EDITION 12

EGAN'S FUNDAMENTALS OF RESPIRATORY CARE

ROBERT M. KACMAREK
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For my wonderful children, Darla, Robert, Julia, Katie, and Callie, some gone too early from my life, who all make it worthwhile, and for Cristina, the love of my life, who has made me whole again.

RMK

I dedicate this work to the memory of my parents, Norma and Alfred Stoller, who instilled the values of rigor and commitment that inform this book; to my wife, Terry Stoller, whose love and support have been the foundation upon which my contribution to this book is possible; to our son, Jake Fox Stoller, whose shining promise gives purpose and illuminates the world; and to generations of Respiratory Therapists, whose daily activities and commitment better our health and give hope.

JKS

To my mother, who is long gone from this earth but continues to be the most dominant, positive influence in my life. Mom taught me many lessons, including that failure is to be expected on the way to success, and excellence can only be achieved through hard work, sacrifice, and perseverance. These lessons have proven invaluable. Hence, my work on this text is dedicated to my mother, Edith; as well as my lovely wife, Laurel; my faculty colleagues and students; fellow respiratory therapists; and the patients we tirelessly serve.

AJH

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PREFACE

Donald F. Egan, MD, the original author of *Egan's Fundamentals of Respiratory Care,* sought to provide a foundation of knowledge for respiratory therapy students learning the practice in 1969. However, the scope of the respiratory care profession is ever-expanding, and the skills and information needed to be an effective respiratory therapist have expanded with it. With improved technology and vast scientific and medical advances, the body of knowledge required for respiratory therapists has increased greatly since the first edition of the text was published.

Now in its twelfth edition, *Egan's Fundamentals of Respiratory Care* encompasses the most relevant information to date and has provided a comprehensive knowledge base for students and professionals for more than 45 years. While these updated editions of *Egan's Fundamentals of Respiratory Care* still accomplish Dr. Egan's original goal—"to present what is felt to be the minimum knowledge for the safe and effective administration of inhalation therapy"—this text also goes far beyond the minimum, delving into important concepts and providing detailed information and resources to enhance student comprehension.

Every editor, guest editor, and contributor to the book is a leading figure in respiratory care, and the vast experience of these individuals ensures that critical content is covered accurately. Using the combined knowledge of these individuals, *Egan's Fundamentals of Respiratory Care* covers the role of respiratory therapists, the scientific bases for treatment, and clinical application skills. With 58 detailed chapters all focused on a unique aspect of respiratory care, *Egan's Fundamentals of Respiratory Care* is without equal in providing the prerequisite information required of a respiratory therapist today.

ORGANIZATION

This edition of the text is organized in a logical sequence of sections and chapters that build on each other to facilitate comprehension of the material. The earlier sections provide a basis for the profession and cover the physical, anatomic, and physiologic principles necessary to understand succeeding chapters. The later chapters address specific cardiopulmonary diseases and the diagnostic and therapeutic techniques that accompany them. Details on preventive and long-term care, as well as Ethics and End of Life, are also provided in the later chapters. In order of presentation, the seven sections are:

I. Foundations of Respiratory Care
II. Applied Anatomy and Physiology
III. Assessment of Respiratory Disorders
IV. Review of Cardiopulmonary Disease
V. Basic Therapeutics
VI. Acute and Critical Care
VII. Patient Education and Long-Term Care

FEATURES

There are many characteristic features throughout the book designed with the student in mind, making *Egan's Fundamentals of Respiratory Care* unique and engaging as a primary textbook. Each chapter begins in a similar manner, outlining the content and drawing attention to what should be mastered through the use of:

- Chapter Objectives
- Chapter Outlines
- Key Terms

The most important features within each chapter are accented by the ample use of figures, boxes, and tables containing key information and by the use of:

- "Rules of Thumb"—"pearls" of information highlighting rules, formulas, and key points necessary to the study of respiratory therapy and to future clinical practice
- "Mini-Clinis"—critical thinking case studies illustrating potential problems that may be encountered during patient care
- Therapist-Driven Protocols—examples of decision trees developed by hospitals and used by respiratory therapists to assess patients, initiate care, and evaluate outcomes

Also, each chapter concludes with:

- A "Summary Checklist" of key points that the student should have mastered on completion of the chapter
- A complete list of references

NEW TO THIS EDITION

This edition has been updated to reflect the most current information in the National Board for Respiratory Care (NBRC) Therapist Exam Content Outline. Also featured is an expanded role for the NBRC Exam Matrix Correlation chart within all of the student and instructor offerings. Several chapters have been added, including Heart Failure; and ethics and end-of-life. Many other chapters have been substantially revised or completely rewritten to reflect the dynamic and expanding field of respiratory care. Furthermore, the content of the entire text has been refined and simplified to be more easily understood and relevant to our key audiences: respiratory therapy students, faculty, and therapists throughout the world.

LEARNING AIDS

Workbook and Evolve Resources

The *Workbook for Egan's Fundamentals of Respiratory Care* is an exceptional resource for students. Offering a wide range of activities, it allows students to apply the knowledge they have gained using the core text. Presented in an engaging format, the workbook breaks down the more difficult concepts and guides students through the most important information. Beyond the many NBRC-style multiple-choice questions in the workbook, students

have access to animations, English/Spanish glossary, student lecture notes, and Body Spectrum, an anatomy coloring book.

Answers to the Workbook are available on the Evolve site. Evolve also includes animations, English/Spanish Glossary, Student Lecture Notes, and Body Spectrum Anatomy Coloring Book.

FOR THE INSTRUCTOR

Evolve Resources

Evolve is an interactive learning environment designed to work in coordination with this text. Instructors may use Evolve to provide an Internet-based course component that expands the concepts presented in class. Evolve can be used to publish the class syllabus, outlines, and lecture notes; set up "virtual office hours" and email communication; and encourage student participation through chatrooms and discussion boards. Evolve also allows instructors to post exams and manage their grade books.

The intuitive and comprehensive Evolve Learning Resources associated with this text provide instructors with valuable resources to use as they teach, including:

- More than 3000 test bank questions available in ExamView
- Comprehensive PowerPoint presentations for each chapter
- An image collection of the figures in the book
- Workbook answer key
- TMC/CSE Correlation Guide

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CONTENTS

SECTION VI Acute and Critical Care

SECTION VII Patient Education and Long-Term Care

1

Early History of Respiratory Care

Robert M. Kacmarek, Albert J. Heuer, and James K. Stoller

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Define respiratory care
- Summarize some of the major events in the history of science and medicine that have directly affected respiratory care
- Explain how the respiratory care profession began
- Describe the historical development of the major clinical areas of respiratory care
- Name some of the important historical figures in respiratory care
- Describe the major respiratory care educational, credentialing, and professional associations
- Explain how the important respiratory care organizations began
- Describe the development of respiratory care education

CHAPTER OUTLINE

KEY TERMS

American Association for Respiratory Care (AARC)
American Respiratory Care Foundation (ARCF)
Board of Medical Advisors (BOMA)
Committee on Accreditation for Respiratory Care (CoARC)
Fellow of the American Association for Respiratory Care (FAARC)
International Council for Respiratory Care (ICRC)
National Board for Respiratory Care (NBRC)
physician assistant
respiratory care
respiratory care practitioner
respiratory therapist (RT)
respiratory therapy

The history of science and medicine is a fascinating topic, which begins in ancient times and progresses to the 21st century. Although respiratory care is a newer discipline, its roots go back to the dawn of civilization. The first written account of positive-pressure ventilation using mouth-to-mouth resuscitation is thought to have been recorded more than 28 centuries ago.[1] Air was thought to be one of the four basic elements by the ancients, and the practice of medicine dates back to ancient Babylonia and Egypt. The progression of science and medicine continued through the centuries, and the development of the modern

disciplines of anesthesiology, pulmonary medicine, and respiratory care during the 20th century depended on the work of many earlier scientists and physicians. This chapter describes the early development of respiratory medicine and the history and development of the field of respiratory care. Specifically, after a historical overview, the birth of respiratory care as a profession is discussed, followed by a discussion of specific therapies (e.g., supplemental oxygen, mechanical ventilation) and a description of various respiratory care organizations (e.g., the American Association for Respiratory Care, the American Respiratory Care Foundation).

DEFINITIONS

Respiratory care, also known as **respiratory therapy**, has been defined as the health care discipline that specializes in the promotion of optimal cardiopulmonary function and health.[2] **Respiratory therapists (RTs)** apply scientific principles to prevent, identify, and treat acute or chronic dysfunction of the cardiopulmonary system.[2] Respiratory care includes the assessment, treatment, management, control, diagnostic evaluation, education, and care of patients with deficiencies and abnormalities of the cardiopulmonary system.[2] Respiratory care is increasingly involved in preventing respiratory disease, managing patients with chronic respiratory disease, and promoting health and wellness.[2]

RTs, also known as **respiratory care practitioners**, are health care professionals who are educated and trained to provide respiratory care to patients. Approximately 75% of all RTs work in hospitals or other acute care settings.[3] However, many RTs are employed in clinics, physicians' offices, skilled nursing facilities, and cardiopulmonary diagnostic laboratories. Others work in research, disease management programs, home care, and industry. RTs are also employed by colleges and universities to teach students the skills they need to become RTs.

A human resources survey conducted in 2014 by the American Association for Respiratory Care (AARC) revealed that there were approximately 172,000 RTs practicing in the United States[3]; this represented a 19% increase over a similar study conducted 4 years earlier in 2009. As the incidence of chronic respiratory diseases continues to increase, the demand for RTs is expected to be even greater in the years ahead. Although the RT as a distinct health care provider was originally a uniquely North American phenomenon, since the 1990s there has been a steady increase in specially trained professionals providing respiratory care worldwide. This trend is referred to as the *globalization of respiratory care.*

RULE OF THUMB Respiratory care has been defined as the health care discipline that specializes in promoting optimal cardiopulmonary function and health.[2] RTs apply scientific principles to prevent, identify, and treat acute or chronic dysfunction of the cardiopulmonary system.

HISTORY OF RESPIRATORY MEDICINE AND SCIENCE

Several excellent reviews of the history of respiratory care have been written; the reader is encouraged to review these publications.[1,4-6] A summary of notable historical events in respiratory care is provided in Tables 1.1. A brief description of the history of science and medicine follows.

Ancient Times

Humans have been concerned about the common problems of sickness, disease, old age, and death since primitive times. Early cultures developed herbal treatments for many diseases, and surgery may have been performed in Neolithic times. Physicians practiced medicine in ancient Mesopotamia, Egypt, India, and China.[1,4,7] However, the foundation of modern western medicine was laid in ancient Greece, with the development of the Hippocratic corpus.[1,4,7,8] This ancient collection of medical treatises is attributed to the "father of medicine," Hippocrates, a Greek physician who lived during the fifth and fourth centuries BC.[1,7,8] Hippocratic medicine was based on four essential fluids, or "humors"—phlegm, blood, yellow bile, and black bile—and the four elements—earth (cold, dry), fire (hot, dry), water (cold, moist), and air (hot, moist). Diseases were thought to be humoral disorders caused by imbalances in these essential substances. Hippocrates believed that an essential substance in air was distributed to the body by the heart.[1] The Hippocratic oath, which admonishes physicians to follow certain ethical principles, is given in a modern form to medical students at graduation.[1,8]

Aristotle (384 to 322 BC), a Greek philosopher and perhaps the first great biologist, believed that knowledge could be gained through careful observation.[1,8] He made many scientific observations, including some obtained by performing experiments on animals. Erasistratus (~330 to 240 BC), regarded by some as the founder of the science of physiology, developed a pneumatic theory of respiration in Alexandria, Egypt, in which air *(pneuma)* entered the lungs and was transferred to the heart.[1,7] Galen (130 to 199 AD) was an anatomist in Asia Minor whose comprehensive work dominated medical thinking for centuries.[1,6,7] Galen also believed that inspired air contained a vital substance that somehow charged the blood through the heart.[1]

The Middle Ages, Renaissance, and Enlightenment Period

The Romans carried on the Greek traditions in philosophy, science, and medicine. With the fall of the Western Roman Empire in 476 AD, many Greek and Roman texts were lost and Europe entered a period during which few advances were made in science or medicine. In the seventh century AD, the Arabians conquered Persia, where they found and preserved many of the works of the ancient Greeks, including the works of Hippocrates, Aristotle, and Galen.[1,7] A golden age of Arabian medicine (850 to 1050 AD) followed.

An intellectual rebirth in Europe began in the 12th century.[1,7] Medieval universities were formed, and contact with the Arabs in Spain and Sicily reintroduced ancient Greek and Roman texts. Magnus (1192 to 1280) studied the works of Aristotle and made many observations related to astronomy, botany, chemistry, zoology, and physiology. The Renaissance (1450 to 1600) ushered in a period of scientific, artistic, and medical advances. Leonardo da Vinci (1452 to 1519) studied human anatomy, determined that subatmospheric intrapleural pressures inflated the lungs,

TABLE 1.1 Major Historical Events in Respiratory Care in the 20th Century

1909	Melltzer (1851–1920; United States) introduces oral endotracheal intubation.
1910	Oxygen tents are in use, and the clinical use of aerosolized epinephrine is introduced.
1911	Drager (1847–1917; Germany) develops the Pulmotor ventilator for use in resuscitation.
1913	Jackson develops a laryngoscope to insert endotracheal tubes.
1918	Oxygen mask is used to treat combat-induced pulmonary edema.
1926	Barach develops an oxygen tent with cooling and carbon dioxide removal.
1928	Drinker develops his "iron lung" negative-pressure ventilator.
1938	Barach develops the meter mask for administering dilute oxygen. Boothby, Lovelace, and Bulbulian devise the BLB mask at the Mayo Clinic for delivering high concentrations of oxygen.
1945	Motley, Cournand, and Werko use intermittent positive-pressure ventilation to treat various respiratory disorders.
1947	The ITA is formed in Chicago, Illinois. The ITA later becomes the AARC.
1948	Bennett introduces the TV-2P positive-pressure ventilator.
1952	Mørch introduces the piston ventilator.
1954	The ITA becomes the AITA.
1958	Bird introduces the Bird Mark 7 positive-pressure ventilator.
1960	The Campbell Ventimask for delivering dilute concentrations of oxygen is introduced.
1961	Jenn becomes the first registered respiratory therapist. Also, metaproterenol, a preferential β-2 bronchodilator, is introduced.
1963	The Board of Schools is formed to accredit inhalation therapy educational programs.
1964	The Emerson Postoperative Ventilator (3-PV) positive-pressure volume ventilator is introduced.
1967	The Bennett MA-1 volume ventilator is introduced, ushering in the modern age of mechanical ventilatory support for routine use in critical care units.
1967	The combined pH-Clark-Severinghaus electrode is developed for rapid blood gas analysis.
1968	The fiberoptic bronchoscope becomes available for clinical use. The Engström 300 and Ohio 560 positive-pressure volume ventilators are introduced.
1969	ARDS and PEEP are described by Petty, Ashbaugh, and Bigelow.
1970	The Swan-Ganz catheter, developed for the measurement of pulmonary artery pressures, is introduced. The ARCF is incorporated. The JRCITE is incorporated to accredit respiratory therapy educational programs.
1971	CPAP is introduced by Gregory. The *Respiratory Care* journal is introduced.
1972	The Siemens Servo 900 ventilator is introduced.
1973	IMV is described by Kirby and Downs. The AAIT becomes the AART.
1974	The IMV Emerson ventilator is introduced.
1974	The National Board for Respiratory Therapy (NBRT) is formed.
1975	The Bourns Bear I ventilator is introduced.
1977	The JRCITE becomes the JRCRTE.
1978	Puritan Bennett introduces the MA-2 volume ventilator. The *AAR Times* magazine is introduced.
1979	AIDS is recognized by the Centers for Disease Control (CDC [later, Centers for Disease Control and Prevention]).
1982	Siemens Servo 900C and Bourns Bear II ventilators are introduced.
1983	The NBRT becomes the National Board for Respiratory Care (NBRC).
1983	President Reagan signs a proclamation declaring National Respiratory Care Week.
1984	Bennett 7200 microprocessor-controlled ventilator is introduced.
1984	The AART is renamed the AARC.
1991	The Servo 300 ventilator is introduced.
1992, 1993	The AARC holds national respiratory care education consensus conferences.
1994	The CDC publishes the first guidelines for the prevention of ventilator-associated pneumonia.
1998	The CoARC is formed, replacing the JRCRTE.

AAIT, American Association for Inhalation Therapist; *AARC*, American Association for Respiratory Care; *ARCF*, American Respiratory Care Foundation; *ARDS*, acute respiratory distress syndrome; *BLB*, Boothby, Lovelace, and Bulbulian; *CoARC*, Committee on Accreditation for Respiratory Care; *CPAP*, continuous positive-airway pressure; *IMV*, intermittent mandatory ventilation; *ITA*, Inhalational Therapy Association; *JRCITE*, Joint Review Committee for Inhalation Therapy Education; *JRCRTE*, Joint Review Committee for Respiratory Therapy Education; *NBRC*, National Board for Respiratory Care; *NBRT*, National Board for Respiratory Therapy; *PEEP*, positive end-expiratory pressure.
Data from references 1, 3–9, 11–14, and 17.

and observed that fire consumed a vital substance in air without which animals could not live.[1,4] Vesalius (1514 to 1564), considered to be the founder of the modern field of human anatomy, performed human dissections and experimented with resuscitation.[1] In 1543, the date commonly given as the birth modern science, Copernicus observed that the planet Earth orbited the sun.[8] Before this time, it had been accepted that Earth was the center of the universe.

The 17th century was a time of great advances in science. Accomplished scientists from this period include Kepler, Bacon, Galileo, Pascal, Hooke, and Newton. In 1628, Harvey fully described the circulatory system.[4,8] In 1662, the chemist Boyle

published what is now known as Boyle's law, governing the relationship between the volume and pressure of a gas.[8] Torricelli invented the barometer in 1650, and Pascal showed that atmospheric pressure decreases with altitude.[1,4] van Leeuwenhoek (1632 to 1723), known as the "father of microbiology," improved the microscope and was the first to observe and describe single-celled organisms, which he called "animalcules."[7]

The 18th-century Enlightenment period brought further advances in the sciences. In 1754, Black described the properties of carbon dioxide, although the discovery of carbon dioxide should be credited to van Helmont, whose work occurred approximately 100 years earlier.[1] In 1774, Priestley described oxygen, which he called "dephlogisticated air."[1,4] Before 1773, Scheele performed the laboratory synthesis of oxygen, which he called "fire air"; a general description of his discovery appeared in 1774, and a more thorough description in 1777.[1,4] Shortly after the discovery of oxygen, Spallanzani worked out the relationship between the consumption of oxygen and tissue respiration.[1] In 1787, Charles described the relationship between gas temperature and volume, now known as Charles' law.[8] In experiments performed between 1775 and 1794, Lavoisier showed that oxygen was absorbed by the lungs and that carbon dioxide and water were exhaled.[1,4] In 1798, Beddoes began using oxygen to treat various conditions at his Pneumatic Institute in Bristol.[1,4]

RULE OF THUMB In 1662, the chemist Boyle published what is now known as Boyle's law, governing the relationship between gas volume and pressure.

Nineteenth and Early Twentieth Centuries

During the 19th century, important advances were made in physics and chemistry related to respiratory physiology. Dalton described his law of partial pressures for a gas mixture in 1801 and his atomic theory in 1808.[8] Young in 1805 and de LaPlace in 1806 described the relationship between pressure and surface tension in fluid droplets.[8] Gay-Lussac described the relationship between gas pressure and temperature in 1808; in 1811, Avogadro determined that equal volumes of gases at the same temperature and pressure contain the same number of molecules.[1,8] In 1831, Graham described his law of diffusion for gases (Graham's law).[8]

In 1865, Pasteur advanced his "germ theory" of disease, which held that many diseases are caused by microorganisms.[8] Medical advances during this time included the invention of the spirometer and ether anesthesia in 1846, antiseptic techniques in 1865, and vaccines in the 1880s.[1,4,7] Koch, a pioneer in bacteriology, discovered the tubercle bacillus, which causes tuberculosis, in 1882, and the vibrio bacterium, which causes cholera, in 1883.[7] He also developed Koch's postulates, which are criteria designed to establish a causative relationship between a microbe and a disease. Respiratory physiology also progressed with the measurement in 1837 of blood oxygen and carbon dioxide content, description around 1880 of the respiratory quotient, demonstration in 1885 that carbon dioxide is the major stimulant for breathing, and demonstration in 1878 that oxygen partial pressure and blood oxygen content were related.[1,4,9] In 1895, Roentgen discovered the x-ray, and the modern field of radiologic imaging sciences was born.[8] Pioneering respiratory physiologists of the early 20th century described oxygen diffusion, oxygen and carbon dioxide transport, the oxyhemoglobin dissociation curve, acid-base balance, and the mechanics of breathing and made other important advances in respiratory physiology.

RULE OF THUMB In experiments performed between 1775 and 1794, Lavoisier showed that oxygen was absorbed by the lungs and that carbon dioxide and water were exhaled.

DEVELOPMENT OF THE RESPIRATORY CARE PROFESSION

Clinical Advances in Respiratory Care

The evolution of the respiratory care profession depended in many ways on developments in the various treatment techniques that matured in the 20th century. As the scientific basis for oxygen therapy, mechanical ventilatory support, and administration of medical aerosols became well established, the need for a health care practitioner to provide these services became apparent. Concurrent with this need was the continuing development of specialized cardiopulmonary diagnostic tests and monitoring procedures, which also required health care specialists to perform.

The first health care specialists in the field were oxygen technicians in the 1940s.[1,4,5] The development of positive-pressure breathing during World War II for breathing support of high-altitude pilots led to its use as a method to treat pulmonary patients and deliver aerosol medications during the 1950s, expanding the role of the oxygen technicians. Inhalation therapists began to be trained in the 1950s, and formal education programs began in the 1960s.[1,4,5] By the end of the 1960s, respiratory care personnel were all referred to as inhalation therapists; they provided oxygen therapy via H cylinders and oxygen tents, masks, and nasal catheters. In addition, these inhalation therapists delivered aerosolized medications and performed intermittent positive-pressure breathing (IPPB) treatments. The development of sophisticated mechanical ventilators in the 1960s and beyond naturally led to a further expansion in the role of RTs, who soon also found themselves responsible for arterial blood gas and pulmonary function laboratories. In 1974, the designation *respiratory therapist* became standard, and the RT became the allied health professional primarily concerned with the assessment, diagnostic testing, treatment, education, and care of patients with deficiencies and abnormalities of the cardiopulmonary system.

RULE OF THUMB When information about the respiratory care profession is being sought, the best place to look is the AARC (see www.AARC.org). The AARC's *Virtual Museum* can be accessed through the AARC website.

Oxygen Therapy

The therapeutic administration of oxygen first occurred in 1798; in 1878, Bert showed that lack of oxygen caused hyperventilation. However, the physiologic basis and indications for oxygen therapy were not well understood until the 20th century.[1,4] Large-scale

Fig. 1.1 The BLB mask (Boothby, Lovelace, and Bulbulian) to administer 80% to 100% oxygen to pilots was introduced during World War II and later used on patients in the 1950s and 1960s.

production of oxygen was developed by von Linde in 1907. The use of a nasal catheter for oxygen administration was introduced by Lane in the same year.[1,4] Oxygen tents were in use in 1910, and an oxygen mask was used to treat combat gas–induced pulmonary edema in 1918.[1] In 1920, Hill developed an oxygen tent to treat leg ulcers, and in 1926, Barach introduced a sophisticated oxygen tent for clinical use. Oxygen chambers and whole oxygen rooms were designed.[1,4] In 1938, a meter mask was developed by Barach to administer dilute oxygen.[1,4] The BLB mask (named for Boothby, Lovelace, and Bulbulian) to administer 80% to 100% oxygen to pilots was introduced during World War II and later used on patients (Fig. 1.1).[1,4] By the 1940s, oxygen was widely prescribed in hospitals, although there was still no good way to measure blood oxygen levels routinely until the mid-1960s, with the introduction of the Clark electrode, followed by the clinical use of the ear oximeter in 1974 and the pulse oximeter in the 1980s.[1,4,5] The Campbell Ventimask—which allowed the administration of 24%, 28%, 35%, or 40% oxygen—was introduced in 1960, and modern versions of the nasal cannula, simple oxygen mask, partial rebreathing mask, and nonrebreathing mask were available by the late 1960s. Portable liquid oxygen systems for long-term oxygen therapy in the home were introduced in the 1970s, and the oxygen concentrator soon followed. Oxygen-conserving devices—including reservoir cannulas, demand pulse oxygen systems, and transtracheal oxygen catheters—were introduced in the 1980s.

The late 1990s saw further advances in home oxygen therapy equipment with the introduction of oxygen concentrators used in conjunction with a pressure booster to allow for the transfilling of small portable oxygen cylinders in the home. Smaller, lightweight portable oxygen concentrators were also introduced. Both of these advances have greatly enhanced the ability of patients receiving long-term oxygen therapy to ambulate beyond the confines of their homes. Furthermore, the National Institutes of Health launched the Long-Term Oxygen Treatment Trial (LOTT), a randomized controlled trial to explore the benefits of supplemental oxygen in patients with chronic obstructive pulmonary disease (COPD) and mild resting hypoxemia (SpO_2 89% to 93%) or with exercise desaturation.[10] In contrast to the case of COPD patients with severe hypoxemia (i.e., resting SpO2 <89%) in whom supplemental oxygen prolongs survival, the findings of LOTT showed that supplemental oxygen did not confer benefit for 2-year mortality or all-cause hospitalization.

RULE OF THUMB In 1974, the designation *respiratory therapist* became standard, and the RT became the allied health professional primarily concerned with the assessment, diagnostic testing, treatment, education, and care of patients with deficiencies and abnormalities of the cardiopulmonary system.

Aerosol Medications

Aerosol therapy is defined as the administration of liquid or powdered aerosol particles via inhalation to achieve a desired therapeutic effect. Bland aerosols (sterile water, saline solutions) or solutions containing pharmacologically active drugs may be administered. In 1802, the use of inhaled *Datura* leaf fumes, which contain atropine, to treat asthma was described.[11] Early use of aerosol medications dates to 1910, when the first use of aerosolized epinephrine was reported. Later, other short-acting bronchodilators—such as isoproterenol (1940), isoetharine (1951), metaproterenol (1961), albuterol sulfate (1980), and levalbuterol (2000)—were introduced, primarily for the emergency treatment of acute asthma attacks.[11] In the late 1990s, long-acting bronchodilators, administered twice daily, were introduced for the maintenance treatment of COPD. Oral and injectable steroids were first used in the treatment of asthma in the early 1950s, and the use of aerosolized steroids for the maintenance of patients with moderate to severe asthma began in the 1970s.[11] Newer medications continued to be developed for aerosol administration, including even longer-acting bronchodilators (once every 24 hours), mucolytics, antibiotics, antiinflammatory agents, and combination drugs such as long-acting bronchodilators and antiinflammatories in a single dose. Along with newer respiratory drugs, newer delivery devices such as dry powder inhalers and innovative designs for small-volume nebulizers have been introduced.

Mechanical Ventilation

Mechanical ventilation involves the use of a mechanical device to provide ventilatory support for patients. In 1744, Fothergill advocated mouth-to-mouth resuscitation for drowning victims.[1,6] During the mid- to late 1700s, there was a great deal of interest in resuscitation, and additional procedures for cardiopulmonary

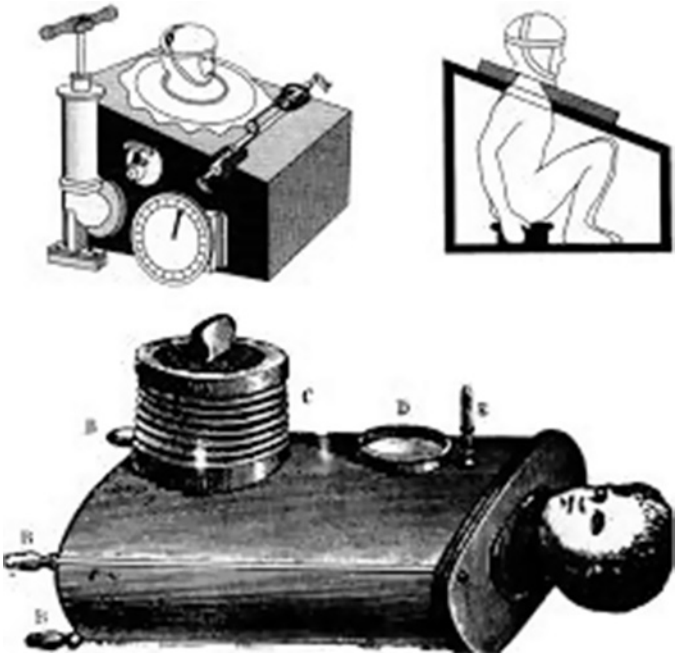

Fig. 1.2 Negative-pressure ventilator used in the mid-1800s. (*Top*, From Dalziel J: On sleep and apparatus for promoting artificial respiration, *BR Assoc Adv Sci* 1:127, 1838; *Bottom*, From Woollam CH: The development of apparatus for intermittent negative pressure respiration, *Anaesthesia* 31[5]:537–547, 1976.)

resuscitation were developed.[1,4,6] Positive-pressure ventilation using a bag-mask system or bellows was suggested. However, the observation that a fatal pneumothorax may result caused this technique to be rejected around 1827.[1,4] Interest in negative-pressure ventilation developed, and the first negative-pressure tank ventilator was described in 1832 (Fig. 1.2).[6] Other negative-pressure ventilators began to appear in the mid-1800s; in 1928, the iron lung was developed by Drinker, an industrial hygienist and faculty member at Harvard University.[1] Emerson developed a commercial version of the iron lung, which was used extensively during the polio epidemics of the 1930s and 1950s (Figs. 1.3 to 1.5).[1,12] The chest cuirass negative-pressure ventilator was introduced in the early 1900s (Fig. 1.6), and a negative-pressure "wrap" ventilator was introduced in the 1950s.[13] Other early noninvasive techniques to augment ventilation included the rocking bed (1950) and the Pneumobelt (1959).[13]

Originally, positive-pressure ventilators were developed for use during anesthesia; later, they were altered for use on hospital wards.[14] Early positive-pressure ventilators included the Drager Pulmotor (Fig. 1.7) (1911), the Spiropulsator (1934), the Bennett TV-2P (1948), the Morch Piston Ventilator (Fig. 1.8) (1952), and the Bird Mark 7 (1958) (Fig. 1.9).[1,14] More sophisticated positive-pressure volume ventilators were developed in the 1960s and included the Emerson Postoperative Ventilator, MA-1 (Fig. 1.10), Engstrom 300, and Ohio 560.[1,14] A new generation of volume ventilators appeared in the 1970s that included the Servo 900 (Fig. 1.11), Bourns Bear I and II, and MA-II. By the 1980s, microprocessor-controlled ventilators began to appear, led by the Bennett 7200 in 1984; in 1988, the Respironics bilevel positive-airway-pressure (BiPAP) device was introduced for providing

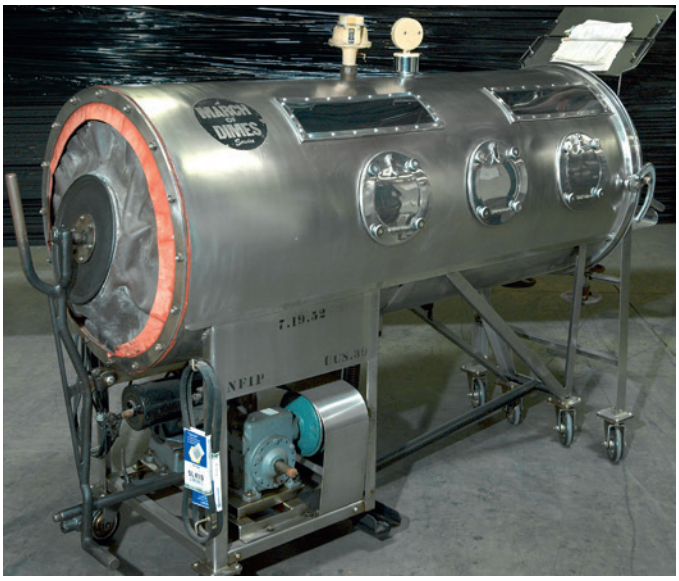

Fig. 1.3 Multiperson negative-pressure ventilation chamber used at Boston Children's Hospital. (From Public Health Image Library (PHIL), Centers for Disease Control and Prevention, Office of the Associate Director for Communications, Division of Public Affairs. CDC/GHO/Mary Hilpertshauser.)

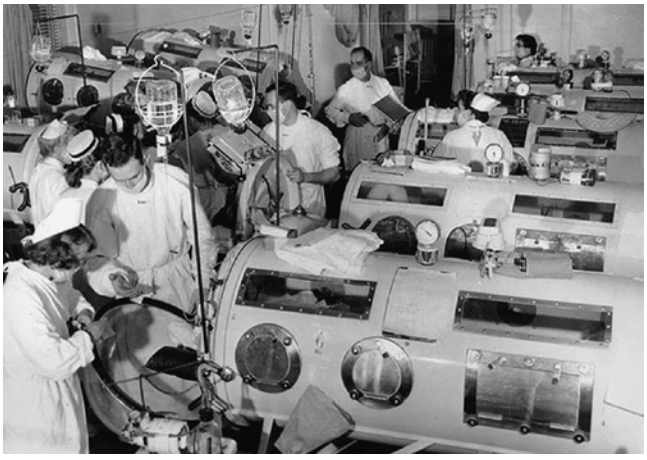

Fig. 1.4 Iron lung patients in a 1950s polio ward. (From the Associated Press and Post-Gazette.com Health, Science and Environment. http://www.post-gazette.com/pg/05094/482468.stm.)

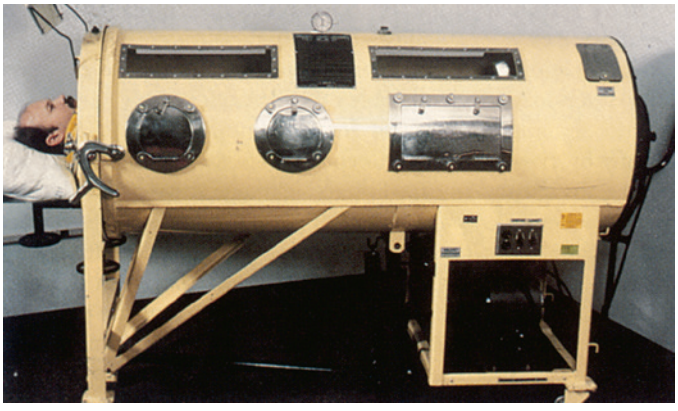

Fig. 1.5 Modern negative-pressure ventilator used in Europe. (From Albert RK, Spiro SG, Jett JR: *Clinical respiratory medicine*, ed 2, Philadelphia, 2004, Mosby)

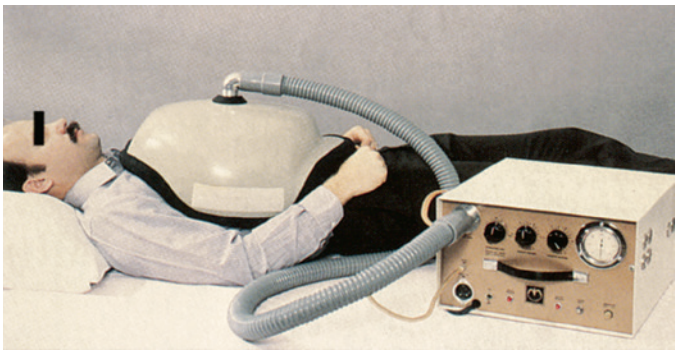

Fig. 1.6 Chest cuirass negative-pressure ventilator. (From Albert RK, Spiro SG, Jett JR: *Clinical respiratory medicine*, ed 2, Philadelphia, 2004, Mosby)

Fig. 1.7 Drager Pulmotor, first half of the 1900s. (From Mushin WW, Rendell-Baker L, Thompson PW, Mapleson WW: *Automatic ventilation of the lungs*, Oxford, 1980, Blackwell Scientific)

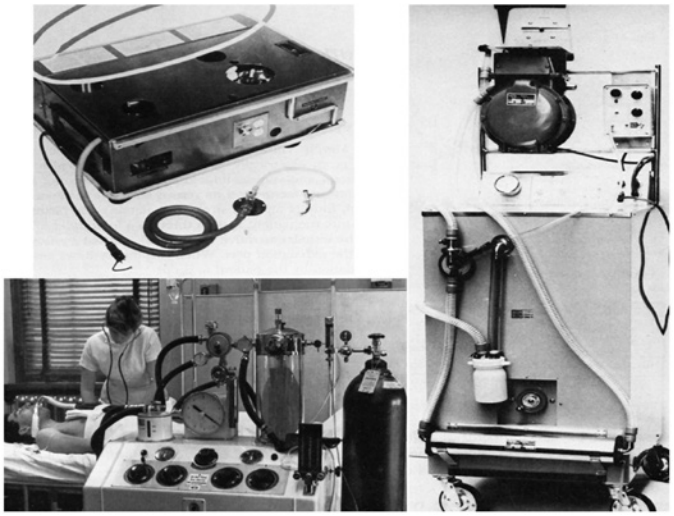

Fig. 1.8 Top left, Morch ventilator; bottom left, Engstrom 300 ventilator; right, Emerson post-op ventilator. (From Mushin WW, Rendell-Baker L, Thompson PW, Mapleson WW: *Automatic ventilation of the lungs*, Oxford, 1980, Blackwell Scientific)

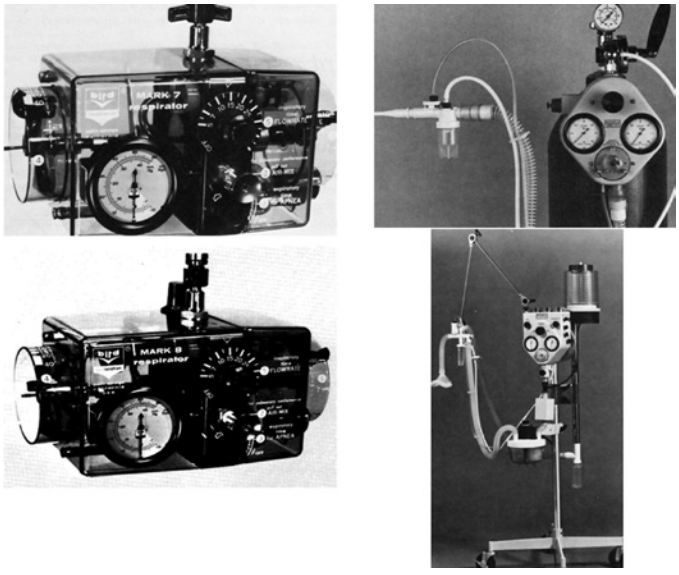

Fig. 1.9 Top left, Bird Mark 7 ventilator; top right, Puritan-Bennett TV-2P ventilator; bottom left. Bird Mark 8 ventilator; bottom right, Puritan-Bennett PR-2 ventilator.

noninvasive positive-pressure ventilation in a wide variety of settings.[1] During the 1990s and beyond, new ventilators have continued to be developed, including the Hamilton G5, Servo I, PB 840, (Fig. 1.12) and Drager V500 and VN500 series (see Chapter 46). Between 1970 and 2004, more than 50 new ventilators with various characteristics were introduced for clinical use.[15,16]

Early mechanical ventilators provided modes for which breaths were delivered according to a preset frequency and inspiratory time regardless of any inspiratory effort on the part of the patient (what anesthesiologists of the time called "controlled" ventilation). The early Bird and Bennett ventilators developed in the 1950s allowed for initiating inspiration by detecting the patient's inspiratory effort, called "assist." This feature was incorporated in later modes that also had preset breath frequency (called *assist/control*, a term that is anachronistic but which persists to this day). The terminology related to modes of ventilation has evolved along with the complexity of ventilator technology (see Chapter 46). In 1967, the addition of positive end-expiratory pressure (PEEP) as a feature was introduced for use in patients dying from the newly described acute respiratory distress syndrome (ARDS). The use of PEEP helped to stabilize the alveoli and

keep them from collapsing at the end of exhalation. Other forms of modern ventilation include intermittent mandatory ventilation (IMV), introduced in 1971, followed by synchronized IMV, in 1975, and mandatory minute volume ventilation in 1977.[1,4] Pressure-support ventilation and pressure-controlled ventilation were introduced in the 1980s, followed by airway pressure release (APRV) ventilation and inverse ratio ventilation. In the 1990s, volume-support ventilation, pressure-regulated volume control, and adaptive support ventilation were introduced. Automatic tube compensation, proportional assist ventilation, neutrally adjusted ventilatory assist, APRV, and other modes of ventilation were introduced around or shortly after 2000. In fact, there are now hundreds of names of modes of ventilation, making a classification system essential for understanding ventilator technology (see Chapter 46).

Because traditional short-term mechanical ventilation, regardless of mode, necessitates using an endotracheal tube, there is always the potential for one or more serious complications. The most common is an infection referred to as ventilator-associated pneumonia (VAP). VAP is a potentially deadly and very costly complication of invasive mechanical ventilation that develops when microorganisms accidentally enter the airway from the mouth and/or gastrointestinal (GI) tract. There has been a concerted effort to try to support inadequate ventilation noninvasively by using a nasal or full-face mask in order to avoid the need for endotracheal intubation and the resultant risk of developing VAP.

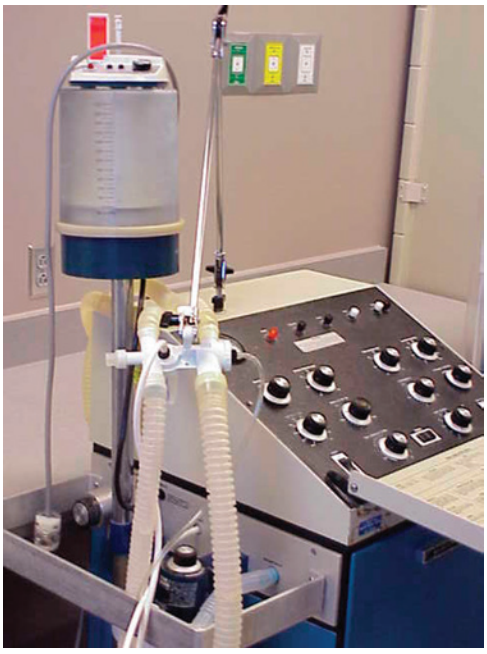

Fig. 1.10 The Bennett MA-1 ventilator, introduced in 1967, played a major role in making mechanical ventilatory support routinely available in intensive care units throughout the world.

Fig. 1.11 Siemens Servo 900.

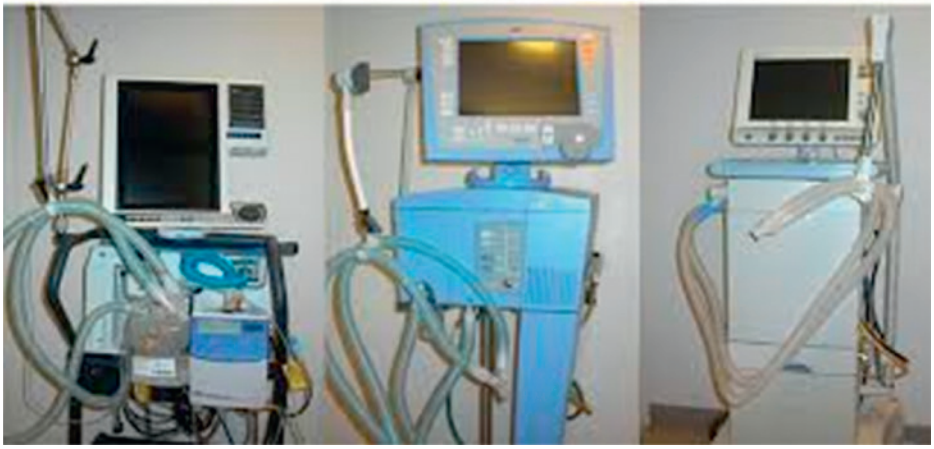

Fig. 1.12 Left, Covidien 840 ventilator; middle, Viaysis Avea ventilator; right, Siemens Servo i ventilator.

Airway Management

Airway management involves the use of various techniques and devices to establish or maintain a functional airway. Tracheotomies may have been performed to relieve airway obstruction in 1500 BC.[6] Galen, the Greek anatomist, described a tracheotomy and laryngeal intubation in 160 AD. Vesalius, another anatomist, described a tracheotomy in an animal in 1555.[1,6] In 1667, Hooke described a tracheotomy and use of a bellows for ventilation.[6] In 1776, tracheal intubation was suggested for resuscitation.[6] In 1880, MacEwen reported successful oral endotracheal intubation in his patients.[6] O'Dwyer further described the technique for endotracheal tube placement. By 1887, Fell had developed a bellows–endotracheal tube system for mechanical ventilation, and this system was used in 1900 to deliver anesthesia.[6]

In 1913, the laryngoscope was introduced by Jackson. Additional early laryngoscopes were designed by Kirstein, Janeway, and others.[1,6] Endotracheal intubation for anesthesia administration was firmly established by World War I. After the war, Magill introduced the use of soft rubber endotracheal tubes, which made blind nasal intubation possible, as described by Magill in 1930.[6] In 1938, Haight advocated nasotracheal suctioning for secretion removal, and in 1941, Murphy described the ideal suction catheter, which included side holes known as "Murphy eyes."[6] The double-lumen Carlen tube for independent lung ventilation was introduced in 1940, followed by a double-lumen tube developed by Robertshaw in 1962. Damage to the trachea by the tube cuff was reduced with the introduction of low-pressure cuffs in the 1970s.[6]

RULE OF THUMB Tracheotomies may have been performed to relieve airway obstruction as early as 1500 BC. Galen, the Greek anatomist, described a tracheotomy and laryngeal intubation in 160 AD. Vesalius, another anatomist, described a tracheotomy in an animal in 1555.

Cardiopulmonary Diagnostics and Pulmonary Function Testing

Pulmonary function testing comprises a wide range of diagnostic procedures to measure and evaluate lung function. The volume of air that can be inhaled in a single deep breath was first measured in 1679, and the lung's residual volume was first measured in 1800.[9] In 1846, Hutchinson developed a water seal spirometer, with which he measured the vital capacity of more than 2000 subjects.[9,17] Hutchinson observed the relationship between height and lung volume and that vital capacity decreases with age, obesity, and lung disease. Hering and Breuer described the effects of lung inflation and deflation on breathing—the Hering-Breuer reflex—in 1868.[4] In 1919, Strohl suggested the use of forced vital capacity (FVC), and in 1948, forced expiratory volume in 1 second (FEV_1) was suggested as a measure of obstructive lung disease by Tiffeneau.[9]

Arterial and venous oxygen and carbon dioxide contents were measured in 1837, and methods to measure blood oxygen and carbon dioxide levels became available in the 1920s. These early methods for measuring blood oxygen, carbon dioxide, and pH were slow and cumbersome. In 1967, combination of the pH, Clark, and Severinghaus electrodes produced a rapid and practical blood gas analyzer for routine clinical use.[1,4] The ear oximeter was introduced in 1974, and the pulse oximeter was introduced in the 1980s. Sleep medicine became well established in the 1980s, and it was then that polysomnography became a routine clinical test, often performed by RTs.

PROFESSIONAL ORGANIZATIONS AND EVENTS

American Association for Respiratory Care

Founded in 1947 in Chicago, the Inhalational Therapy Association (ITA) was the first professional association for the field of respiratory care.[1,4,5] The purpose of the ITA was to provide for professional advancement, foster cooperation with physicians, and advance the knowledge of inhalation therapy through educational activities.[5] The ITA provided a forum to discuss the clinical application of oxygen therapy, improve patient care, and advance the art and science of the field.[1] The ITA had 59 charter members.[1] It became the American Association for Inhalation Therapists (AAIT) in 1954, the American Association for Respiratory Therapy (ARRT) in 1973, and the **American Association for Respiratory Care (AARC)** in 1982.[4,5] The AARC has a formal affiliation with all 50 state respiratory societies (known as *chartered affiliates*), as well as with similar organizations in several foreign countries.[17]

During the 1980s, the AARC began a major push to introduce state licensure for RTs based on the National Board for Respiratory Care (NBRC) credentials.[18] As of 2014, a total of 49 states, the District of Columbia, and Puerto Rico had state licensure

MINI CLINI

Preparing a Presentation for Respiratory Care Week

Problem

You are a staff therapist in a 300-bed hospital. Your supervisor asks you to prepare a 20-minute presentation on the history and development of the respiratory care profession to be presented at the department's annual Respiratory Care Week luncheon. How would you gather the information needed and develop your presentation?

Solutions

First, review this chapter to get an overview of the history and development of the respiratory care profession. You may also want to read one or two of the supplemental references that are cited. Next, go to the AARC website (see www.AARC.org) and review the "Resources" and "Site Map" sections, which list many helpful resources. You should be able to find sections on "The History of the AARC," "Strategic Plan of the AARC," "Position Statements," and "White Papers." There will also be a portal to the AARC's Virtual Museum. You should also find a section on Respiratory Care Week. Review the material that the AARC has provided and develop an outline of your presentation. Your outline may include a brief overview of the history of science and medicine, the development of the respiratory care profession, and the future of respiratory care in the 21st century. Once you have your outline, decide on your delivery method. PowerPoint slides are easy to make and use. If you choose to do a PowerPoint presentation, a good rule of thumb is about one slide per minute, so you would need about 20 slides. Using your outline, begin to develop your presentation.

BOX 1.1 American Association for Respiratory Care Specialty Sections

Adult acute care
Continuing care/rehabilitation
Diagnostics
Education
Home care
Long-term care
Management
Neonatal/pediatrics
Sleep
Surface and air transport

or some other form of legal credentialing required for the practice of respiratory care. State licensing laws set the minimal educational requirements and the method of determining competence to practice. Competency is typically determined by obtaining a passing grade on a credentialing examination (administered by the NBRC) after graduation from an approved training program. State licensing boards also set the number of continuing education credits required to keep a license active.

RULE OF THUMB Founded in 1947 in Chicago, the Inhalational Therapy Association (ITA) was the first professional association for the field of respiratory care. The ITA became the American Association for Inhalation Therapists (AAIT) in 1954, the American Association for Respiratory Therapy (ARRT) in 1973, and the **American Association for Respiratory Care (AARC)** in 1982.

The stated mission of the AARC is to "encourage and promote professional excellence, advance the science and practice of respiratory care, and serve as an advocate for patients, their families, the public, the profession and the respiratory therapist."[19] The AARC serves as an advocate for the profession to legislative and regulatory bodies, the insurance industry, and the general public. To fulfill its mission, the AARC sponsors many continuing educational activities, including international meetings, conferences and seminars, publications, and a sophisticated website (see www.AARC.org).[18] Finally, in an effort to ensure that the unique practice interests of AARC members are addressed (e.g., neonatal/pediatrics, adult acute care, management, home care, diagnostics), members are invited to join one or more of 10 Specialty Sections (Box 1.1) within the AARC designed to facilitate networking and the free exchange of ideas (see Chapter 2 for further details). Annually at the international meeting, the AARC also acknowledges individuals who have contributed to the profession as Fellows of the AARC (FAARC).

RULE OF THUMB The stated mission of the AARC is to "encourage and promote professional excellence, advance the science and practice of respiratory care, and serve as an advocate for patients, their families, the public, the profession, and the respiratory therapist."

Many volunteers who have been elected to the AARC or House of Delegates leadership positions or have been asked to chair important committees started by volunteering at the affiliate level. Student members of the AARC are always welcomed as volunteers, especially at the affiliate level. Student members of the AARC have access to a wide array of resources that can greatly enhance the experience of becoming a professional RT.

Respiratory Care Week

In November 1982, President Reagan signed a proclamation declaring the third week of each October as National Respiratory Care Week. Since then, Respiratory Care Week has become a yearly event to promote pulmonary health and the work of RTs in all care settings. RTs (and students) around the United States use Respiratory Care Week to celebrate their profession and dedication to high-quality patient care. Many respiratory care departments use the opportunity to conduct special events in their hospitals to help raise awareness of the vital role the RT plays as a member of the health care team. Other departments plan community activities to help the public understand the importance of good lung health and the role RTs play in diagnosing and treating breathing disorders. Respiratory Care Week is also an excellent opportunity for respiratory therapy students to become ambassadors of the profession to the rest of the student body. Some respiratory therapy classes conduct free breathing tests on campus, in shopping malls, or in community centers.

Board of Medical Advisors

Because RTs practice under medical direction, the AARC leadership receives formal input from physicians on all matters and questions pertaining to patient care. The **Board of Medical Advisors (BOMA)** is the group of physicians who provide this valuable input (see Chapter 2 for further details).

American Respiratory Care Foundation

Established in 1970 by the AARC, the **American Respiratory Care Foundation (ARCF)** is a not-for-profit charitable foundation that helps promote and further the mission of the AARC. Commonly known as the Foundation, the ARCF collects and manages contributions from individuals, corporations, and other foundations to promote education among RTs and to recognize individual achievements of excellence in clinical practice, chronic disease management, public respiratory health, scientific research, and scholarship (see Chapter 2 for further details).

RULE OF THUMB Established in 1970 by the AARC, the **American Respiratory Care Foundation (ARCF)** is a not-for-profit charitable foundation that helps promote and further the mission of the AARC.

International Council for Respiratory Care

The **International Council for Respiratory Care (ICRC)** is an AARC-sponsored organization dedicated to the globalization of high-quality respiratory care. As mentioned previously, having formally trained professionals working in a dedicated department to assume full responsibility for providing respiratory care

under medical direction was a uniquely North American phenomenon (i.e., both the United States and Canada). However, during the 1970s and 1980s, when many foreign physicians came to the United States to study, they became aware of what an RT was and the important role RTs play in hospitals nationwide. When these physicians returned to their native countries, they wished to have their own specialized teams able to provide the same level of high-quality respiratory care. However, because the health care delivery system is structured differently in each country, the specially trained teams were most often made up of nurses, physicians, or physical therapists, not RTs.

Formed in 1991, the ICRC (in close collaboration with the International Committee of the AARC) began to offer fellowships to interested foreign clinicians that provide the opportunity to visit the United States for 2 weeks before the annual International Respiratory Congress to observe how respiratory care is practiced in various settings. The idea is to allow these international fellows to observe how the various components of respiratory care are practiced throughout the United States. The international fellows can then take back to their home countries ideas and practices that can be integrated into their unique health care delivery systems. The program has been so successful that many countries (e.g., Mexico, Costa Rica, Taiwan) are starting to establish respiratory therapy training programs modeled after the American training system (see Chapter 2 for further details).

National Board for Respiratory Care

The credentialing body for registered RTs began in 1960 as the American Registry of Inhalation Therapists (to test and credential registered therapists), and a certification board was established in 1968 to certify technicians.[1,4] These two groups merged in 1974 as the National Board for Respiratory Therapy, which became the **National Board for Respiratory Care (NBRC)** in 1983.[1,4] Also in 1983, the National Board for Cardiopulmonary Technologists joined the NBRC, and the credentialing examinations for pulmonary function technology were brought in under the respiratory care umbrella.[1,4]

RULE OF THUMB For requirements for testing, examination schedules, study guides, and requirements for maintaining your CRT or RRT credential, check with the NBRC (see www.NBRC.org).

In 1998, the NBRC renamed the lower level *certified respiratory therapist* (*CRT,* or *entry-level respiratory therapist*); the advanced level remained registered respiratory therapist (RRT, or advanced-level respiratory therapist).[20] The NBRC began offering specialty examinations for pulmonary function technology in 1984 and neonatal/pediatrics in 1991. Because of the proliferation of new technologies, other specialty credentials including the adult critical care specialty have been introduced since then (see Chapter 2 for further details).

Committee on Accreditation for Respiratory Care

In 1956, the first guidelines for respiratory care educational programs were published, followed in 1963 by the formation of the Board of Schools to accredit programs.[1] The Board of Schools was replaced by the Joint Review Committee for Inhalation Therapy Education (JRCITE) in 1970, led by Fred Helmholtz, its first chairman.[1,4] The JRCITE became the Joint Review Committee for Respiratory Therapy Education (JRCRTE) in 1977 and then the **Committee on Accreditation for Respiratory Care (CoARC)** in 1996 (see www.COARC.com).[4] Today, respiratory care educational programs in the United States and Canada are accredited by CoARC in collaboration with the Association of Specialized and Professional Accreditors[21,22] (see Chapter 2 for further details).

RESPIRATORY CARE EDUCATION

The first formal educational course in inhalation therapy was offered in Chicago in 1950.[1] In the 1960s, numerous schools were developed to prepare students to become RTs. Early programs concentrated on teaching students the proper application of oxygen therapy, oxygen delivery systems, humidifiers, and nebulizers and the use of various IPPB devices. The advent of sophisticated critical care ventilators, blood gas analyzers, and monitoring devices in the 1960s and 1970s helped propel the RT into the role of cardiopulmonary technology expert.

Respiratory care educational programs in the United States are offered at technical and community colleges, 4-year colleges, and universities. These programs are designed to prepare competent RTs to care for patients. The minimum degree required to become an RT has traditionally been an associate degree.[21] However, many associate degree graduates see great opportunity in pursuing their bachelor's degree and some even higher degrees—master's and doctorates. In an effort to promote bachelor's-level education for respiratory therapy, the CoARC no longer entertains applications for the accreditation of new associate degree programs. At present there are approximately 300 associate, 50 baccalaureate, and 3 graduate-level degree programs in the United States; 19 programs in Canada; and a handful of respiratory care educational programs in Mexico, South America, Japan, India, Taiwan, and other countries.[23,24]

RULE OF THUMB Jobs in management, education, research, or advanced clinical practice normally require bachelor's- or graduate-level educational preparation.

The AARC completed a Delphi study and held two important Education Consensus Conferences in the early 1990s to assess the status of respiratory care education and recommend future direction for the field.[25-28] The first conference suggested that major trends affecting the field were advances in technology; demographic trends and the aging of the population; a need to provide better assessment, outcome evaluation, problem solving, and analytic skills; use of protocol-based care; and the need to increase the focus on patient education, prevention, and wellness, to include tobacco education and smoking cessation.[27] The conference concluded that the curriculum should encompass a broad scope of clinical practice, a significant arts and science

component, emphasis on communication skills, and a minimum of an associate degree to enter practice. The second Educational Consensus Conference, held in the fall of 1993, focused on strategies to implement the recommendations made at the first conference.[28] Both conferences identified the need for more baccalaureate and graduate degree programs in respiratory care. The view that programs should prepare students better in the areas of patient assessment, care plan development, protocols, disease management, pulmonary rehabilitation, research, and geriatrics/gerontology became well accepted.[29,30]

The profession of respiratory care has been described as "a calling or vocation requiring specialized knowledge, methods, and skills as well as preparation, in an institution of higher learning, in the scholarly, scientific, and historical principles underlying such methods and skills."[31] The authors noted that professional roles are different and more complex than technical roles, which are oriented to performing specific tasks as ordered by the physician. Examples of professional roles in respiratory care include patient assessment and care plan development, ventilator management, disease management, pulmonary rehabilitation, and respiratory care consulting services. Technical roles may include basic task performance (e.g., oxygen, aerosol therapy, bronchial hygiene), routine diagnostic testing (e.g., electrocardiography, phlebotomy), and other routine tasks in which little or no assessment is required and decisions are limited to device selection and fine-tuning therapy.[31] In professional practice, the therapist may function as a physician extender who applies protocols or guidelines.[31] Examples include making protocol-based ventilator adjustments, applying assessment-based care plans, and performing advanced procedures such as arterial line insertion and management, intubation and extubation of patients, applying ventilator weaning protocols, and applying advanced cardiopulmonary technologies (e.g., extracorporeal membrane oxygenation, nitric oxide therapy, aortic balloon pumps).

Unfortunately, economic, educational, and institutional forces may limit respiratory care in certain settings to a task-oriented, technical role.[31] However, there are many opportunities for the RT to function as a physician extender, in a role similar to that of the **physician assistant.** Working under the supervision of a physician, the physician assistant may perform many medical procedures that might otherwise be performed by a physician. In a similar way, the respiratory physician extender could improve the quality of care while controlling costs and minimizing unnecessary care. Many authorities believe that the critical thinking, assessment, problem-solving, and decision-making skills needed for advanced practice in the 21st century require advanced levels of education.[31]

In 1998, Hess[32] observed that a task orientation has coincided with a pattern of overordering and misallocation of respiratory care services. Therapist-driven protocols have helped address these concerns by shifting the role of the RT to more of a consultant, allowing him or her to assess the patient and then develop, modify, and implement a care plan once the physician has ordered the protocol.[32] Protocol-based care has been shown to be safe and effective while reducing misallocation of care and helping to control costs.[33,34] Acceptance by physicians of RTs in such consultative roles depends on the professionalism, education, and skill of the RT at the bedside.[32]

In 2001, a report titled *Conference Proceedings on Evidence-Based Medicine in Respiratory Care* was published.[34] Evidence-based practice requires careful examination of the evidence for diagnosis, treatment, prognosis, and, in turn, practice using a formal set of rules.[35] The best evidence is used for clinical decision making, which should lead to optimal respiratory care.[35] Evidence-based practice has been advocated for all respiratory care delivered.

In 2002, the AARC, NBRC, and CoARC published their *Tripartite Statements of Support*, which suggested that all RTs seek and obtain the RRT credential.[36] An AARC white paper followed in 2003, which encouraged the continuing development of baccalaureate and graduate degree programs in respiratory care[37] (see Chapter 2 for further details).

MINI CLINI

Educational Program Advisory Committee

Problem

You are asked to serve on your respiratory care educational program advisory committee. The committee wants to know how respiratory care education has developed and where it should be headed. You are appointed as a member of a subcommittee to research these issues. What should you do?

Solution

You may want to read the sections in this chapter that cover the history and development of respiratory care education to get an overview. You may wish to obtain copies of some of the reference materials that are cited. Items that may be helpful are the AARC Delphi Study,[26] reports of the AARC education consensus conferences,[27,28] and articles about the future of respiratory care.[30-33,37,38] You may wish to review the AARC strategic plan (see www.AARC.org) and AARC statements regarding respiratory care education and credentialing.[11] After reviewing these materials, you should be well prepared to discuss the future direction of your educational program.

SUMMARY CHECKLIST

- RTs apply scientific principles to prevent, identify, and treat acute or chronic dysfunction of the cardiopulmonary system.
- Respiratory care includes the assessment, treatment, management, control, diagnostic evaluation, education, and care of patients with deficiencies and abnormalities of the cardiopulmonary system.
- The AARC is the professional association for the profession.
- RTs work under the direction of a physician who is specially trained in pulmonary medicine, anesthesiology, or critical care medicine.
- The American Registry of Inhalation Therapists was founded in 1960.
- The NBRC, the credentialing board for RTs, was founded in 1974.
- The first Board of Schools was established in 1963.
- The CoARC now accredits respiratory care educational programs.

- As the physiologic basis for oxygen therapy became understood, use of oxygen to treat respiratory disease became established by the 1920s, and oxygen was used routinely in hospitals by the 1940s.
- Use of aerosolized medications for the treatment of asthma began in 1910, with numerous new drugs being developed in the 20th century and continuing up to the present.
- Mechanical ventilation was explored in the 1800s. In 1928, Drinker developed his iron lung; this was followed by the Emerson iron lung in the 1930s, which was used extensively during the polio epidemics of the 1940s and 1950s, and the modern critical care ventilator, which became available in the 1960s.
- The ITA was founded in 1947, becoming the AAIT in 1954, the AART in 1973, and the AARC in 1982.
- The AARC now has 10 specialty sections to provide resources to members based on where they are employed and practice.
- The ARCF offers many scholarships and grants to respiratory therapy students and is promoting advanced training for RTs.
- Although originally found only in the United States and Canada, the practice of respiratory therapy is quickly expanding around the world.
- Respiratory Care Week is a yearly event to promote the profession and raise awareness of the importance of good lung health.
- Many authorities endorse obtaining a bachelor's degree as the minimum credential for respiratory care practice and advanced degrees for research or advisory roles in respiratory care.

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2

The Profession of Respiratory Therapy

Brian K. Walsh

CHAPTER OBJECTIVES

- Describe the roles and function of the American Association for Respiratory Care, National Board for Respiratory Care, and the Commission on Accreditation for Respiratory Care within the respiratory care profession.
- Describe how professional and medical organizations contribute to the development and quality of the medical profession.
- Discuss the scope of respiratory care practice.
- Identify the settings in which respiratory therapists practice.
- Describe the roles and responsibilities of the director, education coordinator, quality assurance coordinator, supervisors/lead therapist, clinical staff, researcher, and medical director.
- Discuss accreditation, credentialing, medical direction, and licensure aspects of the respiratory care profession.
- Identify the roles that each professional respiratory therapist must play in the future growth of the respiratory care profession.

CHAPTER OUTLINE

KEY TERMS

accreditation
American Academy of Sleep Medicine
American Association for Respiratory Care
American Society of Anesthesiologist
American Thoracic Society
Association for the Advancement of Medical Instrumentation
Board of Directors
Board of Medical Advisors
Centers for Medicare and Medicaid Services
clinical staff
CoBGRTE group
credentialing
credentials
department director
educational coordinator
House of Delegates
International Council for Respiratory Care (ICRC)
licensure
medical director
National Association for Medical Direction of Respiratory Care
National Asthma Educator Certification Board

National Board for Respiratory Care
quality assurance coordinator
researcher
***Respiratory Care* journal**
scope of practice
Society of Critical Care Medicine
supervisors/lead therapists
The Joint Commission

INTRODUCTION

The profession of respiratory therapy was officially established in the United States in 1930s[1] and has grown to approximately 172,921 respiratory therapists (RTs).[2] In the early years, RTs were often referred to as "oxygen technicians" or "oxygen orderlies" because most of their activities involved moving compressed cylinders of oxygen and administering oxygen. The majority of these hospital employees were trained on the job. In the late 1940s through early 1950s, short training programs began to appear. The profession of respiratory therapy has grown drastically from those humble days. With the growth of mechanical ventilation therapy and monitoring the side effects of general anesthesia following surgery, the first postoperative care and intensive care units were born. Visionary anesthesiologists and intensivists valued our profession and began to train and use our services as physician extenders to safely and effectively provide mechanical ventilation. Just like oxygen therapy was to the birth of our profession, the volume and complexity of the patients we serve and the advancement of respiratory therapies have not only sustained the profession but have grown it. Currently, respiratory therapy is one of the fastest-growing healthcare professions. This chapter will provide an overview of the profession of respiratory therapy today.

SCOPE OF RESPIRATORY CARE PRACTICE TODAY

According to the **American Association for Respiratory Care** (AARC), "Respiratory Therapists are healthcare professionals whose responsibilities include patient assessment, disease management, diagnostic evaluation, management, education, rehabilitation and care of patients with deficiencies and abnormalities of the cardiopulmonary system. The **scope of practice** includes the application of technology and the use of protocols across all care sites including, but not limited to, the hospital, clinic, physician's office, rehabilitation facility, skilled nursing facility and the patient's home."[3] These responsibilities are supported by education, research, and administration. In addition, RTs perform several diagnostic activities (Box 2.1). The focus of patient and family education activities is to promote knowledge and understanding of the disease process, medical therapy, and self-help. Public education activities focus on the promotion of cardiopulmonary wellness.[3]

We live in exciting times for the profession of respiratory therapy. The information age of the future will be replete with changes in the scope of our practice. The science of respiratory therapy will continue to expand at the same pace as medicine.[4] The scope of practice will continue to incorporate data-driven and evidence-based new technologies, new therapeutic approaches, and data management skills.

BOX 2.1 Respiratory Therapist Diagnostic Scope of Practice Activities

Diagnostic activities include but are not limited to:
1. Obtaining and analyzing physiologic specimens
2. Interpreting physiologic data
3. Performing tests and studies of the cardiopulmonary system
4. Performing neurophysiologic studies
5. Performing sleep disorder studies

Therapy includes but is not limited to:
1. The application and monitoring of medical gases and environmental control systems
2. Mechanical ventilator management
3. Insertion and care of artificial airways
4. Bronchopulmonary hygiene
5. Administration of pharmacologic agents
6. Cardiopulmonary rehabilitation
7. Hemodynamic cardiovascular support
8. Sleep support

PRACTICE SETTINGS

RTs provide hands-on care that ensures people recover from a wide range of medical conditions. RTs get to know their patients and their families and have the gift of helping them through trying times. You will find RTs in a variety of settings from the confines of a climate-controlled hospital or medical office to the extreme temperature changes of interfacility transport (Box 2.2). There are several combinations of practice and patient populations from which an RT can choose to work.

RESPIRATORY THERAPY DEPARTMENT COMPOSITION

Providing respiratory therapy is a business, and over the years, the business of providing respiratory therapy has greatly evolved. Like all well-run health-related businesses, the goal is to provide excellent service to clients. Interestingly, RT departments serve several clients. RT department clients include the patients in which we provide respiratory therapy, the nursing units, and the physicians supported by the department. We often share responsibilities with monitoring, conducting tests, and providing care with the nurses and physicians with whom we work side by side.

The majority of RT departments are centralized, meaning they have centralized leadership, policies, procedures, medical direction, equipment, and staff. However, there are a few hospital systems that embrace a decentralized model. A decentralized model provides RT services as part of a service line with individualized leadership that may or may not be an RT. There are pros and cons to each model, but a discussion of these is outside the scope of this chapter. Although there are different

BOX 2.2 Practice Settings of Respiratory Therapist

- Hospitals: providing respiratory therapy and patient education to individuals suffering from asthma and other respiratory conditions.
- Providing lifesaving therapies:
  - Intensive care units: managing ventilators that keep the critically ill alive.
  - Emergency rooms: delivering lifesaving therapies.
  - Operating rooms or postoperative care units: working with anesthesiologists to monitor patients' breathing during or following surgery.
- Newborn and pediatric care units: helping with conditions ranging from premature birth to cystic fibrosis.
- In patients' homes: providing regular checkups and making sure people have the resources they need to keep them out of the hospital.
- Sleep laboratories: helping diagnose life-altering disorders like sleep apnea.
- Skilled nursing facilities and pulmonary rehabilitation programs: helping older people breathe easier and get more out of life.
- Outpatient specialty clinics or medical offices: conducting pulmonary function testing and providing patient education.
- Hospitals or medical offices: providing smoking cessation programs assisting those who want to kick the habit for good.
- Ground and air transport programs: rushing to rescue people in need of a higher level of care.
- Hospital, insurance companies, or medical offices: providing disease management helping devise care plans for patients with complex respiratory diseases.

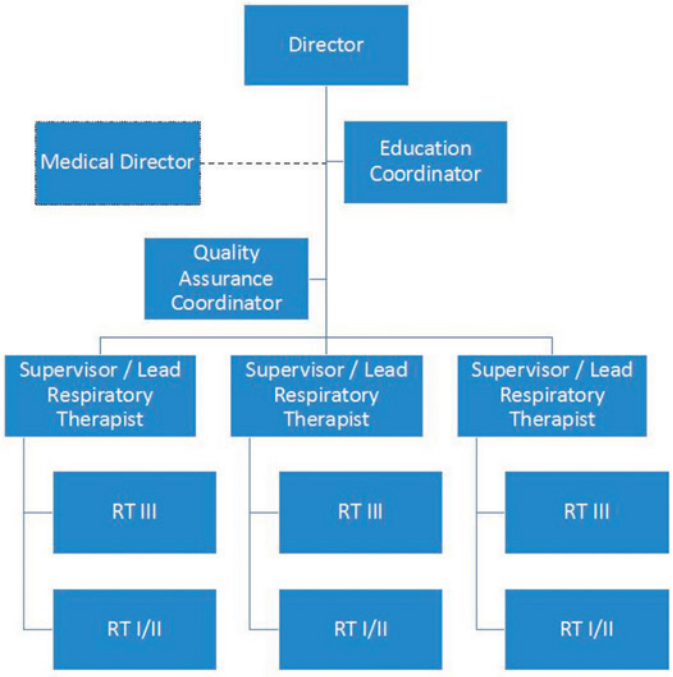

Fig. 2.1 Organizational structure of a typical large respiratory therapy department. *RT*, Respiratory therapist.

compositions of respiratory therapy departments, this section will explore the ideal department. Fig. 2.1 illustrates the typical organization chart for a department with a clinical ladder.

Department Director

The most important element for delivering quality respiratory care is department leadership. The primary leader of the respiratory therapy department is the RT in the role of **department director**. Although this position may have many different names—director, technical director, department chief, manager, etc.—regardless of term used, the department director must be a highly skilled RT, energetic, forward thinking, innovative individual who has as their primary goal quality patient care and the continued development of the department and the profession of respiratory care. For this section we will refer to this individual as the department director. Department direction is often the responsibility of the manager or coordinator of a respiratory therapy department, who must ensure the equipment and the associated policies, procedures, guidelines, and protocols have sufficient quality to ensure the safety, health, and welfare of the patient.

Medical devices are regulated under the *Medical Device Amendment Act* of 1976, which comes under the authority of the U.S. Food and Drug Administration (FDA). The FDA also regulates the drugs that are delivered by RTs. The purpose of the FDA is to establish safety and effectiveness standards and to ensure that these standards are met by equipment and pharmaceutical manufacturers.

Procedures and protocols related to the use of equipment and medications must be written to provide a guide for the RT to follow. This ensures the consistency of the care provided. In addition, equipment must be safety checked and specific maintenance procedures must be performed on a regular basis. Because of rapidly changing respiratory care technology, the job of the Department Director poses significant challenges. Circuit boards and computers have replaced simpler mechanical devices. New medications and delivery devices for the treatment of asthma and newer strategies for treating other respiratory diseases (e.g., ventilatory approaches for acute respiratory distress syndrome [ARDS]) continue to evolve. Individuals responsible for department direction must ensure that these new devices, methods, and strategies are not only effective but also have value.

Educational Coordinator

The **educational coordinator** is tasked with individually assessing the educational needs of the RTs within the department and assigning resources to help reduce educational deficiencies. This includes the development and execution of orientation and continuing competency programs. In addition, this person is part of the leadership of the department and helps develop educational plans related to new technology being evaluated or instituted. In smaller departments this role can be picked up by the director, manager, supervisors, or experienced RTs with an interest in education. This role is essential to ensure the coordination of education to improve quality and compliance with standards and policies and procedures.

Quality Assurance Coordinator

As the profession of respiratory care continues to move from a task and procedure-focused profession to the value associated with those procedures, our quality metrics have changed and become more complex. The **Quality Assurance Coordinator** helps evaluate not only the efficiencies of the **clinical staff** but also the value associated with the practice of respiratory care.

BOX 2.3 Change From the Volume to the Value Paradigm

- Traditional: Efficiency = RVU/FTE
- Value based: Efficiency = Benefit/FTE

Traditionally, efficiencies were determined by the number of procedures (measured by relative value unit (RVU)/time standard) divided by the effort, largely measured by full-time equiveillances (FTEs). This was fairly easy to do, but to measure value, one must take into consideration things such as risk–benefit ratio or define benefit, which can be more difficult (Box 2.3).

Value-based efficiency is determined by the amount of benefit provided by the therapy offered divided by the effort in FTEs. As you can imagine, benefit can be determined in cost savings, survival, or perceived benefit from the patient. Most value-based models use cost as the objective measure. Cost-efficient care is often viewed as higher-quality care.

In addition, as professionals, it is proper for us to determine the quality of care provided by evaluating the care we provide as well as the associated outcomes. This requires resources. As with the educational coordinator in smaller departments, this role can be picked up by the director, manager, supervisors, or experienced RTs with an interest in quality. This role is an integral part of a professional respiratory care department and identifies opportunities to improve the care provided and works hand in hand with other department leaders to develop appropriate action plans.

RULE OF THUMB High-quality care is always safe and efficient.

Supervisors/Lead Therapists

Supervisors or **lead therapists** are roles that are defined by their names. They are often more experienced, are higher credentialed, and hold a higher level of education. These RTs help oversee and ensure the day-to-day functionality of the department by assigning clinical staff to appropriate workloads and areas in which the department provides services. The supervisor or lead therapist is also a clinical resource to assist with advanced procedures (low-volume, higher-risk), emergencies, and consults with difficult to treat patients. The supervisor is also the front-line leader for managerial issues such as personnel disputes or conflict.

Respiratory Therapists

The heart of any respiratory therapy department is their front-line bedside staff. All other roles within the respiratory therapy departments are supportive to these individuals. The product of the department is largely provided by this role group. Most, if not all, clinical staff of the average department must be licensed (registered in Alaska) to provide respiratory therapy. This is a standard that is not negotiable, and it is in the best interest of our patients. Licensed RTs have met a minimum level of competency determined by the **National Board for Respiratory Care** (NBRC) **credentialing** system.

BOX 2.4 Professional Characteristics of a Respiratory Therapist

- Completes an accredited respiratory therapy program
- Obtains professional credentials
- Participates in continuing education activities
  - Adheres to the code of ethics put forth by the institution or state licensing board or both[a]
  - Joins and is actively involved in professional organizations

[a]Ethical standards include respecting the privacy of the patient's personal health information (see Chapters 5 and 7)

Clinical staff are deemed competent and provide the care outlined by the departments policies, procedures, and standards of practice. They often work 12-hour shifts providing care to patients from the youngest (the neonates) to the oldest (the geriatric patients). In larger departments they are often allowed to specialize and work in a specific area of the hospital. Clinical staff are first-line providers of respiratory care but also responders to rapid-response alerts, codes, and disaster/fire emergencies.

The largest personnel group and arguably the most important is the bedside RT. In addition to a competent and dedicated department director and using well-constructed respiratory care policies, procedures, guidelines, and protocols, it is important to have capable RTs able to provide high-quality respiratory care. The quality of RTs depends primarily on their training, education, experience, and professionalism. Training teaches students to perform tasks at a competent level, whereas clinical education provides students with the knowledge they can use in evaluating a situation for making appropriate decisions.[5] Both adequate training and clinical education are required to produce qualified RTs who can assess patients and apply respiratory care procedures.[6] Box 2.4 describes the professional characteristics of an RT.

Medical Director

The **Medical Director** of respiratory care is professionally responsible along with the department director for the quality of clinical care that is delivered (see Box 2.1). The medical director is also responsible for assisting and advising the department director on the management of the respiratory therapy department. Medical direction for respiratory care is usually provided by a pulmonary/critical care physician or an anesthesiologist. Whether the role of a respiratory care service medical director is designated as a full-time or part-time position, it is a full-time responsibility; the medical director must be available on a 24-hour basis to consult with and give advice to other physicians and the respiratory care staff. Box 2.5 describes the responsibilities of a medical director of respiratory therapy.

Perhaps the most important part of providing high-quality respiratory care is to ensure that the care being provided is clinically indicated, the procedure or protocol is based on the most current research, and it is delivered competently. Traditionally, a physician has evaluated patients for respiratory care and has written the specific respiratory therapy orders for the RT to follow. However, such traditional practices often have been associated with what has been called "misallocation of respiratory care."[7–9] Such **misallocation** may consist of ordering therapy

BOX 2.5 Responsibilities of a Medical Director of Respiratory Therapy

- Medical supervision of respiratory therapists in the following areas:
  - General medical, surgical, and respiratory nursing wards
  - Intensive care units
  - Ambulatory care (including rehabilitation)
  - Pulmonary function laboratory
- Approval of department clinical policies and procedures
- Supervision of ongoing quality assurance activities

MINI CLINI

Scope of Practice

Problem: You are a staff therapist in a 300-bed hospital. You have been asked to assist with a procedure you are not sure is within your scope of practice. The physician assures you they are competent and can show you exactly what you should do. How should you investigate whether: (a) the physician is given privileges to perform and (b) you should assist without proper training.

Solution: All hospitals should have a "look-up" reference listing the privileges extended to all healthcare providers. This is usually located within the intranet of the hospital. If you are concerned you do not have the proper training, then you likely do not. You should call your resource or supervisor to confirm, but in an effort to locate a resource who can assist—not in an effort of denying support to a fellow colleague. If your supervisor cannot assist, escalate the concern to the director or medical director for assistance.

that is not indicated, ordering therapy to be delivered by an inappropriate method, or failing to provide therapy that is clinically indicated. Studies show that misallocation of respiratory care occurs frequently and therefore requires focused attention by the department director and medical director to eliminate waste and add value to the care provided by the department.

DESIGNATIONS AND CREDENTIALS OF RESPIRATORY THERAPISTS

The two levels of general practice credentialing in respiratory care are (1) certified respiratory therapists (CRTs) and (2) registered respiratory therapists (RRTs). Students eligible to become CRTs and RRTs are trained and educated in Commission on Accreditation for Respiratory Care (CoARC)-accredited colleges and universities. After completion of an accredited respiratory care educational program, a graduate may become credentialed by taking the written entry-level examination called The Multiple Choice or TMC exam. The exam has one minimum passing score (cut scores) for CRT and a higher cut score that allows the candidate to be eligible to take the clinical simulation examination and become an RRT. Once candidates meet or exceed the higher cut score, they are eligible to take a second exam to determine if they meet the minimum level of competency to become an RRT. Students who complete a 2-year program graduate with an associate degree, and students who complete a 4-year program receive a baccalaureate degree. Some RTs go on to complete a graduate degree (e.g., master's or doctorate) with additional study in the areas of respiratory care, education, management, research, or health sciences. The further development of graduate education in respiratory care has been encouraged by the AARC, and several master's-level RT programs are currently available.[10] Table 2.1 summarizes the distribution of credentialed RTs; organizations overseeing respiratory care education (e.g., CoARC) are reviewed later in this chapter.

TABLE 2.1 Distribution of Active Credentialed Practitioners

Credential Type	Population of Credentialed Practitioners
Certified respiratory therapist (CRT)	82,442
Registered respiratory therapist (RRT)	109,310
Certified pulmonary function technologist (CPFT)	9,614
Registered pulmonary function technologist (RPFT)	4,154
Neonatal/pediatric specialist (CRT-NPS or RRT-NPS)	11,491
Adult critical care specialist (RRT-ACCS)	4,881
Sleep disorders specialist (CRT-SDS or RRT-SDS)	1,044

Note: Based on the 2014 AARC Human Resource Survey.[2] An RT may hold more than one credential.

RULE OF THUMB For testing requirements, examination schedules, study guides, and requirements for maintaining your **credentials**, check with the NBRC website (nbrc.org).

Researcher

A role that has been growing over the years is the role of respiratory therapy **researcher**. As we switch to more value-based care, evidence of the benefit to our practice is paramount. Some department leaders have started to invest into their practice by employing scientists to help research new and old practices and technology in an effort to continuously improve the care the department provides. These individuals are expert clinicians and have advanced degrees in science. This role not only investigates the research questions of the department leaders but also helps the clinical staff in asking and solving their own questions about the care they provide.

PROFESSIONAL RESPIRATORY CARE ORGANIZATIONS TODAY

A profession is often described by its advancing science, technology, and practice; continuous improvement in quality by active participation of its members; maintenance of minimal competency (in our case credentialing); and leadership, research, and innovation. By definition, professionalism is a key attribute to which all RTs should aspire and that must guide respiratory care practice. *Webster's New Collegiate Dictionary* defines a *profession* as "a calling that requires specialized knowledge and often long and intensive academic preparation." A professional is characterized as an individual conforming to the technical and ethical standards of a profession. RTs demonstrate their professionalism by maintaining the highest practice standards, engaging in ongoing learning, conducting research to advance

the quality of respiratory care, and participating in organized activities through professional societies such as the AARC and associated state societies. Therefore it is important to be involved with your professional societies. Box 2.4 lists the professional characteristics of the RT. These characteristics are vitally important because the continued value and progress of the field depends critically on the professionalism of each practitioner.[11]

American Association for Respiratory Care

The AARC is the leading national and international professional organization for RTs. Founded in 1947, the AARC is a not-for-profit professional association with more than 47,000 members. The AARC's membership consists largely of RTs but also includes physicians, nurses, physical therapists, paramedics, and researchers. The AARC serves a larger societal mission to advocate and enhance the professionalism of RTs.

RULE OF THUMB The AARC offers discounted memberships to students.

The art of respiratory care (updates, best practices, opinions, themed highlights, professionalism, humanitarian topics) is supported by the AARC through online and printed version of the professional magazine called the *AARC Times*. In addition, there are "News Now" feeds that you can get via email and multiple social media feeds. The science of respiratory care is supported by the AARC through peer-reviewed publications and journal conferences held by the **Respiratory Care journal**. The respiratory care Journal is composed of an editorial board and editor-in-chief who are researchers and either RTs or physicians.

The AARC has several standing and special committees to support the profession, as well as an executive office that works tirelessly to advance, advocate, and promote the profession of respiratory care. Funding for the operations of the AARC is derived from membership dues, advertisements, grants, and educational programs and conventions. The AARC offers active, student, associate, life, and honorary memberships. The AARC provides some of the highest membership benefits found in health-related professional organizations while maintaining some of the lowest dues. The AARC has multiple specialty sections with several having Board of Director seats to help represent all of the specialization currently afforded RTs.

RULE OF THUMB The AARC is the only professional association dedicated to promoting, advancing, and advocating for respiratory therapists.

Board of Directors

Governance of the AARC comes through the **Board of Directors** (BOD) in conjunction with the **House of Delegates** (HOD). The executive government of the AARC is composed of the Board of Directors made up of no more than 18 active AARC members with at least 5 officers (6 when there is a president-elect) and 12 directors-at-large, and section chairs serving as directors from each of the specialty sections that have at least 1000 members. The AARC BOD members are selected by the membership of the organization. The Executive Director and CEO of the AARC serves as an advisor to the BOD and reports to the current President of the AARC.

House of Delegates

The HOD is a representative body for the chartered affiliate societies. This body is leveraged to help contribute to sustaining, governance, and future growth of the profession through grassroots efforts. The HOD is a vehicle in which the general membership can bring issues or concerns from the local society to the national organization. The HOD is a conduit of information, reporting activities, data, and information to the local level. HOD membership is composed of one to three members from the chartered affiliates. Currently there are 50 delegations representing 48 states. Vermont and New Hampshire, and Maryland and District of Columbia have combined resources to make up one delegation each. The territory of Puerto Rico has its own delegation. The HOD elects officers from its delegation. The officers are Speaker-Elect, Speaker, Immediate Past Speaker, and Treasurer/Secretary.

Board of Medical Advisors

The **Board of Medical Advisors** (BOMA) also helps assist the AARC with governance of practice-related issues and consists of representatives of the AARC's sponsoring organizations: the **American Thoracic Society** (ATS), the American College of Chest Physicians (ACCP), American Academy of Pediatrics (AAP), the American College of Allergy, Asthma, and Immunology (ACAAI), the National Association for Medical Directors of Respiratory Care (NAMDRC), **Society of Critical Care Medicine** (SCCM), and the **American Society of Anesthesiologist**. BOMA consist of no less than 12 members nominated from each sponsoring society. The BOMA chair serves on the AARC BOD, and the chair rotates so that each society will have a representative serve on the BOD.

President's Council

The President's Council is an advisory body composed of past presidents of the AARC. The council has significant experience and wisdom through their activities at the highest position within the AARC. The chair is elected by the members of the President's Council and serves in an advisory position to the BOD.

National Board for Respiratory Care

The NBRC is a voluntary credentialing agency founded in 1960. The NBRC's mission is to promote excellence in respiratory care by awarding credentials based on high competency standards while sharing the profession's goal of protecting and enhancing patient lives. The NBRC has established standards for the credentialing of RTs who work under medical direction and in cooperation with agencies setting educational standards and licensing agencies who provide licensing of RTs. These high standards have been recognized nationally and are the standard for **licensure** in 49 states. The NBRC publishes an electronic newsletter called NBRC Horizons and provides a directory of credentialed individuals. In 2017 the NBRC administered 27,948 examinations.[12]

National Board for Respiratory Care Examinations

Table 2.1 provides an overview of the different professional credentials awarded by the NBRC with an approximate number of practicing individuals with those credentials. The NBRC examinations are graded with a minimum pass level preestablished by the examination committee using a modified Angoff procedure. This accepted psychometric procedure uses the judgements of content experts to determine the number of correct answers required to achieve a passing score for the examinations.[13] The NBRC is governed by a 31-member Board of Trustees composed of representatives from four sponsoring organizations; the AARC, ACCP, ASA, and ATS. A Public Advisor is elected by the board to provide a consumer perspective.

Commission on Accreditation for Respiratory Care

Professional **accreditation** of educational programs in respiratory care assures prospective students, their families, and the general public that the institution meets the minimum professional educational standards for the degree they are offering and there is reasonable evidence that they will continue to meet those standards in the future. The CoARC was founded in 1954 to accredit respiratory care degree programs at the associate, baccalaureate, and master's degree level in the United States and Puerto Rico.

As of December 31, 2017, there were a total of 457 accredited programs. There were 443 Entry into Respiratory Care Professional Practice, 6 sleep specialist programs, and 8 Degree Advancement (DA) programs. Eighty-four percent of the entry to practice programs were at the associate degree, 15% at the baccalaureate degree, and 1% offered at the master's degree level. The BS degree offering has increased 33% since 2011.[14]

RULE OF THUMB CoARC is the accrediting body of respiratory therapy educational programs. CoARC-accredited programs meet the minimum professional educational standards.

American Respiratory Care Foundation

The American Respiratory Care Foundation (ARCF) is dedicated to promoting respiratory health through the support of research, education, and patient-focused philanthropic activities in respiratory care. The ARCF Board of Trustees is composed of respiratory professionals, including emeritus trustees who conduct the business and manage the decisions of the ARCF.

The ARCF supports the RESPIRATORY CARE Journal Conferences, which are conferences designed to be evidence based and timely and provide important information affecting the practice of respiratory care everywhere. These conferences are limited to the faculty and staff of the journal. Each topic is thoroughly presented by an invited expert, followed by heavy discussion among the faculty. The state-of-the-art proceeding appears in a special issue of the journal both in print and online.

As a part of their mission, the ARCF also provides and maintains three Undergraduate Student Awards, four Fellowship Awards, three Research Grants, seven Achievement Awards, and two Literary Awards and heavily support the International Fellowship program. These grants, awards, and recognitions are the output of fundraising. The ACRF could not support research, education, and charitable activities to help improve the quality of our environment if it were not for the generosity of others.[15] The ARCF holds annual fundraising events to ensure the success of the foundation. The AARC supports the ARCF with executive oversight and administrative assistance.

Coalition for Baccalaureate and Graduate Respiratory Therapy Education

The Coalition for Baccalaureate and Graduate Respiratory Therapy Education (CoBGRTE) is organized to help students, faculty members, and the general public learn about baccalaureate and graduate respiratory therapy education in the United States.

The objectives of CoBGRTE are to:

- Award scholarships to baccalaureate and graduate respiratory therapy students.
- Maintain a current roster of baccalaureate and graduate respiratory therapy programs located in regionally accredited colleges or universities in the United States.
- Provide a means of communication among respiratory therapy educators.
- Assist faculty members that are developing curricula for new baccalaureate and graduate respiratory therapy programs.
- Conduct research on respiratory therapy educational programs and the healthcare workforce.
- Engage in study and planning related to the development of new baccalaureate and graduate respiratory therapy programs.
- Assist associate degree respiratory therapy programs in developing consortium and transfer agreements with colleges offering baccalaureate and graduate degrees.
- Advocate for development and establishment of baccalaureate and graduate respiratory therapy programs.

The CoBGRTE Board of Directors consists of 19 professionals in various positions within respiratory therapy. CoBGRTE awards eight merit scholarships and one research scholarship annually and publishes The Coalition Chronicle. The Chronicle helps to highlight programs and best practices of educational institutions. Currently there are 69 institutional members that finically support CoBGRTE.[5]

International Council for Respiratory Care

The **International Council for Respiratory Care (ICRC)** was established in 1991 as a partnership with the AARC and currently consists of 25 member countries. The council is composed of governors from various countries and is a diverse group of worldwide health professions who practice respiratory care within their home country. The ICRC works to address issues affecting educational, medical, and professional trends in the global respiratory care community. As part of their mission to advance the safe, effective, and ethical practice of respiratory care worldwide, the council has been able to do, but not limited to, the following:

1. Develop a Worldwide Code of Ethics within respiratory care.
2. Hold meetings, conferences, and seminars to further open communication, education, and research.
3. Translate popular guidelines and educational resources.

4. Develop an International Education Recognition System (IERS) designed to recognize quality respiratory care education. The IERS grants recognition at three levels; Seminar Recognition (level 1), Program Recognition (level II), and School Recognition (level III).
5. Work with international groups that have like interests, such as the International Standards Organization (ISO), which the ICRC helps develop standards on oxygen therapy.
6. Support the AARC International Fellowship Program.

The AARC supports the ICRC with funding and administrative assistance.

OTHER ORGANIZATIONS AFFECTING RESPIRATORY CARE

National Educator Certification Board

The **National Asthma Educator Certification Board** (NAECB) was established in 2000 to develop and implement qualification/standards, as well as a certification examination for asthma educators on a national level. The goal of the NAECB is to promote optimal asthma management and quality of life among individuals with asthma, their families, and communities by advancing excellence in asthma education through the certified asthma educator (AE-C) process.[6] The 17-member board represents multiple disciplines involved in asthma care and education, including allergy/immunology, behavioral science, emergency medicine, nursing, patient advocacy, environmental health, health education, medicine, pediatrics, pharmacy, public health, pulmonary medicine, and respiratory therapy.

The AE-C–credentialed individual is an expert in teaching, educating, and counseling individuals with asthma and their families in the knowledge and skills necessary to minimize the impact of asthma on their quality of life.[6] RTs make ideal asthma educators because they are very knowledgeable on the optimal uses of medications and delivery devices.

MINI CLINI

Specialty Credentials

Problem: You have successfully obtained your RRT credential and have been practicing for 6 months. You are looking to be promoted and noticed that climbing the clinical ladder in your healthcare system requires specialty credentials within your area of interest. You would like to obtain a specialty credential (RRT-NPS, RRT-ACCS, RRT-SDS, etc.). How do you begin to prepare?

Solution: First you should check your eligibility to be able to sit for the examination. You can find the eligibility criteria on the website of the organization offering the examination. In the case of respiratory therapy the National Board for Respiratory Care (www.nbrc.org) has the majority of exams desired by most respiratory therapist. If you have only 6 months of experience you will not be able to sit for some exams, such as the RRT-ACCS, until you have at least a year of experience. Anticipating becoming eligible, you can leverage the remainder and begin to study. There are several options you can do to self-evaluate and prepare for the successful completion of your specialty examination. The NBRC offers free self-assessments to help identify areas of weakness. Once those areas are identified, you can study to improve your chances of success. In addition, you could take a course or seminar through the AARC or Kettering National Seminars.

Joint Commission

The Joint Commission (TJC) is the United States's predominant standards-setting and accrediting body in healthcare. TJC is an independent, not-for-profit organization that accredits and certifies nearly 21,000 healthcare organizations and programs in the United States.[10] TJC mission is to continuously improve healthcare for the public, in collaboration with other stakeholders, by evaluating healthcare organizations and inspiring them to excel in providing safe and effective care of the highest quality and value.

RTs are directly involved with TJC surveyors when their facilities seek accreditation. Directors of respiratory therapy services are responsible for the core performance measures of patient care related to respiratory care. The AARC works with TJC by appointing members to provide input and influence to the professional and technical advisory committees (PTACs). TJC PTACs are designed to assist in important matters pertaining to its accreditation standards. Periodically, TJC seeks input directly from RTs through a public comment period on proposed standards.

Centers for Medicare and Medicaid Services

The **Centers for Medicare and Medicaid Services** (CMS) is part of the Department of Health and Human Services (HHS). CMS is a federal agency established in 1965 to oversee the Medicare program and works in partnership with state governments to administer Medicaid, Children's Health Insurance Program, and health insurance portability standards. Medicaid gave insurance to eligible people of low-income families, pregnant women, all ages with disabilities, or those who need long-term care.[16] Individual states can tailor their Medicaid programs to best serve the people in their states, so there's a wide variation in the services offered. CMS responsibilities involve the development of policies, guidelines, and procedures used by the intermediaries, carriers, and components of CMS in carrying out their responsibilities for administering the health insurance provisions of the Social Security Act. Respiratory therapy services are specially spelled out within this act.

When the Medicare program was first created, its primary focus was on inpatient acute care. Although the science and practice of respiratory therapy has advanced exponentially since the inception of the Medicare program, Medicare's coverage of respiratory therapy services and RTs has virtually remained as it was in 1965 despite multiple efforts to expand into outpatient, pulmonary rehabilitation, homecare, and now telehealth. This has limited reimbursement of respiratory therapy services largely to the hospital setting.

Association for the Advancement of Medical Instrumentation

The **Association for the Advancement of Medical Instrumentation** (AAMI) is a nonprofit organization founded in 1967 by a diverse community of approximately 7000 professionals. AAMI's mission has been the development, management, and use of safe and effective health technology. One of the best products of the AAMI group is their standards program. The AAMI standards program consists of more than 100 technical committees

TABLE 2.2 Other Organizations That Support the Respiratory Therapy Profession

Organization	Affiliate Membership for RTs	Educational Offerings	Research/Publications	Governmental Affairs and Advocacy
National Association for Medical Direction of Respiratory Care (NAMDRC)	No	Yes	Multiple publication venues and the *Medical Director's Handbook*	Yes
American College of Chest Physicians (ACCP)	Yes	Yes	*CHEST Journal*	Yes
American Thoracic Society (ATS)	Yes	Yes	*American Journal of Respiratory and Critical Care, American Journal of Respiratory Cell and Molecular Biology, and Proceeding of the American Thoracic Society*	Yes
American Society of Anesthesiologists (ASA)	No	Yes	*Anesthesiology*	Yes
Society of Critical Care Medicine	Yes	Yes	*Critical Care Medicine*	Yes
American Academy of Sleep Medicine (AASM)	Yes	Yes	*Journal of Clinical Sleep Medicine*	Yes
American Academy of Pediatrics (AAP)	No	Yes	*Pediatrics*	Yes

and working groups that produce standards, recommended practices, and technical information reports for medical devices. Certainly, respiratory devices are among this group, and AAMI serves as a resource to the respiratory therapy community. With the growth in respiratory technology, this group's role has never been more important.[17]

There are several organizations helping support and contribute to the profession of respiratory care. The respiratory therapy profession works in conjunction with other healthcare professions to deliver the best respiratory care possible. These other professional organizations are largely physician focused but often have memberships for allied health professionals such as RTs. Table 2.2 is a list of organizations, membership offerings, and their contribution to the profession of respiratory care.

RESPIRATORY THERAPY EDUCATION

To become an RT, one must achieve a conferred degree at least at the associate degree level from an a CoARC-accredited institution of higher learning to be eligible to sit for the TMC NBRC examination. This is the primary mechanism for an RT to enter the profession. However, there are additional ways of obtaining entry to practice by obtaining a conferred degree from a baccalaureate and master's degree CoARC-accredited program. In fact, baccalaureate entry to practice has been encouraged by the AARC.[18] In support of the AARC's Position Statement, CoARC started on January 1, 2018 to accredit a new respiratory therapy program only if it confers upon completion a baccalaureate or higher degree.[19] The rationale for furthering the educational level is pretty simple. Over the past 15 years there have been several organizations advocating for the advancement of respiratory care education due to the increasing complexity of the patients we are now serving. This has likely led to the growth of baccalaureate entry to practice programs by 27% from 2011 to 2016.[20] Box 2.6 highlights some of the benefits of baccalaureate education.

According to a study conducted by Varekojis, 70.6% of respiratory therapy department hiring officials indicated they prefer to employ RTs with a baccalaureate degree.[21] These hiring officials specified that an RT with a baccalaureates degree added value to their department in a number of ways, including being prepared: (1) to work effectively with the healthcare team, (2) to complete orientation in a timely and cost-effective manner, (3) to provide evidence-based respiratory therapy services, (4) to provide safe and effective patient care, and (5) for professional advancement.

BOX 2.6 Perceived Benefits of a Baccalaureate Prepared Respiratory Therapist

Associated Benefits of Baccalaureate Education

1. Higher autonomy of practice
2. Better patient outcomes
3. Additional pay
4. Additional soft skills
   - Communication, writing, argument generation, public speaking
5. Recognition as a profession by the department of labor
   - Definition: prolonged course of specialized intellectual instruction[29]
6. Better critical thinking skills

Degree Advancement Programs

Although entry to practice baccalaureate degree programs have grown, there remains a large workforce not at the baccalaureate level. In 2015, the AARC Board of Directors set a goal of 80% of the workforce having or working on their baccalaureate degree by 2020.[22] DA programs are a viable option to help get the current workforce up to the 80% level. The advantage of DA programs is that many of them offer education completely online. In addition, many of them take into consideration students' work and life experience to help get them the maximum number of credits possible.

Bachelor's degree programs often seek to provide students with a foundation for leadership in the profession in the areas of management, supervision, research, education, or clinical specialty areas. To meet the leadership needs of the profession, some baccalaureate programs have already implemented post-baccalaureate certificates or master's degree programs. Clinical areas in which more graduate education programs could be beneficial include critical care, cardiopulmonary diagnostics, clinical research, sleep medicine, rehabilitation, and preparation as a pulmonary physician assistant. There will also be an

increasing demand for RTs with master's and doctoral degrees to serve as university faculty, educators, and researchers.

As exemplified by the 2015 and Beyond project, the knowledge, skills, and attributes needed by RTs will continue to expand, and it will become increasingly difficult to prepare RTs for expanded practice within the credit hour limitations of many existing programs.[4] To alleviate this situation, associate degree programs may develop articulation agreements with 4-year colleges and universities to allow their graduates to complete the bachelor's degree in respiratory care without leaving their home campus; distance education technology will play an important role and allow this to occur at minimal cost.

RULE OF THUMB Promotions to management, education, research, or advanced clinical practice may require bachelor or graduate level educational preparation.

STATE LICENSURE

Licensing of RTs is a mechanism of protecting the public's health, safety, and welfare by mandating a minimal level of competency in respiratory care. For the majority of states, this is the CRT credential; however, there has been a movement to move the entry to licensure to the RRT for all those seeking licensure for the first time. Ohio was the first state to require the RRT credential for licensure in 2015, followed by California (2015), Arizona (2017), New Jersey (2017), New Mexico (2017), Oregon (2018), and Georgia (2019). There are several others states in the process of going to this minimal level of competency. The rationale, as with education, is fairly simple: state licensing boards charged with protecting the safety of the public are asking for a higher level of minimum competency. This is especially important because all RTs trained currently are registry eligible.

RULE OF THUMB States are starting to require the RRT credentials for entry to licensure. Stressing the importance of gaining the RRT credentials.

PROFESSIONALISM

By definition, professionalism is a key attribute to which all RTs should aspire and that must guide respiratory care practice. *Webster's New Collegiate Dictionary* defines a *profession* as "a calling that requires specialized knowledge and often long and intensive academic preparation." A professional is characterized as an individual conforming to the clinical, technical, and ethical standards of a profession. RTs demonstrate their professionalism by maintaining the highest practice standards, engaging in ongoing learning, conducting research to advance the quality of respiratory care, and participating in organized activities through professional societies such as the AARC and associated state societies. Box 2.3 lists the professional characteristics of the RT. We emphasize the importance of these characteristics because the continued value and progress of the field depends critically on the professionalism of each practitioner.[16]

RULE OF THUMB Dedication to a professional practice will ensure the sustainable future of the respiratory therapist.

THE FUTURE OF RESPIRATORY CARE

In 2005, recognizing that many national politicians were beginning to call for an overhaul of the U.S. healthcare delivery system, the AARC Board of Directors began to think strategically, which led to the formation in 2007 of a special task force called 2015 and Beyond. The task force was charged with envisioning potential new roles and responsibilities of RTs by 2015 and beyond. Currently, while beyond 2015, many of the lessons learned or predictions are just as relevant, have come true, or are about to come true.

The leadership of the task force decided to convene three strategic conferences to answer the following five key questions about the profession[23]:

1. How will most patients receive healthcare services in the future?
2. How will respiratory care services be provided?
3. What new knowledge, skills, and attributes will RTs need to be able to provide care that is safe, efficacious, and cost-effective in 2015?
4. What education and credentialing systems will be needed to ensure RTs acquire the new knowledge, skills, and attributes?
5. How should the profession transition from traditional practice to the newer system without adversely affecting the existing workforce?

The initial 2015 and Beyond conference was held in the spring of 2008, and a consensus was reached that there was likely to be[1]:

- Eleven significant changes in how healthcare would be delivered (Box 2.7)
- Nine changes likely to occur in the U.S. healthcare workforce (Box 2.8)
- Five expected changes in how respiratory care services would be provided (Box 2.9)

In the words of one conference organizer, "the take home message was that indeed the scope and depth of respiratory care practice will increase by 2015,"[23] and it certainly has. The second conference was held in the spring of 2009 and built on the findings of the 2008 conference by identifying the competencies needed by graduate RTs and the educational content and curriculum that would be needed to practice in 2015 and beyond. Conference participants agreed that there would be seven major areas of competencies (Box 2.10) that future RTs would need to practice effectively by 2015.[1,4] The third conference was held in the summer of 2010 to determine how the educational programs for entry-level RTs would have to be structured to accomplish the seven major areas of competencies identified during the 2009 conference. The recommendations of the third conference were published in 2011 (Box 2.11).[24]

Although the respiratory care profession is undergoing substantial change, there will be a continuing demand for respiratory care services well into the future because of advances in treatment and technology, increases in the general population, and increases in the elderly population (the baby boomers). A growing

BOX 2.7 Eleven Predicted Changes in Healthcare

1. More patients will be diagnosed with chronic and acute respiratory illnesses.
2. Cost increase will continue, creating challenges for all payers of health services.
3. Personal electronic health records will become more widely used in all healthcare settings.
4. Healthcare clients will pay a greater percentage of the cost but will have more options of care.
5. Retail storefront healthcare and the internet will stimulate consumer-driven cost competition. (Most recent example is Amazon, Berkshire Hathaway, and JPMorgan entering the healthcare arena.)
6. Acute care hospitals will continue to provide episodic, cutting-edge respiratory life support technology, while subacute and homecare providers play important roles in the healthcare continuum.
7. Subacute and long-term care will increase in volume and complexity.
8. The disconnect between prevention and acute care treatment will lessen.
9. All healthcare delivery will undergo increasing scrutiny for quality linked to reimbursement under *Pay for Performance*.
10. New models for the delivery of healthcare will emerge and be tested, such as the Accountable Care Organization and Medical Home.
11. Reimbursement and cost will influence the development and success of these new models.

From Bunch D: 2015 and beyond. *AARC Times* 33:50, 2009.

BOX 2.8 Nine Changes in the Healthcare Workforce

1. There will be national and regional shortages of all healthcare providers.
2. There will be long-term competition for all healthcare professionals
3. The clinical demand will increase at a faster pace than the workforce will be able to expand.
4. The imbalance in jobs and available workforce will be aggravated by the retirement of current providers.
5. Brutal work hours requiring 24/7 staffing will dissuade many individuals from pursuing healthcare careers.
6. Shortage of teaching faculty and a limited number of training programs will limit the number of entrants into allied health professional schools.
7. Traditional clinical sites will be limited in number and variety and will need to be expanded to alternative sites, such as physicians' offices and patients' homes.
8. Newer educational technologic resources will challenge traditional education.
9. Healthcare delivery organizations will find reinvestment in education an attractive way to secure competent and loyal workers.

From Bunch D: 2015 and beyond. *AARC Times* 33:50, 2009.

population will result in increases in asthma, chronic obstructive pulmonary disease (COPD), and other chronic respiratory diseases. There will also be a continuing demand for controlling costs and ensuring that care provided is evidence-based, safe, and effective. Respiratory care will need to be provided using carefully designed policies, guidelines, and protocols to ensure patients get the appropriate care at the right time and that unnecessary care is reduced or eliminated. Aggressive steps to prevent disease and control the cost of chronic respiratory disease will be essential. Effective smoking cessation and tobacco education programs

BOX 2.9 Five Changes Expected in Respiratory Therapy

1. The science of respiratory care will continue to evolve and increase in complexity, and clinical decisions will increasingly be data driven.
2. Patient care teams will become the standard throughout healthcare.
3. New respiratory life-support technologies will be developed and deployed.
4. Reimbursement changes will be the most important impetus for more recognition of the importance of health promotion and disease state management.
5. Concerns over public health issues, military, and disaster response will continue and require new skill sets for all respiratory care providers.

From Bunch D: 2015 and beyond. *AARC Times* 33:50, 2009.

BOX 2.10 Seven Major Areas of Competencies Required by Respiratory Therapists

1. Diagnostics
2. Chronic disease state management
3. Evidence-based medicine and respiratory care protocols
4. Patient assessment
5. Leadership
6. Emergency and critical care
7. Therapeutics

From Barnes TA, Gale DD, Kacmarek RM, Kageler WV: Competencies needed by graduate respiratory therapists in 2015 and beyond. *Respir Care* 55(5):601–616, 2010.

BOX 2.11 Recommendations of the Third 2015 and Beyond Conference

1. Change the Commission on Accreditation for Respiratory Care accreditation standard to require new programs after 2012 to offer a baccalaureate degree in respiratory therapy.
2. Change the Commission on Accreditation for Respiratory Care accreditation standard to require all accredited programs after 2020 to offer a baccalaureate degree in respiratory therapy
3. Retire National Board for Respiratory Care Certified Respiratory Therapist examination after 2014.

Note: Only #1 of the above has been achieved.

and aggressive disease management and pulmonary rehabilitation for patients with moderate to severe asthma, COPD, and other chronic respiratory disease will continue to be needed.

Pulmonary Disease Manager

With increasing shortage of physicians and the growth in volume and complexity of the cardiopulmonary diseased patients, there will be an increasing need for other providers to lead in the management of pulmonary disease. Disease management in general is an approach that teaches patients how to manage and take ownership of their chronic disease. This usually requires a coordinated system of care by an interdisciplinary team. The intent of disease management is to lower the cost of care by properly educating and monitoring patients in a proactive, not reactive way.

The role of disease manager is a natural fit for the RTs. There are several significant studies demonstrating the value of the

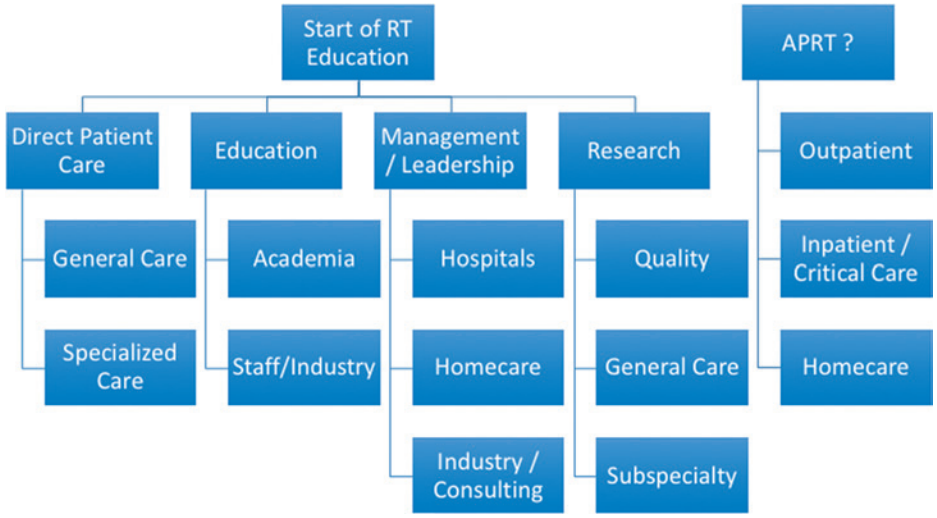

Fig. 2.2 Potential career avenues for respiratory therapists. *APRT,* Advance practice respiratory therapist; *RT,* respiratory therapist.

RTs in this role.[25,26] And it could not have come at a better time. Evidence-based guidelines, practices, and protocols have drastically reduced inappropriate therapies, and department directors have been tasked to appropriately reallocate their FTEs. Although the role is a natural fit for the RT, to be a disease manager requires additional scope of knowledge and skill sets that traditional RTs have not been taught. This is yet a new and exciting avenue for some RT who are interested in this type of care.

Advance Practice Respiratory Therapist

There has been exploration of a new type of RT called the advance practice respiratory therapist (APRT). This concept was developed from the fact that many nonphysician advance practice providers (NPAPPs) such as nurse practitioners and physician assistants lack specialized care for those suffering from cardiopulmonary disease, and there is a growing demand for an NPAPP to assist with this complex patient population. CoARC has established standards for educational institutions to create master's level APRT programs[27]; however, to date not one program has been accredited.

The AARC has put together an APRT Collaborative of key personal from the AARC, NBRC, CoARC, and CoGBRTE to explore the issue further. The committee developed the following working definition:

The APRT is a trained, credentialed, and licensed RT who is employed to provide a scope of practice that exceeds that of the RRT. The aspiring APRT must successfully complete a CoARC-accredited APRT graduate-level education and training program that provides a curricular emphasis that enables the APRT to provide evidence-based, complex diagnostic and therapeutic clinical practice and disease management.[28] Fig. 2.2 demonstrates this possible addition of the APRT pathway. The committee has just completed the following:

1. A literature search of the need of an APRT.
2. Conducted a needs assessment among physicians.
   a. Results are that two in three physicians agree there is a need for an APRT.

Both the literature review and needs assessment will be published in the very near future. This, like the disease manager, is an exciting avenue for those therapists who want to practice at a higher level.

SUMMARY CHECKLIST

- The profession of RT is rapidly growing.
- Respiratory care includes assessment, treatment, management, control, diagnostic evaluation, education, and care of patients with deficiencies and abnormalities of the cardiopulmonary system.
- The AARC is the professional organization for the profession.
- RTs work under the direction of a physician who is trained in pulmonary medicine, anesthesiology, and critical care medicine.
- The NBRC is the credentialing board for RTs.
- CoARC accredits respiratory care educational programs.
- ARCF offers many scholarships and grants to respiratory therapy students and is promoting advanced training for RTs.
- High-quality respiratory therapy can be defined as the competent delivery of indicated respiratory care services in the most efficient way.
- Delivery of high-quality respiratory therapy requires the combined activities of professional and competent RTs who are qualified and led by a competent department director who is assisted by a committed medical director.
- Maintaining and improving quality requires ongoing monitoring of outcomes and testing of the RTs.
- In the future, there will be an increase in demand for respiratory therapy because of advances in treatment and technology; increases in and aging of the population; and increases in the number of patients with asthma, COPD, and other cardiopulmonary diseases.

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3

Quality, Patient Safety, and Communication

Scott P. Marlow and Umur Hatipoğlu

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Define the meaning of *quality* in healthcare services.
- Understand the basic tools used in quality improvement projects.
- Describe established methods of quality improvement such as Six Sigma and lean management.
- Understand the importance of monitoring quality to promote better patient outcomes.
- Identify impediments to care and risk in the direct patient environment.
- State how communication can affect patient care.
- Describe the two-patient identifier system.
- List the factors associated with the communication process.
- Describe how to improve your communication effectiveness.
- Describe how to recognize and help resolve interpersonal or organizational sources of conflict.
- Describe how to apply good body mechanics and posture to moving patients.
- Describe how to ambulate a patient and the potential benefits of ambulation.
- Write definitions of key terms associated with electricity, including voltage, current, and resistance.
- Identify the potential physiologic effects that electrical current can have on the body.
- State how to reduce the risk for electrical shock to patients and yourself.
- Identify key statistics related to the incidence and origin of hospital fires.
- List the conditions needed for fire and how to minimize fire hazards.

CHAPTER OUTLINE

KEY TERMS

accountable care organizations (ACO)
ambulation
ampere
attending
auditory
channel
competencies
current
disease management
feedback
ground
"Jidoka"
lean management
lower confidence limit
macroshock
microshock
ohm
PASS
pay for performance
peer review organization (PRO)
performance improvement
Plan-Do-Study-Act (PDSA) cycle
process control
quality assurance
quality improvement
RACE
resistance
Six Sigma
upper confidence limit
voltage

Provision of high-quality care in a safe environment is the focus of the current healthcare industry. Achieving this goal requires the integration of multiple disciplines, including respiratory therapy. Consequently, respiratory therapists (RTs) should be familiar with the concepts of **quality improvement** as it relates to healthcare.

This chapter will define quality and how it relates to healthcare. We will outline how quality is measured, monitored, enhanced, and adapted to our healthcare environment. Discussions regarding quality in healthcare will demonstrate how RTs share the general responsibilities for providing a safe and effective healthcare environment with nurses and other members of the healthcare team. RTs are also required to have specific technical knowledge of the environment of direct patient care. In addition to technical skills, all healthcare professionals must be able to communicate effectively with each other and with patients and patients' families. This chapter aims to provide the foundational knowledge needed to understand the general aspects of patient safety considerations, communication in healthcare, conflict resolution, and recordkeeping that comprise essential components of high-quality patient care.

QUALITY CONSIDERATIONS

What Is Quality of Medical Care?

The quality of a service or product refers to the sum of its properties that help satisfy the needs of its consumer. High-quality services get high demand and also become a source of pride and financial success for the producer. The Institute of Medicine defines quality of medical care as follows: Quality of care is the degree to which health services for individuals and populations increase the likelihood of desired health outcomes and are consistent with current professional knowledge.[1] The National Academy of Medicine (the successor organization to the Institute of Medicine) suggests the following dimensions in healthcare quality: Safety, Timeliness, Effectiveness, Efficiency, Equity, Patient-centeredness (STEEP). These elements also define the starting points for quality improvement projects in healthcare.

Methods of Quality Improvement

Methods of attaining and ensuring quality were born in the automobile manufacturing industry in Japan, led by American engineers and scientists. These principles were only later adopted in the United States. William Edwards Deming (1900–1993), an electrical engineer and statistician, is credited for laying the foundations of quality control and management. Working first with the Japanese automobile industry and later with Ford Motor Company, Deming suggested that the purpose of an organization is to constantly seek improvement of its product or service aligned with customer needs.[2] Rather than relying on constant inspection, quality should be built into the product from the beginning by design of the process or structure. Emphasis must be placed on the quality of the product and pride in the workmanship rather than on sheer number of units produced. Quality improvement must be everyone's job, starting from executive management to the front-line worker. Deming heavily relied on statistical quality control techniques, established by Walter A. Shewhart

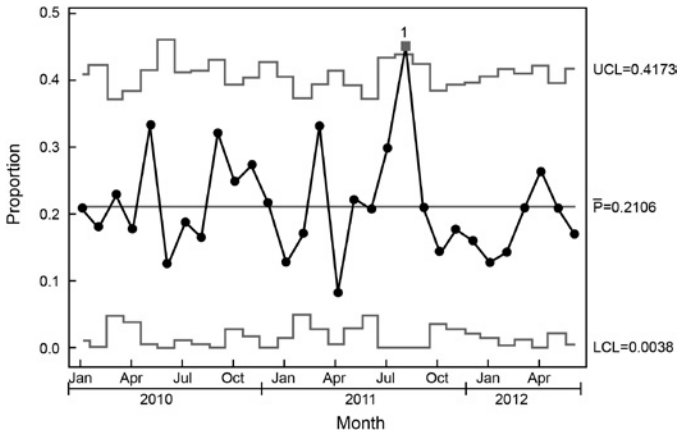

Fig. 3.1 Statistical Process Control Chart Showing Proportion of Patients Having to be Readmitted to the Hospital After Discharge. Upper and lower control limits *(UCL and LCL, respectively)* are marked with gray lines. At approximately September 2011, there appears to be a spike in readmissions to the hospital outside of the UCL that may require investigation.

(1891–1967), another American engineer and scientist. Through statistical **process control** charts (SPCs) discussed in further detail later, Shewhart pointed out that in every process associated with production, there was a variability, which he termed common cause variation. The range of common cause variation can be described with an **upper confidence limit** (UCL) and a **lower confidence limit** (LCL). These limits represent the highest and lowest measurements that are considered normal. A continuous monitoring of the process is possible by taking periodic samples and charting these values on the SPC. Should the sample for any given time interval reveal values outside of the range (e.g., higher or lower than UCL and LCL, respectively), then special cause variation is suspected. Fig. 3.1 depicts an SPC illustrating common and special cause variation. Detecting a special cause variation pattern will require investigation of the process. Shewhart's SPCs continue to form the backbone of continuous quality improvement. Another important contribution to the practice of quality improvement by this brilliant engineer is the **Plan-Do-Study-Act (PDSA)**; or Plan-Do-Check-Act cycle, also known as the Shewhart cycle.

Plan-Do-Study-Act Cycle

The PDSA can be seen visualized as the wheels of the car that is continuous quality improvement. As the wheels of PDSA turn, one gets closer to that difficult-to-achieve "perfect" product or service.

Plan Phase

In the *Plan* phase, clear goals are set for the quality improvement process. Goals should be SMART: Specific, Measurable, Achievable, Realistic, and Time-bound. A SMART goal might be "a 20% increase in referrals to pulmonary rehabilitation on discharge for patients with chronic obstructive pulmonary disease (COPD)." The planned intervention should be stated clearly. For instance, "respiratory therapist stationed on the nursing floor will distribute pulmonary rehabilitation program pamphlets to clinical team and remind clinicians to place the order for patients with COPD."

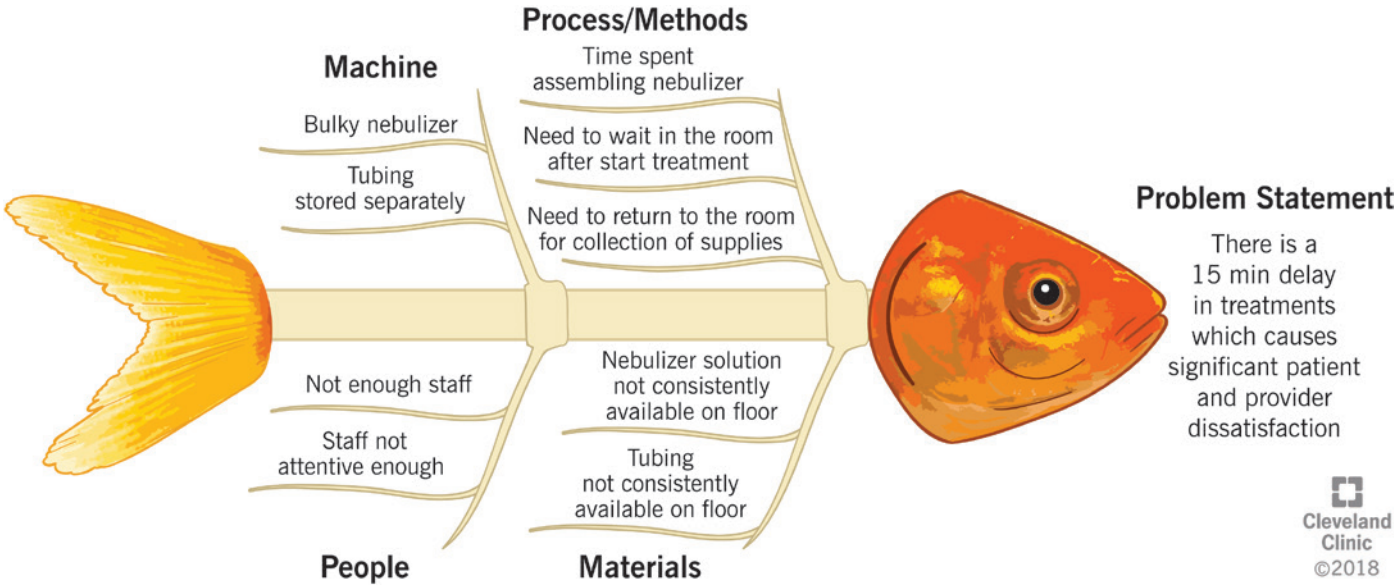

Fig. 3.2 Fishbone diagram. (From Cleveland Clinic, ©2018.)

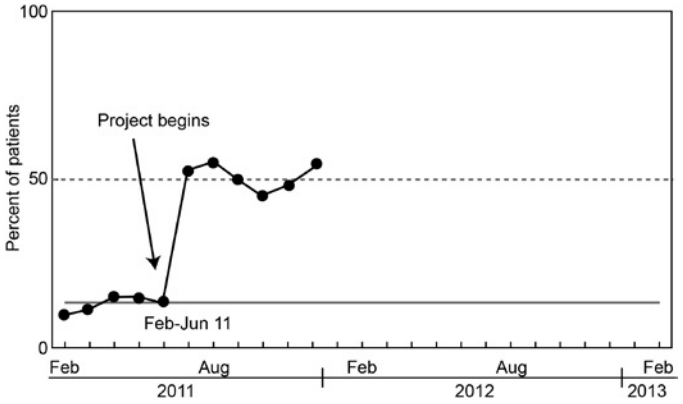

Fig. 3.3 Run chart showing percentage of patients who received pneumonia vaccination over time.

A time limit should be specified, for example, "a 20% increase in referrals to pulmonary rehabilitation on discharge over the next 3 months." During the planning phase, it is also helpful to create a diagram or a flow chart of the process that needs to be improved. The project team may choose to use tools such as the fishbone (or Ishikawa) diagram to systematically evaluate the different factors that affect the process and contribute to the problem, that is, people, technology, environment, materials, equipment, and methods (see Fig. 3.2).

Do Phase

In the *Do* phase, the intervention is begun and observations are recorded. Sometimes, observations may need to be made on a limited sample that is hopefully representative of the entire process. The size of that sample should be determined by statistical methods that may require the help of a quality improvement professional or biostatistician. The observations are plotted on a statistical process chart or its simpler version, a so-called *run chart,* for analysis (Fig. 3.3).

Run charts are graphic representations of data over a period of observation. In contrast to SPCs, there are no defined upper and lower limits. Rather, movement of the data points around the median value (the gray line) is visualized and interpreted. Rules of interpretation are based on statistical principles. A consistent change in the placement of data points on either side of the median indicates special cause variation. The run chart in Fig. 3.3 displays the percentage of patients who have received pneumonia vaccination before discharge from the hospital before and after the onset of a quality improvement project. In this instance, six data points are observed above the median value after the project starts. Five or more points on one side of the median indicates special cause variation (an interpretation rule), in this case the result of an effective project.

Study (or Check) Phase

In the *Study* phase, the observations are analyzed, usually by examination of the process charts. The barriers to achieving the set goals are considered and discussed.

Act Phase

In the *Act* phase, based on the analysis performed in the Study phase, modifications to the intervention are made.

The Plan-Do-Study-Act Cycle Starts Over

The paradigm of the PDSA cycle has served as the foundation for modern quality management systems such as the **lean management** system and **Six Sigma**, which are discussed in the following section.

RULE OF THUMB The crucial components of a quality improvement project are summarized in the PDSA cycle:
Plan: Determine the specific aim, duration, data collection strategy, and team that will run the quality improvement project.
Do: Collect data and record the observations.
Study: Analyze results and derive conclusions.
Act: Change the process for improvement, plan the next cycle.

Six Sigma

By the mid-20th century, it had become obvious to the leading industrial companies that the rate of defective products had to be lowered to maintain market competitiveness and customer loyalty. Developed by the American telecommunications company Motorola, the Six Sigma method for quality improvement recognizes that there is a natural variation in process output that can be measured and monitored over time. Controlling and reducing this variation are the keys to business success. Statistical methods are used to calculate acceptable variation. There has to be a strong commitment on the part of management, from top to bottom, to these principles. The Six Sigma method also is based on the belief that improvement to existing processes is always possible and has to be achieved systematically. Similar to the PDSA cycle, Six Sigma adopts the Define-Measure-Analyze-Improve-Control (DMAIC) cycle for continuous quality improvement.

Define: Describe and validate the problem, create solutions, create a process map, and create a timeline for completion of the project.

Measure: Identify metrics, develop data collection plan, collect baseline data.

Analyze: Evaluate collected data in the measure phase, determine root causes for the problem, and estimate the relative impact of each.

Improve: Discuss, develop, and implement solutions to the root cause(s), and confirm that the intervention is well targeted.

Control: Continue to implement solutions and follow metrics to ensure maintenance and adoption.

Origin of the Term Six Sigma

Sigma (σ) is a Greek letter that is used to note standard deviation in a normally distributed population. Accordingly, one standard deviation from the mean in each direction, that is, ±1 σ, contains approximately 68% of the population. Similarly, two times σ contains 95% and three times σ contains 99%. If one considers a process to operate at 1 σ, then one would have to accept a 68% rate of successful product (or a failure rate of 32%). At the 2 σ level of acceptance, the failure rate would be 5% and at 3 σ, it would be 1%. At Six Sigma, the rate of failure would be 3 in 1 million (or 0.000003). Thus the Six Sigma process has a goal of a very, very small error rate (Fig. 3.4).

Lean Management

Lean management is a business management philosophy that focuses on eliminating waste or non–value-added activities. The origins of lean management are in the Japanese automobile maker, Toyota Motor Company. Lean management is like ergonomics; eliminating waste of time, excess work, and unevenness of product are the goals. This goal is achieved by broadly using the principles of "just in time" (i.e., having equipment, personnel, and supplies at the right place at the right time) and **"Jidoka"** (a joining of automation and human intelligence that results in a higher level of quality control). According to the Jidoka principle, any person involved in a service or manufacturing of product can stop the process if he or she sees a defect.

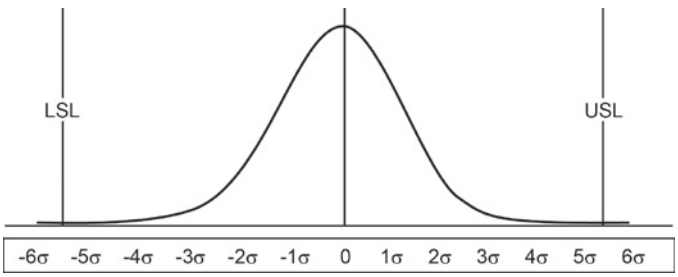

Fig. 3.4 Normal (Gaussian) distribution. *LSL,* Lower specific limit; *USL,* upper specific limit.

Lean management uses tools similar to those in PDSA and Six Sigma, with emphasis on waste elimination. These have been collectively termed the *lean toolbox.* The main instrument is value stream mapping, which is essentially a flow chart with emphasis on identifying value-added activities versus those that are not.

The Evolution of Quality in Healthcare in the United States

As you can see, there are common themes in all quality improvement approaches: Identification of process components, increasing efficiency (reducing waste), standardization (reducing common variation), and a teamwork approach in implementing solutions. Broadly speaking, healthcare delivery systems have been slow to adopt these principles, with the possible exception of laboratory medicine. However, rising healthcare costs have brought about a revolution in how healthcare is delivered in the United States. In line with the *Patient Protection and Affordable Care Act,* the Centers for Medicare and Medicaid Services (CMS) began the Hospital Value-Based Purchasing Program, which rewarded or penalized hospitals based on their performance in the domains of process measures (also called *core measure compliance*), outcomes, patient experience, and efficiency. The Hospital Value-Based Purchasing Program is budget neutral, meaning that superior performance is rewarded and poor performers have to pay a penalty. Funds from the penalties provide the money for the rewards to hospitals that perform well. The federal government also enacted the Hospital Readmissions Reduction Program, which is strictly a penalty program that withholds a certain percentage of entire CMS reimbursements if the hospital has excess readmissions within 30 days of index discharge, compared with the national mean. With these incentives and threats of penalties, the healthcare industry is currently adopting principles of quality improvement quickly.

Disease Management

Disease management refers to an organized strategy of delivering care to a large group of individuals with chronic disease to improve outcomes and reduce cost. Disease management has been defined as a systematic population-based approach to identify persons at risk, intervene with specific programs of care, and measure clinical and other outcomes.[6,7] Disease management programs include four essential components: (1) an integrated healthcare system that can provide coordinated care across the full range of patient needs; (2) a comprehensive knowledge base regarding the prevention, diagnosis, and treatment of disease that guides the plan of care; (3) sophisticated clinical and

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Case Study

Michael Breathewell, a registered respiratory therapist (RRT), is the respiratory therapy manager in the respiratory care department of a 300-bed unit in Our Lady of Sacred Lungs Hospital. Over the past 6 months, he has been made aware, through the newly implemented serious event reporting system (SERS), of the time delay in delivery of scheduled inhaled bronchodilator treatments to patients. There is increasing pressure from physicians, nursing, and administration to fix this problem. After careful review of the cases, Michael determines that the problem occurs throughout all shifts and with different RTs and services involved. He believes that the problem may be due to a system issue and not special cause variation.

There are more than 200 scheduled treatments given per day at the hospital. Tracking each treatment delay on a daily basis would be a huge job. Therefore Michael has to select a sample that represents the time delay for the entire population. He asks the hospital biostatistician for help. Based on several assumptions, the biostatistician determined that 16 randomly sampled events were needed to have a fair idea of the average time delay between scheduled treatments and actual delivery.

Next, Michael asks for the help of a quality improvement professional in choosing the appropriate statistical process control chart for studying and monitoring the process of bronchodilator administration. He then begins collecting and graphing the data.

After a 3-month period of observation, he determines that there is an average of 15 minutes of delay between scheduled time and delivery time per patient (Fig. 3.5).

Michael decides to apply the Plan-Do-Study-Act (PDSA) cycle to tackle the issue.

Plan

Michael calls a brainstorming session with floor respiratory managers and the medical director of respiratory care at this hospital. During the meeting, Michael and the group identify and analyze the problem and map the process. To facilitate the discussion, he uses an Ishikawa fishbone diagram to explore potential causes. Fig. 3.2 shows the completed fishbone diagram. The fishbone allows a systematic discussion of possible contributors to the problem by considering factors related to machines, people, material, and process. The attendees overwhelmingly feel that the bulk of the time is spent getting the nebulizer and tubing, setting up the patient, and then returning back to the room. They also research best practices and conduct a literature review to understand reasons for delay in delivering nebulized treatments.

An attendee points out that administration of bronchodilators via metered dose inhalers (MDIs) has been found to be equivalent in efficacy across different diseases and disease severity.[3–5]

After some deliberation, weighing the balancing measures such as cost difference, the group decides to switch to bronchodilator administration via MDIs with a spacer and to follow time delay between scheduled time of bronchodilator delivery and actual time of delivery. The group decides that a 3-month observation should be enough to determine the effect of the intervention and meet monthly to review results. Michael and the team also identify the measures of success, including monitoring time delay between order entry and administration of the medication and employee satisfaction. Michael meets with hospital administration and with the chief financial officer, getting their support and ensuring financial feasibility of the switch.

Do

The group begins to administer scheduled short-acting bronchodilators by MDI with a spacer throughout the hospital floors. At least 16 observations of bronchodilator administration are made randomly throughout the day and recorded on the statistical process chart. Although the literature provides strong support for this intervention, Michael carefully reviews patient outcomes (e.g., treatment failure that results in a higher level of care or intensive care unit admission) to ensure that the switch to MDIs does not have unintended consequences.

Study

Michael measures the effect of the intervention and sees a trend toward reduction in delay times after 1 month and is pleased. However, some RTs suggest that further reduction in delays might be possible if patients' MDIs and spacers are kept at the bedside.

Act

The suggestion to switch to delivery by MDI is discussed with the committee for pharmacy and therapeutics and is approved. MDIs with the patient's name stamp and spacer are kept at the bedside.

At the end of 3 months, Michael studies the process chart (Fig. 3.6) and notes that delays have been consistently less than the lower confidence limit (LCL) of the original process. He congratulates the entire team and continues to monitor progress. Michael and colleagues plan to refine the intervention through iterative cycles, going back to the plan phase if future results are not as expected or yield unintended consequences.

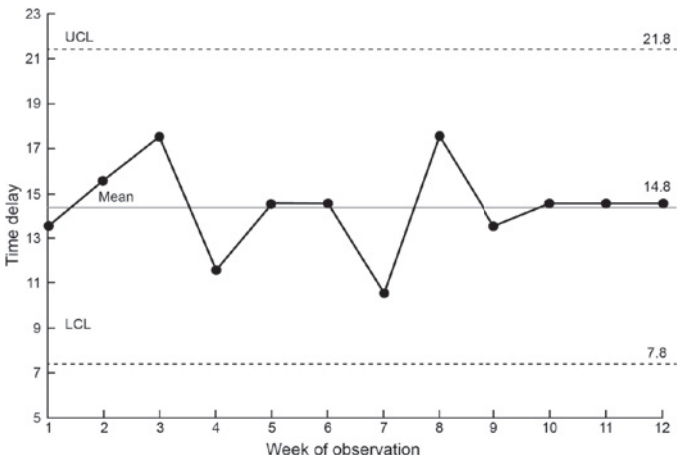


Fig. 3.5 Time delay between scheduled and delivered nebulization. *LCL*, Lower control limit; *UCL*, upper control limit.

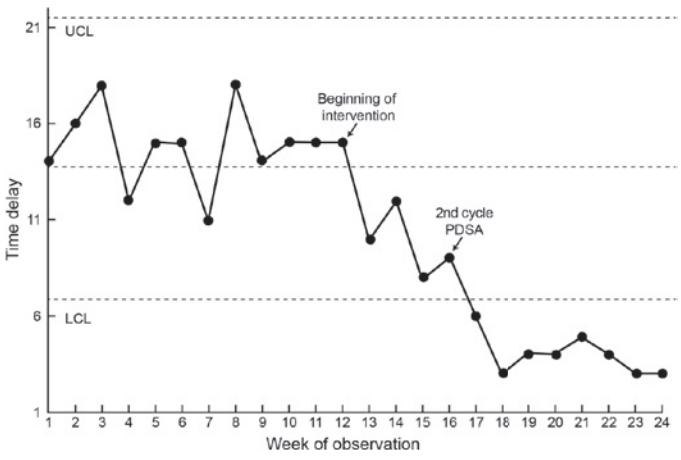


Fig. 3.6 Time delay between scheduled and delivered nebulization. *LCL*, Lower control limit; *PDSA*, Plan-Do-Study-Act; *UCL*, upper control limit.

administrative information systems that can help assess patterns of clinical practice; and (4) a commitment to continuous quality improvement. Disease management programs may be developed for chronic conditions such as asthma, diabetes, COPD, and congestive heart failure.

A disease management program for COPD might be adopted by a healthcare provider, insurance company, or health maintenance organization in defining its practice approach to individuals with COPD. The disease management program might contain algorithms addressing when to suspect COPD, tests to perform (e.g., spirometry, alpha-1 antitrypsin level, diffusing capacity), medications to prescribe based on disease severity, management of exacerbations, and indications for rehabilitation. Disease management programs are often outlined in documents containing branched logic algorithms that specify care. Disease management protocols typically address large groups and are based on an underlying diagnosis rather than on individual signs and symptoms. Other dimensions of the COPD management program may include a data collection activity regarding the number of patients served, the outcomes of care, and, perhaps, the associated costs. In addition, as with quality monitoring in general, ongoing review and periodic updating and revising the care algorithms are important aspects of the program. Chronic care management programs in COPD have been associated with improved quality of life and reduced hospital days.[8] Importantly, RTs can successfully play a central role in the implementation of these respiratory disease specific programs.[9]

Monitoring Quality in Respiratory Care

Beyond ensuring that all elements of a high-quality respiratory care program are in place, quality must be monitored to ensure that it is being maintained. Strategies to monitor quality include intrainstitutional monitoring practices, centralized government monitoring bodies, such as the CMS, and independent agencies such as The Joint Commission (TJC).

Institutional **quality assurance** often uses skills checks or **competencies**. Competence, or the quality of being competent, can be defined as having suitable or sufficient skill, knowledge, and experience for the purposes of a specific task.[10] Competence for a specific skill is frequently determined by observation of the practitioner's performance of the skill according to a prescribed checklist. Annual competency checks are documented for skills and procedures that carry some degree of patient risk (e.g., arterial puncture, aerosol therapy, bilevel positive airway pressure setup).

Although skills checks have traditionally been done in person or with direct supervision of patient care activities, a new dimension of skills training and certification that is being widely implemented is the use of clinical simulation, with either low-fidelity or high-fidelity simulation trainers. Such simulation training, in which RTs use technology that attempts to reproduce reliably a true patient or true patient scenario, is similar to the flight simulator training that commercial airline pilots undergo to achieve certification to fly various airplanes. Simulation training in respiratory therapy may involve intubation, ventilator management, arterial line placement, and optimizing teamwork in acute resuscitation scenarios.[11]

BOX 3.1 Nine Steps for a Quality Assurance Plan

1. Identify problem
2. Determine cause of problem
3. Rank problem
4. Develop strategy for resolving problem
5. Develop appropriate measurement techniques
6. Implement problem-resolution strategy
7. Analyze and compile results of intervention
8. Report results to appropriate personnel
9. Evaluate intervention outcome

Many healthcare organizations, including hospitals, subacute care facilities, and outpatient clinics, seek voluntary accreditation as a way to improve their service and assure the public that they maintain high standards. TJC (as The Joint Commission on the Accreditation of Healthcare) was formed in 1951 by the American College of Surgeons, the American Hospital Association, and the American Medical Association. Accreditation by TJC is based on satisfying specific standards established by professional and technical advisory committees.

TJC requires a hospital service to have a quality assurance plan to provide a system for controlling quality. Nine generally recognized steps for a quality assurance plan are used as the basis for quality assurance programs (Box 3.1).

- Current standards of TJC for accreditation emphasize organization-wide efforts for **performance improvement**. Despite increased emphasis on cost containment, quality care remains the first goal of hospitals and respiratory care services. Performance improvement, also commonly called *continuous quality improvement,* is an ongoing process designed to detect and correct factors that interfere with quality and cost-effective healthcare. This process crosses department boundaries and follows the continuum of the patient's care. TJC develops standards of performance through a rigorous process which is outlined in Box 3.2. The hospital collects, compiles, and analyzes data on its processes to monitor and improve its performance. TJC conducts periodic inspections to ensure adherence to these standards and works with healthcare organizations in their quest to improve performance.

TJC has also adopted a policy to manage serious patient events that result in death, permanent harm, or severe temporary harm, called sentinel events. Sentinel events require immediate attention by the hospital and are subject review by the TJC. Sentinel events necessitate disclosure of the event to the patient and family after stabilizing and supporting the patient in the immediate aftermath. Following a thorough investigation, a root cause analysis is performed in conjunction with the hospital's quality and safety professionals. Once causal and contributing factors are identified, a corrective plan is put in place with a timeline for implementation. The corrective plan may include changes to existing hospital standard operating procedures and policies in an effort to reduce or eliminate the risk of the event happening again. Although submission of sentinel events to the TJC is voluntary, this is encouraged to help others benefit from the lessons learned and allow the hospital an opportunity to consult

BOX 3.2 The Joint Commission (TJC) Development of the Standards for Performance Improvement

- Emerging quality and safety issues are identified through the scientific literature or discussions with TJC's standing committees and advisory groups, accredited organizations, professional associations, consumer groups, or others.
- TJC prepares draft standards using input from technical advisory panels, focus groups, experts and other stakeholders.
- The draft standards are distributed nationally for review and made available for comment on the Standards Field Review page of TJC website.
- After any necessary revisions, standards are reviewed and approved by executive leadership.
- The survey process is enhanced, as needed, to address the new standards requirements, and pilot testing of the survey process is conducted.
- Surveyors are educated about how to assess compliance with the new standards.
- The approved standards are published for use by the field.
- Once a standard is in effect, ongoing feedback is sought for the purpose of continuous improvement.

Adapted from The Joint Commission website. https://www.jointcommission.org/facts_about_joint_commission_accreditation_standards/. Accessed May 5, 2018.

BOX 3.3 Quality Monitoring Benchmarks

- Monitoring the correctness of respiratory care plans
- Monitoring the consistency of formulating respiratory care plans among therapist evaluators
- Evaluating the efficacy of algorithms or protocols
- Evaluating the overall effectiveness of the protocol program

with TJC. If the TJC becomes aware of the event through other means such as patient or family reporting, accredited institutions will be asked to provide a report of the event along with the corrective action plan.

Meeting quality goals is increasingly being tied to reimbursement rates by the CMS and insurers to hospitals; this phenomenon has been called "**pay for performance**."[12] Beyond general monitoring goals for respiratory therapy, use of respiratory care protocols creates the need for additional quality monitoring benchmarks regarding correctness, consistency, efficacy, and effectiveness (Box 3.3).

Specific methods to monitor the quality of respiratory care protocol programs include: conducting care plan audits in real time, ensuring practitioner training by using case study exercises, and using simulation exercises to enhance and to measure the performance of RTs.

Monitoring correctness of respiratory care plans can be accomplished by using a care plan audit system. Care plan auditors must be therapists who are experienced in providing respiratory care and patient assessment. The auditors must also have experience with using the institution's protocol system and in writing care plans. With an auditing system, the auditor writes a care plan for a patient and compares it with the care plan written by the therapist evaluator to determine correctness. A specified number of audits should be performed monthly, with results tabulated and reported monthly or quarterly, depending on the size of the hospital. Feedback must be provided to the evaluators whose care plans are being audited to show their proficiency or to indicate areas that require improvement.

Another monitoring method found useful for respiratory therapy consult services is the case study exercise (or simulated patient scenario exercise). Simulated patient exercises can help determine the consistency of respiratory care plans among therapist evaluators. The scores of individual RTs may be tracked over time to identify problems and assess improvement.

Simulated patient exercises may consist of a set of three or four patient scenarios. All RTs working under the protocol system, whether or not they are evaluators, complete an assessment sheet and, following the associated algorithms, write a care plan for each scenario. The assessment sheets and the care plans are compared with the gold standard, or correct assessments and care plans, as determined by the consensus of the education coordinator and the supervisors. Scores are tabulated for the individual RTs, and the number of errors for each therapy is examined. If a particular therapy consistently has a large number of associated errors, the algorithm is reviewed for errors or vagueness. In some settings a computer-based system that scores the assessments and care plans and provides feedback to the RT has been used.[13] Performance data of individual RTs are maintained in a database to calculate and track aggregate performance statistics.

Peer Review Organizations

In addition to the voluntary accreditation process that healthcare organizations use to help ensure that patients are receiving quality care, the federal government has established an elaborate system of **peer review organizations (PROs)** to evaluate the quality and appropriateness of care given to Medicare beneficiaries. PROs evaluate care provided to individual patients in real time to assess and ensure compliance with federal guidelines.

In recent years, healthcare organizations have attempted to improve the quality of patient care while reducing costs by implementing several innovative healthcare models. Historically, models that were commonly implemented were hospital restructuring and redesign and patient-focused care. Protocols and disease management represent continuing solutions. An Accountable Care Organization (ACO) can be broadly thought of as an emerging model in which a group of healthcare providers aligns and agrees together to try to meet quality and care targets and to receive payments as a collective entity, from which individual payments then can be disbursed. The ACO can benefit as a group from its success and can absorb losses as a group related to its failure to meet the targets. The intent of the ACO is to increase the value of healthcare, which is defined as the quality of care divided by the cost of care. Value is increased when quality increases and/or when the cost of care decreases. Early experience with ACOs indicates a trend for reduced healthcare use without compromising quality.[14]

SAFETY CONSIDERATIONS

Safety is a very important part of ensuring high-quality care. Importantly, patient safety must always be the first consideration

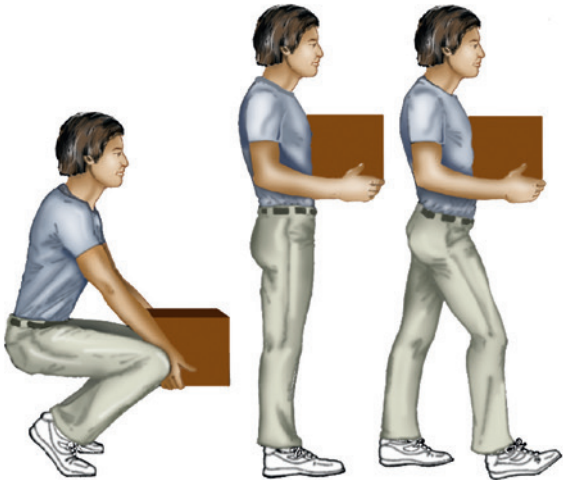


Fig. 3.7 Body mechanics for lifting and carrying objects.

in respiratory care. Although the RT usually does not have full control over the patient's environment, efforts must be made to minimize potential hazards associated with respiratory care. The key areas of potential risk for patients, RTs, and coworkers are patient movement and **ambulation**, electrical hazards, fire hazards, and general safety concerns. Each of these will be discussed as part of attention to providing high-quality, safe care.

Patient Movement and Ambulation

Basic Body Mechanics

Posture involves the relationship of the body parts to each other. A person needs good posture to reduce the risk for injury when lifting patients or heavy equipment. Poor posture may place inappropriate stress on joints and related muscles and tendons. Fig. 3.7 illustrates the correct body mechanics for lifting a heavy object. The correct technique calls for a straight spine and use of the leg muscles to lift the object.

Moving the Patient in Bed

Conscious people assume positions that are the most comfortable. Bedridden patients with acute or chronic respiratory dysfunction often assume an upright position, with their arms flexed and their thorax leaning forward. This position helps decrease their work of breathing. In other cases, patients may have to assume certain positions for therapeutic reasons such as when postural drainage is applied.

Fig. 3.8 shows the correct technique for lateral movement of a bed-bound patient. Fig. 3.9 illustrates the ideal method for moving a conscious patient toward the head of a bed. Fig. 3.10 shows the proper technique for assisting a patient to the bedside position for dangling his or her legs or transfer to a chair.

Ambulation

Ambulation (walking) helps maintain normal body function. Extended bed rest can cause numerous problems, including bed sores and atelectasis (low lung volumes). Ambulation should begin as soon as the patient is physiologically stable and free of severe pain. Ambulation has been shown to reduce the length of hospital stay and 30-day readmissions in hospitalized heart failure patients.[15] RTs may assist to ambulate patients while they

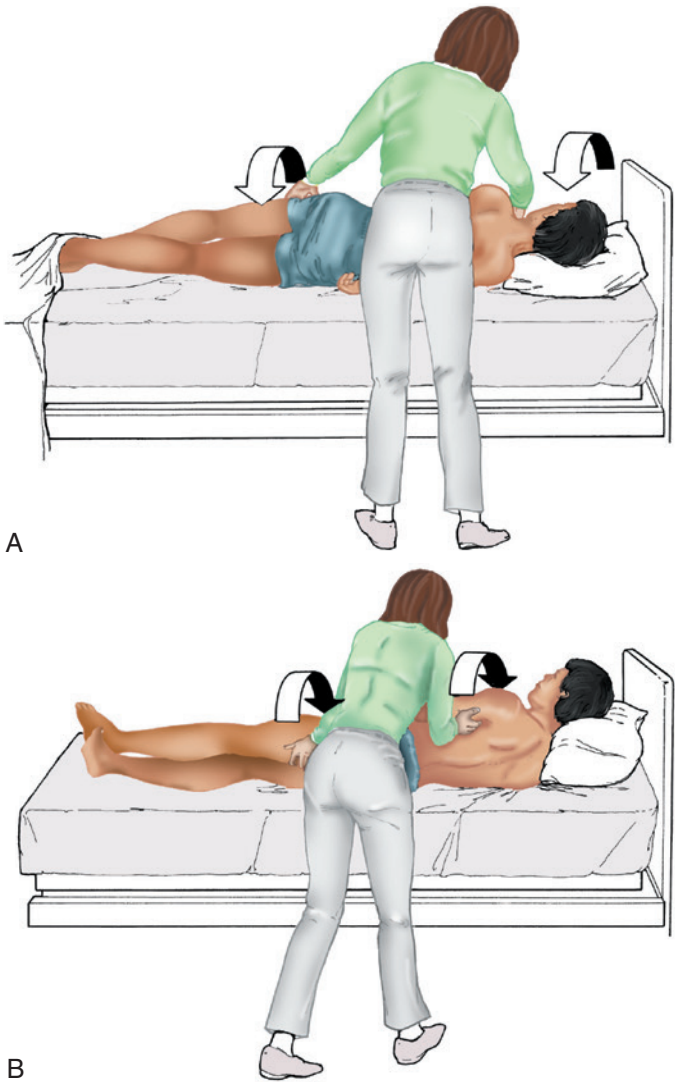


Fig. 3.8 (A) Method to pull a bed-bound patient. (B) Method to push a bed-bound patient.

Fig. 3.9 Method to move a patient up in bed with the patient's assistance.

are on a mechanical ventilator or while on O_2. Early ambulation in Intensive Care Units (ICUs) while on mechanical ventilation has been linked to shorter patient time on mechanical ventilation and is recommended by the American Thoracic Society/American College of Physicians (ATS/ACP).[16,17] Safe patient movement includes the following steps:

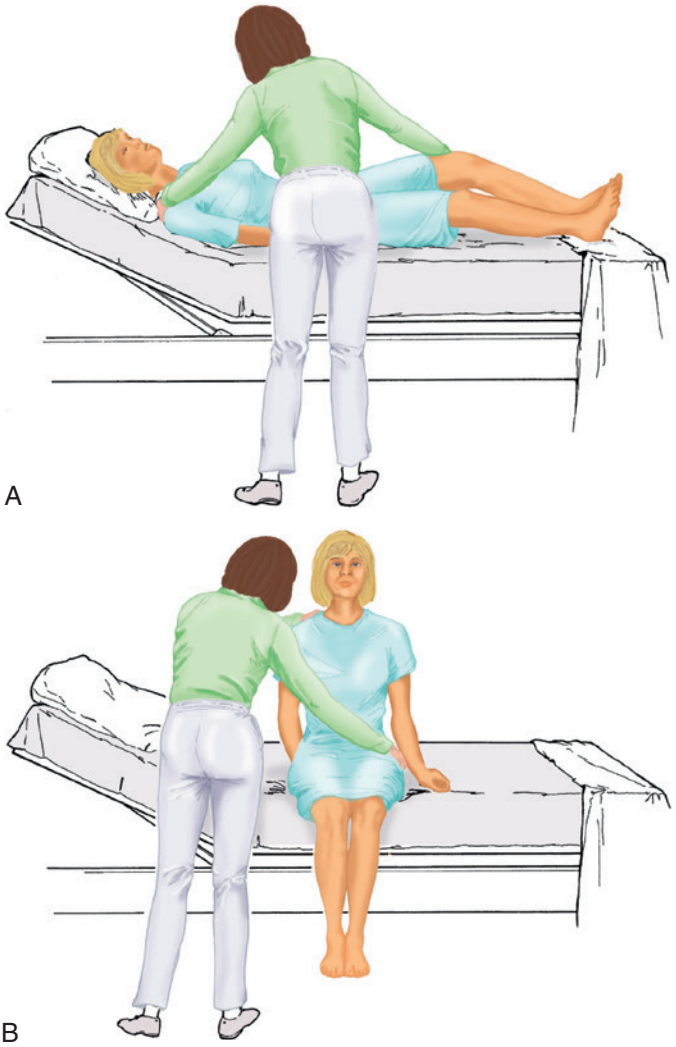


Fig. 3.10 Method to assist a patient in dangling the legs at the side of the bed.

1. Place the bed in a low position and lock its wheels.
2. Place all equipment (e.g., intravenous [IV] equipment, nasogastric tube, surgical drainage tubes) close to the patient to prevent dislodgment during ambulation.
3. Move the patient toward the nearest side of bed.
4. Assist the patient to sit up in bed (i.e., arm under nearest shoulder and one under farthest armpit).
5. Place one hand under the patient's farthest knee, and gradually rotate the patient so that his or her legs are dangling off the bed.
6. Let the patient remain in this position until dizziness or lightheadedness lessens (encouraging the patient to look forward rather than at the floor may help).
7. Assist the patient to a standing position.
8. Encourage the patient to breathe easily and unhurriedly during this initial change to a standing posture.
9. Walk with the patient using no, minimal, or moderate support (moderate support requires the assistance of two practitioners, one on each side of the patient).
10. Limit walking to 5 to 10 minutes for the first exercise.

Monitor the patient during ambulation. Note the patient's level of consciousness, color, breathing, strength or weakness, and complaints such as pain or shortness of breath throughout the activity. Ask the patient about his or her comfort level frequently during the ambulation period. Ensure that chairs are present so emergency seats are available if the patient becomes distressed. Ambulation is increased gradually until the patient is ready to be discharged. Each ambulation session is documented in the patient chart and includes the date and time of ambulation, length of ambulation, and degree of patient tolerance.

Electrical Safety

The potential for accidental shocks of patients or personnel in the hospital exists because of the frequent use of electrical equipment. The presence of invasive devices, such as internal catheters and pacemakers, may add to the risk for serious harm from electrical shock. Although this risk is present, it has been significantly reduced in recent years through a combination of education and more rigid standards for wiring, especially in patient care areas. RTs must understand the fundamentals of electrical safety because respiratory care often involves the use of electrical devices.

Fundamentals of Electricity

Understanding the fundamentals of electricity will enable RTs to create a safe environment for both patients and caregivers.

Electricity moves from point *A* to point *B* because of differences in voltage. **Voltage** is the power potential behind the electrical energy. Low-voltage batteries (e.g., 9 Volt) are sufficient to power a small flashlight but inadequate to power a major appliance such as a microwave oven. Most homes and hospitals are powered with 120-Volt power sources. Power sources that have high voltage have the potential to generate large amounts of electrical current. The current that moves through an object is directly related to the voltage difference between point *A* and point *B* and inversely related to the resistance offered by the makeup of the object. Objects with low resistance (e.g., copper

MINI CLINI

"Tingling" Equipment

Problem

An RT is caring for a patient on a mechanical ventilator that requires both electrical and pneumatic power for operation. When the RT touches the metal housing of the ventilator, a shock is felt. How should the RT handle the situation based on this observation?

Discussion

All therapeutic instruments used in patient care, including mechanical ventilators, should be connected to grounded outlets (three-wire). Because the ground wire is a protection device only and not part of the main circuit, equipment may continue to operate without the clinician being aware that a problem exists. Because the RT felt a tingling sensation when touching the ventilator, this could represent an improper ground and possible serious current leakage. In this situation the RT should immediately take the equipment out of service and get it replaced (while providing backup ventilation). All electrical equipment used in patient care should be routinely checked for appropriate grounding.

wires) allow maximum current to flow through the object. Objects with high resistance (e.g., rubber tubing) allow minimal or no current to flow through the object despite higher levels of voltage.

The simple analogy of water flowing through a piping system is useful to understand electricity. The water pressure level at the source is equivalent to the voltage. Higher water pressure provides the potential for greater water flow or current. The friction (**resistance**) offered by the pipe across the length of the pipe influences the flow exiting the other end. Pipes with lots of friction reduce the water flow (current) greatly. If the friction (resistance) is minimal, the water flow (current) is maximal. Similarly, when voltage is high and resistance is low, electrical current flows easily through the object.

The difference in resistance between two people or two objects explains why the same voltage applied to both can seriously damage one and cause no effect to the other. Two people accidentally touching a "hot" wire with 120 V can experience two completely different sensations. A person with wet skin offers little resistance, and the 120 V passes through the person with high current and can cause serious injury or death. A person with dry skin, which offers high resistance, may not even feel a shock and experiences no injury. The degree of resistance offered by the skin varies from person to person based on the chemistry of the person's skin, the cleanliness of the skin, and the amount of moisture on the surface. For this reason, it is never wise to touch a potentially hot wire even though your skin is dry.

As stated before, voltage is the energy potential from an electrical source, and it is measured with a voltmeter. **Current** is the flow of electricity from a point of higher voltage to one of lower voltage and is reported in **amperes** (amps). Current is measured with an ampmeter. The resistance to electrical current is reported in **ohms**. We can determine the resistance to current for any object by the following equation:

$$\text{Resistance (ohms [}\Omega\text{])} = \text{Voltage (V)/Current (amps [A])}$$

Current represents the greatest danger to you or your patients when electrical shorts occur. Voltage and resistance are important only because they determine how much current potentially can pass through the body. High voltage provides greater potential for high currents, but if resistance is also very high, current would be minimal or nonexistent. Current represents the potential danger to the patient. The harmful effects of current depend on: (1) the amount of current flowing through the body, (2) the path it takes, and (3) the duration the current is applied. Higher currents (>100 milliamps [mA]) that pass through the chest can cause ventricular fibrillation, diaphragm dysfunction (owing to severe, persistent contraction), and death.

Because current is most important, you should be familiar with the equation used to calculate it:

$$\text{Current (A)} = \text{Voltage (V)/Resistance } (\Omega)$$

For example, as long as a person is insulated by normal clothing and shoes and is in a dry environment, a 120 V shock may hardly be felt because the resistance is high in this situation (10,000 Ω). Current can be calculated as:

$$\text{Current (A)} = 120\ \text{V}/10{,}000\ \Omega = 0.012\ \text{A or } 12\ \text{mA}$$

Currents of 12 mA would cause a tingling sensation but no physical damage.

However, if the same person is standing without shoes on a wet floor, a much higher current occurs because the resistance is much lower (1000 Ω). The current is then calculated as:

$$\text{Current (A)} = 120\ \text{V}/1000\ \Omega = 0.12\ \text{A or } 120\ \text{mA}$$

Because the heart is susceptible to any current level greater than 100 mA, 120 mA represents a potentially fatal shock; this is in sharp contrast to the first example, in which the same voltage caused only a tingling sensation.

A shock hazard exists only if the electrical "circuit" through the body is complete, meaning that two electrical connections to the body are required for a shock to occur. In the previous example, the person standing in water with no shoes has "grounded" himself. The finger touching the hot wire provides the input source while the feet standing in water provide the exit to ground. If the same person is wearing rubber boots, the connection to ground does not exist and the current cannot flow through the individual.

In electrical devices, these two connections typically consist of a "hot" wire and a "neutral" wire. The neutral wire completes the circuit by taking the electrical current to a ground. A **ground** is simply a low-resistance pathway to a point of zero voltage, such as the earth (hence the term *ground*).

Fig. 3.11 shows how current can flow through the body. In this case a piece of electrical equipment is connected to an AC

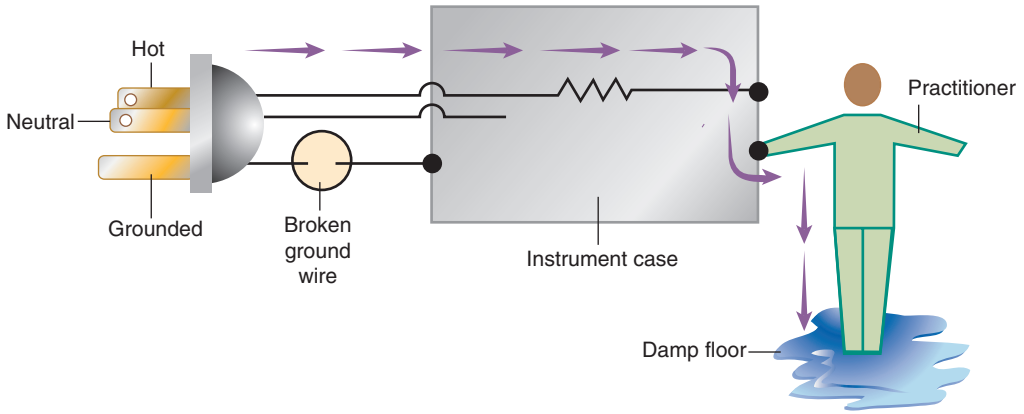


Fig. 3.11 Hazard created by broken ground wire.

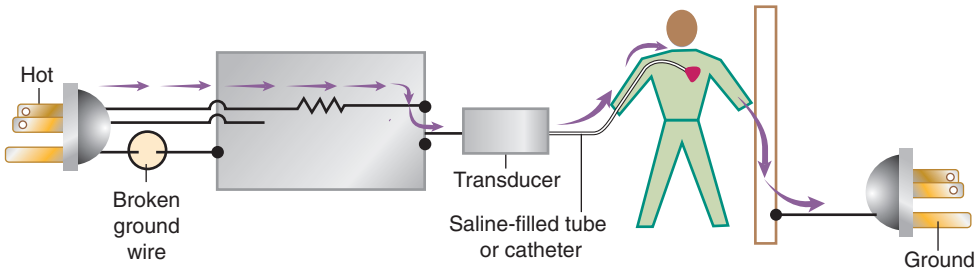


Fig. 3.12 Possible microshock hazard caused by patient grounding.

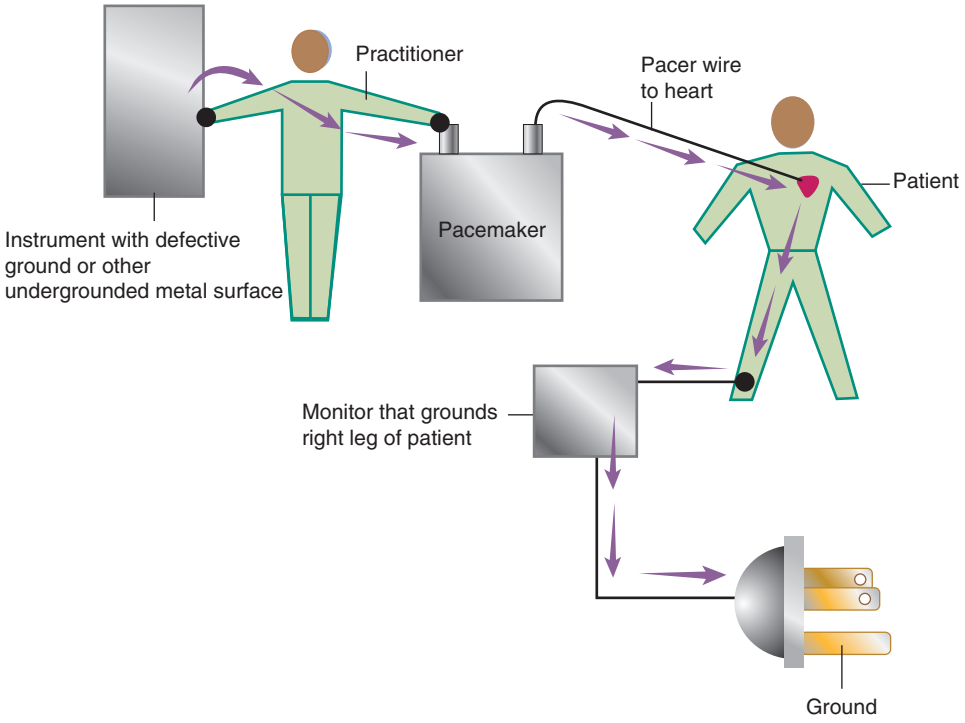


Fig. 3.13 Possible hazard through use of certain cardiac monitors and a pacemaker.

line power via a standard three-prong plug. However, unknown to the practitioner, the cord has a broken ground wire. Normally, current leakage from the equipment would flow back to the ground through the ground wire. However, this pathway is unavailable. Instead, the leakage current finds a path of low resistance through the practitioner to the damp floor (an ideal ground).

Current can readily flow into the body, causing damage to vital organs when the skin is bypassed via conductors such as pacemaker wires or saline-filled intravascular catheters (Figs. 3.12 and 3.13). Even urinary catheters can provide a path for current flow. The heart is particularly sensitive to electrical shock. Ventricular fibrillation can occur when currents of 20 μA (20 microamperes, or 20 millionths of 1 ampere) are applied directly to the heart.

Electrical shocks are classified into two types: macroshock and microshock. A **macroshock** exists when a high current (usually >1 mA) is applied externally to the skin. A **microshock** exists when a small, usually imperceptible current (<1 mA) bypasses the skin and follows a direct, low-resistance path into the body. Patients susceptible to microshock hazards are termed *electrically sensitive* or *electrically susceptible*. Table 3.1 summarizes the different effects of these two types of electrical shock.

Preventing Shock Hazards

Most shock hazards are caused by inappropriate or inadequate grounding. Shock hazards can be eliminated or minimized if wiring in patient care areas is appropriate and if all equipment brought into the patient care area has been Underwriters Laboratories (UL) approved and checked on a regular basis by a qualified person.

Ground Electrical Equipment Near the Patient

All electrical equipment (e.g., lights, electrical beds, ventilators, monitoring or therapeutic equipment) should be connected to grounded outlets with three-wire cords. In these cases the third (ground) wire prevents the dangerous buildup of voltage that can occur on the metal frames of some electrical equipment.

Electrical devices used in hospitals are designed so their frames are grounded, but their connections to the patient are not. In this manner, all electrical devices in reach of the patient are grounded, but the patient remains isolated from ground. Because

TABLE 3.1 Effects of Electrical Shock

Amperes (A)	Milliamperes (mA)	Microamperes (μA)	Effects
Applied to Skin (Macroshock)			
≥6	>6000	>6,000,000	Sustained myocardial contraction followed by normal rhythm; temporary respiratory paralysis; burns, if small area of contact
0.1–3	100–3000	100,000	Ventricular fibrillation; respiratory center intact
0.050	50	50,000	Pain; fainting; exhaustion; mechanical injury; heart and respiratory function intact
0.016	16	16,000	"Let go" current; muscle contraction
0.001	1	1,000	Threshold of perception; tingling
Applied to Myocardium (Microshock)			
0.001	0.1	100	Ventricular fibrillation

Duration of exposure and current pathway are major determinants of human response to electrical shock.
Physiologic effects of AC shocks applied for 1 second to the trunk or directly to the myocardium.

the ground wire is simply a protection device and not part of the main circuit, equipment continues to operate normally even if the ground wire is broken. All electrical equipment must be checked for appropriate grounding on a regular basis by a qualified electrical expert. Patients may wish to use their own continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BiPAP) in the hospital setting. It is important to know your hospital's policy regarding the use of this equipment. If allowed, this equipment should first be checked by the hospital's qualified electrical expert.

Life support devices should be connected to outlets that may function in case of a power failure. These outlets may be denoted by being "red" in color.

Fire Hazards

In 1980, approximately 12,000 healthcare facility fires were officially reported in the United States.[18] During the period of 2011 to 2015, the average annual number of fires in healthcare facilities was 5750.[18] These healthcare facilities include hospitals, hospice facilities, nursing homes, mental health facilities, and doctors' offices or clinics. This significant reduction in healthcare facility fires is primarily due to education and enforcement of strict fire codes.

Hospital fires can be very serious, especially when they occur in patient care areas and when supplemental O_2 is in use. Fires in O_2-enriched atmospheres (OEAs) are larger, more intense, faster burning, and more difficult to extinguish. In addition, some material that would not burn in room air would burn in O_2-enriched air. Hospital fires are also more serious because evacuation of critically ill patients is difficult and slow. For these reasons, hospital fires often cause more injuries and deaths per fire than do residential fires. For a fire to start, three conditions must exist: (1) flammable material must be present, (2) O_2 must be present, and (3) the flammable material must be heated to or above its ignition temperature. When all three conditions are present, a fire starts. Conversely, removing any one of the conditions can stop a fire from starting or extinguish it after it has begun. Fire is a serious hazard around respiratory care patients using supplemental O_2. Although O_2 is nonflammable, it greatly accelerates the rate of combustion. Burning speed increases with an increase in either the concentration or the partial pressure of O_2.

Flammable material should be removed from the vicinity of O_2 use to minimize fire hazards. Flammable materials include cotton, wool, polyester fabrics, bed clothing, paper materials, plastics, and certain lotions or salves such as petroleum jelly. Removal of flammable material is particularly important whenever O_2 enclosures, such as O_2 tents or croupettes, are used. Hyperbaric oxygen chambers are another potential hazard because they supply high concentration of O_2 in a pressurized enclosed environment. These chambers are designed with internal fire suppressants, but steps should be taken to reduce all flammable material.

Ignition sources, such as cigarette lighters, should not be allowed in rooms where O_2 is in use. In addition, the use of electrical equipment capable of generating high-energy sparks, such as exposed switches, must be avoided. All appliances that transmit house current should be kept out of O_2 enclosures. Children should not play with toys that may create a spark when O_2 is in use. RTs must be diligent in educating patients and visitors about the dangers associated with spark-producing items, open flames, and burning cigarettes in the hospital environment, especially in areas with O_2-enriched air.

A frequent source of concern is the presence of static electrical sparks generated by friction. Even in the presence of high O_2 concentrations, the overall hazard from static sparks with the materials in common use is very low. Solitary static sparks generally do not have sufficient heat energy to raise common materials to their flash points. The minimal risk that may be present can be reduced further by maintaining high relative humidity (>60%).

If you identify a fire in a patient care area, you must know what to do. Each hospital must have a core fire plan that identifies the responsibilities of hospital personnel. The plan should be taught to all hospital personnel and practiced with fire drills to reinforce the education. Requirements may include routinely walking the fire exits and reviewing proper fire extinguisher training. Fire extinguisher training includes following the acronym **PASS**:

*P*ull the pin. There may be an inspection tag attached.
*A*im the nozzle. Aim low at the bottom of the fire.
*S*queeze the handle. The extinguisher has less than 30 seconds of spray time.
*S*weep the nozzle across the base of the fire.

The core fire plan follows the acronym **RACE***:*

*R*escue patients in the immediate area of the fire. The person discovering the fire should perform the rescue.

*A*lert other personnel about the fire so they can assist in the rescue and can relay the location of the fire to officials. This step also involves pulling the fire alarm.

*C*ontain the fire. After rescuing patients, shut doors to prevent the spread of the fire and the smoke. In patient care areas, follow your hospital policy regarding turning off O_2 zone valves.

*E*vacuate other patients and personnel in the areas around the fire who may be in danger if the fire spreads.

RTs are frequently key participants in successful handling of hospital fires. First, they know where the O_2 zone valves are located and how to shut them off. Second, they have the knowledge and skills needed to evacuate patients receiving mechanical ventilation or supplemental O_2 to sustain life. Third, they know how to treat and resuscitate victims of smoke inhalation. For these reasons, RTs should be included in all hospital evacuation planning and practices.

General Safety Concerns

In addition to electrical and fire safety, RTs need to be aware of general safety concerns, including the direct patient environment, disaster preparedness, magnetic resonance imaging (MRI) safety, and medical gas safety. Medical gas safety is discussed in more detail in Chapter 41.

Direct Patient Environment

The immediate environment around the patient can create risk for patient safety. Because RTs use medical equipment and participate in direct patient care, it is necessary for RTs to be cognizant of the patient's immediate environment.

To reduce the risk for patient falls and allow easy access to care, the patient care environment should be as free of impediments to care as possible. Use of respiratory supplies and medical equipment by the RT creates an environment that could impede access to care and create a fall risk. It is the responsibility of the RT to position equipment, tubing, and treatments in a way that does not impede access to care and that reduces risk for falls. In addition, when care is completed, the RT should ensure that the patient has easy access to the patient call system.

Magnetic Resonance Imaging Safety

MRI exposes the body to powerful magnetic fields and a small amount of radiofrequency. This powerful magnetic field can create a risk to patients, healthcare workers, and equipment if metal objects containing ferrous-based material, stainless steel or nickel alloys are brought within specified proximity to the field. There are safe proximity areas referred to as *safety zones* or *Gauss lines*. Metal objects can be so forcefully attracted to the magnet of the MRI that they can mimic a missile, causing physical harm. Reports of accidents associated with MRI have involved O_2 cylinders, stethoscopes, scissors, and IV poles. Deaths have been described when O_2 cylinders were pulled into the magnetic area where a patient was lying to undergo an MRI examination. RTs need to become familiar with MRI-compatible ventilators, O_2 supplies, and ancillary equipment. Each radiology department has specific rules and safety precautions that need to be communicated to all patients, caregivers, and healthcare personnel.

Medical Gas Cylinders

Use of compressed gas cylinders by RTs requires special handling. The physical hazards resulting from improper storage or handling of cylinders include increased risk for fire, explosive release of high-pressure cylinders, and the toxic effect of some gases. It is important to store and transport cylinders in appropriate racks or chained containers. Compressed gas cylinders should never be stored without support. Additional information regarding the storage and delivery of medical gases can be found in Chapter 41.

COMMUNICATION

Because the delivery of safe, high-quality healthcare requires interactions among many contributors from different disciplines (e.g., physicians, RTs, nurses), communication is essential to the quality mission of a healthcare organization. Strategies to enhance communication are critical to organizational success.

Communication is a dynamic human process involving sharing of information, meanings, and rules. Communication has five basic components: sender, message, channel, receiver, and feedback (Fig. 3.14).

The sender is the individual or group who transmits the message. The message is the information or attitude that is

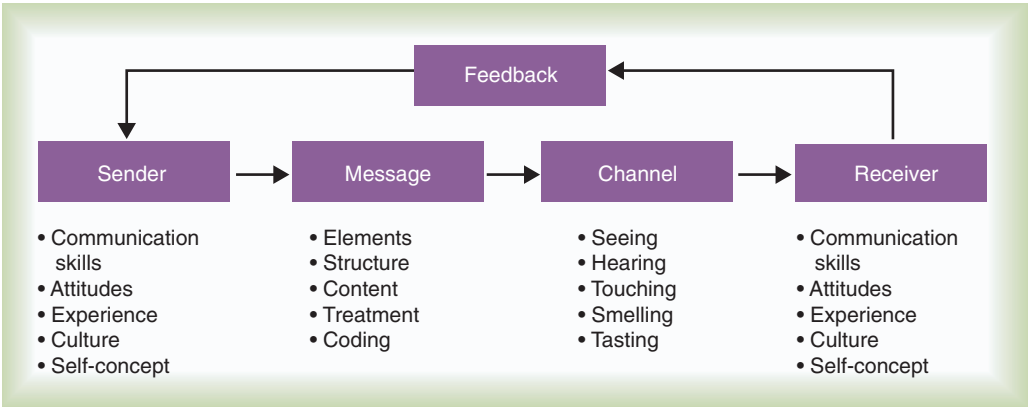


Fig. 3.14 Elements of human communication.

communicated by the sender. Messages may be verbal or nonverbal. Verbal messages are voiced or written. Examples of different kinds of messages are lectures, letters, text messages, and e-mail memos. Nonverbal communication is any communication that is not voiced or written. Nonverbal communication includes gestures, facial expressions, eye movements and contact, voice tone, space, and touch.

The **channel** of communication is the method used to transmit messages. The most common channels involve sight and hearing, such as written and oral messages. However, other sensory input, such as touch, may be used with visual or **auditory** communication. In addition, communication channels may be formal (memos or letters) or informal (conversation).

The receiver is the target of the communication and can be an individual or a group. One-on-one communication is often more effective because both parties can respond to each other. Communication with a group can be more challenging but is a more efficient way to get information to numerous individuals.

The last essential part of communication is **feedback**. Human communication is a two-way process in which the receiver serves an active role. Feedback from the receiver allows the sender to measure communication success and provide additional information when needed.

Communication in Healthcare

Effective communication is the most important aspect of providing safe patient care. The first two 2018 National Patient Safety Goals of TJC are to improve accuracy of patient identification and effectiveness of communicating critical test values among caregivers.[19] All healthcare personnel must correctly identify patients before initiating care using a two–patient identifier system. The patient identifiers can include any two of the following: name, birth date, and medical record number. Effectively communicating critical test values should include a "read back" scenario verifying the reporter and the receiver of the information and accurate reporting and recording of test values. Each institution may have specific values as critical test values; for example, RTs may be expected to report blood gas values of a pH less than 7.20 or a PaO_2 less than 50 mm Hg. The process of the read back scenario is described in Box 3.4.

BOX 3.4 "Read Back" Process to Ensure Accurate Communication of Information

Prescriber/Reporter

- Orders or critical test results are read and clearly enunciated, using two patient identifiers.
- Avoid abbreviations.
- Ask receiver to "read back" the information if this is not done voluntarily.
- Verify with the receiver that the information is correct.

Receiver

- Record the order or value.
- Ask "prescriber/reporter" to repeat if information is not understood.
- "Read back" the information, including two patient identifiers.
- Receive confirmation from the "prescriber/reporter" that the information is correct; if incorrect, repeat the process.

Another setting for improving communication between RTs regards transitions of care or "hand-off" of care; that is, when one RT is telling a colleague about the care of a patient who will be passed to the incoming RT for care. An effective communication tool in this instance may be an SBAR (*S*ituation, *B*ackground, *A*ssessment, and *R*ecommendation).[20] An example of this would be an RT discussing a patient's intolerance to noninvasive ventilation. The *situation (S)* is that the patient was admitted to the intensive care and prescribed noninvasive ventilation but is not tolerating the device. The *background (B)* is that the patient has COPD and was admitted with a high $PaCO_2$ and would benefit from the noninvasive ventilation. The *assessment (A)* is the patient feels "claustrophobic" in the current full-face mask. Finally, the *recommendation (R)* would be to try a smaller, less-confining mask to improve patient comfort.

A second transition of care communication tool is known as I-PASS, which stands for *I*llness severity, *P*atient summary, *A*ction list, *S*ituation awareness and contingency plans and *S*ynthesis by receiver.[21] Considering the same situation as the previous paragraph, the *illness severity (I)* is severe and the *patient summary (P)* is the patient has COPD and was admitted with a high $PaCO_2$. The *action list (A)* is to try to stabilize the patient with noninvasive ventilation. The *situation (S) awareness and contingency plan* are that the patient is not tolerating the noninvasive ventilation and feels claustrophobic. The RT forming the contingency plan of trying a smaller, less-confining mask. Finally, the *synthesis by the receiver (S)* is that during the "hand off" the next shift RT would summarize what has been discussed, ask questions, and restate the actions to take place and attempt to use a smaller more comfortable noninvasive ventilation mask.

As an RT, you will have many opportunities to communicate with patients, other RTs, nurses, physicians, and other members of the healthcare team. Success as an RT depends on your ability to communicate with these key people. Poor communication skills can limit your ability to treat patients, work well with others, and find satisfaction in your employment.

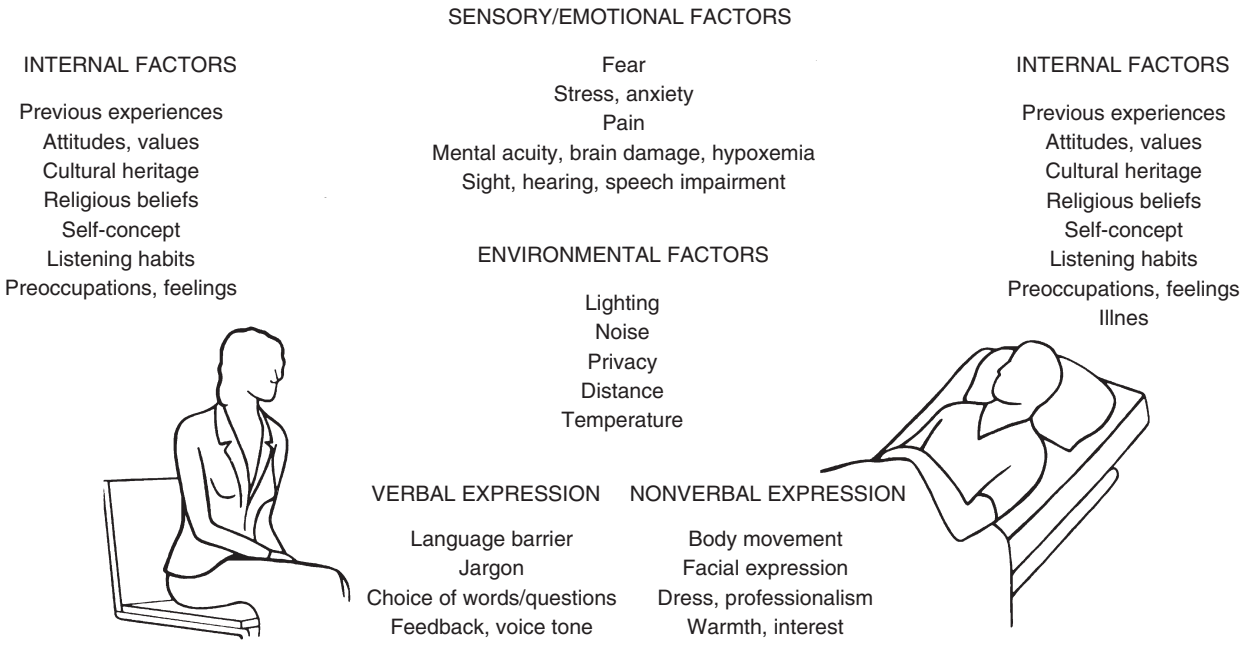
Factors Affecting Communication

Many factors affect communication in the healthcare setting (Fig. 3.15). The uniquely human or "internal" qualities of sender and receiver (including their prior experiences, attitudes, values, cultural backgrounds, and self-concepts and feelings) play a large role in the communication process.

In general, the verbal and nonverbal components of communication should enhance and reinforce each other. Other factors that can affect communication include the patient's direct healthcare environment and their sensory or emotional state. The RT who considers all of these factors will become a better communicator. One example of this is the RT who combines a compassionate-toned verbal message such as, "You're going to be all right now," with a confirming touch of the hand. This communication is sending a much stronger message to an anxious patient than the message provided by either component alone. Several key purposes of communication are summarized in Box 3.5.

Improving Communication Skills

To enhance your ability to communicate effectively, focus on improving sending, receiving, and feedback skills. In



Fig, 3.15 Factors Influencing Communication. (Modified from Wilkins RL, Sheldon RL, Krider SJ: *Clinical assessment in respiratory care*, 6th ed., St. Louis, 2010, Mosby.)

BOX 3.5 Purposes of Communication in the Healthcare Setting

- To establish rapport with another individual, such as a colleague, a patient, or a member of the patient's family
- To comfort an anxious patient by explaining the unknown
- To obtain information, such as during a patient interview
- To relay pertinent information, as when charting the results of a patient's treatment
- To give instructions, as when teaching a patient how to perform a lung function test
- To persuade others to take action, as when attempting to convince a patient to quit smoking
- To educate and confirm understanding as in a "teach back" scenario

addition, identify and overcome common barriers to effective communication.

Practitioner as Sender

Your effectiveness as a sender of messages can be improved in several ways. These suggestions may be applied to the clinical setting as follows:

- *Share information rather than telling.* Health professionals often provide information in an authoritative manner by telling colleagues or patients what to do or say. This approach can cause defensiveness and lead to uncooperative behavior. Conversely, sharing information creates an atmosphere of cooperation and trust.
- *Seek to relate to people rather than control them.* This is of particular significance during communication with patients. Healthcare professionals often attempt to control patients. Few people like to be controlled. Patients feel much more important if they are treated as an equal partner in the

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Patient Communication

Problem

A 73-year-old man with COPD is admitted to the emergency department for acute shortness of breath that is not relieved with rest. The patient has been admitted more than eight times during the past year for various respiratory problems. The patient's physician thinks that this episode may reflect a worsening of his disease process and orders an inhaled bronchodilator via an MDI. After the RT enters the room and introduces herself, the patient becomes quite defensive, stating that he does not need any assistance with treatments and that she should just leave the medication in the room. The RT has not treated the patient in the past and has to decide how to respond to the patient's request.

Discussion

Although this patient exhibited reluctance in allowing the RT to administer the therapy, enough verbal and perhaps nonverbal communication (message) was expressed by the patient (sender) for the RT (receiver) to determine a plan of action. Because human communication is a two-way process, the RT serves an active role for further messages and interaction. This is a key concept for RTs to master because it helps in identifying a patient's problems, evaluating progress, and recommending further respiratory care. The RT must recognize that when an individual verbalizes disagreement with a treatment order and exhibits defensive behavior, the RT must attempt to understand what the patient is saying and must not overreact. The RT could try to put the patient at ease by making eye contact, gesturing effectively, and maintaining a safe distance from the patient when talking. The RT should seek feedback from the patient to ensure that the message was understood as it was intended. In this situation, it may be appropriate for the RT to review and demonstrate MDI use, ask the patient to "teach back" proper inhaler use, and observe the patient self-administering the medication. This process (message) can be repeated until the patient can demonstrate proper technique. Allowing the patient to participate actively in medical care when possible may serve to help him maintain a sense of control over his disease process.

relationship. Explaining procedures to patients and asking their permission to proceed is a way to make them feel part of the decision-making regarding their care.

- *Value disagreement as much as agreement.* When individuals express disagreement, make an attempt to understand what they are saying and do not become defensive. Be prepared for disagreement and be open to the input of others.
- *Use effective nonverbal communication techniques.* The nonverbal communication that you use is just as important as what you say. Nonverbal techniques may include eye contact, effective gesturing, facial expressions, and voice tone. It is important that your nonverbal communication matches what you are saying. It is also important to be aware of cultural differences in nonverbal contact. Some cultures may view direct eye contact as inappropriate, whereas in the United States, most find it an effective communication tool.

Practitioner as Receiver and Listener

Receiver skills are just as important as sender skills. Messages sent are of no value unless they are received as intended. Active listening on the part of the receiver is required. Learning to listen requires a strong commitment and great effort. A few simple principles can help improve your listening skills, as follows:

- *Work at listening.* Listening is often a difficult process. It takes effort to hear what others are saying. Focus your attention on the speaker and on the message.
- *Stop talking.* Practice silent listening and avoid interrupting the speaker during an interaction. Interrupting the patient is a sure way to diminish effective communication.
- *Resist distractions.* It is easy to be distracted by surrounding noises and conversations. This is particularly true in a busy environment such as a hospital. When you are listening, try to tune out other distractions and give your full attention to the person who is speaking.
- *Keep your mind open; be objective.* Being open-minded is often difficult. All people have their own opinions that may influence what they hear. Try to be objective in your listening so that you treat everyone fairly.
- *Hear the speaker out completely before making an evaluation.* Listen to the complete communication, not just the first few words of the speaker. Often, listeners hear the first sentence and tune out the rest, assuming they know what is being said. It is important to listen to the entire message; otherwise, you may miss important information.
- *Maintain composure; control emotions.* Listen authentically to understand. Allowing emotions, such as anger or anxiety, to distort your understanding or drawing conclusions before a speaker completes his or her thoughts or arguments is a common error in listening that is best avoided.
- Active listening is a key component in healthcare communication. Part of active listening is paraphrasing, or repeating back to the patient what you understood the patient to say. This confirms to the patient that you were listening and also allows them to correct any errors you may have made in understanding. Active listening is very important to prevent losing information, which could jeopardize the care you are providing.

Providing Feedback

To enhance communication with others, effective feedback needs to be provided. Examples of effective feedback mechanisms in oral communication with patients include **attending**, paraphrasing, requesting clarification, perception checking, and reflecting feelings:

- *Attending*. Attending involves the use of gestures and posture that communicates one's attentiveness. Attending also involves confirming remarks, such as, "I see what you mean."
- *Paraphrasing*. Paraphrasing, or repeating the other's response in one's own words, is a technique that is useful in confirming that understanding is occurring between the parties involved in the interaction. Note that overuse of paraphrasing can be irritating.
- *Requesting clarification.* Requesting clarification begins admitting that you may have misunderstood, with the goal of better understanding through restating or using alternative examples or illustrations. Overuse of this technique can impair effective communication, especially if it is used in a condescending or patronizing manner. Requests for clarification should be used only when truly necessary and always should be nonjudgmental in nature.
- *Perception checking.* Perception checking involves confirming or disproving the more subtle components of a communication interaction, such as messages that are implied but not stated. For example, the RT might sense that a patient is unsure of the need for a treatment. In this case, the RT might check this perception by saying, "You don't seem to be sure that you need this treatment. Is that correct?" By verifying or disproving this perception, both the healthcare professional and the patient understand each other better.
- *Reflecting feelings.* Reflecting feelings involves the use of statements to determine better the emotions of the other party. Nonjudgmental statements, such as, "You seem to be anxious about (this situation)," provide the opportunity for patients to express and reflect on their emotions and can help them confirm or deny their true feelings.

Minimizing Barriers to Communication

There are many potential barriers to effective communication. A skillful communicator tries to identify and eliminate or minimize the influence of these barriers in all interactions. By minimizing the influence of these barriers, the sender can help ensure that the message will be received as intended. Key barriers to effective communication are the following:

- *Use of symbols or words that have different meanings.* Words and symbols (including nonverbal communication) can mean different things to different people. These differences in meaning derive from differences in the background or culture between the sender and receiver and the context of the communication. For example, RTs often use the letters COPD to refer to patients with COPD caused by long-term smoking. Patients may hear COPD used in reference to them and be confused about the meaning and interpret COPD to mean a fatal lung disease. Never assume that the patient has the same understanding as you do about interpreting commonly used symbols or phrases.

- *Different value systems.* Everyone has his or her own value system, and many people do not recognize the values held by others. A large difference among the values held by individuals can interfere with communication. A clinical supervisor may inform students of the penalties for being late with clinical assignments. If a student does not value timeliness, he or she may not take seriously what is being said.
- *Emphasis on status.* A hierarchy of positions and power exists in most healthcare organizations. If superiority is emphasized by individuals of higher status, communication can be stifled. Everyone has experienced interactions with professionals who make it clear who is in charge. Emphasis on status can be a barrier to communication not only among healthcare professionals but also between healthcare professionals and patients.
- *Conflict of interest.* Many people are affected by decisions made in healthcare organizations. If people are afraid that a decision will take away their advantage or "invade their territory," they may try to block communication. An example might be a staff member who is unwilling to share expertise with students. This person may unfortunately feel that a student is somehow a threat.

Lack of acceptance of differences in points of view, feelings, values, or purposes. Most of us are aware that people have different opinions, feelings, and values. These differences can interfere with effective communication. To overcome this barrier, an effective communicator allows others to express their differences. Encouraging individuals to communicate their feelings and points of view benefits everyone. Not uncommonly, people may think they are always correct. Accepting input from others promotes growth and cooperation.

Feelings of personal insecurity. It is difficult for people to admit feelings of inadequacy. Individuals who are insecure do not offer information for fear they appear ignorant or they may be defensive when criticized, blocking clear communication. To become an effective communicator, identify the purpose of each communication interaction and your role in it. Use specific sending, receiving, and feedback skills in each interaction. Finally, minimize any identified barriers to communication with patients or peers, to ensure that messages are received as intended.

CONFLICT AND CONFLICT RESOLUTION

Conflict is sharp disagreement or opposition among people over interests, ideas, or values. Because no two people are exactly alike in their backgrounds or attitudes, conflict can be found in every organization. Healthcare professionals may experience a great deal of conflict in their jobs. Rapid changes occurring in healthcare have made everyone's jobs more complex and often more stressful. Because conflict is inevitable, all healthcare professionals must be able to recognize its sources and help resolve or manage its effect on people and on the organization.

Sources of Conflict

The first step in conflict management is to identify its potential sources. The four primary sources of conflict in organizations are: (1) ineffective communication, (2) structural problems, (3) personal behavior, and (4) role conflict.

Ineffective Communication

Ineffective communication is the primary source of conflict in organizations. The previously discussed barriers to communication all are potential sources of conflict. If a supervisor is unwilling to accept different points of view for dealing with a difficult patient, an argument may occur. The importance of good communication cannot be overemphasized.

Structural Problems

The structure of the organization itself can increase the likelihood of conflict. Conflict tends to grow as the size of an organization increases. Conflict is also greater in organizations whose employees are given less control over their work and in organizations in which certain individuals or groups have excessive power. Structural sources of conflict are the most rigid and are often difficult to control.

Personal Behavior

Personal behavior factors are a major source of conflict in organizations. Different personalities, attitudes, and behavioral traits create the possibility of great disagreement among healthcare professionals and between healthcare professionals and patients.

Role Conflict

Role conflict is the experience of being pulled in several directions by individuals who have different expectations of a person's job functions. A clinical supervisor is often expected to function both as a staff member and as a student supervisor. Trying to fill both roles simultaneously can cause stress and create interpersonal conflict.

Conflict Resolution

Conflict resolution or management is the process by which people control and channel disagreements within an organization. The following are five basic styles of handling conflict:

1. Competing
2. Accommodating
3. Avoiding
4. Collaborating
5. Compromising

Competing

Competing is an assertive and uncooperative conflict resolution strategy. Competing is a power-oriented method of resolving conflict. A supervisor who uses rank or other forces to attempt to win is using the competing strategy. This strategy may be useful when an unpopular decision must be made or when one must stand up for his or her rights. However, because it often causes others to be quiet and feel inferior, competing should be used cautiously.

Accommodating

Accommodating is the opposite of competing. Accommodating is being unassertive and cooperative. When people accommodate others involved in conflict, they neglect their own needs to meet

the needs of the other party. Accommodation is a useful strategy when it is essential to maintain harmony in the environment. Accommodation is also appropriate when an issue is much more important to one party or the other in a dispute.

Avoiding

Avoiding is both an unassertive and an uncooperative conflict resolution strategy. In avoiding conflict, one or both parties decide not to pursue their concerns. Avoidance may be appropriate if there is no possibility of meeting one's goals. In addition, if one or both of the parties are hostile, avoidance may be a good strategy, at least initially. However, too much avoidance can leave important issues unattended or unresolved.

Collaborating

As a conflict resolution strategy, collaborating is the opposite of avoiding. Collaborating is both assertive and cooperative and often offers the best chance of reaching a mutually beneficial solution. In collaboration, the involved parties try to find mutually satisfying solutions to their conflict. Collaboration usually takes more time than other methods of conflict management and is harder when the involved parties harbor strong negative feelings about each other.

Compromising

Compromising is a middle-ground strategy that combines assertiveness and cooperation. People who compromise give up more than individuals who compete but give up less than individuals who accommodate. Compromise is best used when a quick resolution is needed that both parties can accept. However, because both parties often feel they are losing something with a compromise, compromise should not be used exclusively.

Deciding which type of conflict resolution strategy to use requires knowledge of the context, the specific underlying problem, and the desires of the involved parties.

SUMMARY CHECKLIST

- The quality of a service or product refers to the sum of its properties that serve to satisfy the needs of its consumer.
- Quality improvement is everyone's job.
- Statistical process control and run charts are tools that allow continuous monitoring of quality of service.
- Quality improvement projects involve different phases: Planning the project, implementing the project, analyzing the results, and changing course of action based on analysis.
- Competency is defined as having suitable or sufficient skills, knowledge, and experience for the purposes of the specific task.
- Annual competency checks need to be documented for skills and procedures that pose potential risk to patient safety.
- TJC is an independent, non-for-profit organization that strives to continuously improve quality and safety of healthcare services by setting high standards and evaluating healthcare organizations for adherence.
- TJC requires hospitals to have quality assurance plans and encourages performance improvement efforts.
- Hospital accreditation by TJC is based on satisfying specific standards established by professional and technical advisory committees.
- Good posture is needed when lifting patients or heavy equipment to avoid injury.
- Electrical current (flow) is the dangerous element of electricity. Current is directly related to voltage and inversely related to resistance.
- A microshock is a small, imperceptible current (<1 mA) that enters the body through external wires or catheters; microshocks can cause ventricular fibrillation.
- To avoid electrical hazards, always ground equipment and use only equipment that has been checked for proper wiring.
- Fires in healthcare facilities most often start in the kitchen, but when they occur in patient care areas, loss of life and serious injuries are possible.
- Maintain a safe and clutter-free direct patient care environment.
- Store and transport medical-grade gases in a safe and effective manner.
- Communication skills play a key role in the ability to identify a patient's problems, to evaluate the patient's progress, to make recommendations for respiratory care, and to achieve desired patient outcomes.
- SBAR and I-PASS are two effective communication tools that promote patient safety by improving communication between caregivers
- Individuals' prior experiences, attitudes, values, cultural backgrounds, self-concepts, and feelings play a large role in the communication process.
- To enhance communication ability, focus on improving sending, receiving, and feedback skills; in addition, be able to identify and overcome common barriers to effective communication.
- Choose the best strategy for handling conflict considering knowledge of the context, the specific underlying problem, and the desires of the involved parties.

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4

Principles of Infection Prevention and Control

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CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Define health care–associated infections and state how often they occur
- Describe why infection prevention is important in respiratory care
- Identify and describe the three elements that must be present for transmission of infection within a health care setting
- List the factors associated with an increased risk for hospital-acquired infection
- State the three major routes for transmission of human sources of pathogens in the health care environment
- Describe strategies to control the spread of infection in the hospital
- Describe how to select and apply chemical disinfectants for processing respiratory care equipment
- Describe equipment-handling procedures that help prevent the spread of pathogens
- Identify circumstances when special infection-control procedures are warranted
- State when to use personal protective equipment during patient care
- Describe surveillance with regard to infection control

CHAPTER OUTLINE

KEY TERMS

antiseptic
bactericidal
bacteriostatic
Centers for Disease Control and Prevention (CDC)
cohorting
contact precautions
disinfection
droplet nuclei
droplet precautions
fomites
health care–associated infection
Healthcare Infection Control Practices Advisory Committee
high-efficiency particulate air/aerosol filters
hospital-acquired infections
nosocomial
Occupational Safety and Health Administration
respiratory hygiene/cough etiquette
sporicidal
standard precautions
sterilization
surveillance
virucidal

Patients are at risk for developing infections during their hospital stay. A recent study estimated that 4% of hospitalized patients in the United States develop a health care–associated infection (HAI).[1] To help better understand preventive measures, infections can be categorized by where they originate. Those that develop outside the hospital are called *community onset*. Those that develop in the hospital are called *hospital-onset* or **nosocomial** infections. However, in the current era, patients can receive care in many different settings—the home, the hospital, a skilled nursing facility, or an outpatient treatment center. Patients who are at home but getting care in a nonhospital setting can develop community-onset infections that are related to health care and are not community acquired. The term **health care–associated infection** refers to infections that develop in a patient during the course of medical treatment. There are certain factors that predispose patients to HAIs, including illnesses and treatment regimens which may reduce the immune response to infection; in addition, the use of artificial airways and catheters, which bypass normal barriers to microbes, may play a role. HAIs can also be related to certain pathogens that are more likely to be resistant to one or more classes of antimicrobial agents. For example, *Pseudomonas aeruginosa* is a common cause of hospital-acquired pneumonia; however, it is not routinely seen as a cause of community-acquired disease.

Efforts to decrease **hospital-acquired infection** and HAIs are commonly organized and coordinated by a hospital's Infection Prevention (IP) program. IP programs are charged with reducing the risk for HAIs and thereby protecting patients, employees, and visitors. They do this by providing guidance to their organizations so that they can break the chain of events leading to HAIs. Guidance and prevention efforts are directed at overall organizational structure and systems ("This is what we do as an institution to prevent infection") and at the individual caregiver level ("This is what I do to prevent infection").

Protecting patients and health care professionals against HAIs requires strict adherence to IP procedures. These procedures aim to eliminate the sources of infectious agents, create barriers to their transmission, and monitor and evaluate the effectiveness of control. IP departments coordinate activities and provide guidance to their institutions. Decreasing the risk for HAIs is a major and ongoing responsibility of all health care workers, including respiratory therapists (RTs). To fulfill this responsibility, RTs must be able to select and consistently apply a full spectrum of daily competencies. This chapter provides the foundation needed to assume this important responsibility.

SPREAD OF INFECTION

Three elements must be present for transmission of infection within a health care setting: (1) a *source* (or reservoir) of pathogens, (2) a *route* of transmission for the pathogen, and (3) a *susceptible host* (Fig. 4.1).[2]

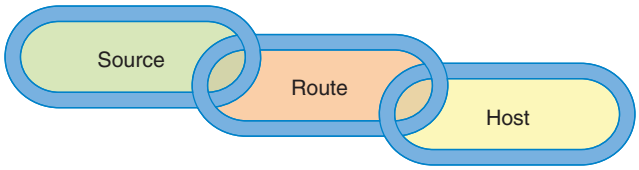

Fig. 4.1 Elements that must be present for infection to spread.

Sources of Infectious Agents

Humans (patients, personnel, or visitors) are the primary source of infectious agents in the health care setting, but inanimate objects (e.g., contaminated medical equipment, linen, medications) have also been implicated in transmission. Patients quickly contaminate their local hospital environment, particularly high-touch surfaces such as call lights, bed rails, tray tables, and bathrooms. People may also serve as their own sources of infection via endogenous flora.

Susceptible Hosts

Susceptibility and resistance to infection vary greatly. Host factors in the acute setting that predispose to HAI can be considered modifiable or nonmodifiable. For example, conditions such as poorly controlled diabetes mellitus, extremes of age, underlying HIV infection, or iatrogenic immunodeficiency (through chemotherapy or anti–tumor necrosis factor inhibitors) can enhance susceptibility to infection and are not readily modifiable in the acute setting. Surgical incisions and radiation therapy impair defenses of the skin and organ space. Medical devices—such as urinary tract catheters, central venous catheters, and endotracheal tubes—increase the risk for infection by interfering with local host defenses and providing a surface for the development of biofilms. The use of a medical device may be unavoidable. However, the risk for infection associated with it can be modified by employing appropriate techniques for its insertion, maintenance, and removal.

Modes of Transmission

The three major routes for transmission of human pathogens in the health care environment are *contact* (direct and indirect), *droplet*, and *airborne*. Table 4.1 provides examples of the common transmission routes for selected microorganisms.[3]

Contact Transmission

Contact transmission is the most common route of transmission and is divided into two subgroups: direct and indirect. *Direct contact transmission* occurs when a pathogen is transferred directly from one person to another. It occurs less frequently than indirect contact in the health care environment but is more efficient. An example of direct contact transmission would be development of respiratory syncytial virus bronchiolitis in a bone marrow transplant recipient owing to transmission of the virus from an ill health care worker who did not perform appropriate hand hygiene before providing care.

Indirect contact transmission is the most frequent mode of transmission in the health care environment and involves transfer of a pathogen through a contaminated intermediate object or person. The most common indirect contact transmission in health care involves unwashed hands of health care personnel that touch an infected or a colonized body site on one patient or a contaminated inanimate object and subsequently touch another patient. Inanimate objects that may serve to transfer pathogens from one person to another are called **fomites.** Indirect contact

TABLE 4.1 Routes of Infectious Disease Transmission

Mode	Type	Examples
Contact	Direct	Hepatitis A
		HIV
		Staphylococcus
		Enteric bacteria
	Indirect	*Pseudomonas aeruginosa*
		Enteric bacteria
		Hepatitis B and C
		HIV
Droplet		*Haemophilus influenzae* (type B) pneumonia and epiglottitis
		Neisseria meningitidis pneumonia
		Diphtheria
		Pertussis
		Streptococcal pneumonia
		Influenza
		Mumps
		Rubella
		Adenovirus
		Rhinovirus
Vehicle	Water-borne	Shigellosis
		Cholera
	Food-borne	Salmonellosis
		Hepatitis A
Airborne	Aerosols	Legionellosis
	Droplet nuclei	Tuberculosis
		Varicella
		Measles
		Smallpox
Vector borne	Ticks and mites	Rickettsia
		Lyme disease
	Mosquitoes	Malaria
	Fleas	Bubonic plague

HIV, Human immunodeficiency virus.

MINI CLINI

Direct Contact Transmission

Problem

For the past few weeks at work it seems as though everyone has had a cold. At the nurses' station there are many people with runny noses all taking their turns at the computer workstations. So far you have dodged the illness, but you worry that someone is going to give it to one of the patients.

Discussion

We should not expect that health care workers will never develop a "cold." Our professional responsibility, however, is to make sure we all do our best to limit the risk of transmitting infection to patients. Basic IP practice accounts for the reality of day-to-day occurrences. For example, appropriate hand hygiene practice includes disinfecting your hands before and after patient contact. Often the importance of hand hygiene before patient contact is underappreciated. Performing hand hygiene prior to touching the patient and his or her immediate environment recognizes the possibility of contaminated keyboards and common work area countertops and prevents transmission of common respiratory viruses to patients.

MINI CLINI

Indirect Contact Transmission

Problem

You are making rounds in the intensive care unit (ICU) with a coworker going from bed space to bed space checking ventilator settings. Your colleague enters a treatment zone without washing his hands, adjusts the ventilator, and prepares to move on to the next patient. He is stopped by the bedside nurse who points out his failure to follow to appropriate hand hygiene practice. Your colleague answers, "I only touched the ventilator. What's the big deal?"

Discussion

Each patient and her or his secretions and excretions are colonized with bacteria. These bacteria promptly inhabit the patient's local environment, including bed rails, bedside tables, chairs, and medical equipment in the near vicinity. Basically, touching the inanimate objects in a patient's room or treatment zone is the same thing as touching the patient. Failure to clean one's hands or appropriately disinfect medical equipment that goes from patient to patient poses a risk of indirect contact transmission. In the previous example, bacteria colonizing a patient's airway would probably also be found on the surfaces of the ventilator. Touching the ventilator without performing appropriate hand hygiene turns the RT's hands into vehicles for pathogen transmission from one bed space to another.

transmission involving fomites can occur when instruments have been inadequately cleaned between patients before disinfection or sterilization.

Droplet Transmission

Droplet transmission is a form transmission via respiratory droplets. Organisms transmitted by respiratory droplets include influenza viruses and *Neisseria meningitidis*. Respiratory droplets are generated when an infected individual discharges large contaminated liquid droplets into the air by coughing, sneezing, or talking. Respiratory droplets are also generated during procedures such as suctioning, bronchoscopy, and cough induction. Transmission occurs when infectious droplets are propelled (usually ≤3 feet through the air) and deposited on another person's mouth or nose. However, experimental studies with smallpox and investigations of outbreaks of severe acute respiratory syndrome (SARS) suggest that droplets from infected patients are rarely able to reach a person 6 feet away.[4]

Airborne Transmission

Airborne transmission occurs via the spread of airborne **droplet nuclei.** These are small particles (≤5 μm in diameter) of evaporated droplets containing infectious microorganisms that can remain suspended in air for long periods and can travel further distances than droplets. Examples of pathogens transmitted via the airborne route include *Mycobacterium tuberculosis*, varicella-zoster virus (chickenpox), and rubeola virus (measles).[4]

Special air handling and ventilation/respiratory protection is required to help prevent airborne transmission, because microorganisms may remain suspended in air and be widely dispersed by air currents before contacting a susceptible host. In addition to airborne infection isolation (AII) rooms, personal respiratory protection with National Institute for Occupational Safety and Health (NIOSH)–approved N-95 or higher respirators is required

MINI CLINI

Droplet Versus Airborne Transmission

Problem

A child with fever and a rash is admitted to the hospital late in the afternoon. He had recently gone on a trip with his family to the Philippines. He continues to be fussy and unhappy. In hopes of improving his spirits, his parents take him down to the playroom for about an hour. There are several other young children in the room, but none comes and plays directly with him. Later that evening, the attending physician makes a diagnosis of measles and the child is moved to a negative air room. The next day the IP team is called and a list is generated of all patients who were in the playroom as the same time as the child.

Discussion

Certain pathogens such as *Mycobacterium tuberculosis*, varicella zoster (chickenpox virus), and rubeola (measles virus) are able to be aerosolized as respiratory droplet nuclei and to travel throughout a room. Not only do they travel, but these small particles remain viable and able to cause infection when inhaled, as their small size makes it easier for them to avoid host defenses in the lungs. Airborne transmission expands the concept of close contact from the 6-foot rule mentioned earlier and focuses on the concept of shared air space—that is, being in the same room as an infected individual for at least an hour. Droplets, on the other hand, which are generated with infections such as influenza and pertussis, are heavier and cannot travel the same distance under usual circumstances, making proximity to the infected individual the main risk.

to prevent airborne transmission.[3] A surgical mask is insufficient to prevent airborne transition.

Miscellaneous Types of Aerosol Transmission

The separation of organisms that are transmitted by aerosols into the categories of droplet and airborne is based on the usual manner in which disease is transmitted. In-depth investigations of outbreaks have demonstrated that the line between these two categories of transmission is sometimes blurry. In certain circumstances, such as during endotracheal intubation and aerosol-generating procedures, there is some evidence that organisms such as influenza and SARS can be transmitted via droplet nuclei. Similarly, norovirus, the most common cause of infectious diarrhea transmitted mainly by contact, can probably also be transmitted by swallowing aerosolized virus from vomitus. Based on these examples, aerosol transmission of droplet nuclei can be further refined as follows[3]:

- *Obligate transmission:* Under natural conditions, disease occurs after transmission of a microorganism only through airborne (droplet nuclei) aerosols. An example of a microorganism spread by obligate transmission is *Mycobacterium tuberculosis*.
- *Preferential transmission:* Natural infection results from transmission through multiple routes, but airborne transmission predominates. Measles is an example of a disease transmitted by preferential transmission.
- *Opportunistic transmission:* Microorganisms that cause disease through other routes—droplet or contact—but only under certain environmental conditions may be transmitted via airborne transmission. An example of such a disease is SARS, which may be transmitted via an aerosol plume originating from sewage. This occurred in the Amoy Gardens housing complex in the Kowloon section of Hong Kong in 2003.[4]

Awareness of these nuances of transmission informs health care workers to wear the appropriate personal protective equipment (PPE) depending on the clinical circumstances. For example, during a bronchoscopy for a patient infected with influenza, the possibility of opportunistic airborne transmission of the virus would lead one to consider wearing an N95 mask as opposed to a regular surgical mask.

Other Sources of Infection Not Involving Person-to-Person Transmission

Common vehicle transmission occurs via exposure to pathogens in contaminated food, water, or medications (e.g., heparin solution). Vector-borne transmission of infectious diseases from insects and rats and other vermin occurs but is of less significance in US health care facilities.

STRATEGIES FOR THE PREVENTION OF INFECTION

Creating a Safe Culture

From an organizational perspective, a crucial first step to decrease the risk for HAIs is the creation by leadership, at all levels, of a culture of safety in which there is a shared commitment to the safety of patients and health care workers. Creating a culture of safety is also the responsibility of each individual health care worker. It is important that each person is empowered and willing to speak up and "stop the line" if the person has a concern that a patient or employee is in an unsafe situation. The Agency for Healthcare Research and Quality, a part of the US Department of Health and Human Services, has developed multiple resources to help organizations improve patient safety. Among the various tools is the ICU-focused Comprehensive Unit-Based Safety Program (CUSP) as well as survey for employees to help an organization assess its culture. Integral to this approach is the concept of a just culture wherein health care workers can report errors and mistakes without fear of reprisal.

Organizations also support best practices for IP by ensuring that the bedside caregiver has the appropriate time, equipment, and training to provide the best possible care. Competent health care workers execute appropriate practice, such as attention to hand hygiene and adherence to IP bundles of care on a daily basis with every patient. Failure to perform these basics is a deviation from good practice and cannot be tolerated. The presence of appropriate systems to deliver care and a committed workforce consistently executing best practices are necessary for an organization to prevent infections reliably.[5]

Maintaining a Healthy Workforce

The day-to-day care of hospitalized patients relies on people. A sick health care worker not only has difficulty executing assignments but could also serve as a source of infection for vulnerable patients. There are multiple different components to maintaining a healthy workforce. The standard and transmission-based precautions described later not only prevent transmission of pathogens from patient to patient but also protect health care

workers. Other efforts employed to protect health care workers are employee immunization and chemoprophylaxis. Certain immunizations are required and others are recommended for health care personnel as well as medical, nursing and allied health students to decrease the risk for infection and the potential for transmission to patients and colleagues.[6] The **Occupational Safety and Health Administration** (OSHA) requires that employers offer hepatitis B vaccination. Vaccinations of health care workers in the absence of evidence of immunity against varicella, rubella, and measles should be strongly encouraged. In addition, health care personnel should receive the adult acellular pertussis vaccine, particularly those who care for young infants and children. Health care personnel without medical contraindications should receive an annual influenza vaccination.[6] The vaccination of health care workers for influenza is the single most effective way to prevent health care–associated influenza. A vaccinated population decreases the risk for presenteeism (health care workers being at work when sick). The importance of receiving an influenza vaccine is reflected in the recent requirement that health care facilities publicly report the vaccination rates of their employees, licensed independent practitioners, volunteers, and adult students.[7] To improve the adherence by health care workers to a vaccination program, many organizations have made adherence to such a program mandatory.

RULE OF THUMB A health care worker with a fever should not report for work. Health care workers who come to work with a potentially contagious disease put their patients and coworkers at risk for becoming ill.

Uncommonly, it is recommended that health care workers take antibiotics in addition to standard and transmission-based precautions and vaccination. Examples of these situations include postexposure prophylaxis after close contact with a patient with meningococcal meningitis or exposure to blood or body fluid of a patient with HIV. One specific situation in which vaccination and chemoprophylaxis are combined is exposure to a patient with *Bordetella pertussis* (whooping cough). Infants can develop severe complications from whooping cough, including death. If health care workers have had close contact with an active case of whooping cough and have contact with infants younger than 1 year of age or women in the third trimester of pregnancy, they should receive prophylaxis in addition to having their vaccination status updated.[3,6]

RULE OF THUMB All health care workers with patient contact should undergo immunization for hepatitis B and varicella (if not immune), pertussis booster, and annual influenza vaccination.

Eliminating the Source of Pathogens

It is impossible to eliminate all pathogens from any working environment. Nonetheless, standard IP procedures always include efforts to eliminate pathogens; therefore recommended practices for cleaning and disinfecting noncritical surfaces in patient care areas should be followed. Procedures designed to remove environmental pathogens fall into two major categories: *general sanitation measures* and *specialized equipment processing.*

General sanitation measures help keep the overall environment clean. General sanitation aims to reduce the number of pathogens to a safe level. This reduction is achieved through sanitary laundry management, food preparation, and housekeeping. Environmental control of the air (using specialized ventilation systems) and water complements these efforts.

The goal of specialized equipment processing is to decontaminate equipment capable of spreading infection. Equipment processing involves cleaning, disinfection, and sterilization (when necessary). Methods that kill bacteria are **bactericidal,** whereas methods and techniques that inhibit the growth of bacteria are **bacteriostatic.** Methods that destroy spores are **sporicidal,** and methods that destroy viruses are **virucidal.**

Interrupting Transmission

General sanitation measures and equipment processing have limits. To prevent the spread of infections between patients and to keep themselves healthy, health care personnel must take measures to stop infection. Best practices to limit the transmission of pathogens in the hospital have been put forth by the **Healthcare Infection Control Practices Advisory Committee** (HICPAC) and the **Centers for Disease Control and Prevention (CDC)**. These recommendations include standard precautions and transmission-based precautions.[3]

Standard Precautions

The term **standard precautions** refers to the simplest level of infection control based on the recognition that all blood, body fluids, secretions, and excretions (with the exception of sweat) may contain transmissible infectious agents. Standard precautions are intended to be applied to the care of all patients in all health care settings all the time. This is the primary strategy for the prevention of health care–associated transmission of infections among patients and health care personnel. To reduce the risk for infection, a health care worker should employ PPE, which refers to various barriers used alone or in combination to protect mucous membranes, skin, and clothing from contact with infectious agents. Gloves, gowns, masks, eye protection, and face shields should be used depending on the anticipated exposure.

The application of standard precautions by health care personnel during patient care depends on the nature of the interaction and the potential for blood, body fluids, or pathogen contact. For some patient care situations, only gloves are required. In other cases, gloves, gowns, and face shields may be required. Box 4.1 describes standard precautions, including hand hygiene; use of gloves, masks, and eye protection; equipment handling; and patient placement.

Hand Hygiene

The importance of hand hygiene to reduce the transmission of infectious agents cannot be overemphasized and is an essential element of standard precautions.[8] Hand hygiene includes handwashing with either plain or **antiseptic**-containing soap and water for at least 15 seconds or the use of alcohol-based products (gels, rinses, and foams). In the absence of visible soiling of hands, approved alcohol-based products are preferred over antimicrobial or plain soap and water because of their superior

BOX 4.1 Standard Precautions

Hand Hygiene
- Perform hand hygiene before and after patient contacts, immediately after removing gloves, and when otherwise indicated to avoid cross contamination.
- Perform hand hygiene after touching blood, body fluids, secretions, excretions, and contaminated items, even if wearing gloves.
- Perform hand hygiene between tasks and procedures on the same patient if cross contamination of different body sites is possible (e.g., tracheostomy care after assistance with a bedpan).
- Use an approved alcohol-based product for routine hand hygiene. If hands are visibly soiled, use soap and water.

Gloves
- Perform hand hygiene before and after removing gloves.
- Wear clean gloves when touching blood, body fluids, secretions, excretions, and contaminated items.
- Don clean gloves just before touching mucous membranes and non-intact skin.
- Change gloves between tasks and procedures on the same patient after contact with infectious material.
- Remove gloves promptly after use, before touching non-contaminated items and environmental surfaces, and before going to another patient.

Masks, Eye Protection, Face Shields
- Wear a mask and eye protection or a face shield to protect mucous membranes of the eyes, nose, and mouth during procedures and patient care activities that are likely to generate splashes or sprays of blood, body fluids, secretions, and excretions.

Gowns
- Wear a clean gown to protect skin and prevent soiling of clothing during procedures and patient care activities that are likely to generate splashes or sprays of blood, body fluids, secretions, or excretions.
- Remove a soiled gown as promptly as possible and perform hand hygiene to avoid transfer of microorganisms to other patients or environments.

Patient Care Equipment
- Handle used patient care equipment soiled with blood, body fluids, secretions, and excretions in a manner that prevents skin and mucous membrane exposures, contamination of clothing, and transfer of microorganisms to other patients and environments.
- Do not use reusable equipment to care for another patient unless it has been cleaned and reprocessed appropriately.
- Discard single-use items properly.

Occupational Health and Blood-Borne Pathogens
- Exercise extreme caution when handling needles, scalpels, and other sharp instruments or devices; when cleaning used instruments; and when disposing of used needles.
- Never recap used needles, handle them using both hands, or point toward any part of the body.
- Do not remove used needles from disposable syringes by hand, and do not bend, break, or otherwise manipulate used needles by hand.
- Place used disposable syringes and needles, scalpel blades, and other sharp items in appropriate puncture-resistant containers; place reusable syringes and needles in a puncture-resistant container for transport to the reprocessing area.
- Use mouthpieces, resuscitation bags, or other ventilation devices as an alternative to mouth-to-mouth resuscitation methods in areas where the need for resuscitation is predictable.

Patient Placement
- Place patients who contaminate the environment or who do not (or cannot be expected to) assist in maintaining appropriate hygiene or environmental control in a private room.
- If a private room is unavailable, consult with infection preventionist regarding patient placement.

microbicidal activity, reduced drying of skin, and convenience. It should be noted; however, that alcohol-based products are not effective against certain spore-forming microbes (discussed later in this chapter), including *Clostridium difficile*. In addition, the quality of performing hand hygiene can be affected by the type and length of fingernails and the wearing of jewelry. Artificial fingernails and extenders should not be worn by health care workers because of their association with infection.[8] Fig. 4.2 illustrates the proper technique for handwashing.

Gloves

Gloves protect both patients and health care workers. They protect patients from exposure to pathogens that may be carried on the hands of health care workers. Gloves protect caregivers from contamination when they are contacting blood, body fluids, secretions, excretions, mucous membranes, and nonintact skin of patients and when they are handling or touching visibly or potentially contaminated patient care equipment and environmental surfaces.[8]

Caregivers should wear sterile gloves whenever they are performing invasive procedures. A single pair of nonsterile disposable gloves (e.g., latex, nitrile) may be used for routine patient care.

MINI CLINI

When to Use Soap and Water Versus Alcohol-Based Hand Hygiene Products

Problem

A patient is admitted to the hospital and diagnosed with *C. difficile* infection. You have finished your interaction with the patient and are getting ready to leave the room. You reach for the alcohol-based hand disinfectant dispenser. The infectious disease physician who is in the room asks you to use soap and water instead. You ask her why.

Discussion

The introduction of alcohol-based hand sanitizers has helped hospitals to improve their hand hygiene compliance. They are effective, easy to use, generally easier on the skin, and convenient. However, alcohol is not effective against spore-forming bacteria. The most common spore-forming bacterium encountered in health care today is *C. difficile*. In order to remove spores from the hands, the mechanical action of soap and water is necessary. An alcohol-based product can be used for hand hygiene on entering the room, but soap and water should be used after contact with the patient and his or her environment.

Hand hygiene should always be performed before donning gloves. Gloves should be changed between each patient contact and after any direct contact with infectious material, even if a caregiver is in the middle of a procedure. After removing the gloves, caregivers always must clean their hands. Gloves may have small, invisible defects or may be torn during use. The hands can also be contaminated during removal of the gloves. For these reasons, the wearing of gloves should never be used as a substitute for hand hygiene.

Mouth, Nose, Eye, and Face Protection

Face protection is an important component of standard precautions because the mucous membranes of the eyes, nose, and mouth are particularly vulnerable to some types of pathogens. Masks protect mucosal surfaces against splashes or sprays, but they should not be confused with the particulate respirators recommended for protection from small particles (as described subsequently for airborne isolation [AI]). The wearing of masks, eye protection, and face shields in specified circumstances when exposures are likely to occur (e.g., in the bronchoscopy suite) is mandated by the OSHA Bloodborne Pathogen Standard.

Respiratory Protection

Respiratory protection (use of NIOSH-approved N-95 or higher level respirator) is intended for diseases (e.g., *M. tuberculosis*) that could be transmitted by the airborne route.[3] Health care

Fig. 4.2 Steps for handwashing. (A) Thorough wetting of hands. (B) Washing around wrist and forearm. (C) Scrubbing palm of hand. (D) Washing between digits on back of hand.

Continued

Fig. 4.2, cont'd (E) Washing around the cuticle. (F) Drying hands with clean towel. (G) Using towel to turn off faucet.

workers should be fit tested to ensure that they are wearing the appropriate respirator and can feel confident in their safety while caring for patients. If a health care worker cannot be fitted with an appropriate respirator, a powered air-purifying respirator should be made available for use. The term *respiratory protection* has a regulatory context that includes components of a program required by OSHA to protect workers. It requires (1) medical clearance to wear a respirator, (2) provision and use of appropriate NIOSH-approved fit-tested respirators, and (3) education in respirator use.

Gowns, Aprons, and Protective Apparel

Isolation gowns and other apparel (aprons, leg coverings, boots, or shoe covers) also provide barrier protection and can prevent the contamination of clothing and exposed body areas from blood and body fluid contact and transmissible pathogens (e.g., respiratory syncytial virus and *C. difficile*). Selection of protective apparel is dictated by the nature of the interaction of the health care worker with the patient, including the anticipated degree of body contact with infectious material.[3] In most instances, gowns are worn only if contact with blood and body fluids is likely. Clinical coats and jackets worn over clothing are not considered protective apparel. Isolation gowns should always be donned with gloves and other protective equipment as indicated. As with gloves and masks, a gown should be worn only once and then discarded. In most situations, aseptically clean, freshly laundered, or disposable gowns are satisfactory. In addition to the gowns and other apparel described in this section, RTs and other clinicians may be required to take additional precautions such as wearing hair coverings to enter certain restricted hospital settings such as an operating room or cardiac catheterization lab, as may be needed in responding to a *code blue*.

Cough Etiquette

The emergence of novel respiratory viruses such as SARS and Middle East respiratory syndrome (MERS) along with pandemic H1N1 influenza have reinforced the need for a strategy for preventing transmission of respiratory infections at the first point of contact within a health care setting (e.g., physician's office), termed **respiratory hygiene/cough etiquette.** This concept is a component of standard precautions.[3] The elements of respiratory hygiene/cough etiquette include (1) education of health

BOX 4.2 Contact Precautions (used *in addition to* standard precautions)

- Place the patient in a private room; if a private room is unavailable, cohorting is acceptable.
- Perform hand hygiene and don gown and gloves to enter room whether or not direct patient contact is anticipated. Wear clean gloves when entering the room.
- Remove gown and gloves before leaving the patient's environment and perform hand hygiene.
- After glove removal and hand hygiene, ensure that hands do not touch potentially contaminated environmental surfaces or items in the patient's room.
- Limit transport of the patient from the room to essential purposes only.
- When possible, dedicate the use of noncritical patient care equipment to a single patient or patient cohort.
- If use of common equipment or items cannot be avoided, ensure that it is adequately cleaned and disinfected before use on another patient.

BOX 4.3 Droplet Precautions (used *in addition to* standard precautions)

- Place the patient in a private room; if a private room is unavailable, cohorting is acceptable.
- Special air handling and ventilation are unnecessary, and the door may remain open.

Mask

- Perform hand hygiene and put on a surgical mask before entering the room.
- Remove mask before exiting the room and perform hand hygiene.
- Limit movement and transport of the patient from the room to essential purposes only.
- If transport or movement is necessary, minimize droplet transmission by having the patient wear a surgical mask.

MINI CLINI

Isolation Methods

Problem

A serious influenza outbreak occurs in a local long-term care facility. You are called to the emergency department (ED) because four of the sickest patients are being admitted together to your hospital for treatment. Currently no private rooms are available for these patients. Outline the key isolation methods you would apply to help prevent the spread of influenza in your institution.

Discussion

Influenza spreads via the droplet route. Both standard and droplet precautions must be applied for these patients. When these patients are being transported out of the ED, you must make sure that they are wearing surgical masks. Because private rooms are unavailable, these patients must be grouped or **cohorted** together. Cohorting should, if at all possible, be done only with patients known to have the same disease. If this is not feasible, the patients must be separated from other patients by at least 3 feet. Special air handling and ventilation are unnecessary, and the door may remain open. In addition to following standard precautions, all caregivers and visitors should wear surgical masks when within 3 feet of these patients (or entering the room). All remaining patients at the long-term care facility should be immunized with the flu vaccine (if this has not already been done) and be given antiviral prophylaxis.

care personnel, patients, and visitors; (2) posted signs in language appropriate to the population served with instructions for patients and accompanying family members or friends; (3) source control measures (covering the mouth and nose with a tissue when coughing or placing a surgical mask on a coughing person when possible); (4) hand hygiene after contact with respiratory secretions; and (5) spatial separation (≥3 feet from persons with respiratory infections in common waiting areas).

Transmission-Based Precautions

Transmission-based precautions are for patients who are known or suspected to be infected with pathogens that require additional control measures to prevent transmission. There are three categories of transmission-based precautions based on the primary route by which the pathogen is transmitted: contact precautions, droplet precautions, and AII (see earlier section titled "Modes of Transmission"). Whether used alone or in combination, these precautions are always used in addition to standard precautions.[3]

Contact precautions are intended to reduce the risk for transmission by direct or indirect contact with the patient or the patient's environment. Contact precautions require health care personnel and visitors to wear gowns and gloves for all interactions that may involve contact with the patient or the patient's environment. Contact precautions are most commonly employed to decrease the spread of multidrug-resistant organisms such as *C. difficile*. Contact precautions are described in Box 4.2.

Droplet precautions are employed for patients with presumed or confirmed infection with organisms known to be transmitted by respiratory droplets such as influenza (see the earlier discussion). Droplet precautions are described in Box 4.3. Precautions for use when cough-inducing and aerosol-producing procedures are being performed are described in Box 4.4.

Airborne infection isolation refers to isolation techniques intended to reduce the risk for selected infectious agents transmitted by small droplets of aerosol particles (e.g., *M. tuberculosis*).[6] Persons who enter an AII room must wear respiratory protection (an NIOSH-approved N-95 or higher respirator). Patients should be placed in a single-patient AII room equipped with special air handling AII means not only wearing respiration protection as outlined earlier but also placing patients in a single patient room with ventilation capacity that meets the American Institute of Architects/Facility Guidelines Institute standards (monitored negative pressure relative to surrounding area, minimum of two outdoor air changes per hour, minimum of 12 total air changes per hour for new construction or 6 air changes per hour for existing buildings, and air exhausted directly to the outside).[9] These types of rooms are less formally known as "negative air rooms." The airflow in the room is directed away from the door and exhausted outside. In settings where AII cannot be implemented because of limited resources, physical separation, the masking of patients and respiratory protection for health care personnel should be implemented to reduce the likelihood of airborne transmission. Box 4.5 describes airborne precautions that should be used in addition to standard precautions.

BOX 4.4 Guidelines for Cough-Inducing and Aerosol-Generating Procedures

- Cough-inducing procedures include endotracheal intubation and suctioning, diagnostic sputum induction, aerosol treatments (e.g., pentamidine therapy), and bronchoscopy.
- Cough-inducing procedures should not be performed on patients who may have infectious tuberculosis unless the procedures are essential and can be performed with appropriate precautions.
- All cough-inducing procedures performed on patients who may have infectious tuberculosis should be performed using booths or special enclosures; if this is not feasible, a room that meets the ventilation requirements for airborne infection isolation can be used.
- After the completion of cough-inducing procedures, patients who may have infectious tuberculosis should remain in their isolation rooms or enclosures until coughing subsides. They should be required to cover their mouths and noses with tissues when coughing.
- Before the enclosure or room is used for another patient, enough time should be allowed to pass for at least 99% of airborne contaminants to be removed (this time varies according to the efficiency of the ventilation or filtration system).

BOX 4.5 Airborne Precautions (used *in addition to* standard precautions)

- Place the patient in a private negative-pressure room that has 6–12 air changes per hour and either safe external air discharge or high-efficiency particulate air filtration of recirculated air.
- Keep the room door closed and the patient in the room.
- If a private room is unavailable, cohorting is acceptable.
- Perform hand hygiene and don respiratory protection when entering the room of a patient with known or suspected infectious pulmonary tuberculosis.
- Remove respiratory protection and perform hand hygiene after leaving the room.
- Susceptible persons should not enter the room of patients known or suspected to have measles (rubeola) or varicella (chickenpox) if other immune caregivers are available; individuals who are immune to measles or varicella need not wear respiratory protection.
- Limit transport of the patient from the room to essential purposes only.
- If transport or movement is necessary, minimize patient dispersal of droplet nuclei by having the patient wear a surgical mask.

Protective Environment

A specialized engineering approach to protect highly immunocompromised patients is a protective environment. Such an environment is used for patients with allogeneic hematologic stem cell transplants to minimize the number of fungal spores in the air.[3] Studies showing outbreaks of aspergillosis associated with construction support the importance of minimizing spore counts. Air quality for patients with hematologic stem cell transplants is improved by a combination of environmental controls that include (1) high-efficiency particulate air (HEPA) filtration of incoming air, (2) directed room airflow, (3) positive room air pressure relative to the corridor, (4) well-sealed rooms to prevent the infiltration of outside air, (5) ventilation to provide 12 or more air changes per hour, (6) strategies to reduce dust, and (7) the prohibition of dried or fresh flowers and potted plants in the room.

Cystic Fibrosis Patients

A patient population of particular interest to RTs are those with cystic fibrosis (CF). Patients with CF are at risk for recurrent respiratory infection, developing bronchiectasis, and acquiring resistant pathogens. Respiratory infection can trigger declines in lung function that require hospitalization. Guidance for IP and control in this unique patient population was updated in 2013. This updated guidance starts with the premise that all people with CF could have pathogens in their respiratory tracts that are transmissible to other people with CF. In addition to emphasizing standard precautions and hand hygiene, the standard of care is to manage CF patients with contact precautions in both the inpatient and outpatient settings. It is also recommended that CF patients wear masks whenever they are outside their hospital room or exam room.[10]

Transport of Infected Patients

By limiting the transport of patients with contagious diseases, the risk for cross infection can be reduced. However, infected patients sometimes do need to be transported; when that occurs, the patient must wear appropriate barrier protection (mask, gown, impervious dressings) consistent with the route and risk for transmission.[3] If a patient on respiratory precautions is being manually ventilated during transport, make sure that a filter is in place on the expiratory side of the manual resuscitator device. Health care personnel receiving the patient must be notified of the patient's impending arrival and what infection control measures will be required.

RULE OF THUMB Apply standard precautions when you are caring for patients.

1. Wash your hands after touching blood, body fluids, or contaminated items (even if gloves were worn).
2. Wear fresh, clean gloves for all tasks and procedures involving potential contact with blood, body fluids, or contaminated items. Perform hand hygiene prior to donning gloves.
3. Exercise extreme caution when you are handling sharps.
4. Handle soiled equipment in a manner that prevents skin and mucous membrane exposures, contamination of clothing, and transfer of microorganisms to other patients and environments.[6]

Medical Devices and Bundles

A large percentage of HAIs are device-related infections, including ventilator-associated pneumonia (VAP), catheter-related bloodstream infection, and catheter-associated urinary tract infection (CAUTI). The best way to decrease host susceptibility to a device-related infection is first to limit device use and second to ensure that devices are placed and maintained appropriately. Prevention bundles—defined as the use of multiple different evidence-based best practices to prevent device-related infection—have been shown to decrease the incidence of HAIs significantly.[11,12] Exactly how much each component of a bundle contributes to a reduction in infection is often difficult to determine. There are bundles for placement of central vascular catheters, placement and maintenance of urinary catheters, and the management of patients on ventilators. Several different variations

MINI CLINI

Spread of Infection

Problem

You work in the neonatal intensive care unit (NICU) of a large urban hospital. Over the last 2 days, many infants in the unit have developed serious *Staphylococcus aureus* infections. Identify the most likely source and route of transmission and suggest ways to prevent the spread of this serious infection.

Discussion

In hospitals, *S. aureus* commonly colonizes the skin of both health care professionals and visitors. Neonates are very susceptible hosts because of their poor immunity. *Staph* infections are transmitted mainly by direct contact (see Table 4.1). To help prevent the spread of this infection to the newborn infants, you should try to disrupt the transmission route. Meticulous attention to hand hygiene and use of gloves would help. In addition, you could isolate the infected neonates from uninfected infants (**cohorting**) and, in an effort to identify patients who may be colonized, begin screening the umbilicus and nares of each infant in the NICU for *Staph.*

TABLE 4.2 Equipment Processing Definitions

Term	Definition
Cleaning	Removal of all foreign material (e.g., soil, organic material) from objects
Disinfection (general term)	Inactivation of most pathogenic organisms excluding spores
Disinfection, low level	Inactivation of most bacteria, some viruses and fungi, without destruction of resistant microorganisms such as *Mycobacterium tuberculosis* or bacterial spores
Disinfection, intermediate level	Inactivation of all vegetative bacteria, most viruses, most fungi, and *M. tuberculosis* without destruction of bacterial spores
Disinfection, high level	Inactivation of all microorganisms *except* bacterial spores (with sufficient exposure times, spores may also be destroyed.)
Sterilization	Complete destruction of all forms of microbial life

of VAP bundles have been described. Common components to most include maintaining the head of the bed above 30 degrees, routine mouth care with chlorhexidine, minimizing sedation (daily sedation vacation), and appropriate assessment of a patient's ability wean and be liberated from mechanical ventilation.[12] Other practices commonly included in VAP bundles are venous thromboembolism prophylaxis and stress ulcer prophylaxis, although these practices do not have a direct effect on the risk for pneumonia. Institutions should be committed to these processes of care, and individual health care workers should be familiar with these practices and use them on a routine basis.[12–14] Compliance with bundles can be tracked over time as part of process improvement projects. Each individual component can be tracked, or all components can be tracked in an all-or-none total appropriateness of care manner.

DISINFECTION AND STERILIZATION

Medical instruments are used in tens of millions of procedures in the United States every year. When properly performed, cleaning, disinfection, and sterilization processes can reduce the risk for infection associated with the use of invasive and noninvasive medical instruments. Although a detailed review of disinfection and sterilization is beyond the scope of this chapter, overall principles are discussed, particularly as they pertain to the use of bronchoscopes. The interested reader is referred to detailed guidance available from the CDC.[15] Table 4.2 lists definitions of the steps involved in equipment reprocessing.

The Spaulding Approach to Disinfection and Sterilization of Patient Care Equipment

In 1968, Earle H. Spaulding published his approach to disinfection and sterilization, which was based on the degree of risk for infection involved in the use of the item in patient care.[16] The three categories he described were critical, semicritical, and noncritical (Table 4.3). *Critical* items are those that enter normally sterile tissue or the vascular system. Based on the high risk for infection if such an item is contaminated with pathogens, including bacterial spores, these items should be purchased sterile or be sterilized after each use. *Semicritical* items come into contact with mucous membranes or nonintact skin; this category includes most respiratory equipment. These items should be free of all microorganisms before use, although small numbers of bacterial spores may be present. Semicritical items require at least high-level disinfection using chemical disinfectants. *Noncritical* items come into contact with intact skin (an effective barrier to most microbes) only. These items may include noncritical patient care items and noncritical environmental surfaces. Most noncritical reusable items (e.g., bedpans, patient bed rails, blood pressure cuffs) may be decontaminated where they are used and do not have to be transported to a central processing department.

Personnel responsible for these tasks must make sure that reprocessing is done per device manufacturer guidelines using products registered with the US Environmental Protection Agency (EPA) or cleared by the US Food and Drug Administration (FDA). Health care workers should wear appropriate PPE while cleaning, disinfecting, or sterilizing medical equipment to protect themselves from potentially infectious material as well as the chemical products used in the process.

Cleaning

Medical equipment must be cleaned and maintained according to the manufacturer's instructions. Cleaning is the first step in all reprocessing of equipment, including that undergoing low- or high-level disinfection and sterilization. Cleaning involves removing all dirt and organic material from equipment, usually by washing (see Table 4.3).[15] Failure to clean equipment properly can render all subsequent processing efforts ineffective. Cleaning should occur in a designated location with separate dirty and clean areas. Before being cleaned, the equipment should be disassembled per the manufacturer's recommendations and examined for worn parts. Disassembly helps to ensure thorough exposure to the cleaning agent.

Because water alone cannot dissolve organic matter, detergents or enzymatic cleaners combined with friction (rubbing and/or

TABLE 4.3 Processing of Medical Equipment According to Infection Risk Categories

Category	Description	Examples	Processing
Critical	Devices introduced into the bloodstream or other parts of the body	Surgical devices Intravascular catheters Implants Heart-lung bypass components Dialysis components Bronchoscope forceps/brushes	Sterilization
Semicritical	Devices that directly or indirectly contact mucous membranes	Bronchoscopes Oral, nasal, and tracheal airways Ventilator circuits/humidifiers Pulmonary function testing mouthpieces and tubing Nebulizers and their reservoirs Resuscitation bags Laryngoscope blades/stylets Pressure, gas, or temperature probes	High-level disinfection
Noncritical	Devices that touch only intact skin or do not contact patient	Face masks Blood pressure cuffs Ventilators	Detergent washing Low- to intermediate-level disinfection

Modified from Chatburn RL, Kallstrom TJ, Bajasouzian S: A comparison of acetic acid with a quaternary ammonium compound for disinfection of hand-held nebulizers. *Respir Care* 34:98–109, 1989.

brushing) should be used to clean all internal and external surfaces of equipment. Enzymatic cleaners are neutral detergents with added enzymes that help to remove organic (proteinaceous) material from equipment. Some EPA-registered products combine a germicide with a detergent, providing the dual action of cleaning and disinfection. This combination type of product is generally appropriate for use on noncritical items such as stethoscopes, intravenous pumps, and ventilator surfaces, which must be cleaned and low-level disinfected before use on another patient.

Although careful cleaning removes most pathogens from the equipment, it cannot eliminate the risk for infection. For this reason, semicritical and critical medical equipment must then undergo either high-level disinfection or sterilization, respectively.

Disinfection

Disinfection describes a process that destroys the vegetative form of many or all pathogenic organisms except spores on medical equipment or other inanimate objects.[15] Spores are forms that a bacterium can assume when under physical and chemical stress that makes them resistant to routine disinfection measures. Spores can survive in the environment for an extremely long time. A few *high-level* disinfectants kill spores with prolonged exposure times (hours) and are called *chemical sterilants*. Disinfection can involve either physical or chemical methods. The most common physical method of disinfection is *pasteurization*. Many chemical methods are used to disinfect respiratory care equipment.

Chemical Disinfection

Chemical disinfection involves the application of chemical solutions to contaminated surfaces or equipment. Numerous disinfectants are used alone or in combination in the health care setting, including alcohol, chlorine and chlorine products, glutaraldehyde, iodophors, phenolics, quaternary ammonium compounds, peracetic acid, and hydrogen peroxide. In most cases, a given product is designed for a specific purpose and should be used in a certain manner; the label should be read carefully. Table 4.4, excerpted from the CDC Guideline for Sterilization and Disinfection in Healthcare Facilities, summarizes common chemical disinfectants and their activity against various pathogens.[15] Health care facilities should select disinfectant agents that best meet their overall needs. Each product manufacturer's recommendations for the amount, dilution, and contact time of disinfectants should be followed. A comprehensive overview of disinfectants in the hospital can be found in the CDC Guideline.[15]

The FDA provides a list of cleared chemical disinfectants that can be used for high-level disinfection of semicritical medical devices.[17] Examples of cleared agents include 2.4% or greater glutaraldehyde, 0.55% orthophthaldehyde (OPA), 3100 to 3800 ppm peracetic acid, and 2.0% hydrogen peroxide. The choice of agent used in high-level disinfection is dictated by the device manufacturer. For high-level disinfection to be effective, cleaned equipment must be completely immersed in the disinfectant solution. After a set "contact" time, the equipment is removed, rinsed in sterile or filtered water (to remove toxic residues), and thoroughly dried. Equipment must be handled and stored carefully to prevent recontamination during subsequent reassembly, packaging, and storage.

Sterilization

Sterilization destroys all microorganisms on the surface of an article or in a fluid, which prevents transmission of pathogens associated with the use of that item. Both physical and chemical means can achieve sterilization. Physical methods include various forms of heat (via steam) and ionizing radiation. Chemical methods of sterilization include low-temperature sterilization technologies such as ethylene oxide (ETO) gas. Table 4.5, excerpted from the CDC Guidelines, compares and contrasts the major methods of sterilization.[15]

Medical devices that have contact with sterile body tissues or fluids are critical items and should be sterile before use. If the

TABLE 4.4 Comparison of the Characteristics of Selected Chemicals Used as High-Level Disinfectants or Chemical Sterilants

	Hydrogen Peroxide (7.5%)	Peracetic Acid (0.2%)	Glutaraldehyde (≥2.0%)	Orthophthalaldehyde (0.55%)	Hydrogen Peroxide/Peracetic Acid (7.35%/0.23%)
HLD claim	30 min at 20°C	NA	20–90 min at 20°C –25°C	12 min at 20°C, 5 min at 25°C in AER	15 min at 20°C
Sterilization claim	6 h at 20°C	12 min at 50°C –56°C	10 h at 20–25°C	None	3 h at 20°C
Activation	No	No	Yes (alkaline glut)	No	No
Reuse life[a]	21 days	Single use	14–30 days	14 days	14 days
Shelf-life stability[b]	2 years	6 months	2 years	2 years	2 years
Disposable restrictions	None	None	Local[c]	Local[c]	None
Materials compatibility	Good	Good	Excellent	Excellent	No data
Monitor MEC[d]	Yes (6%)	No	Yes (≥1.5%)	Yes (0.3% OPA)	No
Safety	Serious eye irritant (safety glasses)	Serious eye and skin irritant (conc soln)[e]	Respiratory irritant	Eye irritant, stains skin	Eye irritant
Processing	Manual or automated	Automated	Manual or automated	Manual or automated	Manual
Organic material resistance	Yes	Yes	Yes	Yes	Yes
OSHA exposure limit	1 ppm TWA	None	None[f]	None	HP-1 ppm TWA
Cost profile (per cycle)[g]	+ (manual), ++ (automated)	+++++ (automated)	+ (manual), ++ (automated)	++ (manual)	++ (manual)

[a]Number of days a product can be reused as determined by reuse protocol.
[b]Time a product can remain in storage (unused).
[c]No US Environmental Protection Agency regulations, but some states and local authorities have additional restrictions.
[d]Minimum effective concentration is the lowest concentration of active ingredients at which the product is still effective.
[e]Conc soln, concentrated solution.
[f]The ceiling limit recommended by the American Conference of Governmental Industrial Hygienists is 0.05 ppm.
[g]Per-cycle cost profile considers cost of the processing solution (suggested list price to health care facilities in August 2001) and assumes maximum use life (e.g., 21 days for hydrogen peroxide, 14 days for glutaraldehyde), five reprocessing cycles per day, 1-gallon basin for manual processing, and 4-gallon tank for automated processing.
AER, Automated endoscope reprocessor; *HLD,* high-level disinfectant; *MEC,* minimal effective concentration; *NA,* not applicable; *OPA,* orthophthaldehyde; *OSHA,* Occupational Safety and Health Administration; *TWA,* time-weighted average for a conventional 8-hour workday; +, least expensive; +++++, most expensive.
Data from Rutala WA, Weber DJ, and the Healthcare Infection Control Practices Advisory Committee (HICPAC). Centers for Disease Control and Prevention: guidelines for sterilization and disinfection in healthcare facilities, Atlanta, 2008. http://www.edu.gov./hicpac/.pdf/guidelines.

MINI CLINI

Selection of a Disinfectant

Problem

You work in the pulmonary function laboratory of a community hospital. Immediately after performing spirometry on a patient, you learn that he has been admitted and tests positive for pulmonary tuberculosis. You also remember seeing him cough into the spirometer. You have four more patients scheduled for spirometry testing beginning in 45 minutes. How should you process the spirometer to prevent the transmission of the tuberculosis?

Discussion

All disposable single-patient-use components (e.g., mouthpiece, filter) should be changed between patients. Internal components of spirometers are not routinely sterilized or high-level disinfected between patients. If reusable components are present, they should be cleaned and disinfected or sterilized between all patients per the equipment manufacturer's instructions for use. The equipment surface should be cleaned and low-level disinfected after each patient use with hospital- and manufacturer-approved products. All patients should be treated as potentially infectious and the equipment maintained and reprocessed properly to prevent the transmission of disease.

object is heat resistant, steam sterilization is usually recommended. However, increases in the use of medical devices that are heat and moisture sensitive (e.g., plastic) have necessitated the development of low-temperature sterilization technology. These include but are not limited to ETO, hydrogen peroxide gas plasma, and peracetic acid. A review of the commonly used sterilization technologies with a summary of advantages and disadvantages can be found in the updated CDC Guideline for Disinfection and Sterilization in Healthcare Facilities.[15] Following is an overview of a few of these technologies.

Steam Sterilization

Moist heat in the form of steam under pressure is the most common, most efficient, most reliable, and easiest sterilization method. Steam sterilization, using an autoclave, is accomplished by exposing medical devices to direct contact with steam at the required temperature and pressure for the specified time. Medical equipment must always be thoroughly cleaned before sterilization because materials that remain on the surfaces of equipment interfere with the effectiveness of the sterilization process. Clean equipment is wrapped in muslin, linen, or paper or placed in specially designed rigid containers, all of which are easily penetrated by steam. Items must be properly loaded in the autoclave to ensure

TABLE 4.5 Advantages and Disadvantages of Accepted Methods for Equipment Sterilization

Sterilization Method	Advantages	Disadvantages
Steam	Nontoxic to patient, staff, environment Cycle easy to control and monitor Rapidly microbial Least affected by organic/inorganic soils among sterilization processes listed Rapid cycle time Penetrates medical packing, device lumens	Deleterious for heat-sensitive instruments. Microsurgical instruments damaged by repeated exposure. May leave instruments wet, causing them to rust. Potential for burns.
Hydrogen peroxide gas plasma	Safe for the environment Leaves no toxic residuals Cycle time is 28–75 min (varies with model type) and no aeration is necessary Used for heat- and moisture-sensitive items because process temperature is <50°C Simple to operate, install (208 V outlet), and monitor Compatible with most medical devices Requires electrical outlet only	Cellulose (paper), linens, and liquids cannot be processed. Sterilization chamber size from 1.8–9.4 feet^3 total volume (varies with model type). Some endoscopes or medical devices with long or narrow lumens cannot be processed at this time in the United States (see manufacturer's recommendations for internal diameter and length restrictions). Requires synthetic packaging (polypropylene wraps, polyolefin pouches) and special container tray. Hydrogen peroxide may be toxic at levels >1 ppm TWA.
100% Ethylene oxide (ETO)	Penetrates packaging materials, device lumens Single-dose cartridge and negative-pressure chamber minimizes potential for gas leak and ETO exposure Simple to operate and monitor Compatible with most medical materials	Requires aeration time to remove ETO residue. Sterilization chamber size 4.0–7.9 feet^3 total volume (varies with model type). ETO is toxic, a carcinogen, and flammable. ETO emission regulation by states but catalytic cell removes 99.9% of ETO and converts it to CO_2 and H_2O. ETO cartridges should be stored in flammable liquid storage cabinet. Lengthy cycle/aeration time.
ETO mixtures: 8.6% ETO/91.4% HCFC; 10% ETO/90% HCFC; 8.5% ETO/91.5% CO_2	Penetrates medical packaging and many plastics Compatible with most medical materials Cycle is easy to control and monitor	Some states (e.g., California, New York, Michigan) require ETO emission reduction of 90%–99.9%. CFC (inert gas that eliminates explosive hazard) banned in 1995. Potential hazards to staff and patients. Lengthy cycle/alteration time ETO is toxic, a carcinogen, and flammable.
Peracetic acid	Rapid cycle time (30–45 min) Low temperature (50°C–55°C) liquid-immersion sterilization Environmentally friendly by-products Sterilant flows through endoscope, which facilitates salt, protein, and microbe removal	Point-of-use system, no sterile storage. Biologic indicator may be unsuitable for routine monitoring. Used for immersible instruments only. Some material incompatibility (e.g., aluminum anodized coating becomes dull). One scope or a small number of instruments processed in a cycle. Potential for serious eye and skin damage (concentrated solution) with contact.

CFC, Chlorofluorocarbon; *HCFC,* hydrochlorofluorocarbon; *ETO,* ethylene oxide; *TWA,* time-weighted average.
Data from Rutala WA, Weber DJ, and the Healthcare Infection Control Practices Advisory Committee (HICPAC), Centers for Disease Control and Prevention: Guidelines for sterilization and disinfection in healthcare facilities, Atlanta, 2008. http://www.edu.gov./hicpac/.pdf/guidelines.

adequate exposure to steam. The higher the temperature and pressure of the sterilizer, the shorter the time needed for sterilization. The combination most commonly used for autoclaving is 15 psi at 121°C for a minimum of 30 minutes. After sterilization, the packaging prevents recontamination during handling and storage. Numerous quality-control monitors (mechanical, chemical, and biologic) are used to ensure that adequate sterilization has taken place. Steam sterilization is generally not suitable for heat-sensitive equipment such as bronchoscopes.

Immediate-Use Sterilization

Immediate-use (previously referred to as *flash* sterilization) steam sterilization (IUSS) is a modification of conventional steam sterilization in which the item is placed in an open tray or a specially designed container to allow for the rapid penetration of steam.[15] IUSS is not recommended as a routine method of sterilization for many reasons, including lack of timely biologic indicators to monitor performance, lack of protective packaging following sterilization, and risk of contamination of sterilized items during transport to point of use. It is considered an acceptable practice for processing cleaned patient care items that cannot be packaged, sterilized, and stored before use. IUSS use only for the sake of convenience (e.g., to save time or to limit purchase of additional instrumentation) should be discouraged.

Low-Temperature Sterilization Technologies

Low-temperature (<60°C) sterilants are needed for sterilizing temperature- and moisture-sensitive medical devices and equipment. Low-temperature sterilant technology includes ETO, hydrogen peroxide gas plasma, ozone, vaporized hydrogen peroxide, and peracetic acid.[15] ETO, a commonly used process, is reviewed in the following paragraphs.

ETO is a colorless toxic gas and potent sterilizing agent. Because it is active at ambient temperatures and harmless to rubber and plastics, ETO is a good sterilant for items that cannot be autoclaved. Similar to steam, ETO penetrates most packaging materials. Were it not for its many hazards, ETO would be the ideal sterilant.[18] However, acute exposure to ETO gas can cause airway inflammation, nausea, diarrhea, headache, dizziness, and seizures. Chronic exposure to the gas is associated with respiratory infections, anemia, and altered behavior. Residual ETO left on processed equipment can cause tissue inflammation and hemolysis. When combined with water, ETO forms ethylene glycol, which can also irritate tissues. Other potential problems include carcinogenic, mutagenic, and teratogenic effects. ETO concentrations greater than 3% are explosive.

ETO requires special attention to general safety precautions, equipment preparation, and sterilization cycle parameters. In addition, because ETO is absorbed by many materials, residual ETO must be removed from equipment after sterilization via a process called *aeration*.

EQUIPMENT-HANDLING PROCEDURES

Equipment-handling procedures that help prevent the spread of pathogens include maintenance of in-use equipment, proper reprocessing of reusable equipment, and application of single-patient-use disposables instruments.

Maintenance of In-Use Equipment

In-use respiratory care equipment that can spread pathogens includes nebulizers, ventilator circuits, bag-valve-mask devices (manual resuscitators), and suction equipment. Oxygen therapy and pulmonary function equipment is also implicated as potential sources of HAIs.

Nebulizers

Because they produce aerosols capable of spreading pathogenic microbes, large volume (Jet) nebulizers remain among the most common types of respiratory equipment linked to HAIs.[19] Small-volume medication nebulizers (SVNs) can also produce bacterial aerosols. SVNs have been linked with health care–associated pneumonia, including Legionnaires' disease, resulting from either contaminated medications or contaminated tap water used to rinse the reservoir. General procedures designed to prevent nebulizers from spreading pathogens are presented in Box 4.6.[19]

The Cystic Fibrosis Foundation recommends strict adherence to the nebulizer instructions already mentioned and provides additional recommendations for the use of nebulizers on CF patients in the hospital setting. These include dedicating reusable nebulizers to a single patient and discarding disposable nebulizers every 24 hours. Additional recommendations for care of this patient population can be found in the Cystic Fibrosis Foundation Guideline: Infection Prevention and Control Guideline for Cystic Fibrosis.[20]

Ventilators and Ventilator Circuits

The internal workings of ventilators are uncommon sources for infection; this is partly a result of the widespread use of **high-efficiency particulate air/aerosol (HEPA) filters**, which have an efficiency rate of 99.97%, and the use of sheathed suction catheters, which help to reduce endotracheal tube contamination. An inspiratory HEPA filter (placed between the machinery and the external circuit, proximal to any humidifier) can eliminate bacteria from the driving gas and prevent retrograde contamination back into the machine. An expiratory filter using a heated thermistor to prevent condensation performs the same function and still protects the internal ventilator components. Expiratory filters also prevent pathogens from being expelled into the surroundings from the patient's expired air.

The external ventilator circuitry poses the most significant contamination risk, particularly in systems using heated humidifiers. The humidifiers themselves are rarely the problem. Bubble or wick designs produce little or no aerosol and pose minimal infection risk. In addition, heating the humidifier reduces or eliminates growth of most bacterial pathogens. However, because tap water or distilled water may harbor heat-resistant pathogens, sterile water should still be used to fill bubble-type humidifiers.

The primary problem stems from contaminated condensate in the inspiratory limb of the ventilator circuit. Most often, the source of this contamination is the patient. Spillage of contaminated condensate into the patient circuit and the patient occurs when the tubing or the patient is moved, increasing the risk for self-infection. In addition, microorganisms in this condensate can be transmitted to other patients via the hands of the health care worker handling the fluid if he or she is negligent. This is another reason why it is crucial for RTs to practice hand hygiene before and after contact with every patient. Contact with the patient's ventilator is considered contact with the patient's body.

BOX 4.6 Procedures to Minimize Infection Risk With Nebulizers

Large-Volume Nebulizers and Mist Tents

- Always fill nebulizer reservoirs with sterile water.
- Fill fluid reservoirs immediately before use; do not add fluid to replenish partially filled reservoirs. If fluid is to be added, discard the remaining old fluid first.

Use sterile water for rinsing nebulizers and other semicritical equipment items after they have been cleaned or disinfected.

- Do not use large-volume room air humidifiers that create aerosols unless they can be sterilized or subjected to high-level disinfection at least daily and filled only with sterile water.
- Use mist tents and their nebulizers and reservoirs that have undergone sterilization or high-level disinfection, and replace them between patients.

If mist tents are changed for use on the same patient, perform low-level disinfection of the unit and allow to air dry.

Small-Volume Nebulizers

- Between treatments on the same patient, clean, disinfect, rinse with sterile water, and air dry.

Store in a manner that prevents contamination.

- Do not share small-volume nebulizers between patients without performing sterilization or high-level disinfection on the units.
- Use only sterile fluids for nebulization and dispense these fluids aseptically.
- When possible, use single-use medication vials; if using multidose vials, handle, dispense, and store them according to manufacturer's instructions and check expiration dates.

BOX 4.7 Procedures to Minimize Infection Risk With Mechanical Ventilators

- Do not routinely sterilize or disinfect the internal workings of ventilators.
- Do not routinely change the ventilator circuit more often than every 48–72 hours with HME.
- Sterilize or high-level disinfect reusable breathing circuits and humidifiers.
- Periodically drain tubing condensate away from patient and discard.
- Wash hands after draining tubing condensate or handling the fluid.
- Do not place bacterial filters distal to humidifier reservoirs.
- Use sterile water to fill bubble humidifiers.
- Use sterile distilled water to fill wick humidifiers.
- Change HMEs according to manufacturer's recommendation and when you observe evidence of gross contamination or mechanical dysfunction.
- Do not routinely change HME breathing circuits while in use.

HME, Heat-and-moisture exchanger.

BOX 4.8 Procedures to Minimize Infection Risk With Oxygen Therapy Apparatus

- Humidifiers are not needed with flows <4 L/min.
- When needed and whenever possible, prefilled, sterile, disposable humidifiers should be used.
- With reusable humidifiers, fluid reservoirs should be filled immediately before use with sterile distilled water.
- Fluid must not be added to replenish partially filled reservoirs. If fluid is to be added, discard the remaining old fluid first, then clean and dry the reservoir before refilling.
- The tubing and oxygen delivery device should be changed between patients; prefilled, sterile, disposable humidifiers do not need to be changed between patients in high-use areas such as the recovery room.
- Prefilled disposable humidifiers can be used safely for 30 days.

One way to address this problem is by reducing or eliminating circuit condensation. This is easily achieved by using heated wire circuits or a *heat-and-moisture exchanger* (HME). Available guidance does not recommend daily changing of HMEs. These devices should be inspected daily and replaced if contaminated with patient secretions or if flow resistance has increased. HMEs can be used safely for 48 hours; with some patient populations they may be used for up to 7 days.[21]

Based on current knowledge, both the CDC and the American Association for Respiratory Care (AARC) have developed guidelines addressing ventilator-associated infection control.[22] Box 4.7 provides general procedures for minimizing HAIs associated with ventilator use. Mechanical ventilation exposes the patient to the risk for VAP; therefore and the frequency of circuit changes and the relationship to VAP have been investigated.[12] Current guidelines suggest that ventilator circuits should not be changed routinely for infection control purposes; however, they should be changed when they are visibly soiled or malfunctioning.[23]

Bag-Mask Devices

Bag-mask devices are a source for colonizing both the airways of intubated patients and the hands of medical personnel.[24] Nondisposable bag-mask devices should be sterilized or high-level disinfected between patients. In addition, the exterior surface of any bag-mask device should be cleaned of visible debris and disinfected at least once a day.

Suction Systems

Tracheal suctioning increases the risk for infection. Proper hand hygiene and gloving help to minimize this risk. Although much has been made of the IP advantages of sheathed suction systems over open ones, evidence is mixed as to whether sheathed systems are clearly superior. However, guidance recommends in-line suctioning as part of a VAP reduction program.[23] There is no need to change a closed-system suction catheter daily. To minimize the risk for cross contamination during suctioning with an open system, a fresh, sterile, single-use catheter should be used on each patient. In addition, only sterile fluid should be used to remove secretions from the catheter. Last, both the suction collection tubing and collection canister should be changed between patients except in short-term care units, where only the collection tubing need be changed.

Oxygen Therapy Apparatus

O_2 therapy devices pose much less risk than other in-use equipment but still pose a potential infection hazard. In-use nondisposable O_2 humidifiers have a contamination rate of 33%. Conversely, prefilled sterile disposable humidifiers present a negligible infection risk.[25] On the basis of this knowledge, procedures that can help to prevent O_2 therapy apparatus from spreading pathogens are outlined in Box 4.8.

Pulmonary Function Equipment

The inner parts of equipment for pulmonary function testing are not a major source for spread of infection. However, contamination of external tubing, connectors, rebreathing valves, and mouthpieces can occur during testing. These components should be cleaned and subjected to high-level disinfection or sterilization between patients.[19,26] The common practice of using HEPA filters to isolate the spirometer from the patient makes sense logically but has yet to be proved either effective or necessary in preventing HAI.

Other Respiratory Care Devices

Use of other respiratory care equipment—including O_2 analyzers, the handheld bedside spirometer, and circuit probes—has been linked to hospital outbreaks of gram-negative bacterial infections.[19] The most likely transmission route is direct patient-to-patient contact via either the device itself or the contaminated hands of caregivers. The best way to control this problem is with proper hand hygiene and sterilization or high-level disinfection of the devices between patients.

Reprocessing Reusable Equipment

Improperly reprocessed reusable equipment is another potential source of pathogens. General principles for cleaning, disinfection, and sterilization were provided previously. This section presents specific guidelines for reprocessing reusable respiratory care equipment and a special section on bronchoscope disinfection.

BOX 4.9 Factors to Consider in Processing Reusable Equipment

- Information found in equipment manufacturer's instructions for use
- Infection risk (critical, semicritical, noncritical)
- Material and equipment configuration
- Available hospital reprocessing resources
- Relative cost (labor and materials)

Respiratory Care Equipment

Several factors must be considered in selecting a reprocessing method for reusable respiratory care equipment (Box 4.9). The most critical is compliance with the equipment manufacturer's instructions for use, which at a minimum should agree with the device's infection risk (critical, semicritical, or noncritical). These reprocessing instructions must be matched to the resources available for disinfection and sterilization in the health care facility. Each reusable device should undergo the most effective and least costly processing approach available. When reusable equipment cannot be successfully reproccessed, the use of single-patient-use disposable items should be considered.

Bronchoscope reprocessing. Bronchoscopes routinely become contaminated with high levels of organisms because of the body cavities in which they are used. The benefits of these medical devices are numerous; however, proper reprocessing is crucial. HAIs associated with bronchoscopes have been most reported with *M. tuberculosis*, nontuberculosis mycobacteria, and *P. aeruginosa*.[26] The most common reasons for transmission include failure to adhere to recommended cleaning and disinfection procedures, failure of automated endoscope reprocessors (AERs), and flaws in design. Flexible endoscopes are particularly difficult to disinfect; hence meticulous cleaning must precede any sterilization or high-level disinfection process.

The FDA has issued communications regarding the safe reprocessing of bronchoscopes.[27,28] The key components to such reprocessing are precleaning at the point of use, leak testing, manual cleaning, high-level disinfection, rinsing, drying, and storage (Box 4.10).[15] AERs offer many advantages over manual disinfection because they limit the opportunity for process variation. Regardless of whether disinfection is done manually or with an AER, all personnel involved in bronchoscope reprocessing should be given appropriate education and hands-on training, with assessment of competency initially as well as at designated intervals. Training should also be given when new equipment or disinfection technologies are introduced. Strict adherence to bronchoscope, AER, and chemical manufacturers' instructions for reprocessing is essential, as is attention to recommended preventative maintenance.

Disposable Equipment

An important alternative to reprocessing equipment continually is employing single-patient-use disposable devices. In the past, only O_2 therapy devices (i.e., masks, cannulas), suction apparatus (i.e., catheters, tubing), and some supplies were disposable. Today, manufacturers provide a range of disposable devices, including humidifiers, nebulizers, incentive spirometers, ventilator circuits, bag-valve-masks, and monitoring transducers.

Three major issues are involved in using disposable devices: *cost*, *quality*, and *reuse*. Cost issues boil down to straightforward dollar comparisons between purchasing and processing reusable devices versus stocking and distributing disposable devices. Good comparisons take into account direct and indirect costs (e.g., personnel, inventory, and maintenance) and risk factors. Most recent findings support the cost-effectiveness of disposable devices over reusable devices in respiratory care.

Even with cost savings, many quality issues persist. Although disposable devices generally perform well, poor quality control remains a problem.[24] Respiratory care managers must carefully evaluate disposable devices being considered for bulk purchase before they are put to clinical use. To ensure reliability, this evaluation should include physical testing of multiple units of each model being assessed. Simply put, the lowest-priced equipment is not always the best. A flimsy nasal cannula that does not stay

BOX 4.10 Key Components of Bronchoscope Sterilization or Disinfection

Bronchoscope disinfection involves five key steps after point-of-use precleaning and leak testing:

1. *Clean:* Mechanically clean internal and external surfaces, including brushing internal channels and flushing each internal channel with water and a detergent or enzymatic cleaner.
2. *Disinfect:* Immerse bronchoscope in high-level disinfectant or chemical sterilant, perfuse disinfectant into all channels, and expose for product-specific time.
3. *Rinse:* The bronchoscope and all channels should be rinsed with sterile water, filtered water, or tap water.
4. *Dry:* Rinse insertion tube and inner channels with alcohol and dry with forced air after disinfection and before storage.
5. *Store:* The bronchoscope should be stored in a way that prevents recontamination (e.g., hung vertically in an enclosed cabinet).

Data from Rutala WA, Weber DJ, and the Healthcare Infection Control Practices Advisory Committee (HICPAC), Centers for Disease Control and Prevention: Guidelines for sterilization and disinfection in healthcare facilities, Atlanta, 2008. http://www.edu.gov./hicpac/.pdf/guidelines.

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Bronchoscope Reprocessing

Problem

You are responsible for reprocessing bronchoscopes used in the procedural area. After the point-of-use precleaning of the bronchoscope, you transport it in a biohazard-labeled container to the reprocessing room. While you are performing the leak test, you notice a continuous stream of bubbles in the water and determine that the bronchoscope has failed the leak test. Outline what you should do next.

Discussion

When a bronchoscope fails a leak test, there is the potential for water to penetrate the inside of the bronchoscope, leading to potential damage to the scope and the inability to perform adequate cleaning and high-level disinfection or sterilization. The bronchoscope should be immediately removed from the water and the endoscope manufacturer contacted for further instructions.

BOX 4.11 Precautions for Fluids and Medications

- Sterile fluids should always be used for tracheal suctioning and to fill nebulizers and bubble humidifiers. These fluids should be dispensed aseptically.
- Sterile water should be used when equipment is being rinsed. If tap water must be used, either an alcohol rinse must follow or the equipment must be thoroughly air-dried before use.
- If a large stock bottle of sterile fluid must be reused, the container must be resealed and dated after opening. Remaining fluid should be discarded within 24 h.
- When multidose medication vials are being used, they must be handled, dispensed, and stored according to the manufacturer's instructions (on the label or package insert). A medication must not be used after its expiration date.

in the patient's nose may render such therapy ineffective and can potentially harm the patient. Finally, bedside clinicians must carefully inspect and confirm the operation of any disposable device before use.

Reusing high-cost, high-volume disposable equipment may save hospitals money. However, the practice of reusing devices labeled by the manufacturer for "single-use only" raises significant safety concerns and issues of negligence. The FDA provides stringent regulations for reprocessing and reusing single-use devices.[29] A reused single-use device must comply with the same regulatory requirements of the original manufactured device, including but not limited to submitting documents for premarket notification or approval, submitting adverse event reports, and meeting manufacturing and labeling requirements. The US Centers for Medicare and Medicaid Services recommends that the reprocessing of single-use devices be performed by an FDA-approved third-party reprocessor and not by hospitals.

Fluid and Medication Precautions

Unit dosing has decreased but not eliminated the infection hazard associated with medications. Box 4.11 outlines several simple procedures designed to help prevent cross contamination while using fluids and medications.

Handling Contaminated Articles and Equipment

Reusable contaminated items should be enclosed in a biohazard-labeled impervious bag or rigid container before removal from a patient's room. This practice helps prevent accidental exposure of both personnel and the environment to contaminated articles. After containment, reusable patient-care equipment must be returned to the applicable processing area.

When contaminated single-use devices are being discarded, facility policy should be followed in compliance with both OSHA and any applicable local, state, or federal regulations. Needles and other single-use sharp instruments should be discarded in an appropriate sharps container at the point of use.

Handling Laboratory Specimens

When laboratory specimens (e.g., sputum) are being gathered, extreme care must be taken to prevent contamination of the external surface of the container. If the outside of the container is contaminated, the caregiver must either disinfect it or place it in an impervious bag. To minimize the likelihood of laboratory specimens leaking during transport, they should always be placed in a sturdy container with a secure lid. When a specimen from a patient on isolation precautions is being handled, the container must be placed in an appropriately labeled, impervious bag before it is removed from the room. It should also be noted that special handling procedures may be warranted for specific clinical situations, such as the use of a special dual-vessel sputum trap used for acid-fast bacilli for a patient suspected of having tuberculosis.

SURVEILLANCE FOR HOSPITAL-ACQUIRED INFECTIONS

Surveillance is an ongoing process of monitoring patients and health care personnel for the acquisition of infection, colonization of pathogens, or both. It is one of the five key recommended components of an IP program; the others are *investigation*, *prevention*, *control*, and *reporting*.[2] Surveillance is a systematic process designed to review and analyze HAI data on patients. These data can be used to provide outcome measurements, which may include assessing the effectiveness of HAI reduction interventions, identifying clusters or outbreaks, and identifying opportunities to intervene to prevent the transmission of pathogens in the health care environment.

Generally an IP committee establishes surveillance policies and an infection preventionist or epidemiologist administers them. The following principles should be a part of any IP surveillance program[2]: (1) use of standard definitions for HAIs; (2) use of microbiology-based data (when available), including resistance patterns for pathogens of significance (e.g., *S. aureus*); (3) establishment of risk stratification for infection risk when available (e.g., ventilator days, device days); (4) monitoring the results prospectively and identifying trends indicating unusual rates of infection or transmission within the facility; and (5) providing feedback to stakeholders within the institution (e.g., surgical-site infection rates reported back to individual surgeons). It is also common for IP programs to oversee hand hygiene and the maintenance of standard precautions.

Most hospitals perform surveillance for device-related infections: central line–associated bloodstream infections (CLABSI), CAUTIs, and VAPs. Surveillance is performed by applying the definitions of the National Healthcare Safety Network (NHSN). It is also usual to track certain organisms, including *C. difficile* infection and methicillin-resistant *S. aureus* infection. Increasingly, there are regulatory mandates for the public reporting of surveillance results.

Traditionally, VAP was tracked and a standardized definition was employed. The VAP surveillance definition has significant limitations, including a lack of sensitivity and specificity and the subjectivity involved in interpreting radiographic findings as well as clinical signs and symptoms of a patient's condition.[12] A new way of evaluating the development of complications in ventilated adult patients has recently been developed and publicized by the NHSN.[30] Instead of following patients only for the development of VAP, surveillance is performed to look for ventilator-associated events (VAEs). The VAE surveillance definition is based on objective criteria that may identify a number of conditions or complications in mechanically ventilated adult patients that could potentially contribute to a VAP.

VAEs are broken down into three tiers: ventilator-associated condition (VACs), infection-related ventilator-associated complication (IVACs), and possible VAP (PVAP) (Fig. 4.3). VAE surveillance starts with the identification of a VAC defined as an increase in the daily minimum positive end-expiratory pressure (PEEP) or daily minimum fraction of inspired oxygen (FiO_2) for 2 calendar days or longer after a period of stability. An IVAC is considered to be present if a VAC has been identified and a patient has an elevated temperature or white blood cell count and new antibiotics have been started and administered for 4

Patient has a baseline period of stability or improvement on the ventilator, defined by ≥2 calrendar days of stable or decreasing daily minimum* FiO_2 or PEEP values. The baseline period is defined as the 2 calendar days immediately preceding the first day of increased daily minimum PEEP or FiO_2.
*Daily minimum defined by lowest value of FiO_2 or PEEP during a calendar day that is maintained for >1 h.

After a period of stability or improvement on the ventilator, the patient has a least one of the following indicators of worsening oxygenation:
1) Increase in daily minimum* FiO_2 of ≥0.20 (20 points) over the daily minimum FiO_2 of the first day in the baseline period, sustained for ≥2 calendar days.
2) Increase in daily minimum* PEEP values of ≥3 cmH_2O over the daily minimum PEEP of the first day in the baseline period†, sustained for ≥2 calendar days.

Ventilator-Associated Condition (VAC)

On or after calendar day 3 of mechanical ventilation and within 2 calendar days before or after the onset of worsening oxygenation, the patient meets both the following criteria:
1) Tempered >38˚C or <36˚C, **OR** white blood cell count ≥12,000 cells/mm^3 or ≤4000 cells/mm^3.
AND
2) A new antimicrobial agent(s) (see Appendix for eligible antimicrobial agents) is started, and is continued for ≥4 qualifying antimicrobial days (QAD).

Infection-Related Ventilator-Associated Complication (IVAC)

On or after calendar days 3 of mechanical ventilation and within 2 calendar days before or after the onset of worsening oxygenation, ONE of the following criteria is met **(taking into acount organism exclusions specified in the protocol):**

1) Criterion 1: Positive culture of one of the following specimens, meeting quantitative or semi-quantitative thresholds as outlined in protocol, without requirement for purulent respiratory secretions:
   - Endotracheal aspirate, ≥10^5 CFU/mL or corresponding semi-quantitative result
   - Bronchoalveolar lavage, ≥10^4 CFU/mL or corresponding semi-quantitative result
   - Lung tissue, ≥10^4 CFU/g or corresponding semi-quantitative result
   - Protected specimen brush, ≥10^3 CFU/mL or corresponding semi-quantitative result
2) Criterion 2: Purulent respiratory secretions (defined as secretions from the lungs, bronchi, or trachea that contain ≥25 neutrophils and ≤10 squamous epithelial cells per low-power field [lpf, x100)† **PLUS** organism identified from one of the following specimens (to include quantitative culture, or quantitative/semi-quantitative culture without sufficient growth to meet criterion #1):
   - Sputum
   - Endotracheal aspirate
   - Bronchoalveolar lavage
   - Lung tissue
   - Protected specimen brush

   † If the laboratory reports semi-quantitative results, those results must correspond to the quantitative thresholds. See additional instructions for using the purulent respiratory secretions criterion in the VAE Protocol.
3) Criterion 3: One of the following positive tests:
   - Organism identified from pleural fluid (where specimen was obtained during thoracentesis or initial placement of chest tube and NOT from an indwelling chest tube)
   - Lung histopathology, defined set as (1) abscess formation or foci consolidation with intense neutrophil accumulation in bronchioles and alveoli; set as (2) evidence of lung parenchyma invasion by fungi (hyphae, pseudohyphae or yeast forms); set as (3) evidence of infection with the viral pathogens listed below based on results of immunohistochemical assays, cytology, or microscopy performed on lung tissue
   - Diagnostic test for *Legionella* species
   - Diagnostic test on respiratory secretions for influenza virus, respiratory syncytial virus, adenovirus, parainfluenza virus, rhinovirus, human metapneumovirus, coronavirus

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Possible Ventilator-Associated Pneumonia (PVAP)

Fig. 4.3 Ventilator-associated events *(VAE)* surveillance algorithm. *PEEP,* Positive end expiratory pressure. (From Centers for Disease Control and Prevention.)

or more days. PVAP is present if an IVAC has been identified in a patient with positive culture results meeting specific threshold values or purulent respiratory secretions and a positive culture result that does have sufficient growth to meet the threshold values. VAE surveillance is a new practice in surveillance in that it tries to examine the overall safety of ventilator therapy rather than focusing only on infection-related outcomes. Conduct of this surveillance requires a partnership among IP, critical care physicians, and RTs.

The surveillance activities of an IP program are most effective when they generate actionable data that are communicated to the bedside caregiver in a timely fashion. These data can become the basis for continuous improvement in the delivery of care. Infection preventionists must communicate the results of surveillance activities to bedside caregivers in a meaningful way so that continuous improvements in care can occur based on local data. Health care workers must be willing to accept surveillance data in the way it is intended, not as a punitive grade but as a tool to encourage reflection on current processes for delivering care. All health care workers should be aware of the rates of adherence in their area to bundles, hand hygiene, and HAI and should seek out their infection preventionist with any questions, observations, and suggestions on how care could be improved.

SUMMARY CHECKLIST

- The five major routes for transmission of pathogens are contact, droplet, airborne, common vehicle, and vector borne.
- IP procedures involve (1) eliminating the sources of infectious agents, (2) creating barriers to their transmission, and (3) monitoring and evaluating the effectiveness of control.
- Failure to clean equipment properly can render all subsequent processing efforts ineffective.
- Physical or chemical disinfection destroys the vegetative form of pathogenic organisms but cannot kill bacterial spores.
- Glutaraldehyde (used for 20 minutes) is the most common option for high-level disinfection of semicritical respiratory care equipment.
- ETO is best suited for the sterilization of critical moisture- or heat-sensitive items; heat-stable critical items should be steam sterilized.
- Among respiratory care equipment, large-volume nebulizers have the greatest potential to spread infection.
- Ventilator circuits should be changed when visibly soiled or malfunctioning.
- HMEs may be used up to 96 hours before they need to be changed.
- Single-use items should be reused only if there is hard documented evidence that reprocessing poses no threat to the patient, does not alter the function of the device, and FDA guidelines are being followed. The use of a third-party reprocessor is recommended.
- Sterile fluids must always be used for tracheal suctioning and to fill nebulizers and humidifiers.
- Hand hygiene must be performed before and after any patient contact, even when gloves are used.
- Standard precautions must be used in caring for all patients, regardless of their diagnosis or infection status.
- Masks, goggles, or a face shield must be worn during any procedure that can generate splashes or sprays of blood, body fluids, secretions, or excretions.
- Special infection-control protocols may have to be followed for specific situations such as the shoe coverings and special handwashing protocols that may be warranted when one is preparing to enter a restricted environment such as the operating room and cardiac catheterization lab.
- RTs must be familiar with the overall IP program, including surveillance policies and procedures.

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5

Ethical and Legal Implications of Practice

Anthony L. DeWitt

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Summarize the philosophical foundations of ethics.
- Explain what constitutes an ethical dilemma and how such dilemmas arise in healthcare.
- Describe how professional codes of ethics apply to ethical decision-making.
- Explain how traditional ethical principles are useful in resolving ethical dilemmas.
- Describe the information that should be gathered before making an ethical decision.
- Explain how the systems of civil and criminal law differ.
- Describe what constitutes professional malpractice and negligence.
- Explain how a respiratory therapist can become liable for wrongful acts.
- List the elements that constitute a practice act.
- Explain how licensing affects legal responsibility and liability.
- Describe how changes in healthcare delivery have shaped the ethical and legal aspects of practice.
- Summarize the basic elements of the *Health Insurance Portability and Accountability Act* of 1996 (HIPAA).
- Discuss the Patient Protection and Affordable Care Act.
- Summarize the basic elements of the National Labor Relations Act.
- Discuss elements of the False Claims Act.
- Describe the role of advance directives and living wills in healthcare.

CHAPTER OUTLINE

KEY TERMS

advance directives
assault
autonomy
battery
beneficence
benevolent deception
breach of contract
compensatory justice
confidentiality
consequentialism
defendant
distributive justice
double effect
formalism
informed consent
intuitionism
justice
libel
living will
malpractice
negligence
nonmaleficence
plaintiff
qui tam

res ipsa loquitur
rule utilitarianism
slander
strict liability
tort
veracity
virtue ethics

An effective respiratory therapist (RT) must possess excellent clinical skills and an understanding of the business of healthcare. The healthcare industry, similar to all industries, must deliver services in an atmosphere in which ethical and legal considerations are an integral part of the organizational culture. RTs regularly find themselves in circumstances that require them to make choices or take actions that have ethical and legal consequences. In society, ethics and law help maintain order, stability, and accountability. In professional practices, ethics guide RTs in carrying out their duties in a moral way. Law establishes the minimum legal standards to which practitioners must adhere. Although not always the case, ethical practice may require a standard above that of legal practice. The tension between these two competing values can sometimes cause problems.

The force behind law is threefold: (1) state statutes regulate individual conduct by imposing criminal and sometimes civil penalties on those whose conduct is considered to be against public policy by the state or federal government. The sanctions range from fines to imprisonment; (2) state statutes and professional boards regulate the practice of therapists and set minimum standards for competent practice as well as requirements for continuing education. Violation of licensing statutes and regulations can result in fines or discipline or revoking of the individual practitioner's license; and (3) the common law of civil liability for negligent and intentional acts imposes a duty to pay compensation to individuals who are injured. Civil judgments are usually monetary—they do not involve prison terms.

Punishment for ethical misconduct ranges from a loss of professional standing to expulsion from the profession or professional societies. Punishment by the state board in one state will usually result in reciprocal discipline in any other state where a practitioner holds a license to practice. In some cases, particularly those involving patient injury, ethical misconduct leading to state sanctions on the right to practice, and legal consequences, in the form of criminal penalties or civil judgments, may result from the same incident. The distinction between illegal acts and unethical behavior is not always obvious but is straightforward. *An illegal act violates the standards of conduct set down for all citizens (e.g., domestic assault), whereas ethical misconduct usually relates to violations of professional and ethical norms established by the profession as a whole*. A given act may fit any one of the following categories, depending on the circumstances and the ethical orientation of the person involved: ethical and legal, unethical but legal, ethical but illegal, or unethical and illegal.

For example, a therapist who spends 30 minutes after clocking out visiting with a patient because the patient has no family is performing an act that is both ethical and legal. However, if the purpose of the visit is to encourage the patient to offer her monetary gratuities for this extra visitation, the act would be *legal but unethical* because it seeks to take advantage of the emotional vulnerability of a patient. If the same patient were a prisoner subject to a restriction on their right to visitation by the state and the therapist knowingly violated the prohibition against visitation in violation of a state statute, the act *would not be unethical* (because the act does not violate the standards of the profession) *but may well be illegal* under state law. Finally, if the purpose of the visit was to rummage through a demented patient's valuables for the purpose of taking his or her credit card and checkbook, the act would be *both unethical* (because it would be exploiting the patient's mental vulnerabilities in violation of professional norms) *and illegal* (because it would be theft in violation of state criminal laws). It is important to note that under the ethical guidelines in every state, a practitioner who knows about unethical or illegal conduct, yet does not report that conduct to the proper authorities, is similarly committing an unethical (and in some cases, illegal) act.

This chapter provides a foundation of principles related to the ethical and legal practice of respiratory care.

PHILOSOPHICAL FOUNDATIONS OF ETHICS

Although an in-depth discussion of philosophy is beyond the scope of this chapter, you should realize that ethics has its origins in philosophy. *Philosophy* may be defined as the love of wisdom and the pursuit of knowledge concerning humankind, nature, and reality.[1] *Ethics* is one of the disciplines of philosophy which is primarily concerned with the question of how we should act. Although ethics may share common origins with the disciplines of law, theology, and economics, as an applied practice, ethics is clearly different from these disciplines.[1] Ethics can be described philosophically as a moral principle that supplements the golden rule and can be summed up by a commitment to "respect the humanity in persons."[2]

ETHICAL DILEMMAS OF PRACTICE

The growth of respiratory care has paralleled the development of advanced medical technology and treatment protocols. At the same time, during the 1970s and through the present, the medical community has experienced rising expectations about acceptable standards of care and patient outcomes. This is due to an ever-growing and sophisticated patient population fueled by medical benefit packages from the government and employers, as well as increased accessibility of information on the internet. In the latter part of the 1990s, managed care strategies and other cost-containment methods adopted by most third-party payers slowed the growth of the healthcare industry. The ethical and legal issues faced by RTs, although changed in many cases, continued to grow. In the earlier period, RTs faced ethical dilemmas and legal issues associated with patient expectations, staffing, and quality of care, among others. RTs continue to face ethical dilemmas and legal

issues. Such dilemmas may include the rationing of care, dealing with conflicts associated with third party–imposed standards of care, and delivery of the appropriate standard of care in the face of cost constraints and corporate influence. Staffing issues continue to be a problem and contribute to many of the ethical and legal concerns faced by RTs. As respiratory care continues to mature as a profession and resources are stretched, these challenges are likely to increase. The 21st century has brought one particular challenge, although not new to healthcare or to RTs: a heightened awareness of the patient's right to privacy. The *Health Insurance Portability and Accountability Act* of 1996 (HIPAA), discussed later in this chapter, is currently a major consideration for RTs as they perform their jobs. It also has brought new opportunities in the form of the *Patient Protection and Affordable Care Act* of 2010 (PPACA). The PPACA has improved access to healthcare and increased reimbursement for patient care services, as well as creating disease management opportunities for RTs. Changes in control of the government, insurance cost inflation, lack of affordable coverage, and increasing demand for Medicaid services are likely to force changes to the PPACA and to the healthcare universe in general. There is significant pressure to revise or replace the PPACA.

RTs work in complex healthcare settings. As a result, there are many types of ethical dilemmas that may face the RT on a regular basis. The healthcare industry continues to be in a period of dynamic change, bringing many new challenges. New technologic and management methods are continuously being introduced to accomplish the missions and goals of healthcare organizations. Over the past decade, there has been an almost complete change from a relatively open fee-for-service system to one in which care is managed in some fashion and the fees are in some form of capitated payment. These changes often create serious ethical dilemmas.

For example, managed care uses a concept known as "restrictive gatekeeping." Restrictive gatekeeping requires patients to obtain prior approval from their third-party payer, usually an insurance company, before hospitalization and before certain procedures. When the hospital admission or procedure is approved, specific requirements or limitations are usually associated with the patient's care. As a result, healthcare workers, including RTs, may find themselves captive to third-party payers' demands related to the cost of services than by medical considerations of the patient's needs. Under these circumstances, healthcare workers may feel frustrated and helpless if they believe a patient needs care beyond that approved by the third-party payer. Ethics may impose a duty on professionals to interact with and press for change with the third party.

The rationing of care continues to be a side effect of staffing patterns created by managed care and by the pressure to decrease the cost of healthcare. An RT working in an understaffed department may decide that a patient can really do without therapy because the department is short staffed and the patient is really not going to get better anyway. Although this may sound, at first, like a case of simple neglect of duty, it is also an ethical dilemma. Unless this decision is supported by a treatment protocol approved by the medical director and medical staff, it may violate professional norms and be unethical. Approaches to settling ethical dilemmas range from specific solutions such as a code of ethics for the RT profession to a general approach such as an ethical theory.[3]

CODES OF ETHICS

A *code of ethics* is an essential part of any profession that claims to regulate itself. Adopting a code of ethics is one way in which an occupational group establishes itself as a profession. A code may try to limit competition, restrict advertisement, or promote a particular image in addition to providing rules for conduct.[4]

The American Association for Respiratory Care (AARC) has adopted a Statement of Ethics and Professional Conduct. The current code appears in Box 5.1. This code represents a set of general principles and rules that have been developed to help ensure that the health needs of the public are provided in a safe, effective, and caring manner. The most difficult ethical decisions arise from situations in which two or more right choices are incompatible, in which the choices represent different priorities, or in which limited resources exist to achieve a desired end. Ethicists readily admit that reducing these issues to simple rules is not an easy task.

BOX 5.1 American Association for Respiratory Care Statement of Ethics and Professional Conduct (Revised 2009).

In the conduct of professional activities, the respiratory therapist shall be bound by the following ethical and professional principles. Respiratory therapists shall:

- Demonstrate behavior that reflects integrity, supports objectivity, and fosters trust in the profession and its professionals. Actively maintain and continually improve their professional competence and represent it accurately.
- Seek educational opportunities to improve and maintain their professional competence and document their participation accurately.
- Perform only those procedures or functions in which they are individually competent and that are within the scope of accepted and responsible practice.
- Respect and protect the legal and personal rights of patients they treat, including the right to informed consent and refusal of treatment.
- Divulge no confidential information regarding any patient or family unless disclosure is required for responsible performance of duty or required by law.
- Provide care without discrimination on any basis, with respect for the rights and dignity of all individuals.
- Promote disease prevention and wellness.
- Refuse to participate in illegal or unethical acts and refuse to conceal illegal, unethical, or incompetent acts of others.
- Follow sound scientific procedures and ethical principles in research.
- Comply with state or federal laws that govern and relate to their practice.
- Avoid any form of conduct that creates a conflict of interest and shall follow the principles of ethical business behavior.
- Promote healthcare delivery through improvement of the access, efficacy, and cost of patient care.
- Encourage and promote appropriate stewardship of resources.

MINI CLINI

Conflicting Obligations

Problem

Mary Smith, a registered RT with 18 years' experience, has worked for a large regional medical center for the past 10 years. She is generally happy with her work but is concerned about the financial stability of the hospital. As a result, she has signed on with a temporary agency to ensure that she will have work in case the hospital closes. On one of her scheduled days off, Mary Smith agrees to work a shift for the temporary agency at another hospital. Two hours before her shift is scheduled to begin, she receives a telephone message from the medical center where she is employed. Her supervisor asks Mary Smith to report to work at the medical center because the only experienced therapist on the shift has been in an automobile accident. Mary Smith is torn between her obligation to the medical center where she has worked for 10 years and the agency.

Discussion

Professionalism and ethics generally require a commitment to one's duties. In this situation, Mary Smith must consider not only her duty but also the consequences of each decision that she might make. In either case, there is the possibility that her decision will leave a staffing shortage at one of the hospitals.

Discussion Questions

Should Mary Smith cancel her shift with the agency, although she has agreed to give the agency a 4-hour notice except in an emergency? Should she work the shift at the agency as scheduled, using the rationale that she did not create the staffing problem at the medical center? Should she call her supervisor, explain the situation, and ask for help in making the right decision, realizing that the final decision would still be hers? Should she call her supervisor and tell the supervisor that she is ill and cannot come in and report to the agency job?

Guidance

In general, a therapist's loyalty should be to the primary institution that employs her. In this situation the hospital has invested time, money, and benefits, as well as training, in the therapist, and the therapist owes the institution a duty of loyalty. Saying "I didn't create the problem" does not solve the problem. The agency may be annoyed at the change of plans but likely has others to call. The same does not appear to be true of the hospital. Calling the supervisor makes the problem a shared problem, and that is probably not fair to the supervisor because the supervisor did not seek outside employment. Thus this situation requires the therapist to consider her duty of loyalty to her employer and do the right thing.

In addition to the moral obligations that ethical duties impose on RTs, ethical obligations are often cited in legal proceedings as a tool of cross-examination. If an RT expresses opinions or is accused of actions that would violate the ethical duties of the profession, the RT's ignorance of ethical standards during cross-examination can have a powerful effect on a jury.

ETHICAL THEORIES AND PRINCIPLES

Ethical theories and principles provide the foundation for all ethical behavior. Contemporary ethical principles have evolved from many sources, including Aristotle's and Aquinas' natural law, Judeo-Christian morality, Kant's universal duties, and the values characterizing modern democracy.[5,6] Although controversy exists, most ethicists agree that principles like autonomy, veracity, nonmaleficence, beneficence, confidentiality, justice, and role fidelity are the primary guiding principles in contemporary ethical decision-making.[1,5]

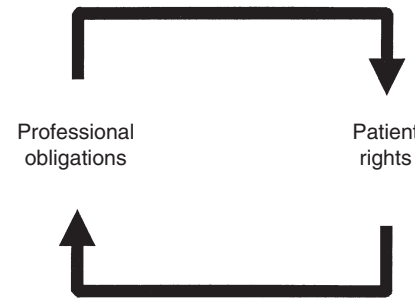

Fig. 5.1 Reciprocal relationship between professional obligations and patient rights.

Each of these ethical principles, as applied to professional practice, consists of two components: a *professional duty* and a *patient right* (Fig. 5.1). The principle of autonomy requires that healthcare professionals uphold the freedom of will and freedom of action of others. The principle of beneficence requires healthcare professionals to further the interests of others, either by promoting their good or by actively preventing their harm. The principle of justice obliges healthcare professionals to ensure that others receive what they rightfully deserve or legitimately claim.

Expressed in each duty is a reciprocal patient right. Reciprocal patient rights include the right to autonomous choice, the right not to be harmed, and the right to fair and equitable treatment. More specific rules can be generated from these general principles of rights and obligations, such as those included in a code of ethics.

Autonomy

The principle of **autonomy** acknowledges the personal liberty of patients and their right to decide their own course of treatment and follow through on a plan on which they freely agree. It is from this principle that rules about **informed consent** are derived. As such, before many medical interventions can be performed, the patient must be *informed* as to what is being done, as well as the risks and benefits. Then they exercise their autonomy and freely decide to give or withhold *consent* for that procedure. Under the principle of autonomy, the use by an RT of deception or coercion to get a patient to give consent is unethical.

Chapter 58 discusses how autonomy and other ethical principles are integrated into end-of-life patient care.

Veracity

The principle of **veracity** (accuracy or truthfulness) is often linked to autonomy, especially in the area of informed consent. In general, veracity requires that the healthcare provider tell the consenting individual the whole truth about the choices inherent in medical care. This means providing not only information about the benefits of a particular course of action but also what might go wrong and what kinds of frequent complications occur.

MINI CLINI

Patient Rights

Problem

An RT working at a hospital receives a physician order to administer an aerosolized bronchodilator treatment to a 26-year-old female patient with asthma admitted for suspected pneumonia. The patient refuses the treatment on entering the room, stating that she is having a "bad day" today and does not want to be bothered by anyone. The patient is regarded as being competent and fully capable of making healthcare decisions for herself. How should the RT handle this situation?

Discussion

The RT must acknowledge and respect the patient's right to decide freely whether or not to allow the respiratory care treatment. According to the principles of ethical theory and conduct, healthcare professionals have an obligation to promote patient autonomy by permitting freedom of will and freedom of action. It is also important that neither coercion nor deception be used to get a patient to reverse his or her decision to refuse a treatment. According to the American Hospital Association statement called "The Patient Care Partnership," the patient has the right to refuse treatment and to be informed of the medical consequences of her action.

Problems with the veracity principle revolve around such issues as benevolent deception. In actions of **benevolent deception**, the truth is withheld from the patient for, supposedly, his or her own good.

When the caregiver decides to withhold the truth from a conscious, well-oriented adult, the decision affects the interactions between healthcare providers and the patient and has a chilling effect on the trusting relationship that is necessary for good care. In a poll conducted by the Louis Harris group, 94% of Americans surveyed indicated that they wanted to know everything about their cases, even the dismal facts. Other than with pediatrics and rare cases in which there is evidence that the truth would lead to a harm (e.g., suicide), the truth, provided in as pleasant a manner as possible, is the best policy.[7]

Truth telling also can involve accuracy in documentation and medical recordkeeping.

The RT could talk to the patient and explore what the term "bad day" means to her. It might be that she is not feeling well because of breathing problems from her asthma condition and worsening symptoms of possible pneumonia. The RT has an important role in ensuring that the patient understands the benefits of the respiratory treatment and the health consequences of refusal so that the patient can make a well-informed decision. If the RT approaches the patient in a professional, nonthreatening manner, she may feel more at ease and be willing to discuss in greater depth why she does not want to take the treatment. Some patients refuse therapy initially only to change their minds after discussion with the RT. Others may refuse therapy but permit the RT to assess them, including listening to breath sounds. This may at least provide the patient care team with some insight as to whether some alternative intervention may be warranted. Should the patient still refuse the treatment after discussion with the RT, the RT should not judge the patient, even if he or she disagrees with the patient's decision. The RT should document the patient's decision and the information provided to the patient in the medical record and notify the physician.

Nonmaleficence

The principle of **nonmaleficence** requires healthcare providers to avoid harming patients. It is sometimes difficult to uphold this principle in modern medicine because, in many cases, drugs and procedures have secondary effects that may be perceived as harmful. Procedures carry risks of side effects and complications, not all of which can be predicted. For example, an RT might ask whether it is ethical to give a high dose of steroids to an asthmatic patient, knowing the many potentially harmful consequences of these drugs. However, RTs should understand that many helping actions inevitably have both a positive effect and other potentially bad effects. **Double effects** are common. The key is the *first intent*. In this example, if the first intent of giving the steroids is good, the possible harmful effect is viewed as an unintended result.

Beneficence

The principle of **beneficence** raises the "do no harm" requirement to an even higher level. Beneficence requires that healthcare providers go beyond doing no harm and contribute actively to the health and well-being of their patients. Many quality-of-life issues are included within this dictum. Currently, practitioners of medicine possess the technology to keep some individuals alive well beyond any likelihood of meaningful recovery. This technology presents dilemmas for practitioners who have the ability to prolong life but not the ability to restore any uniquely human qualities or enhance the quality of that prolonged existence.

The Mini Clini involves the ethical principles of veracity and the duty of candor to third parties. Therapists have fought hard for professional recognition, and selling test results undermines the entire profession. The ethical principle of veracity is among the most important of the ethical principles because it has the potential to do the most damage if it is violated.

One approach in this situation is for the RT to tell the patient that the physician will interpret the studies and provide a full report at the next office visit. All final discussion of results must ultimately go through the physician.

Some individuals interpret the principle of beneficence to mean that they must do everything to promote a patient's life, regardless of how useful the life might be to that individual. Other professionals in the same situation might believe they are allowing the principle to be better served by doing nothing and allowing death to occur without taking heroic measures to prevent it. In an attempt to allow patients to participate in resolving this dilemma, legal avenues, called **advance directives**, have been developed.[8] Advance directives allow a patient to give direction to healthcare providers about treatment choices in circumstances in which the patient may no longer be able to decide competently. The two types of advance directives currently available are the *living will* and the *durable power of attorney for healthcare*. A durable power of attorney for healthcare allows the patient to identify another person to carry out his or her wishes with respect to healthcare should he be unable to express his opinion, whereas a **living will** states a patient's healthcare preferences in writing.

MINI CLINI

Veracity

Problem

Jon performs pulmonary function testing, including blood gases, for his hospital. Many of the patients he sees are attempting to qualify or requalify for continuous reimbursement for home oxygen use. To qualify, the patient's PaO_2 must be less than 60 mm Hg on room air at rest. A patient who has home O_2 therapy is attempting to requalify although her condition has improved from 1 year earlier. Her blood gas results show a PaO_2 of 63 mm Hg. The patient's husband asks Jon if there is anything he can do, while relating how greatly his wife benefits from the O_2. Jon tells the husband that there is nothing he can do and assists the husband in taking the patient out to her car. At the car, the husband pulls out his wallet, shows it to Jon, and repeats the question.

Discussion Points

RTs have an obligation to carry out their duties in the most competent and professional manner possible. Failure to do so may represent both an ethical dilemma and a legal issue. Similarly, RTs have a duty to be truthful with third parties who may rely on their clinical results.

Discussion Questions

What is the potential ethical dilemma in this situation? What ethical principles are involved here? What other ways could Jon have chosen to handle this situation?

Guidance

The ethical dilemma here is whether to accept cash to change a blood gas result, and there should be no question about the right answer. It is never acceptable to accept money from patients for either doing your job or failing to do your job. It creates a situation in which a clinician feels obligated to perform additional or, in this case, unlawful acts for the patient. It may also create the risk that the patient will expect further unethical conduct in exchange for cash. Falsification of medical records can result in both civil and criminal liability. Accepting money to change the test result could be viewed as receiving a kickback under the federal Anti-Kickback statute, which carries criminal penalties. It could be viewed as an unlawful and unethical act by the state licensure board. Worse, it erodes the trust of other health professionals—including physicians, nurses, and other RTs.

Of these two options the durable power of attorney for healthcare is the best option because it provides an individual who can take legal action on behalf of the patient if questions arise. However, it is worth noting that the durable power of attorney cannot be used to avoid a conscious, competent patient's wishes. As a result of the *Patient Self-Determination Act* of 1990, most states require that all healthcare agencies receiving federal reimbursement under Medicare/Medicaid legislation provide adult clients with information on advance directives.[8,9] Chapter 58 discusses in more detail ethical situations related to end-of-life patient care.

Confidentiality

The principle of **confidentiality** is based on the Hippocratic Oath; it was later restated by the World Medical Association in 1949. The principle of confidentiality requires healthcare providers to "respect the secrets which are confided even after the patient has died."[10] Confidentiality often must be balanced against other principles, such as beneficence. Notably, state laws require a breach of confidence under certain conditions (e.g., reporting gunshot wounds or child abuse) in which risk to other parties may result from not disclosing events or results.

The main ethical issue surrounding confidentiality is whether more harm is done by occasionally violating its mandate or by always upholding it regardless of the consequences. This limitation to confidentiality is known as the *harm principle*. This principle requires that practitioners refrain from acts or omissions in which foreseeable harm to others could result, especially when the others are vulnerable to risk. This principle would require that confidentiality be maintained for a patient with acquired immunodeficiency syndrome (AIDS) in matters involving his or her landlord. In this case, confidentiality is justified because the landlord is not particularly vulnerable. However, if the patient were planning to marry, the harm principle would require that confidentiality be broken because of the special vulnerability of the future spouse.

Confidentiality is usually considered a qualified, rather than an absolute, ethical principle in most healthcare provider–patient relationships. These qualifications are often written into codes of ethics. The American Medical Association Code of Ethics, Section 9, provides the following guidelines: "A physician may not reveal the confidences entrusted to him in the course of medical attendance or the deficiencies he may observe in the character of patients, unless he is required to do so by law or unless it becomes necessary in order to protect the welfare of the community or a vulnerable individual." Under the requirements of public health and community welfare, there is often a legal requirement to report such things as child abuse, poisonings, industrial accidents, communicable diseases, blood transfusion reactions, narcotic use, and injuries caused with knives or guns.[11] In many states, child abuse statutes protect the healthcare practitioner from liability in reporting even if the report should prove false as long as the report was made in good faith. Failure to report a case of child abuse can leave the practitioner legally liable for additional injuries that the child may sustain after being returned to the hostile environment. Some states, such as Missouri, provide a testimonial privilege to physicians, whereas others, such as Alabama, do not recognize a testimonial privilege for caregivers.

Breaches of confidentiality more often result from careless slips of the tongue than from purposeful actions. Trading gossip about patients is unprofessional, unethical, and, in certain cases, illegal. Risks for inadvertent disclosure increase markedly when RTs may exchange information on social media such as Facebook and LinkedIn. The fact that a group is restricted to physicians or therapists does not immunize an RT from liability should confidential information be disclosed. Such information should never be placed in such social media networks, because doing so violates the rights of individual patients and certain laws discussed later in this chapter.

The only exception to the rule of confidentiality regarding Mary's neighbor is if Mary is assigned to provide care to her as a treating RT. Only then does she have a need to know what is in the chart and what is wrong with her neighbor, but even then, the wiser course, because of the close relationship, would be for Mary to ask that she be excused from this case and that someone else handle the clinical duties for the patient.

RULE OF THUMB Patient information should be discussed **only** in private and with persons who have a legitimate reason and need to know.

Because of the widespread use of computerized databases, confidential information, previously highly protected, is currently relatively easy to obtain. Clinical data are available for close scrutiny by the clerical staff, laboratory personnel, and other healthcare providers. The widespread use of these data systems also threatens patient confidentiality. In an attempt to reduce this threat, most clinical databases are restricted to use by only the healthcare workers who have a need to know. In addition to being unethical, a respiratory therapist who reads the file of a patient whom he or she is not treating would likely be in violation of institutional policy. The following accompanying Mini Clini provides an example.

MINI CLINI

Confidentiality

Problem

Mary, an RT, is working the evening shift at a large urban medical center when she receives a telephone call from a friend telling her that her next door neighbor has been admitted to the medical center. Mary's first thought is to check the neighbor's file on the computer system to see why her neighbor has been hospitalized.

Discussion Point

Mary knows that the medical center has a policy that employees are to access only the charts for which they have a clinical reason to do so.

Discussion Questions

Should Mary access this chart via the computer system? If she does, what kind of violation will she be committing—ethical, legal, or both? What ethical principles, if any, would apply here? What is the harm in simply checking the computer on this patient? Is anyone likely to know if Mary accesses this patient's information?

Guidance

The answer here is straightforward. She should absolutely not access her neighbor's medical record. The policy is there to keep the facility compliant with the Health Insurance Portability and Accountability Act and with state laws regarding privacy. Mary runs the risk for being fired because this action violates hospital policy. What harm does looking at the computer do? It erodes the confidentiality that patients expect. The far greater harm will be to Mary's reputation and future employability. If Mary does this, she will certainly be found out because the electronic medical record system has an "audit trail" that indicates who accessed the record and when. Mary will face hospital discipline for the policy violation (likely termination), and she may face criminal charges or civil administrative penalties under state and federal law for breaches of patient confidentiality. This action also places Mary at risk for a civil lawsuit for invasion of privacy.

Why? If the patient has an illness that carries any stigma with it (human immunodeficiency virus [HIV] infection, pediculosis capitis, etc.), the patient will likely be very embarrassed if her neighbor knows about it. In addition, if the patient's other neighbors learn about the condition from another source, Mary will be suspected. This will have consequences at work. For this reason, Mary should steer clear of this patient's medical record.

Despite medical and sociologic advances, potential violations of the individual's right to privacy in certain populations, such as patients with AIDS, pose a special risk because disclosure may result in economic, psychologic, or physical harm to the patient. RTs should adhere to the dictum found in the Hippocratic Oath: "What I may see or hear in the course of the treatment or even outside of treatment of the patient in regard to the life of men, which on no account one must spread abroad, I will keep to myself, holding such things to be shameful to be spoken about."[12]

Justice

The principle of **justice** involves the fair distribution of care. Rising healthcare expectations, along with the decreased availability of care because of cost, are making this principle an important one for healthcare workers. Population trends and the increasing cost pressure from Medicaid and Medicare will continue to make justice a challenge in delivering respiratory care.

Efforts to achieve a balance between increasing healthcare expenses and cost pressure may lead to some form of rationing of the delivery of healthcare services. This type of justice is properly referred to as **distributive justice**.

A second form of justice seen in healthcare is **compensatory justice**. This form of justice calls for the recovery for damages that were caused by the action of others. Damage awards in civil cases of medical malpractice or negligence are examples of compensatory justice. Compensatory justice often has been cited as playing a major role in increasing the cost of healthcare. However, the Congressional Budget Office estimates that less than 2% of the cost of healthcare is related to medical malpractice. Nationally, 75% of medical negligence cases that go to trial are won by the medical provider. However, one problem with studying the impact of "malpractice" on healthcare costs is that malpractice is rarely admitted and is frequently not black and white. Damages may be caused by, or multiplied by, malpractice but often are simply the result of the normal progression of disease. This is why causation in medical negligence cases is so important.

Role Duty

Because no single individual can be solely responsible for providing all of a patient's healthcare needs, modern healthcare is necessarily a team effort. There are more than 100 allied health professions, and allied health workers (excluding nursing and physicians) provide approximately 60% of all patient care. Each of the allied health professions has its own practice area, defined by tradition or by licensure law. Practitioners must understand the limits of their role and to practice with fidelity. For example, because of differences in *role duty,* an RT might be ethically obliged not to tell a patient's family how critical the situation is, instead having the attending physician do so.[3] The previous Mini Clinis addressed role duty, and the accompanying Mini Clini presents another example of the ethics of role duty.

There are both legal and ethical components to the problem. The nurse had a good-faith belief that blood gas levels were required based on her understanding of the pulse oximeter. Her belief was wrong but reasonable. It is easily corrected with some training, and it is far better to discover this problem with an

MINI CLINI

Role Duty

Problem

Sue, an RT, receives a request to perform a blood gas analysis for a patient on a ventilator because, as reported by the nurse, the patient's oxygen saturation is only 61%. The patient has an order to obtain blood gas values as needed. As the nurse and RT look at the blood gas results, they both are surprised because the saturation is now 93%. The nurse suggests repeating the blood gas examination. The RT is about to comply until she notes the oximeter display on which the nurse is relying shows the patient with an O_2 saturation of 93% and a pulse rate of 61 beats/min.

Discussion Point

Teamwork and role delineation are both essential components of good patient care. Each practitioner also has an obligation to perform his or her duties in the most competent and professional manner possible.

Discussion Questions

What kind of issue or dilemma exists here—legal, ethical, or both? What should the RT do at this point? Should an incident report be written and, if so, by whom?

Guidance

The dilemma here is to explain the nurse's mistake in a way that does not jeopardize the working relationship with the nurse, while at the same time protecting the patient and the facility. Clearly a second blood gas value should not be obtained. Placement of the oximeter should be checked, and, if the oximeter is functioning properly, then it should be believed.

error that does not harm a patient as opposed to an error in which patient harm might have resulted.

The first issue is to explain the way the oximeter works and the meaning of the readings. Many nurses fail to understand the oxyhemoglobin dissociation curve and, as a result, interpret data from oximeters incorrectly. A therapist's job is to educate both patients and other caregivers and to do so in a professional and nonjudgmental manner.

The second issue is to evaluate the level of risk. There is very limited legal risk in this situation because the patient simply was not harmed by the error. However, the ethical duty of veracity and the duty of loyalty to the employer create a tension regarding the filing of an incident report. Incident reports are necessary to protect the institution.

The nurse may be very reluctant to write an incident report about this event because it makes her look bad. Sadly, in some institutions, incident reports are used incorrectly as a disciplinary tool instead of as a method of reporting errors from which systems can be improved, so the nurse may not wish to write an incident report, but the therapist must insist in this case. In the current era, ensuring high-quality care is so important that hospitals must establish a culture in which reporting errors is encouraged and, in fact, expected as every caregiver's obligation to use the experience of errors and "near miss" errors to improve care.

Why must a report be filed regarding the current event? First, the incident carried with it a strong presumption that risk to patients was present because the nurse did not understand the limits of the technology. Second, although a bad outcome was averted, at least one unnecessary blood gas level was obtained and a second was advocated. Third, the therapist is involved because she should have checked the oximeter before doing the first blood gas measurement to determine that the equipment was operating within specifications, so there is error on both sides of the issue. Even if the nurse does not write an incident report, the incident report should be written by the therapist and the mistake disclosed to the physician. Teamwork and a commitment to high-quality care for patients requires honesty and full disclosure. Hospitals must ensure that reporting such events causes a focus on the process of care and opportunities to improve rather than on punishing the caregivers involved. When the culture is guided by the principle of justice, the result of filing an incident report will be to address any knowledge gaps among caregivers regarding oximetry but not to punish the specific nurse.

In general, incident reports are good things because they help to identify system errors and the need for education or training. They are also a valuable resource for attorneys defending medical negligence cases.

ETHICAL VIEWPOINTS AND DECISION-MAKING

In deciding ethical issues, some practitioners try to strictly interpret one or more of the aforementioned ethical principles. Other practitioners seek to decide the issue solely on a case-by-case basis, considering only the potential good (or bad) consequences. Still other practitioners would appeal to the image of a "good practitioner," asking themselves what a virtuous person would do in a similar circumstance. Finally, many practitioners acknowledge that they largely follow their intuition for making ethical decisions. These different viewpoints represent the four dominant theories underlying modern ethics.[5,13] The viewpoint that relies on rules and principles is called **formalism**, or duty-oriented reasoning. The viewpoint in which decisions are based on the assessment of consequences is called **consequentialism**. The viewpoint that asks what a virtuous person would do in a similar circumstance is called **virtue ethics**. When intuition is involved in the decision-making process, the approach is called **intuitionism**.

First of all, there is no "right" answer. The life of a 78-year-old man is no less valuable than the life of a 25-year-old woman. They are both equal under the law and from an ethical point of view, but the therapist cannot be in two places at once. Thus, irrespective of whether it is fair, a choice must be made. Triage is the principle that guides the approach to these situations. According to the 2014 Unabridged *Webster's Third New International Dictionary,* the term *triage* comes from the French verb *trier,* meaning to separate, sift, or select. Triage originated from the need to treat multiple wounded soldiers with limited resources. Wounded soldiers were initially assigned into three categories: (1) those who would likely live without medical aid, (2) those who would likely die no matter what was done, and (3) those for whom immediate treatment would likely be lifesaving. In this situation, the therapist has to sort through two choices.

MINI CLINI

Role Duty

Problem

Courtney is the lone RT on duty on the midnight shift in a small, 65-bed rural hospital. She likes working at the small hospital and knows most of the patients and their conditions by memory. The night is quiet and uneventful until 2:00 a.m., when a code is called for a patient in the intensive care unit (ICU). Courtney immediately heads for the ICU while mentally noting the condition of the patient on whom the code has been called. She remembers that the patient is 78 years old and has chronic obstructive pulmonary disease (COPD). Just as she nears the ICU, a second code is called for a patient in a room just outside of the ICU. Courtney quickly jogs her memory and remembers that this patient is a 25-year-old woman with diabetes who has just given birth to a baby girl.

Discussion Point

The lone RT can attend to only one code, although she has an obligation to provide the best care possible to all patients. There is no protocol of which the RT is aware that would provide guidance about which patient she should help first. At the time the second code is called, she is at an equal distance from both patients.

Discussion Questions

Is this RT facing an ethical dilemma? If so, what guiding principle or principles should be relied on to determine the best course of action? Which patient should the RT help first?

Guidance

The ethical dilemma here is one that arises more frequently than most clinicians realize. Fortunately, however, because it is not new, there are certain principles that can be used to help guide decision-making.

Between the two patients, there is a strong likelihood that no matter what is done for the 78-year-old patient, that patient will expire given his diagnosis and comorbidities. The young woman likely has the greatest chance for survival, so that lifesaving care will likely benefit her more than the 78-year-old patient. These are the factors that could be used to make the decision, but ultimately, the decision belongs to the therapist. No one can say whether one choice is better than the other. Ethics rarely involves the choice between good and evil, it usually involves a choice between good and better, or better and best. Because the lines are so gray, it is easy to cross them.

Formalism

Formalist thought believes that certain features of an act determine its moral rightness. In this framework, ethical standards of right and wrong are described in terms of rules or principles. These rules function apart from the consequences of a particular act. An act is considered morally justifiable only if it upholds the rules or principles that apply.

The major problem with this duty-oriented approach is the chance of inconsistency.

Consequentialism

For the consequentialist, an act is judged to be right or wrong based on its consequences. Each possible act is evaluated in terms of the relative amount of good (over evil) that it would cause. The most common application of consequentialism judges acts according to the *principle of utility*. The principle of utility, in its simplest form, aims to promote the greatest general good for most people.

Critics of this approach claim that it has two basic flaws. First, analyzing and weighing the amount of good over evil that might occur is not always possible. Second, relying on the principle of utility alone can result in actions that are incompatible with ordinary judgments about right and wrong. A classic example of this problem can be seen in the true World War II case of the battle for North Africa. In this scenario, there were two groups of soldiers but only enough antibiotics for one group. One group required the medication for syphilis contracted in the local brothels; the other group needed antibiotics for wounds sustained in battle. The dilemma arose as to who should receive the antibiotics. The actual decision in this case was based not on the desire to distribute the drug justly but rather on the need to obtain a quick victory with as few casualties as possible. The scarce medication was given to the soldiers who were "wounded" in the brothels rather than in battle because these soldiers could be restored quickly and returned to the frontlines to aid the war effort.

Mixed Approaches

Mixed approaches to moral reasoning try to take advantage of the strengths of two major lines of ethical thought. One approach, called **rule utilitarianism**, is a variation of consequentialism. Under this framework, the question is not which act has the greatest utility but which rule would promote the greatest good if it were generally followed.

To the rule utilitarian, truth-telling is necessary not because it has any underlying moral rightness but because it promotes the greatest good in professional-patient relationships. Specifically, if truth-telling were not followed consistently, trusting relationships between patients and healthcare professionals would be impossible.

The rule utilitarian approach is probably the most appealing and useful to healthcare professionals. This approach is appealing because it addresses both human rights and obligations and the consequences of actions. However, although it has some value as an ethical framework, it has the disadvantage of being quite variable among caregivers. Where caregivers have different values and different educational levels, ethical decision-making using this tool frequently is inconsistent.

Virtue Ethics

A theory of virtue ethics has evolved based in part on the limits of both formalism and consequentialism. Virtue ethics is founded not in rules or consequences but in personal attributes of character or virtue. Under this formulation, the first question is not, "How do I act in this situation?" but rather, "How should I carry out my life if I am to live well?" or "How would the good RT act?"

Virtue-oriented theory believes that professions have historical traditions. Individuals entering a profession enter into a relationship not only with current practitioners but also with the practitioners who have come before them. According to this perspective, the established practices of a profession can give guidance, without an appeal to either the specific moral principles

or the consequences of an act.[3] When the professional is faced with an ethical dilemma, he or she need only envision what the "good practitioner" would do in a similar circumstance. It is hard to imagine the good RT stealing from the patient, charging for services not provided, or smothering a patient with a pillow.

Rapidly changing fields such as respiratory care pose some problems for virtue ethics. What might be considered good ethical conduct at one time might be deemed wrong the next time. An example of this change over time is an RT who is asked not only to disconnect a brain-dead patient from a ventilator but also to remove the feeding tubes and intravenous lines.

In addition to the difficulty with changing values in virtue ethics, it provides no specific directions to aid decision-making. The heavy reliance of virtue ethics on experience rather than on reason makes creative solutions less likely. Finally, practitioners often find themselves in conflicting role situations for which virtue ethics has no answers. A good example is an RT who practices the virtue of being a good team player but is confronted with the need to "blow the whistle" on a negligent or incompetent team member.[3] Despite these limitations, virtue ethics is probably the way most practitioners make their ethical decisions.

Intuitionism

Intuitionism is an ethical viewpoint that believes that there are certain self-evident truths, usually based on moral sayings like "treat others fairly." The easiest way to understand intuitionism is to think of as many timeless sayings as you can. These sayings may range from "do not kill" to "look before you cross the street."[6] As a decision-making tool, intuitionism is not helpful, mostly because it depends on the intuitional abilities of the specific caregiver.

Comprehensive Decision-Making Models

To aid in the process of decision-making in bioethics, several comprehensive models have been developed. Fig. 5.2 shows one example of a comprehensive decision-making model that combines the best elements of formalism, consequentialism, and virtue ethics. As is evident in this approach, the ethical problem is framed in terms of the conditions and who is affected. Initially, an action is chosen based on its expected results. The possible consequences of this decision are compared with the human values underlying the problem. The short test of this comparison is a simple restatement of the golden rule, that is, "Would I be satisfied to have this action performed on me?" A simpler but nonetheless comprehensive model is used by many ethicists. The model uses eight key steps (Box 5.2).

BOX 5.2 Ethical Decision-Making Model.

1. Identify the problem or issue.
2. Identify the individuals involved.
3. Identify the ethical principle or principles that apply.
4. Identify who should make the decision.
5. Identify the role of the practitioner.
6. Consider the alternatives (long-term and short-term consequences).
7. Make the decision (including the decision not to act).
8. Follow the decision to observe its consequences.

With or without these models, RTs are often at a double disadvantage in ethical decision-making because RTs not only must live with their own decisions but also must support (and act on) the decisions of their physician colleagues. Unless excellent communication exists, misunderstandings can occur. Such misunderstandings may be an important factor in the high job stress and burnout in respiratory care.

Ethics, decision-making, and communication skills are crucial parts of training for RTs. The specialty requires practitioners who can go beyond simple assertions of right or wrong and provide justifications that are both right and reasoned. Many hospitals have ethics boards or committees to review and set policy and to assist in making informed ethical decisions. In addition to administrators and medical staff members, these committees may include a member of the lay public, a chaplain, and one or more experts in bioethics.

A major factor in the disciplinary decisions of professional boards is frequently whether the acts of the RT conformed to the ethical standards of the profession. Nearly every respiratory care practice act has ethical principles contained in the statute and codified in state regulations. Every RT should be aware of his/her state's ethical practice requirements.

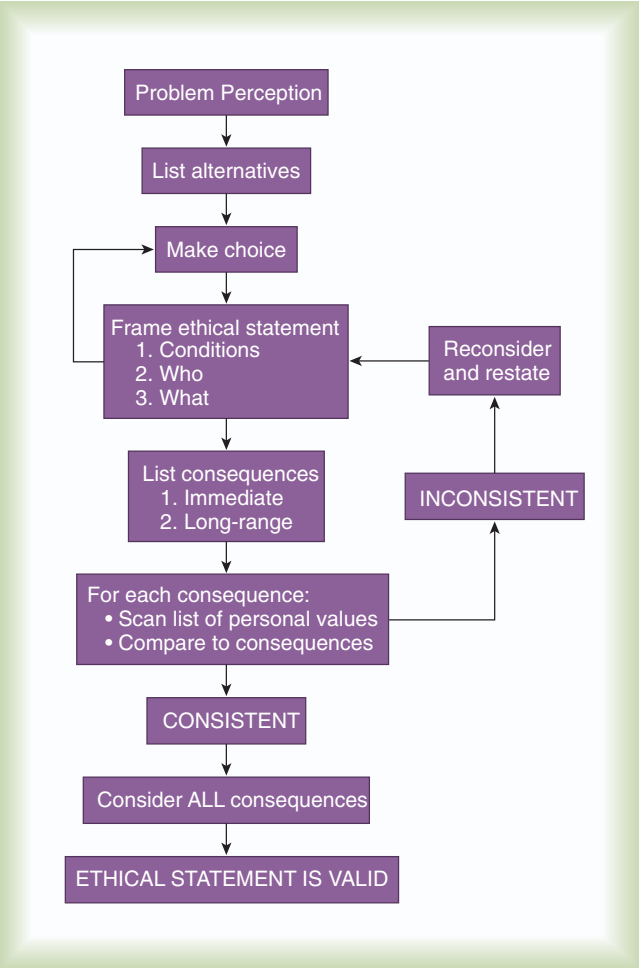

Fig. 5.2 Comprehensive ethical decision-making model. (Redrawn from Brody H: *Ethical decisions in medicine*, ed 2, Boston, 1981, Little, Brown.)

RULE OF THUMB Never attempt to make ethical decisions for others. You can make them only for yourself.

LEGAL ISSUES AFFECTING RESPIRATORY CARE

When errors in practice cause patient injury or death, the possibility of professional liability results.

Currently, many hospitals and healthcare organizations have adopted processes to lessen the risk of being sued. These quality review processes involve rapidly investigating sentinel events (an unanticipated event with serious physical or psychological consequences) and, where errors are made, telling the patient that an error has occurred followed by an immediate apology. In those instances where there is compensable injury, immediate compensation is offered. This process has reduced medical liability costs for some providers.[14-18]

Despite these processes, patient errors may lead to suits and go to the courts. The problem of professional liability in the delivery of healthcare is significant. Professional liability may contribute to increasing healthcare costs. Limits on medical liability have been key factors in recent legislation; however, these limits often suffer from constitutional flaws.[19]

Practitioners are caught in the middle. On one hand, they are required to keep costs down. On the other hand, they are faced with a level of consumerism that holds them accountable when medical errors result from scarcity of resources. Fortunately, very few cases actually wind up going to court, and most therapists will practice their entire career without ever going to court for a medicolegal claim.

Systems of Law

Under our legal system, the law is divided into two broad classes: *public law* and *civil law.* Public law deals with the relationships of private parties and the government. Civil law is concerned with the recognition and enforcement of the rights and duties of private individuals and organizations.

Public (Criminal and Administrative) Law

The two major divisions of public law are *criminal law* and *administrative law.* Criminal law deals with acts or offenses against the welfare or safety of the public. Offenses against criminal law are punishable by fines, imprisonment, or both. In these cases the accuser is the state and the person prosecuted is the **defendant**.

Administrative law consists of the countless regulations set by government agencies. Healthcare facilities face a large number of administrative and agency rules that affect almost every aspect of operation. RTs are required to abide by these rules and regulations.

Civil Law

Private or civil law protects private citizens and organizations from others who might seek to take unfair and unlawful advantage of them. If an individual believes that his or her rights have been violated, the individual can seek settlement in the civil courts. In these cases the individual bringing the complaint is known as the **plaintiff** and the individual accused of wrong is the **defendant**. Civil courts, usually in the form of juries, decide between the two parties with regard to the degree of wrong and the level of awards required. The category of civil law that is best related to respiratory care is called tort law.

Tort law. A **tort** is a civil wrong, other than a breach of contract, committed against an individual or property, for which a court provides a remedy in the form of an action for damages. Causes for the complaints may range from assault and battery to invasion of privacy. The basic functions of torts are to keep the peace between individuals and to replace vengeance between individuals with a settlement. There are three basic forms of torts: *negligent torts, intentional torts,* and torts in which liability is assessed regardless of fault (as in the case of manufacturers of defective products). The basic difference between negligent and intentional torts is the element of intent. An intentional tort always involves a willful act that violates another person's interest. A negligent tort does not have to involve any action at all. Instead, a negligent tort can consist of an omission of an action or a failure to carry out a professional duty.

Professional negligence. **Negligence** is the failure to perform one's duties competently. For example, to clarify negligence to juries in Missouri, the state's jury instructions state:

> The term *negligent* or *negligence* as used in this [these] instruction[s] means the failure to use that degree of skill and learning ordinarily used under the same or similar circumstances by the members of defendant's profession.[20]

Negligence may involve acts of commission or omission. The tort of negligence is concerned with the compensation of an individual for loss or damages arising from the unreasonable behavior of another. For example, the normal standard for the claim in an automobile accident is the duty imposed on individuals not to cause risk or harm to others, the standard being what a reasonable and prudent person should have foreseen and avoided. Professional negligence is different because the duty is defined by other professionals and, for that reason, requires expert testimony to establish.

In negligence cases the breach of duty often involves the matter of foreseeability. Cases in which the patient falls, is burned, is given the wrong medication, or is harmed by defects in an apparatus often revolve around the duty of the healthcare provider to anticipate the harm. Duty is imposed by law. Courts tell us the following about duty:

> *For purposes of determining whether a duty exists, this Court has defined foreseeability as the presence of some probability or likelihood of harm sufficiently serious that ordinary persons would take precautions to avoid it. The existence of a mere possibility is insufficient. Id. The test is not the balance of probabilities, but of the existence of some probability of sufficient moment to induce the reasonable mind to take the precautions which would avoid it.*
>
> ***Lopez v. Three Rivers Elec. Co-op., 26 S.W.3d 151, 156 (Mo. 2000)***

For the tort of negligence to be a valid claim, the four conditions listed in Box 5.3 must be met.

The assessment of what is reasonable and prudent for an RT can be determined by guidelines established by a professional

BOX 5.3 Elements of Negligence.

- The practitioner owes a duty to the patient.
- The practitioner breaches that duty.
- The breach of duty was the cause of damages.
- Damage or harm came to the patient.

group (e.g., the AARC), by direct expert testimony, or by circumstantial evidence. The legal principle ***res ipsa loquitur*** (the thing speaks for itself) may apply where a court determines under the facts that the circumstantial evidence rises to a level to permit its assertion. *Res ipsa loquitur* is sometimes invoked to show that the harm would not ordinarily have happened if the individuals in control had used appropriate care. In these cases, negligence is established by inference.

For a claim of *res ipsa loquitur* to be supported, three basic conditions must be met: (1) The harm was such that it would not normally occur without someone's negligence. (2) The action responsible for the injury was under the control of the defendant. (3) The injury did not result from any contributing negligence or voluntarily assumed risk on the part of the injured party. An example of *res ipsa loquitur* might be the failure to recognize that a patient's right main stem bronchus had been intubated with a resultant pneumothorax. For negligence to occur, the breach in duty also must cause damage or injury to the individual. The injured party must file the lawsuit within the time frame set by the statute of limitations. The term *injury,* in this sense, may include not only physical harm but also mental anguish and other invasions of the patient's rights and privileges. The claim must be established by a preponderance of the evidence to prevail. Essentially this means that a jury must be convinced that it is more likely than not that negligence occurred.

For the tort of negligence to result in liability, the breach of duty must be shown to be the cause of the injury. *Causation* revolves around whether the acts of negligence were the cause in fact and the legal cause of the damages. *Causation in fact* means simply that the negligent act of the caregiver caused the damages. *Proximate causation*, or *legal causation*, usually turns on foreseeability and whether it is fair to impose damages on a defendant.

Factual causation usually is a question for the jury. It is best illustrated in the context of a motor vehicle accident. If a car runs a stop sign but does not hit anyone, the driver may well be negligent, but no one could sue because the driver did not cause any harm. If there is a collision, there is harm flowing directly from the failure to stop. In most states the act of negligence does not have to be the only cause; it only has to be one cause. Sometimes this is referred to in jury instructions as a requirement that the defendant's actions "caused or contributed to cause" the injury. Ordering O_2 turned off on a severely hypoxemic patient might be the direct cause of the patient's injury, but the therapist's acting on that order instead of questioning it could be thought of as a contributing cause.

Proximate causation is based on foreseeability. It tends to be a retrospective analysis. If an RT fails to check a ventilator as required, it is foreseeable that the patient could develop a compromised airway and sustain brain damage or die. The RT's failure would be both the factual and the legal cause of the injury. However, proximate causation also comes into play when there are multiple wrongdoers. For example, a nurse requests a therapist's help to place a patient on the bedside commode. The therapist is unaware that the patient's systolic blood pressure is 60 mm Hg by Doppler. The patient bears down, experiences a cardiac arrest, and dies. Although the actions of the therapist in helping to move the patient to the commode are the cause in fact, the therapist might escape liability because it was not foreseeable that helping the nurse to move the patient would result in the patient's death. This is because the therapist was not aware of the blood pressure issue.

Most medical negligence lawsuits are defended by lawyers, and the first line of defense is always a claim that no matter what the medical error was, it was not the cause in fact of the patient's death. This is frequently possible because only a very limited number of patients actually get autopsies. There may be no demonstrative evidence or pathology report detailing what caused the patient's death. This is sometimes fatal to a claim of medical negligence, particularly where courts have adopted the scientific analysis set out in the Supreme Court's Daubert v. Merrell-Dow decision. In federal courts and in some state courts, the failure to have a scientific basis for an expert's opinion, one that is based on data that support the conclusions, means a jury may never hear the case.

Causation is often difficult to prove. In a situation in which the leads were reversed in a patient receiving a dual-chamber pacemaker, the heart, on autopsy, showed focal areas of inflammation. The defendant had a pathologist testify that the most likely cause of death was not the failure to place the pacemaker leads in the correct position, but rather, a particularly virulent virus (never identified) that caused rhythm disturbances and death. In nearly every case, one of the primary defenses will always be a lack of medical causation. Under the *Daubert* standards, such an opinion might not be allowed into evidence.

Damages are another factor in negligence lawsuits. There are three kinds of damages: economic, noneconomic, and punitive. Economic damages are awarded for economic loss. For example, a working wife and mother killed in a vehicular accident leaves a family without a caregiver for the children and without the $45,000 a year salary she earned. Her economic damages include both the salary figure (adjusted for inflation and wage increases over her work life) and the cost of replacing the home care she rendered to her family.

Noneconomic damages include pain, suffering, disability, disfigurement, and loss of the enjoyment of life. Although economic damages can be guided by hard numbers, juries are often left to decide the value of a person's pain or suffering. Through tort reform laws, many states have limited the amounts that can be awarded for these elements of damage, but in some states those caps have been overturned.

Punitive damages are damages that are awarded to punish wrongful conduct and discourage future unlawful conduct. Punitive damages are quite rare in medical negligence cases except where alcohol or drug use by caregivers is involved or where there is overwhelming negligence that is equivalent to intentional conduct. Some states also limit these damages.

Malpractice. **Malpractice**, as a form of negligence, can involve professional misconduct, unreasonable lack of skill or fidelity in professional duties, evil practice, or unethical conduct. There are three classifications of malpractice: (1) *Criminal* malpractice includes crimes such as assault and battery or euthanasia (handled in criminal court). (2) *Civil* malpractice includes negligence or practice below a reasonable standard (handled in civil court). (3) *Ethical* malpractice includes violations of professional ethics and may result in censure or disciplinary actions by licensure boards.

Intentional torts. An intentional tort is a wrong perpetrated by someone who intends to do the act and, possibly, intends to do the harm. Intentional torts must be intentionally performed to produce the harm or must be performed with the belief that a harmful result was likely to follow. Unlike negligent torts, intentional torts are done with the goal of producing harm. Thus, in intentional torts, both actual and punitive damages may be awarded. Examples of intentional torts are acts that involve fraud, defamation of character, invasion of privacy, deceit, infliction of mental distress, and assault and battery.

In the hospital the unwarranted discussion of the patient's condition, diagnosis, or treatment for purposes other than the exchange of information could be regarded as intentional tort. Under the general title of defamation of character are the torts of libel and slander. **Slander** is the verbal defamation of an individual by false words by which his or her reputation is damaged. **Libel** is printed defamation by written words, cartoons, and such representations to cause the individual to be avoided or to be criticized. Libel and slander do not exist unless they are seen or heard by a third person. If the practitioner directed such remarks only to the individual involved, it would not be slanderous; if the remark was made in the presence of a third party, it might constitute slander. Torts involving defamation are subject to short statutes of limitation and are generally disfavored in the law. The First Amendment to the Constitution may even provide a shield against slander or libel in many cases.

It is especially important to avoid unauthorized disclosure of patient information in cases involving diseases such as AIDS, where there may be a social or medical stigma attached. Several states currently have civil liability and criminal penalties for the release of confidential human immunodeficiency virus (HIV) test results in which the breach of confidence causes economic, psychologic, or bodily harm to the patient.

An **assault** is an intentional act that places another person in fear of immediate bodily harm. Threatening to injure someone through some overt act (e.g., swinging a bat at a person, even if it misses) is considered an act of assault. **Battery** represents unallowed, nonconsensual physical contact with another person. In the classic act of assault and battery, one individual threatens injury through some overt act (throws a punch) and injures another through an overt act (connects with the punch).

Although battery is an unusual charge against a clinician (because of the nature of the work), it creates special problems. The major element of battery is physical contact without consent. When a practitioner performs a procedure without the patient's consent, this contact may be considered battery. In most instances, there is an implied consent, created when the patient seeks care from the physician. This implied consent allows the healthcare giver to perform ordinary procedures without written consent. In all cases of unusual, difficult, or dangerous procedures, such as surgery, the courts require written consent. For this reason, to avoid being accused of battery, RTs should always explain all procedures involving physical contact to their patients before they proceed. If a patient refuses something like a blood gas test, in the absence of some other factor that makes the test absolutely necessary (such as an immediate life-threatening situation in which the patient is not competent to refuse), the patient's refusal should be honored.

There are two general defenses against intentional torts. The first defense is that there was no intent to harm and that only clinicians who engage in intentional conduct are liable. For example, if a practitioner fainted during a procedure and caused the patient injury, he or she would not be liable because the action was involuntary. The second defense is that the patient gave consent for the procedure. If the patient consented to the action, knowing the risks involved, the practitioner would not be liable.

Strict liability. **Strict liability** is a theory in tort law that can be used to impose liability without fault, even in situations in which injury occurs under conditions of reasonable care. The most common cases of strict liability are cases involving the use of dangerous products or techniques. Courts have imposed this principle on medical equipment manufacturers and on hospitals. However, strict liability generally has not been applied to actions by healthcare givers. However, medical providers can be liable under strict liability in certain circumstances.

RTs have for years modified pieces of medical equipment to perform ordered therapies. For example, inhaled pulmonary vasodilators such as nitric oxide (INO) and nebulized epoprostenol (IEPO) provide relief in cases of severe pulmonary hypertension. However, if delivery systems have been modified or "cobbled together" to provide these therapies and the equipment fails, strict liability could be the result.

Breach of contract. **Breach of contract** is a more unusual legal claim than is negligence. This claim is based on the theory that when a healthcare professional renders care, an implicit or explicit professional-patient "contract" is established. Essentially, the contract requires that the healthcare professional places the patient's welfare as the foremost concern, to act only in the patient's behalf, to protect the patient's life, to preserve the patient's health, to relieve suffering, and to protect privacy. When the patient is injured as a result of the services rendered under this contract, the patient may claim that the failure of the healthcare professional to perform the service competently is a breach of the contract. Most state laws do not permit this kind of action, and those that do require high standards for proof.

RTs are responsible for their actions, as are members of all other professions. When these actions result in the injury of another, the injured party may turn to the courts. If the RT, while acting for the physician, injures the patient through some negligent act, the patient may sue both the RT and the physician.

Civil suits. Civil action can be brought for many reasons, such as to challenge a law or to prevent an activity. However, as in the case of malpractice suits, most civil suits seek monetary

damages. The following scenario is an example of a situation that might involve the RT. The physician intends to order 0.5 mL of a bronchodilator for a 3-year-old asthmatic patient but inadvertently prescribes 5.0 mL of the drug. Because of the overdose given by the RT, the child dies.

A clearly articulated legal principle in negligence is that the more vulnerable the patient, the greater is the caregiver's duty to protect them from reasonably foreseeable harms. When the order is unclear or seems inappropriate under this principle, clinicians have an obligation to clarify the order rather than blindly give the medication and risk harm.

The suit could be brought against the physician for negligence for ordering the overdose, against the nurses and RT for failing to recognize that the dose was incorrect for the child, and, possibly, against the pharmacist for failing to gain adequate information as to the nature of the patient so that an appropriate dosage could be calculated. The plaintiff would base the secondary charges against the nurses and allied health practitioners on the theory that they missed an opportunity to correct the first wrongdoer's mistake.

Medical negligence insurance is a topic that deserves special mention here. Insurance is always based on a contract between an insurance company (insurer) and the person they insure (insured). Insurance policies are the product of negotiation between the person or entity insured and the insurer. The policy has several important parts. One names the person or entity insured. The next names the harms for which the insurance is provided, and the third provides the exclusions from coverage. For example, a hospital might buy a policy of insurance that covers the hospital and its corporate entities from claims of negligence by its employees. The policy covers the hospital, not the employees. Sometimes, however, an entity will enter into an agreement with an insurer to insure "other named insureds." In that instance it might offer protection to certain employees it names or to certain officers of the corporation, but a person is covered by an insurance policy only if they are listed or identified as a "named insured."

A healthcare organization's insurance relationship is usually managed by the risk management department. The risk manager will buy the insurance and seek legal advice from the hospital's general counsel (a law firm hired to provide advice on legal issues). Although the risk management department may tell employees that they are "covered by" the hospital's medical liability insurance, this is frequently not the case because it is a rare policy that actually names employees as named insureds. In fact, the insurance company usually has what is called a "subrogation clause" in the policy that would permit it to pursue an individual employee for indemnity or contribution in the event the insurer is forced to pay money on behalf of the hospital.

Medical liability insurance policies provide two main benefits. They provide a team of lawyers to defend any claims brought against the insured, and they provide a fund of money to pay any claims that must be paid either as a result of settlement or verdict. Under the law in most states, an insurance company has a broad duty to defend its insured.

If the hospital in which the RT works does not provide malpractice insurance for the RT by making them a named insured under the hospital's policy, then the therapist should carry their own policy of malpractice insurance. Professional liability insurance is available through the AARC's preferred provider, and it provides RTs with an attorney not only to represent them in the case of a malpractice lawsuit but also in those rare instances in which a professional board questions the conduct of the RT. All RTs should have malpractice insurance, preferably that which is personally obtained to supplement any policy of their employers. Should a judgment result, it protects the RT not only from the plaintiff but also from any settling defendant who attempts to point the finger at the RT. In addition, RTs should adhere to professional legal advice and not try to "go it alone" in a malpractice case. Sometimes well-meaning but poorly informed risk professionals tell therapists that having their own insurance is likely to get them sued. This is simply untrue.

Helping Avoid Lawsuits

There is no foolproof formula for avoiding lawsuits; the right to bring suit is protected by the United States Constitution, but the simplest and most effective way of avoiding lawsuits is both providing excellent care that meets professional standards and documenting that care carefully.

For example, in the case of routine ventilator care, frequent documentation of tube position and suctioning is vital to show that the patient's airway was protected and that therapists were aware of the patient's condition. Documentation of an Allen test before an arterial blood gas measurement shows attention to detail and documents that the patient's circulation was assessed. Knowing both what to do and how to do it are critical to avoiding litigation, but demonstrating that this knowledge was rightly applied with precise, accurate documentation is critical to establishing that a therapist acted correctly.

Another aspect of avoiding suit is to ensure that your RT license is active and that you are up-to-date with your institution's practice policies, procedures, and standards of care. A thorough understanding of national standards of care and relevant clinical practice guidelines and documented attendance at continuing education seminars also go a long way toward demonstrating professionalism.

Moreover, managing risk is important for every clinician. It should be an ongoing component of departmental operation. Risks to patients and staff should be sought out, identified, and mitigated where possible. One method of doing this is risk auditing.

A risk audit involves an objective look at the organizations practices and methods from the standpoint of both prior litigation at that facility, as well as other litigation at other facilities. Where systems have failed at other facilities, the same systems may be predicted to fail at the audited facility. Risk auditing is best done by persons who do not have a vested interest in either the organization or its constituents. As one example, a neutral risk auditor may see safety and security hazards that a hospital security office has overlooked for years. A clinician who did not write the hospital's protocols and procedures may well spot potential areas of risk that the author either did not recognize or purposefully minimized out of unconscious bias. Risk auditing is not a guarantee of risk reduction, but it is a very important part of the overall risk management process.

Ongoing quality improvement is another way to accomplish risk reduction. Measurements of quality indicators and measures of the effectiveness of quality interdiction efforts give professionals a yardstick by which to measure success. Professional development, in addition to teaching new methods and procedures, should also routinely address documentation standards and how to manage the risks associated with patient care.

Even if everyone does every possible thing right, there is no guarantee that a health professional will not be sued. Just as there are "professionals" with medical degrees who will testify that everything was done properly when standards of care were actually violated, so too are there people who are willing to say anything on behalf of a plaintiff in a lawsuit. Once a professional satisfies the baseline requirements of an expert witness (skill and expertise in the field and exposure to the facts of the case sufficient to form an opinion), in most cases his or her opinion will become evidence in a malpractice suit. Notably, federal courts adopted the Daubert standard for expert testimony several years ago and have demanded that professionals testifying bring with them some evidence that their opinion is not based on unscientific personal opinions. More state courts are adopting this standard as well, and this may make it more difficult for experts on both sides of litigation to manufacture expert opinions out of whole cloth. Still, malpractice insurance as well as having a good legal team are the best safeguards a clinician has to protect against liability.

Not all cases wind up in court. Sometimes, when the parties are willing, a lawsuit can be avoided with mediation, whereby all involved parties agree to settle a case outside of the courts under specified terms. However, when any potential legal claim or lawsuit surfaces, decisions about how to proceed should be made only with full input of institutional risk management and legal counsel experienced in professional negligence defense.

In recent years, the experience of several large hospital systems has suggested that active risk management practices and appropriate patient experience policies are two of the most effective tools to prevent malpractice litigation. Unhappy patients are identified quickly, and corrective action is undertaken immediately. A commitment to a great patient experience will produce listening that often results in better clinical decision-making, thereby lessening the risk of a malpractice lawsuit. The best way to avoid a malpractice suit is to develop a good, sound relationship with the patient that communicates to the patient that he or she is important and valued.

Health Insurance Portability and Accountability Act of 1996

In August 1996, the U.S. Congress enacted HIPAA,[21] which required, among other things, the establishment of Standards for Privacy of Individually Identifiable Health Information. These standards, which have become known as the Privacy Rule, strengthened the need to treat medical records and information as confidential. The primary goal of the rule was to strike a balance between protecting individuals' health information and not impeding the exchange of information needed to provide quality healthcare and protect the public's health and well-being.

The Privacy Rule applies to all healthcare providers, health plan providers (with some exceptions, such as small employer plans with fewer than 50 participants administered solely by the employer), and healthcare clearinghouses. An example of a healthcare clearinghouse is an entity that processes insurance claims for payment. The basic goal of the Privacy Rule is to protect all "individually identifiable health information," commonly referred to as *protected health information*. Protected information includes any record or information that would or could identify or reveal: (1) an individual's past, present, or future physical or mental health or condition; (2) the provision of healthcare to the individual; or (3) the past, present, or future payment for the provision of healthcare to the individual. Protected health information includes information in any format, which may include patient charts (electronic or paper), faxes, e-mails, or other records. The Privacy Rule specifies proper methods for the normal and appropriate conduct of healthcare treatment and business for all "covered entities," individuals, and organizations that have a legitimate need to access and use the information. Consent of the individual is not required for these covered entities.[22]

Medical Supervision

RTs are required by their scope of practice to work under competent medical supervision. This requirement creates not only a professional relationship but also a legal one. If the RT is employed by the physician, the physician is liable under the doctrine of *respondeat superior* for the RT's actions. If the RT is employed by the hospital, the hospital is liable for the RT's actions for the same reason. Under the laws of some states, the supervising physician may still be liable even if the RT is employed by the hospital where the legal theory involves a failure to supervise.

Simply because you know Ms. Smith and her family, it is not sufficient to disclose information. Written authorization is required by HIPAA. Verbal authorizations are not permitted because: (1) you have no way to prove that it happened, and (2) the patient may later change his or her mind or forget who was authorized. Thus, until you know that the person is authorized in writing to receive the information, you may not disclose protected health information.[22]

Even though it may be difficult to tell a family member of a patient that you cannot share information over the phone, that is the answer that you must give. You may not say that Ms. Smith is in the bathroom because it is not true. There is no ethical exception that permits lying to family members. Lying erodes trust in the healthcare system.

Under the doctrine of medical supervision, the physician assumes responsibility for the wrongful actions of the RT as long as such negligence occurred in the course of the employer-employee relationship. For this liability to apply, two conditions must be met: (1) the act must be within the scope of employment, and (2) the injury caused must be the result of an act of negligence. If the RT acted outside of his or her scope of practice, as outlined by licensure laws or by institutional regulations, the court would have to decide whether the physician would still be liable. If the RT, while in the patient's room to deliver an aerosol treatment, went beyond the normal scope of practice and adjusted

MINI CLINI

Health Insurance Portability and Accountability Act

Problem

You, the RT, are in Ms. Smith's room tending to her respiratory equipment when the telephone rings. Ms. Smith and some of her family members are well known to you because of her many previous hospitalizations. During this hospitalization, Ms. Smith's condition has progressively worsened, and today has been a particularly bad day for her. At this point, she is having serious difficulty moving and even talking. As the telephone rings, she looks at you and in a barely audible voice asks you to please answer the telephone. You do so, and the person on the other end identifies herself as Ms. Smith's granddaughter. You tell Ms. Smith that her granddaughter is on the telephone, but Ms. Smith simply looks away. You tell the granddaughter that Ms. Smith cannot talk right now and to call back later. The granddaughter asks you why Ms. Smith cannot talk, along with a series of specific questions about her condition.

Discussion

As the RT, how should you handle this situation?

1. What HIPAA guidelines, if any, are applicable in this case?
2. Because you know Ms. Smith and her family, is it permissible to answer the granddaughter's questions?
3. To avoid alarming the granddaughter, should you say Ms. Smith is asleep or in the bathroom?

Guidance

The first question is whether HIPAA applies. HIPAA pertains to "the individual's past, present or future physical or mental health or condition." HIPAA requires that protected healthcare information never be disclosed to those who are not authorized to receive it, and the rule requires a written authorization of who can receive protected health information by the patient. Until you verify that the person on the other end of the phone is authorized in writing to receive information, you cannot disclose anything. You also may have no way of knowing whether this really is the granddaughter of the patient, even if you think you recognize the voice. The hospital has specific policies regarding the release of information, and you must follow those to protect yourself from any allegation of wrongdoing.

cervical traction, causing injury, it is doubtful that the physician could be held fully responsible. However, the hospital, as a corporate entity, could be held responsible for the actions of its employees.

Historically, RTs have not been named individually as defendants in malpractice cases because the law generally has not focused on their role as specialized healthcare providers separate from the healthcare facility. Either the hospital or the physician is usually named as the defendant for the acts of the practitioner. RTs in these cases have been viewed simply as employees, merely carrying out the orders of a supervising physician. However, with the increased application of state licensure regulations governing respiratory care, and especially with the development of respiratory care protocols giving RTs more autonomy, this relative protection from liability is changing rapidly. As RTs are given more discretion and are permitted to exercise independent judgment, their decision-making is likely to be more frequently called into question in court.

Scope of Practice

One measure of professionalism is the extent to which the group is willing to direct its own development and regulate its own activities. This self-direction is carried out mainly through professional associations and state licensure boards, which try to ensure that professionals exhibit minimum levels of competence.

Basic elements of a practice act. Some practice acts emphasize one area over another, but most acts address the following elements:

- Scope of professional practice
- Requirements and qualifications for licensure
- Exemptions
- Grounds for administrative action
- Creation of examination board and processes
- Penalties and sanctions for unauthorized practice

Licensure laws and regulations. In licensure legislation, there is always a clause specifying a scope of practice. The scope-of-practice statutes give general guidelines and parameters for the clinician's practice. Deviation from these statutes could create legal risk. Ideally, the original language of a licensure law should be broad enough to account for changes in practice without requiring continual updating. Continuing education and regular review of the practice act are essential to ensure compliance with both the statute and evolving rules of the practice act.

Providing emergency care without physician direction. One unique area that allows practice without the direction of a competent physician is that of rendering emergency medical care to injured persons. Good Samaritan laws protect citizens from civil liability for any errors they make while attempting to give emergency aid. Most states have legislated Good Samaritan statutes to encourage individuals to give needed emergency medical assistance. It is necessary for this aid to be given in good faith and free of gross negligence or willful misconduct. However, it is unlikely that the RT would be protected for giving aid that went beyond the expected skills of the individual or aid that went beyond that which could be defined as first aid. For example, risks of an RT's performing a tracheostomy would likely not be protected under Good Samaritan rules, which generally apply only to roadside accidents and emergency situations outside the hospital.

INTERACTION OF ETHICS AND THE LAW

A good example of the interaction of ethics and the law in respiratory care is the growth of the field into home care and durable medical equipment supply. This growth has led to new relationships between these elements of the healthcare system and has created the potential for unethical and unlawful activity. If a practitioner accepts some payment, such as a finder's fee or percentage of the total lease costs for referring patients to a particular home care company or equipment service, he or she should be prepared to face charges of unethical and perhaps illegal practice.

Several federal and many state statutes address the legality of such transactions. In general, these statutes say that knowingly

or willfully soliciting, receiving, offering, or paying directly or indirectly any payment in return for Medicare business is a crime. Violation of these statutes carries for a possible prison sentence, a substantial fine, or both. In addition, violation of the statutes by an organization can result in exclusion from Medicare and other federal healthcare programs.

In recent years, hospitals have been encouraged to appoint a corporate compliance officer (CCO) to oversee the hospital's business practices and ensure that the hospital conforms to the law. Most hospitals use a toll-free anonymous number to allow employees who wish to remain anonymous to report wrongful activity. If the practitioner is aware of others who are engaged in these practices, he or she should report these activities to the appropriate state or federal healthcare agency. To aid the clinician in maintaining an ethical stance on these new issues, the AARC has established a position statement about ethical performance of respiratory home care.

PROFESSIONAL LICENSURE ISSUES

Because nearly every state has currently passed some form of licensure for RTs, more RTs are being disciplined for various offenses related to the practice of respiratory care. Fortunately, most RTs serve their entire professional careers and never have a problem with their professional boards. There are four significant things that RTs can be aware of now that would help prevent problems with their professional boards later.

Licensure Statute

All RTs should know in detail the requirements of their respiratory care practice act. They should know what is expected of them in terms of obtaining licensure and in the requirements to remain licensed. Some states require that RTs report certain behavior, such as violation of statutes by another RT. The California Respiratory Care Act states that the supervisors of RTs terminated for cause should be reported to the state as well.

The second thing that all RTs should do to protect themselves against licensure issues is to purchase an insurance policy that covers professional discipline. Most policies available for purchase by RTs provide coverage of both malpractice liability and professional discipline.

Understanding the Causes of Discipline

A review of professional discipline cases available from publicly available sources, including the California Board for Respiratory Care, reveals that the most frequent causes of professional discipline are as follows:

- Substance abuse
- Domestic violence
- Sexual abuse
- Gross incompetence

Even in cases in which the cause of discipline is domestic violence or sexual abuse of another person, some form of substance abuse is often a contributing factor. Alcohol violations (driving while intoxicated, driving while impaired) are often the most frequent violation that bring an RT face to face with his or her professional board. RTs with alcoholism or a significant drug habit are almost certain to come before their professional board. Sometimes, employers and supervisors take the position that as long as such a problem does not affect a person's work at the facility, they should not address it. However, even in cases in which an RT does not use drugs or alcohol at work, the disease process is affecting his or her judgment and decision-making and should be addressed. A supervisor who fails to report a substance abuser of any kind is asking for legal trouble, in the form of either a damages lawsuit or a visit from the professional board. Academic RTs should be especially vigilant with students and should insist on substance abuse counseling for any student who appears to have such a problem.

Any good attorney will tell you that it is far better to defend a wrongful termination lawsuit than a wrongful death lawsuit. If you are wrong about the termination, the employee can be rehired. There is no remedy for the patient when an employee's substance abuse leads to a patient's death.

Engaging Counsel

If approached by the professional board, an RT should never talk to investigators without having an attorney present. Every investigation is, by its nature, oppressive and burdensome, and an attorney ensures that the RT's rights are respected and protected. Often in cases in which an RT has allegedly violated the professional code or engaged in conduct that merits discipline, an attorney can help negotiate a better resolution than the RT could without the help of a professional.

RESPIRATORY THERAPISTS WHO SPEAK OUT ABOUT WRONGDOING

RTs are in a unique position to help protect patients from multiple harms. Sometimes, RTs have a duty to speak out about problems or issues in the department under the protocols of the institution for addressing these concerns. Usually working with a CCO is the most effective way to affect change inside an organization. However, sometimes the person who speaks out and identifies a problem faces retaliation. Several federal laws protect RTs who, because of their respect for ethical issues, speak out about wrongdoing. However, although these statutes may offer a cause of action for damages after a wrongful termination, they are generally ineffective in preventing termination. One should not assume that because a law says retaliation is unlawful that individuals might nonetheless decide to take their chances and fire a whistleblower.

Patient Protection and Affordable Care Act

In 2010 Congress passed the PPACA in an attempt to reform healthcare. Challenges to the PPACA are still finding their way through the state and federal courts, and results to date have been mixed. One thing that the statute did was improve whistleblower protections for hospital workers. Section 1558 of the PPACA amends the *Fair Labor Standards Act* of 1938 (FLSA) stating that an employer cannot discriminate "against any employee with respect to his or her compensation, terms, conditions, or other privileges of employment" because the employee, among other things:

1. Provided, caused to be provided, or is about to provide or cause to be provided to the employer, the Federal Government, or the attorney general of a state information relating to the violation of, or any act or omission the employee reasonably believes to be a violation of, any provision of this title;
2. Actually did or is about to assist, participate, or testify in a proceeding about such violation; or
3. Objected or refused to participate in any activity or task that the employee "reasonably believed" to be in violation of the statute or any rule or regulation promulgated under the statute.

Any employee who believes that he or she has been discharged or discriminated against in violation of the FLSA is entitled to seek relief using the extensive whistleblower protections contained in the *Consumer Product Safety Improvement Act* of 2008. These procedures include filing a complaint concerning discrimination or retaliation with the Department of Labor, going through an administrative process to determine whether the employee's conduct was "a contributing factor in the unfavorable personnel action" alleged by the employee, and providing for the filing of a civil action in federal court after exhaustion of the administrative remedies provided by the statute.

National Labor Relations Act

Although the *National Labor Relations Act* (NLRA) is usually thought of as a "union" statute, the NLRA provides protections to hospital workers whether they are organized into a union or not. Specifically, the NLRA provides for protection where a worker engages in actions for the benefit of all employees. For example, when an RT approaches the supervisor on behalf of all the workers on the second shift to request that shift differentials be increased, that RT—who is engaged in what is called "protected concerted activity"—cannot be discharged for acting on behalf of the other RTs in the department. When an RT is discharged for such an offense, the RT has 180 days in which to make a complaint to the local office of the NLRA. No attorney is necessary to make such a complaint.

False Claims Act

Buried in the banking section of the United States Code is a little-known statute called the *False Claims Act* (FCA) (31 USC §3729).

Perhaps the most powerful part of the statute is the part that permits an employee with knowledge of fraud or false billing to file a lawsuit against the company or organization engaging in fraud. For example, when an emergency medical technician (EMT) knows that his employer is giving away free ambulance services to nursing homes in exchange for the Medicare business of the nursing homes, the EMT could file an FCA case against the employer. If the EMT then follows with a lawsuit against the ambulance company for such false billing or claim, it is known as a ***qui tam*** (Latin for suing for one's self). Often the plaintiff, or the person initiating the lawsuit, may be entitled to a percentage of the financial amount recovered.

The government investigates such lawsuits and frequently intervenes in them. Where the government intervenes, the employee who blows the whistle stands to receive an award of up to 25% of the amount the government recovers. In recent years the United States has recovered greater than $3 billion in fraudulently paid claims, most of which came from employees who blew the whistle on the fraud of their employers or competitors.

Much like the PPACA and the Civil Rights Act, the FCA prohibits retaliation against employees who report fraud.

HEALTHCARE AND CHANGE

The healthcare industry is experiencing rapid change relating to how services are funded and how patients and healthcare workers interact. These changes are occurring at the same time that ethical demands of practice are also increasing.

Socrates demanded that professionals acknowledge the social context of their activities and recognize their obligations toward the segment of society that they profess to serve. As this analysis of ethical reasoning and the law has made clear, only by identifying, justifying, and prioritizing basic principles of human values can the RT resolve the difficult questions of professional behavior consistently. To the extent that clearly stated principles guide our choices and actions, all parties involved will be well served.

RULE OF THUMB The letters RCP are used to indicate "respiratory care practitioner." They also suggest three important characteristics of the RT when confronted with ethical dilemmas:

- *R*espect
- *C*ompassion
- *P*rofessionalism

Healthcare Advance Directives

Recognizing the right of competent adults to exercise choices concerning their healthcare, all 50 states and the District of Columbia have adopted some form of healthcare advance directives. As discussed in Chapter 58, the advance directive instruments are state regulated.

SUMMARY CHECKLIST

- Ethical dilemmas occur when there are two equally desirable or equally undesirable choices. Ethical dilemmas may involve situations that are either legal or illegal.
- Ethical dilemmas in respiratory care involve scope of practice, confidentiality, working within levels of professional responsibility, professional development issues, staffing patterns, or recordkeeping.
- Professional codes of ethics are general guidelines established to identify ideal behaviors of members of a professional group. These codes are often simplistic and tend to deal with behavior over which there is little disagreement.
- Traditional ethical principles are rooted in philosophical thought and include autonomy, beneficence, confidentiality, role fidelity, justice, nonmaleficence, and veracity. These principles are used in the ethical decision-making process.

- There are two basic ethical theories: formalism and consequentialism. The most commonly used ethical decision-making model is the mixed approach. The mixed approach combines components of formalism, consequentialism, and modern decision-making theory.
- The basic information that must be identified before a reasoned ethical decision is made includes the problem or issue, the individuals involved, and the ethical principle or principles that apply; a determination of who should make the decision; and the role of the practitioner.
- Public law deals with the relationships of private parties and the government. Civil law is concerned with the recognition and enforcement of the rights and duties of private individuals and organizations.
- Professional malpractice is negligence in which a professional has failed to provide the care expected, resulting in harm to someone. Examples of situations that RTs might encounter include attempting procedures beyond the practitioner's skill level, failure to perform a duty as assigned, or failure to perform the duty correctly.
- Like members of other professions, RTs are responsible for their actions. If their actions result in injury to others, the injured party or parties are entitled to seek redress in the courts.
- A professional license provides a framework under which a licensee carries out his or her duties. Because licensure acts define who can perform specified duties, it is expected that the duties will be performed in a responsible manner and the professional will be responsible for his or her actions. The purpose of licensure is to provide for the public's safety. The best ways for RTs to avoid medicolegal risk are to practice competently within the scope of practice and to document care that was delivered.
- Patients nowadays are better educated and hold higher expectations from healthcare practitioners. Many patients are assuming responsibility for their own healthcare, placing the healthcare practitioner into the role of consultant.

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6

Physical Principles of Respiratory Care

Daniel F. Fisher

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Describe the properties of gases
- Discuss three common temperature scales and how to convert from one system to another
- Describe the mechanisms of heat transfer
- Describe the properties of liquids and how these properties influence flow
- Describe those factors that affect pressure within a liquid
- Discuss what surface tension is and its relationship to radius of an object
- Describe the mechanisms responsible for the change of state to a vapor and the energy required to make the transition
- Describe the effects that both vaporization and condensation have on internal energy
- Describe the factors that influence the capacity of air to hold water vapor
- Describe the concept of relative humidity and how it is determined
- Describe gas diffusion and what
- Discuss the application of Dalton's law of partial pressures
- Describe how gases can dissolve into liquids and what affects its solubility
- Discuss the combined gas laws and the interrelationships between temperature, pressure, and gas volume
- Describe the concepts of both critical temperature and critical pressure
- Describe various kinds of fluid flow and what causes a transition from one kind of flow to another
- Describe how Boyle's law is applied
- Describe the changes to pressure in a fluid when flow is increased
- Describe the Venturi effect

CHAPTER OUTLINE

KEY TERMS

absolute humidity
adiabatic
adhesion
ATPS
Avogadro constant
Avogadro's law
Bernoulli principle
boiling point
Boyle's law
BTPS
buoyancy
capillary action
Charles law
Coanda effect
cohesion
condensation
conduction
convection
convection currents
critical temperature
Dalton's law
density
dew point
diffusion
evaporation
flow resistance
fractional concentration
Gay-Lussac's law
Graham's law
Henry's law
hygrometer
humidity deficit
jet entrainment
Joule-Thompson effect
kinetic energy
laminar flow

Laplace's law
latent heat of fusion
latent heat of vaporization
law of continuity
laws of thermodynamics
melting point
meniscus
molar volume
partial pressure
Pascal's principle
percent body humidity
Poiseuille's law
pressure
polycythemia
potential energy
radiation
Raynold's number relative humidity (RH)
shear rate
solubility coefficient
specific gravity
STPD
strain-gauge pressure transducers
sublimation
surface tension
tension
thermal conductivity
thermodynamics
turbulent flow
van der Waals forces
vaporization
Venturi effect
viscosity
water vapor pressure

STATES OF MATTER

There are three primary states and one secondary state of matter: solid, liquid, gas, and plasma. Fig. 6.1A–D depicts simplified models of these states of matter.

Solids have a fixed volume and shape. The molecules that make up the solid have the shortest distance to travel until they collide with one another. This motion has been referred to as a "jiggle." Solids have a high degree of internal order; their atoms or molecules are limited to back-and-forth motion about a central position, as if held together by springs (see Fig. 6.1A). Solids maintain their shape because their atoms are kept in place by strong mutual attractive forces, called ***van der Waals forces***.[1]

Liquids have a fixed volume but adapt to the shape of their container. If a liquid is not held within a container, the shape is determined by numerous internal and external forces. Liquid molecules exhibit mutual attraction. However, because these forces are much weaker in liquids than in solids, liquid molecules can move about freely (see Fig. 6.1B). This freedom of motion explains why liquids take the shape of their containers and are capable of flow. However, similar to solids, liquids are dense and cannot be compressed easily.

In a *gas,* molecular attractive forces are very weak. Gas molecules, which lack restriction to their movement, exhibit rapid, random motion with frequent collisions (see Fig. 6.1C). Gases have no inherent boundaries and are easily compressed and expanded. Similar to liquids, gases can flow. For this reason, both liquids and gases are considered fluids. Gases have no fixed volume or shape. Both of these qualities depend on local conditions for the gas.

Plasma has been referred to as a fourth state of matter. Plasma is a combination of neutral atoms, free electrons, and atomic nuclei. Plasmas can react to electromagnetic forces and flow freely, similar to a liquid or a gas (see Fig. 6.1D). Although

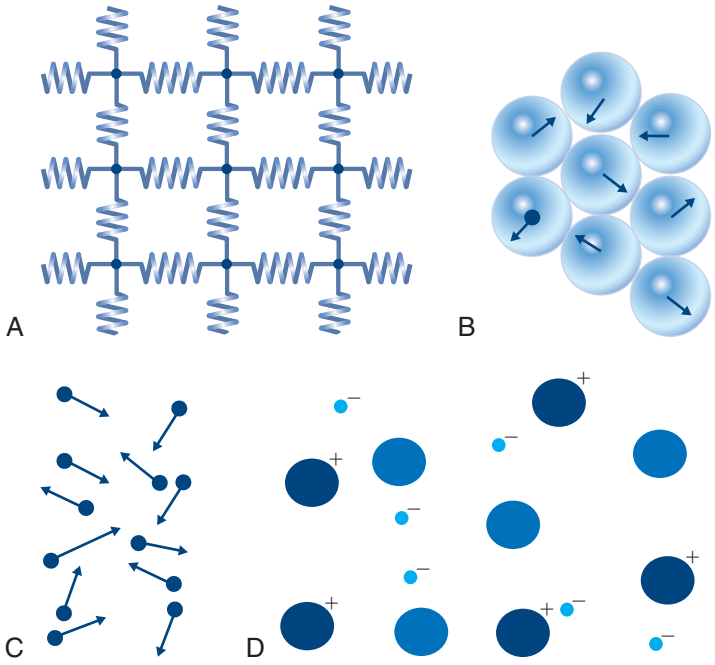

Fig. 6.1 Simplified Models of the Four States of Matter. (A) Solid (rigid network of interconnected springs). (B) Liquid (freely moving spheres with no space among them). (C) Gas (small rapidly moving particles with a lot of space among them). (D) Plasma (small rapidly moving charged particles with a lot of space among them).

mentioned here for the sake of completeness, plasmas are not discussed further because at this time they are not known to be relevant to the practice of respiratory care.

Internal Energy of Matter

The atoms that make up all matter are in constant motion at normal temperatures.[2] This motion results from *internal energy*. There are two major types of internal energy: (1) **potential energy** and (2) **kinetic energy**. Potential energy is referred to as the energy of position—that is, the energy possessed by an object balanced on a shelf. Potential energy is a result of the strong attractive forces between molecules. These intermolecular forces are why solids are rigid and liquids have viscosity and cohesiveness. These same intermolecular forces are not as strong in gases. Kinetic energy is the energy of motion, such as that of a falling object. Most internal energy in gases is in the form of kinetic energy.

Laws of Thermodynamics

The term **thermodynamics** can refer to either the science of studying the properties of matter at various temperatures or the kinetics (speed) of reactions of matter at various temperatures. From the study of physics, we take special notice of the **laws of thermodynamics**. These laws describe how fundamental physical quantities (temperature, energy, and entropy) behave under various circumstances and forbid certain phenomena (such as perpetual motion). A basic knowledge of these principles is helpful in understanding many aspects of respiratory care. Of particular interest is the first law of thermodynamics, one version of which states that an increase in the internal energy of a closed system can only be the result of work performed on the system. Work can be viewed as the process of transferring energy to or from a system. The increase in internal energy of a system can be observed as an increase in heat (as with a humidifier) or pressure (as during mechanical ventilation).

Heat Transfer

When two objects exist at different temperatures, the first law of thermodynamics tells us that heat will move from the hotter object to the cooler object until both objects' temperatures are equal. This is an example of transitioning from a higher state of energy to a lower state. Two objects with the same temperature exist in thermal equilibrium. Heat can be transferred in four ways: (1) *conduction,* (2) *convection,* (3) *radiation,* and (4) *evaporation and condensation*.

Conduction

Heat transfer in solids occurs mainly via conduction. **Conduction** is the transfer of energy by direct contact between hot and cold molecules. How well heat transfers by conduction depends on both the number and the force of molecular collisions between adjoining objects.

Heat transfer between objects is quantified by using a measure called ***thermal conductivity***. Table 6.1 lists the thermal conductivities of selected substances in centimeter-gram-second (cgs) system units. As is evident, solids (especially metals) tend to have high thermal conductivity. This is why metals feel cold to the touch even when they are at room temperature. In this case, the high thermal conductivity of metal quickly draws heat away from the skin, creating a feeling of "cold." In contrast, with fewer molecular collisions than in solids and liquids, gases exhibit low thermal conductivity.

TABLE 6.1 Thermal Conductivities in (cal/s)/(cm² °C/cm)

Material	Thermal Conductivity (k)
Silver	1.01
Copper	0.99
Aluminum	0.50
Iron	0.163
Lead	0.083
Ice	0.005
Glass	0.0025
Concrete	0.002
Water at 20°C	0.0014
Asbestos	0.0004
Hydrogen at 0°C	0.0004
Helium at 0°C	0.0003
Snow (dry)	0.00026
Fiberglass	0.00015
Cork board	0.00011
Wool felt	0.0001
Air at 0°C	0.000057

From Nave CR, Nave BC: *Physics for the health sciences,* ed 3, Philadelphia, 1985, WB Saunders.

Convection

Heat transfer in both liquids and gases occurs mainly by convection. **Convection** involves the mixing of fluid molecules at different temperatures. Although air is a poor heat conductor (see Table 6.1), it can efficiently transfer heat by convection. To do so, the air is first warmed in one location and then circulated to carry the heat elsewhere; this is the principle behind forced-air heating in houses and convection heating in infant incubators. Fluid movements carrying heat energy are called *convection currents*.

Radiation

Radiation is another mechanism for heat transfer. Conduction and convection require direct contact between two substances, whereas radiant heat transfer occurs without direct physical contact. Heat transfer by radiation occurs even in a vacuum, as when the sun warms the earth.

The concept of radiant energy is similar to that of light. Radiant energy given off by objects at room temperature is mainly in the infrared range, which is invisible to the human eye. Objects such as an electrical stove burner or a kerosene heater radiate some of their energy as visible light. In the clinical setting, radiant heat energy is commonly used to keep newborn infants warm.

Evaporation and Condensation

Vaporization is the change of state from liquid to gas. Vaporization requires heat energy. According to the first law of

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Problem

Bulk storage of oxygen in liquid form for hospitals consist of two basic components, a large tank to hold the liquefied gas and a vaporizer, which is a tower containing radiator fins. The liquid oxygen flows from the bulk storage unit into the vaporizer, which allows ambient temperatures to heat the liquid, converting it into gas. This is an efficient method to store a large quantity of oxygen in a relatively small space. For more information on the bulk storage of medical gases, see Chapter 41.

Discussion

The liquefication of gases depends on two factors; a critical temperature and a critical pressure. Without one, the gas will not change to a liquid. The molecules of a liquid are closer together than those of a gas. The **density** of liquid oxygen is about 1000 times greater than that of gaseous oxygen.

thermodynamics, that energy must come from the surroundings. This phenomenon is illustrated by the bulk storage of oxygen at hospitals and health care facilities. In such cases, large quantities of compressed and liquefied oxygen is kept in tanks; it is then exposed to ambient temperatures and vaporized into its gaseous form in order to be made available for patient use (see Chapter 41). In one form of vaporization, called *evaporation*, heat is taken from the air surrounding the liquid, cooling the air. In warm weather or during strenuous exercise, the body takes advantage of this principle of *evaporative cooling* by producing sweat. The liquid sweat evaporates and cools the skin.

Condensation is the opposite of evaporation. In condensation, gases become liquids. Because vaporization takes heat from the air around a liquid (cooling), condensation must give heat back to the surroundings (warming). A refrigerator (or air conditioner) works on the principle of repeated vaporization cycles. The food cools as it passes energy through the walls of the refrigerator into pipes containing condensed refrigerant. The refrigerant warms, vaporizes, and expands. Then a compressor condenses the refrigerant again, releasing heat that is carried away to the atmosphere by a radiator. The condensed refrigerant is then passed by the food and the cycle repeats. The whole system is basically a heat pump transferring thermal energy from the food to the atmosphere. The next section expands on the concept of change of state and provides more detail on the processes of vaporization and condensation.

Temperature

Temperature and kinetic energy are closely related.[2] Temperature is a measurement of heat. Heat is the result of molecules colliding with one another. The temperature of a gas, with most of its internal energy spent keeping molecules in motion, is directly proportional to its kinetic energy. In contrast, the temperatures of solids and liquids represent only part of their total internal energy.

Absolute Zero

In concept, absolute zero is the lowest possible temperature that can be achieved. That is the temperature at which there is no kinetic energy. Because there is no energy, the molecules cease to vibrate and the object has no heat that can be measured. This temperature is defined to be absolute zero. Although researchers have come close to attaining absolute zero, no one has actually achieved it; this is due to the third law of thermodynamics, which states that absolute zero is impossible to achieve.

Temperature Scales

Multiple scales can be used to measure temperature. The Fahrenheit and Celsius scales are based on properties of water (freezing and boiling). A third scale, the Kelvin scale, is based on molecular motion. Absolute zero provides a logical zero point on which to build a temperature scale. In the International System of Units (SI), temperature is measured in Kelvin (K), with a zero point equal to absolute zero (0 K).[3-7] Because the Kelvin scale has 100 degrees between the freezing and **boiling points** of water, it is a centigrade, or 100-step, temperature scale. The Kelvin scale has the unique quality of being based on the triple-point definition for water (the temperature at which all three phases of water exist). This temperature happens to be approximately 273 K (0.0°C).[5-7]

The cgs temperature system is based on Celsius (C) units. Similar to the Kelvin scale, the Celsius scale is a centigrade scale (100° between the freezing and boiling points of water). However, 0°C is not absolute zero but instead is the freezing point of water.

In Celsius units, kinetic molecular activity stops at approximately −273°C. Therefore 0 K equals −273°C, and 0°C equals 273 K. To convert degrees Celsius to degrees Kelvin, simply add 273:

$$K = °C + 273$$

For example:

$$25°C = 25 + 273 = 298\,K$$

Conversely, to convert degrees Kelvin to degrees Celsius, you simply subtract 273. For example:

$$310\,K = 310 - 273 = 37°C$$

The Fahrenheit scale is the primary temperature scale in the foot, pound, and second (fps) or British system of measurement. Absolute zero on the Fahrenheit scale equals −460°F.

To convert degrees Fahrenheit to degrees Celsius, use the following formula:

$$°C = (°F - 32)/1.8$$

For example:

$$°F = 98.6$$

$$°C = (98.6 - 32)/1.8$$

$$°C = 37$$

To convert degrees Celsius to degrees Fahrenheit, simply reverse this formula:

$$°F = (1.8 \times °C) + 32$$

For example:

$$°C = 100$$

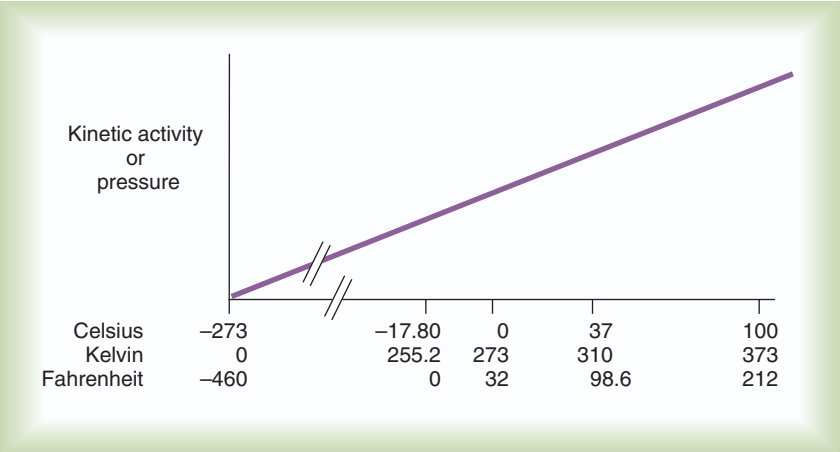

Fig. 6.2 Linear Relationship Between Gas Molecular Activity, or Pressure, and Temperature. The graph shows comparable readings on three scales for five temperature points.

$$°F = (1.8 \times 100) + 32$$

$$°F = 212$$

Fig. 6.2 shows the relationship between the kinetic activity of matter and temperature on all three common temperature scales. For ease of reference, four key points are defined: (1) the zero point of each scale, (2) the freezing point of water (0°C), (3) body temperature (37°C), and (4) the boiling point of water (100°C).

CHANGE OF STATE

All matter can change state. Because respiratory therapists work extensively with both liquids and gases, they must have a good understanding of the key characteristics of these states and the basic processes underlying their phase changes.

Liquid-Solid Phase Changes (Melting and Freezing)

When a solid is heated, its molecular kinetic energy increases. This added internal energy increases molecular vibrations. If enough heat is applied, these vibrations eventually weaken the intermolecular attractive forces. At some point molecules break free of their rigid structure and the solid changes into a liquid.

Melting

The changeover from the solid to the liquid state is called *melting*. The temperature at which this changeover occurs is the **melting point**.[2] The range of melting points is considerable. For example, water (ice) has a melting point of 0°C, carbon has a melting point of greater than 3500°C, and helium has a melting point of less than −272°C.

Fig. 6.3 depicts the phase change caused by heating water. At the left origin of −50°C, water is solid ice. As the ice is heated, its temperature increases. At its melting point of 0°C, ice begins to change into liquid water. However, the full change to liquid water requires additional heat. This additional heat energy changes the state of water but does not immediately change its temperature.

The extra heat needed to change a solid to a liquid is the **latent heat of fusion**. In cgs units, the latent heat of fusion is defined as the number of calories required to change 1 g of a solid into a liquid without changing its temperature. The latent heat of fusion of ice is 80 cal/g, whereas the latent heat of fusion of oxygen is 3.3 cal/g. This change of state, compared with simply heating a solid, requires enormous energy.

RULE OF THUMB The latent heat of fusion of ice is 80 cal/g, which is about 24 times more than the latent heat of fusion of oxygen, which is why oxygen is a gas at room temperature and ice becomes a liquid.

Freezing

Freezing is the opposite of melting. Because melting requires large amounts of externally applied energy, you would expect freezing to return this energy to the surroundings, and this is exactly what occurs. During freezing, heat energy is transferred from a liquid back to the environment, usually by exposure to cold.

As the kinetic energy of a substance decreases, its molecules begin to regain the stable structure of a solid. According to the first law of thermodynamics,[4] the energy required to freeze a substance must equal that needed to melt it. The freezing and melting points of a substance are the same.

Sublimation is the term used for the phase transition from a solid to a vapor without becoming a liquid as an intermediary form. An example of sublimation is dry ice (frozen carbon dioxide). Dry ice sublimates from its solid form into gaseous CO_2 without first melting and becoming liquid CO_2. This sublimation occurs because the vapor pressure is low enough for the intermediate liquid not to appear.

RULE OF THUMB The term *vapor pressure* refers to the tendency of a liquid to change to a gaseous state. In a closed system, the amount of liquid changing into vapor equals the amount of vapor condensing back into a liquid.

Properties of Liquids

Liquids exhibit flow and assume the shape of their container. Liquids also exert pressure, which varies with depth and density.

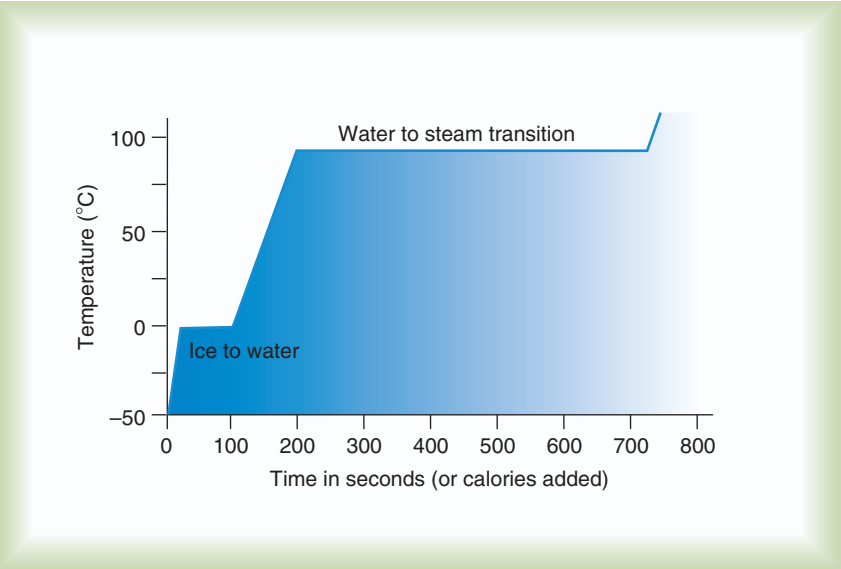

Fig. 6.3 Temperature as a function of time for 1 g of water heated at the rate of 1 cal/s. (Modified from Nave CR, Nave BC: *Physics for the health sciences*, ed 3, Philadelphia, 1985, WB Saunders.)

Variations in liquid pressure within a container produce an upward supporting force, called *buoyancy*.

Although melting weakens intermolecular bonding forces, liquid molecules still attract one another. The persistence of these cohesive forces among liquid molecules helps explain the physical properties of viscosity, **capillary action**, and **surface tension**.

RULE OF THUMB Surface tension always forces a liquid have the smallest possible surface area. That is why aerosol droplets are round. A sphere has the smallest surface area.

Pressure in Liquids

Liquids exert pressure, which has the dimensions of force per unit area. The *pressure* exerted by a liquid depends on both its *height* (depth) and *weight density* (weight per unit volume), which is shown in equation form as follows:

$$P_L = h \times d_w$$

where P_L is the static pressure exerted by the liquid, h is the height of the liquid column, and d_w is the liquid's weight density.

For example, to compute the pressure at the bottom of a 33.9-feet (1034-cm)-high column of water (density = 1 g/cm^3), you would use this equation:

$$\begin{aligned} P_L &= h \times d_w \\ &= 1034\ \text{cm} \times (1\ \text{g/cm}^3) \\ &= 1034\ \text{g/cm}^2 \end{aligned}$$

The answer (1034 g/cm^2) also equals 1 atmosphere of pressure (atm), or approximately 14.7 lb/in^2. This figure does not account for the additional atmospheric pressure (P_B) acting on the top of the liquid. The total pressure at the bottom of the column equals the sum of the atmospheric and liquid pressures. In this case, the total pressure is 2068 g/cm^2, equal to 29.4 lb/in^2, or 2 atm.

As shown in Fig. 6.4, the pressure of a given liquid is the same at any specific depth (h), regardless of the container's shape. This is because the pressure of a liquid acts equally in all directions. This concept is called the ***Pascal's principle***.

Buoyancy (Archimedes Principle)

Thousands of years ago, Archimedes showed that an object submerged in water appeared to weigh less than it did in air. This effect, called *buoyancy,* explains why certain objects float in water. Liquids exert buoyant force because the pressure below a submerged object always exceeds the pressure above it. This difference in liquid pressure creates an upward or supporting force. According to the Archimedes principle, this buoyant force must equal the weight of the fluid displaced by the object. The buoyant force (B) may be calculated as follows:

$$B = d_w \times V$$

where d_w is weight density (weight/unit volume) and V is volume of displaced fluid. If the weight density of an object is *less* than that of water (1 g/cm^3), it will displace a weight of water greater than its own weight. In this case, the upward buoyant force will overcome gravity and the object will float. Conversely, if an object's weight density exceeds the weight of water, the object will sink.

Clinically, this principle is used to measure the specific gravity of certain liquids. The term ***specific gravity*** refers to the ratio of the density of one fluid compared with the density of another reference substance, which is typically water. Fig. 6.5 shows the use of a hydrometer to measure the specific gravity of urine. The specific gravity of gases can also be measured. In this case, O_2 or hydrogen is used as the standard instead of water.

Gases also exert buoyant force, although much less than that provided by liquids. Buoyancy helps keep solid particles suspended

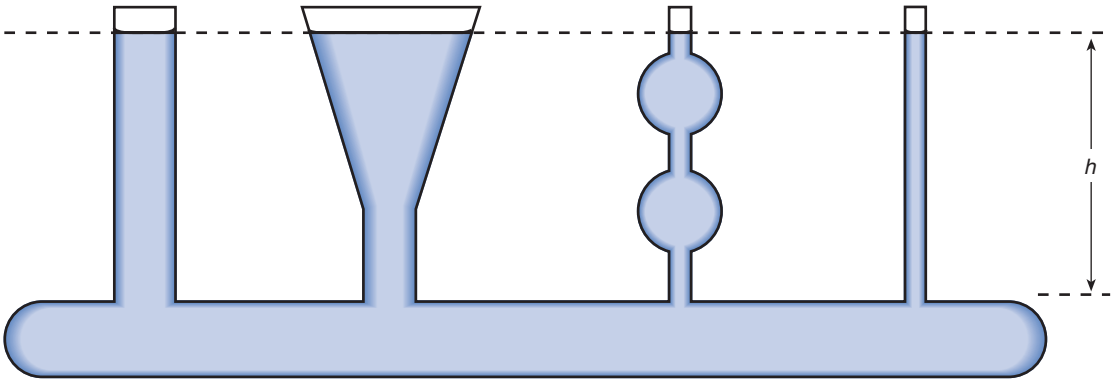

Fig. 6.4 Pascal's Principle. Liquid pressure depends only on the height (*h*) and not on the shape of the vessel or the total volume of liquid. (Modified from Nave CR, Nave BC: *Physics for the health sciences*, ed 3, Philadelphia, 1985, WB Saunders.)

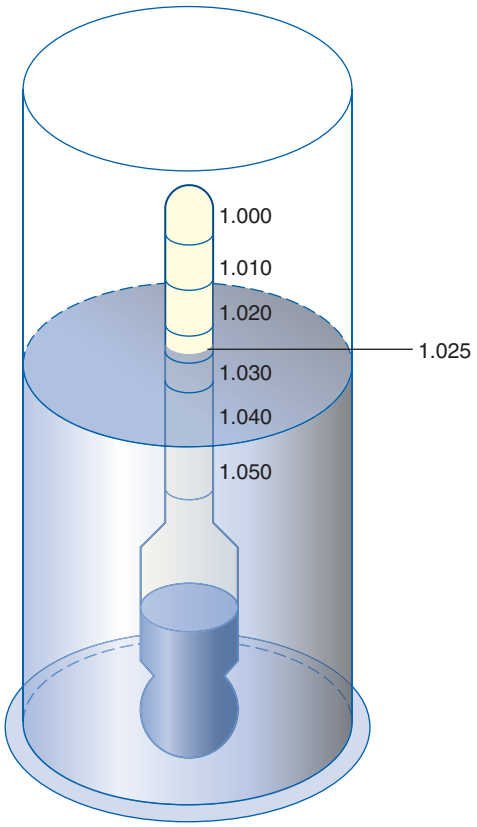

Fig. 6.5 Using a Hydrometer to Measure the Specific Gravity of a Urine Specimen. The scale value of 1.025 indicates that this urine sample has a weight density 1.025 times greater than that of water.

in gases. These suspensions, called *aerosols,* play an important role in respiratory care. More detail on the characteristics and use of aerosols is provided in Chapters 39 and 40.

Viscosity

Viscosity is the force opposing a fluid's flow and is similar to friction in solids. The viscosity of a fluid is directly proportional to the cohesive forces between its molecules. The stronger these cohesive forces are, the greater the fluid's viscosity. The greater a fluid's viscosity, the greater its resistance to deformation and the greater its opposition to flow.

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Problem

Aerosols are not suspended in heliox as well as they are in air.

Discussion

Aerosols are made of either droplets of liquids or fine particles suspended in a gas. By changing the density of the gas as during heliox therapy, the buoyancy of the gas also changes, which will affect the ability to suspend the aerosol because the weight volume of the gas has changed and the volume displaced has changed. For more information on aerosol therapy, see Chapters 39 and 40. For information about heliox, see Chapter 42.

The understanding of viscosity leads to the concept that fluids move in discrete cylindrical layers, called *streamlines.* This pattern of motion is called ***laminar flow***. Laminar flow is viewed as concentric layers of fluid flowing parallel to the tube wall at velocities that increase toward the center. As shown in Fig. 6.6, frictional forces between the streamlines and the tube wall impede movement of the outer layers of a fluid. Each layer, moving toward the center of the tube, hinders the motion of the next inner layer less and less.

The difference in the velocity among these concentric layers is called the ***shear rate*** and is simply a measure of how easily these layers separate. Shear rate depends on two factors: (1) the pressure pushing or driving the fluid, called the *shear stress,* and (2) the viscosity of the fluid. Shear rate is directly proportional to shear stress and inversely proportional to viscosity.

In uniform fluids such as water or oil, viscosity varies with temperature. Because higher temperatures weaken the cohesive forces between molecules, heating a uniform fluid reduces its viscosity. Conversely, cooling a fluid increases its viscosity. This is why a car's engine is so hard to start on a cold winter morning. The oil becomes so viscous that it impedes movement of the engine's parts.

Blood, in contrast to water or oil, is a complex fluid that contains not only liquid (plasma, which is 90% water) but also cells in suspension. For this reason, blood has a viscosity approximately five times greater than that of water. The greater the viscosity of a fluid, the more energy is needed to make it flow. The heart works harder to pump blood than it would if it were

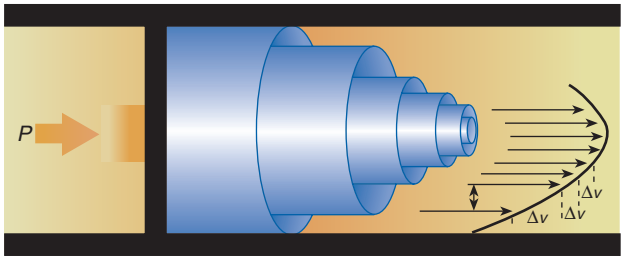

Fig. 6.6 Effects of shear stress or pressure *(P)* on shear rate (velocity gradient *[v]*) in a newtonian fluid. (Modified from Winters WL, Brest AN, editors: *The microcirculation*, Springfield, IL, 1969, Charles C Thomas.)

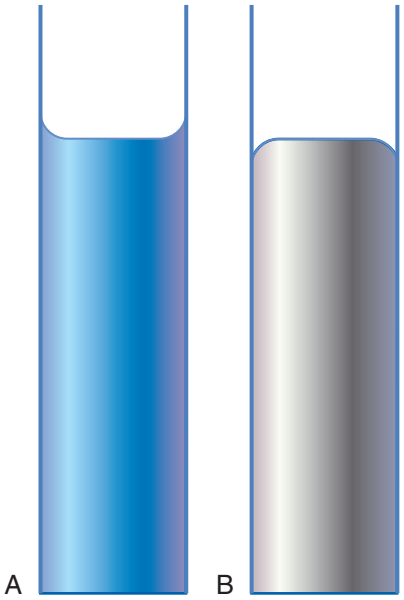

Fig. 6.7 The Shape of the Meniscus Depends on the Relative Strengths of Adhesion and Cohesion. (A) Water: Adhesion stronger than cohesion. (B) Mercury: Cohesion stronger than adhesion.

pumping water. The heart must perform even more work when blood viscosity increases, as occurs in **polycythemia** (an increase in red blood cell concentration in the blood).

RULE OF THUMB Although an 80% helium/20% oxygen mixture (heliox) is less dense than air, it actually has a slightly higher viscosity than air at room temperature. This is because the molecular distance between helium and oxygen is less than that between nitrogen and oxygen.

Cohesion and Adhesion

The attractive force between like molecules is called *cohesion*. The attractive force between unlike molecules is called *adhesion*. These forces can be observed at work by placing a liquid in a small-diameter tube. As shown in Fig. 6.7, the top of the liquid forms a curved surface, or **meniscus**. When the liquid is water, the meniscus is concave because the water molecules at the surface adhere to the glass more strongly than they cohere to each other (see Fig. 6.7A). In contrast, a mercury meniscus is convex (see Fig. 6.7B). In this case, the cohesive forces pulling the mercury atoms together exceed the adhesive forces trying to attract the mercury to the glass.

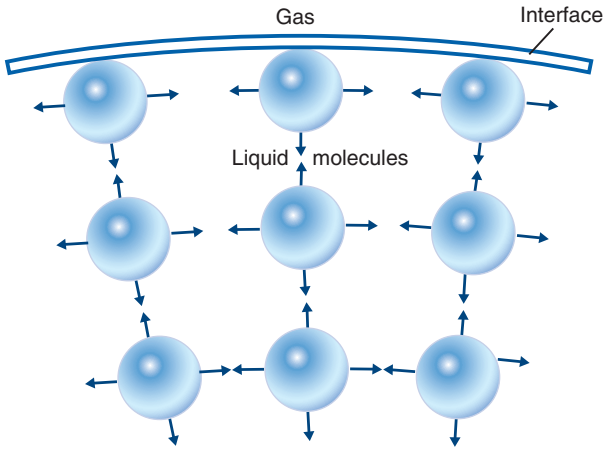

Fig. 6.8 The Force of Surface Tension in a Drop of Liquid. Cohesive force *(arrows)* attracts molecules inside the drop to one another. Cohesion can pull the outermost molecules inward only, creating a centrally directed force that tends to contract the liquid into a sphere.

TABLE 6.2 Examples of Surface Tension

Substance	Temperature (°C)	Surface Tension (dynes/cm)
Water	20	73
Water	37	70
Whole blood	37	58
Plasma	37	73
Ethyl alcohol	20	22
Mercury	17	547

Surface Tension

Surface tension is a force per unit length (equivalent to surface energy density) exerted by like molecules at the surface of a liquid. A small drop of fluid provides a good illustration of this force. As shown in Fig. 6.8, cohesive forces affect molecules inside the drop equally from all directions. However, only inward forces affect molecules on the surface. This imbalance in forces causes the surface film to contract into the smallest possible surface area, usually a sphere or curve (meniscus). This phenomenon explains why liquid droplets and bubbles retain a spherical shape.

Surface tension is quantified by measurement of the force needed to produce a "tear" in a fluid surface layer. Table 6.2 lists the surface tensions of selected liquids in dynes per centimeter (cgs). For a given liquid, surface tension varies inversely with temperature: The higher the temperature, the lower is the surface tension. Surface tension plays an important role in determining the relative sizes of connected alveoli (Fig. 6.9). To understand this, consider a spherical bubble of air in a liquid (analogous to an alveolus). According to the **Laplace's law**, the pressure inside the bubble varies directly with the surface tension of the liquid and inversely with its radius. Internal surface tension (T) will attempt to contract the bubble but is opposed by the resulting pressure inside the bubble (P). The law of Laplace defines the relationship between surface tension and the radius of a sphere (the "radius of curvature"):

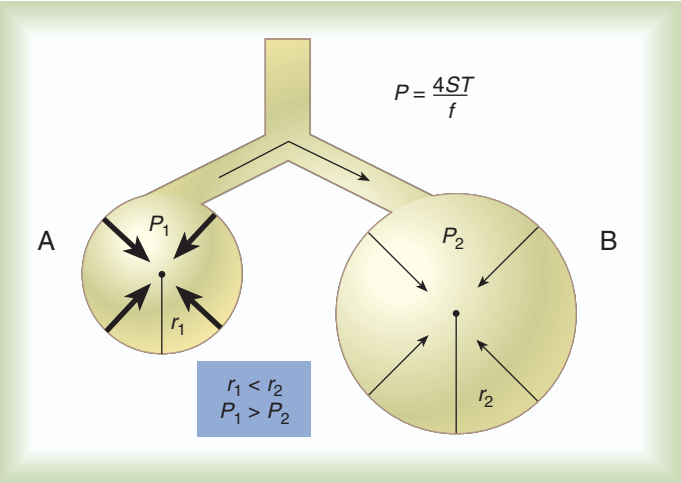

Fig. 6.9 Laplace Relationship. Two bubbles in a liquid matrix (models of alveoli). They have different sizes but the same surface tension. Bubble A, with the smaller radius, has the greater inward or deflating pressure and is more prone to collapse than the larger bubble, B. Because the two bubbles are connected, bubble A would tend to deflate and empty into bubble B. Conversely, because of the greater surface tension of bubble A, it would be harder to inflate than bubble B.

$$P = \frac{2T}{R}$$

For a structure such as a soap bubble, which has two liquid-air surfaces (and hence twice the surface tension) the equation is

$$P = \frac{4T}{R}$$

Fig. 6.9 suggests that if two alveoli of different sizes are connected, the smaller one will tend to empty into the larger one. However, this does not happen because, in reality, the two alveoli would have different surface tensions. This is because of the thin layer of surfactant inside the alveoli that counteracts the surface tension. As the radius of the alveoli decreases, its internal surface area also decreases but the volume of surfactant stays the same. The thickness of the layer of surfactant increases, which decreases the surface tension. Therefore all other factors being equal, the two alveoli will reach equilibrium, at which point they have the same radius. Abnormalities in alveolar surface tension occur in certain clinical conditions, such as *prematurity.* These abnormalities may result in the collapse of alveoli secondary to high surface tension.

Capillary Action

Capillary action is a phenomenon in which a liquid in a small tube moves upward, against gravity. Capillary action involves both adhesive and surface tension forces. As shown in Fig. 6.10A, the adhesion of water molecules to the walls of a thin tube causes an upward force on the edges of the liquid and produces a concave meniscus.

Because surface tension acts to maintain the smallest possible liquid-gas interface, instead of just the edges of the liquid moving up, the whole surface is pulled upward. The strength of this force depends on the amount of liquid that contacts the tube's surface.

MINI CLINI

Varying Alveolar Diameter

Problem

From the description in the text, two connected alveoli of unequal diameters will eventually achieve the same volume and diameter.

Discussion

Surfactant decreasing the surface tension helps to explain this phenomenon. When the diameter of the alveolus is decreased, the thickness of the surfactant increases which decreases the surface tension in the alveolus. The lowered surface tension makes it easier to inflate the already partially inflated alveolus. Assuming a closed system, the larger-diameter alveolus has a slightly larger pressure than the smaller-diameter alveolus, which will lead to equilibrium.

Because a small capillary tube creates a more concave meniscus and a greater area of contact, liquid rises higher in tubes with smaller cross-sectional areas (see Fig. 6.10B).

Capillary action is the basis for blood samples obtained by use of a capillary tube. The absorbent wicks used in some gas humidifiers are also an application of this principle, as are certain types of nebulizers and even surgical dressings.

RULE OF THUMB: Capillary Action The concept of capillary action can be seen in many small-volume jet nebulizers. Inside of the nebulizer chamber there is a thin fluid pathway allowing capillary action to bring the medication up from the reservoir.

Liquid-Vapor Phase Changes

Only after ice completely melts does additional heat increase the temperature of the newly formed liquid (see Fig. 6.3). As the water temperature reaches 100°C, a new change of state begins—from liquid to vapor. This change of state is called *vaporization.* There are two different forms of vaporization: *boiling* and *evaporation.*

Boiling

The *boiling point* of a liquid is the temperature at which its vapor pressure exceeds atmospheric pressure. When a liquid boils, its molecules must have enough kinetic energy to force themselves into the atmosphere against the opposing pressure. Because the weight of the atmosphere retards the escape of vapor molecules, the greater the ambient pressure, the greater is the boiling point. Conversely, when atmospheric pressure is low, liquid molecules escape more easily and boiling occurs at lower temperatures. This is why cooking times must be increased at higher altitudes.

Although boiling is associated with high temperatures, the boiling points of most liquefied gases are very low. At 1 atm, O_2 boils at −183°C.

Energy is also needed to vaporize liquids, as with other phase changes. The energy required to vaporize a liquid is the **latent heat of vaporization**. In cgs units, the latent heat of vaporization is the number of calories required to vaporize 1 g of a liquid at its normal boiling point.

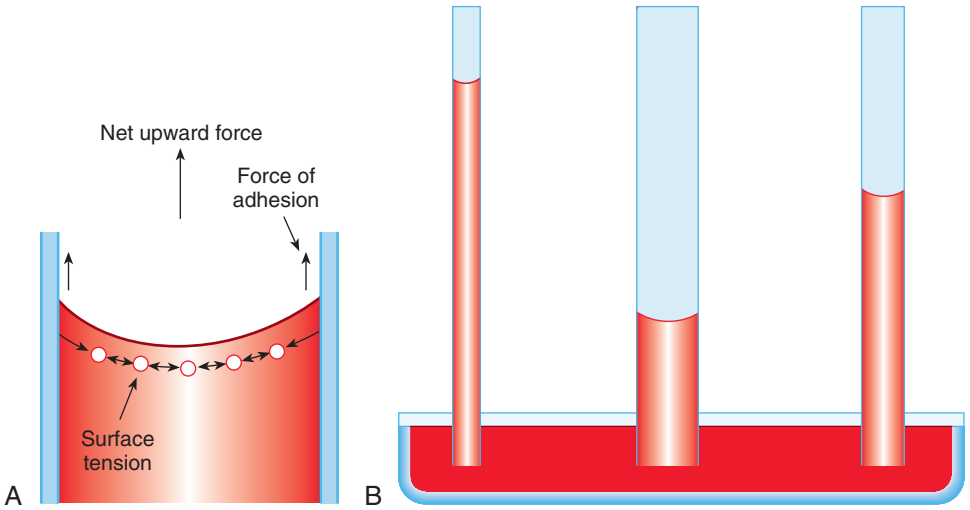

Fig. 6.10 Capillary Action. (A) Adhesion and surface tension contribute to capillary action (capillarity). (B) The liquid rises highest in the smallest tube. (Modified from Nave CR, Nave BC: *Physics for the health sciences*, ed 3, Philadelphia, 1985, WB Saunders.)

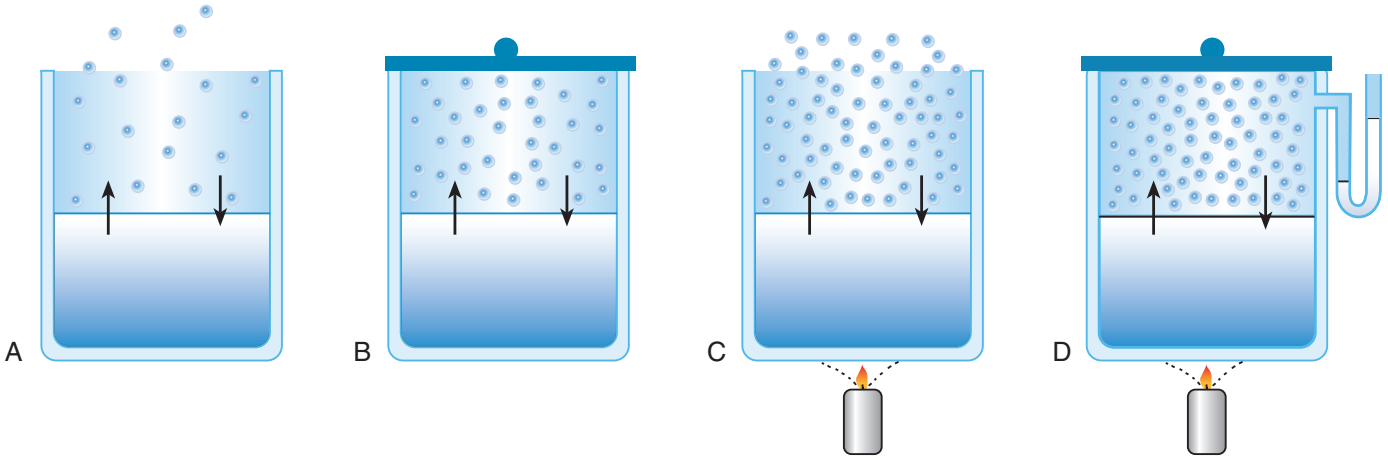

Fig. 6.11 Factors Influencing Vaporization of Water. See text for details.

Melting weakens attractive forces between molecules, whereas vaporization eliminates them. Elimination of these forces converts essentially all of the internal energy of a substance into kinetic energy. For this reason, vaporization requires substantially more energy than melting. As shown in Fig. 6.3, almost seven times more energy is needed to convert water to steam (540 cal/g) than is needed to melt ice.

Evaporation, Vapor Pressure, and Humidity

Boiling is only one type of vaporization. A liquid can also change into a gas at temperatures lower than its boiling point through a process called *evaporation*. Water is a good example (Fig. 6.11). When at a temperature lower than its boiling point, water enters the atmosphere via evaporation. The liquid molecules are in constant motion, as in the gas phase. Although this kinetic energy is less intense than in the gaseous state, it allows some molecules near the surface to escape into the surrounding air as water vapor (see Fig. 6.11A).

After water is converted to a vapor, it acts like any gas. Not to be confused with visible particulate water, such as mist or fog, this invisible gaseous form of water is called *molecular water*. Molecular water obeys the same physical principles as other gases and exerts a pressure called ***water vapor pressure***. This pressure needs to be considered when gas exchange is being calculated (see Chapter 12).

Evaporation requires heat. The heat energy required for evaporation comes from the air next to the water surface. As the surrounding air loses heat energy, it cools. This is the *principle of evaporative cooling*, which was previously described.

If the container is covered, water vapor molecules continue to enter the air until it can hold no more water (see Fig. 6.11B). At this point, the air over the water is saturated with water vapor. However, vaporization does not stop when saturation occurs. Instead, for every molecule escaping into the air, another returns to the water reservoir. These conditions are referred to as a *state of equilibrium*.

Influence of temperature. No other factor influences evaporation more than temperature. Temperature affects evaporation in two ways. First, the warmer the air, the more vapor it can hold. Specifically, the capacity of air to hold water vapor increases

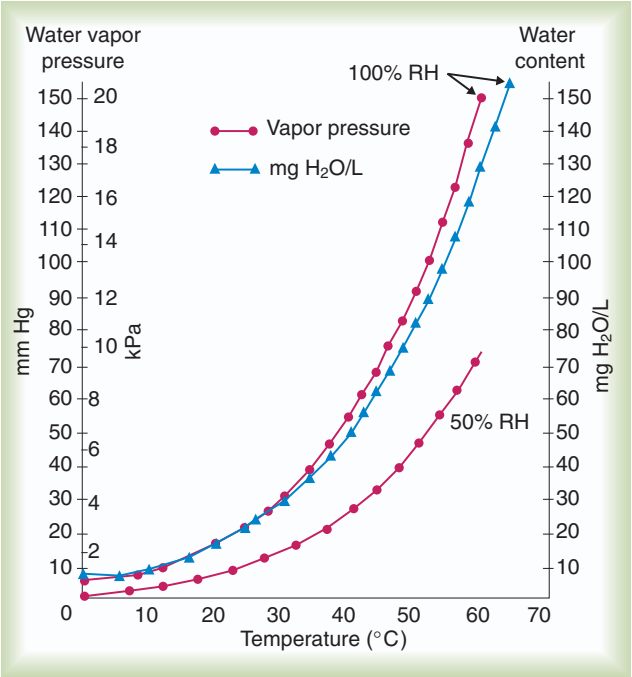

Fig. 6.12 Water vapor pressure (P_{H_2O}) and absolute humidity (mg H_2O/L) curves for gas that is fully saturated (relative humidity [RH] = 100%) and gas that is half saturated (RH = 50%).

TABLE 6.3 Vapor Pressure and Absolute Humidity for Air Saturated With Water Vapor

Temperature (°C)	Vapor Pressure (mm Hg)	Water Vapor Content (mg/L)	ATPS to BTPS Correction Factor[a]
20	17.50	17.30	1.102
21	18.62	18.35	1.096
22	19.80	19.42	1.091
23	21.10	20.58	1.085
24	22.40	21.78	1.080
25	23.80	23.04	1.075
26	25.20	24.36	1.068
27	26.70	25.75	1.063
28	28.30	27.22	1.057
29	30.00	28.75	1.051
30	31.80	30.35	1.045
31	33.70	32.01	1.039
32	35.70	33.76	1.032
33	37.70	35.61	1.026
34	39.90	37.57	1.020
35	42.20	39.60	1.014
36	44.60	41.70	1.007
37	47.00	43.80	1.000

[a]Correction factors are based on 760 mm Hg pressure.
ATPS, Ambient temperature and pressure saturated; *BTPS,* body temperature and pressure saturated

with temperature. The warmer the air contacting a water surface, the faster is the rate of evaporation.

Second, if water is heated, its kinetic energy is increased and more molecules are helped to escape from its surface (see Fig. 6.11C). Last, if the container of heated water is covered, the air again becomes saturated (see Fig. 6.11D). However, the heated saturated air, compared with the unheated air (see Fig. 6.11B), now contains more vapor molecules and exerts a higher vapor pressure (as shown by the manometer in Fig. 6.11D). The temperature of a gas affects both its capacity to hold molecular water and the water vapor pressure.

The relationship between water vapor pressure and temperature is shown graphically in Fig. 6.12. The left vertical axis plots water vapor pressure in both millimeters of mercury (mm Hg) and (kilopascals [kPa], which is another unit of pressure, where 1 kPa = 7.5 mm Hg). The horizontal axis plots temperatures between 0°C and 70°C. This graph shows that the greater the temperature, the greater the saturated water vapor pressure *(bold red dots)*. Table 6.3 lists actual water vapor pressures in saturated air in the clinical range of temperatures (20°C to 37°C).

Humidity. Water vapor pressure represents the kinetic activity of water molecules in air. For the actual amount or weight of water vapor in a gas to be determined, the water vapor content or absolute humidity must be measured.

Absolute humidity can be measured by weighing the water vapor extracted from air using a drying agent. The common unit of measure for absolute humidity is milligrams of water vapor per liter of gas (mg/L). Absolute humidity values for saturated air at various temperatures are plotted against the right vertical axis of Fig. 6.12. The middle column of Table 6.3 lists these absolute humidity values for saturated air between 20°C and 37°C.

A gas does not have to be fully saturated with water vapor. If a gas is only half saturated with water vapor, its water vapor pressure and absolute humidity are only half that in the fully saturated state. Air that is fully saturated with water vapor at 37°C and a pressure of 760 mm Hg has a water vapor pressure of 47 mm Hg and an absolute humidity of 43.8 mg/L (see Table 6.3). However, if the same volume of air were only 50% saturated with water vapor, its water vapor pressure would be 0.50 × 47 mm Hg, or 23.5 mm Hg, and its absolute humidity would be 0.50 × 43.8 mg/L, or 21.9 mg/L.

When a gas is not fully saturated, its water vapor content can be expressed in relative terms using a measure called ***relative humidity (RH)***. The RH of a gas is the ratio of its actual water vapor content to its saturated capacity at a given temperature. RH is expressed as a percentage and is derived with the following simple formula:

$$\text{RH}(\%) = \frac{\text{Content}}{\text{Capacity}} \times 100\%$$

For example, saturated air at a room temperature of 20°C has the capacity to hold 17.3 mg/L of water vapor (see Table 6.3). If the absolute humidity is 12 mg/L, the RH is calculated as follows:

$$\begin{aligned}\text{RH} &= 12\,\text{mg/L} / 17.3\,\text{mg/L} \times 100\% \\ &= 0.69 \times 100\% \\ &= 69\%\end{aligned}$$

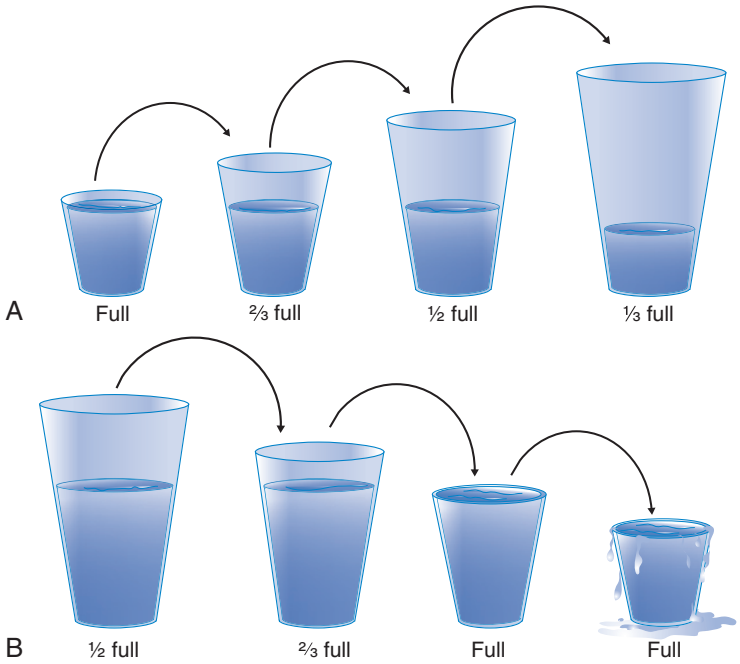

Fig. 6.13 Relative Humidity Analogy. (A) The effect of increasing capacity without changing content, as when heating a saturated gas. (B) The effect of decreasing capacity, as when cooling a gas. See text for details.

Actual water vapor content does not have to be measured for RH to be computed. Instruments called ***hygrometers*** allow measurement of RH using a wide variety of ingenuous mechanisms based on the effects of humidity on, for example, temperature through evaporation (psychrometers), the length of a human hair, or electrical capacitance and resistance.

When the water vapor content of a volume of gas equals its capacity, the RH is 100%. When the RH is 100%, a gas is fully saturated with water vapor. Under these conditions, even slight cooling of the gas causes its water vapor to turn back into the liquid state—a process called *condensation.*

Condensed moisture deposits on any available surface, such as on the walls of a container or delivery tubing or on particles suspended in the gas. Condensation returns heat to and warms the surrounding environment, whereas vaporization of water cools the adjacent air.

If air that is at an RH of 90% is cooled, its capacity to hold water vapor decreases. Although the water vapor capacity of the air decreases, its content remains constant. With a lower capacity but the same content, the RH of the air must increase. Continued cooling decreases the air's water vapor capacity until it eventually equals the water vapor content (RH = 100%). When content equals capacity, the air is fully saturated and can hold no more water vapor.

Because RH never exceeds 100%, any further decrease in temperature causes condensation. The temperature at which condensation begins is called the ***dew point***. Cooling a saturated gas below its dew point causes increasingly more water vapor to condense into liquid water droplets.

Fig. 6.13 provides a useful analogy of the relationship between water vapor content, capacity, and RH. The various-sized glasses represent the capacity of a gas to hold water vapor. The larger the glass, the greater is its capacity. The water in the glasses represents the actual water vapor content. A glass that is half full is at 50% capacity, or 50% RH. A full glass represents the saturated state, which is equivalent to 100% RH.

Fig. 6.13A, shows what happens when a saturated gas is heated. Warming a gas increases its capacity to hold water vapor but does not change its content. This is equivalent to pouring the contents of the full glass on the *left* in Fig. 6.13A into progressively larger glasses. The amount of water does not change, but as the glasses get larger, they become less full. We started with a full glass (100% RH) but end up with one that is only one-third full (33% RH).

A decrease in capacity would have the opposite effect. In Fig. 6.13B, we start with a large glass that is half full (50% RH). The capacity of the glass is decreased by pouring the water into progressively smaller glasses (equivalent to decreasing the gas

MINI CLINI

Problem

A common problem noticed when active humidification is being provided to a patient on a ventilator is that water will collect in the breathing circuit. This condition is commonly known as "rain-out."

Discussion

Rain-out happens when a warmer, fully saturated gas cools. The decrease in temperature lowers the capacity of the gas to hold water, and the excess condenses—it "rains" within the circuit. To combat this, some humidifier manufacturers add a heating wire within the circuit to counter the heat loss and decrease the amount of condensation. The water condensing within the tubing is directly related to a change in relative humidity because the warmer gas has a greater capacity to carry the water than the cooler gas. For more information about ventilator circuits see Chapter 46.

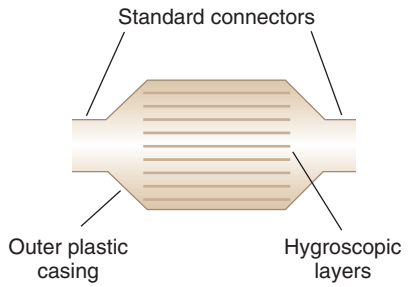

Fig. 6.14 Hygroscopic condenser humidifier.

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Condensation and Evaporation

A good clinical example of condensation and evaporation is the hygroscopic condenser humidifier, a form of an artificial nose (Fig. 6.14). These devices consist of a sponge-like material encased in plastic. When a patient exhales into an artificial nose, the warm, saturated expired gas cools, causing condensation on the absorbent surfaces. As condensation occurs, heat is generated in the device. When the patient inhales through the device, the inspired gases are warmed and the previously condensed water evaporates, aiding in airway humidification. Chapter 39 provides more detail on humidification devices, including the artificial nose.

temperature). Eventually the water volume is enough to fill a smaller glass (100% RH). What happens if we try to empty this full glass into an even smaller one? Because the smaller glass has less capacity, the excess content must spill over. This spillover is analogous to the condensation occurring when a saturated gas cools below its dew point. However, although condensation has removed the excess moisture from the air, the smaller glass is still full (100% RH).

In clinical practice, two additional measures of humidity are used: **percent body humidity** (BH) and **humidity deficit**. The BH of a gas is the ratio of its actual water vapor content to the water vapor capacity in saturated gas at body temperature (37°C). The BH is the same as RH except that the capacity (or denominator) is fixed at 43.8 mg/L:

$$\text{BH}(\%) = \frac{\text{Content (mg/L)}}{43.8} \times 100\%$$

The humidity deficit is associated with a BH of less than 100% and represents the amount of water vapor the body must add to the inspired gas to achieve saturation at body temperature (37°C). To compute the humidity deficit, simply subtract the actual water vapor content from its capacity at 37°C (43.8 mg/L).

Influence of pressure. High temperatures increase vaporization, whereas high pressures impede this process. Water molecules trying to escape from a liquid surface must push their way out against the opposing air molecules. If the surrounding air pressure is high, there are more opposing air molecules and vaporization decreases; alternatively, low atmospheric pressures increases vaporization.

Influence of surface area. The greater the available surface area of the gas in contact with air, the greater is the rate of liquid evaporation. This statement can be easily proved by comparing how quickly equal volumes of water evaporate under dry conditions from a flat plate versus from a tall narrow glass. The water spread over a flat plate evaporates more quickly compared with the same amount of liquid in a tall narrow glass. This principle is applied to the design of certain humidifiers to increase their ability to put water vapor into the passing gas.

Properties of Gases

Gases share many properties with liquids. Specifically gases exert pressure, are capable of flow, and exhibit the property of viscosity. However, in contrast to liquids, gases are readily compressed and expanded and fill the spaces available to them through **diffusion**.

Kinetic Activity of Gases

Because the intermolecular forces of attraction of a gas are so weak, most of the internal energy of a gas is kinetic energy. *Kinetic theory* says that gas molecules travel about randomly at very high speeds and with frequent collisions.

The velocity of gas molecules is directly proportional to temperature. As a gas is warmed, its kinetic activity increases, its molecular collisions increase, and its pressure increases. Conversely, when a gas is cooled, molecular activity decreases, particle velocity and collision frequency decrease, and the pressure decreases.

Molar Volume and Gas Density

A major principle governing chemistry is the **Avogadro's law**. It states that the 1-g atomic weight of any substance contains exactly the same number of atoms, molecules, or ions. This number, 6.023×10^{23}, is the **Avogadro's constant**. In SI units, this quantity of matter equals 1 mole.

Molar volume. The Avogadro's law states that equal volumes of gases under the same conditions must contain the same number of molecules. At a constant temperature and pressure, 1 mole of a gas should occupy the same volume as 1 mole of any other gas. This ideal volume is termed the *molar volume.*

At standard temperature (0.0°C) and pressure (760 mm Hg) dry **(STPD)**; the ideal molar volume of any gas is 22.4 L. In reality there are small deviations from this ideal. For example, although the molar volumes of both O_2 and nitrogen are 22.4 L at STPD, the molar volume of CO_2 is closer to 22.3 L. These values are used to calculate gas densities and convert dissolved gas volumes into moles per liter.

Density. Density is the ratio of the mass of a substance to its volume. A dense substance has heavy (high atomic weight) particles packed closely together. Uranium is a good example of a dense substance. Conversely, a low-density substance has a low concentration of light atomic particles per unit volume. Hydrogen gas is a good example of a low-density substance.

In clinical practice, weight is often substituted for mass, and weight density (weight per unit volume [d_w]) is actually measured. Solid or liquid weight density is commonly measured in grams per cubic centimeter. For gases, the most common unit is grams per liter. Because weight density equals weight divided by volume, the density of any gas at STPD can easily be computed by dividing its molecular weight (gmw) by the universal molar volume

BOX 6.1 Examples of Gas Densities d_w at Standard Temperature and Pressure, Dry

d_w O_2 = gmw/22.4 = 32/22.4 = 1.43 g/L
d_w N_2 = gmw/22.4 = 28/22.4 = 1.25 g/L
d_w He = gmw/22.4 = 4/22.4 = 0.179 g/L
d_w CO_2 = gmw/22.4 = 44/22.4 = 1.97 g/L

of 22.4 L (22.3 for CO_2). Box 6.1 provides examples of gas density calculations.

For the density of a gas mixture to be calculated, the percentage or fraction of each gas in the mixture must be known. To calculate the density of air at STPD, the following equation is used:

$$d_w \text{ air} = (FN \times gmwN) + (FO_2 \times gmwO_2)/22.4 \text{ L}$$
$$d_w \text{ air} = (0.79 \times 28) + (0.21 \times 32)/22.4$$
$$d_w \text{ air} = 1.29 \text{ g/L}$$

FN and FO_2 equal the **fractional concentrations** of N and O_2 in air.

Gaseous Diffusion

Diffusion is the process whereby molecules move from areas of high concentration to areas of lower concentration. *Kinetic energy* is the driving force behind diffusion. Because gases have high kinetic energy, they diffuse most rapidly. However, diffusion also occurs in liquids and can occur in solids. Gas diffusion rates are quantified using the **Graham's law**. Mathematically, the rate of diffusion of a gas (D) is inversely proportional to the square root of its gram molecular weight:

$$D_{gas} \propto \frac{1}{\sqrt{gmw}}$$

According to this principle, light gases diffuse rapidly, whereas heavy gases diffuse more slowly. Because diffusion is based on kinetic activity, anything that increases molecular activity quickens diffusion. Heating and mechanical agitation speed diffusion.

Gas Pressure

Whether free in the atmosphere, enclosed in a container, or dissolved in a liquid such as blood, all gases exert **pressure**. In physiology, the term *tension* is often used to refer to the pressure exerted by gases dissolved in liquids. The pressure or tension of a gas depends mainly on its kinetic activity. In addition, gravity affects gas pressure. Gravity increases gas density, increasing the rate of molecular collisions and gas tension; this explains why atmospheric pressure decreases with altitude.

Pressure is a measure of force per unit area. The SI unit of pressure is the N/m^2, or Pascal (Pa). Pressure in the cgs system is measured in dynes/cm^2, whereas pounds per square inch (lb/in^2 or psi) is the British foot-pound-second (fps) pressure unit. Pressure can also be measured indirectly as the height of a column of liquid, as is commonly done to determine atmospheric pressure in a barometer.

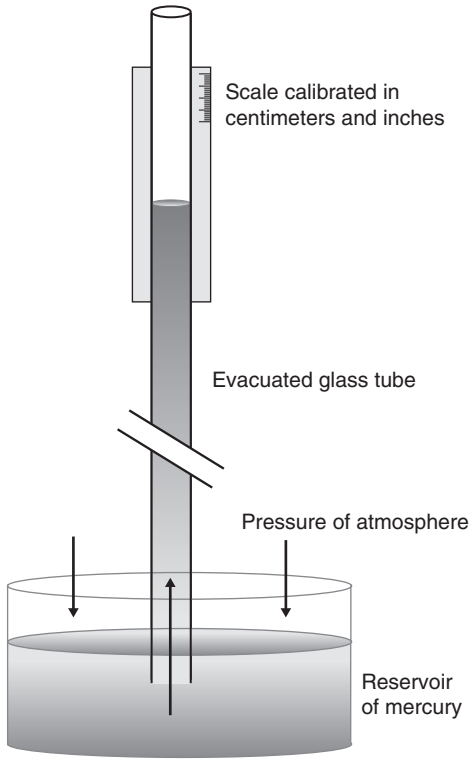

Fig. 6.15 Major components of a mercury barometer.

MINI CLINI

Problem
Gas transfer across the alveolar-capillary membrane is largely due to pressure gradients between the gas in the alveolus and the capillary.

Discussion
The partial pressure of oxygen in the alveolus (PaO_2) for a person breathing ambient air is 150 mm Hg. The partial pressure of carbon dioxide within the alveolus should be 0 mm Hg. In the capillary, the conditions are reversed. The partial pressure of carbon dioxide is about 40 mm Hg and the partial pressure of oxygen is also approximately 40 mm Hg.

If we look at this as two compartments, the oxygen tension in the alveolus is greater than that in the venous blood and will diffuse into the blood to be carried by hemoglobin. The venous tension for CO_2 is greater, so it will diffuse across the alveolar-capillary membrane into the alveolus to be expelled on expiration. Conditions that can impede gas exchange are pulmonary fibrosis, pulmonary edema, poor ventilation, and changes in perfusion. See Chapter 12 on gas exchange.

Measuring atmospheric pressure. A barometer consists of an evacuated glass tube approximately 1 m long. This tube is closed at the top, with its lower, open end immersed in a mercury reservoir (Fig. 6.15). The pressure of the atmosphere on the mercury reservoir forces the mercury up the vacuum tube a distance equivalent to the force exerted. In this manner, the height of the mercury column represents the downward force of atmospheric pressure and is measured in either inches (British) or millimeters (metric). Barometric pressure is reported with readings such as 30.4 inches of mercury (Hg) or 772 mm Hg; this means that the atmospheric pressure is great enough to support a column of mercury 30.4 inches or 772 mm in height.

Alternatively, the term *torr* may be used in pressure readings. Torr is short for Torricelli, the seventeenth-century inventor of the mercury barometer. At sea level, 1 torr equals 1 mm Hg. A pressure reading of 772 torr is the same as 772 mm Hg.

The height of a column of mercury is not a true measure of pressure. Height is a linear measure, whereas pressure represents force per unit area. The pressure exerted by a liquid is directly proportional to its depth (or height) times its density:

$$\text{Pressure} = \text{Height} \times \text{Density}$$

At sea level, the average atmospheric pressure supports a column of mercury 76 cm (760 mm) or 29.9 inches in height. If we also know that mercury has a density of 13.6 g/cm^3 (0.491 lb/in^3), the average atmospheric pressure (P_B) is calculated as follows:

$$\text{cgs units:} \quad P_B = 76\ \text{cm} \times 13.6\ \text{g/cm}^3 = 1034\ \text{g/cm}^2$$

$$\text{fps units:} \quad P_B = 29.9\ \text{in} \times 0.491\ \text{lb/in}^3 = 14.7\ \text{lb/in}^2$$

These two measures, 1034 g/cm^2 and 14.7 lb/in^2, are considered standards in the cgs and British fps systems, each being equivalent to 1 atm.[4-7]

Similar to any solid material, a barometer's housing reacts to temperature changes by expanding and contracting. In addition, the mercury column acts like a large thermometer. Both pressure and temperature affect the mercury level of a barometer. For accuracy, the reading must be corrected for temperature changes.

Clinical pressure measurements. Mercury is the most common fluid used in pressure measurements both in barometers and at the bedside. Because of the high density (13.6 g/cm^3) of mercury, it assumes a height that is easy to read for most pressures in the clinical range. Water columns can also be used to measure pressure (in centimeters of water [cm H_2O]), but only low pressures. Because water is 13.6 times less dense than mercury, 1 atm would support a water column 33.9 feet high or about as tall as a two-story building.

Both mercury and water columns are still used in clinical practice, especially when vascular pressures are being measured. However, these traditional tools are rapidly being replaced by mechanical or electronic pressure-measuring devices. Even so, these new instruments must be calibrated against a mercury or water column before being used to make measurements.

The simplest mechanical pressure gauge is the *aneroid barometer,* which is common in homes. An aneroid barometer consists of a sealed evacuated metal box with a flexible, spring-supported top that responds to external pressure changes (Fig. 6.16). This motion activates a geared pointer, which provides a scale reading analogous to pressure.

This same concept underlies the simple mechanical manometers used to measure blood or airway pressure at the bedside (Fig. 6.17). However, rather than the pressure acting externally on the sealed chamber, the inside is connected to the pressure source. In this manner, the flexible chamber wall expands and contracts as pressure increases or decreases.

A flexible chamber can also be used to measure pressure electronically. These devices are called ***strain-gauge pressure transducers***. In these devices, pressure changes expand and contract a flexible metal diaphragm connected to electrical wires (Fig. 6.18). The physical strain on the diaphragm changes the amount of electricity flowing through the wires. By measuring this change in electrical voltage, we are indirectly measuring changes in pressure. Most modern medical devices use small solid-state piezoelectric pressure sensors. These devices work on the principle that certain materials generate an electrical charge in response to applied mechanical stress.

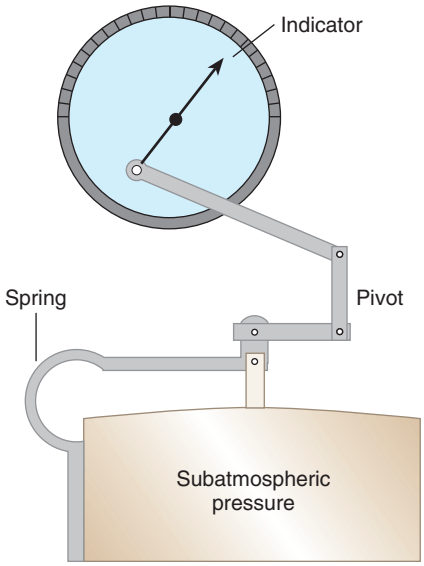

Fig. 6.16 Aneroid Barometer.

Fig. 6.17 Mechanical manometer used to measure a patient's airway pressure.

Although millimeters of mercury and centimeters of water are still the most common pressure units used at the bedside, they do not represent the SI standard. The SI unit of pressure is the kilopascal (kPa); 1 kPa equals approximately 10.2 cm H_2O or 7.5 torr. To convert between these pressure units accurately, use the factors provided in the rear inside cover of this book.

RULE OF THUMB One kilopascal equals approximately 10.2 cm H_2O or 7.5 mm Hg (torr). A pressure of 10 kPa equals approximately 100 cm H_2O or 75 mm Hg. Conversely, a pressure of 60 cm H_2O equals approximately 6 kPa.

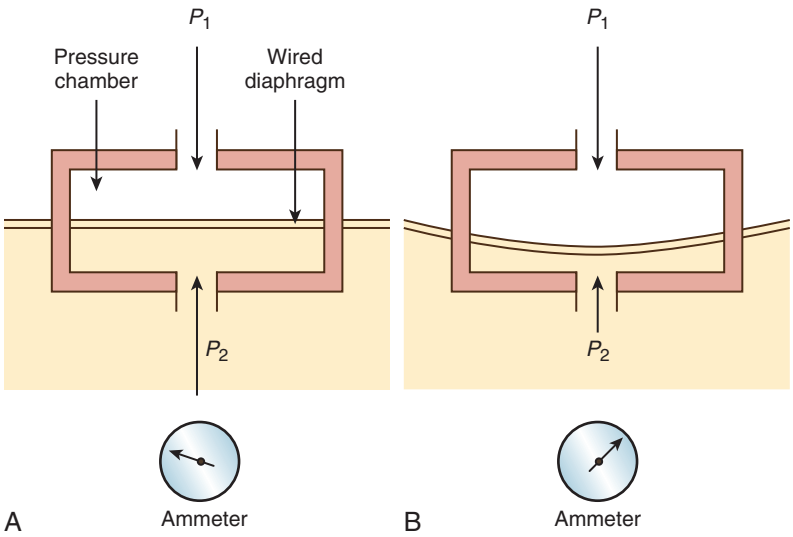

Fig. 6.18 Strain-Gauge Pressure Transducer. (A) No pressure is applied. (B) Pressure is applied to the transducer. An ammeter shows a change in electrical current proportional to the magnitude of pressure applied.

Partial Pressures (the Dalton's Law)

Many gases exist together as mixtures. Air is a good example of a gas mixture, consisting mainly of O_2 and N_2. A gas mixture, similar to a solitary gas, exerts pressure. The pressure exerted by a gas mixture must equal the sum of the kinetic activity of all its component gases. The pressure exerted by a single gas in a mixture is called its **partial pressure**.

The Dalton's law describes the relationship between the partial pressure and the total pressure in a gas mixture. According to this law, the total pressure of a mixture of gases must equal the sum of the partial pressures of all component gases. The principle states that the partial pressure of a component gas must be proportional to its percentage in the mixture.[8]

A gas making up 25% of a mixture would exert 25% of the total pressure. For consistency, the percentage of a gas in a mixture is usually expressed in decimal form, using the term *fractional concentration*. A gas that is 25% of a mixture has a fractional concentration of 0.25. For example, air consists of approximately 21% O_2 and 79% N. To compute the partial pressure of each component, simply multiply the fractional concentration of each component by the total pressure. Assuming a normal atmospheric pressure of 760 torr, the individual partial pressure is computed as follows:

$$\text{Partial pressure} = \text{Fractional concentration} \times \text{Total pressure}$$

$$PO_2 = 0.21 \times 760 \text{ torr} = 160 \text{ torr}$$

$$PN = 0.79 \times 760 \text{ torr} = 600 \text{ torr}$$

As predicted by the Dalton's law, the sum of these partial pressures equals the total pressure of the gas mixture.

What if the total pressure changed? Changes in barometric pressure, in addition to minor fluctuations caused by weather, are mainly a function of altitude. Considering only O_2, we know that its fractional concentration, or fractional inspired O_2 (FiO_2), remains constant at approximately 0.21. At a P_B of 760 torr, the pO_2 is equal to 0.21 × 760, or 160 torr. At an altitude of 25,000 feet, the FiO_2 of air is still 0.21. However, the P_B is only 282 torr, and the resulting pO_2 is 0.21 × 282, or 59 torr, just more than one-third of that available at sea level. Because the pO_2 (not its percentage) determines physiologic activity, high altitudes can impair O_2 uptake by the lungs. Mountain climbers must sometimes use supplemental O_2 at high altitudes for this reason. By increasing the amount of O_2 to more than 0.21, we can raise its partial pressure and increase uptake by the lungs. For a practical application of this principle, see the accompanying Mini Clini.

MINI CLINI

Why Are Oxygen Masks Needed on Airplanes?

Problem

People who have traveled by air are familiar with the safety instructions given by the crew before flight. Instructions include how to use the O_2 masks. When and why are these masks needed?

Discussion

At a typical cruising altitude of 30,000 feet, the P_B outside the airplane cabin is approximately 226 torr. The inspired partial pressure of O_2 (PiO_2) is calculated as follows:

$$PiO_2 = 0.21 \times 226 \text{ torr} = 47 \text{ torr}$$

If the cabin were to depressurize, travelers inside would be exposed to this low PiO_2. At this PiO_2, most people become unconscious within seconds and eventually die due to lack of O_2 (anoxia).

To overcome this problem, emergency O_2 masks are available when the cabin depressurizes. These masks, assuming a tight fit, probably provide approximately 70% O_2, or an FiO_2 of 0.70. The PiO_2 of a person wearing a mask under these conditions is calculated as follows:

$$PiO_2 = 0.70 \times 226 \text{ torr} = 158 \text{ torr}$$

This PiO_2 (about the same as at sea level) is sufficient to keep the passengers alive until the crew can bring the plane down to a safe altitude.

In contrast, high atmospheric pressures increase the partial pressure of inspired O_2 (PiO_2) in an air mixture. Pressures above atmospheric are called *hyperbaric pressures*.[9] Hyperbaric pressures commonly occur only in underwater diving and in special hyperbaric chambers.[9] For example, at a depth of 66 feet under the sea, water exerts a pressure of 3 atm, or 2280 mm Hg (3 × 760). At this depth, the O_2 in an air mixture breathed by a diver exerts a PO_2 of 0.21 × 2280, or approximately 479 mm Hg. This is nearly three times the PO_2 at sea level.

The same conditions can be created on dry land in a *hyperbaric chamber*. Hyperbaric chambers are used for controlled depressurization of deep-sea divers and to treat certain types of diving accidents. Clinically, hyperbaric chambers and O_2 are used together to treat various conditions, including carbon monoxide poisoning and gangrene. Chapter 42 provides more details on this use of high-pressure O_2.

Solubility of Gases in Liquids (the Henry's Law)

Gases can dissolve in liquids. Carbonated water and soda are good examples of a gas (CO_2) dissolved in a liquid (water). The **Henry's law** states that at a constant temperature, the amount of a given gas that dissolves in a given type and volume of liquid is directly proportional to the partial pressure of that gas in equilibrium with that liquid. For O_2 dissolved in blood, the equation is:

$$C_{dO_2} = kP_{O_2}$$

where C_{dO_2} = the quantity of O_2 dissolved in the blood at standard temperature and pressure dry conditions (milliliters per deciliter of blood, equivalent to mL/100 mL, also called volume percent) and k = s the constant of proportionality, or **solubility coefficient** (for blood k = 0.0031 mL/mm Hg/dL blood at 37°C). Note that this term shows up in the equation for the total O_2 content of blood (see Chapter 12). For example, if the PaO_2 is 100 mm Hg, the content of dissolved O_2 is:

$$C_{dO_2} = 0.0031 \times 100 = 0.3 \text{ mL/dL}$$

Temperature plays a major role in gas solubility. High temperatures decrease solubility, and low temperatures increase solubility. This is why an open can of soda may still fizz if left in the refrigerator but quickly goes flat when left out at room temperature. The effect of temperature on solubility is a result of changes in kinetic activity. As a liquid is warmed, the kinetic activity of any dissolved gas molecules is increased. This increase in kinetic activity increases the escaping tendency of the molecules and partial pressure. As an increasing number of gas molecules escape, the amount left in a solution decreases rapidly. For a practical application of this principle, see the accompanying Mini Clini, which discusses blood gases and patient temperature.

GAS BEHAVIOR UNDER CHANGING CONDITIONS

Gases, with large distances between their molecules, are easily compressed and expanded. When a gas is pressurized, the molecules are squeezed closer together. If a gas-filled container could be enlarged, the gas would expand to occupy the new volume. Fig. 6.19 illustrates the concepts of gas compression and expansion.

MINI CLINI

Blood Gases Versus Patient Temperature

Problem

Respiratory therapists (RTs) frequently need to sample and measure the partial pressures of O_2 and CO_2 in patients' arterial blood. These samples are called *arterial blood gas* (ABG) samples. Typically ABG samples are measured in analyzers kept at a normal body temperature of 37°C. However, not all patients have normal body temperatures. Many are feverish (hyperpyrexia), and some have low body temperatures (hypothermia). What effect does this have on the measurements?

Discussion

The direct relationship between temperature and partial pressure causes higher arterial PaO_2 and $PaCO_2$ readings at higher temperatures. At 37°C, the arterial PaO_2 in a normal adult is approximately 100 torr. However, at 47°C, the PaO_2 would be nearly twice as high. A smaller increase from 37°C to 39°C increases the arterial PaO_2 less markedly from 100 torr to approximately 110 torr. Likewise, an increase in temperature increases the arterial $PaCO_2$. Arterial $PaCO_2$ values increase approximately 5% per degree Celsius. An increase in temperature from 37°C to 39°C increases the $PaCO_2$ by approximately 10%, from 40 to 44 torr.

The reverse is also true. Decreased temperatures decrease the arterial partial pressures of O_2 and CO_2. Correction equations are available to help compute these corrections; however, they correct only for the relationship between temperature and pressure and do not take into account metabolic and cardiovascular changes that accompany a change in a patient's temperature. For this reason, the use of corrected PaO_2 and $PaCO_2$ readings remains controversial.

Gas Laws

Several laws help to define the relationships among gas pressure, temperature, mass, and volume (Table 6.4). Using these laws,[10,11] the behaviors of gases under changing conditions can be predicted. Underlying all these laws are three basic assumptions: (1) no energy is lost during molecular collisions, (2) the volume of the molecules themselves is negligible, and (3) no forces of mutual attraction exist between these molecules. These three assumptions describe the behavior of an "ideal gas." Under normal conditions, most gases exhibit ideal behavior.

The **Boyle's law** states that with constant temperature, the volume and pressure are indirectly proportional. That is, as the pressure is increased, the volume will decrease. The **Charles law** states that with pressure constant, the volume of a gas is directly proportional to its temperature. A warm gas will take up more volume than a cooler gas at the same pressure. This effect can be seen with mechanical ventilators (see Chapter 46).

RULE OF THUMB: The Boyle's Law The Boyle's law is used in pulmonary function labs that perform body plethysmography. This is accomplished by placing the subject into a sealed box and having him or her take a series of breaths through a mouthpiece that is connected to the outside. Within the mouthpiece is a small shutter that, when closed, will block the tube for a moment. The minute changes measured with the shutter closed are then used to help calculate lung volumes. See Chapter 20 for pulmonary function testing.

The **Gay-Lussac's law** assumes that gas volume is constant and pressure and temperature are directly proportional to one

MINI CLINI

Variations From Ideal Gas Behavior: Expansion Cooling and Adiabatic Compression

Boyle's law describes gas behavior under constant temperature, or isothermal conditions.[10] During isothermal conditions, the temperature of an ideal gas should not change with either expansion or contraction. For example, if an ideal gas were to escape rapidly from a high-pressure cylinder into the atmosphere, its temperature should not change. The rapid expansion of real gases causes substantial cooling. This phenomenon of expansion cooling is called the ***Joule-Thompson effect***.

A rapidly expanding gas cools because the attractive force between its molecules is broken. Because the energy needed to break these forces must come from the gas itself, the temperature of the gas must decrease. This decrease in temperature, depending on the pressure drop that occurs, can be large enough to liquefy the gas. This is the primary method used to liquefy air for the production of O_2 because the gas achieves both the critical pressure and temperature.

Isothermal processes keep gas temperature constant. The internal energy will remain constant. In an ***adiabatic*** *process,* the container is insulated, resulting in no heat transfer into or out from the system. If the volume increases, the internal energy decreases to perform the work and thus the temperature decreases. If the volume is increased, the internal energy is also increased, resulting in a higher temperature.

another. As a gas is cooled, the pressure will decrease, and as the gas is heated, the pressure will increase. This is a result of molecular motion based on temperature. With a "hot" gas, more molecules are colliding, thus increasing the pressure. Cooling the gas decreases the collisions. If these three laws are combined algebraically, they are commonly referred to as *the combined gas laws.*

Measuring the volume of a gas may change slightly due in part to the flexibility of the container in which the gas is kept. Avogadro's number refers to the number of molecules in a mole. If we take number of moles into account, this removes the influence of the container's flexibility. The revised formula is now:

$$PV = nRT$$

where P = pressure, V = volume, and n = number of moles, R is the universal gas constant, which is equal to the work per degree per mole, and T = temperature.

Effect of Water Vapor

In clinical practice, most gas law calculations must take into account the presence of water vapor. Water vapor, similar to any gas, occupies space. The dry volume of a gas at a constant pressure and temperature is always smaller than its saturated volume. The opposite is also true. Correcting from the dry state to the saturated state always yields a larger gas volume.

The pressure exerted by water vapor is independent of the other gases with which it mixes, depending only on the temperature and RH. The addition of water vapor to a gas mixture always lowers the partial pressures of the other gases present. This fact becomes relevant when discussing the partial pressure of gases in the lungs, where the gases are saturated with water vapor at body temperature.

Corrected Pressure Computations

To compute the new or corrected partial pressure of a gas after saturation with water vapor, the following formula is applied:

$$P_C = F_{gas} \times (P_T - P_{H_2O})$$

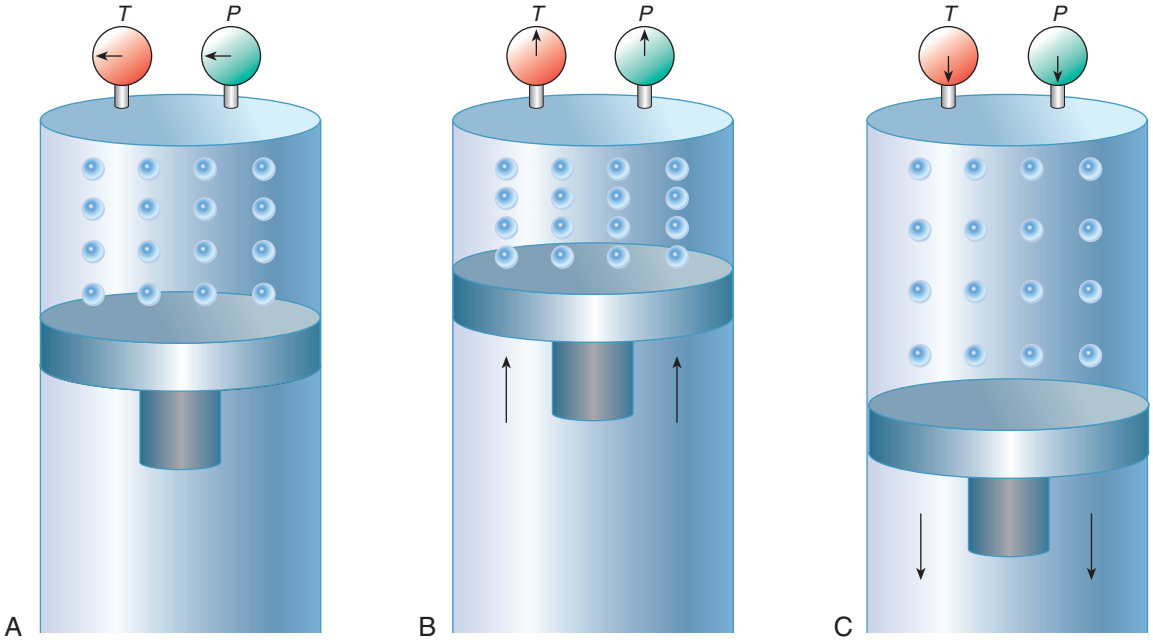

Fig. 6.19 A mass of gas in the resting state exerts a given pressure (*P*) at a given temperature (*T*) in cylinder A. In cylinder B, as the piston compresses the gas, the molecules are crowded closer together, and the increased energy of molecular collisions increases both the temperature and the pressure. Conversely, as the gas expands in cylinder C, molecular interaction decreases and the temperature and pressure decrease.

TABLE 6.4 Laws Describing Gas Behavior Under Changing Conditions

Gas Law	Basic Relationship	Constants	Description	Working Formula[a]	Clinical Applications
Boyle's law	$P \times V = k$	Temperature, mass	Volume of a gas varies inversely with its pressure	$P_1V_1 = P_2V_2$	Ventilation (see Chapter 11) Body plethysmography (see Chapter 20) Compressed volume (see Chapter 46)
Charles' law	$\frac{V}{T} = k$	Pressure, mass	Volume of gas varies directly with changes in its temperature (K)	$\frac{V_1}{T_1} = \frac{V_2}{T_2}$	ATPS to BTPS corrections (see earlier in this chapter)
Gay-Lussac's law	$\frac{P}{T} = k$	Volume, mass	Pressure exerted by a gas varies directly with its absolute temperature	$\frac{P_1}{T_1} = \frac{P_2}{T_2}$	Cylinder pressures (see Chapter 41)
Combined gas law	$PV = nRT$	—	Interaction of above (none held constant)	$\frac{P_1V_1}{nT_1} = \frac{P_2V_2}{nT_2}$	Complex interactions of variables

[a]Use the working formulas to calculate the new value of a parameter when a gas undergoes a change in *P*, *V*, *n*, or *T*. For example, to solve for a new volume (*V*) using Boyle's law, you would simply rearrange its working equation as follows:

$$V_2 = V_1 \times P_1/P_2$$

where n = mass; P = pressure; R = the gas constant (a combined constant of proportionality); T = temperature (K); V = volume.

where P_C = the corrected gas pressure, F_{gas} = the fractional concentration of the gas in the gas mixture, P_T = the total gas pressure of the mixture, and P_{H_2O} = the water vapor pressure at the given temperature (see Table 6.3). If only a single gas is present, F_{gas} equals 1, and the formula can be simplified:

$$P_C = (P_T - P_{H_2O})$$

Correction Factors

Correction factors can be used to convert gas volumes from one set of conditions to another. Such computations are common in pulmonary function laboratories and are also common to mechanical ventilators. For example, suppose you set a tidal volume on a ventilator to 500 mL. If the ventilator's output control valve metered out 500 mL and the gas was heated and humidified to body conditions (fully saturated at 37°C), then the gas volume would increase because of the heat and addition of water vapor. But how much would it increase? To find out, we must use conversion equations. As it turns out, the volume increases to 562 (assuming ambient barometric pressure of 760 mm Hg) which is a significant increase of 12%. The current standard of care for mechanical ventilation places emphasis on accurately dosing tidal volume to approximately 6 mL/kg. To maintain the desired accuracy, most manufacturers of intensive care unit ventilators correct the set tidal volume to convert from ambient temperature and pressure dry (ATPD) conditions to body temperature and pressure saturated (**BTPS**) conditions, which in this case would mean decreasing the volume exiting the control valves by 62 mL. Such conversions are important for research when evaluating the performance of mechanical ventilators in terms of volume delivery accuracy. In that case, the experiment generally involves measuring gas at ATPD and then converting to BTPS to make a fair comparison to the ventilator's display (which is corrected to BTPS).

In gas volume conversions, the four most common computations are as follows ATPD to BTPS, **ATPS** to BTPS, ATPS to STPD, and STPD to BTPS. Table 6.5 has the correction factors for 760 mm Hg, 20°C, and 17.5 mm Hg water vapor pressure.

TABLE 6.5 Correction Factors for Various Conditions

Condition	Correction Factor
ATPD → BTPS	1.1278
ATPS → BTPS	1.1018
ATPS → STPD	0.9770
STPD → BTPS	1.2104

Assuming ambient pressure of 760 mm Hg, 20°C (68°F), Water vapor pressure of 17.50 mm Hg.
ATPD, Ambient temperature and pressure dry; *ATPS,* Ambient temperature and pressure saturated; *BTPS,* body temperature and pressure saturated; *STPD,* standard temperature (0.0°C) and pressure (760 mm Hg) dry.

Properties of Gases at Extremes of Temperature and Pressure

Most gases exhibit ideal behavior under normal conditions. However, gases can deviate from these expectations, especially at the extremes of pressure and temperature.

Weak attractive forces (van der Waals forces) between gas molecules oppose their kinetic activity. Both temperature and pressure affect these forces. At high temperatures the increased kinetic activity of gas molecules far overshadows these forces. However, at very low temperatures, kinetic activity lessens and these forces become more important. Likewise, very low pressures permit gas molecules to move freely about with little mutual attraction. In contrast, high pressures crowd molecules together, increasing the influence of these forces.

The actual space occupied by gas molecules can also influence their behavior. At low pressure, the total mass of matter in a gas is a negligible fraction of the total volume. However, molecular density becomes important at very high pressures, altering the expected relationship between pressure and volume.

Critical Temperature and Pressure

For every liquid, there is a temperature above which the kinetic activity of its molecules is so great that the attractive forces

TABLE 6.6 Critical Temperature Points of Three Gases

Gas	°C	°F	Atmosphere
Helium (He)	–267.9	–450.2	2.3
Oxygen (O_2)	–118.8	–181.1	49.7
Carbon dioxide (CO_2)	31.1	87.9	73.0
Nitrous oxide (N_2O)	36.5	97.7	71.8

cannot keep them in a liquid state. This temperature is called the ***critical temperature***. The critical temperature is the highest temperature at which a substance can exist as a liquid. The pressure needed to maintain equilibrium between the liquid and gas phases of a substance at this critical temperature is the *critical pressure*. Together, the critical temperature and pressure represent the critical point of a substance.

The critical temperature of water is 374°C. At this temperature, a pressure of 218 atm is needed to maintain equilibrium between the liquid and gaseous forms of water. No pressure can return water vapor to its liquid form at a temperature greater than 374°C.

Compared with liquids, gases have much lower critical points. Table 6.6 lists the critical points of four gases used in clinical practice: O_2, He, CO_2, and N_2O. The critical temperatures of O_2 and He are well below the normal room temperature of 20°C (68°F).

The concept of critical temperature can be applied to distinguish between a true gas and a vapor. A true gas, such as O_2, has a critical temperature so low that at room temperature and pressure it cannot exist as a liquid. In contrast, a vapor is the gaseous state of a substance coexisting with its liquid or solid state at room temperature and pressure. This is why molecular water is referred to as *water vapor*.

The concept of critical temperature and pressure also helps explain how gases are liquefied. A gas can be liquefied by being cooled to below its boiling point. Alternatively, a gas can be liquefied by being cooled to less than its critical temperature and then being compressed. The more a gas is cooled below its critical temperature, the less pressure will be needed to liquefy it. However, under no circumstances can pressure alone liquefy a gas existing above its critical temperature.

According to these principles, any gas with a critical temperature above ambient should be able to be liquefied simply by having pressure applied. Both CO_2 and N_2O have critical temperatures above normal room temperature (see Table 6.6). Both gases can be liquefied by simple compression and stored as liquids at room temperature without cooling. However, both liquefied gases still need to be stored under pressure, usually in strong metal cylinders.

Liquid O_2 is produced by separating it from a liquefied air mixture at a temperature below its boiling point (–183°C or –297°F). After it is separated from air, the O_2 must be maintained as a liquid by being stored in insulated containers below its boiling point. As long as the temperature does not exceed –183°C, the O_2 remains liquid at atmospheric pressure. If higher temperatures are needed, higher pressures must be used. If at any time the liquid O_2 exceeds its critical temperature of –118.8°C, it converts immediately to a gas.

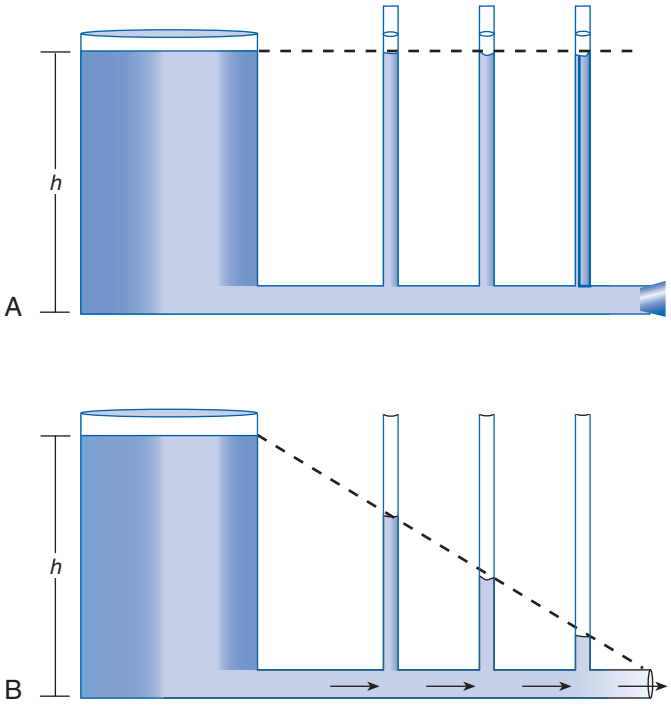

Fig. 6.20 (A) The pressure is the same at all points along the horizontal tube when there is no flow. (B) A progressive decrease in pressure occurs as the fluid flows. (Modified from Nave CR, Nave BC: *Physics for the health sciences*, ed 3, Philadelphia, 1985, WB Saunders.)

FLUID DYNAMICS

So far, liquids and gases have been presented under static, or nonmoving, conditions. However, both liquids and gases can flow. Flow is the bulk movement of a substance through space. The study of fluids in motion is called *hydrodynamics*. Because many respiratory care devices use hydrodynamic principles, the RT must have a good understanding of the basic concepts governing fluids in motion.

Pressures in Flowing Fluids

As we have seen, the pressure of a static liquid depends solely on the depth and density of the fluid. In contrast, the pressure exerted by a liquid in motion depends on the nature of the flow itself. As shown in Fig. 6.20A, the pressure exerted by a static fluid is the same at all points along a horizontal tube, depending only on the height (h) of the liquid column. However, when the fluid flows out through the bottom tube, the pressure progressively decreases all along the tube length (see Fig. 6.20B). In addition, the decrease in pressure between each of the equally spaced vertical tubes is the same.

The decrease in fluid pressure along the tube reflects a cumulative energy loss, as predicted by the second law of thermodynamics.[4] Available energy decreases because frictional forces (flow resistance) oppose fluid flow. Frictional resistance to flow exists both within the fluid itself (viscosity) and between the fluid and

MINI CLINI

Differential Pressure Pneumotachometer

Problem

It is often necessary to measure and record changes in airflow as a patient breathes. How can we apply the formula for resistance to measure and record airflow?

Discussion

Airflow can be measured using a device called a *pneumotachometer*. One of the simplest designs is the differential pressure pneumotachometer. A differential pressure pneumotachometer incorporates a flow tube with a known and constant resistance. If the formula for resistance is rearranged to solve for flow, it appears as follows:

$$\Delta\dot{V} = k \times \Delta(P_1 - P_1)$$

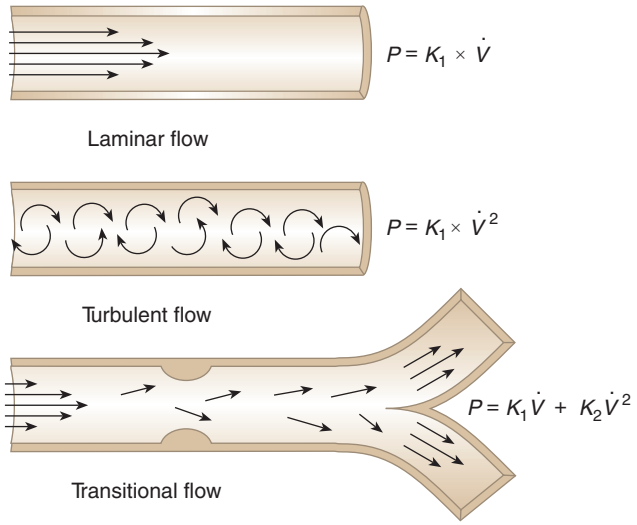

Fig. 6.21 Three patterns of flow—laminar, turbulent, and transitional. (Modified from Moser KM, Spragg RG: *Respiratory emergencies*, ed 2, St Louis, 1982, Mosby.)

the tube wall. Generally, the greater the viscosity of the fluid and the smaller the cross-sectional area of the tube, the greater is the decrease in pressure along the tube.

For any given tube length, **flow resistance** is defined as the pressure difference between two points along the tube at a given flow:

$$R = \frac{\Delta(P_1 - P_2)}{\Delta\dot{V}}$$

where R = resistance (cm H_2O/L/s, the most common units in pulmonary physiology), P_1 = the pressure (cm H_2O) at the upstream point (point 1), P_2 = the pressure at the downstream point (point 2), and $\dot{V}$ = the flow (L/s). This equation has wide application in pulmonary physiology and respiratory care. The accompanying Mini Clini provides a good example of such application.

Patterns of Flow

The pressure difference that results from flow also varies with the pattern of flow. There are three primary patterns of flow through tubes: laminar, turbulent, and transitional (Fig. 6.21).

Laminar Flow

As discussed earlier, during laminar flow, a fluid moves in discrete cylindrical layers or streamlines (see Fig. 6.6). The difference in pressure required to produce a given flow, under conditions of laminar flow through a smooth tube of fixed size, is defined by the **Poiseuille's law**[12]:

$$P_1 - P_2 = \frac{8nL\dot{V}}{\pi r^4}$$

where P_1 = the pressure (dyne/cm^2; equal to 0.001 cm H_2O) at the upstream point (point 1), P_2 = the pressure at the downstream point (point 2), n = viscosity (dyne • s/cm^2, called poise), L = length (cm), r = radius (cm) and $\dot{V}$ = the flow (mL/min). The viscosity of air is approximately 1.9×10^{-4} poise; for water it is approximately 8.90×10^{-3} poise. A pressure of 1 cm H_2O is about 980 dyne/cm^2.

Occasionally flow resistance is expressed in terms of the Poiseuille equation as:

$$R = \frac{\Delta P}{\dot{V}} = \frac{8nL}{\pi r^4}$$

which indicates that resistance is very sensitive to changes in tube radius (e.g., doubling the tube radius decreases the resistance by a factor or $2^4 = 16$). Another way to view this is that increasing the tube radius by 19% will increase the flow by 100% (i.e., double the flow; $1.19^4 = 2.0$).

Turbulent Flow

Under certain conditions the pattern of flow through a tube changes significantly, with a loss of regular streamlines. Instead, fluid molecules form irregular eddy currents in a chaotic pattern called *turbulent flow* (see Fig. 6.21). This changeover from laminar to turbulent flow depends on several factors, including fluid density (d), viscosity (n), linear velocity (v), and tube radius (r). In combination, these factors determine **Reynold's number** (Re)[13]:

$$Re = \frac{\rho v d_h}{\mu}$$

where ρ is the density of the fluid (kg/m^3), v is the velocity of the fluid (m/s), d_h is the diameter of the tube (m), and μ is the dynamic viscosity of the fluid [(kg/(m s)]. Flow is considered to be laminar when Re is less than 2000, transitional when it is between 2000 and 3000, and turbulent when it is above 3000. Turbulence is favored by increased fluid velocity, increased fluid density, increased tube diameter, and decreased fluid viscosity. In the presence of irregular tube walls, turbulent flow can occur when Re is less than 2000.[14]

Flow through a tube with constant resistance is directly proportional to the pressure difference ($P_1 - P_2$) across the tube. By measuring this pressure difference we can calculate flow. To ensure

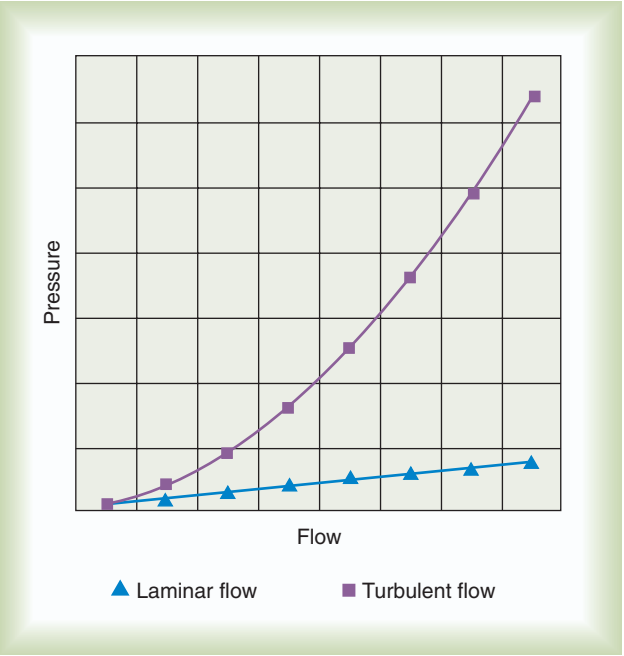

Fig. 6.22 Relationship between driving pressure and flow under laminar and turbulent conditions.

linearity between pressure and flow, the pneumotachometer is usually designed so that the flow pattern through the tube remains laminar, which simplifies calibration and use by having only one constant value for k.[14] This technique is at the heart of many pulmonary function laboratory procedures and is also used by some mechanical ventilators that have flow sensors at the airway opening portion of the patient circuit.

When flow becomes turbulent, Poiseuille's law no longer applies. Instead, the pressure difference across a tube is defined as follows:

$$P_1 - P_2 = \frac{fL\dot{V}^2}{4\pi^2 r^5}$$

where ΔP = the driving pressure, f = a friction factor based on the density and viscosity of the fluid and the tube wall roughness, L = the tube length, and $\dot{V}$ = the fluid flow.

Fig. 6.22 compares the relationship between pressure and flow under laminar and turbulent conditions. As can be seen, when flow is laminar (Poiseuille's law), the relationship between driving pressure and flow is linear. However, when flow becomes turbulent, driving pressure varies with the square of the flow ($\dot{V}^2$). To double flow under laminar conditions, it is necessary only to double the driving pressure. To double flow under turbulent conditions, the driving pressure would be increased fourfold.

Transitional Flow

Transitional flow is a mixture of laminar and turbulent flow. Flow in the respiratory tract is mainly transitional. When flow is transitional, the total driving pressure equals the sum of the pressures resulting from laminar and turbulent flow, as follows:

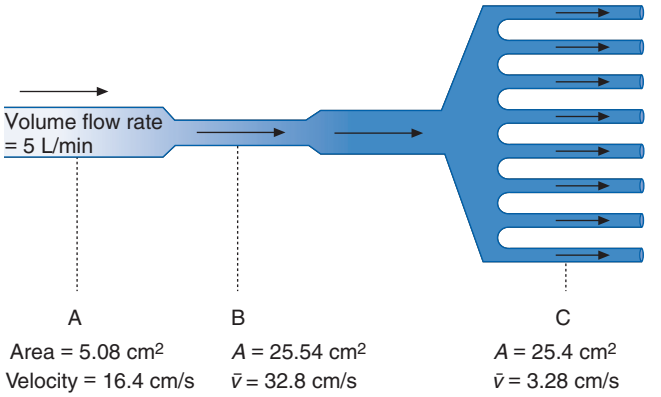

Fig. 6.23 Fluid velocity, at a constant flow, varies inversely with the cross-sectional area of the tube. (Modified from Nave CR, Nave BC: *Physics for the health sciences*, ed 3, Philadelphia, 1985, WB Saunders.)

$$P_1 - P_2 = (k_1 \times \dot{V}) + (k_2 \times \dot{V}^2)$$

where k_1 and k_2 = factors indicating the respective contribution of laminar and turbulent flow to overall driving pressure. When flow is mainly laminar, the pressure varies linearly with the flow. When flow is mainly turbulent, driving pressure varies exponentially with the flow. With all else equal, pressures generated during laminar flow are most affected by fluid viscosity, whereas fluid density is the key factor when flow is turbulent.

Flow, Velocity, and Cross-Sectional Area

Clinically, the most common units of measurement describing flow are liters per minute (L/min) or liters per second (L/s). In contrast, velocity is a measure of linear distance traveled by the fluid per unit of time. Centimeters per second (cm/s) is a common velocity unit used in pulmonary physiology.

Although fluid flow and velocity are different measures, the two concepts are closely related. The key factor relating velocity to flow is the cross-sectional area of the conducting system. Fig. 6.23 shows this relationship.

Throughout the tube, the fluid flows at a constant rate of 5 L/min. At *point A*, with a cross-sectional area of 5.08 cm^2, the velocity of the fluid is 16.4 cm/s. At *point B*, the cross-sectional area of the tube decreases to 2.54 cm^2, half its prior value. At this point, the velocity of the fluid doubles to 32.8 cm/s. At *point C*, the passage divides into eight smaller tubes. Although each tube is smaller than its "parent," together they provide a 10-fold increase in the cross-sectional area available for flow compared with *point B*. The velocity of the fluid decreases proportionately, from 32.8 to 3.28 cm/s.

These observations show that the velocity of a fluid moving through a tube at a constant flow varies inversely with the available cross-sectional area. This relationship is called the ***law of continuity***. Mathematically, the equation is as follows:

$$(A_1 \times v_1) + (A_2 \times v_2) + (A_n \times v_n) = k$$

where A = the cross-sectional area of the tube; v = the velocity of the fluid; 1, 2, and n = different points in the tube; and k = a constant value.

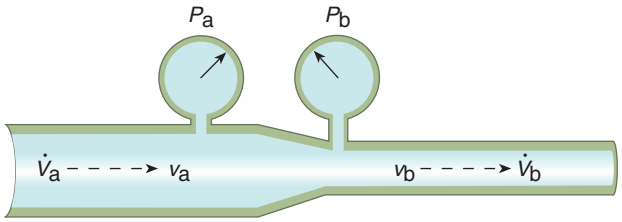

Fig. 6.24 According to the Bernoulli theorem, lateral pressure of a flowing fluid must vary inversely with its velocity. $\dot{V}_a$, flow in tube "a"; v_a, velocity in tube "a"; v_b, velocity in tube "b"; $\dot{V}_b$, flow in tube "b"; P_a, lateral wall pressure in tube "a"; P_b, lateral wall pressure after restriction (see text).

Although the principle holds true only for incompressible liquids, the qualitative features are similar for gas flow. This principle also underlies the application of nozzles or jets in fluid streams. Nozzles and jets are simply narrow passages in a tube designed to increase fluid velocity. A garden-hose nozzle is a good example of this principle in action. Clinically, jets are used in many types of respiratory care equipment, including pneumatic nebulizers (see Chapter 40) and gas entrainment or mixing devices (see Chapter 42).

Bernoulli Principle

Daniel Bernoulli, a Swiss physicist, described the effects of increasing the rate of flow of a fluid. The **Bernoulli principle** states that as the flow increases, the pressure in the fluid will decrease along with its potential energy. The loss of the potential energy is due to a change in location from a higher to a lower position. The decrease in pressure is due to fewer molecular collisions because of the increased flow. The Bernoulli equation is:

$$p + \tfrac{1}{2}\rho v^2 + \rho g y = \text{Constant}$$

where p = pressure at some point in a tube, ρ = fluid density, v = fluid velocity, g = acceleration due to gravity, and y = elevation of the pressure point above a reference plane. Fig. 6.24 shows this relationship. Fluid is flowing through a tube at a point with a certain velocity (v_a) and a lateral pressure (P_a). According to the law of continuity, as the fluid moves into the narrow or constricted portion of the tube, its velocity must increase ($v_b > v_a$). According to the Bernoulli theorem, the higher velocity at point b should result in a lower lateral pressure at that point ($P_b < P_a$). As a fluid flows through the constriction, its velocity increases and its lateral pressure decreases.

This equation also helps demonstrate how heliox therapy works. The equation implies that the lower the density, the higher is the velocity (and hence flow) for the same inspiratory effort (driving pressure) or the lower is the pressure for the same velocity—either way lowering the effort for someone struggling to breathe.

A special application of the Bernoulli prinicple is the **Venturi effect**. The Venturi effect describes the flow of a gas through a constriction and the subsequent drop in pressure at the constriction. As the gas passes from a larger bore through a constriction, the flow increases and the pressure perpendicular to the constriction decreases. The Venturi effect can be used for measuring gas flow in ventilators.

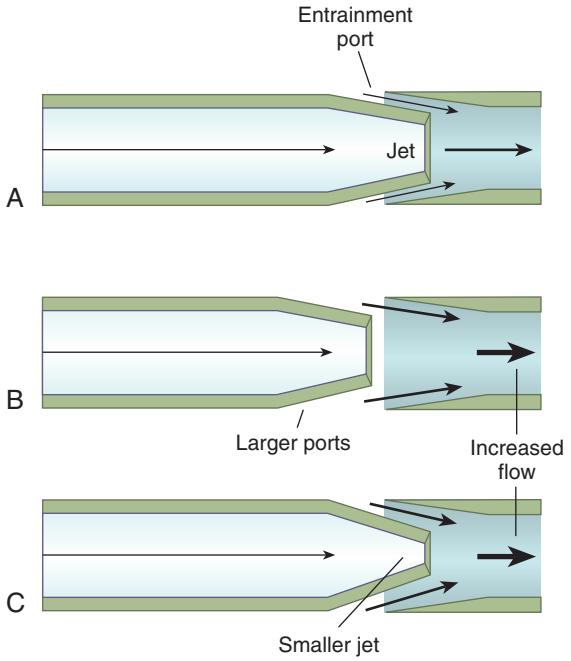

Fig. 6.25 Air Injector. (A) Basic design. (B) Greater entrainment and total flow occurs with larger entrainment ports. (C) Alternatively, a smaller jet increases source gas velocity and entrains more air.

Fluid Entrainment

Jet entrainment is the design principle used in simple O_2 masks with variable FiO_2 settings, although they are often mistakenly called *Venturi masks*. In this case, a pressurized gas, usually O_2, serves as the primary flow source. This pressurized gas passes through a nozzle or jet, beyond which is an air entrainment port (Fig. 6.25A). In this case, air entrainment occurs as a consequence of fluid viscosity. The viscous shearing force that exists between moving and static layers of gas causes the non-moving gas (room air) to be dragged into the moving stream of O_2.[15] The amount of air entrained depends on both the diameter of the jet orifice and the size of the air entrainment ports. For a fixed jet size, the larger the entrainment ports, the greater is the volume of air entrained, the higher is the total flow, and the lower is the FiO_2 (see Fig. 6.25B). The entrained volume can still be altered, with fixed entrainment ports, by changing the jet diameter (see Fig. 6.25C). A large jet results in a lower gas velocity and less entrainment, whereas a small jet boosts velocity, entrained volume, and total flow.

Fluidics and the Coanda Effect

Fluidics is a branch of engineering that applies hydrodynamic principles in flow circuits for purposes such as switching, pressure and flow sensing, and amplification. Because fluidic devices have no moving parts, they are very dependable and require little maintenance.

The primary principle underlying most fluidic circuitry is a phenomenon called *wall attachment*, or the **Coanda effect**. This effect is observed mainly when a fluid flows through a small orifice with properly contoured downstream surfaces.[16] We know that a jet or nozzle entrains any surrounding fluid, such as air,

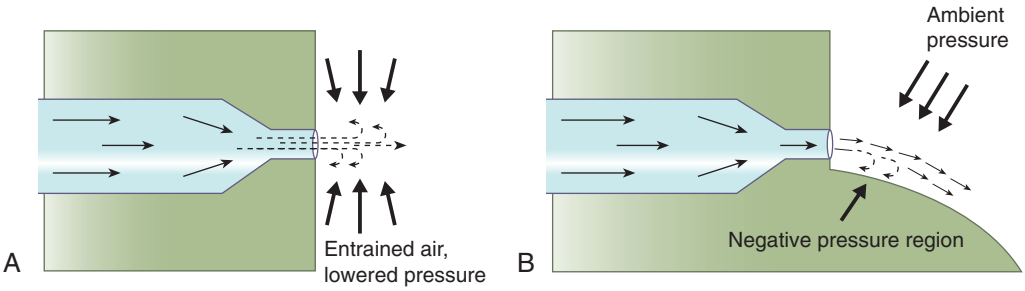

Fig. 6.26 Coanda Wall Effect. (A) Entrainment into the fluid stream. (B) Wall attachment initiated by negative pressure near wall.

into the primary flow stream (Fig. 6.26A). If a carefully contoured curved wall is added to one side of the jet (see Fig. 6.26B), the pressure near the wall becomes negative relative to atmospheric pressure. The atmospheric pressure on the other side of the gas stream pushes it against the wall, where it remains "locked" until interrupted by some counterforce. By carefully extending the wall contour, we can deflect the fluid stream through a full 180-degree turn.

Various fluidic devices can be designed using this principle, including on/off switches, pressure and flow sensors, and flow amplifiers. These individual components can be combined into *integrated fluidic logic circuits,* which function much like electronic circuit boards but without the need for electrical power.

SUMMARY CHECKLIST

- Gases have no inherent boundary, are readily compressed and expanded, and can flow.
- Three temperature scales are in common use: Kelvin (SI), Celsius (cgs), and Fahrenheit (fps); conversion among these scale units can be done by using simple formulas.
- Transfer of heat energy can occur by conduction, convection, radiation, and evaporation.
- Liquids exert pressure and exhibit the properties of flow, buoyant force, viscosity, capillary action, and surface tension.
- The pressure exerted by a liquid depends on both its height (depth) and weight density.
- Surface tension forces increase the pressure inside a liquid drop or bubble; this pressure varies directly with the surface tension of the liquid and varies inversely with the radius.
- A liquid can vaporize by either boiling or evaporation; in evaporation, the required heat energy is taken from the air surrounding the liquid, cooling the air.
- Vaporization causing cooling and condensation causes warming of the surroundings.
- The capacity of air to hold water vapor increases with temperature.
- Relative humidity (RH) is the ratio of water vapor content (absolute humidity) to saturated water vapor capacity; for a constant content, cooling increases RH and warming decreases RH.
- The rate of diffusion of a gas is inversely proportional to its molecular weight.
- The total pressure of a mixture of gases must equal the sum of the partial pressures of all component gases.
- The volume of a gas that dissolves in a liquid equals its solubility coefficient times its partial pressure; high temperatures decrease gas solubility, and low temperatures increase gas solubility.
- Volume and pressure of a gas vary directly with temperature; however, with constant temperature, gas volume and pressure vary inversely.
- The critical temperature of a substance is the highest temperature at which it can exist as a liquid; gases with critical temperatures higher than room temperature can be stored under pressure as liquids without cooling.
- Under conditions of laminar flow, the difference in pressure required to produce a given flow is defined by Poiseuille's law.
- Boyle's law explains the relationship between pressure and volume of a gas.
- Charles' law explains the relationship between volume and temperature of a gas.
- Gay-Luccac's law explains the relationship between temperature and pressure of a gas.
- When the flow of gas increases, the pressure downstream will decrease, this is called the Bernoulli principle.
- The Venturi effect is an application of Bernoulli's principle using gases.

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7

E-Medicine in Respiratory Care

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CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Define electronic health records (EHR) and their major uses in medicine and respiratory care.
- State the differences between the EHR and the electronic medical record (EMR).
- Describe the role of telehealth in healthcare in the delivery of healthcare services
- Identify the value of E-medicine applications in informatics and clinical decision support.
- Describe E-medicine applications in clinical care and management.
- Evaluate the trustworthiness and accuracy of health information sources.
- Describe major uses of E-medicine applications in healthcare administration.
- Outline steps necessary to maintain security and confidentiality of EHR.
- Describe major E-medicine applications in respiratory care education and training.
- Discuss the future of E-medicine.

CHAPTER OUTLINE

KEY TERMS

benchmarking
business intelligence
central line-associated blood stream infection (CLABSI)
clinical decision support
clinical simulation
closed-loop ventilation
computerized physician order entry (CPOE)
continuing respiratory care education
continuous quality improvement
electronic health record (EHR)
electronic medical record (EMR)
enterprise software packages
E-medicine
health informatics
Health Information Technology for Economic and Clinical Health (HITECH) Act
information retrieval
key performance indicators (KPIs)
learning management systems
Merit-based Incentive Payment System (MIPS)
m-health
picture archiving and communication systems (PACS)
point-of-care testing
root-cause analysis
telehealth
telemedicine
telemonitoring
value-based purchasing

E-Medicine is the term that relates to the use of computerized or digital technology to enhance efficiency and effectiveness of healthcare in general and more specifically in patient care. E-Medicine was initially used to describe the use of basic computer applications in clinical care, recordkeeping, and healthcare education. However, because of significant and widespread technologic advancements, the term *E-medicine* now refers to a wide array of hardware and software applications used in essentially every facet of healthcare delivery and services. As a vital part of the patient care team, respiratory therapists (RTs) need to understand, and be proficient in, many aspects of E-medicine. This chapter describes digital applications related to electronic health records, direct clinical care, disease management, healthcare administration, health information sources, healthcare delivery, and healthcare training and education.

THE ELECTRONIC HEALTH RECORD AND THE ELECTRONIC MEDICAL RECORD

A transformation has taken place in the recent past whereby medical records formerly maintained primarily in paper form are now almost exclusively computerized and are maintained as part of the patient's **electronic health record (EHR)**. A closely related but different term is the **electronic medical record (EMR)**, which represents the computerized record produced every time the patient (or consumer) uses healthcare services. The EHR is the sum of all EMRs produced by a patient during the different encounters with various healthcare entities throughout a lifetime. Unlike the EHR, which is owned by the patient, the EMR (the "chart") is owned by the hospital or healthcare delivery organization.[1] The terms *EHR* and *EMR* are so closely related that for simplicity we will use the term *EHR* to describe both concepts for the rest of this chapter.

RULE OF THUMB The record for a patient admission or healthcare event can be found in the electronic medical records, or EMR. The sum of all EMRs of a patient can be found in the patient's electronic health records, or EHR.

Nonclinical information such as patient demographics (e.g., age, gender, religion), health insurance, and financial records are also now electronic. Likewise, clinical information, including the patient's history and physical examination information, progress notes, physician orders, laboratory and other testing results, vital signs trending, and other information formerly found only in the hard-copy chart are now in electronic form. This information is now readily available to authorized clinicians and the patient via secured personal computers and mobile devices. In addition to being able to access existing medical information, new records can be more readily entered and updated, making most EHRs more current than paper records. Medical imaging and laboratory tests generally become a part of the EHR immediately as the results are finalized. The net impact of these factors is that the EHR has helped make disease diagnosis quicker and more accurate by facilitating the efficient access of medical records.[2,3]

EHRs are also proving to be a significant asset in the realm of patient treatment. When coupled with other computerized tools such as clinical decision support (CDS) applications, EHRs have enhanced treatment and disease management, as discussed in more detail later. The core functions of EHRs are shown in Box 7.1.

BOX 7.1 Core Functions of Electronic Health Records

- Medical records
- Results reporting
- Computerized physician order entry
- Clinical decision support
- Electronic communication
- Channels between healthcare providers and patients
- Patient-entered data

EHRs are more than a repository for medical records and patient-related information. EHRs are also a rich source of information that can be used in a variety of applications, including quality improvement and regulatory compliance, as detailed later in this chapter. EHRs also can serve as a vital source of data for conducting research, as discussed in Chapter 8 of this text.

Computerized Physician Order Entry

A subset of EHRs is the **computerized physician order entry (CPOE)** system. CPOE systems is a required feature for hospitals seeking to demonstrate meaningful use of EMR systems and qualify for federal financial incentives.[4]

CPOEs allow new orders to be electronically transmitted to the EHR and ancillary departments such as the pharmacy, physical therapy, respiratory department, and so on, saving time and reducing transcription errors resulting from handwriting clarity issues. Built-in stopgaps and prescribing templates alert physicians about potential problems such as incorrect dose, formulary issues, potential side effects, and drug interaction concerns. The interfacing of CPOE systems with other hospital computer systems also alerts RTs and other clinicians of new, expired, or changed orders.

CPOE systems have a substantial impact on patient care in areas where the potential for medical error is high, and the clinical workflow is complex such as intensive care units (ICUs), emergency rooms (ERs), and operating rooms (ORs).[5] Thus CPOE has helped facilitate patient care and reduce medical errors.[6] All of these factors combined to make EHR and CPOE systems value-added features for healthcare organizations, clinicians, and patients alike. Indeed, EHRs and other computerized applications are helping transform medicine and enhancing both efficiency and effectiveness in essentially all aspects of healthcare and respiratory care.[7]

RULE OF THUMB CPOE systems are the standard of care for large, complex healthcare institutions to meet national required guidelines to prevent and eliminate preventable medical errors. CPOE improves accuracy and communication of physician orders and therapies among the institution and healthcare providers.

Enterprise Software Packages

An issue that had plagued healthcare organizations and our healthcare system involves the use of separate software packages for individual organizational functions, including but not limited to EHRs. In the past, the need for one such system to interface or "communicate" to another was dealt with on an as-needed basis through software "patches" and upgrades. Over time these separate software packages, which were originally designed to stand alone or provide a specific or limited number of functions, became inefficient and much less able to meet the increasingly sophisticated and numerous requirements of healthcare organizations, including hospitals and departments within them. At about the same time that this problem was reaching critical proportions, the US government (as part of a larger legislative initiative) passed the ***Health Information Technology for Economic and Clinical Health Act of 2009***, or the HITECH Act, as part of a national strategy for building a national health information infrastructure (Fig. 7.1). The HITECH Act provided the Health and Human Services (HHS) Department with the authority to establish programs to improve healthcare quality, safety, and efficiency through the promotion of health IT, including EHRs and private and secure electronic health information (EHI) exchange.[8]

Among other things, HITECH provided financial incentives to hospitals, physicians, and other health service providers who demonstrated that they are *meaningfully* using their EHRs by meeting predefined standards for a number of objectives. These objectives related to the submission of patient data to authorized third-party surveillance registries, making clinical data including lab values, vital signs, and office visit summaries more easily available to patients via secure internet sources, as well as interfacing multiple functions together, such as EHRs with CPOE.[9-11]

In October 2016, the Centers for Medicare and Medicaid Services (CMS) **Merit-based Incentive Payment System (MIPS)** replaced the Medicare EHR Incentive Program for eligible clinicians (also known as meaningful use) originally found in the HITECH Act. MIPS now replaces meaningful use, but it still aims to achieve the same objectives, including but not limited to improving quality, safety, and efficiency, and reducing health disparities, engaging patients and family, improving care coordination, and maintaining privacy and security of patient health

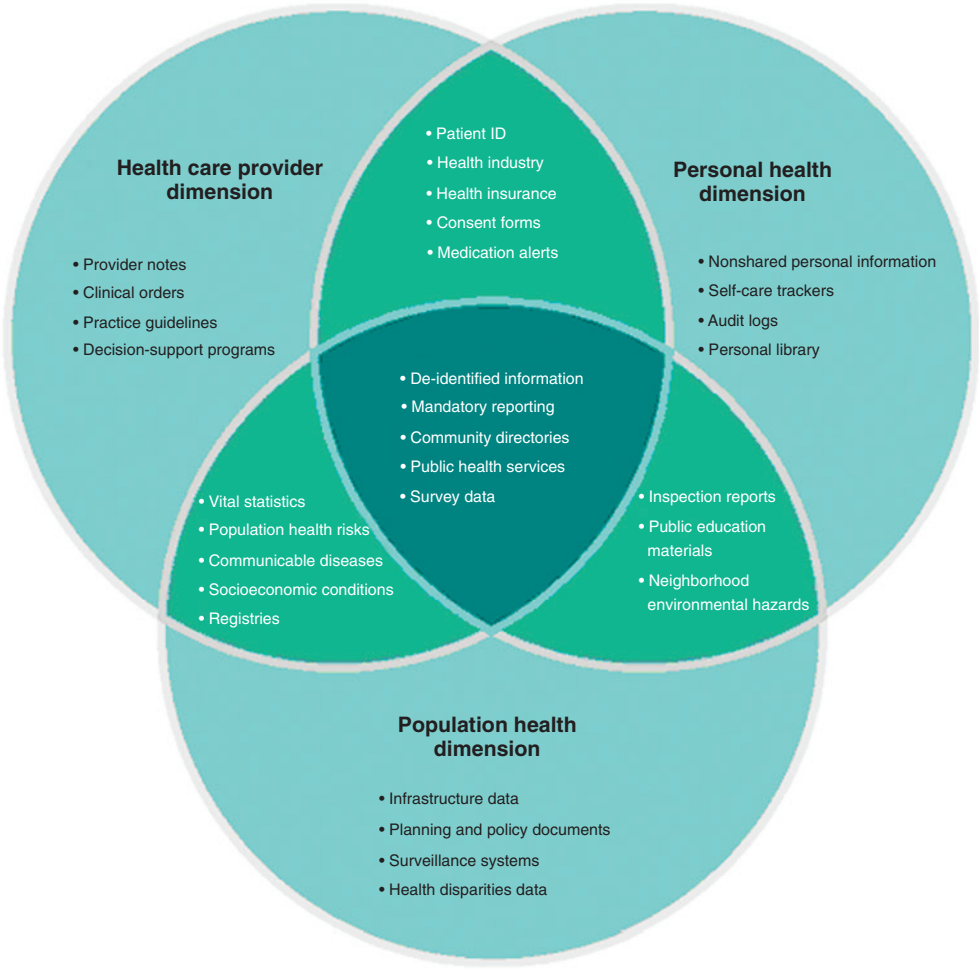

Fig. 7.1 Electronic health records: dimensions of the national health information structure. (From U.S. Department of Health and Human Services. Information for health: a strategy for building the national health information infrastructure. http://aspe.hhs.gov/sp/NHII/Documents/NHIIReport2001/default.htm. [Accessed 25.09.2006].)

TABLE 7.1 Top Vendors of Enterprise Electronic Health Record Systems (October 2011 to October 2012)

Vendor	Location	Website
Allscripts	Chicago, IL	http://www.allscrips.com
Cerner Corp.	Kansas City, MO	http://www.cerner.com
CPSI	Mobile, AL	http://www.cpsinet.com
Eclipsys	Atlanta, GA	http://www.allscripts.com
Epic Systems Corp	Verona, WI	http://www.epic.com
Healthcare Management Systems	Nashville, TN	http://www.wns.com
Healthland	Minneapolis, MN	http://www.healthland.com
McKesson Provider Technologies	Alpharetta, GA	http://www.mckesson.com
Meditech	Westwood, MA	http://ehr.meditech.com
Siemens Healthcare	Malvern, PA	http://www.healthcare.siemens.com

Modified from Top vendors of enterprise EMR systems. Modern Healthcare 2012.

information. Additional information about HITECH and additional regulatory guidelines regarding the use of information technology can be found at www.healthit.gov.

To address these regulatory demands, hospitals and other healthcare providers increasingly use a single comprehensive software system or **enterprise software package** designed to provide integrated functionality to enhance both efficiency and effectiveness, as well as comply with current CMS and HHS information technology (IT) regulations. A variety of such software packages are available to healthcare organizations (Table 7.1). Enterprise EHR vendors such as Meditech, Epic, and Cerner continue to dominate the industry year after year, but small and specialty vendors can still hold their own.[10] In addition to serving as a secure repository for EHRs, these software packages provide integrated functionality for a multitude of purposes, such as CPOE sytems, RT documentation of therapy given, test results, patient education resources, and so on. Other purposes are for the retrieval, review, and interpretation of existing records, such as those used to provide direct patient care, or for nondirect care functions, such as billing, process improvement, regulatory reporting, or other similar functions discussed later in this chapter.[6] Nowadays, enterprise software systems that interface the EHRs with functions relevant to respiratory care and other clinical departments are the standard of care.

APPLICATIONS FOR PATIENT CARE

Applications in Diagnostics

Because the EHR contains an abundance of important clinical information, the RT needs to be able to promptly access and interpret key elements of it to assist the patient care team in accurately diagnosing, managing, and treating the patient's condition. This may involve hemodynamic monitoring, blood gas, and point-of-care testing (POCT), medical imaging applications, and pulmonary function testing (PFT), among others.

MINI CLINI

Central Line–Associated Blood Stream Infection

Problem

An ARDS patient is being hemodynamically monitored using a PAC. The catheter was inserted 5 days ago. The patient has developed a fever of 101.9°F, tachycardia, and tachypnea (HR 110 beats/min, RR 28 breaths/min) with decreased urine output. Sepsis caused by a **Central Line-associated Blood Stream Infection (CLABSI)** is suspected.

Discussion

The PAC was introduced in 1971 for the assessment of heart function at the bedside. Since its introduction, its use has generated controversy regarding the benefits and potential harms caused by this invasive form of hemodynamic monitoring.[12]

Hemodynamic Monitoring

In hemodynamic monitoring, bedside monitors and stand-alone devices can calculate cardiac output (CO), monitor intravascular fluid volume, and provide cardiac parameters and indices using both invasive and noninvasive applications. However, invasive methods using a pulmonary artery catheter or PAC (see Chapter 52) have a multitude of complications, including the risk for infection and death.

As a result, the rapid evolution of E-medicine technologies has allowed for the development of safer noninvasive hemodynamic monitoring applications in perioperative and intensive care medicine. According to clinical studies, these technologies can provide CO readings noninvasively and continuously with minimal complications. Like most new technologies, their performance and accuracy need further validation. These new applications might prove to be innovative tools for the assessment of advanced hemodynamic monitoring without the drawbacks of invasive techniques.[11]

Pulmonary arterial catheterization is an invasive procedure. Inflation of the catheter once in a PA may cause rupture of that vessel with disastrous consequences. Furthermore, the continual presence of a PAC (more than 72 hours) increases the likelihood of CLABSI and endocarditis.[12]

If sepsis-related symptoms are noticed, removal and culture of the catheter must be done without delay. If advanced monitoring of hemodynamic parameter is still necessary, a non-invasive method must be used to avoid further complications and increased morbidity.

General strategies for prevention of catheter-related infections in adult and pediatric patients include (1) education of healthcare personnel regarding the indications for PAC use and proper procedures for insertion and maintenance; (2) periodically assessing knowledge of and adherence to guidelines for all personnel involved in the insertion and maintenance of a PAC; and (3) allowing only trained personnel to maintain and manage PACs.[13]

Blood Gas Laboratories and Point-of-Care Applications

The accuracy and precision of blood gas data influence clinical decisions and patient safety. Computerized blood gas analyzers and computer-assisted quality assurance measures in a blood

gas laboratory are crucial functions in a respiratory care department. Quality assurance data are necessary for accreditation of blood gas laboratories by the College of American Pathologists (CAP), the Clinical Laboratory Improvement Amendments (CLIA), and the Joint Commission (TJC). Blood gas laboratory applications interface analyzers with the patient's EHR to make blood gas results immediately available at the point of care and alert the clinician of critical results. In addition, this interfacing enables the storage, maintenance, retrieval, billing, and quality assurance of the blood gas analyzer data.

Point-of-care testing (POCT) refers to blood gas analysis performed at or near the site of a patient, in a setting that is different from a normal hospital clinical laboratory. POCT testing reduces the time required to produce blood gas test results (turnaround time) and thus improves clinical care and decision-making for the clinician. POCT applications integrate seamlessly with the HER, allowing for immediate reporting of results and flagging of critical values. POCT applications can be used in a variety of clinical settings, including the OR, critical care unit, emergency department (ED), maternity unit, and outpatient clinic.[14]

Medical Imaging and Picture Archiving and Communication Systems

Remote access to a patient's imaging studies (see Chapter 21) has become an essential element in the delivery of care. Clinical integration of all these imaging modalities with the EHR is critical to help in the diagnosis of the pulmonary patient and to improve patient care and patient safety. A **picture archiving and communication system (PACS)** is an application that allows for imaging storage, portability, communication, and clinical integration of all imaging modalities with the EHR.[15] Advances in technology and computer applications have allowed for PACS enterprise systems to flourish. In addition to the advantages mentioned earlier, current PACS applications have enhanced medical treatment and research by providing a variety of digital tools for the manipulation and interpretation of radiologic images, including three-dimensional imaging and three-dimensional printing technology.

Pulmonary Function Testing and Interpretation

Essentially the older volume displacement and spirograph PFT systems have been replaced by those that use different technology methods and computer interfaces to measure, display, and interpret the results. Similarly, most hospitals interface their PFT systems with the EHR, which allows clinicians to access reports and graphics from multiple workstations and remote devices.

Interpretation of Pulmonary Function Tests

Computer algorithms use standard reference-predicted values and formulas to aid in the interpretation of PFTs, including spirometry, lung volume, diffusing capacity, and bronchodilator response. The algorithms compare the patterns of the patient's measured values with reference values based on age, height, gender, and race. These algorithms are used by computers to classify the patterns of the patient's measured values as either normal or abnormal with degrees of severity. However, qualified interpreters must consider the effect of patient effort and other factors on the computer-assisted interpretation of PFTs. Physician review and confirmation of computer-generated PFT results is always required.

MINI CLINI

Computer-Assisted Interpretations of Pulmonary Function Tests in an Individual Patient

Problem

A patient with alpha$_1$-antitrypsin deficiency has repeat PFTs, including a diffusing capacity of the lung for carbon monoxide (DLCO). Based on a computer-assisted interpretation, there appears to be a remarkable decrease in the percent-of-predicted value for DLCO. It was previously normal; now it is 68% of predicted, indicative of emphysema. An effective therapy, pooled human plasma alpha-1 antitrypsin, is available but expensive. What additional information should the clinician evaluate?

Discussion

The clinician should determine (1) the actual observed DLCO values of the previous and repeat test and (2) whether the computer-assisted interpretations are based on different reference values among the tests. If the computer-assisted percent-of-predicted values for each test were based on different sets of reference values, it could account for the change in DLCO. Further investigation of the results is warranted before final diagnosis and treatment.

Applications in Treatment

Many current devices, therapies, and protocols developed in the last decade rely on technologic advances generated by E-medicine applications. These applications can be used in acute or nonacute settings by RTs to provide support and care for the pulmonary patient.

Applications in the Acute Care Setting

Mechanical ventilators. Most mechanical ventilators use microprocessors with complex software applications to deliver, monitor, and in some cases independently manage (**closed-loop ventilation**) ventilator modes.[16] A "mode" of ventilation is defined as a predetermined pattern of patient-ventilator interaction. Modes can be quite complex, as explained in detail in Chapter 46. Some modes, such as neurally adjusted ventilatory assist (NAVA), aim to enhance the patient-ventilator synchrony via automation that is highly responsive to the patient's respiratory needs.[17]

Microprocessors also provide for graphic outputs and touch screens and interfaces, control ventilator alarms, data trending, and archive the history of set and measured values and settings, which can be downloaded and used later for review. Current conventional ventilators allow for updating and adding new modes of ventilation via software updates by their manufacturer. It is worth mentioning that all data taken or physically downloaded from any medical device in use is consider protected health information (PHI) and, hence, subjected to all HIPPA and other regulatory guidelines.

Protocols for ventilator weaning and management of certain respiratory conditions (e.g., acute respiratory distress syndrome) coupled with the trending capabilities of today's microprocessor

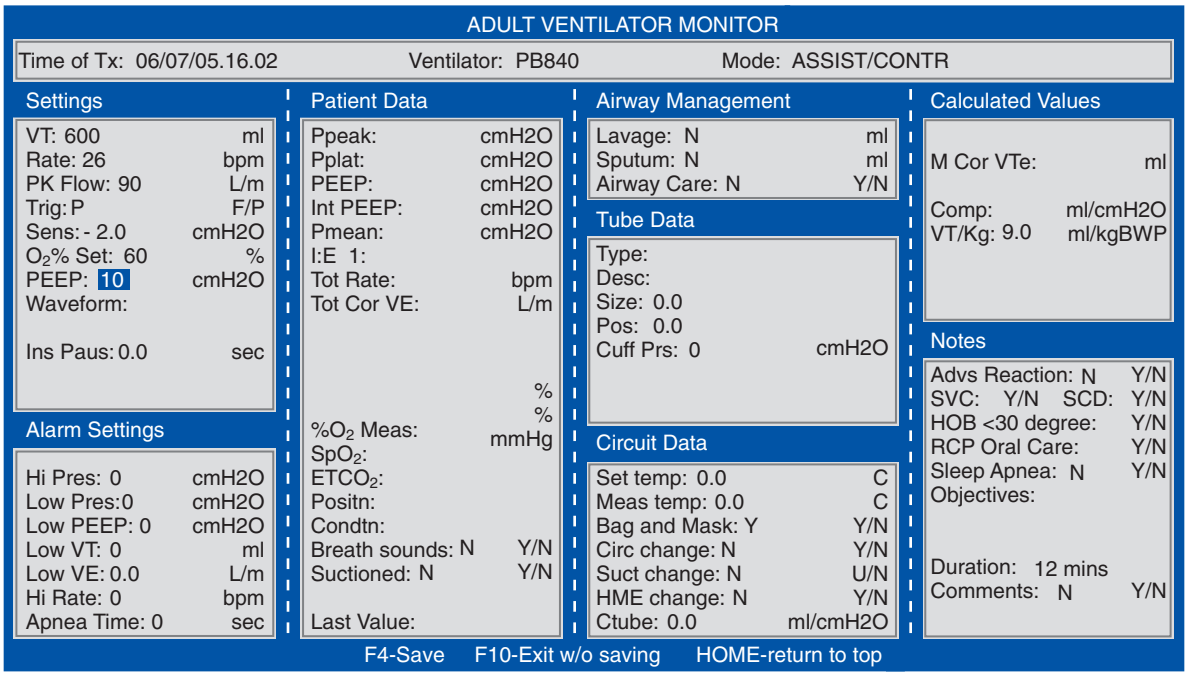

Fig. 7.2 Automated ventilator charting.

ventilators has improved patients' outcomes and decreased length of stay (LOS; see Chapter 53).

Complete, accurate, and consistent documentation of ventilator settings is key to achieve these goals. However, manual ventilator charting is frequently incomplete, inaccurate, and inconsistent, particularly regarding nomenclature.[18] Computerized ventilator charting applications have the potential to improve the quality and consistency of ventilator documentation, especially when fully integrated with the patient's EHR. It should be noted, however, that to capitalize on these advantages, computerized charting templates must be designed to be intuitive and efficient to avoid placing an unnecessary administrative burden on RTs or other clinicians using them. Automated ventilator charting takes computerized ventilator charting a step further by periodically transferring selected data from the ventilator to the digital charting template, which is then *verified* by RT.[19] Fig. 7.2 is an example of a computer screen for automated charting.

Closed-loop ventilation. Limited, proprietary computerized, closed-loop weaning software packages are available that automate weaning according to set physiologic parameters. The automated weaning program adjusts levels of support to keep patients in a normal range of intermittently monitored respiratory rate, tidal volume, and exhaled carbon dioxide. Preliminary research has shown mixed results when comparing manual protocols to automated weaning systems.[20]

These closed-loop protocols have the potential to reduce the time spent on mechanical ventilation and ICU LOS in addition to manpower savings. However, their effect on morbidity and mortality are still questionable. Even though no trial has found any harm associated with automated weaning, there is a need for more research in this area before these automated systems can be routinely used effectively.[21]

RULE OF THUMB It is important to understand that not every patient is suitable for automated weaning. Patient selection and close monitoring are essential for any weaning approach to succeed and improve patient outcomes without causing harm.

Therapist-driven protocols. Therapist-driven protocols can shorten LOS and improve health outcomes.[22] Based on patient assessment, RTs use protocols to initiate, allocate, titrate, and discontinue respiratory care. Consistency and timeliness of implementation are keys to the effectiveness of protocols. Automation of protocols at the point of care can help RTs address these concerns. An automated protocol for discontinuation of the mechanical ventilation program on the EMR can decrease the time to the first spontaneous breathing trial and the LOS in the ICU compared with a protocol without automation.[23] These protocols allow the RTs to enter information about each mechanically ventilated patient in the EMR throughout the shift. When the patients meet preset criteria, the computer application prompts the RTs to conduct a spontaneous breathing trial to help determine the patient's readiness for ventilator discontinuation.

Applications in Nonacute Care Settings and Chronic Diseases

Management of chronic diseases presents a serious challenge to the US healthcare system. Today, heart disease, cancer, and stroke account for over half of all deaths—the result of an epidemiologic transition from acute infectious diseases to noninfectious chronic diseases as the predominant causes of morbidity and mortality.[24] As of 2017, approximately half of all adults in the United States have one or more chronic health conditions.[25] As baby boomers continue to age, the proportion of the US population 65 years

old and older is expected to double. There is much interest in optimizing chronic disease management through advances in E-medicine technologies such as Telehealth (discussed later in the chapter) to improve health outcomes in a cost-effective manner and be able to reach a large number of individuals. This is particularly noteworthy given the focus by the US government on reducing short-term (within 30 days) hospital readmissions. Hospitals have begun being penalized for excessive short-term readmissions for their patients with certain conditions, including chronic obstructive pulmonary disease (COPD) and heart failure. To address this initiative, hospitals and other healthcare providers have developed an array of protocols to address the main reasons for such readmissions. These protocols often emphasize patient and family education and follow-up and often use computer applications to help accomplish this.[26,27]

Asthma. E-Medicine applications for asthma management include interactive internet applications, such as games for children, web applications linked to cell phones for personalized or automated voice or text messaging, and other telemonitoring applications. Many of these applications use monitored patient data to tailor the adjustment to the plan of care. Some provide for personalized goals, calendars, and reminders via texts or e-mails. Educational tools include audiovisuals, games, and quizzes. In patients with persistent asthma, evidence from research studies shows that these E-Medicine applications can result in an improvement in asthma knowledge, self-management skills, peak flow rates, and adherence to inhaled corticosteroid controller medications and fewer symptoms, missed school days, nighttime awakenings, activity limitations, ED visits, and hospitalizations.[28-31]

Chronic obstructive pulmonary disease. Increasingly, COPD management and mild exacerbations are being managed in the home (e.g., Emphysema, Chronic Bronchitis and Cystic Fibrosis [CF]). Web-based telemonitoring systems, smartphones, and mobile phones with computer applications extend the reach of healthcare providers into the home. E-Medicine applications for patients with COPD facilitate education, self-management, and timely feedback from healthcare providers (Fig. 7.3).

Patients generally have a positive attitude about the role of this technology, and the quality of the transmitted data is generally good.[32] Improved outcomes include earlier identification of deteriorating symptoms, better response to exacerbations, increased rate of sustained exercise after pulmonary rehabilitation, and decreased ED visits and hospitalizations.[32-34] However, evidence to date suggests that telehealth for COPD delivers similar rather than better outcomes than the "usual care" provided to people allocated to control groups which may, of course, be better than routinely available usual care.[35-37]

Fig. 7.3 Telehealth homepod. (Courtesy Tele Health Ltd. Dublin, Ireland.)

Applications in Disease and Infection Prevention

As explained earlier, the federal government has committed unprecedented resources to support the adoption and use of EHRs.[38] Ultimately, the aim of MIPS is to better clinical outcomes, improve population health outcomes, increase transparency and efficiency, empower individuals, and improve research data on health systems.[8] Payments by third-party payers to health service providers are specifically tied to the achievement of advances in healthcare processes and outcomes. Disease prevention and patient education are intrinsically part of these processes.

In some cases, computer applications are being used to identify patients who are at high risk for accidents such as falls or healthcare-acquired infections. In one study, researchers developed and validated a computer-based application which was used to screen hospitalized patients who are predisposed to contracting C. difficile infection, so measures could be adopted to reduce the infection risk.[39]

Treatment of Tobacco Use and Dependence

In the United States, tobacco use and dependence is the leading preventable cause of death and chronic diseases.[40] Healthcare costs attributable to tobacco use are quite significant. Effective evidence-based treatments are available, but their implementation by healthcare providers is lagging.[41] RTs can play a vital role in the treatment of tobacco-related diseases and are now using E-medicine as an aid to help tobacco users to quit smoking.

E-Medicine, including phone-based applications, provides exciting new components of treatment for tobacco use and dependence. With the extensive reach of the internet and the demonstrated efficacy of some applications, the potential impact on health outcomes is immense. More than 10 million internet users have searched for online information about how to quit smoking.[42]

Internet-based treatment programs can recruit tobacco users via search engines, or they can be an adjunct to telephone *quitline* counseling. Fig. 7.4 shows the *smokefree.gov* tobacco treatment website. When E-medicine applications are tailored to individual tobacco users, with frequent automated contacts via e-mail or text messages, rates of long-term abstinence from tobacco use are similar to those with traditional evidenced-based interventions.[42-45]

Consistent with the US Public Health Service clinical practice guideline recommendations for a high-intensity, multicomponent approach, web-based applications can provide both counselings that promote tailored quit strategies and tobacco cessation medications that have been approved by the US Food and Drug Administration.[46] These applications can provide sustained access to virtually limitless numbers of participants and are therefore very cost-effective. Table 7.2 lists some websites related to the treatment of tobacco use and dependence.

Fig. 7.4 Example of a web-based tobacco cessation resource. (From http://smokefree.gov.)

TABLE 7.2 Websites Related to the Treatment of Tobacco Use and Dependence

Organizations	Website
Association for the Treatment of Tobacco Use and Dependence	http://www.ATTUD.org
Centers for Disease Control and Prevention	http://www.cdc.gov/tobacco/quit_smoking/
International Tobacco Control Policy Evaluation Project	http://www.ITCProject.org
QuitNet	http://www.quit.com/
US Department of Health and Human Services	http://www.SmokeFree.gov
US Surgeon General's Office	https://www.surgeongeneral.gov/priorities/prevention/strategy/tobacco-free-living.html
Society for Research on Nicotine and Tobacco	http://www.TreaTobacco.net
Tobacco Free Kids	http://www.TobaccoFreeKids.org
World Health Organization, Tobacco Free Initiative	http://www.WHO.int/tobacco

Education of the Public and Healthcare Consumer

Today's savvy healthcare consumers understand that access to good information is essential to health-related decision-making. The Pew Internet and American Life Project found that more than 80% of internet users report seeking health information online; for those with chronic conditions, the rate is 86%.[47] Those percentages will most likely increase over the coming years.

E-Medicine applications offer unique public access to health education materials through the use of a variety of interactive tools such as websites, videos and graphics, chat rooms, e-mail, games, social media, and so on, through any web-enabled device. RTs should not underestimate the impact of these applications on public health education and disease prevention.

The amount of data available on health-related and wellness-related issues increases each year exponentially. RTs play an important role in helping their pulmonary patients assess accurate information found on E-medicine applications. Box 7.2 lists the factors to consider when educating pulmonary patients on evaluating the worthiness of E-medicine sources.[48]

BOX 7.2 Factors to Consider When Reviewing E-Medicine Sources

- Web address:
  - .com—A website most likely to a for-profit company
  - .org—A website most likely from a nonprofit organization
  - .edu—A website published by an educational institution such as a university
  - .go—A web page that belongs to a governmental organization
- When assessing credibility, consider the following:
  - Who are the authors?
  - What are their credentials?
  - Is there a hidden agenda?
  - Who published the information?
  - Is the information peer reviewed?
- When assessing accuracy, consider the following:
  - Is the information current?
  - Is the information supported by facts?
  - Is the information based on scientific evidence?
  - Is the original source listed?
  - Do other sources back up the information?
- Red flags to consider:
  - Anonymous information.
  - There appears to be a conflict of interest.
  - The information presented is one-sided or biased.
  - The information is outdated.
  - There is a claim of a miracle or secret cure.
  - No evidence is cited.
  - The grammar is poor and words are misspelled.

MINI CLINI

Cystic Fibrosis Online Resources

Problem

Shawn, a 17-year-old CF patient, is preparing to move away for college. He would like to research the World Wide Web to find out which options he has to manage his disease while away from home and ask an RT for additional suggestions.

Discussion

A simple online search using the words "CF," "CF resources," or "traveling with CF" done in any commonly available search engine such a Yahoo search, Bing, or Google will render a plethora of results that may answer Shawn's questions. However, the RT should warn Shawn of selecting only those resources that are sponsored or created by recognizable government or private for-profit organizations that provide a strong background and support in their recommendations. The RT should warn Shawn of for-profit private companies that will appear in his search trying to sell CF-related merchandises rather than provide honest, unbiased advice.

INFORMATICS AND CLINICAL DECISION SUPPORT

Health informatics, which refers to the use of information technology in healthcare, combines advances in computer science

and technology to improve clinical care, manage the health of populations, and accelerate research.

Business Intelligence

Business intelligence refers to a set of tools that permit capture, storage, and transformation of data into useful and actionable information. In healthcare, business intelligence tools are used to capture and integrate clinical data with relevant financial and operational data. **Key performance indicators (KPIs)** are indicators of quality and efficiency that are selected based on reporting or operational requirements. Commercially available business intelligence systems allow KPIs to correlate with dimensions that typically include person, time, place, and so forth. For example, a hospital may be interested in ventilator-associated conditions and ventilator-associated events. In this case, KPIs may include daily ventilator census and incidence of pneumonias and other ventilator associated conditions, which is then correlated with other data such as practitioners involved in the care of the patient before the event, hospital unit, date of occurrence, medication administer, and so on. This information allows an institution to not only report on the aggregate rate of incidents or events (such as ventilator-associated pneumonias [VAP]) but also recognize patterns relating to specific units and caregivers. Business intelligence also can be quite useful in research, especially in accessing data for retrospective clinical studies, as discussed in Chapter 8.

Clinical Decision Support

Clinical decision support (CDS) has been defined as "Health information technology functionality that builds upon the foundation of an EHR to provide persons involved in care processes with general and person-specific information, intelligently filtered and organized, at appropriate times, to enhance healthcare delivery and outcomes."[49,50] Examples of CDS include computerized alerts and reminders, such as notification to a therapist that the selected tidal volume exceeds the recommended range for a patient, based on predicted body weight and calculated using a previously recorded height measurement. CPOE systems, discussed previously in this chapter, frequently incorporate decision support alerts for drug-drug interactions and drug-allergy reactions. More advanced implementations may include examples of drug-disease interactions or contraindications, such as when the selected drug dose is high for a patient whose latest creatinine value indicates renal impairment. More complex clinical guidelines, such as for weaning from mechanical ventilation, may be embedded within the EHR system. Condition-specific order sets, such as "care paths" for patients admitted with COPD or asthma can guide the caregivers to ensure the provision of evidence-based care.

Documentation templates are frequently used for decision support where rules are embedded into the logic behind the templates. As an example, a template for charting may direct the therapist to chart breath sounds and then subsequently direct them to record the type of sounds and location in the chest. Similar directions also may be used to prompt the RT for ventilator setting changes resulting from changes in patient status.

Summaries of patient data and patient lists created based on specific criteria are other examples of decision support. For example, a worklist may summarize patients who have been on noninvasive ventilation longer than a specified time and are therefore appropriate candidates for evaluation for skin breakdown.

Evidence Supporting Clinical Decision Support

Several studies have evaluated the usefulness of CDS in patient care. CDS has demonstrated value in identifying high-risk patients using blood gas and laboratory results,[51-53] as a diagnostic aid, and in early identification of patients for intervention.[54,55] Knowledge-based systems have been shown to improve automated surveillance for the detection of healthcare-associated infections (HCAIs) in ICUs[56] and weaning from mechanical ventilation.[57]

Mobile Applications (m-Health)

Increasingly, mobile applications are being used to not only provide information to users but also capture healthcare data. Mobile phones, watches, tablets, and similar devices are becoming increasingly important in monitoring and delivery of healthcare interventions. They function as pocket computers, due to their advanced digital features, enhanced preferences, and diverse capabilities.[58] Their sophisticated sensors and complex software applications make the mobile healthcare-based applications more feasible and innovative (**m-health**). In a number of scenarios, user-friendliness, convenience, and effectiveness of these systems have been acknowledged by both patients as well as healthcare providers.[59] Applications such as Fitbit and the Apple Health app (among others) allow remote users to visualize streaming vitals sign data and graphics, monitor and transmit body measurements, monitor health indices related to sleep health, nutrition, reproductive health, and daily activities. At the consumer level, m-health applications are driving consumer engagement via telehealth, consumer education, and health applications that use mobile devices as a data collection and management tool.

RULE OF THUMB To benefit from m-health applications, consumers must be cautious and smart on their selection and use. Too much unnecessary information can lead to information overload and making wrong healthcare decisions. Physician guidance is always recommended when making decisions or when interpreting information based on m-health apps.

Administrative Decision Support

Administrative decision support using electronic data takes two main forms, which could be considered as external and internal benchmarking. External benchmarking is most prominently represented by the American Association for Respiratory Care (AARC) Benchmarking System, which facilitates identification and adoption of best practices among similar respiratory care departments. Internal benchmarking is exemplified by the hospital business review process. This form of benchmarking involves the creation and tracking of relevant quality and productivity metrics to inform internal process improvement activities.

American Association for Respiratory Care Benchmarking System

In the 1950s, the Xerox corporation invented a process called **benchmarking** as a way to identify and adopt best practices that have developed among similar organizations.[60] In 1989, Robert

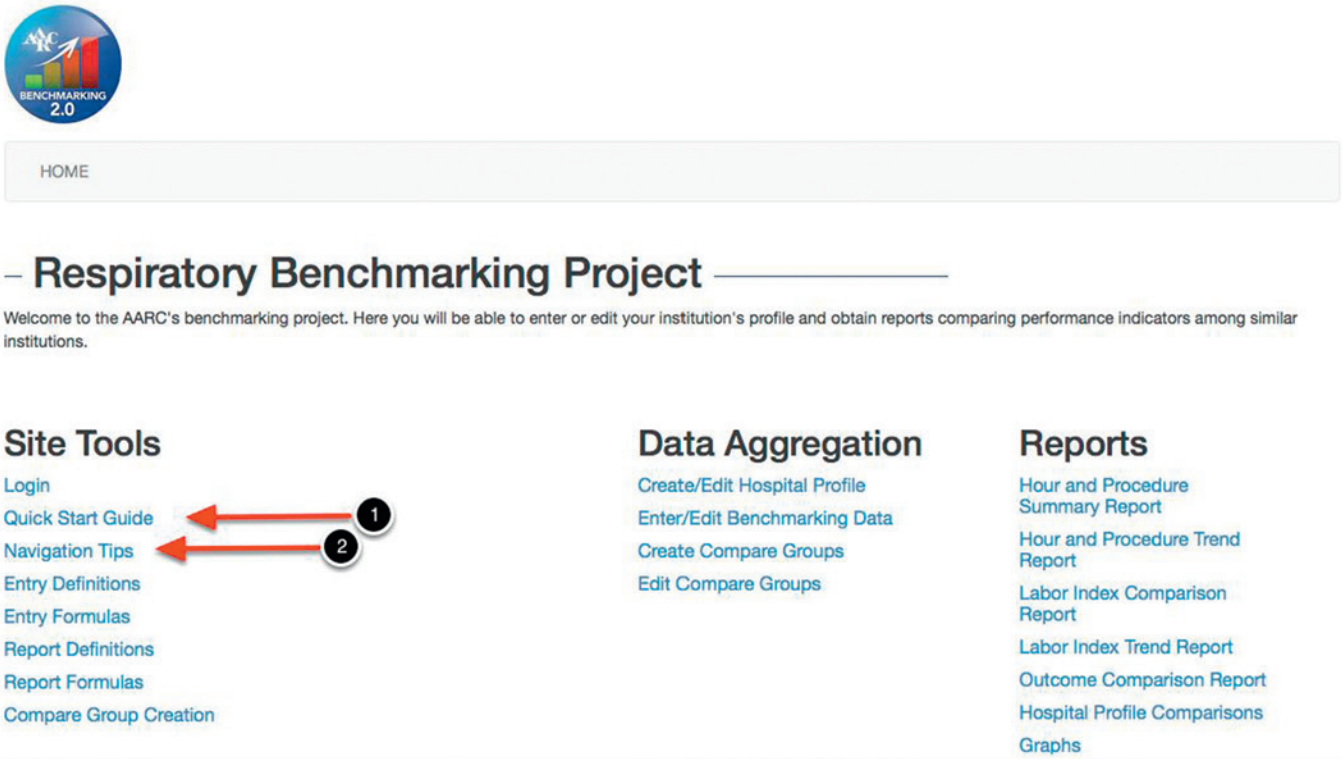

Fig. 7.5 Example of the AARC benchmarking project 2.0. (From American Association for Respiratory Care. *Respiratory Benchmarking Project.* Irving, TX.)

Camp wrote one of the first textbooks on benchmarking,[61] outlining four basic steps: (1) know your operation, (2) know the industry leaders or competitors, (3) incorporate the best, and (4) gain superiority.

Early in 2006, the leadership of the AARC, recognizing the need to establish a valid benchmarking resource for respiratory care, created an official benchmarking website designed for respiratory care department managers (http://www.aarc.org/resources/tools-software/benchmarking/). Department managers who are members (i.e., have a paid subscription to the AARC benchmarking system) may enter their department's profile, including information on structure and function as well as personal contact information, although an anonymous option is provided.[62] Next, managers enter productivity data monthly. This activity builds the communal database from which benchmarking reports are generated by all members (Fig. 7.5).

Best practices are identified using reports. A manager creates a report based on a "compare group" comprising several other departments that are similar in structure and function. This compare group is identified by performing searches on the database using various criteria from the profile and studying the profiles of the departments matching those criteria. The report has two sections. The first section gives numeric values for various productivity metrics (definitions are available on the AARC benchmarking website) that indicate the department's percentile ranking.[63] The manager is given the option of entering the desired percentile ranking, and the report will then calculate the opportunity (both regarding dollars and number of staff positions) associated with improving the percentile ranking. The second section of the report is a list of all the departments in the compared group ranked according to percentile on each of the productivity metrics. This section of the report allows the department manager to identify the top performers.[64] The next step for the manager is to study the profiles and monthly productivity data of the top performers to find clues about how they are achieving best practices. The AARC Benchmarking System has grown and evolved since its inception and continues to provide essential information to forward-thinking managers. It is a valuable tool for maintaining a completive advantage in the ever more demanding and competitive US healthcare environment.

Research

Research is based on data (facts) that can be transformed into information (facts that answer questions). Thus any of the sources of data described earlier are potential research tools. Online databases provide both the framework and content for designing research studies (e.g., PubMed). Private databases (e.g., productivity and hospital business review resources) support internal process improvement initiatives.[65,66] These issues are discussed in Chapter 8.

TELEHEALTH AND TELEMONITORING

Telehealth (previously known as **telemedicine**) involves the use of telecommunications to provide health information and health-related services care across distance. Telehealth has recently reemerged as a potentially effective way to address diverse problems in modern healthcare by increasing the quality, accessibility, utilization, efficiency, and effectiveness of healthcare, with the added advantage of cost reduction.[67,68] Telehealth can allow for

the evaluation, diagnosis, treatment, monitoring, triage, consultation, and follow-up of patients without travel.[69,70]

According to the CMS, telemedicine seeks to improve a patient's health by permitting two-way, real-time interactive communication between the patient and the physician or practitioner at a distant site. This electronic communication means the use of interactive computerized telecommunications equipment that generally includes audio and video equipment. Telemedicine is viewed as a cost-effective alternative to the more traditional in-person way of providing medical care, such as face-to-face consultations or examinations between the clinician and patient.[71] A form of telemedicine is **telemonitoring**, which involves the use of telecommunications and information technology to provide access to health assessment, diagnosis, intervention, consultation, supervision, and information across distance.

Although best practices in this area are still emerging, telemedicine and telemonitoring are gaining ground in the management of all type of patients, including those with pulmonary disease. In some cases, it has facilitated the timely diagnosis and treatment of patients with limited access to healthcare facilities. In particular, patients in remote geographic locations or those with limited mobility such as ventilator-dependent individuals with severe neuromuscular disease have benefited from telemedicine.[72] Computer interfaces for telemonitoring facilitate patient assessment through the two-way transmission of key clinical data such as vital signs, pulmonary function measures, and patient-ventilator data, and even the patient's physical appearance captured by computer web cameras. Similar monitoring also can facilitate the early detection of, and intervention for, any deterioration in a patient's condition. Such inventions have been shown to be helpful in reducing doctor visits and hospital admissions, a benefit to the patient and the economics of healthcare.[73]

Also, telemedicine has proved useful in facilitating the patient's participation in computer-based disease management programs. In particular, selected telemedicine applications have been created that bundle patient education, disease management, interactive communication, and other features. Such multipronged systems have been shown to be effective in helping reduce chronic disease exacerbations and related hospital admissions and re-admissions, as well as enhancing the daily functioning and quality of life of patients with asthma and COPD.[74] Other telemedicine programs have shown promise in helping overcome logistical barriers such as transportation and scheduling that too often prevent individuals from participating in valuable disease management programs. In particular, telemedicine has helped facilitate the participation of COPD patients in remote access pulmonary rehabilitation programs in which they otherwise would not have been able to participate.

Furthermore, their participation in such computer-aided rehabilitation programs has permitted these patients to achieve similar benefits associated with traditional rehabilitation programs (see Chapter 56), such as demonstrable enhancement in their tolerance for activities of daily living (ADL).[75]

Like many aspects of E-medicine, telemedicine seems to be in its infancy. As healthcare resource limitations and cost-containment pressures continue, as well as improvements in the applications and the efficiencies they offer, it appears inevitable that use of this and related technologies will expand and become commonplace in healthcare and more specifically in respiratory care.

SOURCES OF HEALTH INFORMATION

Considering that almost half of adults in the United States have limited health literacy, E-medicine applications have the potential to improve our patients' level of health literacy if used appropriately.[76] Low health literacy compromises patient safety, limits the overall quality of healthcare, and accounts for increased healthcare costs. When patients have poor knowledge about their disease and the management of it, positive outcomes become more difficult to achieve.[77]

Health Information Sources for Respiratory Therapists and Other Clinicians

Effective **information retrieval** is essential to evidence-based respiratory care. It enhances clinical expertise by providing information for the development of evidence-based, therapist-driven protocols, and it aids in clinical decision-making for the clinician. Although assessment skills of RTs generally sharpen with experience, their knowledge of the most up-to-date therapies and guidelines may diminish over time.[78] However, the best available medical evidence is highly dynamic and the amount of available information is staggering. RTs need to be knowledgeable about efficient ways to access, filter, process, and retrieve relevant information effectively. They also must be prepared to guide increasingly sophisticated patients and healthcare consumers, many of whom actively seek medical information on the internet in the use and validity of that information.

E-Medicine applications are a far-reaching, rich source of information. RTs can use search engines such as PubMed, MEDLINE, and Google Scholar to access, filter, and retrieve manuscripts and other sources for clinical practice guidelines, evidence-based systematic reviews of clinical questions, accrediting agencies, or other relevant sources of important information (Table 7.3; see Chapters 2 and 8).

Health Information Sources for Consumers

As discussed earlier, patients increasingly seek knowledge about diseases and treatments on their own. However, many users neglect to scrutinize the quality or source of this information, which is largely unregulated. Selected resources for pulmonary patients are listed in Table 7.4 and include the AARC website for patients (http://www.yourlunghealth.org), the websites of the National Lung Health Education Program (http://www.nlhep.org) dedicated to COPD patients, and MedlinePlus.gov of the National Library of Medicine. MedlinePlus features online interactive tutorials, practical instructional handouts for patients, a medical encyclopedia, and videos of surgical procedures.

APPLICATIONS IN HEALTHCARE ADMINISTRATION

E-Medicine applications also play an integral role in helping respiratory care managers and leaders maximize the value they add to

TABLE 7.3 Helpful Websites for Respiratory Therapists

Organizations	Website
American Academy of Allergy, Asthma, and Immunology	http://www.aaaai.org
American Academy of Pediatrics	http://www.aap.org
American Academy for Sleep Medicine	http://www.aasmnet.org
American College of Allergy, Asthma, and Immunology	http://www.acaai.org
American Association for Respiratory Care	http://www.aarc.org
American Cancer Society	http://www.cancer.org
Alpha-1 Foundation	https://www.alpha1.org/
American College of Chest Physicians	http://www.chestnet.org
American Heart Association	http://www.heart.org
American Lung Association	http://www.lung.org
American Thoracic Society	http://www.thoracic.org
ARDS Network	http://www.ardsnet.org
Centers for Disease Control and Prevention	http://www.cdc.gov
Cochrane Collaboration	http://www.cochrane.org
Committee on Accreditation for Respiratory Care	http://www.coarc.com
Cystic Fibrosis Foundation	http://www.cff.org
Global Initiative for COPD	http://www.goldcopd.com
National Board for Respiratory Care	http://www.nbrc.org
National Heart, Lung, and Blood Institute	http://www.nhlbi.nih.gov/health-pro
Society for Critical Care Medicine	http://www.sccm.org
US Surgeon General	http://www.surgeongeneral.gov

COPD, Chronic obstructive pulmonary disease.

TABLE 7.4 Helpful Websites for Pulmonary Patients

Organizations	Website
Medical Associations	
American Academy of Allergy, Asthma, and Immunology	http://www.aaaai.org
American Academy for Sleep Medicine	http://www.aasmnet.org
American College of Chest Physicians	http://www.chestnet.org
American Thoracic Society	http://www.thoracic.org
Alpha-1 Foundation	https://www.alpha1.org
Society of Critical Care Medicine	http://www.sccm.org
Patient Education and Support Organizations	
American Association for Respiratory Care	http://www.aarc.org http://www.yourlunghealth.org
American Heart Association	http://www.heart.org/heartorg
American Lung Association	http://www.lungusa.org
Cystic Fibrosis Foundation	http://www.cff.org
COPD Foundation	http://www.copdfoundation.org
Global Initiative for COPD	http://www.goldcopd.com
Healthways	http://www.QuitNet.com
National Lung Health Education Program	http://www.nlhep.org
SmokeFree: US Department of Health and Human Services	http://www.SmokeFree.gov
Government Agencies	
Centers for Disease Control and Prevention	http://www.cdc.gov
Food and Drug Administration (FDA)	http://www.fda.gov
Health Information Technology Regulations	https://www.healthit.gov
National Heart, Lung, and Blood Institute (NHLBI)	http://www.nhlbi.nih.gov
National Institutes of Health (Medline)	http://www.nlm.nih.gov/medlineplus/
National Library of Medicine	http://www.nlm.nih.gov

COPD, Chronic obstructive pulmonary disease.

their healthcare organizations. In addition to the benchmarking resources and business intelligence concepts described earlier in this chapter, there are other highly useful digital applications related to documentation, workload, and staffing; financial and quality management; human resources; regulatory compliance; and similar tools related to management and administration.

Documentation, Workload, Staffing, and Scheduling

Increasingly, the comprehensive software systems used by healthcare organizations provide features that support department-specific functions, including those essential to respiratory care departments. These software packages enable respiratory care department managers to retrieve, sort, and use information-relevant managing strategic functions such as resources use, staffing, productivity, and financial management. In addition, such software systems can link these strategic functions with day-to-day operations, such as using hospital census (e.g., percentage occupancy) and acuity (e.g., average severity of illness) data, helping determine how many RTs are needed during a given shift or other period to adequately handle such a patient load. These same data can be used by most such systems to calculate the productivity of an individual RT or the department as a whole. Often such productivity results are expressed as a percentage of a certain benchmark or reference range. For example, if the productivity expectation for an RT is to complete 24 aerosol treatments for an 8-hour shift (assuming no other workload), but because of several call-outs, the RT is assigned and completes 30 such treatments, then that therapist would have a productivity percentage of 125% (30 [actual] / 24 [assigned]). Fig. 7.6 shows an example of a worksheet for workload calculation. These software packages also facilitate computerized documentation, including ventilator-patient monitoring or charting the delivery of all forms of respiratory therapy, through computers or remote devices interfaced with the EHR. These documentation systems not only provide a record of the care provided and patient's response but are also interfaced with other facets of the comprehensive software platform, including those for billing and quality assurance.[79]

Financial Management

Computer hardware and software are universally used in the financial aspects of healthcare. The more predominant uses relate to financial accounting applications, including billing and accounts receivable, as well as managerial accounting functions, which encompass financial statement reporting, budgeting, and

Bennett Memorial Hospital

Workload Estimate for 3 Shifts by Zone

Procedure Name	Time Standard	Number of Orders	------Shift One------ # of Txs	Work Units	------Shift Two------ # of Txs	Work Units	------Shift Three------ # of Txs	Work Units
CCU								
ABG	20	3	3	60	3	60	3	0
AIRWAY CARE	25	1	1	0	1	0	1	0
ASSESSMENT	30	1	1	30	1	0	1	0
CPAP	5	1	1	5	1	5	1	5
EKG	22	1	1	22	1	22	1	0
EQUIPMENT CHANGE	10	1	1	10	1	0	1	0
MED NEB	13	2	2	26	2	26	2	26
METER DOSE INHALER	7	3	3	42	3	35	3	35
O2/LPM	5	1	1	15	1	10	1	10
O2/VENTI MASK	5	1	1	5	1	5	1	5
SPONTANEOUS MECHS	25	1	1	25	1	25	1	0
VENT CARE/ADULT	12	2	2	0	2	0	2	0
Total by Zone		18	18	240	18	188	18	81
# of Therapists Required for Zone				0.53		0.42		0.18
PEDS								
MED NEB	13	1	1	26	1	26	1	26
Total by Zone		1	1	26	1	26	1	26
# of Therapists Required for Zone				0.06		0.06		0.06
RICU								
AIRWAY CARE	25	1	1	0	1	0	1	0
CPT	20	1	1	40	1	40	1	0
EKG	22	1	1	22	1	22	1	0
MED NEB	13	1	1	26	1	26	1	26
METER DOSE INHALER	7	1	1	0	1	0	1	0
O2/AEROSOL	5	1	1	5	1	5	1	5
O2/LPM	5	1	1	5	1	5	1	5
Total by Zone		7	7	98	7	98	7	36
# of Therapists Required for Zone				0.22		0.22		0.08
SICU								
ABG	20	2	2	40	2	40	2	0
AIRWAY CARE	25	2	2	0	2	0	2	0
CPR	30	1	1	30	1	30	1	0
CPT	20	1	1	40	1	40	1	40
INCENT SPIROMETER	10	1	1	20	1	20	1	0
METER DOSE INHALER	7	3	3	49	3	42	3	14
O2/AEROSOL	5	1	1	5	1	5	1	5
O2/LPM	5	1	1	5	1	5	1	5
VENT CARE/ADULT	12	2	2	0	2	0	2	0
Total by Zone		14	14	189	14	182	14	64
# of Therapists Required for Zone				0.42		0.40		0.14

Fig. 7.6 Clinivision Mobile Patient Charting. Workload estimate for three shifts by zone. This report is grouped by zone and then the procedure to show the estimate for the number of procedures, work units, and therapists required. (Image used by permission from Nellcor Puritan Bennett LLC, Boulder, Colorado, doing business as Covidien.)

forecasting. *Accounts receivable* is a fancy term for billing for and monitoring of the reimbursement of services provided. Most of the billing to CMS and private health insurance providers and monitoring of such payments by hospitals is done through electronic software platforms. Often this process is facilitated by features within the healthcare organization's EHR system, which accesses a portal to the payment system of CMS or another reimbursement source.[79]

The financial accounting systems facilitate billing and interface closely with the managerial platforms used for financial statement

and budgeting. For example, once the software recognizes that a payment has been made by CMS, higher level financial statements such as the income statement can be immediately updated to show an increase in the revenue received. Software applications have enhanced managerial accounting functions in other ways, by facilitating the budgeting process, which ensures the healthcare organizations and respiratory departments have adequate resources to provide their services and perform their functions. Likewise, computer software permits faster and often more accurate financial forecasting, as well as the ability to make predictions under various economic and environmental scenarios.[80]

Quality Assurance

Computer software applications are a vital tool in healthcare quality assurance. Chapter 3 of this text provides some detail on the principles of and tools used for quality assurance in respiratory care and healthcare in general. However, it is important to note that many tools used in the **continuous quality improvement** (CQI) model, for both enhancing and monitoring quality, are computer-based. For example, a **root-cause analysis** is a process by which the underlying primary, secondary, and other notable causes of a medical error or other safety issues are identified, and then an action plan is created and implemented. Finally, an ongoing monitoring system is put in place to evaluate the plan's effectiveness, and software applications are commonly used to perform such an analysis. Respiratory care departments use software applications that track quality data such as unplanned extubations and noninvasive mask-induced skin breakdowns, to examine trends and the potential impact of corrective action.[81]

Regulatory Compliance

In a similar way that accounts payable systems of healthcare organizations use portals to facilitate reimbursement of services rendered, shared applications exist for the reporting of key compliance and regulatory data. For example, compliance with the meaningful-use objectives of the MIPS discussed earlier in this chapter is done in this manner. In addition, CMS has introduced the **value-based purchasing** system, whereby reimbursement by CMS to hospitals and healthcare providers is partially based on their ability to meet a predefined set of standards. Reporting by hospitals to CMS for this program and other similar ones, such as 30-Day Short-Term Readmission Rates, are monitored through similar computer-based reporting systems.[82]

Web Analytics

Web analytics is a generic term that encompasses the study of the impact of a website on its users. It employs software to measure trends such as how many people visited a website, how many of those visitors were first-time or repeat visitors, how they came to the site (i.e., if they followed a link to get to the site or came there directly), what keywords they searched within the site's search engine, how long they stayed on one or more web pages, what links they clicked on when they left the site, and other similar trends. Using insights gained from web analytics, healthcare institutions can build, optimize, and deliver experiences that are engaging, relevant, and personal aimed to attract the health customer, improve health scores, and optimize outcomes.

Healthcare organizations are using web analytics software for many other additional purposes. In the realm of business management and administration, healthcare organizations are using web analytics to measure trends of current and potential customers, to help make predictions about future market conditions, and as an aid in strategic business decisions. Many clinical applications for web analytics are gaining popularity, including to track usage of educational websites that are designed as patient resources—for example, those used to for patients with chronic disorders such as COPD, CF, diabetes, and neuromuscular diseases.[83]

Human Resources

In addition to their use in staffing and scheduling described earlier in this chapter, computer databases have proved to be invaluable tools for human resource functions of healthcare facilities and those more specific to respiratory care departments by enabling them to maintain employee records, track training and education, and keep abreast of licensure and credentialing renewals, among many other similar applications. In addition, web resources have proved invaluable in helping recruit talented staff. The AARC website has a "Job Bank" feature that enables employers to post openings and furnishes qualified candidates with instructions on how to apply. Many state societies for respiratory care offer similar resources, and there are many proprietary recruitment websites, including Monster.com, Indeed.com, and ZipRecruiter.com.

Beyond this, many healthcare organizations are using web resources to help evaluate job candidates. In addition to being able to search state agencies to confirm a candidate's licensure and the National Board for Respiratory Care (NBRC) websites to determine credentialing status, preemployment criminal background checks can be easily done through services offered on the web for a fee-for-service basis. Furthermore, although it is controversial, employers are increasingly performing credit checks and reviewing the social media profiles and patterns during the screening process of candidates.[84]

Privacy and Confidentiality

The *Health Insurance Portability and Accountability Act* (HIPAA) of 1996 established standards and safeguards to protect the confidentiality of medical records, including those maintained on computers and other similar devices. Essentially all EHR software offered by reputable sources must be HIPAA compliant, and healthcare organizations are required to have their staff trained on performing their functions within the guidelines of this law. However, in some ways, technologic advancements are threatening the protections offered by HIPAA. Increasingly, health information maintained and transmitted on portable devices such as laptop computers, tablets, watches, and smartphones is circulating outside the HIPAA-protected zone. Such information is increasingly kept on, or downloaded to, storage devices such as "thumb drives" or in remote computerized servers known as "the cloud" that may not meet HIPAA standards.

Furthermore, clinical datasets and databases originally intended for one purpose, such as regulatory compliance reporting or for clinical purposes, are being acquired by other organizations for different purposes, such as research and marketing. The required

protection of all PHI within such data sets is not always properly done, which poses further threats to patient confidentiality. Patient information on social media is another area of concern. Although it will take some time for our governmental regulators to enact updated legislation to address the impact that such technology has had on HIPAA compliance and patient privacy and confidentially, such regulation will eventually be adopted. In the meantime, RTs need to be ever mindful to protect and respect the confidentiality of patient information and to ensure such data are used only for its intended purpose (see the Rule of Thumb). Failure to comply with HIPAA regulations is a serious violation of federal law with financial and legal consequences for those involved.[85]

RULE OF THUMB Users can take steps to help prevent computer infiltration by malicious software by doing the following:

- Never share or use their password on public unsecured devices.
- Regularly update their computers with security patches from authorized sources only according to their IT Department guidelines.
- Install a virus scanning program and regularly update it.
- Most importantly, users should be careful when opening e-mail file attachments and refrain from downloading and installing applications from unknown sources.

APPLICATIONS IN TRAINING AND EDUCATION

Computing plays a central role in the education of respiratory care students, credentialing of graduates of educational programs, and continuing education for RTs.

Clinical Simulations

Computerized **clinical simulations** are a powerful learning tool. Computer-based simulation is a long-standing educational method for hazardous occupations that have shown remarkably low rates of failure (e.g., airline pilots, members of the military, astronauts, and nuclear power plant operators). Healthcare education has progressed to include the use of computer-based, full-body manikins and high-fidelity clinical simulators. These devices feature software to program clinical scenarios and simulated vital signs and physical examination findings that either improve or deteriorate in response to the actions of the learners. The simulators can reproduce situations requiring complex airway management or advanced life support. In virtual surgical simulators, certain devices allow learners to exert force against simulated tissue that offers realistic resistance, and in virtual bronchoscopy simulators, vocal cord movements are exhibited that are synchronous with the phases of breathing and cough.

Learners can better immerse themselves in carefully planned case scenarios and performing in a manner similar to that of real clinical situations (Fig. 7.7). They develop psychomotor, critical thinking, decision-making, and team-building skills. In contrast, traditional methods of didactic education in combination with clinical apprenticeships can result in increased knowledge, but limited, inconsistent experiential learning opportunities and experiences. Clinical simulators allow for more in-depth and consistent evaluation of learners' competencies in a safe environment. They are an excellent tool to help respiratory care departments meet TJC requirement of demonstrating the competencies of respiratory care staff in an ongoing and consistent manner.[86] Recommended steps in clinical simulation education are diagrammed in Fig. 7.8.

Clinical simulators are particularly valuable for learning how to function in rare but high-risk clinical situations. Training via simulators has resulted in improved performance of healthcare providers in emergency airway management, advanced life support, bronchoscopy, and surgery. Computer-based simulators also have become a useful tool in promoting and optimizing the use of interprofessional teams within clinical settings.[87,88] Clinical simulators have the potential to reduce medical errors and improve patient safety. Simulations promote relatively comprehensive learning and allow for performance in clinical settings to become more refined and automatic (Box 7.3).

Fig. 7.7 Clinical simulation benefits students. (From Cummings CW, et al: *Cummings otolaryngeal: head and neck surgery*, ed 2, St Louis, 2005, Mosby.)

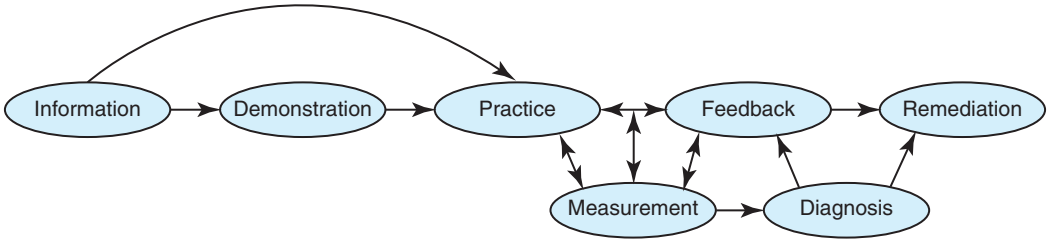

Fig. 7.8 Steps in clinical simulation education.

Student name and initiator name	Date and IP address View record	Submission date Delete record	Patient and competency and summary	Clinical instructor	Clinical site and location	Area device
Kumar Patel Tonya Cook	Wednesday, December 16, 2009 144.30.0.221	Wednesday, January 6, 2010 at 1:42 PM 144.30.0.221	Adult vital signs Satisfactory	Tonya Cook	Baptist Health Clinic	Adult floor web
Kumar Patel Heather Neal-Rice	Saturday, April 3, 2010 144.30.0.221	Saturday, April 3, 2010 at 4:37 PM 144.30.0.221	Adult x-ray interpretation Satisfactory	Michael Anders	St. Vincent Infirmary Medical Center Clinic	Medical ICU web
Kumar Patel Tonya Cook	Tuesday, October 20, 2009 144.30.0.221	Tuesday, January 5, 2010 at 3:57 PM 144.30.0.221	Adult nasal cannula Satisfactory	Tonya Cook	Baptist Health Clinic	Adult floor web

Fig. 7.9 DataArc documentation of clinical competencies. (Courtesy DataArc LLC, League City, TX.)

BOX 7.3 Learner Objectives in Clinical Simulation

- Interpret data
- Recognize and prioritize problems
- Make decisions
- Observe consequences of decisions
- Develop leadership skills
- Develop interpersonal communication skills
- Develop team-building skills
- Use available resources
- Manage stress and crisis

Full-Scale Physiologic Clinical Simulators

There are several full-scale, physiologic, clinical simulators available, two of which are SimMan (Laerdal Medical, Wappingers Falls, NY) and the Human Patient Simulator (HPS; CAE Healthcare, Quebec, Canada). These simulators generate physiologic functions, including pulse, blood pressure, cardiac rhythm, breathing, exhaled carbon dioxide, lung compliance, and bowel sounds. Interdisciplinary teams can practice scenarios such as cardiac defibrillation, hemodynamic monitoring, apnea, right mainstem intubations, tension pneumothoraces, anesthesia administration, occluded endotracheal tubes, high-pressure alarm limits during mechanical ventilation, and loss of medical gas.

Clinical Education Applications

Management of clinical education involves a significant amount of documentation, tracking, scheduling, evaluations, clinical competencies, reporting, and compliance with accreditation standards. E-Medicine software applications have been developed to help educators manage each of these aspects of the clinical education process.

These applications are secured, password-protected, web-based database management systems for documenting and reporting clinical educational activities for allied health professions, including respiratory care programs. These electronic records help both students and faculty members track student progress in completing required competencies as they progress through their clinical rotation assignments (Fig. 7.9). Functions may include the following:

- Immunization and background check information tracking
- Streamlined data entry process minimizing data entry duplication that can occur between clinical sites, students, and the academic program.
- A daily log for completed procedures and activities for students and instructor
- Competency evaluations
- Automated surveys to accommodate questionnaires for students, graduates, and clinical affiliates as required by accrediting agencies
- Cloud-based data and backup storage

A variety of such software applications is available to educational institutions. These include DataArc (http://www.dataarc.ws), Medhub (http://www.medhub.com), and Typhoon Group (http://www.typhongroup.com), among others. Students and faculty can use any web-enabled device, including smartphones, to access these applications to record and monitor academic progress.

National Board for Respiratory Care Credentialing

The NBRC uses computerized credentialing examinations for the written exams and the clinical simulation examinations (CSEs). Candidates must go to a designated testing center, sit at a monitored computer terminal, and take the examination during the designated timeframe. Once candidates are done with the examination, they receive their score immediately. In addition, to achieve the advanced credentialing level or Registered Respiratory Therapist (RRT) designation, candidates must demonstrate their ability to gather and interpret clinical information and then make or recommend clinical actions based on a clinical scenario. In the computerized CSE, RRT candidates must complete a series of case-based simulations and demonstrate that they have adequately mastered the management of major respiratory diseases (Fig. 7.10).

Continuing education is mandatory for national credentialing for the NBRC and often a requirement for most state licensure. Credentials awarded by the NBRC are valid for 5 years and are subject to renewal through the Continuing Competency Program (CCP) requirements. A new Credential Maintenance Program (CMP) will replace the CCP starting in 2019. RTs can renew their credentials by provide evidence to the NBRC that they are continuing to meet current standards of practice and have all

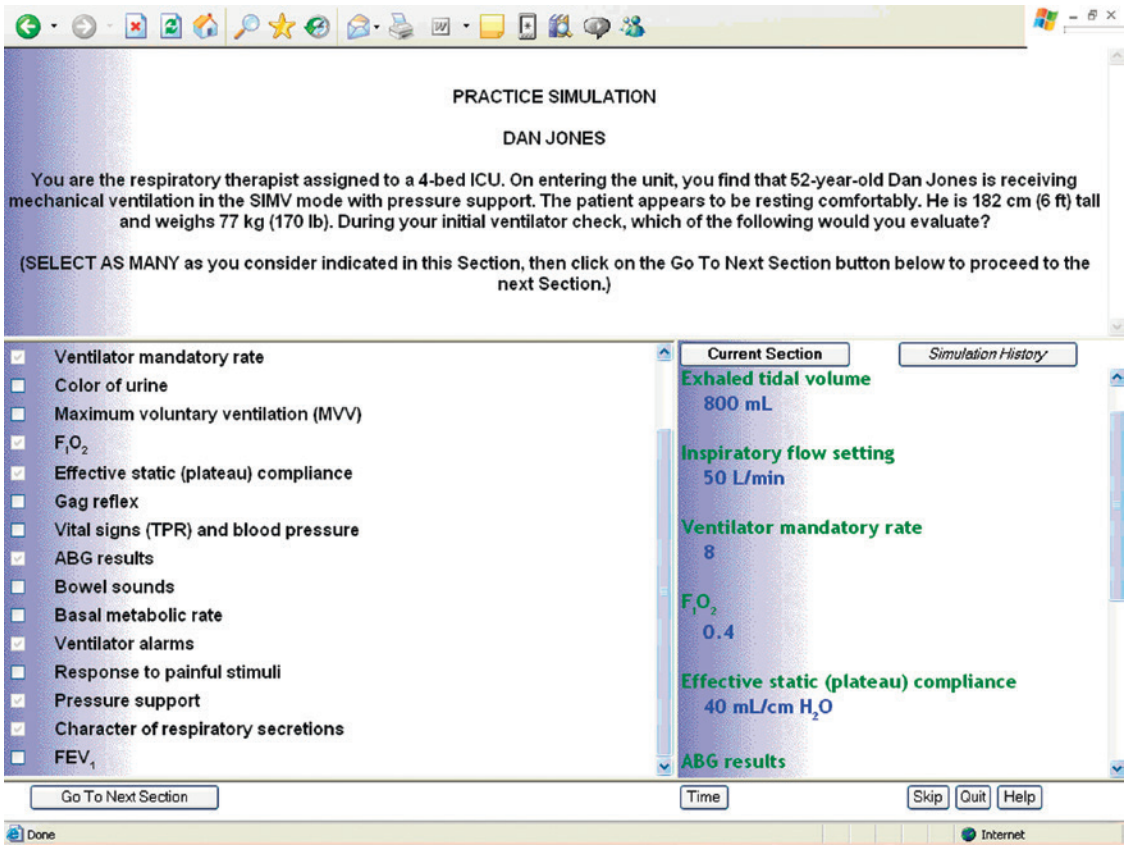

Fig. 7.10 National Board for Respiratory Care. Practice simulation problem. (Courtesy NBRC, Olathe, KS.)

the requirements for renewal. In addition, the new CMP will allow RTs to test their current skills and knowledge via a mobile device, tablet, or personal computer awarding credits toward their credential renewal.

Web-based **continuing respiratory care education** (CRCE) courses, which have been preapproved or outright sponsored by the AARC, offer RTs an easily accessible, efficient, and cost-effective means of meeting continuing education requirements for CCP and state licensure purposes, as well as keeping current in their profession.

Learning Management Systems

To an increasing extent, respiratory care educators use online, web-based **learning management systems** (LMS) platforms such as Moodle or Blackboard to augment traditional classroom courses known as web-enhanced courses or deliver entirely web-based courses (Fig. 7.11). This technology improves access and management of course content for web-enhanced courses. Web-delivered courses make respiratory care education possible for students who might not otherwise be able to attend respiratory care programs such as those requiring flexible schedules or students in remote rural areas. Other adjunctive applications, such as Adobe Connect and Zoom Video communications, permit live interaction between the student and faculty. Students can talk to their instructors and classmates via live audiovisual platforms. Participants also can have asynchronously access to archived classes, discussion boards, and related course content and other material by the use of podcasts or recorded sessions.

American Association for Respiratory Care

The AARC provides many continuing education opportunities online (see http://www.aarc.org). Webinars and text-based courses are available in both live and asynchronous formats. RTs may earn CRCE credits by completing these courses (Fig. 7.12). The AARC also provides web-based CRCE credits through the *Respiratory Care* journal. RTs can read the journal, use a copy of the test that appears in the journal to draft answers, and then complete the web-based test on the journal website (http://www.aarc.org/education/online-courses/crce-through-the-journal). The AARC maintains a transcript of members' CRCE credits, which RTs can access on the AARC website. These records can be electronically transferred to the NBRC for credentialing renewal.

In addition, to facilitate electronic networking among RTs, the AARC offers Specialty Sections and Roundtables. Each Specialty Section features an e-mail listserv for discussions, e-newsletters, e-bulletins, and a website. The AARC connect discussion boards (http://connect.aarc.org/home) also offers a wealth of information and networking opportunities to all RTs across the nation and the world.

FUTURE OF E-MEDICINE

The second decade of the 21st century will probably be best known for the radical transformation of healthcare, using information technology advances, particularly in emerging economies.[89] In the future, computerized technologic applications described

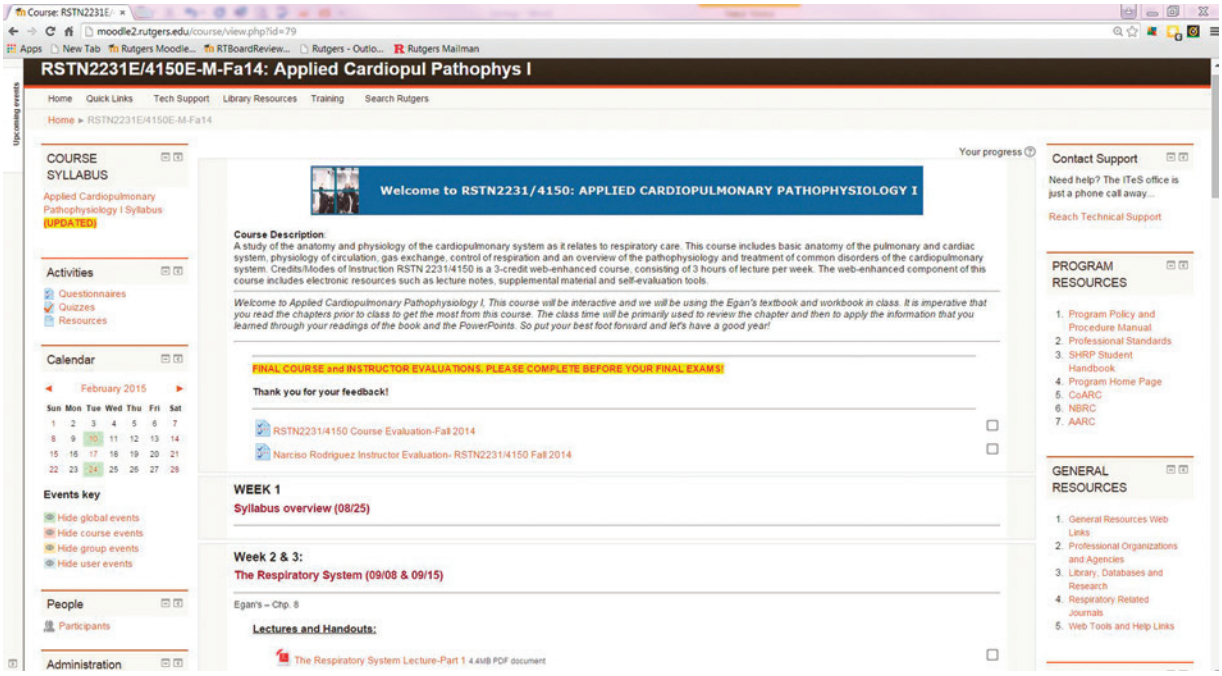

Fig. 7.11 Moodle Learning Management System Course homepage. (Courtesy Rutgers School of Health Professions, Respiratory Care Program–North, Newark, NJ.)

Fig. 7.12 American Association for Respiratory Care, Continuing Respiratory Care Education, web-based courses. (Courtesy AARC, Irving, TX.)

in this chapter, such as telemedicine and closed-loop decision-making on mechanical ventilators, will be more widespread, as well as refined and improved, and most likely able to do more in much less time. In addition, new digital applications will emerge, including a vast assortment of diagnostic, treatment, educational, and disease management applications available to patients and clinicians alike. The current technology coupled with new developments hold great promise for helping optimize the large-scale effectiveness and efficiency our healthcare system, as well as providing notable benefits to healthcare organizations and clinicians, including the RTs operating within it.

SUMMARY CHECKLIST

- E-Medicine relates to the use of computerized or digital technology to enhance efficiency and effectiveness of healthcare in general and more specifically patient care.
- EMRs represent the computerized records produced every time a patient (or consumer) uses health services.
- The EHR is the sum of all EMRs produced by the different encounters of the consumer with various healthcare entities throughout a lifetime.
- CPOEs allow new orders to be electronically transmitted to the EHR and ancillary departments such as the pharmacy, physical therapy, respiratory department, and so on, saving time and reducing transcription errors resulting from handwriting clarity issues.
- CPOE systems are the standard of care for large, complex healthcare institutions to meet national required guidelines to prevent and eliminate preventable medical errors.
- Enterprise software packages are designed to provide integrated functionality for healthcare organizations to enhance both efficiency and effectiveness of patient care.
- E-Medicine applications can be used in acute or nonacute settings by RTs to provide support and care for the pulmonary patient.
- Health informatics combines advances in computer science and technology to improve clinical care, manage the health of populations, and accelerate research.
- To comply with regulatory demands, hospitals and other healthcare providers increasingly use a single comprehensive software system or enterprise software package designed to provide integrated functionality to enhance both efficiency and effectiveness, as well as comply with current CMS and HHS IT regulations.
- POCT refers to blood gas analysis performed at or near the site of a patient, in a setting that is different from a normal hospital clinical laboratory. POCT testing reduces the time required to produce blood gas test results (turnaround time) and thus improves clinical care and decision-making for the clinician.
- A PACS is an application that allows for imaging storage, portability, communication, and clinical integration of all imaging modalities with the EHR.
- Most mechanical ventilators use microprocessors with complex software applications to deliver, monitor, and in some cases independently manage (closed-loop ventilation) ventilator modes.
- Therapist-driven protocols can shorten LOS and improve health outcomes.
- E-Medicine applications for asthma management include interactive internet applications, such as games for children, web applications linked to cell phones for personalized or automated voice or text messaging, and other telemonitoring applications.
- In patients with persistent asthma, evidence from research studies shows that these E-medicine applications can result in an improvement in asthma knowledge, self-management skills, peak flow rates, and adherence to inhaled corticosteroid controller medications and fewer symptoms, missed school days, nighttime awakenings, activity limitations, ED visits, and hospitalizations.
- E-Medicine applications for patients with COPD facilitates education, self-management, and timely feedback from healthcare providers.
- E-Medicine applications offer unique public access to health education materials through the use of a variety of interactive tools such as websites, videos and graphics, chat rooms, e-mail, games, social media, and so on, through any web-enabled device.
- Health informatics refers to the use of information technology in healthcare, combining advances in computer science and technology to improve clinical care, manage the health of populations, and accelerate research.
- Business intelligence refers to a set of tools that permit capture, storage, and transformation of data into useful and actionable information.
- KPIs are indicators of quality and efficiency that are selected based on reporting or operational requirements.
- CDS provides general and person-specific information, intelligently filtered and organized, at appropriate times, to enhance health and healthcare.
- Benchmarking includes four basic steps: (1) know your operation, (2) know the industry leaders or competitors, (3) incorporate the best, and (4) gain superiority.
- Telehealth (previously known as telemedicine) involves the use of telecommunications to provide health information and health-related services care across distance.
- Telehealth and telemonitoring allow for the evaluation, diagnosis, treatment, monitoring, triage, consultation, and follow-up of patients without travel.
- The internet is a rich source of information for RTs and patients when the quality and source of information are appropriate.
- Information retrieval is essential to practice evidence-based respiratory care. It enhances clinical expertise by providing information for the development of evidence-based, therapist-driven protocols, and it aids in clinical decision-making for the RT.
- E-Medicine applications also play an integral role in helping respiratory care managers and leaders maximize the value they add to their healthcare organizations.
- Computers and digital information can be useful to clinicians in optimizing the quality of care and to patients and their families participating in care plans.

- Common sense is the best prevention against infiltration by malicious software.
- Emerging computer applications are expected to support management of chronic disease and potentially reduce medical errors.
- The role of computer applications in clinical care, diagnostics, management, and education is essential and will continue to expand.

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8

Fundamentals of Respiratory Care Research

Robert L. Chatburn

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Explain why research activities are important in healthcare.
- Describe several sources of information that are commonly used during a literature search.
- Review the various roles of those involved in conducting research.
- Argue the importance of evidence-based medicine and note its limitations.
- Compare and contrast the types of research design.
- Describe strategies for getting started in research.
- Describe and give examples of how to develop a study idea and write a research protocol.
- Describe the three basic formats for publishing a research study.

CHAPTER OUTLINE

KEY TERMS

bibliographic database
case report
cohort study
co-investigators
consultant
evidence-based medicine
hypothesis
Institutional Review Board
meta-analysis
null hypothesis
observational cohort study
peer review
portals
pre-experimental
principal investigator
PubMed
***P*-value**
quasi-experimental
randomized controlled trial
research
scholarship
scientific experiment
scientific method
study subject
true-experimental

OVERVIEW OF RESPIRATORY CARE RESEARCH

The main purpose of this chapter is to help you become an educated consumer of medical research. It will present a brief overview[1] of how to search and evaluate the published literature in a particular area. In addition, this chapter will also review the specific steps in conducting research and presenting your results in a scholarly manner. But if you want to actually perform research, to be a respiratory care scientist, the best thing you can do is find a mentor—someone who has experience conducting scientific studies and publishing the results. A mentor can help you turn the ideas in this chapter into practical realities.

RULE OF THUMB **Research** involves a scientific and systematic exploration of new knowledge. **Scholarship** entails sharing the methods and findings of existing research and knowledge through presentations at professional events, as well as publishing textbooks and journal articles. The chances that any of us will become a famous researcher may be slim. For example, at last count (2014), there are about 173,000 people practicing respiratory therapy in the United States. Of those, approximately 48,000 are members of the American Association for Respiratory Care (AARC) as of 2018. Only 500 were listed as researchers (authors of abstracts) at the 2017 annual AARC Congress. Thus only 0.3% of practicing therapists and 1% of AARC members (at most) are expected to be actively involved in research projects. Yet every one of the 173,000 people in the respiratory care field needs to know how to read and understand scientific articles in medical journals. The same holds true for all healthcare workers. Even if you never conduct a study, you must be familiar with the basic concepts of research to practice as a professional whose understanding grows from a scientific basis for respiratory care practice and from continuing education.

The Importance of Research in Healthcare

Academic medicine has three basic missions: to heal, to teach, and to discover. Scientific research is the underlying theme that ties these activities together. These activities imply several classes of stakeholders: clinicians (who need the ability to assess the usefulness of new equipment and treatments), educators (who need the ability to find, summarize, and present evidence for clinical activities), administrators (who need to evaluate the quality of services and the validity of policies/procedures), and finally researchers (who need to be able to generate new ideas that inform the other stakeholders). *The one skill that is common to all these stakeholders is the ability to read and critically evaluate published scientific reports.* Without this skill, no meaningful evaluation of current practices can be made and no research can be planned.

HOW TO REVIEW AND EVALUATE THE LITERATURE

Students who have grown up in the digital age are quite familiar with finding information on the internet. Practically everybody has a smartphone, and, in my experience, it is not uncommon for a therapist or medical resident to look up the answer to a clinical question in a matter of seconds during bedside rounds. Here is a true story: An experienced colleague and I were helping a young physician write a research protocol. One of his outcome variables was some measure of atelectasis. I asked him how he would quantitate that outcome. He suggested that maybe he could create some kind of score. I said that I had done that a number of years ago in a paper by myself and a co-author named Deakins. Almost before I had completed the sentence, my colleague had entered our names into a Google Scholar[2] search and had the paper on the screen with the method for creating an atelectasis score. All this took less than 60 seconds. That is the power of knowledge in the information age!

Unfortunately, not all sources of information are equally reliable. Let's take a look at what is available.[3]

Bibliographic Databases

A database is a structured collection of facts. A list of names and phone numbers on a piece of paper is a database. A spreadsheet containing a business profit and loss statement is a database. And of course, a project created with a software database design program (e.g., Microsoft Access) is a database. A bibliographic, or library database, contains books, book chapters, reports, citations, abstracts, and either the full text of the articles indexed or links to the full text. Perhaps the most popular **bibliographic database** is **PubMed**, a service of the US National Library of Medicine that includes over 18 million citations from MEDLINE and other life science journals for biomedical articles back to 1948.[4] PubMed includes links to full text articles and other related resources in medicine, nursing, dentistry, veterinary medicine, healthcare systems, and preclinical sciences. It provides a *Clinical Queries* search filters page as well as a *Special Queries* page. The site also provides automatic e-mailing of search updates, the ability to save records, and filters for search results using "My NCBI." The My NCBI feature is particularly useful because it will periodically e-mail you results of automatic searches on subjects and authors of interest to you, saving you a lot of time in just keeping up to date, aside from any focused research.

Synthesized Databases

Synthesized databases are prefiltered records for particular topics. They are usually subscription-based with relatively large fees. This type of database may provide the "best" evidence without extensive searches of standard bibliographic databases. The gold standard and leading database in this category is the Cochrane Collaboration.[5] UpToDate is another subscription-based service.[6] It claims to be the largest clinical community in the world, dedicated to synthesizing knowledge for clinicians and patients.

Portals

Portals are web pages that act as a starting point for using the web or web-based services. One example of a subscription-based service is ClinicalKey,[7] which provides links to books, journals, Clinics in Medicine, patient education resources, and images. Another example is Ovid,[8] which provides links to books, journals, evidence-based medicine (EBM) databases (e.g., Cochrane Collaboration), and the Cumulative Index to Nursing and Allied Health Literature (CINAHL). Most medical libraries will have subscriptions to both of these services.

Electronic Journals and Books

We are rapidly reaching the point at which all medical journals are available online. Some are available *only* online. You should already be reading the *Respiratory Care Journal*.[9] Full text versions of *Respiratory Care Journal* articles are available online back to January 2003. Open Forum abstracts (i.e., abstracts presented at the annual AARC Congress) are also available.

There are many sources of electronic versions of textbooks available on the internet. From the PubMed homepage, select Books (instead of PubMed) from the drop-down menu in the upper left-hand corner of the page. Enter a search term, and you will get a results page with links for books and figures from

books. Subscription services include Oxford Reference Online,[10] STAT!Ref (a great source for nursing and drugs),[11] and Safari Books Online (an excellent source of technical reference books).[12] Again, your medical library will probably have subscriptions to these services. Another great book resource is Amazon.[13] Amazon sells new books, but many times you can find used editions for a fraction of their original cost.

RULE OF THUMB If you don't want to buy a book from Amazon, just use the website to get ideas before you go to the library. This is also a quick way to get the publisher information if you need to reference a book you do not have.

General Internet Resources

Google and Google Scholar are perhaps the most popular of the general internet search engines. Other options come and go, and, ironically, the best way to find new ones is to do a Google search on "search engines." But remember, these sites generally use proprietary search algorithms rather than controlled vocabularies like PubMed. As a result, you are likely to get unexpected results.

Suggestions for Conducting Searches

The first and most important suggestion I can offer is to talk to a professional librarian. These people can show you all the tricks of the trade—things you never imagined could be done. And in some cases, they will even do the search for you. Some libraries offer free courses on how to use all kinds of software tools for conducting searches.

When searching PubMed or Medline, there are tutorials on how to successfully navigate a search on a clinical topic. For example, when searching PubMed, it is helpful (but not necessary) to use Medical Subject Heading or MeSH terms (check the PubMed tutorials for an explanation).

Finally, bibliographic software such as EndNote[14] or RefWorks[15] can be extremely useful for keeping track of related articles and formatting them to meet the specifications of journals to which a researcher may submit an article of their own. These programs let you import the results of your reference searches into your own database for future use. If you are an author, they will also help you manage the references in your manuscripts. Programs like these will save you a lot of time and effort. Two free alternatives are Zotero[16] and Mendeley.[17]

Before moving on, I want to call your attention to another challenge. Just finding a source of research information is not enough. You must know how to read it. A great resource on this topic is a comprehensive book called *Studying a Study and Testing a Test: Reading Evidence-Based Health Research* by Richard Riegelman, MD, MPH, PhD. Also try typing in the search criteria "Gordon Guyatt how to read" to find a series of articles on how to read various kinds of study reports.

EVALUATING THE QUALITY OF RESEARCH

Not all research is created equal. Just because a research project is published does not necessarily mean that it has held up to scrutiny by experts. However, some journals or more accurately the articles published in them are what is called **peer reviewed**. In essence, this means that the papers in them have been reviewed often multiple times, by experts, and usually only after several drafts do they get published. The peer-review process is discussed in more detail later in this chapter. One way to determine whether a journal or article is peer-reviewed is to see if it is included or indexed in Pubmed or Medline, which generally means it is peer-reviewed. For example, *Respiratory Care Journal* is a peer-reviewed journal; however, the *AARC Times* is not.

Evidence-Based Medicine

Another important concept regarding high-quality care is **evidence-based medicine**.[18] EBM refers to an approach to determining optimal clinical management based on several practices as follows: (1) a rigorous and systematic review of available evidence, (2) a critical analysis of available evidence to determine which conclusions are most sound and applicable, and (3) a disciplined approach to incorporating the literature with personal practice and experience. In a broader context, EBM can be thought of as understanding and using the best quality evidence available (i.e., the best-designed, most rigorous clinical trials) to support the most appropriate and correct possible clinical decisions. Nevertheless, EBM is far from perfect, including problems with ignoring clinical judgment and patient values, placebo effects, and poor systematic reviews comprising a large portion of EBM literature.[19]

In rating the quality of scientific evidence, one needs to recognize the various types of study designs from which scientific evidence comes.[20] The simplest and least rigorous design is a single **case report**, in which a new clinical issue or problem is described in a single patient. A description of the favorable outcome of using a new mode of mechanical ventilation in one patient with refractory hypoxemia is an example of a single case report. Although single case reports have value in pointing out new insights and new possibilities for treatment, disease associations, or disease causation, they cannot prove the effectiveness of a treatment or the causality of a risk factor. This is because, by nature, they lack a control or comparison group (i.e., a group that is similar to the patient or patients described, differing only in whether the risk factor of interest was present or the treatment of interest was applied). Collecting a group of patients with similar clinical features is called a case series. A series may have greater impact than a single case report because it suggests that the issue is more general than in a single patient alone. However, like a single case report, a case series cannot prove the efficacy of a treatment or the causality of a risk factor because no comparison or control group is included.

Cohort studies compare the clinical outcomes of two groups (cohorts). A cohort is a group of patients who share some defining characteristic, such as age or disease. Cohort studies generally have greater scientific rigor than case studies or case series and consist of two broad types of study design: **observational cohort studies** and **randomized controlled trials** (RCT). An observational cohort study compares the outcomes between two groups of patients, with the treatment allocated to one group but not the other. For example, an observational cohort study of a new protocol for mechanical ventilation would compare

outcomes (e.g., duration of ventilation) between two groups of similar patients. One group would be managed by protocol and the other by routine choices made by physicians. The key idea is that the groups are not selected by an intervention of the investigator. Rather, the investigator simply observes the treatment process and outcomes, and then assesses the strength of the relationship between the two. The study is "controlled" for confounding factors by including other common characteristics of the cohort in the statistical analysis. But such a study cannot be used to infer causation (correlation does not imply causation).

In contrast, a RCT mitigates confounding factors by randomly assigning study participants into either a treatment group (e.g., a ventilator management protocol) or the "control" group (usual management by physician preference). This is usually considered the strongest study design because it has the least risk of bias. This allows both researchers and consumers of the research to confidently attribute outcome differences between the two groups to the treatment, and if performed properly, RCTs can be used to infer causation (i.e., treatment-caused measured outcome).

Different types of RCTs exist and include the parallel-control study and the crossover study (Fig. 8.1). Parallel-control treatment studies compare two groups: one receives the treatment being studied, and the other receives the control treatment. Outcomes in the two groups are compared, especially regarding the main outcome of interest in the study. For example, a parallel-control randomized trial of low-stretch ventilation for ARDS would be composed of one group of patients receiving low-stretch ventilation and another (otherwise similar) group receiving higher stretch ventilator settings. The two groups would be compared on key outcomes, such as survival, discharge from the intensive care unit, and organ system failures. This design was used in the ARDSNet trial that showed the superiority of using a tidal volume of 6 mL/kg (ideal body weight) in managing patients with acute respiratory distress syndrome (ARDS).[22]

MINI CLINI

Study Designs[21]

Three characteristics are seen in a **scientific experiment**: (1) *manipulation* of an independent (treatment) variable, (2) *control* of all other variables except for the dependent (outcome) variable, and (3) *observation* of the change, if any, in the dependent variable.

A research design that plans for manipulation, observation, and control is thus an experimental research design—that is, a plan for a scientific experiment. This will not be the case in nonexperimental research design.

The major purpose of a research design, especially in clinical research, is *control* of potential nuisance variables. There are four methods of control commonly used in experimental research design: (1) random selection of sample and random assignment to groups, (2) matching of subjects between groups or grouping of subjects based on a nuisance variable to achieve homogeneity (e.g., grouping based on age or weight), (3) including a nuisance variable as a treatment variable, and (4) statistical removal of a nuisance variable through analysis of covariance.

The first three methods are of *experimental* control, whereas the last is a *statistical* control. The advantage of the first method, randomization, is that random or chance assignment can be expected to even out any nuisance variables far all groups, whether a nuisance variable is known in advance or not. The second method of control is frequently seen when subjects are used as their own controls in a before and after study, or in studies of paired twins. A blocking design, termed a *randomized block*, will be illustrated when presenting common designs.

Experimental research designs are distinguished from the weakest to the strongest, on the basis of the amount of control employed, using the following terms:

Pre-experimental: There is little or no control of extraneous nuisance variables. Such a design is often useful for a pilot study.

Quasi-experimental: Designs lack full control of all variables, but there is an effort to compensate with other controls. Usually, randomization is lacking, perhaps because of ethical constraints in choosing or assigning subjects to treatment.

True experimental: Designs provide full control of variables by one or more of the methods previously described (e.g., RCTs).

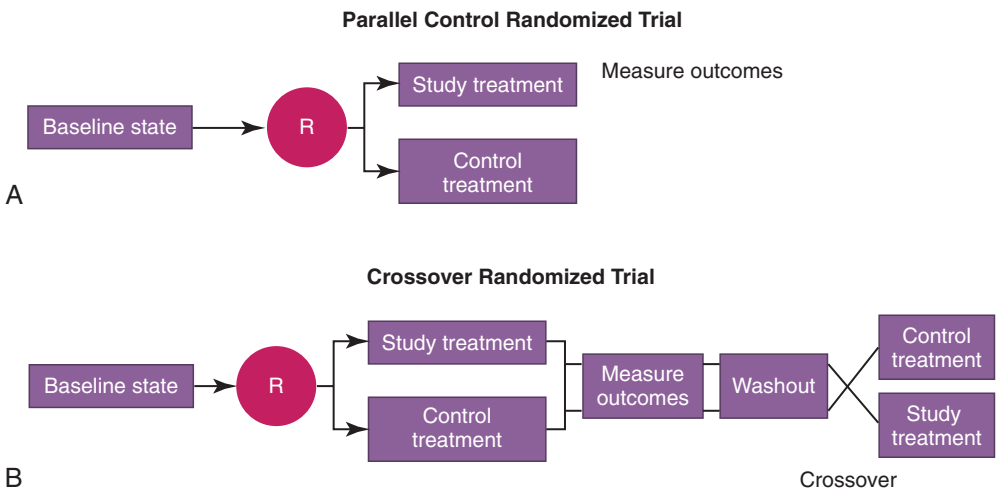

Fig. 8.1 Study Design of the Two Types of Randomized Controlled Trial: Parallel-Control and Crossover. In a parallel-control trial, after randomization (*R*), one group receives the study treatment, while the control group receives the comparison treatment (possibly a placebo). At the end of the subsequent observation period, study outcomes are measured, and the trial is over. In a crossover trial, one group initially receives the study treatment and the other group receives the comparison treatment; outcomes are measured; and after a washout period (see text), each group receives the alternative treatment for another period, after which outcomes are measured again.

In the other type of RCT—the crossover trial—the study treatment is first administered to one group of study subjects while the other group receives the control or comparison treatment. Then, after measuring outcomes and a subsequent "washout period" (in which the effects of the initial treatment wear off), the group initially given the study treatment receives the control treatment and the group initially given the control treatment receives the study treatment. The crossover study design offers a statistical advantage of greater power to detect a difference between the compared groups. This means that fewer study participants are required to find a statistically significant difference, if one exists. However, crossover studies can be performed only when the effects of the initial treatment administered to the first study group can wear off completely, allowing the study group to return to its baseline state before the alternative treatment is administered. When the effects of treatment are permanent (e.g., surgery, radiation therapy), a crossover trial involving that treatment cannot be done because washout of the treatment effect is not possible.

EBM requires knowledge of how to analyze the results of clinical trials (e.g., RCTs and observational cohort studies) and how to apply the results of such research to high-quality clinical practice. Another method of EBM is systematically reviewing the available literature, called **meta-analysis**. A meta-analysis of a clinical question (e.g., does a low-stretch mechanical ventilation strategy improve survival in ARDS?) identifies, analyzes, and summarizes the body of literature that meets specific criteria about this topic by assessing the quality of the available evidence and giving greater weight to better designed, more rigorous studies and less to, or even excluding, weaker ones.

Sometimes, meta-analyses pool the actual data from different trials together when pooling is scientifically and statistically permissible. In other instances (called narrative analyses), the meta-analysis simply evaluates the quality of the data from each available trial (based on explicit methodological criteria) to offer a conclusion about the clinical issue. A meta-analysis performed as part of an evidence-based approach to determining the optimal ventilatory approach for ARDS might weigh the results of large randomized clinical trials of low-stretch versus conventional tidal volume approach mechanical ventilation more heavily than the results of small observational studies. Such narrative meta-analyses have for many years been an important component of professional society guidelines for managing specific diseases. For example, a 2003 evidence-based review of the management of individuals with alpha-1 antitrypsin deficiency issued experts' recommendations for testing for this genetic cause of chronic obstructive pulmonary disease (COPD). A level A recommendation (i.e., that testing should be performed) was issued to test all symptomatic adults with airflow obstruction on pulmonary function tests (whether carrying the diagnosis of emphysema, COPD, or asthma in which airflow obstruction fails to reverse completely with bronchodilators), asymptomatic individuals with persistent airflow obstruction on pulmonary function tests with identifiable risk factors (e.g., cigarette smoking, occupational exposure), individuals with unexplained liver disease, and adults with the skin condition necrotizing panniculitis.[23] Although the hope is that issuing such evidence-based guidelines will improve the care that such individuals receive by allowing clinicians to access efficiently the best available information, experience suggests that clinicians may sometimes be slow to adopt the best available evidence in caring for their patients.[24]

RULE OF THUMB The randomized controlled clinical trial is often considered to be the most rigorous type of study design to prove the efficacy of a treatment. The optimal randomized controlled clinical trial is designed to be free from bias that can confuse the study results.

Some authors point out that EBM does not differ from prior practice in which clinicians were called on to analyze carefully available data and make clinical judgments based on the best quality information available. However, EBM specifies precise methods for analyzing available information and allowing the clinician to judge best practices. As a measure of the importance of EBM in respiratory care, several articles in *Respiratory Care Journal* considered the effectiveness of RTs and of various respiratory care treatment modalities using an evidence-based approach.[25-27] The Clinical Practice Guidelines of the AARC are being systematically reviewed to reflect the rigorous techniques of EBM and to ensure that guidelines for respiratory care management reflect the best available evidence.[27] The proof that low-stretch ventilation is associated with improved survival in patients with ARDS and the methods used to enhance awareness of this best practice are further examples of evidence-based medical practice.

RULE OF THUMB Various scales exist to rate evidence. One such scale rates evidence on a scale from Grade A to Grade D, as follows:

Evidence Grades

Grade A: Scientific evidence provided by randomized, well-designed, well-conducted, controlled trials with statistically significant results that consistently support the guideline recommendation.

Grade B: Scientific evidence provided by well-designed, well-conducted observational studies with statistically significant results that consistently support the guideline recommendation.

Grade C: Scientific evidence from bench studies, animal studies, and case studies.

Grade D: Expert opinion provides the basis for the guideline recommendation, but scientific evidence either provided inconsistent results or was lacking.

Finally, as mentioned previously, an important aspect of ensuring that only high-quality evidence gets published in medical journals is the so-called peer-reviewed process. Peer review means that when a paper is submitted for consideration to publish in a medical journal (like *Respiratory Care*), reviewers who are experts in the subject are selected by the journal editor and invited to read the paper and submit to the journal editor their structured assessment of the paper. In general, peer reviews are invited by two to four reviewers for every submitted paper. This assessment by each reviewer covers all aspects of the submitted paper—for example, the results, the analysis, the figures, title, abstract, text, and so on. The structured reviews are then submitted by the reviewer to the journal editor who synthesizes the

different reviews of the paper and then sends to the authors of the paper a summary of these reviews. The summary indicates whether the paper is accepted to publish or rejected, or—most commonly—how the paper should be revised in order to be considered further for publication. If the authors can respond to the reviewers' and editor's comments, the paper may later be accepted for publication.

HOW TO BEGIN DOING RESEARCH

Suppose that just being an educated consumer of research is not enough for you. You want to do your own research projects or at least participate as part of a research team. Another way to begin in research is to find out who is doing the research in an area in which you are interested and volunteer to help out. This could involve assisting in screening, recruiting, and enrolling research participants or simply collecting data.

Increasingly, healthcare organizations and related educational institutions are establishing formal or informal mentoring programs, which may include research and other similar projects. RTs can inquire with their manager or supervisors if such opportunities exist. In any event, those interested in research need to be prepared to commit a significant amount of time and effort.

Also, remember that some forms of research are easier to accomplish than others. For example, publication of your research often involves the preparation and presentation of a poster at a professional event (e.g., the annual AARC Congress). Similarly, preparing an abstract, which is a short (often less than 300 words) summary of a research or quality improvement project for a journal, may be a good way to begin and help advance your career as well. Maybe you are involved in a quality improvement project and need to know the basics of research methodology. Hopefully, you have decided to be the next leading scientist in the respiratory care field.

Whatever your motivation, I remind you that your first task is to find a mentor. After that, find a good textbook. There have been only two textbooks on respiratory care research. One is fairly new,[21] and the other is out of print[28] (but still very useful if you can find a used one on Amazon.com). Of course, there are many other fine textbooks on healthcare research, and I suggest you consider as many as you can find (again, search Amazon.com). Back in 2004, *Respiratory Care Journal* dedicated a whole issue to research and publication. It contained 19 articles written by the leaders in respiratory care research. I highly recommend that you find and read it (*Respiratory Care*, October 2004, Volume 49, Number 10).

In the next sections, we will look briefly at the major skills required to design, conduct, and report healthcare research.

How to Develop a Study Idea

No doubt, the biggest hurdle for someone new to research is how to generate an idea worthy of investigation. You need passion and time. Those outside the research community often say that emotion and personal belief play no part in the scientific method and that only through detached objectivity can the truth be revealed. If this were, in fact, the case, there would be no human scientists. Without passion, there could be no **hypothesis**, without a hypothesis there could be no experiment, and without experimentation there would be no science. Choosing and defining a research topic are the first steps in applying the scientific method to a clinical research problem. This process implies concern or doubt about some concept or observation, usually based on the observer's experience from clinical practice. Indeed, the scientific method itself can be viewed as nothing more than organized curiosity. Curiosity about the details of one's everyday activity provides the motivation for finding out how or why events are related. Curiosity and the creative energy it produces are vital ingredients of a productive research effort. The scientific method simply provides a standardized and efficient technique for describing relationships among events in a way that can be verified by other observers. You can think of the scientific method as a way of creating beliefs based on evidence.

Your interest may be stimulated in a number of ways. One of the most obvious ways is to read medical journals. Often one investigator's results will not completely answer the questions that another investigator seeks to answer. Perhaps the authors themselves suggest areas in which further work needs to be done (usually found in the discussion section of a scientific paper). Occasionally, the results of an article contradict those of a previous study, creating the need for yet another look at the research problem. Review articles that cover the state of the art in some area of research are especially useful in helping you generate ideas along these lines. The basic concept to remember is that research breeds more research and that the truth in scientific research is defined when the results of earlier experiments and studies can be reproduced consistently by others.

RULE OF THUMB Richard Feynman, who received the Nobel Prize in Physics in 1965, once said, "Science is the belief in the ignorance of experts."

Trying to develop research topics from personal experience is often the most frustrating approach for the beginning researcher. The natural tendency is to choose a general problem that everyone seems to recognize but no one does anything about. The difficulty lies in trying to narrow the general idea to a specific problem statement.[29] There are at least two reasons for this. First, a general problem, by its nature, is often spoken about in vague, undefined terms. Second, in attempting to explicitly describe the problem, it may appear to be overwhelming. One may easily become frustrated to the point of not being able to write anything.

One way to avoid this situation is to start small. Begin with a specific incident that stimulated either curiosity or irritation. *Simply state what you see happening and why it is important.* Write a narrative, first-person account of the incident. Now you can begin to review the literature, using key definitions related to your study idea to speed the search. Try to find similar problems in other disciplines to create original experimental approaches. For example, many problems concerning clinical measurement (e.g., airway pressure measurement) have been solved in the context of electrical or mechanical engineering. Keep in mind that not all ideas you have will be practical to study. When searching the literature, consider whether the experimental methods you will use are feasible for your situation (Box 8.1).

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What Is the Scientific Method?

The scientific method is usually thought of as a series of steps that lead from question to answer (and then usually to more questions).

1. Formulate a Problem Statement
   Research projects usually start out as a vague perception of some problem, either real or imagined. The first step is to refine this vague notion into a concise statement, usually only one or two sentences in length. Think in terms of (a) what you see happening and (b) why it is important. For example, if you find a coin lying on the ground, your problem statement might be "I need to identify this coin so I can decide whether or not to spend it."
2. Generate a Hypothesis
   The hypothesis is a short statement that describes your belief or supposition about a specific aspect of the research problem. The hypothesis is what you test with an experiment. Nobody knows where hypotheses come from; forming one is a creative act. All you can do is prepare yourself by thoroughly studying all aspects of the problem so your mind becomes a fertile ground for hypotheses to grow. Continuing with our example, we might hypothesize that "the coin is a penny."
3. Define Rejection Criteria
   The purpose of the experiment is to provide data. We will use the data to either reject the hypothesis as false or else accept it for the time being as a useful assumption. The fact that we can never prove the truth of a hypothesis leads us to focus on trying to prove it false. We prove a hypothesis is false by comparing the experimental data to a set of criteria we have established before the experiment began. If the experimental data do not meet the criteria, we reject the hypothesis (hence the name "rejection criteria"). In order to define the rejection criteria, we need to specify what we can measure during the experiment. For example, we could measure the coin's diameter and note its color.
4. Make a Prediction
   Next, we make a prediction based on our hypothesis that specifies the rejection values. For example, we can say, "If the coin is a penny, it will have a diameter of 1.9 centimeters and a copper color." The rejection criteria are thus: diameter = 1.9 centimeters and color = copper.
5. Perform the Experiment
   The rejection criteria determine the measurements that are required in the experiment. Many factors are involved with designing experiments, some of which we will discuss in the next section. Much of experimental design is based on statistical theory, which is beyond the scope of this chapter. However, the basic idea is to determine (a) what variables to measure, (b) how the measurements should be made, and (c) what experimental units (subjects) will be used for making measurements. In our simple example, we have only one experimental unit (the coin) and we need only a ruler and our eyes for making the measurements.
6. Test the Hypothesis
   It is the hypothesis, not the experimental subject, which is being tested (despite the fact that we say things like, "The patient was tested for cystic fibrosis."). The hypothesis is tested by comparing the experimental data to the rejection criteria. If the data contradict the prediction we made, then the hypothesis is rejected. If not, the hypothesis is accepted as possibly true until further data can be obtained. For example, suppose that the diameter of the coin is 2.1 centimeters and it is silver. Obviously, we would reject the hypothesis that it was a penny. We would then create a new hypothesis (perhaps that the coin was a dime) and a new prediction (based on the diameter and color of a dime). But suppose the diameter is indeed 1.9 centimeters and the color is copper. Does that mean it is definitely a penny? What if there is a foreign coin that just happens to have those characteristics? So, we simply acknowledge that we may be wrong but until we have further information, we will suppose the coin is a penny. This example shows that we can do everything right in terms of following the scientific method and still end up with a wrong conclusion. It also shows the critical nature of selecting the right rejection criteria and making accurate measurements. It also shows how science usually produces more questions than it answers.

BOX 8.1 Factors Affecting the Feasibility of a Research Project

1. Significance or potential benefits of study results
2. Measurability of research variables
3. Duration and timing of study
4. Availability of research subjects
5. Availability of equipment and funds
6. Knowledge and experience of investigators

Once you have clarified your study purpose through your literature review, the next step is to develop a formal problem statement. This problem statement is the foundation of the actual study design. It dictates the concepts and methods used to gather data. It also determines the theoretical context in which the conclusion will be interpreted. From the problem statement comes either a brief statement of the study purpose(s) or a hypothesis statement. A hypothesis is a supposition or proposed explanation for an observation. For example, here is an actual problem statement from a published abstract:

> *Protective lung ventilation requires calculation of predicted body weight from gender and height. Thus, inaccuracy of height data in the electronic health record (EHR) is a risk factor for volutrauma. A study showed that bedside tape measurements or visual estimates of height in ventilated patients may be highly inaccurate but that height predicted by ulnar length might be an alternative. In our institution, height records are often based on patient self-reporting, with uncertain accuracy. The purposes of this study were: (1) to evaluate the difference between patient height of unknown origin recorded in the EHR and predicted height from ulnar length, and (2) to determine the effect of height difference in setting tidal volume during ventilation.*[30]

This is a descriptive study. There are no predetermined hypotheses. But such a study might generate hypotheses to test in future studies (e.g., error in height determination is associated with increased duration of mechanical ventilation). Here is an example of another published abstract with explicit hypotheses:

> *The FiO_2 for constant flow (CF) oxygen therapy via nasal cannula depends on a combination of factors, including breathing frequency and the anatomic reservoir (AR). Patients with COPD have end expiratory flows which do not reach zero, potentially eliminating the AR and decreasing FiO_2. Pulsed flow (PF) devices that do not depend on the AR and FiO_2 should not be affected by loss of the AR. The purpose*

of this study was to test 2 hypotheses: (1) loss of AR reduces FiO_2 for CF, and (2) loss of AR does not affect FiO_2 for PF.[31]

Creating clear statements of study purpose or hypotheses is a key element for success in research. The purpose or hypothesis makes clear what the experimental method should be. The methods section of your study protocol is related to the purpose or hypothesis because it dictates what the outcome variables are and how to measure them, as well as how to analyze the data and what statistical tests to use.

RULE OF THUMB One of the best study ideas for a beginning respiratory therapy researcher is to do a device evaluation (particularly a new device).[32] This kind of study is usually very inexpensive (vendors often donate or loan equipment and supplies) and does not require approval by the institutional review board (IRB; as is required for studies of human subjects).

Key Roles in Research

People play different roles in a research project. The **principal investigator** is the one who is ultimately responsible for completing the study in compliance with all applicable rules and regulations, and for adhering to the protocol approved by the IRB. **Co-investigators** have a range of roles spanning screening/entering subjects into the study (including obtaining informed consent, if applicable), collecting and analyzing data, and finally assisting with writing the abstract and manuscript for publication. The study may include the help of **consultants**, such as statisticians, who may give advice before, during, and after the study. If the study is funded, there may be a host of people involved with the business and legal aspects of partnership with a funding agency. Last but not least, there are the **study subjects**, who are people (or animals or even inanimate objects) who meet the entry criteria and are enrolled in the study.

How to Write a Study Protocol

Whether you are doing a small process improvement project, a device evaluation, or a major RCT, you need a written study plan. Here are three reasons why: First, the process of writing it out will help you clarify the goals of the study and methods of investigation. The realization that problems in approach or analysis exist may not become clear until ideas are committed to paper. Second, you often must present a plan to obtain permission or approval to proceed with the study. Permission may need to be sought from a funding source, IRB, department manager, or student advisor before a study may begin. Third, the research plan, or research protocol, as it is often called, provides an operational guide for the entire research team. Successful coordination of study personnel is all but impossible without a detailed protocol. For these reasons, a properly formulated proposal is an essential first step in the research process. An example of a protocol outline, as might be required for review before gaining permission from an IRB for human studies, is shown in Box 8.2. The outline in Box 8.2 might seem like overkill, but you can simplify it to fit your needs, and it will impose discipline in the planning stages of your project. Another reason to do this is that it serves as the outline for any publication you may consider once the study is completed.

BOX 8.2 Elements of a Protocol for Submission to an Institutional Review Board

1. Name of investigator/co-investigator
2. Title of project
3. Introduction
4. Purpose, specific aims, and hypotheses
5. Study design
   a. Population
   b. Specific procedures
   c. Financial considerations
      - Compensation to subjects
      - Extra costs incurred for purposes of the study
   d. Risks and benefits
6. Consent form
   a. Purpose of the study and individual participation
   b. Study and procedures
   c. Risks and benefits
   d. Alternatives and withdrawal
   e. Treatment after the study
   f. Financial considerations (cost responsibility statement)
   g. Confidentiality statement
   h. Identification of persons obtaining consent

How to Analyze the Data

You don't have to be a statistician to conduct research. However, you do need to understand some basic concepts, even if only to be able to communicate with a statistician consultant. Of course, you also have to understand at least some of the terminology just to be able to read a scientific paper. Space does not permit us to explore this topic in detail,[21] but in general, all research papers contain at least some descriptive data analyses, such as mean values and standard deviation (or perhaps median values and ranges), along with confidence intervals and percentile plots. If the purpose of the paper is to determine the interval within which future measurements of a variable might lie, the Bland-Altman analysis is very popular in medical journals.[33] If the purpose of the paper is to test one or more hypotheses, the statistical tests used depend on the type of data elements in the study (e.g., Are the data continuous variables, dichotomous ["yes/no"] or categorical variables [e.g., groups]?). In general, the test yields a *P*-value that is used to determine if you should reject the **null hypothesis** (the guess that there is no difference between values of a statistic like a percentage or mean value). Percentages are compared with either a Fisher exact test (for small sample sizes) or a chi square test. If two mean values are to be compared, the most common procedure is a t-test; when more than two means are to be compared, we generally use some form of analysis of variance (ANOVA).

Some suggestions for self-study are given in Boxes 8.3 and 8.4. If you are not familiar with any of the terms or topics in the boxes, study those. Textbooks are a good resource, and the internet is a rich source of online texts, tutorials, and even statistical calculators. Box 8.3 lists some basic concepts for making experimental measurements. Box 8.4 lists some basic concepts

BOX 8.3 Basic Concepts for Making Experimental Measurements

- Basic measurement theory
  - Accuracy
  - Precision
  - Inaccuracy, bias, and imprecision
  - Linearity
  - Calibration
  - Sources of bias (systematic error)
  - Sources of imprecision (random error)
- Measuring specific variables
  - Pressure
  - Flow
  - Volume
  - Humidity
- Computerized data acquisition
  - Sensors
  - Analogue to digital conversion
  - Signal processing software

BOX 8.4 Basic Concepts in Statistics.

- Levels of measurement
  - Nominal
  - Ordinal
  - Continuous
- Significant figures
- Rounding off
- Descriptive statistics
  - Data representation
    - Graphs
    - Tables
  - Measures of the typical value of a set of numbers
    - Mean, median, mode
  - Measures of dispersion
    - Standard deviation, variance, coefficient of variation
  - Correlation and regression
- Inferential statistics
  - The concept of probability
  - The normal distribution and standard scores
  - Sampling distributions
  - Confidence intervals
  - Error intervals
  - Data analysis for device evaluation studies
  - Interpreting manufacturers' error specifications
  - Hypothesis testing
  - Type I and II errors
  - Power analysis and sample size
  - Rules of thumb for estimating sample size
  - Clinical importance versus statistical significance
  - Matched versus unmatched data

in statistics. There are hundreds, perhaps thousands, of statistical procedures used to analyze data once they are collected. Fortunately, there are only a handful of procedures that are used most of the time in the medical literature. If you learn nothing else, you should be familiar with calculating the mean and standard deviation of a set of numbers. As discussed previously, you should know what a *P*-value is, when to use nonparametric procedures

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What Is a P-Value?

There are two ways to define the term ***P*-value** seen so often in published studies. One way is the strictly correct statistical way, which requires much background knowledge about probability and hypothesis testing. The other way is more intuitive and appropriate for consumers of research. I think of it this way: when testing a hypothesis, we want to know if we should accept it or not. By accepting it, we consider it provisionally "true" until further evidence proves it false. But the fact that we can never perform all possible experiments to test the hypothesis means that we have to accept that there is some chance we are wrong (i.e., the hypothesis is actually false). For example, suppose we compare two mean values. Is their difference "statistically significant"? The *P*-value gives us the probability that the difference occurred by chance (acknowledging measurement errors), instead of some underlying cause that makes them truly different. By convention, if the *P*-value is <.05 (meaning a less than 5% or "1 in 20" chance), then we conclude that the difference is probably not due to chance and that the difference is significant. However, another issue is whether the difference is also "clinically important," and that is generally a matter of professional judgment, not statistics.

For some measurements (e.g., the FEV1, 6-minute walk distance, the St. George's Respiratory Questionnaire), the so-called "minimally important clinical difference (MCID)" has been determined. The MCID defines the difference between two values of that measurement that is considered to be clinically important.

(e.g., Fisher Exact and Chi-square) versus parametric methods (e.g., t-test and ANOVA). You do not need special statistical software; for many purposes, a Microsoft Excel spreadsheet functions quite well both for creating data collection forms and doing simple statistical procedures. Again, the internet has many tutorials showing how to do these things. Finally, Fig. 8.2 is an algorithm showing how to select the most appropriate statistical procedure for a given set of data.

RULE OF THUMB Although you should be somewhat skeptical about what you read in Wikipedia (http://www.wikipedia.org), I have found it to be a rich and very detailed source of information about statistical concepts.

HOW TO SUBMIT A PAPER FOR PUBLICATION

Once you have completed a research project, you need to communicate the results. As a healthcare researcher, you will encounter three basic ways to formally present your findings: the abstract, the poster, and the paper. Abstracts and papers are published in electronic and/or printed form in medical journals. Posters are presented in person at medical conventions. All three venues share the same basic outline structure: Introduction, Methods, Results, and Discussion (or Conclusions). As with conducting the research itself, publishing your results requires much practice under the tutelage of an experienced mentor.

How to Write the Abstract

An abstract is a condensed version of a research paper that appears at the beginning of the publication. Many readers skim the abstract to see if they are interested enough to read the whole paper.

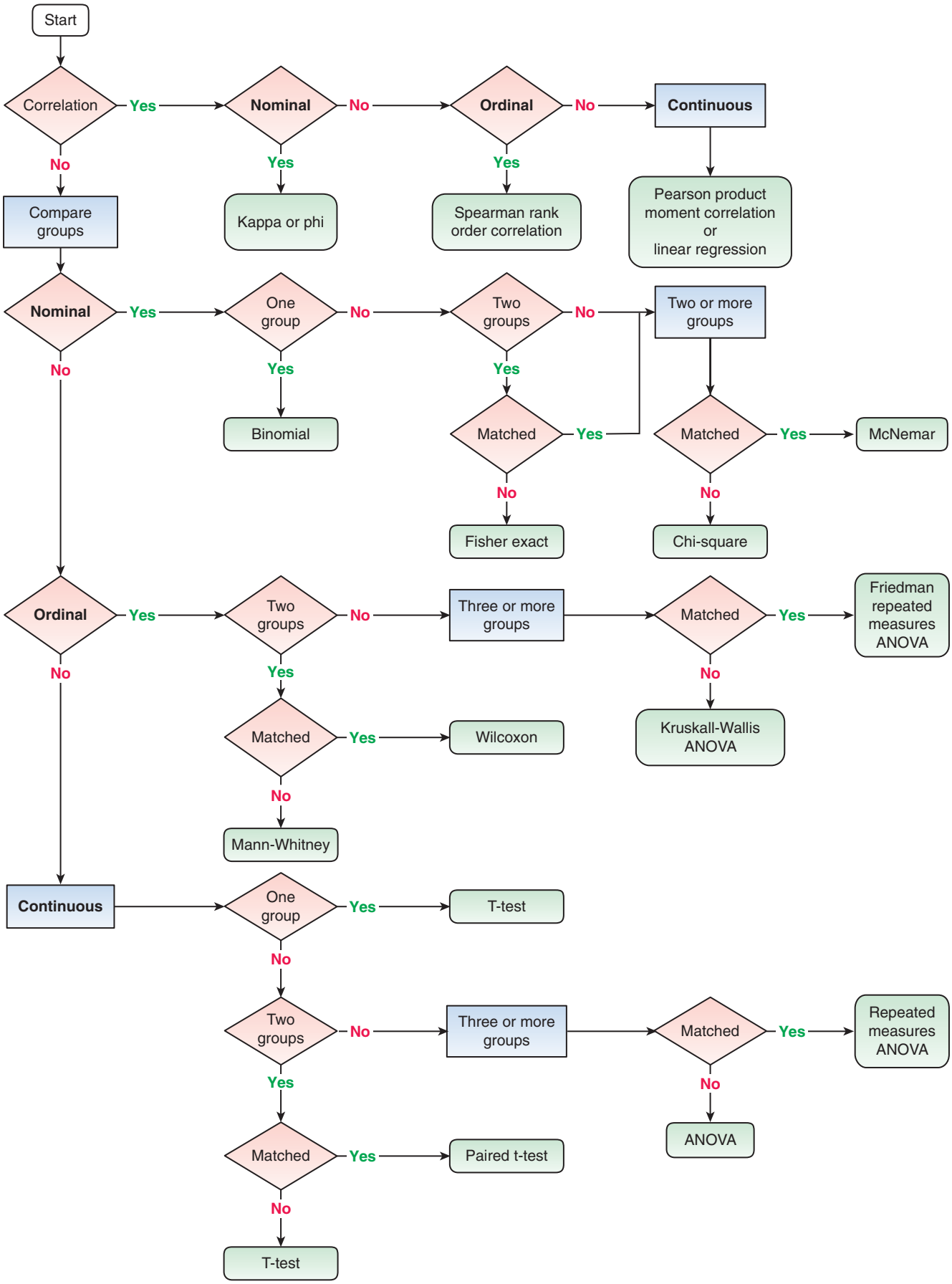

Fig. 8.2 Statistics selector algorithm.

Some readers do not have enough time to read anything more than abstracts. For these reasons, the abstract is an important element of a published paper. Furthermore, abstracts are sometimes published alone. For example, *Respiratory Care Journal* devotes one issue each year (usually the November issue) to abstracts describing studies that were presented at the AARC Congress, the profession's annual scientific meeting.

Writing a good abstract is an art.[34] Most journals restrict the length of the abstract (e.g., 300 words or 2500 characters), so the challenge is to balance brevity with clarity and explicitness. Abstracts can be either structured (with specific topic headings like Background/Introduction, Methods, Results, and Conclusions) or unstructured (with no such headings in the abstract). My approach to a structured abstract is to start with the text I wrote for the research protocol, including the Introduction (study purpose, hypothesis) and Methods (outcome measures, procedures, data analysis). Then, because most journals restrict your abstract to having a single graphic (if any), I create one illustration (table or graph) that summarizes the data. Next, I simply describe that illustration in the Results section of the abstract. After that, I look again at the study purpose and/or hypothesis statements in the Introduction to the abstract. These are the key ideas that must be included in the Discussion/Conclusion section of the abstract. I explain how the results address the hypothesis and how I interpret the data. I may even provide a speculation or suggestion for further study.

My first draft of an abstract may be 1000 words or more, which is way too long (the limit in *Respiratory Care Journal* is 2500 characters for a stand-alone abstract and 300 words in an abstract for a paper). Now the process of shortening or redaction begins. I read each word of every sentence and see which I can eliminate or replace with shorter ones or with abbreviations. If abbreviations are used, they should be placed in parentheses after the full word the first time they are used in the paper, to indicate the meaning of the abbreviation. *The idea is to decrease word count while increasing clarity*. It usually takes three or four passes through the entire abstract before the number of words is within the limit specified in the Instructions to Authors provided by the journal publisher (usually available on the web site for the journal). Needless to say, this process goes much more smoothly if you have an experienced mentor by your side. I find that if I have everything I need from the study, including the illustration, writing an abstract takes about 2 hours (but this is after 40 years of practice).

Once completed, the abstract is usually submitted online for peer review by the editors and reviewers of the medical journal. Fig. 8.3 shows what such an abstract looks like after submitting online and conversion to a PDF file.

CONTROL ID: 2017986

TITLE: OPTIMUM VENTILATION FOR LUNG DONORS

AUTHORS (LAST NAME, FIRST NAME): Cole, Stephanie [1]; Chatburn, Robert L.[1]; Mireles-Cabodevila, Eduardo[1]

INSTITUTIONS (ALL): 1. Respiratory Institute, Cleveland Clinic, Cleveland , OH, United States.

Abstract body: Lung donors are a unique subset of the population of ventilated patients because (a) they typically have normal lungs (those with lung disease are usually excluded from the donor program) and (b) they are often passive, ie, not able to trigger the ventilator (due to brain death). Mascia et al suggest a lung protective strategy using a pressure control (PC) mode [JAMA 2010;304(23):2620-2627]. Others [Arch Surg 2011;146(3):325-328] specifically suggest Airway Pressure Release Ventilation (APRV). The purpose of our study was to compare the potential lung protective value of three different PC modes: Pressure Control Continuous Mandatory Ventilation (PC-CMV), APRV, and Mid Frequency Ventilation [MFV; Resp Care 2008;53(12):1669-1677]. We hypothesized that the mode with the highest frequency would result in the lowest V_T and the highest potential for lung protection. **METHOD:** A passive patient was modeled (ALS 5000 lung simulator ImgMar Medical) using published parameters for normal ventilated humans: resistance = 15 cm H_2O/L/s, compliance = 39 mL/H_2O. Targets: minute alveolar ventilation (MV_A) = 2.5 L/min, totalPEEP = 8 cm H_2O. Ventilator settings were derived from published studies. PC-CMV: f =14/min, inspiratory pressure above PEEP (IP) = 9 cm H_2O, PEEP = 8 cm H_2O, T_I = 1 s. APRV f = 9/min, IP 18 cm H_2O, PEEP = 0 cm H_2O, T-low = 0.7 s. MFV: f = 90/min IP = 17 cm H_2O, PEEP = 1 cm H_2O, I:E = 1:1. For MFV, optimum frequency was determined by increasing the frequency and decreasing the set PEEP to maintain the target totalPEEP until the set PEEP reached 0 or no further V_T reduction was observed. Volume measurements were made with the ASL 5000. Mean V_Ts were compared with ANOVA ($P < 0.05$ considered significant). **RESULTS:** Actual MV_A was APRV = 2.7 L/min, PC-CMV = 2.5 L/min, MFV = 2.3 L/min. MV_A error for APRV due to interaction of autoPEEP and V_T; for MFV error due to inability to set fractional IP, necessary at high frequencies. MFV had the lowest V_T ($P = 0.001$; see Figure). Mean airway pressures (cm H_2O) were: APRV = 18, PC-CMV = 10, MFV = 11. Strain (V_T/end expiratory volume) for each mode was: APRV = 1.29, PC-IMV = 0.96, MFV = 0.44. **CONCLUSION:** This model study confirms that maximizing ventilatory frequency results in the lowest V_T and hence the highest potential for lung protection.

DISCLOSURES: Chatburn consults for Hamilton, Invacare, and IngMar. Chatburn and Mireles-Cabodevila hold patent for MFV.

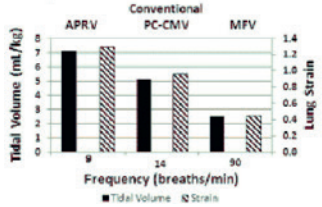

Fig. 8.3 Abstract after online submission and conversion to PDF file. (Courtesy Robert L Chatburn, Cleveland Clinic, Cleveland, Ohio.)

How to Make a Poster

If your abstract is accepted for publication (through the process called peer-review mentioned above), you may be invited to present a poster version at a medical convention, along with all the other studies from other authors that have been accepted. A poster allows a bit more freedom in terms of space.[35] You generally are allowed to create a paper or cardboard poster fitting a space of approximately 4 feet tall by 6 feet long. The way I do it is to create a template in Microsoft PowerPoint (using a custom slide size, 36 inches wide by 20 inches in height in Landscape orientation). On this template, there are text boxes and graphics. Make sure the graphics are at least 300 dots per inch (dpi), usually TIFF files. If the graphics are not in the right format or have a resolution less than 200 dpi, they may look grainy when printed. Once the poster is created in PowerPoint (Fig. 8.4), the file is taken to a printer (university or hospital art department or commercial establishment like Kinkos) and printed on a very large piece of poster paper (I use 42 by 74 inches). You can then roll it up and transport it in a special tube (cardboard—cheap; plastic—less cheap) made for the purpose (available at art supply stores). Such a tube is small enough to take as a carryon on a plane. It is always a good idea to also take a PDF of the poster on a flash drive to the meeting in the rare case that the poster is damaged in transport; that has happened! Posters are usually presented in a group of maybe 10 to 15 abstracts in small meeting rooms. The paper posters are hung on stands, and visitors walk around reading them and discussing them with the authors. In some cases, each author is given a few minutes at a podium to verbally summarize the study and answer questions.[36] Poster sessions can be an excellent way of networking with leaders in the field, as many will look for posters in their areas of interest and come by to meet the authors and discuss the findings.

How to Write a Paper

If writing an abstract takes an experienced researcher 2 hours, then a full paper takes 20 to 100 hours. A paper has the same basic outline as an abstract or poster (Introduction, Methods, Results, Discussion, or Conclusions) but goes into much greater detail. It also has an extra component, the References section.[37] The Introduction of the paper can start with the full text of the Introduction from your research protocol. There is no word limit for the Introduction (within reason), but most journals have a maximal word count for the full text of the paper (usually in the range of 2000 to 3000 words, depending on the journal). The purpose of the Introduction is to provide a brief background explaining why the study was conducted and why it is of interest. A statement of the research problem or hypothesis should be included. The references cited in the Introduction (if any) should support the theoretical framework of the hypothesis, although an in-depth explanation should be saved for the Discussion section. The Introduction should also contain definitions of the general concepts discussed in the manuscript. Frequently used terms can be abbreviated after first being spelled out fully in the opening paragraphs.

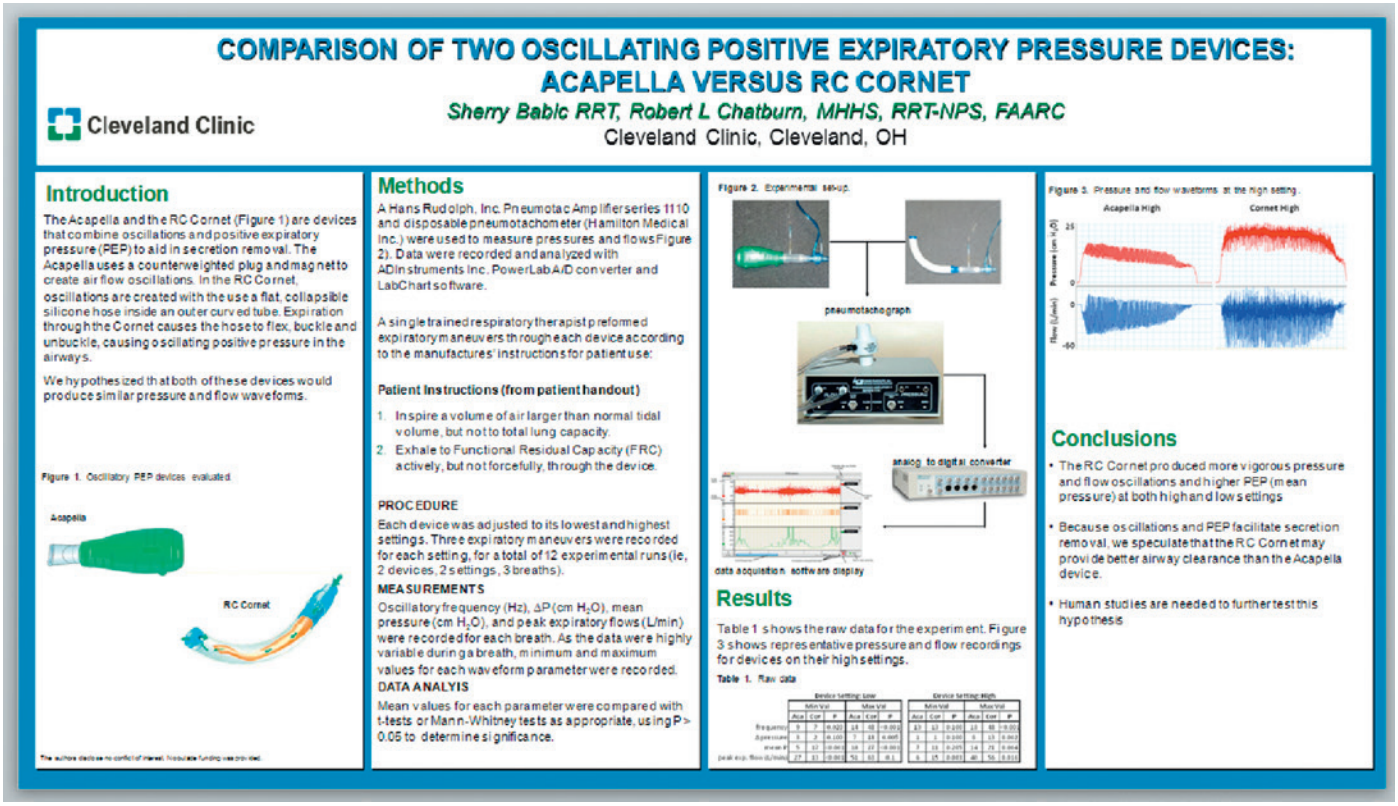

Fig. 8.4 Example poster created in PowerPoint. (Courtesy Robert L Chatburn, Cleveland Clinic, Cleveland, Ohio.)

RULE OF THUMB Not including the hypothesis is a common mistake among beginners. Describing the hypothesis or research problem in the Introduction of the paper sets the stage for the Methods (which must describe how the hypothesis was tested), the Results (which must correspond to all the methods described), and the Discussion (which tells how the results addressed the hypothesis, discusses how this paper extends existing knowledge, and comments about limitations of the paper and further research opportunities to answer the questions posed in the paper).

The purpose of the Methods section is to explain to the reader exactly what was done to answer the research question and/or test the hypotheses described in the Introduction.[38] *The key concept here is that the reader must be given enough detail to be able to repeat the study,* including all assumptions, calculations, and statistical procedures and descriptions of all equipment used. Amazingly, many published papers are weak in this respect. The Methods section may contain several subdivisions; description of experimental subject population, inclusion, and exclusion criteria by which subjects are selected to participate in the research study, explicit experimental procedures, data analysis procedures, and so on. An essential component of the Methods section is a complete description of any equipment used to gather the data. The calibration procedure for each measuring device should be described, along with any pertinent validation procedures. The procedure used to gather the data should be described. This description might include an outline of the experimental protocol that was approved by the hospital's **Institutional Review Board** (IRB), the body that oversees research, is primarily in change of protecting human subjects and whose approval is needed before any research on human subjects can be conducted. If the study involves humans, state that IRB approval was received before collecting data (as is required). A description of the experimental procedure should include the actual steps involved in gathering the data and the time elapsed during each phase of the experiment. Any problems or unforeseen events that occurred during the study should be mentioned. The information in this section should be detailed enough to guide other researchers who might wish to verify the results in their own studies. The Methods section also will help the reader evaluate the quality of the data gathered during the study. Finally, the Methods section should include a brief description of how the data were analyzed. Provide a short discussion of the statistical procedures used and why they were appropriate for the experimental design. Unless the procedures were unusual, do not give the statistical equations used. However, many statistical procedures are based on certain assumptions about how the data were gathered (e.g., normality of the data or independence of data points used in a linear regression). Thus enough information should be provided for the reader to evaluate the validity of any underlying statistical assumptions and, hence, the adequacy of the analysis. The specific statistical software that was used (if any) should also be cited in the Methods section.

The Results section of the paper presents the data gathered from the experiments. The order in which the information is given should correspond to the organization of the Methods section. In that section, the reader is introduced to the step-by-step procedure used to study a particular problem. An expectation has been created in the reader's mind for the result of each step of the procedure. Therefore, the results should be presented in a logical progression from the beginning to the end of the experiment. This progression helps to assure the reader of the thoroughness of the experimental technique. The actual presentation of the data can take many forms. Use tables to summarize large amounts of raw data.[39] Each table should be constructed so that its meaning is clear without having to refer to the text. The idea is to summarize and guide the interpretation of large amounts of data and to reduce the time necessary to read the article. If the table appears to be too large or complex, make use of figures or graphs. Again, you do not need special statistical software; Microsoft Excel is an excellent tool for making tables and graphs. The information presented in the Results section is usually in the form of "bare facts," with little or no explanation of its significance. Interpretation of the data is presented in the Discussion section. Of course, this is a general rule and may be suspended at times if it is felt that elaboration of some point would help the reader's flow of understanding. The responsibility for interpreting the generalizability of the results ultimately rests with the reader who must ask, "Does this result apply to my patients?" As mentioned previously, the significance of any statistical hypothesis test is usually reported in terms of a *P*-value. Differences associated with *P*-values less than 0.05 are considered significant by convention in medical studies. This means that the chance of the conclusion being wrong (i.e., that the null hypothesis is rejected when it should actually not be rejected) is 1 in 20 or less.

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Obtaining IRB Approval

At my institution (Cleveland Clinic), research protocols are submitted to an IRB portal online. The first step is to specify the type of protocol (minimal risk/exempt or standard IRB review) and enter the title of the study. The next steps include identifying the principal investigator and co-investigators, and study sponsors (if any). Next is a summary of the protocol and procedures, including study population (and recruitment procedures), study aims, data analysis, data security and safety monitoring plans, and consent form. These may all be cut and pasted from the text version of the protocol. You will also need to upload a full text version of the protocol and any data collection forms. Next an e-mail will be sent to all of the investigators asking them to digitally sign a form indicating that they have reviewed the protocol and declaring any potential conflicts of interest. Once all signatures are obtained, the protocol can be submitted for review. There are three basic routes to approval: (1) a quality improvement project that is deemed not to be human research and given quick approval, (2) an expedited review for studies qualifying as "exempt" (such as surveys or educational research where no subject identifiers are collected), and (3) full review of the protocol, the consent form, and the data collection forms. The review process is similar to the review of a paper for publication in that the IRB will often have questions or suggestions for modifying the protocol. The review process may take days to weeks, depending on the type of review and how complicated the study is. If you are not affiliated with an organization that has an IRB (e.g., a home care company), you may hire a private IRB found by searching the internet. IRB's are certified and overseen by the government.

In the Discussion section, the author must show how the results answer the research question that was first described in the Introduction.[40] The results of statistical hypothesis tests must be translated into conclusions about the research hypotheses stated in the Introduction. The implications and practical meaning of the study results should be explained. Also, the Discussion should interpret the results in the face of earlier studies' conclusions. Specifically, how does the current study extend or add new knowledge to what is already known and accepted? Does it contradict previous findings, and, if so, what is the proposed reason? In addition, the Discussion should describe the limitations of the study design, any problems encountered, and any recommendations for future studies. The process of interpreting the results concerns not only the data produced by the study but also relates that data to other studies and theoretical frameworks. The Discussion is the appropriate place to include detailed reviews of other related research, including references, which would help develop the reader's perspective and appreciation for the significance of the study.

Some journals require a separate Conclusion statement at the end of the paper. The conclusions made should be briefly explained, including reasons for rejecting alternative interpretations. In addition, there should be a statement regarding the population to which the results can be generalized. Because the implications of a given study are usually speculative, it is appropriate to use words that are somewhat tentative in nature. For example, "The results of this study suggest that…" or, "Because of the significant differences found, it may be possible to…" Such language emphasizes the fact that your interpretation is itself a hypothesis that may be tested by further research.

How to Respond to Reviews

Once your paper is completed and submitted to a journal for review, it will be given to two or three peer reviewers. These are your scientist peers who have expertise in the area of research described in your paper. They are invited by the editor of the journal to review the paper you submitted and will read and critique everything about your paper, from what words you use, to what measurements you made, to what statistical procedures you used. Based on their careful examination of your manuscript, the peer reviewers will then recommend to the journal editor one of three outcomes which the journal will communicate to you (usually without revealing the names of the peer reviewers)—that is, that (1) your paper should not be considered for publication, (2) your paper is rejected but (with luck), there is an opportunity to revise and resubmit, or (3) the paper should be accepted as is without any further revision. Rarely does a paper get accepted without any suggested revisions. The main reasons that papers get rejected are given in Box 8.5.[41] Rates of rejection vary by the journal, with some journals with the highest so-called impact factor, rejecting the vast majority of submitted papers.

BOX 8.5 The 10 Most Frequent Reasons for Manuscript Rejections

1. Inappropriate statistics
2. Inappropriate interpretation of results
3. Instrumentation insufficient for the study purpose
4. Inadequate or biased sampling of experimental subjects
5. Unclear, poorly written, or overly complex text
6. Insufficient (or absent) problem statement
7. Inaccurate or inconsistent data
8. Incomplete, inaccurate, or outdated literature review
9. Insufficient data
10. Defective tables or figures

Modified from Pierson DJ: The top 10 reasons why manuscripts are not accepted for publication. *Respir Care* 49:1246, 2004.

MINI CLINI

Having a paper rejected is like being told your child is ugly and stupid. Most people react with negative emotions and give up. But (hopefully) if you can get past that phase, you have several options. First, examine whether the reviewers' comments are justified. Sometimes they have just misunderstood what you did. If the comments are justified, see what you can do to make the required changes. In general, you will be given a list of reviewers' comments. In your response, you need to repeat each of the reviewer's comments and then give your explicit answers and what you did to achieve the requested change in the manuscript. (I use a numbered list to keep track of everything in this so-called *point-by-point response* that must accompany any resubmission.) Keep three things in mind: (1) The time spent in revision is generally only a small fraction of the time already invested—you should not give up if you receive a rejection with an opportunity to revise. (2) Most manuscripts require revision and you are not being singled out. (3) Authors have the right to overrule a reviewer's objection, but they must adequately support their points of view and convince the editor that they are right and that the reviewer's point is in error. When the revision is complete, resubmit the manuscript. Depending on the journal, it may take as many as three rounds of revisions before a manuscript is accepted and ready for publication. Most journals now have online submission sites.

Above all, BE PERSISTENT!

SUMMARY

Hopefully, this chapter has introduced you to the importance and methods of scientific research and has helped you become an educated consumer of medical research. Not everybody is cut out to be a scientist. But, as professionals, everyone practicing respiratory care has the responsibility to intelligently evaluate what they are doing in light of scientific evidence. Unfortunately, most of the things we do in medicine are not supported by strong evidence, despite the wealth of information in printed medical journals and on the internet (in the form of databases, portals, and electronic media). And even when evidence is available, it is often controversial. We rarely know anything for sure, and we only have varying degrees of confidence. On the one hand, this situation is frustrating. On the other hand, there is no doubt that we are progressing. Which would you prefer—your least favorite health maintenance organization today or the best medicine of 100 years ago? Our current situation provides infinite possibilities for anyone who has an interest in research and the willingness to help clarify the confusion just a bit. If you have enough interest (and hopefully a mentor), you can begin to create basic study ideas and conduct experiments. With perseverance, it is

quite possible for you to get your abstract accepted in *Respiratory Care Journal* and present your poster at the Annual AARC Congress. Even if your personal goals do not include becoming a scientist, you should publish at least one abstract in your career to understand what is involved with moving the profession forward as a clinician, educator, or administrator. Generating new knowledge and research is critical to preserving the profession of respiratory care.

RULE OF THUMB Even after doing research, we may still be confused, but we believe we are confused at a higher level about more important things.

SUMMARY CHECKLIST

- All healthcare professionals have the responsibility to intelligently evaluate their policies and procedures in light of the latest scientific evidence.
- Information required to evaluate professional practice can be found from various printed and digital media including medical journals and on the internet (in the form of databases, portals, and electronic media).
- Reviewing the scientific evidence can also be useful in identifying potential topics worthy of research. Many journal articles will specifically mention such areas for future research.
- Research ideas can be obtained from reading research and from simply observing daily practice. General ideas can be turned into statements of study purpose by describing what you see happening and why it is important.
- When reviewing the literature or actually conducting research, the RT should understand the various types of research design.
- Literature reviews are conducted using various forms of online databases, portals, and electronic journals and books—plus the library of course.
- An important concept regarding high-quality care is EBM, which refers to an approach to determining optimal clinical management.
- Research results can be disseminated in three main ways: abstracts, poster presentations, and papers in peer-reviewed medical journals.

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9

The Respiratory System

Narciso E. Rodriguez and Siddharta Silva

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- State the major developmental events of the respiratory system.
- Describe how genes control lung development.
- Describe the key elements of normal fetal circulation.
- State what happens to the respiratory system at birth.
- Describe the developmental events in the respiratory system that continue after birth.
- Identify the main structures in the thorax and describe their functions.
- Identify and describe the primary and accessory muscles of respiration.
- Describe the pulmonary and bronchial circulations structure and functions.
- Describe how somatic and autonomic nervous systems connect to and control the lungs and respiratory muscles functions.
- Identify the major structures of the upper respiratory tract and their function.
- Describe how the lungs are organized into lobes and segments and the airways that participate in gas exchange.
- Describe mucus production and their role in the respiratory system.
- Describe the structure and organization of the respiratory bronchioles and alveoli.
- Describe the blood-gas barrier and how gas exchange occurs.

CHAPTER OUTLINE

KEY TERMS

accessory muscles of breathing
acinus
alae
alveolar-capillary membrane
alveolar period
alveoli
anatomic deadspace
angle of Louis
anterior nares
apexes
canals of Lambert
canalicular stage
carina
chorionic villi
cilia
Clara cells
costal cartilage
costal groove
costophrenic angle
cricoid cartilage
diaphragm

ductus arteriosus
ductus venosus
embryonic period
epiglottis
epistaxis
eustachian tubes
external nares
external respiration
false ribs
fetal lung fluid
fetal period
fissures
floating ribs
foramen ovale
gel layer
gladiolus
glottis
grunting
hard palate
hilum
hypopharynx
hypoplastic lungs
intercostal nerves
intervillous spaces
internal respiration
L/S ratio
laryngopharynx
larynx
manubrium
mediastinum
mucociliary escalator
nasopharynx
oligohydramnios
oropharynx
P_{50}
palate
palatine folds
parietal pleura
patent ductus arteriosus (PDA)
pharynx
phrenic nerves
pleurisy
pleural space
pleural fluid
pores of Kohn
primary lobule
pseudoglandular stage
pulmonary surfactant
respiratory bronchioles
saccular stage
soft palate
sol layer
spiral arteries
sternal angle
sternum
suprasternal notch
terminal bronchioles
thoracic inlet
thyroid cartilage
tonsillectomy
trachea
true ribs
turbinates
type I pneumocyte
type II pneumocyte
uvula
vallecula
visceral pleura
xiphoid process

The primary function of the respiratory system is gas exchange, that is, the continuous absorption of oxygen and the elimination of carbon dioxide. This exchange between the alveolar gas and the blood is termed **external respiration**. This process supports the **internal respiration**, which is the exchange of gases between blood and tissues at the cellular level. To carry out external respiration, the respiratory system must bring gas into close contact with the flowing blood in the pulmonary circulatory system.[1] This close "match" of gas and blood across a large but extremely thin blood-gas barrier membrane enables gas exchange to occur via simple diffusion due to gas pressure gradients.

RULE OF THUMB External respiration or gas exchange occurs at the alveolar level by gas passively diffusing, due to pressure gradients, across the alveolar-capillary membrane.

The respiratory system includes the upper airways, chest wall, respiratory muscles, lower airways, pulmonary blood vessels, support nerves, and lymphatics. Development of these organs occurs from embryo to fetus, to infant and child, through puberty, and into young adulthood. A gradual loss of lung tissue and functional changes start at about age 40 and continue until death. During the lifespan of a human, the respiratory system maintains external respiration by matching large amounts of air with a proportional amount of blood flow in the lungs.[2] Approximately 250 million liters of each are moved and matched during an average lifespan. The respiratory system normally moves this amount of air and blood flow with a minimal amount of work and effort. It also humidifies and warms inspired air while removing inhaled contaminants and filtering out chemicals and small blood clots deposited or formed in the blood. The respiratory system is regulated by the nervous system, with a feedback mechanism capable of increasing or decreasing function in response to changing demands.[1]

The respiratory therapist (RT) needs a sound understanding of the development of, and of the fully developed "normal" anatomy and physiology of the respiratory system. Such an understanding helps assess and treat those with pulmonary disorders and supports the role of the RT in providing respiratory health in the community.

DEVELOPMENT OF THE RESPIRATORY SYSTEM

The developing human undergoes a remarkable transformation from a single cell to an individual with a nearly complete set of organ systems. The developmental phases of a fertilized egg are divided into the *embryonic* and *fetal periods*. The **embryonic period** occurs during the first 8 weeks of pregnancy. Major organs will develop during this period. The **fetal period** occurs during the remaining 32 weeks of pregnancy. During this period, the organs continue to develop and refine their structure and function.[3]

The respiratory system develops during these periods as a fluid-filled structure playing no role in gas exchange yet must be developed sufficiently to assume this important activity at the time of birth. Its development is a continuous process that begins in the early stages of the embryonic period and extends for years after birth.[2] The embryo is made up of three distinct germinal tissue layers that ultimately form all tissues and organs: *endoderm, mesoderm,* and *ectoderm*. From these three layers, the organs and systems develop (Table 9.1).

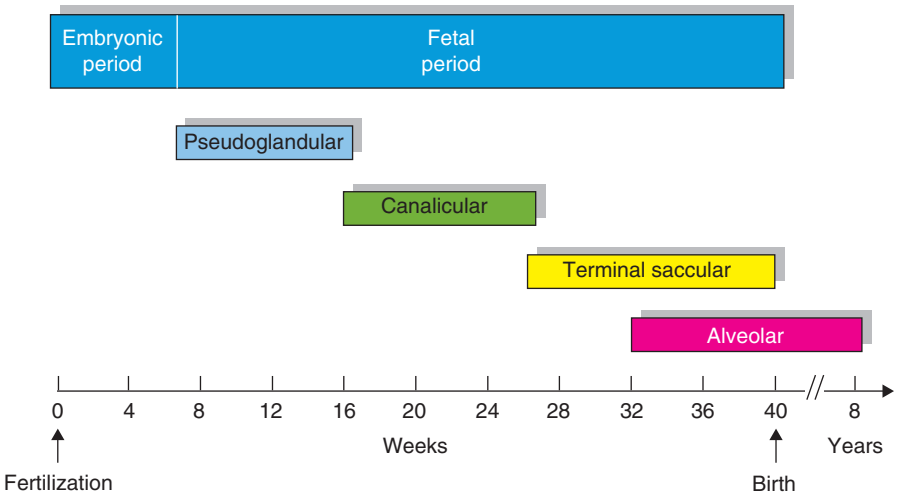


Fig. 9.1 Major phases of respiratory development.

TABLE 9.1 Structures Arising From the Three Germ Layers

Endoderm	Mesoderm	Ectoderm
Respiratory tract	Dermis and muscles	Epidermis, hair, and nails
Digestive tract, bladder, and thyroid	Bone, connective and lymph tissue	Lens of eyes and skin glands
Liver and pancreas	Reproductive and cardiovascular system	Central and peripheral nervous system

The development of the respiratory system has been categorized into various stages.[2] Fig. 9.1 shows the various stages of lung development, and Table 9.2 summarizes the major developmental events in each phase. Respiratory development begins in the embryonic period on approximately day 22 after fertilization. A primitive laryngotracheal tube forms from a groove in the fourth pharyngeal pouch. From that groove a tracheal bud forms by the end of the fourth week of life (Fig. 9.2). During week five of development, the tracheal bud continues to develop and bifurcates into left and right primary bronchial buds (see Fig. 9.2C).

Injury to the embryo or genetic damage during the embryonic period of development can lead to many congenital anomalies, including tracheoesophageal fistulas, esophageal atresia, choanal atresia, pulmonary hypoplasia, and complex heart and vascular anomalies discussed later in this text (Table 9.3).[4,5]

At approximately 6 weeks of development, lung and airway growth has the appearance of a glandular structure—hence the name of the second phase of development, the ***pseudoglandular stage*** (Fig. 9.3). For the next 10 weeks, the growth and branching of the tracheobronchial tree and pulmonary vasculature continue and culminate with the formation of the terminal and respiratory bronchioles. The distinction between these two types of bronchioles is important. **Terminal bronchioles** are *conducting airways* only and do not participate in gas exchange. Respiratory bronchioles have more superficial capillaries and are capable of gas exchange.[3]

Branching and dividing of the tracheobronchial tree occur in several ways. The epithelial lining of the airways begins to differentiate into columnar epithelia in the proximal airways and differentiates into cuboidal epithelia in the more distal bronchioles (Fig. 9.4A). Development of *cilia, mucous glands,* and *goblet cells*—which line most of the conducting airways—occurs at this time.[2]

Beginning with the trachea and moving distally, the amount of cartilage supporting the airway decreases as smooth muscle cells in the middle layer of the airway increase. Altered development of smooth muscle, cartilage, and vascular structures can lead to congenital pulmonary disorders, such as tracheomalacia and anomalous pulmonary arteries, causing vascular rings to encircle and "narrow" the airway (see Table 9.3).

The ***canalicular stage*** (see Fig. 9.4B) begins at week 16 and continues until week 26. The canalicular stage overlaps with the pseudoglandular stage because the superior regions are developing slightly faster than the inferior regions. During this phase, primary changes include the development of two to four more generations of respiratory bronchioles from each terminal bronchiole. In the last several weeks of this stage, the region beyond each terminal bronchiole forms the functional structure called the **acinus**, the basic gas-exchanging unit of the lung. At this time, the two primary epithelial cell types that cover the gas-exchange surface begin to appear, type I and type II pneumocytes. At the end of the canalicular period (24 to 26 weeks of gestation), the fetus, if born, is generally capable of sufficient gas exchange and can survive if supported with supplemental O_2, ventilatory support, and surfactant administration.

During the terminal ***saccular stage*** (see Fig. 9.4C), more terminal bronchioles and their associated acini form and develop from 26 weeks to birth. The formation of the total number of terminal bronchioles is complete at the end of this phase. The cuboidal epithelia that line the blind tubules of the acinus continue to differentiate into rounded secretory cells (type II pneumocytes) and flatter squamous epithelial cells (type I pneumocytes). Capillaries continue to form near and bulge from the surface of the acinus. Although some type II pneumocytes form by 20 weeks of gestation, they are in such small numbers and of such primitive function that their impact on lung function is marginal. From this point until birth, there is rapid growth in the

TABLE 9.2 Developmental Events of the Cardiopulmonary System

Period		Gestational Age	Developmental Event(s)
Embryonic Period		20–22 days	Primordial pharyngeal arches form
		21–23 days	Primordial respiratory cells form on fourth pharyngeal pouch, primordial heart starts forming
		26th day	Laryngotracheal bud forms
		4th week	Primitive trachea develops
		5th week	Primary bronchial buds form, laryngeal structures develop
		6th week	Segmental and subsegmental bronchioles form
Fetal Period	***Pseudoglandular Stage***	7th week	Diaphragm complete
		8th week	Heart complete, fetal circulatory pattern begins to develop
		10th week	Pulmonary lymphatic structures develop
		12th week	Major arteries formed
		13th week	Major airway epithelia and mucus-producing cells formed, smooth muscle cells developing
		14th week	Principal arteries formed
		16th week	Terminal bronchioles and associated pulmonary vessels form
		16th–17th week	Respiratory bronchioles and immature acini begin to form
	Canalicular Stage	20th–24th week	Type I and II pneumocytes begin to appear and replicate
		24th–26th week	Pulmonary capillaries develop at surface of acinus, immature surfactant begins to appear in lung fluid
			Alveolar-capillary membrane able to support gas exchange
	Terminal-Saccular Stage	26th week–birth	Terminal saccules increase in number, pulmonary capillary density and proximity increase, type I and II pneumocytes continue to multiply, surfactant production increases, extrauterine life possible with support
	Alveolar Stage	32th–40th week	Immature alveoli begin to form and increase in number; surfactant production matures
		40th week	50 million immature alveoli formed
Postnatal Period		Birth	First breath and lung fluid cleared, adult circulatory pattern established
			Fusion of double alveolar capillary network into a single layer
		Birth-8–10 years	470 million mature alveoli formed
		8–22 years	Enlargement of terminal bronchioles and alveoli

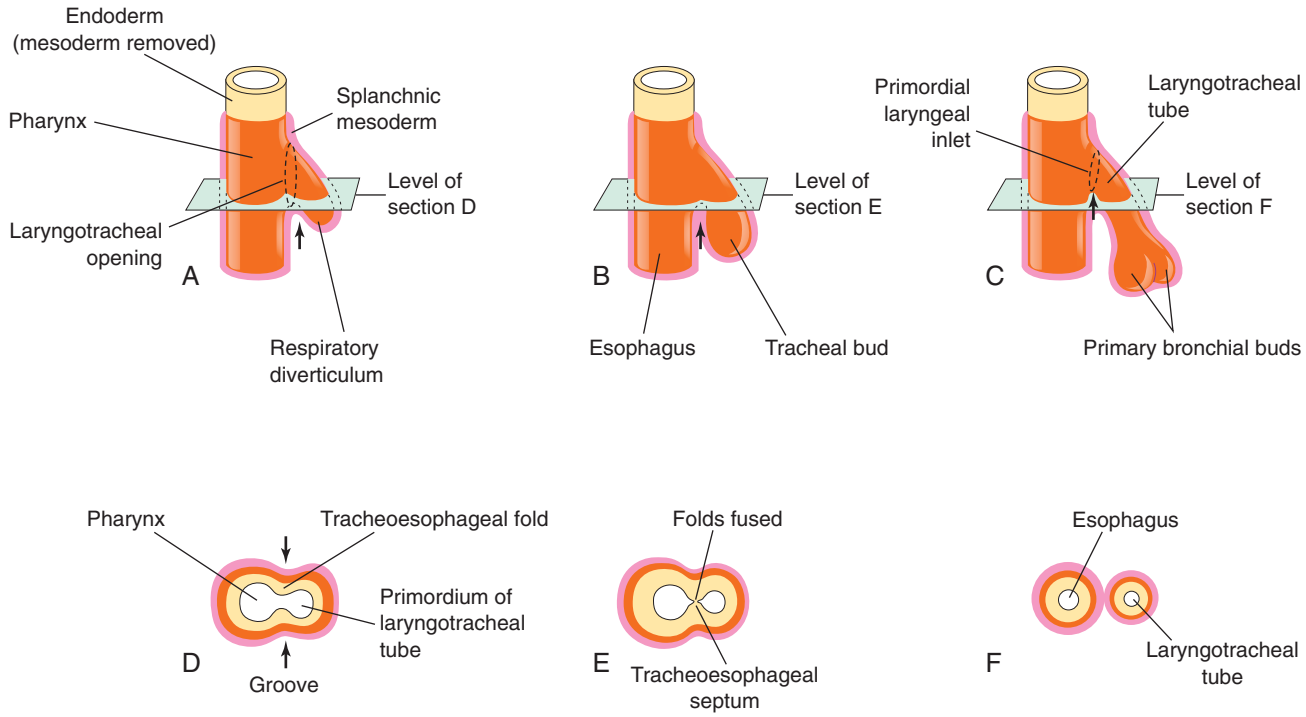


Fig. 9.2 Successive Stages in the Development of the Respiratory System From the Primitive Foregut. (A–C) Lateral views of the caudal part of the primordial pharynx showing the respiratory diverticulum and partitioning of the foregut into the esophagus and laryngotracheal bud. (D–F) Transverse sections illustrating the formation of the tracheoesophageal septum and showing how it separates the foregut into the laryngotracheal bud and esophagus. (From Moore KL, Persaud TVN: The respiratory system. In Moore KL, Persaud TVN, editors: *The developing human: clinically oriented embryology*, ed 8, Philadelphia, 2008, WB Saunders.)

TABLE 9.3 Congenital Malformations Associated With Abnormal Lung Growth

Period	Malformation
Embryonic	Pulmonary agenesis
	Tracheal or laryngeal agenesis or stenosis
	Bronchial malformation
	Ectopic lobes
	A-V malformations
	Congenital lobar cysts
Pseudoglandular	Cystic adenomatoid malformation
	Pulmonary sequestration
	Lung hypoplasia
	Lung cysts
	Congenital pulmonary lymphangiectasia
	Congenital diaphragmatic hernia (CDH)
Canalicular	Lung hypoplasia
	Respiratory distress syndrome (RDS)
	Acinar dysplasia
Saccular/alveolar	Pulmonary hypoplasia
	Respiratory distress syndrome/chronic lung disease of prematurity
	Acinar dysplasia
	Alveolar capillary dysplasia

Adapted from Joshi S, Kotecha, S: Lung growth and development, *Early Human Development* 83(12):789–794, 2007.

number of alveolar ducts and sacs formed from the respiratory bronchioles.

The type I pneumocytes in the saccule walls thin and stretch to cover the walls of this region. Type I cells become the primary gas-exchange cells in the lung with a close approximation to the developing pulmonary capillaries. Type II pneumocytes form and secrete the vital pulmonary surfactant that is necessary to alter surface tension and help keep the lungs inflated.[5]

The development of mature **alveoli**, accompanied by capillary proliferation around their outside walls, marks the final phase of lung development and is known as the ***alveolar period*** (see Fig. 9.4D). This phase begins at about week 32 of gestation and continues for years after birth. During this phase, the terminal saccules develop pouch-like regions called *alveoli* within their walls, resulting in greater numbers of alveoli that enlarge to a mature state over time. Premature infants younger than 32 weeks are at greater risk for developing respiratory distress due, among other reasons, to the lack of mature alveoli and mature surfactant in their lungs (see Mini Clini).

A full-term newborn has approximately 50 million alveoli; this number continues to increase until approximately 2 to 3 years after birth.[3,5] The alveoli are lined with type I and II pneumocytes covering the pulmonary capillaries forming just below the basement membrane.

As mentioned before, human **pulmonary surfactant**, which promotes lung inflation and protects the alveolar surface, begins to be produced around 24 to 25 weeks of development by type II pneumocytes. It is composed primarily of phospholipids, a

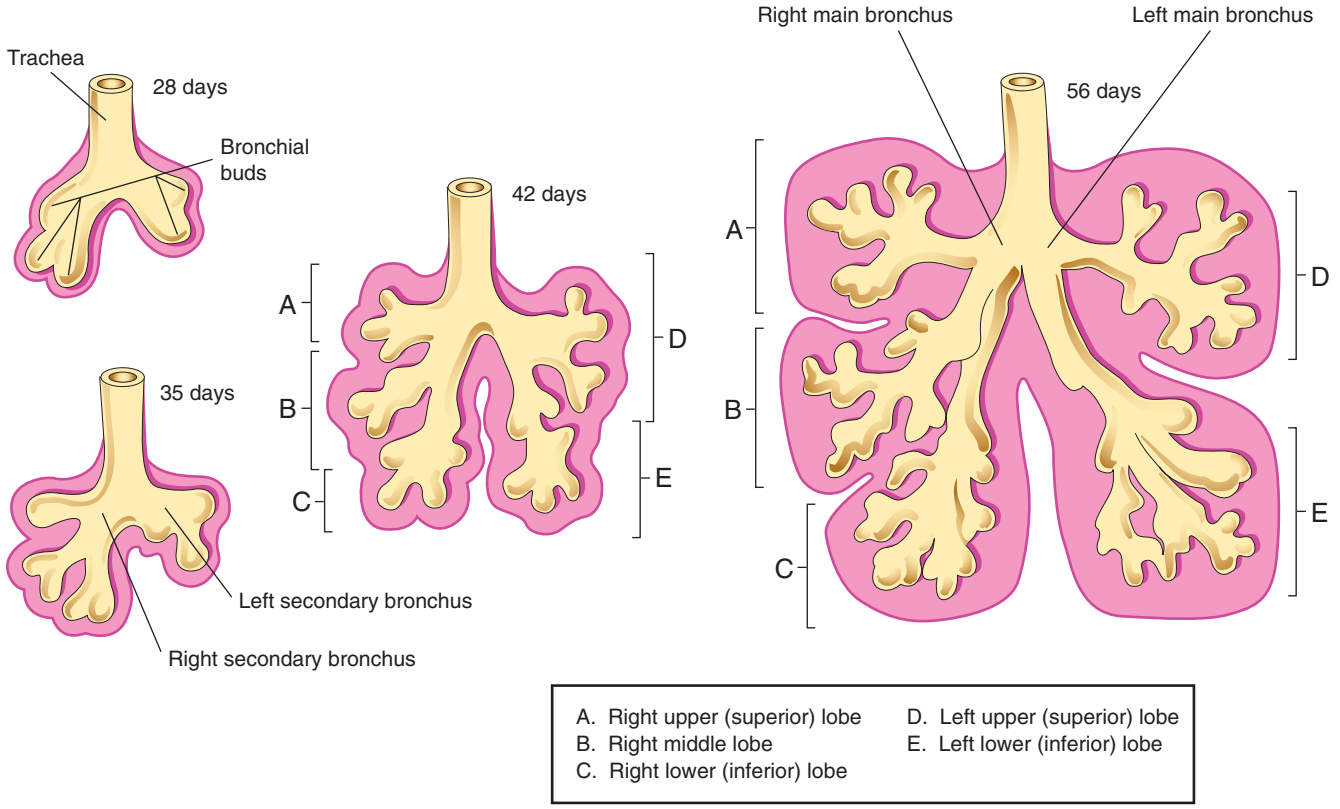


Fig. 9.3 (A–E) Various stages in the growth of the bronchi as the lungs enter the pseudoglandular period of development. (From Moore KL, Persaud TVN: The respiratory system. In Moore KL, Persaud TVN, editors: *The developing human: clinically oriented embryology,* ed 8, Philadelphia, 2008,WB Saunders.)

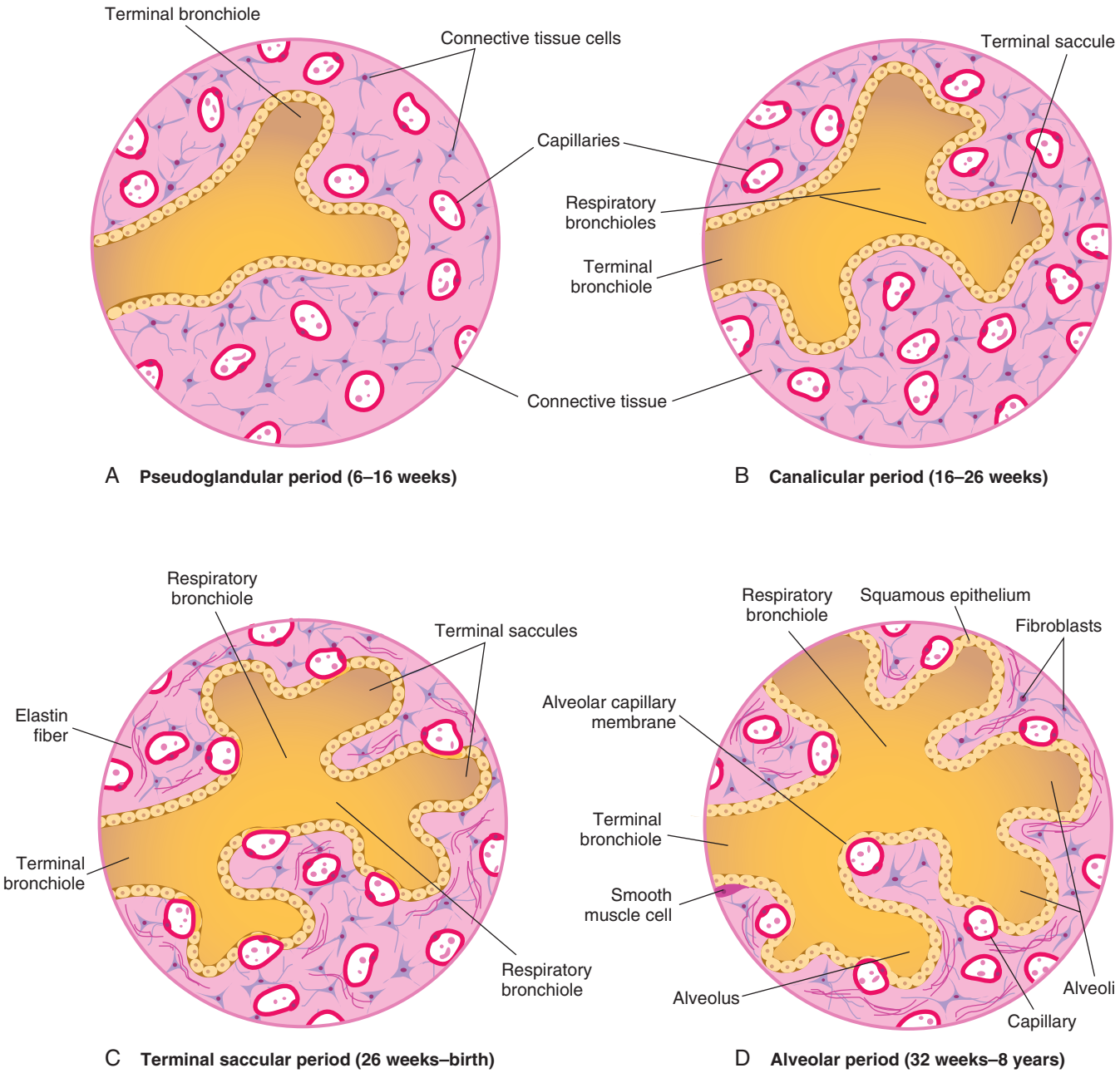


Fig. 9.4 Histologic Changes That Illustrate Various Periods of Airway Development. (A and B) There is considerable distance between the air within the airways and blood within the capillaries. (C and D) The air-blood distance is considerably thinner and more supportive of effective gas exchange. (From Moore KL, Persaud TVN: The respiratory system. In Moore KL, Persaud TVN, editors: *The developing human: clinically oriented embryology*, ed 8, Philadelphia, 2008, WB Saunders.)

small amount of protein (types SP-A, SP-B, and SP-C), and a trace of carbohydrates (Table 9.4).[6,7] Early research in pulmonary surfactants centered on the phospholipid components, mainly phosphatidylcholine (lecithin [L] and sphingomyelin [S]) and phosphatidylglycerol (PG). The amount of these phospholipids (the ***L/S ratio*** and *PG concentration*) provides a predictive index of the lung maturity in a fetus before birth and the risks for the development of respiratory distress.[8] An L/S ratio ≥ 2 indicates a relatively low risk for the development of Infant Respiratory Distress Syndrome (IRDS or RDS), whereas an L/S ratio of less than 1.5 is associated with a high risk.

Surfactant production is regulated by numerous hormones, genes, and factors, including glucocorticoids.[7] Glucocorticosteroid production increases at the end of gestation and stimulates receptors in type II pneumocytes, further increasing surfactant production and improving the L/S ratio.

A distinctive function of the developing lung is the formation of relatively large amounts of **fetal lung fluid** that passes into the amniotic fluid. Fetal lung fluid is a unique combination of plasma ultrafiltrate from the fetal pulmonary microcirculation, components of pulmonary surfactant, and other fluids from pulmonary epithelial cells and the developing fetus.[2] This fluid

MINI CLINI

Lung Maturity and Respiratory Distress Syndrome

Problem

Why are premature babies at a higher risk of developing respiratory distress syndrome (RDS)? What are the signs of RDS in newborns? What are common respiratory interventions/treatments implemented to alleviate or de-escalate this situation?

Discussion

Strong evidence reveals an inverse relationship between low gestational age and increased respiratory dysfunction. Premature infants younger than 32 weeks are at greater risk for developing RDS due to the lack of mature alveoli and mature surfactant in their developing lungs. Surfactant deficiency increases surface tension in the alveoli, resulting in microatelectasis, low lung volumes, and alveolar damage.

Signs and symptoms of RDS usually occur at birth or within the first few hours that follow. They include:

- Rapid, shallow breathing
- Sharp pulling in of the chest below and between the ribs with each breath (retractions)
- Grunting sounds
- Flaring of the nostrils
- Low L/S ratio

Recommended respiratory interventions are:

- Surfactant replacement therapy
- Noninvasive ventilation (continuous positive airway pressure/noninvasive positive-pressure ventilation [CPAP/NIPPV])
- Oxygen therapy
- Antenatal corticosteroid administration
- Intubation/ventilatory support
- If pulmonary hypertension present, inhaled nitric oxide (INO) therapy should generally be initiated (see Chapter 42).

is constantly produced and replaced, keeping the fetal lung inflated at a slightly higher positive pressure than the amniotic fluid pressure. This phenomenon is important in stimulating normal lung development and keeping the lungs "inflated" in uterus.[9] A developing fetus begins to make periodic and irregular respiratory efforts beginning mid-gestation but moves little or no fluid in and out of the lungs until birth. At term, the fetal lung is filled with approximately 40 mL of fetal lung fluid. Conditions that lead to inadequate fetal breathing and low amounts of amniotic fluid formation (**oligohydramnios**) are linked to incomplete inflation and incomplete development of the lungs (**hypoplastic lungs**) (see Table 9.3).

TRANSITION FROM UTERINE TO EXTRAUTERINE LIFE

At birth, the lungs undergo a rapid and remarkable transition. A fluid-filled organ that possesses very little circulation incapable of sufficient gas exchange becomes an air-filled organ that receives the entire cardiac output from the right heart. It then carries and delivers all gas necessary for gas exchange to sustain life for the newborn infant.[10]

TABLE 9.4 Composition of Pulmonary Surfactant

Component	Approximate Content
Phospholipids	**85%**
Phosphatidylcholine (PC)	76.3%
Dipalmitoylphosphatidylcholine	47.0%
Unsaturated phosphatidylcholine	29.3%
Phosphatidylglycerol (PG)	11.6%
Phosphatidylinositol (PI)	3.9%
Phosphatidylethanolamine	3.3%
Sphingomyelin (SM)	1.5%
Other	3.4%
Neutral Lipids[a]	**5%**
Cholesterol, free fatty acids	
Proteins[b]	**10%**
SP-A	++++
SP-B	+
SP-C	+
SP-D	++
Other	

[a]There is about 5% neutral lipid, most of which is cholesterol and free fatty acids. There is relatively little triglyceride and cholesterol ester.

[b]The composition of the surfactant proteins is not known precisely, but on a mass basis there appears to be more SP-A than SP-D and more SP-A than SP-B and SP-C. However, there is significant uncertainty about the exact values for SP-B and SP-C.

Adapted from Watson RJ, Leland GD: Alveolar epithelium and pulmonary surfactant. In Mason RJ, Ernst JD, Murray JF, et al., editors: *Murray and Nadel's textbook of respiratory medicine*, ed 6, Philadelphia, 2016, WB Saunders.

Placental Structure and Function

Survival of the embryo/fetus requires an effective circulatory interface with the circulation of the mother, which is provided by the placenta.[11] Within 1 week of uterine implantation, vascular projections called ***chorionic villi*** arise from the chorion of the embryo and penetrate the uterine endometrium. As gestation proceeds, the villi increase in number and complexity, erode the endometrium, and create irregular pockets called ***intervillous spaces*** in the placenta, which fill with maternal blood. The maternal blood flowing through the intervillous spaces bathes the embryonic villi and creates an O_2-rich and nutrient-rich blood environment where exchange occurs.

The maternal uterine tissues and blood vessels of the fetal chorionic villi make up the bulk of the placenta. Fig. 9.5 shows a cross-section of a well-developed placenta. Maternal blood flows into the intervillous space through the ***spiral arteries***, whereas fetal blood is supplied to the villi from two umbilical arteries. Maternal and fetal blood come into close proximity but *remain separated* by an embryonic membrane that permits the exchange of O_2, CO_2, water, ions, various metabolic molecules, and hormones.[10]

Various chemicals, hormones, bacteria, and viruses can also cross the intervillous space and cause a variety of fetal developmental problems. Oxygenated fetal blood leaves the chorionic

MINI CLINI

Surfactant Replacement Therapy and Respiratory Distress Syndrome

Problem

Why is surfactant replacement therapy essential for the prevention and treatment of RDS?

Discussion

Surfactant is a coating on the inside lining of the alveoli. This coating makes it easier for the alveoli to expand during breathing with minimal effort. It also keeps the alveoli from collapsing and sticking together during exhalation. Surfactant production begins in the lungs between 24 and 35 weeks of gestation.

Insufficient surfactant leads to reduced pulmonary compliance and increased surface tension inside the immature alveoli. This lack of surfactant results in increased work of breathing during inspiration and risk of alveoli collapse during exhalation followed by a reduction in total surface area for gas exchange (microatelectasis), as well as a decrease in the alveolar-capillary diffusion capacity.

RDS is a disease of surfactant deficiency in preterm newborn infants. Neonates born at the extremes of viability (≤28 weeks gestational age) have immature lungs with severe deficiency of surfactant production. Babies who have RDS are given surfactant until their lungs mature enough to sustain spontaneous ventilation and adequate gas exchange. Surfactant replacement therapy prevents alveolar collapse and is supplemented with oxygen therapy or mechanical ventilation to help the premature lung develop.

Surfactant often is given right after birth in the delivery room. It also may be given several times in the days that follow, until breathing improves.

TABLE 9.5 Approximate Normal Values of Blood Gases and Acid-Base in Fetal and Maternal Blood

Value	Maternal Intervillous Blood	Fetal Umbilical Artery Blood	Fetal Umbilical Venous Blood
pH	7.38	7.36	7.39
PCO_2 (mm Hg)	42	47	43
PO_2 (mm Hg)	50	19	30

villi capillaries through placental venules and returns to the fetus through a single umbilical vein.

Many factors enhance the delivery of O_2 to fetal tissues. The partial pressure gradient for O_2 between maternal blood and fetal blood drives the diffusion of O_2 into fetal blood within the chorionic villi capillaries.[12,13,14] Maternal arterial blood has a partial pressure of O_2 (PO_2) of approximately 100 mm Hg and mixes with the blood in the intervillous space, producing a mean PO_2 of approximately 50 mm Hg. Fetal blood that enters the villi has a PO_2 of approximately 19 mm Hg, and the pressure gradient between maternal and fetal blood PO_2 (~30 mm Hg) causes O_2 to diffuse into fetal blood. Blood leaving the villi and entering the umbilical vein has a PO_2 of approximately 30 mm Hg. Table 9.5 summarizes the approximate normal gas and acid-base values in normal fetal umbilical arteries and veins and maternal intervillous blood. Assessment of umbilical vein blood gas data (cord blood gas) shortly after birth is a method of determining the degree of fetal asphyxiation during the birth process by mainly assessing the pH.

Fetal pH is normally 0.1 unit lower than maternal pH. The mean umbilical arterial blood pH, base deficit, and gas values for premature and term infants are almost identical.[12] The risk of neonatal morbidity is inversely related to pH, with the highest risks at the lowest pHs.[13]

RULE OF THUMB A practical pH threshold for defining pathologic fetal acidemia is an umbilical artery pH < 7.00, which occurs in 3.7 per 1000 nonanomalous term births.[13] Umbilical artery between pH > 7.00 and < 7.20 or < 7.10 has been proposed as the threshold for identifying fetuses with abnormal fetal heart rate tracings who might benefit from intervention before the development of pathologic fetal acidosis and fetal injury.[14]

The O_2 content and delivery by fetal blood are almost the same as adult blood despite the much lower PO_2. This is due to several factors, including the relatively higher content of hemoglobin (18 g/dL) and hematocrit (54%) in fetal blood and the presence of fetal hemoglobin (HbF). Fetal hemoglobin has an increased affinity for O_2, and a more pronounced Bohr effect (reduced oxyhemoglobin affinity with acidosis) to enhance O_2 release (see Chapter 12).[15] Fig. 9.6 illustrates how the increased O_2 affinity is manifested by a leftward shift of the fetal oxyhemoglobin dissociation curve. The **P_{50}** (PO_2 that saturates 50% of the hemoglobin) is 6 to 8 mm Hg less than the P_{50} for adult hemoglobin (HbA), which indicates the degree of the shift toward higher affinity. At birth, approximately 70% of circulating hemoglobin is HbF.[16]

RULE OF THUMB At birth, approximately 70% of circulating hemoglobin is HbF. HbA gradually replaces HbF during the first 6 months of extrauterine life as HbA genes in bone marrow switch on and HbF genes in the liver are switched off.

Fetal Circulation

Fetal circulation is different from the circulation of the neonate after birth.[10] Three important bypass pathways (shunts) function in the developing fetus to enhance the flow of blood to the developing organs: ductus venosus, ductus arteriosus, and foramen ovale. Oxygenated blood from the placenta is carried in the umbilical vein back to the fetal circulation via the hepatic circulatory system (Fig. 9.7). Approximately *one-third* of this blood flows to the lower trunk and extremities. The other *two-thirds* flows through the ***ductus venosus***, bypassing the liver's circulation, and flows to the inferior vena cava. This better-oxygenated blood in the inferior vena cava mixes with the venous blood returning from the lower trunk and extremities entering the right atrium. Approximately 50% of this blood is shunted from the right atrium into the left atrium through an opening in the interatrial septum called the ***foramen ovale***. Left atrial blood flows to the left ventricle and then to the ascending aorta, where it continues to the brain, brachiocephalic trunk, and descending aorta. Venous blood from the superior vena cava is directed

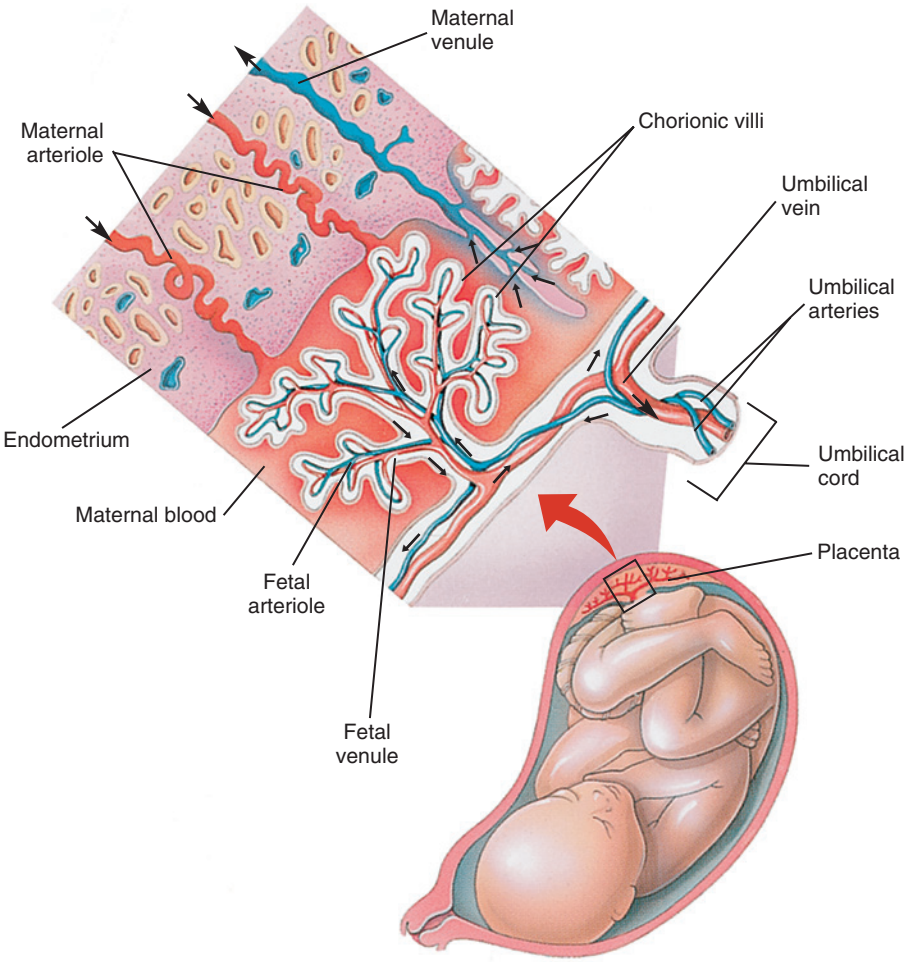


Fig. 9.5 Cross-sectional view through the placenta showing the spiral arteries that supply maternal blood to the intervillous spaces. The fetal villi, immersed in maternal blood, are supplied with blood from the umbilical arteries and drain their blood back through the umbilical vein. (From Thibodeau GA, Patton KT: *Anatomy and physiology,* ed 7, St Louis, 2010, Mosby.)

downward through the right atrium into the right ventricle and then into the main pulmonary artery.

In the fetus, the relatively low PO_2 and various prostaglandins in the fetal blood cause pulmonary vasoconstriction leading to increased pulmonary vascular resistance resulting in pulmonary artery pressures being higher than aortic blood pressure. As a result, 90% of the blood flow entering the pulmonary artery takes the path of least resistance by shunting through the **ductus arteriosus** (a muscular vessel attached to the trunk of the pulmonary artery and the aorta) and flowing to the aorta. Only 10% flows into the lungs. Blood flowing through the ductus arteriosus mixes with blood flowing through the aorta, routing into the systemic circulation. Some of this blood flows to the gut, lower extremities, and placenta. Two umbilical arteries carry blood from the fetal abdominal aorta to the placenta, carrying out fetal-maternal gas and nutrient exchange.[17]

RULE OF THUMB Before birth, 90% of the fetal blood bypasses the pulmonary circulation through the foramen ovale and the ductus arteriosus (right-to-left shunting). Any additional shunting after birth is considered an anomaly.

Cardiopulmonary Events at Birth

Various mechanisms work together to reduce and clear the amount of lung fluid at birth in preparation for alveolar gas exchange.[18] Days before birth, the epithelial surfaces of the lung stop the production of lung fluid, which is actively absorbed back into the fetal circulation. During normal vaginal delivery, approximately one-third of the lung fluid is cleared through compression of the thorax in the birth canal. The pulmonary capillaries and lymphatics clear the remaining fluid. A cesarean section (C-section) can lead to small amounts of fetal lung fluid to remain in the lungs leading to lung complications such as transient tachypnea of the newborn (TTN).

A newborn must develop very high transpulmonary pressure gradients during the first few breaths to open the alveoli and replace the remaining lung fluid with air to establish a stable lung volume for gas exchange (Fig. 9.8). These large pressure gradients overcome the forces of fluid viscosity in the airways and surface tension in the alveoli. The pressure-volume changes occurring during these first breaths are shown in Fig. 9.8.[9] At first, no air enters the newborn lung until the transpulmonary pressure gradient exceeds 40 cm H_2O. As lung volume increases

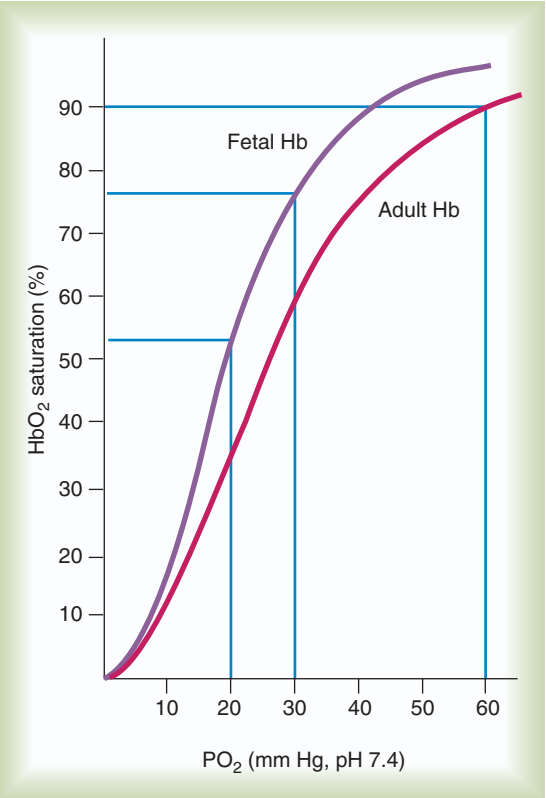


Fig. 9.6 Fetal hemoglobin (Hb) has a leftward shift of the oxyhemoglobin (HbO_2) dissociation curve compared with adult Hb, indicating a greater affinity for O_2. (Modified from Koff PB, Eitzman DV, Neu J: *Neonatal and pediatric respiratory care*, St Louis, 1988, Mosby.)

with each breath, decreasing amounts of pressure are needed to overcome the opposing forces in subsequent breaths. The volume trapped in the lung stabilizes quickly and is crucial to normalize gas exchange after birth.

The stimulus for these initial respiratory efforts is sent via peripheral and central chemoreceptors (transient increased on PCO_2 and decreased PO_2 during birth) and augmented further by skin thermoreceptors (being born into a cold environment). The first breath is triggered by new tactile and thermal stimuli. Also, as the placental gas transfer is suddenly interrupted, the newborn becomes hypoxic, hypercapnic, and acidotic, triggering strong inspiratory efforts.[10]

Fig. 9.9 summarizes the major cardiopulmonary changes that occur during the transition from a fluid-filled lung to an air-filled lung. As the lung expands with air, and gas exchange starts within the lung, pulmonary blood PO_2 increases, PCO_2 decreases, and pH increases; this results in pulmonary vasodilation, lower pulmonary vascular resistance, and constriction of the ductus arteriosus, which facilitates greater blood flow through the pulmonary circulation.

Ductus arteriosus closure is stimulated further by the loss of maternal prostaglandins. The combination of increasing alveolar air content and constriction of the ductus arteriosus promotes progressive improvement in the matching of ventilation and blood flow. A **patent ductus arteriosus (PDA)** after birth is an abnormal condition that usually resolves on its own. Failure to close occurs in the presence of a critical congenital heart defect (CCHD) where a PDA is needed to maintain adequate right-to-left circulation or death may occur.[19]

After the clamping of the umbilical cord, cessation of umbilical and placental blood flow causes the closure of the ductus venosus and a rapid increase in systemic vascular resistance. As systemic vascular resistance increases, left-sided heart pressures increase. Left atrial pressures also increase as a result of increased pulmonary blood flow that returns from the lungs. With left-sided heart pressures now higher than right-sided pressures, the foramen ovale closes.

When this last right-to-left shunt closes, the transition between fetal and extrauterine circulations is functionally complete. The full transition occurs later as the ductus arteriosus and foramen ovale close anatomically through fibrosis. Anatomic closure of the ductus normally occurs within 3 weeks of birth. Permanent closure of the tissue flap covering the foramen ovale may take several months.[10]

All of these changes normally occur during the first few minutes after birth and allow the newborn to achieve normal gas exchange.

RULE OF THUMB Many abnormal conditions can interfere with the fetal transition to extrauterine life. These events can lead to persistence of the fetal circulation (right-to-left shunting) and cardiorespiratory failure.

POSTNATAL LUNG DEVELOPMENT

Upper Airway

The infant's airways, distal lung tissue, and pulmonary capillary bed all continue to grow and develop after birth. Although the general pattern is well developed at birth, both the upper and the lower airways continue to change.

Fig. 9.10 shows the relative differences in the upper airway in relation to body size in an infant and an adult. The greater relative weight of the head can cause acute flexion of the cervical spine in infants with poor muscle tone. Infant neck flexion can cause acute airway obstruction. Although the head is larger, an infant's nasal passages are proportionately smaller than those of an adult. Also, the infant's jaw is much rounder, and the tongue is much larger relative to the size of the oral cavity.[20] These anatomic differences increase the likelihood of airway obstruction when an infant becomes unconscious and loses muscle tone.

RULE OF THUMB: Infant Airway Obstruction During neonatal or infant resuscitation, the baby's head and neck should be neutral or slightly extended in the sniffing position to avoid airway obstruction and collapse and provide effective ventilations.

Most infants breathe preferentially through the nose. However, most term newborn infants shift to oral breathing in response to nasal occlusion and hypoxia.[21] At approximately 4 to 5 months of age, most infants are capable of full oral ventilation.[22]

A newborn's **larynx** lies higher in the neck than the larynx of an adult, with the glottis located between C3 and C4, and is more funnel-shaped than that of an adult. In a child, the narrowest region of the upper airway is through the cricoid cartilage,

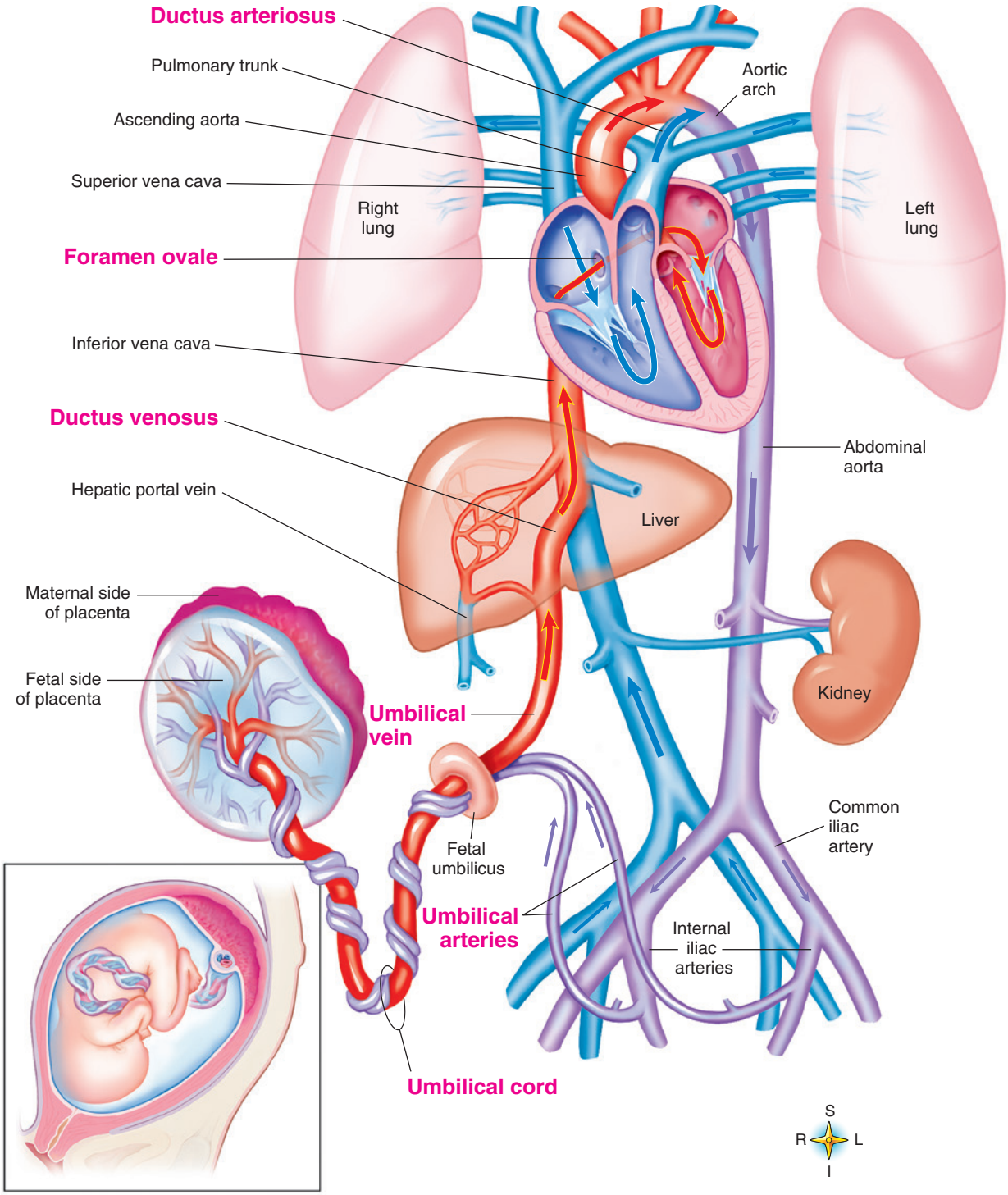


Fig. 9.7 Fetal Circulation Before Birth. Special features (shown in *red*) include the umbilical cord, two umbilical arteries, one umbilical vein, ductus venosus, foramen ovale, and ductus arteriosus. (From Thibodeau GA, Patton KT: *Anatomy and physiology*, ed 7, St Louis, 2010, Mosby.)

rather than the glottis, as in adults. The **epiglottis** of an infant is longer and less flexible than the epiglottis of an adult and lies higher and in a more horizontal position. During swallowing, the infant's larynx provides a direct connection to the nasopharynx. This connection creates two nearly separate pathways, one for breathing and one for swallowing, allowing infants to breathe and suckle at the same time. The anatomic descent of the epiglottis begins at 2.5 to 3 months of age. Mechanical and chemical irritant laryngeal reflexes develop at birth and can initiate protective laryngeal closure; these reflexes can trigger prolonged apnea in some and may be a cause of sudden infant death syndrome (SIDS).[23]

The large conducting airways of infants are shorter and narrower than the airways of adults. The normal newborn trachea

is approximately 5 to 6 cm long and 4 mm in diameter, whereas in small preterm infants, it may be only 2 cm long and 2 to 3 mm in diameter. Because of the smaller airways, a newborn's anatomic deadspace is proportionately smaller than the anatomic deadspace of an adult, being approximately 1.5 mL/kg of body weight.[24]

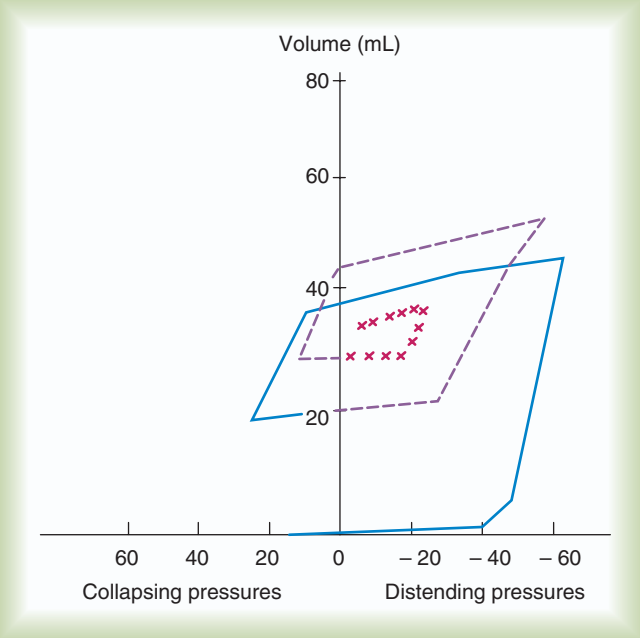


Fig. 9.8 Pressure-volume changes in the human neonate during the first three breaths after birth: first breath (—), second breath (---), and third breath (xxx). (Modified from Taeusch WH, Ballard RA, Gleason, CA: *Avery's diseases of the newborn*, ed 8, Philadelphia, WB Saunders, 2005.)

Fig. 9.11 compares the tracheal anatomy in an adult and newborn. The mainstem bronchi branch off from the trachea in the infant at less acute angle than in the adult. Like in adults, the right mainstem bronchus of the infant is still more in line with the trachea, promoting right mainstem intubation when airways or suction catheters are inserted too deeply. Mean airway diameter, from main bronchi to respiratory bronchioles, increases approximately 2 to 3 times from birth to adulthood.[21]

Smooth muscle is present in the airways of a neonate down to the level of the respiratory bronchioles and continues to increase until the infant is approximately 8 months old. Distinct C-shaped

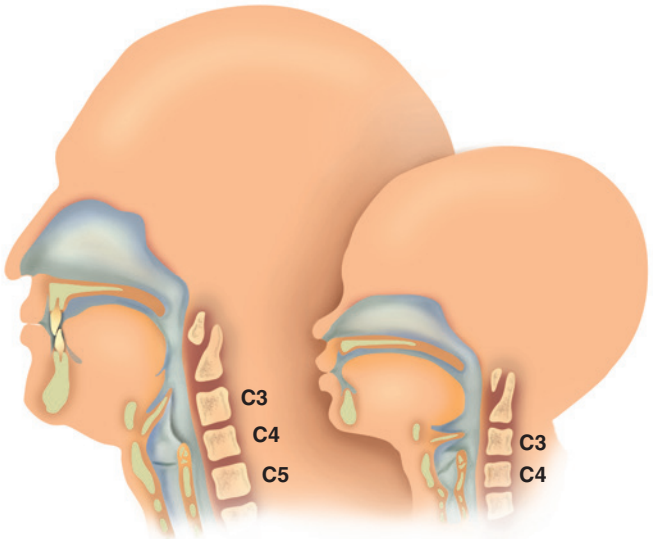


Fig. 9.10 Adult and pediatric upper airways.

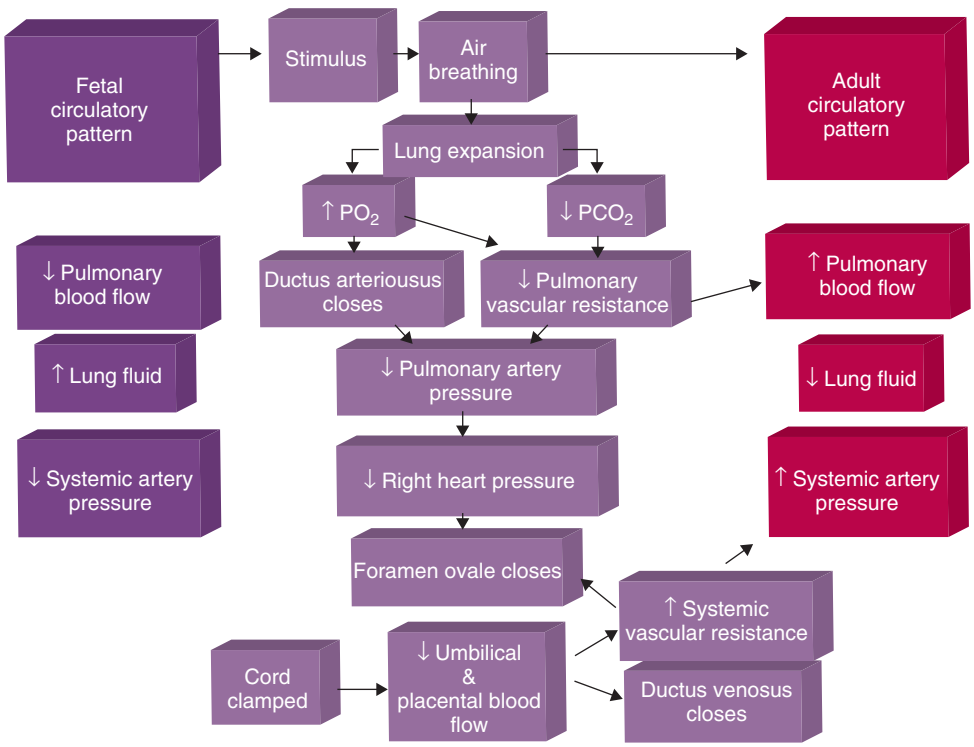


Fig. 9.9 Major cardiopulmonary changes during the transition from the fetal to the adult circulatory pattern.

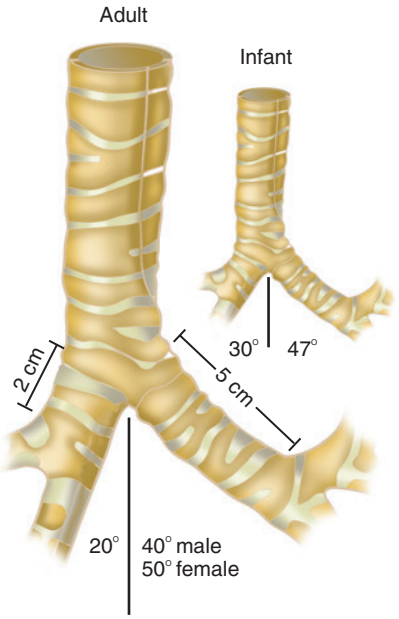


Fig. 9.11 Adult and infant tracheas showing the different angles of main stem bifurcation.

rings of cartilage are found in the trachea and mainstem bronchi of the neonate. The amount of cartilage progressively decreases in the more distal bronchi and eventually disappears in airways smaller than 2 mm in diameter.

Despite the presence of cartilage in the central airways of an infant, the trachea and larger bronchi of a neonate lack the rigidity of adult central airways. The compliant nature of these airways makes them prone to collapse and compression.

RULE OF THUMB Chest retractions in a neonate or infant, evident by the use of accessory muscles in the neck, rib cage, sternum, or abdomen, occur when lung compliance is poor or airway resistance is high.

Lower Airway and Alveoli

The human lung continues to develop alveoli for years until it reaches a stable stage, at which the total number has increased to approximately 480 million alveoli.[25] All development is generally complete by 10 years of age, with most occurring in the first to the second postnatal year.[26] By adulthood, the lungs have a gas exchange surface area of approximately 140 m^2.

Development of Vascular, Lymphatic, and Nervous Systems

The basic structure of the pulmonary circulation is complete at birth. The main pulmonary arterial trunk arises from the right ventricle and divides into left and right pulmonary arteries, which supply each lung. These arteries divide further to form direct or conventional arteries and supernumerary arteries. Both types of pulmonary arteries come together to supply blood to large clusters of alveoli that are supplied by a single bronchiole. Most of the growth in the vascular system that occurs after birth includes further smooth muscle growth within the walls of arteries and arterioles and greater density and refinement of the arterioles and capillaries in the distal airway region.[27]

The respiratory system is a unique organ in that it receives a double blood supply: one from the left ventricle and one from the right ventricle. The right heart supplies the bulk of the flow to the pulmonary circulation. The left heart supplies a smaller amount of flow (approximately 1% to 2% of cardiac output) to the bronchial arteries, which arise from the aorta and supply oxygenated blood to the tracheobronchial tree. The bronchial arteries supply O_2 to the airway tissue, blood vessels, nerves, lymphatics, and visceral pleura. O_2 is also directly absorbed across the airway lumen. Although the pulmonary and bronchial circulations have entirely different origins and purposes, they mix and supply blood flow to the microcirculation of the alveoli; this provides some collateral circulation and allows the shunting of blood. The lung's double circulation benefits the entire lung and helps compensate for deficiencies or disease processes that can affect either circulation.

The lymphatic vessels, located in the connective tissue tracts of the lung, surround the bronchi bronchioles, blood vessels, nerves, and pleural membrane. They play a central role in the control of fluid and protein balance within the lung and house various defensive cells. Fluid collected from the pleural space and interstitium is carried by the pleural capillaries and vessels through the lymphatic system back to the root of the lung (hilum), where numerous lymph nodes are located.[28]

Before birth, neuronal centers in the brainstem (medulla oblongata and pons) form the automatic control of breathing. At this time various afferent and efferent nerves form to sense and control different aspects of the respiratory system. The **phrenic nerves** and **intercostal nerves** are the primary components of the somatic (motor) nervous system that carry nerve signals from the brainstem to the respiratory muscles. They innervate the diaphragm (phrenic nerves) and intercostal muscles (intercostal nerves). These muscles are primarily responsible for expanding of the thorax during inspiration and allow exhalation by relaxing, letting the thorax and lungs recoil back to their pre-inspiratory position.

Visceral control of the smooth muscle of the respiratory system is carried out by branches of the sympathetic and parasympathetic nervous systems and chemical mediators transported to the lungs via the pulmonary circulation. Nerve fibers from the brainstem and spinal cord enter the lungs and grow in the same connective tissue tracts that surround the airways and house the blood and lymphatic vessels long before birth. These nervous fibers stimulate the smooth muscles of the bronchioles to cause bronchodilation (sympathetic fibers), the mucous glands to produce mucus (parasympathetic), and the blood vessels to cause vasoconstriction (sympathetic). Cranial nerve X (*vagus* nerve) carries motor and sensory signals of the parasympathetic system throughout the airways and the lungs (vagal innervations). Branches from each thoracic spinal nerve carry sympathetic motor and sensory signals to and from the lungs.[29]

Chest Wall Development, Diaphragm, and Lung Volume

The thoracic wall in infants is more compliant, and its muscles less developed than the muscles of adults, providing little structural support. The infant thoracic cage is also more box-like,

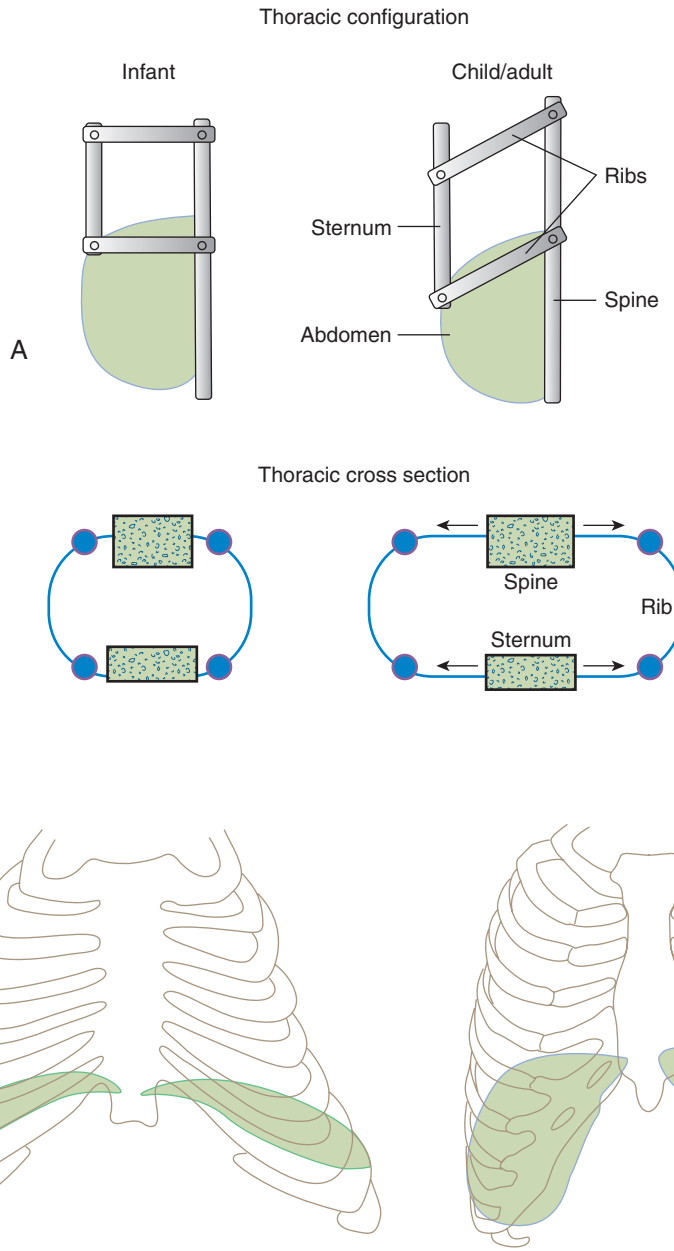


Fig. 9.12 (A) Changes in angularity of ribs and spine and cross-sectional shape of the thorax from an infant to an older child and adult. (B) Anterior views of a newborn *(left)* and adult *(right)* rib cage and the relative position of the diaphragm *(shaded portions)*. (Modified from Taussig LM, Landau LI, editors: *Pediatric and respiratory medicine*, ed 2, St Louis, 2008, Mosby.)

with the ribs being more horizontally oriented or elevated than that of adults (Fig. 9.12A). Also, the **diaphragm** inserts into the thoracic cage in a more horizontal plane decreasing the effective ability to enlarge the thorax (see Fig. 9.12B).

As infants inhale, the diaphragm moves down, but the flexible chest wall moves very little in the anteroposterior dimension as the chest wall muscles attempt to pull it upward and outward. Compounding this situation is a proportionately larger abdominal visceral content in neonates and infants that restricts the vertical motion of the diaphragm. The ribs take on a progressively downward slope as a child grows, and by 10 years of age, the rib cage has the configuration seen in adults. Ossification of the ribs and sternum normally completes by 25 years of age, and this, combined with muscular development, results in a stiffer chest wall that moves more in the anteroposterior dimension with each inspiratory effort.

The balance of these static forces results in reduced lung volume in an infant. Proportionately lower lung volumes can lead to early airway closure, widespread alveolar collapse (atelectasis), ventilation/perfusion mismatch ($\dot{V}/\dot{Q}$), and resultant hypoxemia. The combination of a reduced lung volume and high O_2 demands renders the infant more susceptible to profound hypoxemia in situations disturbing ventilation, lung volume, or $\dot{V}/\dot{Q}$ mismatching. Infants possess a remarkable ability to elevate their lung volume dynamically. Infants in distress can actively increase lung volume by trapping gas, improving $\dot{V}/\dot{Q}$ matching

and gas exchange. Infants accomplish gas trapping by actively using the diaphragm during exhalation. This active diaphragmatic compression slows exhalation, by closing the vocal cords and narrowing the glottis. The combination of these two maneuvers effectively regulates volume in the lung and dynamically elevates lung volume. The narrowing of the glottis or larynx during exhalation is referred to as "laryngeal braking" or "grunting." Infants in respiratory distress commonly grunt, a manifestation of laryngeal braking.[30] A more compliant chest wall contributes to suprasternal, substernal, intercostal, and subcostal retractions in distressed infants and young children (see Mini Clini).

MINI CLINI

The Significance of Thoracic Soft Tissue Retractions

Supraclavicular and intercostal retractions are inward movements of the soft tissues above the clavicle and between the ribs of the chest wall during inspiration. This inward movement causes the clavicle and ribs to stand out prominently during inspiratory efforts.

Problem

Why do infants and some adults in respiratory distress with severe airway obstruction or reduced compliant ("stiff") lungs exhibit thoracic soft tissue retractions?

Discussion

The pressure within the intrapleural space is slightly negative (–3 to –5 cm H_2O) because of the tendency of the lung to collapse and the rib cage to expand outward. This pressure becomes more negative (–5 to –10 cm H_2O) during inspiration. The respiratory muscles enlarge the chest as the diaphragm descends and the intrathoracic volume increases. During respiratory distress and airway obstruction, a much greater inspiratory effort is required. This increased effort translates into a much greater decrease in intrathoracic and pleural pressures (–10 to –40 cm H_2O). This greater decrease in intrathoracic and pleural pressures "sucks" the soft tissues inward and causes soft tissue retractions. These retractions significantly increase the patient's work of breathing.

RULE OF THUMB ***Grunting*** is an expiratory sound caused by the sudden closure of the glottis during exhalation to maintain functional residual capacity (FRC) and prevent alveolar atelectasis. Because lung compliance is worse at very low or very high FRC, achieving and maintaining physiologic FRC in infants is essential in the management of respiratory disorders with poor compliance, such as RDS or TTN.

RESPIRATORY SYSTEM IN THE ADULT

Surface Features of the Thorax

At birth, the thorax has a smaller transverse (side to side) dimension. Thoracic size and volume increase throughout childhood and especially during the adolescent growth spurt. When evaluating lung size and volume throughout puberty and into adulthood, boys and men are consistently found to have larger lungs than age-matched and height-matched girls and women.[31]

Imaginary lines are commonly used to establish reference points and identify landmarks on the thorax. These lines and points help identify the location of underlying structures and the location of abnormal findings. On the anterior chest, the *midsternal line* divides the thorax into equal halves. The left and right *midclavicular lines* are parallel to the *midsternal line*. These are drawn through the midpoints of the left and right clavicles (Fig. 9.13). The *midaxillary line* divides the lateral chest into equal halves. The *anterior axillary* line is parallel to the midaxillary line. It is situated along the anterolateral chest. The *posterior axillary* line is also parallel to the midaxillary line. It is located on the posterolateral chest wall (Fig. 9.14). Three imaginary vertical lines are located on the posterior thorax. The *midspinal* line divides the posterior chest into two halves. The left and right *midscapular* lines are parallel to the midspinal line. They pass through the inferior angles of the scapulae in a relaxed upright subject (Fig. 9.15).

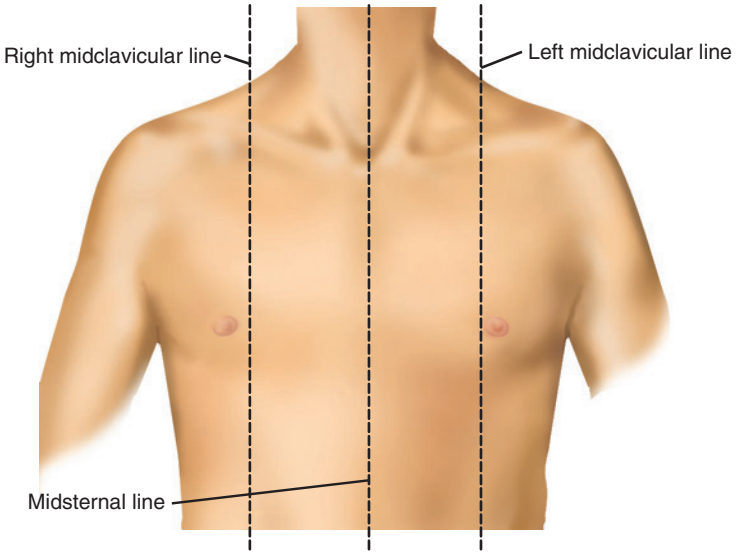


Fig. 9.13 Anatomic reference lines on the anterior chest wall.

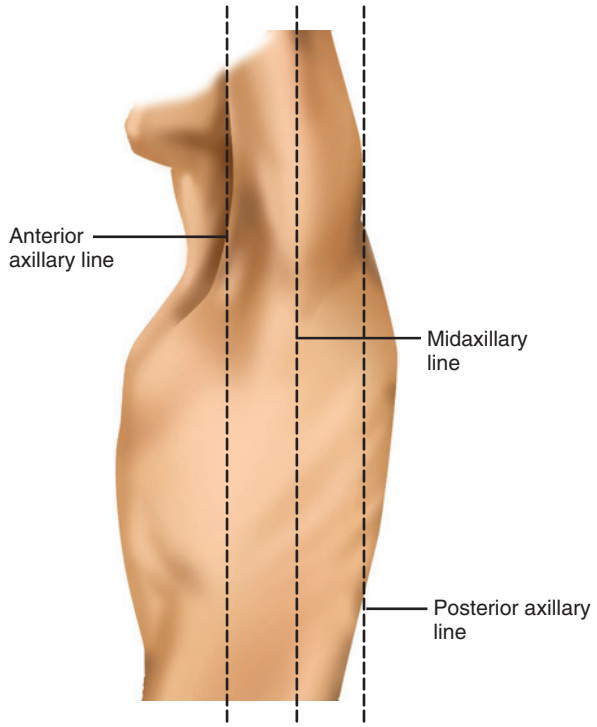


Fig. 9.14 Anatomic reference lines on the lateral chest wall.

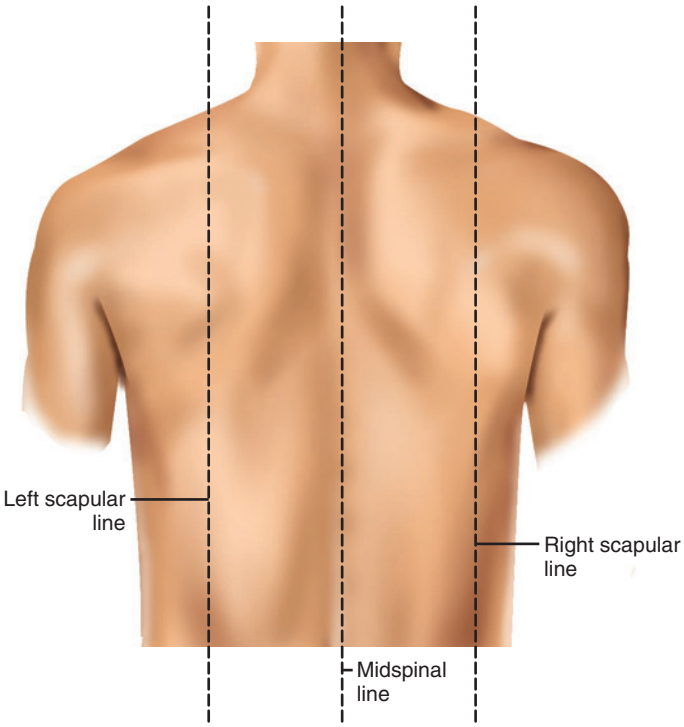


Fig. 9.15 Anatomic reference lines on the posterior chest.

RULE OF THUMB: Anatomic Directions Descriptions of various anatomic structures often use the following terms:

Anterior, anteriorly, ventral	Front of the body, toward the front
Posterior, posteriorly, dorsal	Back of the body, toward the back
Anteroposterior	In a direction from the front to the back
Lateral, laterally	Side of the body, toward the side
Medial, medially	Midline of the body, toward the midline

Components of the Thoracic Wall

The thoracic cavity is formed by the tissues of the chest, upper back, and diaphragm.[32] It is a cone-shaped cavity that houses the lungs, heart, and the contents of the mediastinum (Figs. 9.16 and 9.17). It protects the vital organs within and is capable of changing shape to enable air to be moved into and out of the lungs. The thoracic cavity is formed from epithelial, connective, and muscle tissues.

The various parts of the thoracic wall are shown in Fig. 9.18. The outer covering of the thorax is formed by the integumentary system, which includes skin, hair, subcutaneous fat, and breast tissues. Skeletal muscle tissue forms the various muscles of the chest and back and lies over and between the ribs. The ribs lie in the inner portion of the thoracic wall. The inner layer of the thoracic wall in contact with the lungs is lined with a serous membrane called the **parietal pleura**. It is opposite to another serous membrane called the **visceral pleura**, which covers the outer surface of the lungs. A thin, fluid-filled pleural space forms between the parietal and visceral pleural membranes facilitating lung movement and avoiding friction.

The rigidity of the thorax is provided by the bone tissue of the rib cage. The bony parts of the rib cage include the sternum, ribs, thoracic vertebral bones, scapula, and clavicle (Fig. 9.19). The **sternum** is a long, vertical flat bone found on the anterior side that is composed of three bones: the **manubrium**, the body (or **gladiolus**), and the **xiphoid process**. The superior edge of the manubrium forms a shallow depression that is known as the **suprasternal notch** (or jugular notch). The fused connection between the manubrium and the body is known as the **sternal angle**; it is also known as the ***angle of Louis***. The sternal angle is an external marker of the point where the trachea divides into the left and right main stem bronchi (the carina). A cartilaginous joint called the **costal cartilage** is on the lateral edges of the manubrium and sternal body and forms the attachment between the ribs and sternum. This joint allows the rib cage to bend and permits the thorax to increase and decrease in size as we breathe.[33]

RULE OF THUMB Where the manubrium and body of the sternum meet, the anterior chest wall shows a slight depression that forms an oblique angle (when viewed from the side). This depression is referred to as the *angle of Louis*. Beneath this important landmark is the carina, where the trachea divides into the right and left main stem bronchi.

The rib cage is formed by 12 pairs of ribs.[32] Rib pairs 1 through 7 are known as the **true ribs** because they are attached directly to the sternum. The first ribs and the upper sternum form the opening into the thorax that is called the ***thoracic inlet***, or *operculum*. Ribs 8 through 12 are called **false ribs** because they are neither directly nor indirectly attached to the sternum. The vertebrochondral rib pairs 8, 9, and 10 are indirectly attached to

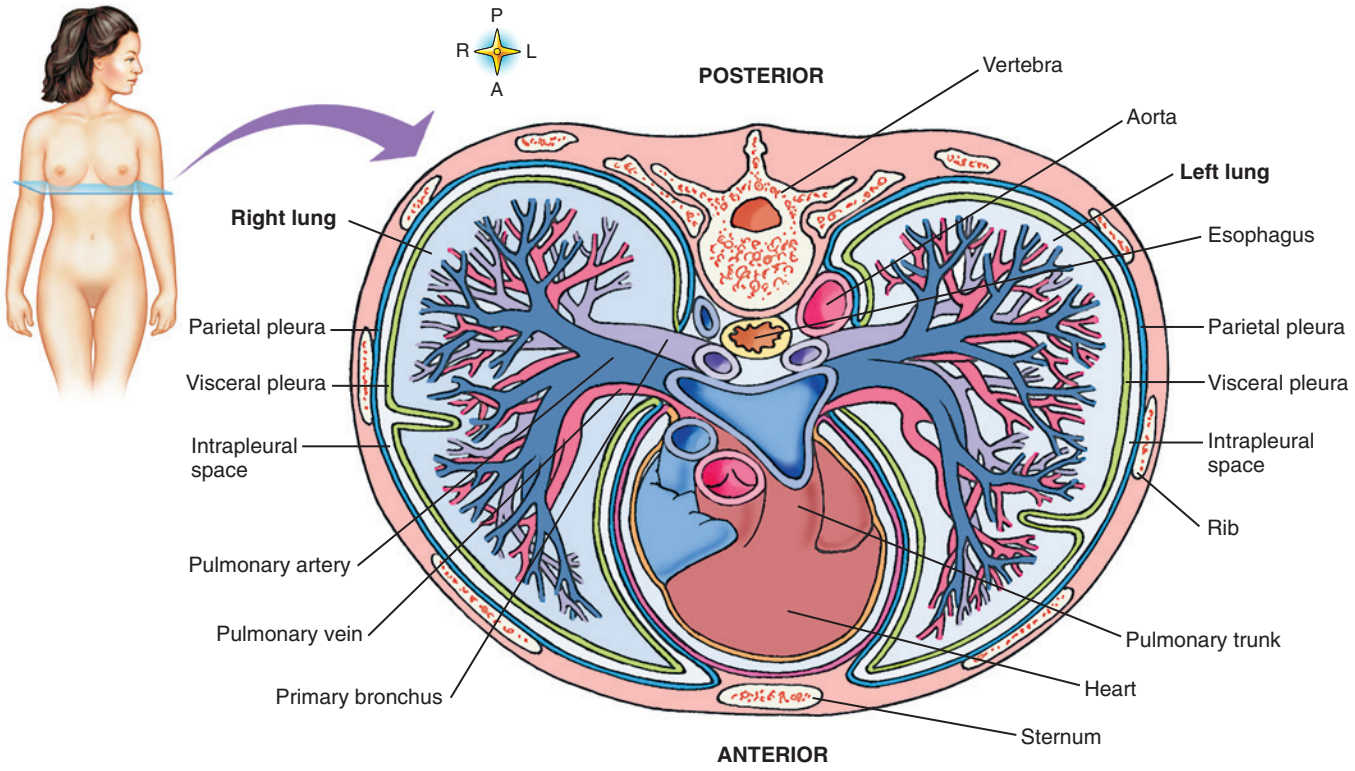


Fig. 9.16 Transverse sectional view of the thorax showing its contents. (From Thibodeau GA, Patton KT: *Anatomy and physiology*, ed 7, St Louis, 2011, Mosby.)

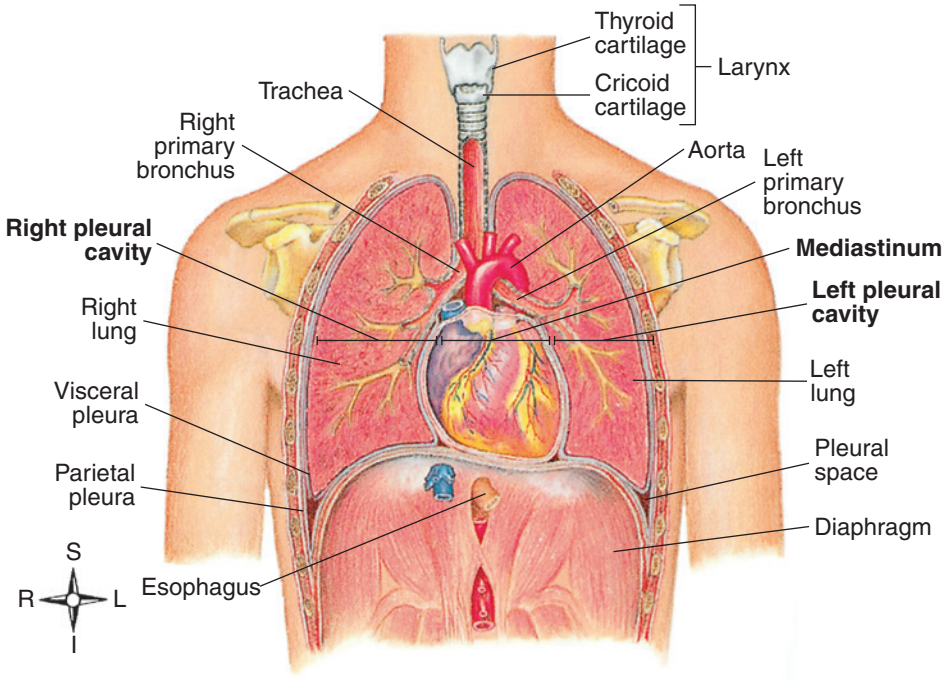


Fig. 9.17 Sectional view of the thoracic cavity divided into the left and right pleural cavities and the central mediastinal cavity. (From Thibodeau GA, Patton KT: *Anatomy and physiology*, ed 3, St. Louis, Mosby, 1996.)

the sternum through a common cartilaginous strap. Rib pairs 11 and 12 are called **floating ribs** because they are not attached to the sternum.

Each rib has a sternal end; a long, curved, and relatively flat body; and a head that articulates with the thoracic vertebrae (Fig. 9.20). Intercostal muscles lie between the ribs and hold them together. Just below each rib, in their inner surface is the **costal groove**. The costal groove contains an intercostal artery, vein, and nerve, supplying blood flow and innervation to that region of the chest wall (see Fig. 9.18).

RULE OF THUMB Numerous procedures require entry into the pleural cavity, such as thoracentesis or chest tube insertion. Punctures made during these procedures are always done directly above a selected rib upper border to avoid injuring important structures. The intercostal nerves, veins, and arteries all lie in the costal groove groove in the lower third of each rib.

The upper and lateral regions of the thorax house the bones of the pectoral girdles. The pectoral girdle on each side is formed by the clavicle and scapula.[32] The scapula forms the socket for the shoulder joint and is stabilized or moved by skeletal muscles of the upper back. The clavicle supports and stabilizes the shoulder joint through a flexible attachment to the manubrium of the sternum.

Rib Movement

The various ribs move in different ways, and some may move more than others at different times. The first rib moves slightly, raising and lowering the sternum. Its slight motion increases the anteroposterior diameter of the chest. This action is not used during quiet breathing and becomes active only under conditions that require increased ventilation or deep breathing. Ribs 2 through 7 can move simultaneously about two axes (Fig. 9.21). As each rib rotates about the axis of its neck, its sternal end rises and falls. This movement increases the anteroposterior thoracic diameter in what is commonly referred to as a "pump handle" motion (see Fig. 9.21B). At the same time, the rib moves about its long axis from its angle at the sternum. This motion causes the middle part of the rib to move up and down in what is commonly described as a "bucket handle" (see Fig. 9.21A). The compound action of ribs 2 through 7 changes both the anteroposterior and the transverse dimensions of the chest in an upward and outward motion during inspiration. Ribs 8 through 10 rotate in a pattern similar to that of ribs 2 through 7. However, the elevation of the anterior ends of these ribs produces a small backward movement of the lower sternum that slightly reduces the anteroposterior thoracic diameter. Outward rotation of the middle section of these ribs increases the transverse diameter of the thorax. Ribs 11 and 12 participate in changing the contour of the chest in a minor way as they are pulled upward and outward in a "caliper" motion.[34]

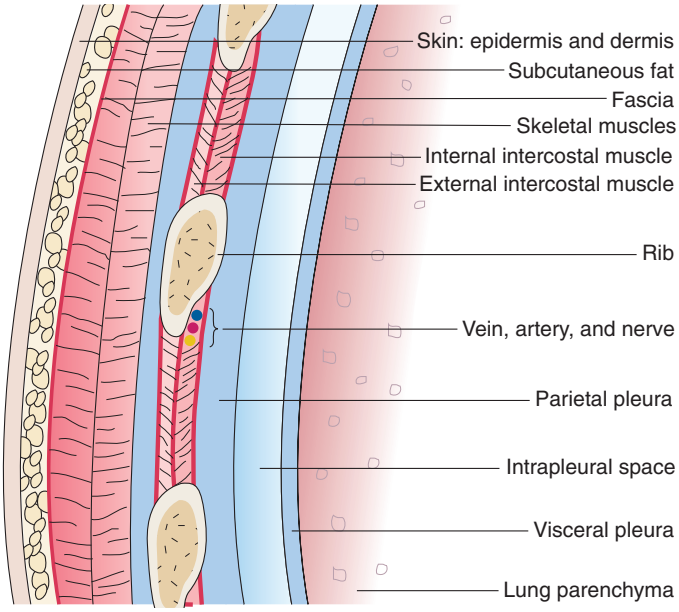


Fig. 9.18 Sectional view of the thoracic wall. (From Hicks GH: *Cardiopulmonary anatomy and physiology*, Philadelphia, 2000, WB Saunders.)

Respiratory Muscles

Changes in thoracic cavity dimension during breathing are the product of tension developed by various skeletal muscles known as the *respiratory muscles*.[35] Their origins, insertions, innervation, and actions are summarized in Tables 9.6 and 9.7. The diaphragm and intercostal muscles are the primary muscles of ventilation. They are active both while at rest and when the individual exhibits stress-induced increases in breathing. The **accessory muscles of breathing** assist the diaphragm and intercostal muscles when ventilatory demand increases. The scalene, sternocleidomastoid, pectoral, and abdominal wall muscles are the predominant accessory muscles. Other abdominal and chest wall muscles may function as accessory muscles when needed.

The diaphragm is a thin, musculotendinous, dome-shaped structure that separates the thoracic and abdominal cavities (Fig. 9.22).[36] It originates from the chest and abdominal wall and converges in a central tendon at the top of its dome. The diaphragm is a highly aerobic and fatigue-resistant muscle compared with other skeletal muscles and more capable of long-term rhythmic contraction.

TABLE 9.6 Respiratory Muscles That Expand the Thorax During the Inspiratory Phase

Muscle	Origin	Insertion	Innervation	Action
Diaphragm	Xiphoid process, lower lateral ribs, lumbar vertebra	Central tendon of the dome	Phrenic nerves (C3-C5)	Diaphragm moves downward; abdominal wall forced outward
External intercostals	Upper ribs	Lower ribs	Intercostal nerves (T1-T12)	Lift ribs upward
Scalene	Lower five cervical vertebrae	Ribs 1 and 2	Cervical nerves (C5-C8)	Lifts ribs 1 and 2
Sternocleidomastoids	Manubrium and clavicle	Mastoid process of occipital bone	Accessory nerves (cranial nerve XI)	Lift sternum
Trapezius	Occipital bone, C7-T12 vertebrae	Scapula and clavicle	Accessory nerves (cranial nerve XI)	Stabilizes head
Pectoralis minor	Anterior region of ribs 3–5	Scapula	Pectoral nerves (C6-C8)	Lifts upper ribs
Pectoralis major	Clavicle and sternum	Humerus	Pectoral nerves (C5-C8)	Lifts sternum

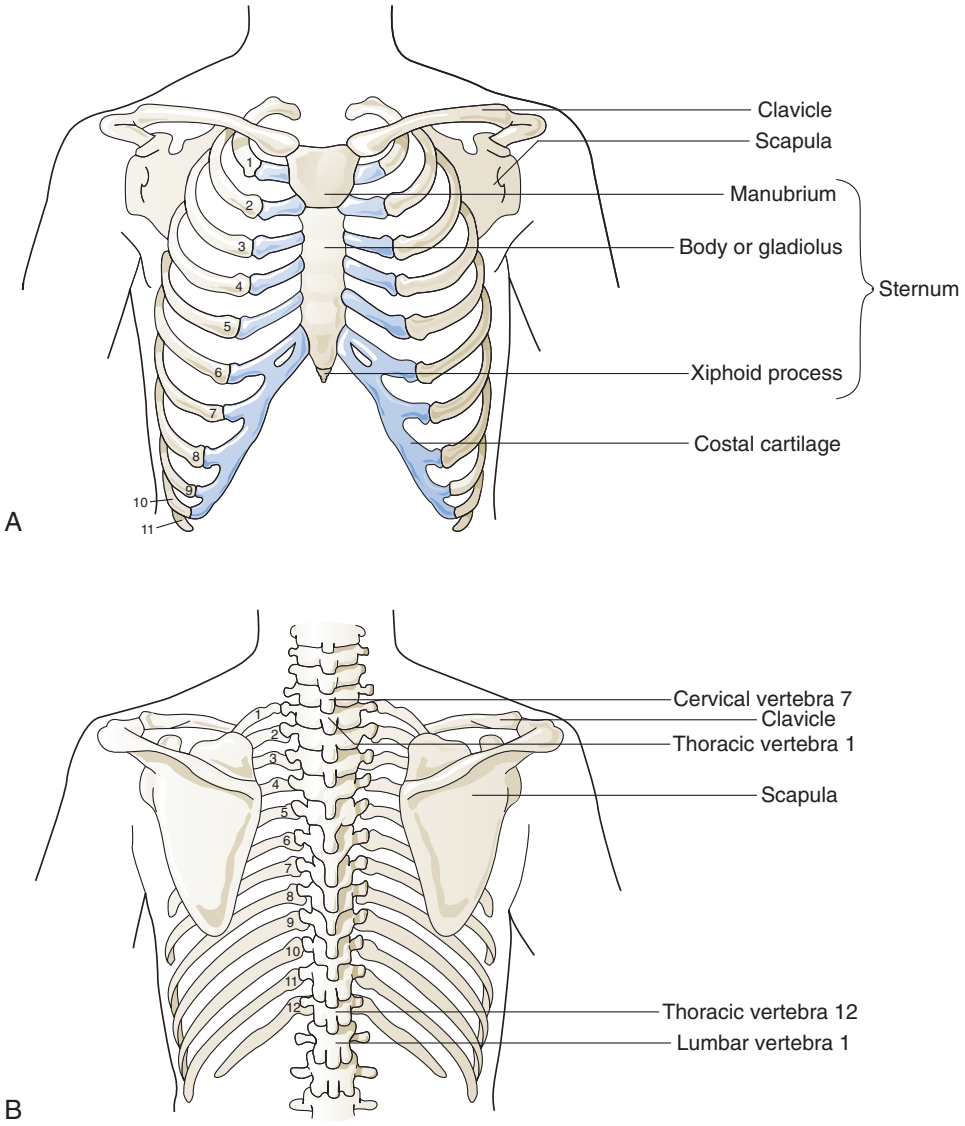


Fig. 9.19 (A) Anterior and (B) posterior views of the bones of the thorax. (From Hicks GH: *Cardiopulmonary anatomy and physiology*, Philadelphia, 2000, WB Saunders.)

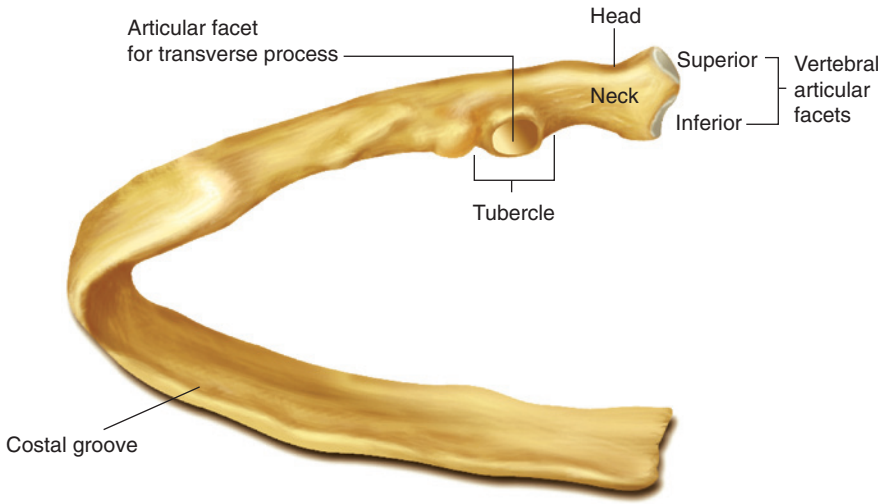


Fig. 9.20 Typical Middle Rib as Viewed From the Posterior. The head end articulates with the vertebral bones, and the distal end is attached to the costal cartilage of the sternum.

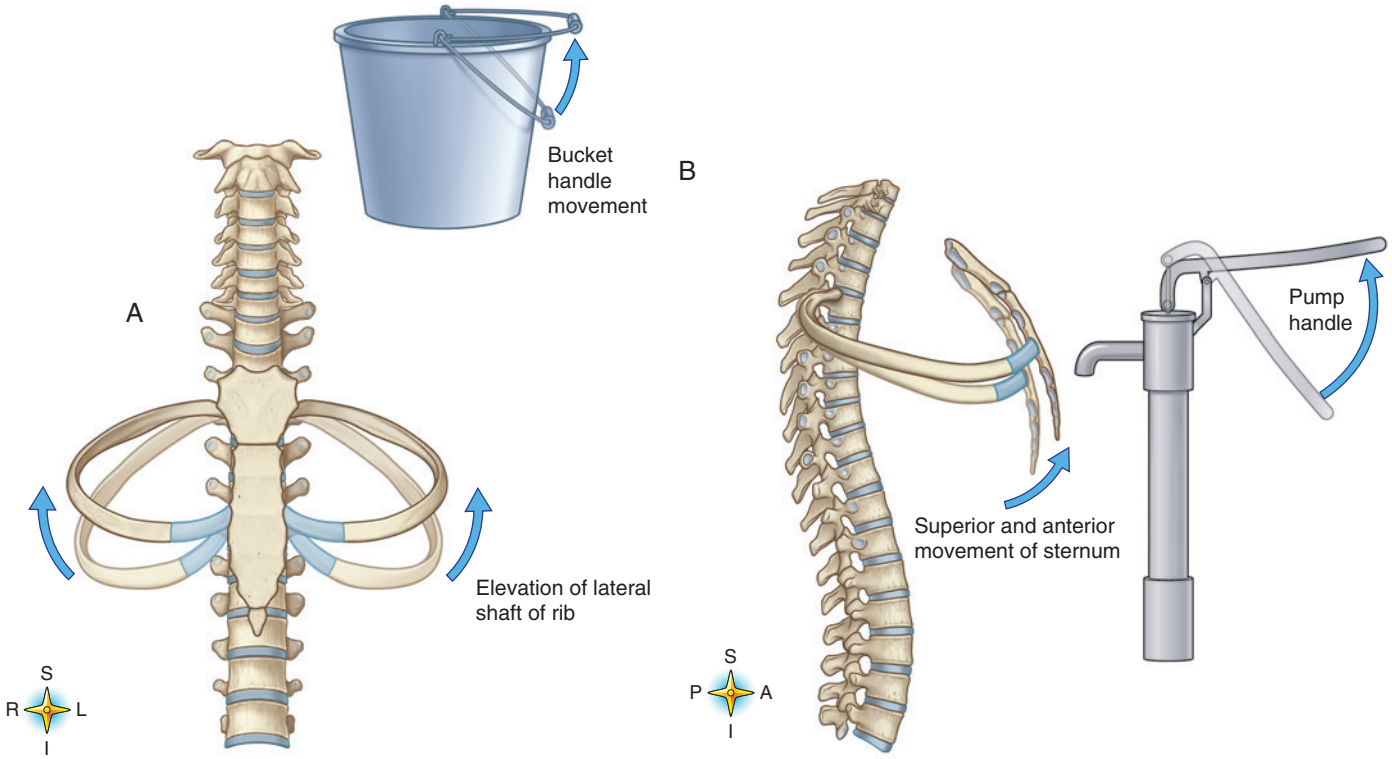


Fig. 9.21 (A) "Bucket handle" type and (B) "pump handle" type of rib motions. (From Thibodeau GA, Patton KT: *Anatomy and physiology*, ed 7, St Louis, 2011, Mosby.)

TABLE 9.7 Respiratory Muscles That Compress the Thorax During the Expiratory Phase

Muscle	Origin	Insertion	Innervation	Action
Internal intercostals	Lower ribs	Upper ribs	Intercostal nerves (T1-T12)	Pull ribs down
External oblique	Anterior lower eight ribs	Linea alba and iliac crest	Lower intercostal and iliohypogastric nerves (T7-T12)	Pulls abdominal wall inward
Internal oblique	Lumbar vertebrae, iliac crest, and inguinal ligaments	Costal region of ribs and pubis	Lower intercostal and iliohypogastric nerves (T10-T12 and L1)	Pulls abdominal wall inward
Transverse abdominis	Costal region of lower ribs, iliac crest, and inguinal crest	Linea alba	Lower intercostal and iliohypogastric (T7-L1)	Pulls abdominal wall inward
Rectus abdominis	Costal region and ribs 5–7	Pubis	Lower intercostal and iliohypogastric (T7-T12)	Pulls abdominal wall inward
Serratus anterior	Costal region of upper eight ribs	Scapula	Long thoracic nerves (T5-T7)	Compresses thorax when the arm is stabilized
Serratus, posterior superior	Lower cervical and upper thoracic vertebrae	Posterior ribs 2–5	Intercostal nerves	Pulls ribs downward
Serratus, posterior inferior	Lower thoracic and upper lumbar vertebrae	Posterior ribs 9–12	Thoracic nerves	Pulls ribs downward
Latissimus dorsi	Lower thoracic, lumbar, sacral vertebrae, ilium, and lower ribs	Humerus	Thoracodorsal nerve (C6-C8)	Compresses thorax when the arm is stabilized

In an upright position and with the diaphragm relaxed, the liver forces the dome of the right hemidiaphragm upward approximately 1 cm higher than the left hemidiaphragm at the end of a quiet exhalation. The highest portion of the right dome sits at the 8th or 9th thoracic vertebra posteriorly and at the 5th rib anteriorly. The left diaphragmatic dome sits at the 9th or 10th thoracic vertebra posteriorly and the 6th rib anteriorly. The movements of the hemidiaphragms are synchronous in healthy subjects. When lying down in a supine position, the weight of the abdominal contents forces the diaphragm farther up into the thoracic cavity. During quiet breathing, the diaphragm is responsible for approximately 75% of the change in thoracic volume.[37] When the muscle fibers of the diaphragm are tensed during inspiration, the dome of the diaphragm is pulled down 1 to 2 cm; this results in enlargement of the thoracic cavity and compression of the abdominal contents. During maximal

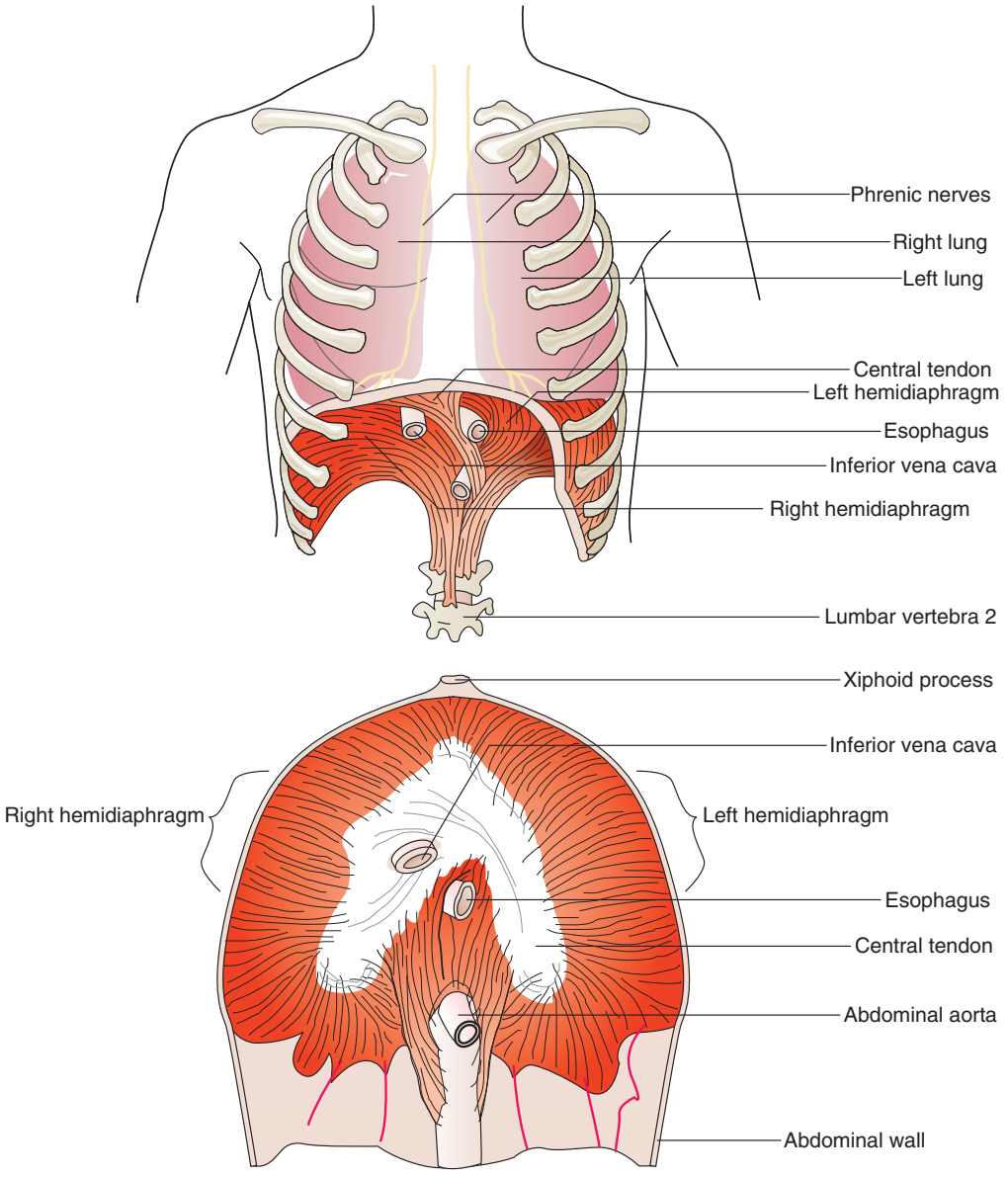


Fig. 9.22 The diaphragm originates from the lumbar vertebrae, lower ribs, xiphoid process, and abdominal wall and converges in a central tendon. Note the locations of the phrenic nerves and openings for the inferior vena cava, esophagus, and abdominal aorta. (From Hicks GH: *Cardiopulmonary anatomy and physiology*, Philadelphia, 2000, WB Saunders.)

inspiration, the diaphragm can be pulled down approximately 10 cm. Exhalation is passive and results when diaphragmatic tension decreases, and the diaphragm returns to its relaxed position.

Increased lung volume (e.g., hyperinflation, air-trapping) causes the diaphragm to drop and flatten out. Contraction of a flattened diaphragm can result in tension on the lower ribs that causes them to be pulled inward, resulting in compression of the thoracic cavity. This condition can occur in individuals with severe gas trapping as a result of emphysema or asthma. To compensate, these individuals must recruit other muscles to enlarge the thorax. Less efficient breathing and excessive muscle work results. Non-pulmonary diseases also can affect diaphragmatic function. Abdominal wall muscle tensioning *(splinting)* cause by pain, abdominal distention with fluid *(ascites)*, or other causes of rigidity of the abdominal wall muscles can interfere with diaphragmatic descent during inspiration.

Functionally, the diaphragm is divided into a right and a left hemidiaphragm. Each hemidiaphragm is innervated by a phrenic nerve that arises from branches of spinal cervical nerves C3, C4, and C5.[36] Spinal cord injuries at or above the level of the third cervical vertebrae may result in diaphragmatic paralysis. In this situation, the individual loses *all* nervous control of the respiratory muscles and is unable to breathe spontaneously. Unilateral phrenic nerve injury or disease to one side can spare the other nerve and permit unilateral ventilation.

Although the diaphragm is the primary ventilatory muscle, it is not essential for survival. Limited, short-term ventilation is possible using accessory muscles even if the diaphragm is paralyzed.

MINI CLINI

Lung Hyperinflation in Emphysema

Emphysema is a disease characterized by the destruction of the elastic alveolar tissue of the lungs. This destruction causes the emphysematous lung to have less elastic recoil than a normal lung.

Problem

Why do patients with severe emphysema have enlarged or overinflated lungs? How does hyperinflation interfere with breathing? What can be done to alleviate the problem?

Discussion

The pathologic findings of emphysema include the destruction of elastic fibers in the alveolar region, reduced lung recoil, and expansion of the remaining lung tissue. As the disease progresses, the tendency of the lungs to collapse (because of their inherent elasticity) becomes less than the normal outward expanding force of the rib cage (because of its higher elasticity). The stronger outward expanding force of the rib cage expands the lungs, increases their volume, and results in overinflated lungs at the end of a normal, resting exhalation.

Hyperinflation "flattens" the diaphragm for similar reasons, making it less effective during inspiration, and increasing the work of breathing. Loss of elastic tissues allows small airways to collapse, resulting in air trapping and exaggerating hyperinflation.

Therapy for emphysema is directed at reducing the effects of air trapping. Administration of bronchodilators and corticosteroids may improve airway opening, reducing trapped gas and the work of breathing. Maneuvers such as pursed-lip breathing also may assist in reducing gas trapping by splinting open the airways and facilitating exhalation. Lung reduction surgery may be an option for selected patients.

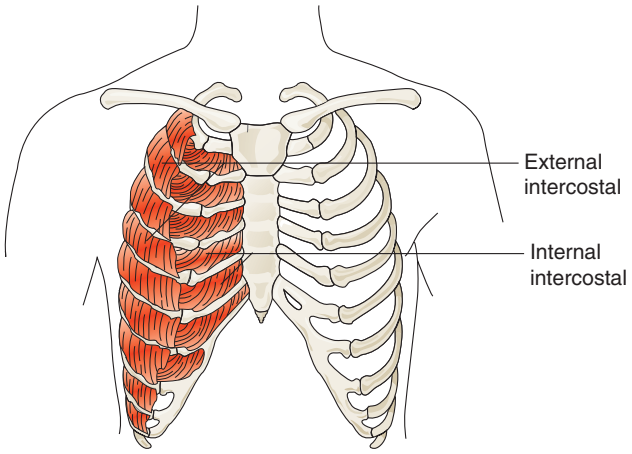


Fig. 9.23 The external intercostal muscles lift the inferior ribs and enlarge the thoracic cavity. The internal intercostal muscles compress the thoracic cavity by pulling the ribs together. (From Hicks GH: *Cardiopulmonary anatomy and physiology*, Philadelphia, 2000, WB Saunders.)

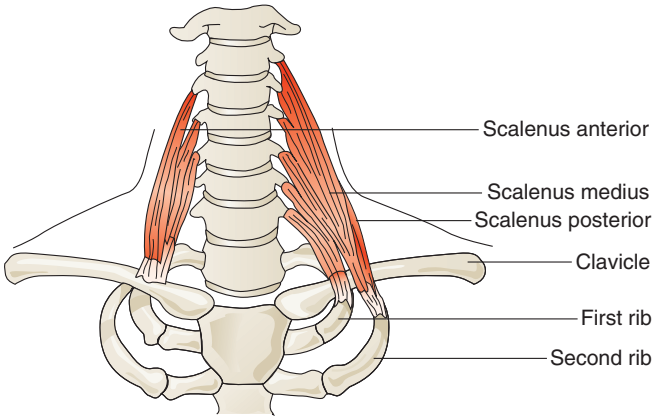


Fig. 9.24 The scalene muscles originate from the lower cervical vertebrae and lift the clavicle and first two ribs. (From Hicks GH: *Cardiopulmonary anatomy and physiology*, Philadelphia, 2000, WB Saunders.)

Because exhalation is *passive*, the diaphragm normally does not actively participate in exhalation. During exhalation, it returns to its resting position during the passive recoil of the lungs and thorax. Though not typically active during exhalation, the diaphragm plays an important role in maintaining the FRC of the lungs. It maintains a level of contraction or "tonicity" that helps to manage FRC levels, effectively helping with oxygenation and ventilation of the lungs.[38]

During forced exhalation, abdominal wall muscles compress the abdominal cavity and increase intraabdominal pressure. The diaphragm is forced upward, and the lungs compressed, forcing gas from them. The diaphragm performs important functions other than ventilation; it aids in generating high intraabdominal pressures by remaining fixed while the abdominal muscles contract (*Valsalva maneuver*), facilitating vomiting, coughing, sneezing, defecation, and parturition.

As previously discussed, during quiet breathing, the diaphragm does most of the work. The accessory muscles of breathing are slightly active during quiet breathing and become more active with forceful breathing as discussed earlier in the chapter.

The accessory muscles of inspiration include various muscles in the neck, chest, and upper back. The external intercostal muscles (Fig. 9.23) originate on the upper ribs and attach to the lower ribs. The fibers of these muscles run at an oblique angle between the ribs. When they generate tension, the ribs lift upward and cause the thoracic cavity to enlarge the thorax (Hamberger mechanism, better known as the "bucket handle" mechanism). Nerve signals are received from the intercostal nerves that arise from thoracic spinal nerves (T1 to T12). They are more active during the inspiratory phase of forceful breathing and are thought to play a role in stabilizing excessive rib motion during forceful breathing.[38]

Three pairs of scalene muscles (scalenus anterior, scalenus medius, and scalenus posterior) arise from the lower five or six cervical vertebrae and insert on the clavicle and first two ribs (Fig. 9.24). They lift the upper chest when active. The scalene muscles are slightly active during resting inhalation and become more active with forceful inspiration, especially when ventilatory demands increase.[38] Such instances may occur in healthy subjects during exercise or in patients who have pulmonary disease. In healthy subjects, inspiratory efforts against a closed glottis or obstructed airway activate the scalene muscles. When alveolar pressure decreases to −10 cm H_2O, scalene muscles are active in all subjects. The scalene muscles are largely inactive during expiratory efforts but can become active to fixate the ribs as abdominal muscles contract during forceful exhalation such as coughing.

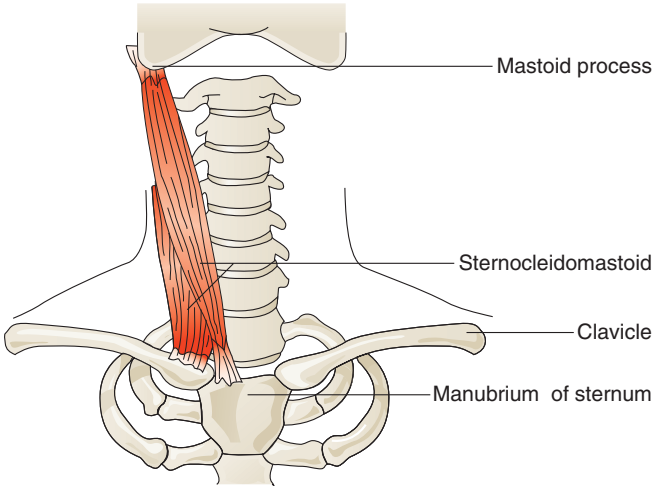


Fig. 9.25 The sternocleidomastoid muscles originate from the manubrium and clavicle and insert on the mastoid process of the temporal bone. They lift the upper thorax when the trapezius stabilizes the head. (From Hicks GH: *Cardiopulmonary anatomy and physiology*, Philadelphia, 2000, WB Saunders.)

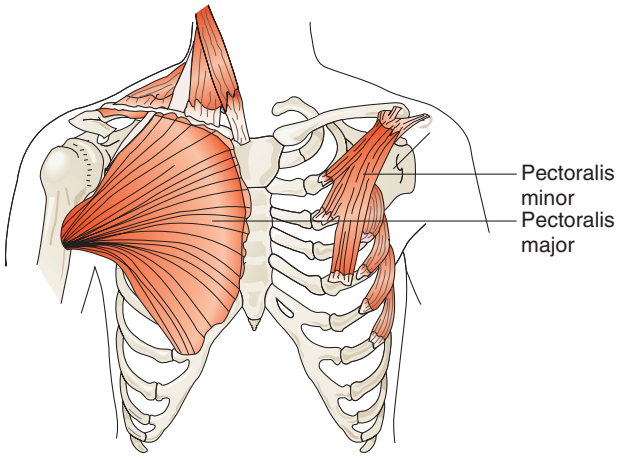


Fig. 9.26 The pectoralis major and minor can lift and enlarge the thorax when the arms are braced by leaning forward on the elbows (tripod position). (From Hicks GH: *Cardiopulmonary anatomy and physiology*, Philadelphia, 2000, WB Saunders.)

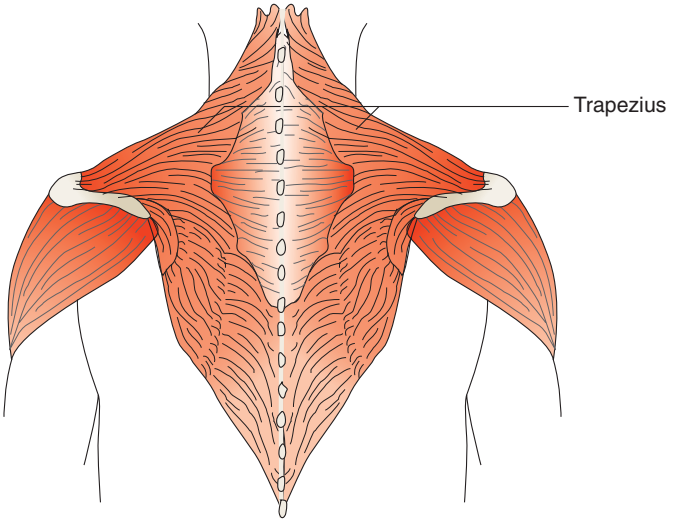


Fig. 9.27 The trapezius assists forceful inspiration primarily by stabilizing the head, which allows the sternocleidomastoid to lift the anterior thorax. (From Hicks GH: *Cardiopulmonary anatomy and physiology*, Philadelphia, 2000, WB Saunders.)

The sternocleidomastoid muscles (Fig. 9.25) originate from the manubrium and clavicle and insert on the mastoid process of the temporal bone. Normally, this muscle flexes and rotates the head and is active during shoulder shrugging. When the head is held in an upright position by tensing the trapezius muscle of the upper back and neck, the sternocleidomastoid muscles can function to lift the upper chest. These muscles are active during forceful inspiration and become visible as thick bands on either side of the neck during the inspiratory phase in an individual who is in respiratory distress. This motion increases the anteroposterior diameter of the chest.[34]

RULE OF THUMB Patients with advanced chronic obstructive pulmonary disease (COPD) often use accessory muscles to assist the flattened diaphragm, helping relieve their work of breathing. The muscle groups used include the shoulder and neck muscles. To use these muscles, the shoulder girdle must be stabilized. Patients with COPD often do this by supporting their forearms or elbows on a stationary object in front of them, forming a "tripod" position. This immobilizes the shoulders and allows the accessory muscles to raise the anterior chest wall increasing the depth of a breath.

The major and minor pectoralis muscles are broad fan-shaped muscles of the upper anterior chest (Fig. 9.26). The pectoralis major originates on the humerus and inserts onto the clavicle and sternum. The pectoralis minor originates from the anterior region of ribs 3 through 5 and inserts onto the scapula. They normally function to adduct the arms in a hugging motion. They are also capable of generating some anterior thoracic lift when the arms are braced on a surface in front of a subject (tripod position). Individuals who have chronic shortness of breath often use these muscles by sitting in the "tripod" position (see Rule of Thumb).[39]

The trapezius muscles are flat, triangular muscles located on the upper back and neck (Fig. 9.27). Their action is to rotate the scapulae, lift the shoulders, and flex the head up and back. During forceful inspiration, they become more active by helping stabilize the head and allowing the sternocleidomastoid muscles to lift the thorax.

The accessory muscles of exhalation become active during forceful breathing (see Table 9.7). Generally, these muscles compress the thoracic cavity and facilitate exhalation. The internal intercostal muscles (see Fig. 9.23) lie between the ribs and just behind the external intercostal muscles. The muscle fibers of the internal intercostal muscles run downward and less obliquely than the external intercostal muscle fibers causing these muscles to pull the ribs together, which results in compression of the thoracic cavity. They are stimulated by branches of the intercostal nerves and are most active during forceful exhalation. They also become active toward the end of deep inhalation and antagonize the lifting effect of the external intercostal muscles, which effectively stabilizes rib motion during forceful exhalation.[34,37]

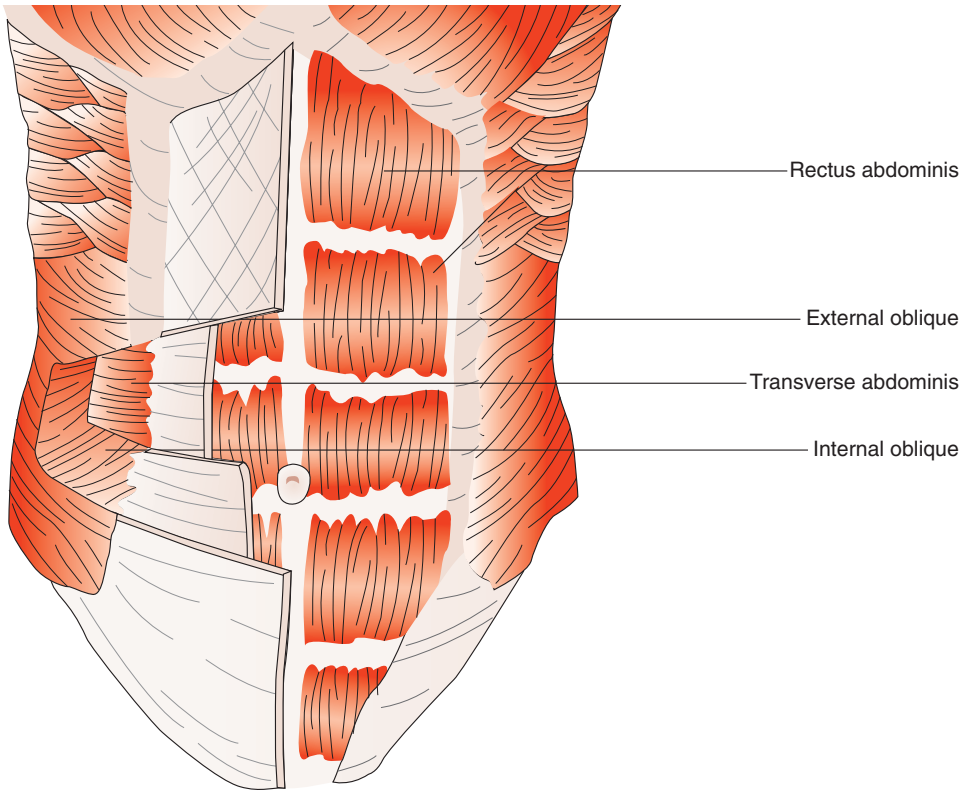


Fig. 9.28 The abdominal wall muscles compress the thoracic cavity by compressing the abdominal wall and forcing the diaphragm upward. (From Hicks GH: *Cardiopulmonary anatomy and physiology, Philadelphia,* 2000, WB Saunders.)

When the abdominal wall muscles contract, they compress the abdominal cavity. This compression forces the diaphragm upward, compressing the thoracic cavity. The abdominal muscles include pairs of external oblique, internal oblique, transverse abdominis, and rectus abdominis muscles (Fig. 9.28).[40] The external oblique muscles are the outermost layer of the abdominal wall and lie over the lateral aspects of the abdominal cavity. The internal oblique muscles lie just underneath the external oblique muscles. They originate on the lumbar vertebrae, iliac crest, and inguinal ligaments, inserting into the pubis and costal region of the lower ribs; this results in a fiber orientation that is at right angles to the external oblique muscles. The transverse abdominis muscles lie below the internal oblique muscles. Muscle fibers of the transverse abdominis run around the lateral wall of the abdomen. The rectus abdominis muscles are a pair of muscular bands that run vertically on the anterior surface of the abdomen. These muscular bands arise from the pubis, travel upward over the abdominal cavity, and insert into the costal region of ribs 5, 6, and 7 and the xiphoid process of the sternum.

Abdominal wall muscles are active during resting and forceful exhalation.[41] They become more active when the elastic recoil of the lung and thorax cannot provide the needed expiratory flow during forceful exhalation, such as coughing, sneezing, talking loudly, and playing wind-powered musical instruments. The transverse abdominis is the most active muscle of the group during resting and forceful exhalation in most body positions. The least active muscles are the rectus abdominis. The abdominal muscles also can contribute to inspiration by contracting at end-exhalation. This contraction reduces end-expiratory lung volume, so the chest wall can recoil outward, assisting the next inspiratory effort.[42]

Elevating abdominal pressure increases both the length and the radius of curvature of the diaphragm. These effects result in greater trans-diaphragmatic pressure for a given contractile tension. In patients with COPD, any increase in ventilatory demand significantly increases the use of the abdominal muscles. Loss of effective use of the abdominal wall muscles results in a marked inability to exhale forcefully and to cough effectively.

Pleural Membranes, Space, and Fluid

The thoracic cavity is subdivided into the **mediastinum** and the left and right pleural cavities. The centrally located mediastinum contains the trachea, esophagus, heart, great vessels, and other organs.[43] The left and right pleural cavities contain the lungs. As previously mentioned, the surfaces of the inner thoracic wall, mediastinum, and lungs are covered with serous membranes called the *pleural membranes* (see Fig. 9.17). The parietal pleural membrane lines the chest wall and mediastinum, whereas the lungs are covered by the visceral pleura.

The parietal and visceral membranes are constructed from a thin surface layer of mesothelial cells, and below the layer of mesothelial cells is a layer of connective tissue that houses blood vessels, lymphatic vessels, and nerve fibers.[44] Numerous microscopic openings, called *stomata,* are found in the surface of the pleura and are surrounded by mesothelial cells. The stomata open into the lymphatic drainage system of the pleural

membrane. The parietal pleura contains sensory fibers that are responsible for the painful sensation that is associated with inflammation of the pleura—a condition called ***pleurisy***.

The space between the membranes is called the ***pleural space*** and is filled with approximately 0.26 mL/kg, or about 18 mL in a 70-kg adult, of pleural fluid.[44] ***Pleural fluid*** is a clear fluid with a pH of 7.60 to 7.65 that has few cells, a small amount of protein (about 1 g/dL), and glucose and electrolytes in concentrations that approximate those of plasma. The small volume of pleural fluid is spread out over the entire surface of both lungs and functions as a lubricant to reduce friction as the lungs move within the thorax. It acts as an airtight seal that keeps together the two pleural membranes.

Pleural fluid is secreted and reabsorbed by the two pleural membranes. A little more than half of the pleural fluid is thought to be produced by the parietal pleura. Pleural fluid is formed from the systemic blood flow to each pleura. Blood pressure-driven filtration is supplied to the parietal pleura by blood flow from the intercostal arteries. The bronchial circulation of the lung supplies most of the blood flow to the visceral pleura.

It is estimated that the pleurae produce 150 to 250 mL of pleural fluid per day.[45] Most of the fluid is thought to be absorbed by the visceral pleura capillaries. From there the fluid is carried to the hilar region, where it enters the major lymphatic vessels draining back to the subclavian veins and right heart.[46]

The angle where the costal parietal pleura joins the diaphragmatic parietal pleura is known as the **costophrenic angle**. It is located in the right and left lateral and inferior regions of the thoracic cavities. This angle is clearly visible and is an important landmark in the normal chest radiograph. Normally it is a sharp angle of approximately 30 to 45 degrees. Abnormal excess of fluids between the visceral and parietal pleura tend to pool here in an upright individual. This pooling of fluid causes the angle to appear blunted or flattened to 90 degrees when viewed in the chest radiograph.

Mediastinum

The mediastinum lies between the left and right pleural cavities that contain the lungs (see Figs. 9.16 and 9.17). The mediastinum is bounded on either side by the pleural cavities, anteriorly by the sternum, posteriorly by the thoracic vertebrae, inferiorly by the diaphragm, and superiorly by the thoracic inlet. The mediastinum can be subdivided into three compartments. Between the sternum and pericardium is an anterior compartment (the anterior mediastinum) containing the thymus gland and lymph nodes. The middle compartment (the middle mediastinum) contains the pericardium, heart, great vessels, phrenic and upper portions of the vagus nerves, trachea, portions of the right and left main stem bronchi, and lymph nodes. The posterior compartment or posterior mediastinum contains the thoracic aorta, esophagus, and thoracic duct (Box 9.1). Also found in the posterior mediastinum are the sympathetic nervous system ganglionic chains and lower portions of the vagus nerve and lymph nodes.[43]

Lungs

The lungs are multi-lobed, cone-shaped, sponge-like organs that lie within the pleural cavities (Fig. 9.29). They are pink at birth and develop a gray coloration with age. Average adult lungs are hollow, low-density organs that occupy a volume of approximately 3.5 L and weigh approximately 900 g.[44] The organs within the mediastinum bulge into the left hemithorax, resulting in a narrower and slightly smaller left lung. The liver below the right lung elevates the right diaphragm and results in a slightly shorter right lung.

The lungs extend from the diaphragm 1 to 2 cm above the medial third of the clavicles on the top. The uppermost regions are called the **apexes**. At end-exhalation, the anterior lower lung borders extend to approximately the 6th rib at the midclavicular line. Laterally, the lower lung border is at the 8th rib at the

BOX 9.1 Mediastinal Contents

- Anterior mediastinum
  - Thymus gland
  - Lymph nodes
- Middle mediastinum
  - Pericardium
  - Heart
  - Great vessels
  - Phrenic nerve
  - Upper portions of the vagus nerves
  - Trachea
  - Right and left main stem bronchi
  - Lymph nodes
- Posterior mediastinum
  - Thoracic aorta
  - Esophagus
  - Thoracic duct

MINI CLINI

Penetrating Chest Injury

Normally, the parietal and visceral pleurae are in physical contact with one another and are separated by only a thin liquid film or fluid. This film provides a cohesive force that resists separation of the membranes. When the respiratory muscles move the rib cage outward in an inspiratory effort, the lungs are pulled by the cohesive forces between the parietal and visceral pleurae. The elastic recoil forces of the lungs resist this outward movement creating a negative pressure inside the pleural space (–3 to –5 cm H_2O).

Problem

A person sustains blunt force traumatic injury to the left chest. The fractured ribs are forced through the chest wall and parietal pleura, puncture the visceral pleura and lacerate the lung. What happens to the lungs and the pleural space?

Discussion

The lung on the affected side collapses as air and blood leak from the lacerated lung into the pleural space. As air and blood enter the pleural space (hemopneumothorax), the parietal and visceral pleurae separate. The chest wall expands outward, and the elastic recoil of the lung causes it to collapse inward. Both structures recoil in opposite directions as the pleural space between them separates, creating paradoxical movement. Treatment of a hemopneumothorax involves inserting a chest tube into the chest cavity and applying vacuum to remove the air and blood, re-expanding the lung and sealing the pleural space again.

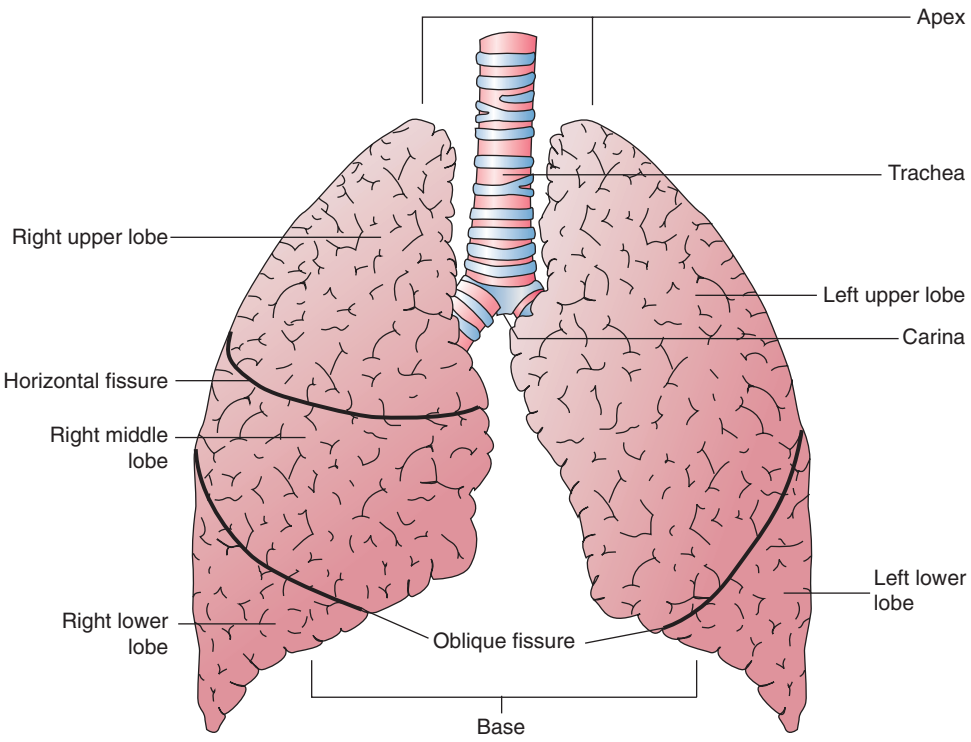


Fig. 9.29 Anterior view of the lungs showing the lobes and fissures. (From Hicks GH: *Cardiopulmonary anatomy and physiology*, Philadelphia, 2000, WB Saunders.)

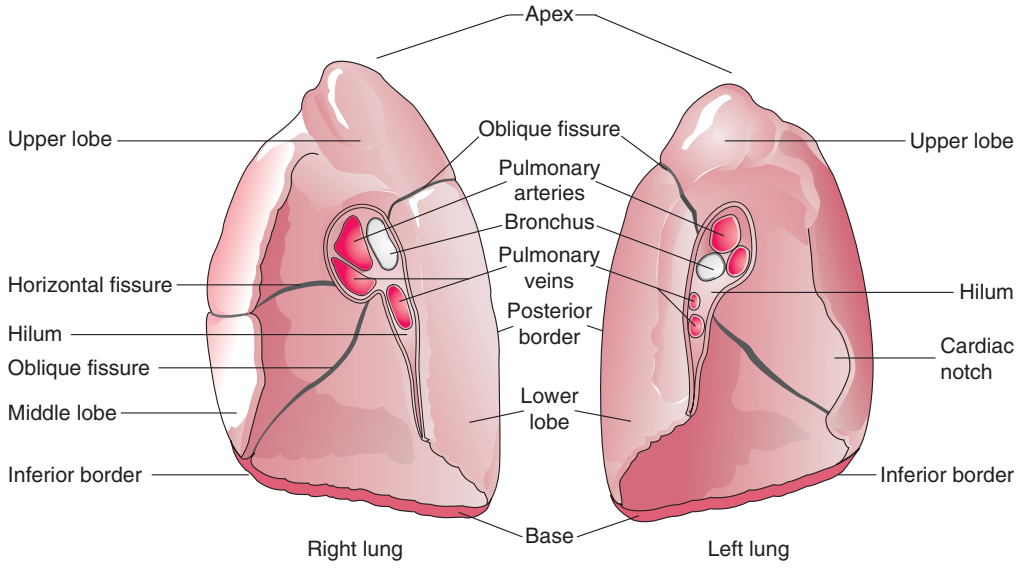


Fig. 9.30 The medial surfaces of the lungs. (From Hicks GH: *Cardiopulmonary anatomy and physiology*, Philadelphia, 2000, WB Saunders.)

midaxillary line. The top of the lungs, viewed posteriorly, extend upward from the 8th or 9th thoracic vertebra to the 1st thoracic vertebra. The diaphragm rises and falls, with resting breathing between the 9th and 12th thoracic vertebrae.

The anterior, lateral, and posterior lung surfaces lie and move against the thoracic inner wall. The medial surfaces of the lungs lie in close contact with the mediastinal surfaces. Fig. 9.30 shows the medial surfaces of the lungs and the opening in this region known as the ***hilum***. The main stem bronchi, blood vessels, lymphatics, and nerves that enter or exit the lung all pass through the hilum.

Each lung is divided into two or three lobes (see Fig. 9.29) separated by one or more **fissures**. The right lung has an upper, a middle, and a lower lobe. The left lung has only an upper and a lower lobe. Both lungs have an oblique fissure beginning on the anterior chest at approximately the 6th rib at the midclavicular line. These fissures extend laterally and upward until they cross the 5th rib on the lateral chest in the midaxillary line.

The fissures continue to the posterior chest to approximately the 3rd thoracic vertebra. The right lung also has a horizontal or "minor" fissure that separates the upper and middle lobes. Under normal conditions, this horizontal fissure extends from the 4th rib at the sternal border to the 5th rib at the midaxillary line.

The lungs are elastic organs that can expand when inflated with air and recoil back to their resting volume when exhalation occurs (see Chapter 11). Three different fiber systems form a scaffold that supports the structure of the lungs as tension develops in them with inflation.[47] The axial system, primarily composed of collagen and reticulin fibers, originates in the hilum and extends outward in all of the airway walls almost all the way to the alveolar region. The septal fiber system composed of collagen, reticulin, and elastin, supports the alveolar walls and capillaries. The peripheral fiber system, primarily composed of collagen, originates in the outer viscera and extends into the lung tissue to divide the lung tissue effectively into interlobular regions.

Collectively, these connective tissue fibers provide support to the airway walls, lungs, and the gas-exchange membrane as it is stretched during inflation. When a lung is removed from the chest cavity, the lung quickly collapses to a smaller size. The same occurs if air or fluid enter into the pleural space; it is possible that individual lobes can collapse as the result of airway obstruction and gradual diffusion of air from the lobe (absorption atelectasis).

PULMONARY VASCULAR, LYMPHATIC, AND NERVOUS SYSTEMS

The vascular supply of the lungs is composed of the pulmonary and bronchial circulations. The pulmonary circulation carries mixed venous blood from the systemic circuit to the lungs for gas exchange. The bronchial circulation provides systemic arterial blood to the airways and pleura supporting their metabolic needs. A network of lymphatics is also involved in fluid transport from the lungs. The lymphatic system removes fluid from the lung tissue and pleural space and returns it to the systemic circulation. The nervous system of the lungs acts to sense when lung function needs to be adjusted to maintain adequate oxygenation and ventilation.

Pulmonary Circulation

Pulmonary circulation is supplied with blood from the right heart (Fig. 9.31). O_2-reduced systemic venous blood flows to the right heart via the inferior and superior venae cavae. This blood is pumped to the lungs by the right ventricle through the pulmonic semilunar valve and into the trunk of the pulmonary artery. The trunk of the pulmonary artery passes upward and divides into right and left pulmonary arteries just below the point of tracheal bifurcation (the carina) into left and right main stem bronchi. The pulmonary arteries accompany the right and left main stem bronchi through the hilar opening into the lungs and continue dividing along with the airways. These divide to form two types of arteries: conventional, which continue to follow the airway branching, and supernumerary, which branch at 90-degree angles from the conventional arteries and travel outside the common path. Both sets of arteries form arterioles, connecting to and supplying blood to the microcirculation of the respiratory zone of the lung.

The pulmonary arterial system continues to divide into increasing numbers all the way to the distal airspaces. They subdivide, forming dense "sheet-like" beds of alveolar capillaries located within the walls of the alveoli, just below approximately 90% of the alveolar surface (Fig. 9.32). The wall of the pulmonary capillary is formed by endothelial cells. At rest, the pulmonary capillary bed contains 60 to 80 mL of blood and can expand to 200 mL through dilation and recruitment of collapsed capillaries during conditions of higher cardiac output (e.g., exercise).[48] Pulmonary blood is collected from the capillaries by the pulmonary venules, combining into larger veins. Similar to their arterial counterparts, the veins also form conventional and supernumerary types of

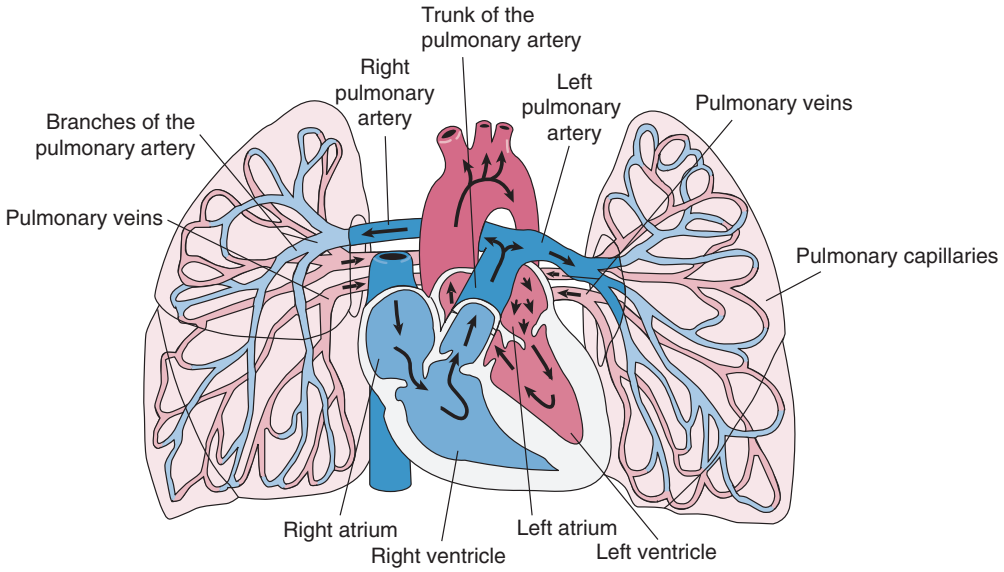


Fig. 9.31 The pulmonary circulation. (From Hicks GH: *Cardiopulmonary anatomy and physiology*, Philadelphia, 2000, WB Saunders.)

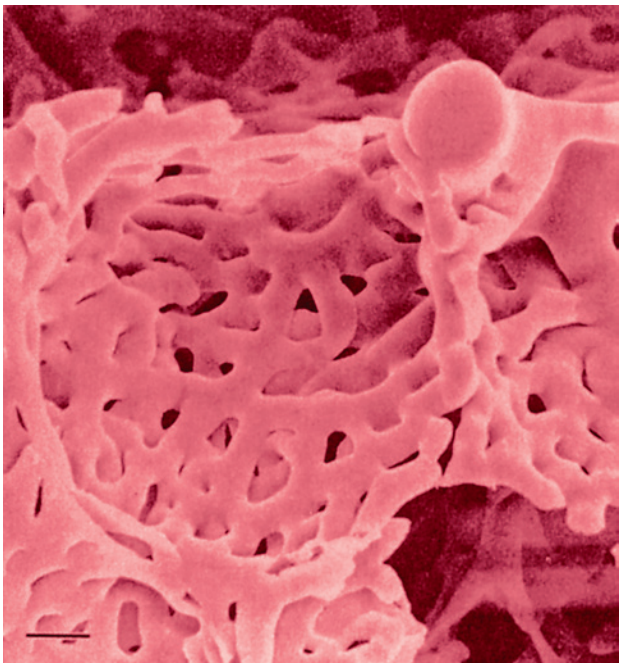


Fig. 9.32 Scanning electron photomicrograph at a high magnification of plastic cast of alveolar capillaries of the pulmonary circulation (black bar, 10 µm). (From Thibodeau GA, Patton KT: *Anatomy and physiology*, ed 7, St Louis, 2010, Mosby.)

veins that drain blood from the pulmonary capillary beds. The pulmonary veins possess less smooth muscle in their medial walls and have thinner walls than similar-sized pulmonary arteries. The veins follow the same connective tissue path that houses the bronchi and arteries, merging into larger and fewer vessels. Four major pulmonary veins (superior and inferior veins from each lung) exit through the hila and return arterialized blood to the left atrium of the heart for delivery to the systemic circulation (Fig. 9.33).

RULE OF THUMB The pulmonary artery and its branches are the only arteries in the body to carry deoxygenated blood. The pulmonary veins are the only veins that carry oxygenated blood back to the left side of the heart.

Respiratory Function of Pulmonary Circulation

The pulmonary circulation has several different functions.[48] The primary function of the pulmonary circulation is to deliver blood to the alveolar-capillary bed for the exchange of O_2 and CO_2 with alveolar gas, delivering it to the left heart. The second function is to serve as a barrier between the interstitial spaces and airspaces of the lung on one side and the blood within the capillaries on the other. Less than 0.3 µm thick, the endothelial capillary membrane is an active barrier that controls the exchange of fluid and solutes crossing it. In doing so, it plays a crucial role in the regulation of the fluid balance within the lungs. Injury to the pulmonary capillary often disrupts the fluid balance, resulting

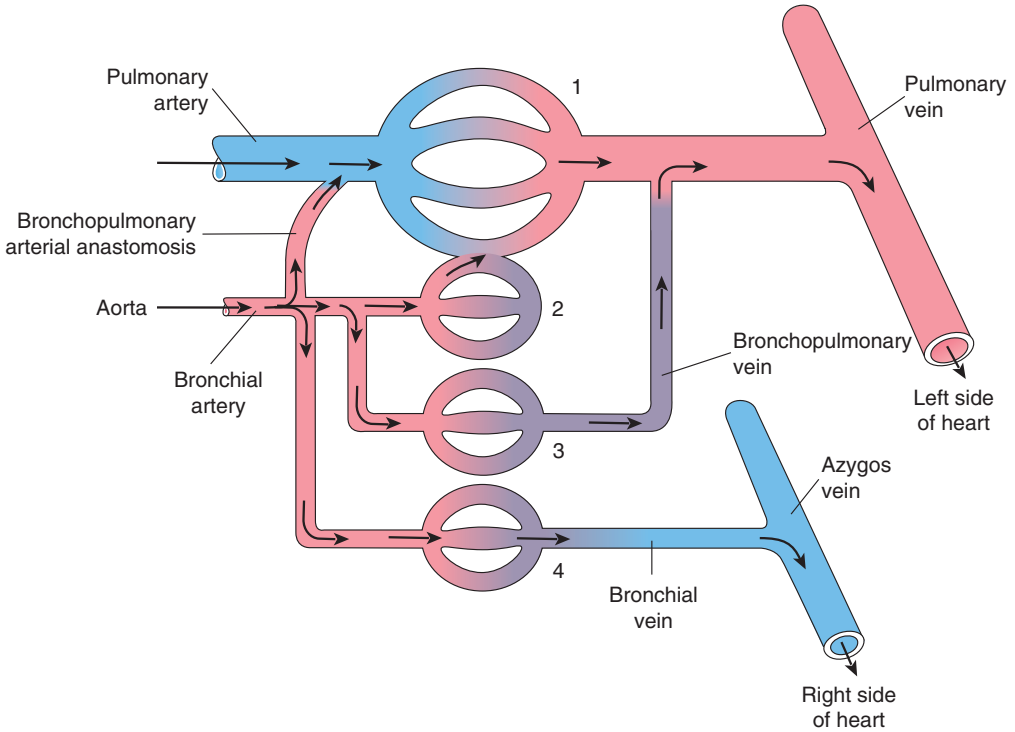


Fig. 9.33 Schematic Depiction of the Interconnection of Pulmonary and Bronchial Circulations. Bronchial blood flows to the pulmonary artery *(1),* through the capillary bed of the large airways and pleura and into pulmonary capillaries *(2),* through the bronchopulmonary veins and into the pulmonary veins *(3),* and through the bronchial vein and on to the azygos vein *(4).* The route through the bronchopulmonary vein allows less oxygenated blood to mix with the better-oxygenated blood, which returns to the left side of the heart. (From Hicks GH: *Cardiopulmonary anatomy and physiology*, Philadelphia, 2000, WB Saunders.)

TABLE 9.8 Resting Hemodynamic Values in Adult Systemic and Pulmonary Vascular Systems

Parameter	Systemic Circuit	Pulmonary Circuit
Blood flow (cardiac output, L/min)	5	5
Arterial blood pressure (mm Hg)	120/80	25/10
Vascular resistance (dynes/s/cm^{-5})	1200	120

in excessive fluid leaks and the formation of pulmonary edema. The third function is non-respiratory, involving the production, processing, and clearance of various chemicals and blood clots.

Table 9.8 compares the hemodynamic parameters of the systemic and pulmonary circulatory systems.[49] Although the entire cardiac output passes through both pulmonary and systemic circuits, the pulmonary circulation offers much lower resistance and consequently has much lower blood pressure. The low vascular pressures within the pulmonary circuit are essential in the maintenance of fluid balance at the alveolar-capillary interface. The pulmonary capillaries are exposed to vascular pressures of approximately 7 to 10 mm Hg. Increased pressure in the pulmonary circulation can occur with mitral valve disease or congestive (left) heart failure, disrupting fluid balance and leading to excessive fluid leakage, fluid accumulation, and alveolar congestion, which can impair gas exchange and lead to hypoxia.

The low vascular pressures of the pulmonary circulation result in regional blood flow within the lungs that is highly influenced by gravity (dependent areas), airway pressure, and gas exchange.[48] In the upright lung, blood pressure in the pulmonary arteries increases approximately 1 cm H_2O for each 1 cm traversed downward from the apex to the base.

Pulmonary blood flow distribution is highly dependent on gravitational effects. In the normal upright human lung, pulmonary blood flow decreases approximately linearly with distance up the lung, reaching very low values at the apex. Blood flow distribution in the lungs is divided into three zones according to the relative magnitudes of the pulmonary arterial, alveolar, and venous pressures (Fig. 9.34).[16]

Zone 1 is that region of the lung above the level at which pulmonary arterial pressures are lower than alveolar pressures; in other words, in this region, alveolar pressure exceeds arterial pressure and the collapsible capillaries close because the pressure inside exceeds the pressure outside. In *Zone 2* the blood flow is determined by the difference between arterial and alveolar pressures, rather than by the expected arterial-venous pressure difference. *Zone 3* is that part of the lung in which venous pressure exceeds alveolar pressure. Blood flow increases as one moves vertically down this zone due to the progressive distention from the increasing transmural pressure (intravascular pressure increasing down the zone while alveolar pressure is constant).

Areas of regional lung hypoxia, because of reduced ventilation, congestion, or airway obstruction, can result in local pulmonary arterial vasoconstriction and cause blood flow to shift from these areas toward areas of higher O_2 content and pulmonary vasodilation.[16]

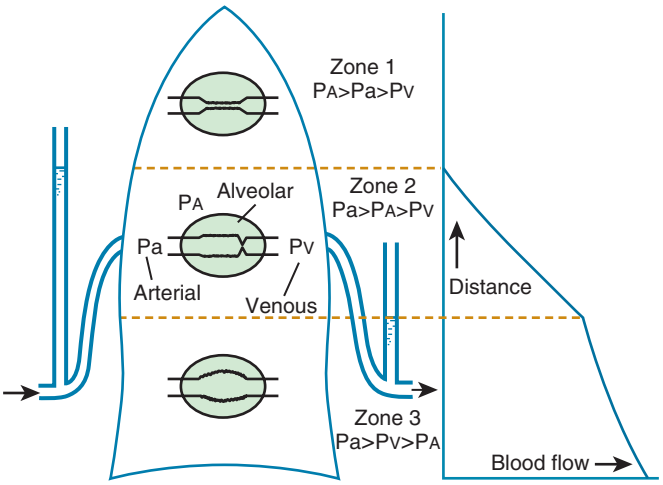


Fig. 9.34 Three-zone model designed to account for the uneven topographic distribution of blood flow in the lung. *Pa*, Pulmonary arterial pressure; *PA*, pulmonary alveolar pressure; *Pv*, pulmonary venous pressure. From Broaddus: Murray & Nadel's Textbook of Respiratory Medicine, 6th Edition, ed 6, St. Louis, 2013, Mosby.)

RULE OF THUMB As a consequence of having low blood pressure in some areas of the pulmonary circulation and being susceptible to gravity, the blood flow is much *higher* in the lung bases in resting upright subjects than in the lung apices. Gravity-related effects also occur in supine or recumbent positions but are less pronounced.

Non-respiratory Function of the Pulmonary Circulation

The pulmonary circulation also serves as a blood reservoir for the left ventricle.[16,48] This reservoir maintains stable left ventricular volumes despite small changes in cardiac output. The pulmonary blood volume (approximately 600 mL) is sufficient to maintain normal left ventricle filling for several cardiac cycles. This reservoir is important if filling of the right heart is momentarily decreased or interrupted.

The pulmonary circulation also acts as a filter for the systemic circulation. The capillaries have an inner diameter of approximately 7 to 10 μm and theoretically trap particles (e.g., blood clots) down to this size before they enter the systemic circulation, where blockages could be life-threatening.

The lungs also play an active role in the clearance, activation, and release of various biochemical factors.[48] They are responsible for the synthesis, activation, inactivation, and detoxification of many bioactive substances. Angiotensin I is converted to its active form (angiotensin II) as it circulates through the lung. Various proinflammatory cytokines are also released from the lung when it is injured or repetitively overinflated during mechanical ventilation.[50]

Bronchial Circulation

A separate arterial supply system called the *bronchial circulation* supplies blood to the airways from the trachea to the bronchioles and most of the visceral pleurae.[51] The metabolic needs of the lung are comparatively low, and much of the lung parenchyma

is oxygenated by direct contact with the inhaled gas. The bronchial circulation is a branch of the systemic circuit and is supplied with blood from the aorta via minor thoracic branches. Blood flow through the bronchial circulation constitutes approximately 1% to 2% of the total cardiac output.

A single right bronchial artery supplying the right lung arises from the upper intercostal artery, the right subclavian artery, or an internal mammary artery. Two bronchial arteries supply the left lung and branch directly from the upper thoracic aorta. Bronchial arteries follow their respective bronchi. The bronchial arterial circulation terminates in a plexus of capillaries joining the alveolar-capillary bed. Bronchial venous blood drains through the *azygos, hemiazygos,* and *intercostal* veins to the right atrium. Some drain through the pulmonary capillaries to the pulmonary veins and into the left atrium. Fig. 9.33 shows the interrelationship and comingling of the pulmonary and bronchial circulatory systems.

The bronchial and pulmonary circulations share an important compensatory relationship.[51] Decreased pulmonary arterial blood pressure tends to cause an increase in bronchial artery blood flow to the affected area. This compensation minimizes the danger of pulmonary infarction, as sometimes occurs when a blood clot (pulmonary embolus) enters the lung. Similarly, loss of bronchial circulation can be partially offset by increases in pulmonary arterial perfusion. The adult lung does not require the bronchial circulation to remain viable, as evidenced by the success of lung transplantation, which does not preserve the bronchial circulation. However, this circulation plays a more important role in lung development, helps to preserve gas exchange during various congenital cardiac conditions, and appears to compensate in certain pulmonary diseases.

Lymphatics

The lymphatic system of the lungs is an extensive system of lymphatic vessels, lymph nodes, the tonsils, and the thymus gland.[28] The primary function of the lymphatic system is to clear fluid from the interstitial and pleural spaces to help maintain the fluid balance in the lungs. The lymphatic system also plays an important role in the specific defenses of the immune system. It removes bacteria, foreign material, and cell debris via the lymph fluid and through the action of various phagocytic cells (e.g., macrophages), providing defense against foreign material and cells that can penetrate deep into the lung. It also produces various lymphocytes and plasma cells to aid in defense. Both roles are essential for maintaining the normal function of the respiratory system.

Most of the pulmonary lymphatic system consists of superficial and deep vessels—the superficial (pleural) vessels that drain the lung surface and the deep (peri-bronchovascular) conduit-like vessels that travel through the connective tissue tracts.[28] Both drain the lymphatic capillaries in the respective regions. The deeper lymph vessels are closely associated with the small airways but do not extend into the walls of the alveolar-capillary membranes. The lymphatic vessels are thin-walled vessels that contain little connective and muscle tissue in their walls.

Lymph fluid is collected by the loosely formed lymphatic capillaries and drains through the lymph vessels toward the hilum.

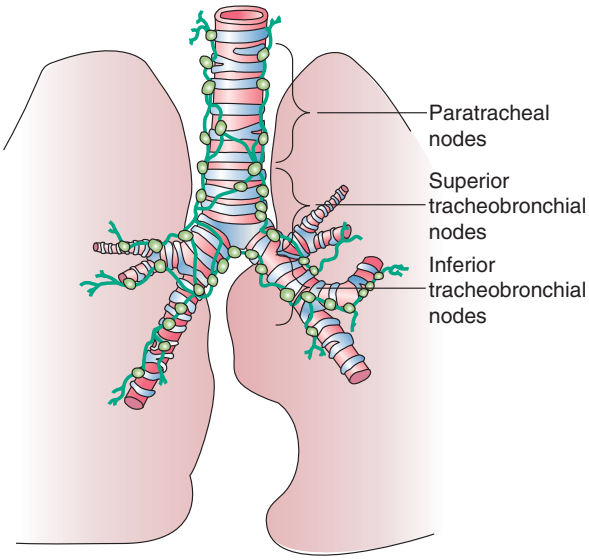


Fig. 9.35 Mediastinal and paratracheal pulmonary lymph nodes. (From Hicks GH: *Cardiopulmonary anatomy and physiology*, Philadelphia, 2000, WB Saunders.)

The fluid is propelled through the lymphatic system by the collective actions of valves that direct flow toward the hilum. The combined milking actions of smooth muscle contractions in the deeper conduit-like vessels and the cycle of ventilation act as a pump and squeeze the lymphatic vessels. Lymph fluid flow from the lungs can be increased after an injury to the pulmonary capillaries that results in increased leakage (e.g., acute ARDS) or from pulmonary capillary hypertension secondary to heart disease (e.g., left-sided heart failure).

The lymph vessels emerge from the hilum of each lung and drain lymph fluid through a series of lymph nodes clustered around each hilum and the mediastinum. From there, lymph fluid travels through various lymph nodes within the mediastinum (Fig. 9.35). The lymph fluid rejoins the general circulation after passing through the right lymphatic or thoracic duct, draining into the jugular, subclavian, or innominate veins. The lymph fluid mixes with blood and returns to the heart.

Lymphatic channels are not usually visible on chest radiographs. They may be detected if distended or thickened by disease. The "butterfly" pattern that radiates from the hilar region of both lungs during the acute development of pulmonary edema is thought to be the result of interstitial and lymph vessel distention with fluid. In this situation, the lymphatic drainage system has been overwhelmed by a sudden and excessive surge of fluid from the circulation. The development of a pleural effusion suggests that the lymphatic system is unable to remove excess fluid in the lung.

Neural Control of the Lungs

All of the major structures of the respiratory system are innervated by branches of the peripheral nervous system: the autonomic and somatic branches (Fig. 9.36).[52] Their primary functions are to (1) maintain homeostasis by regulating the depth and rate of breathing, bronchomotor tone, airway secretion, and other

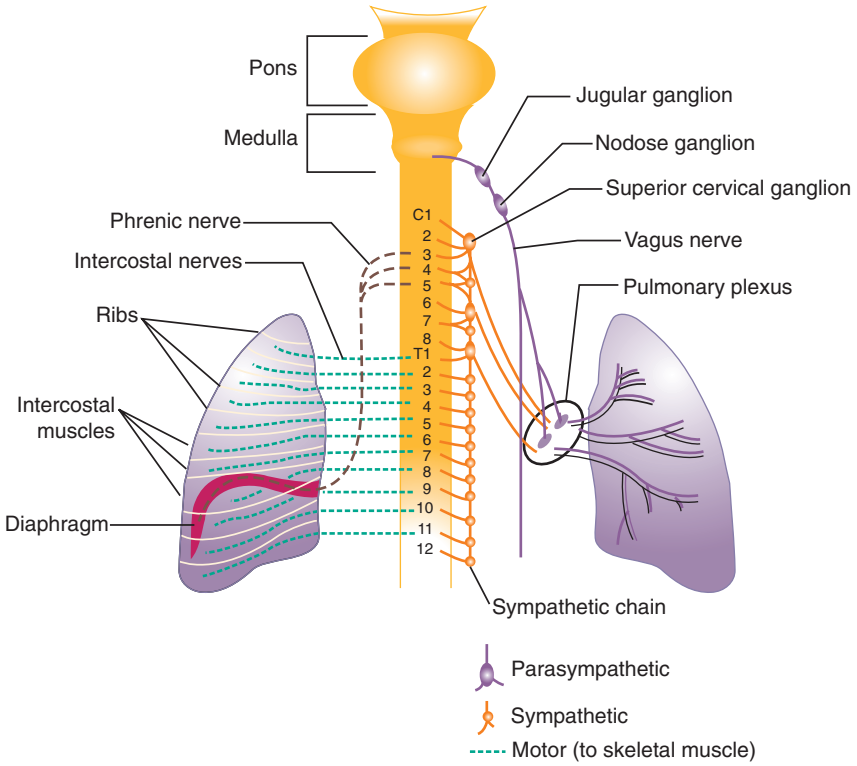


Fig. 9.36 Schematic of the autonomic innervation (motor and sensory) of the lung and the somatic (motor) nerve supply to the intercostal muscles and diaphragm. (Modified from Murray JF: *The normal lung*, ed 2, Philadelphia, 1986, WB Saunders.)

TABLE 9.9 Summary of Important Airway Reflex Responses That Contribute to the Neural Control of the Lung

Regulation of respiratory system	Breathing pattern	Inflation reflex (Hering-Breuer)	Suppresses inspiration to initiate expiration Controls the depth of breathing
		Head's reflex	Stimulates a deeper breath rather than inhibiting further inspiration It may prevent alveolar collapse by producing occasional deep breaths or gasps It also may be responsible for gasping in newborn infants as they progressively inflate their lungs
	Airway smooth muscle	Parasympathetic-bronchospasm Sympathetic-bronchodilation	
	Airway secretion	Activation of C-fibers reflexively stimulates submucosal gland secretion in the trachea	
	Cough reflex	A full-fledged cough action may come from activation of multiple types of airway sensors	
Regulation of cardiovascular system	Cardiac function	Lung inflation at low pressure causes reflex tachycardia, whereas inflation at higher pressure causes bradycardia	
	Vascular resistance	Activation of C-fibers causes significant systemic hypotension, which results from vasodilation in addition to bradycardia and decreased stroke volume	
	Bronchial circulation	Stimulation of C-fibers produces bronchial vasodilation	

cardiopulmonary functions under both healthy and disease conditions; and (2) initiate important defense reflexes that protect the lung and body from potential health-hazardous effects of air-borne particulates and chemical irritants (Table 9.9).[53,54]

The somatic system provides voluntary and automatic motor control and sensory innervation to the chest wall and respiratory muscles. Most of the major motor nerves that carry nervous signaling to the respiratory muscles are summarized in Tables 9.6 and 9.7. The autonomic nervous system signaling to and from the lungs is carried through *afferent* (summarized in Table 9.10 and Box 9.2) and *efferent* pathways. These pathways carry unconscious autonomic nervous system motor signals to and from smooth muscles, airway lumen, and glands, and various sensory signals to and from the brain.

Autonomic innervation of the lungs is carried from the brainstem through branches of the right and left vagus nerves (cranial nerve X) and from the spinal cord to four or five thoracic sympathetic ganglia that lie just laterally to the spinal cord.[55] Both contribute fibers to the anterior and posterior pulmonary plexus at the root of each lung. From these plexuses, sympathetic and parasympathetic fibers enter the lung through the hilum and innervate various structures.

TABLE 9.10 Summary of Vagal Afferent Pathways That Contribute to the Neural Control of the Lung

Laryngeal afferents	Recurrent laryngeal nerves Superior laryngeal nerve (internal and external branches)	• Cold receptors • Drive receptors (contraction) • Pressure receptor	Reflex responses to prevent upper airway collapsing and preserve its patency in wakefulness and sleep
	Myelinated and unmyelinated afferents	• Sensitive to chemical and mechanical stimulation and are responsible for eliciting the protective reflex responses (e.g., apnea, cough, etc.) against inhaled irritants • Can be activated by high concentration (>8%) of CO_2 • Stimulated by solution lacking permanent anions (e.g., chloride ion) administered topically or by aerosol	
Bronchopulmonary afferents	Slowly adapting receptors (SARs) or *pulmonary stretch receptors*	• Found along the airways with the density being highest in the trachea and gradually decreasing along the airways to the lung periphery • They are mechanoreceptors and insensitive to chemical stimulation • During eupneic breathing, they discharge regularly, characterized by increased response during lung expansion and decreased response during lung deflation • They adapt very slowly to maintain lung inflation, and their stimulation can be sustained for as long as an hour	
	Rapidly adapting receptors (RARs)	• Distributed along the airways with a high density in the large airways and the carina • Classified as mechanoreceptors • Sense changes in lung volume and mechanics • Stimulated mainly by the rate of change in the amplitude of stimulation. In quiet breathing, many RARs are inactive and others discharge irregularly • Most activity occurs during the lung inflation phase • RARs respond to changes in lung volume, flow rate, airway pressure, the rate of change of airway pressure, and lung stiffness	
	Deflation-activated receptors (DARs)	• Found along the airways but their exact location (in muscle or mucosal layers) has not been defined • Possibly activated by mechanical forces in the lung	
	High-threshold Aδ receptors (HTARs)	• Found in the large airways and in lung periphery, often located near the hilum • Stimulated by hypertonic saline, hydrogen peroxide, bradykinin • Many afferent properties and reflex functions attributed to RARs may belong to HTARs	
	C-fiber afferents (also called juxtacapillary or *J receptors*)	• Stimulated by chemical stimulants delivered intravenously or by aerosol • Distributed from the trachea to the lung periphery • Represent ~80% of the vagal bronchopulmonary afferents • Activated by a variety of endogenous and exogenous agents, such as hydrogen ions, adenosine, reactive oxygen species (ROS), capsaicin, and phenyldiguanide • Also activated by changes in osmolarity and temperature	
		Pulmonary C-fibers	• Receive blood supply from pulmonary circulation and are often located in the lung periphery • Respond to a stimulant with short latency
		Bronchial C-fibers	• Perfused by systemic circulation via the bronchial artery • Often located in large airways and superficially in the lumen
Nonadrenergic, noncholinergic (NANC) system		• Travels within the vagus nerve to each lung • Releases a neurotransmitter that promotes the production of nitric oxide • Causes the relaxation of airway smooth muscle and dilation • Capable of bronchoconstriction through the local reflex release of substance P (a peptide protein) and neurokinin A	
Cough receptors	• Initiate the cough reflex • Located mainly in different regions of the respiratory tract, including larynx, tracheobronchial tree, and alveoli		

Efferent Pathways

The parasympathetic nervous preganglionic fibers exit the brainstem via the two vagus nerves. On entry into the chest, the vagus nerve branches to the larynx. This branch is called the *recurrent laryngeal nerve.* Each vagus nerve also develops a branch called the *superior laryngeal nerve.* The external branch of this nerve supplies the cricothyroid muscle. The internal branch provides sensory fibers to the larynx. The recurrent laryngeal nerves provide the primary motor innervation to the larynx. Damage to laryngeal nerves can cause unilateral or bilateral vocal cord paralysis, depending on which branches are involved. Hoarseness, loss of voice, and an ineffective cough may result.

After forming ganglia and postganglionic nerve fibers, parasympathetic and sympathetic nerve fibers enter the lung through the hilum and run parallel to the airways as they branch (Fig. 9.37). Parasympathetic fibers form their ganglia much closer to the target tissues (e.g., bronchioles, glands, and blood vessels) and have much shorter postganglionic nerve fibers. Most of the sympathetic fibers form their ganglia along the spinal cord and then form longer postganglionic fibers that penetrate the lungs and end on the airway smooth muscle and glands. Both

sympathetic and parasympathetic postganglionic efferent fibers innervate the smooth muscle and glands of the airways and the smooth muscles of the pulmonary arterioles. They influence the diameter of the airway by causing more or less tension in the smooth muscles that wrap around the airway, and they also influence glandular secretion. The smooth muscles in the medial wall of the pulmonary arterioles cause constriction when tensed and dilation when relaxed. The combined effects of the parasympathetic and sympathetic nervous activity, which generally oppose each other's action, result in a balanced control of airway tone, vessel diameter, and glandular secretion.[55]

The parasympathetic postganglionic fibers generally secrete acetylcholine as their primary neurotransmitter when they receive signals from the brainstem. Acetylcholine binds to M_3 muscarinic cholinergic receptors, causing airway smooth muscle constriction, blood vessel dilation, and glandular secretion. The sympathetic postganglionic fibers are much less developed in comparison. The sympathetic postganglionic fibers in the lung primarily secrete norepinephrine. The adrenal glands release epinephrine into the circulation when they receive sympathetic signals from the spinal cord. Epinephrine and norepinephrine bind to α-adrenergic and β-adrenergic receptors of blood vessels. This binding causes dilation and relaxation in the β-adrenergic receptors of the bronchial airway and vessel smooth muscles.

The airways are provided with a third autonomic pathway that is neither parasympathetic nor sympathetic in action. The nonadrenergic, noncholinergic (NANC) system nerve fibers travel within the vagus nerve to each lung. For additional description of this system's roles in lung innervation refer to Table 9.10.[56]

Box 9.3 lists the most common effects of the parasympathetic system stimulation that affect the lungs and other organs by using the pneumonic SLUG BAM (the first initial for all of its manifestations).

BOX 9.2 Summary of Sympathetic Afferent Pathways' Roles in the Neural Control of the Lung

- Sympathetic afferents travel with their efferent counterpart
- Their cell bodies reside in the dorsal root ganglion (DRG) and fibers travel through the white ramus communicans to the paravertebral ganglia as well as the prevertebral ganglia
- Have much more diffused sensory territory than the vagal afferent system
- Stimulation of pulmonary sympathetic afferents fibers alters breathing pattern
- They are believed to mediate the pain sensation, especially when pain arising from the pleural region is involved
- Respiratory sensations, such as dyspnea, air hunger, tightness of chest, airway irritation, and urge to cough, are generated by sensory signals related to breathing or arising from the respiratory structures
- These sensations involve multiple sensors located in different parts of the respiratory systems and neural pathways, and complex signal processing in specific neural structures and regions in the central nervous system (CNS)

BOX 9.3 Effects of the Parasympathetic Nervous System (SLUG BAM Pneumonic)

- **S**alivation/↑ secretions/sweating
- **L**acrimation
- **U**rination
- **G**astrointestinal upset
- **B**radycardia/bronchoconstriction/bowel movement
- **A**bdominal cramps/anorexia
- **M**iosis (pupils become constricted)

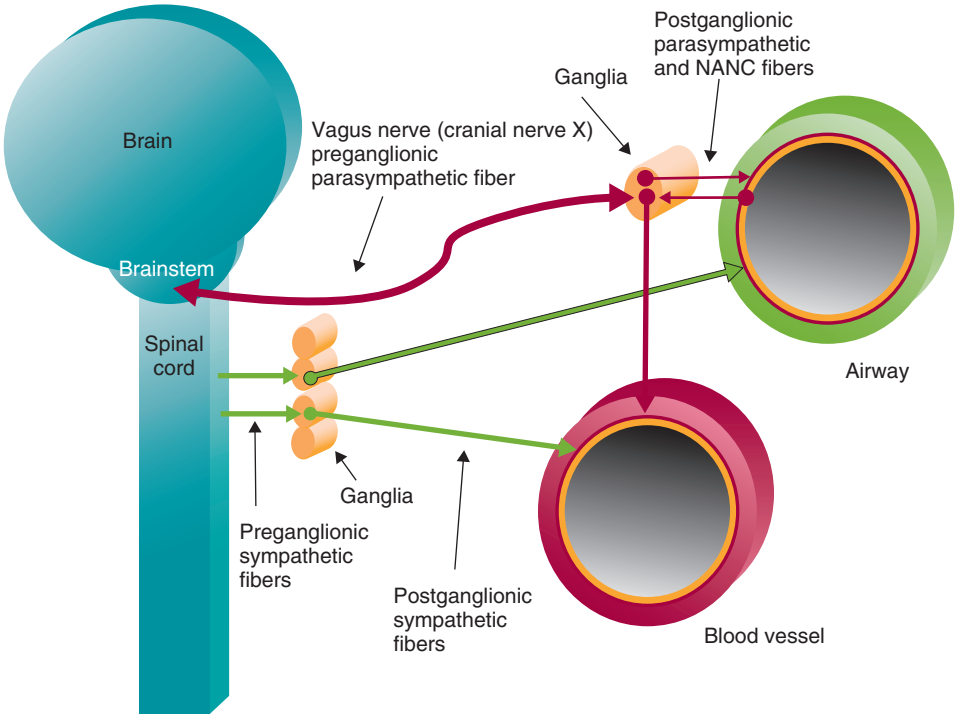


Fig. 9.37 Schematic of sympathetic, parasympathetic, and nonadrenergic, noncholinergic *(NANC)* neural fiber connections to the airways and blood vessels of the lungs.

Afferent Pathways

Most afferent fibers follow pathways from the lungs to the central nervous system in the vagus nerve. The vagus afferent pathways are activated by a variety of different receptors within the lung that are sensitive to inflation, deflation, and chemical stimulation.[57]

Slow-adapting receptors (SARs) are concentrated in the small and medium-sized airways and are closely associated with the airway smooth muscle. SARs, also known as pulmonary stretch receptors, are activated by an increase in tension in the walls of airways, thereby providing information about increases in lung volume. In the mucosal layer of the airway, rapid-adapting receptors (RARs) sense changes in tidal volume, respiratory rate, and lung compliance, responding to a wide variety of mechanical and chemical irritants. Also, a variety of other chemical and congestion sensors, when active, seem to modify the sensation of breathing and modify the breathing pattern (e.g., cough reflex and response to alveolar congestion). Additional receptors are located outside the lungs; they include respiratory muscle proprioceptors that sense the stretch state of the muscles and peripheral chemoreceptors that sense the chemical condition of blood (e.g., O_2, CO_2, and hydrogen ion concentration) that are involved in the control of ventilation (see Table 9.10).

Pulmonary stretch slow-adapting and RAR progressively discharge during lung inflation and are linked to inhibition of further inflation. This is a type of negative feedback known as the *inflation reflex*. It was originally described by Hering and Breuer and continues to bear their names (the *Hering-Breuer reflex*). The inflation reflex is thought to be actively involved with controlling the depth of breathing and may affect the duration of the expiratory pause between breaths. The inflation reflex is probably very weak or absent during quiet breathing in healthy adults, but there appears to be evidence of its activity in newborns (see Table 9.9).[53]

Irritant or mechanical rapid adapting receptors are found mainly in the posterior wall of the trachea and at bifurcations of the larger bronchi. These receptors respond to various mechanical, chemical, and physiologic stimuli, such as physical manipulation or irritation, inhalation of noxious gases, histamine-induced bronchoconstriction, asphyxia, and microembolization of the pulmonary arteries. Stimulation of the irritant RARs can result in bronchoconstriction, hyperpnea, glottic closure, cough, and sneeze.[58] Stimulation of these receptors also can cause a reflex slowing of the heart rate (bradycardia). This response is referred to as the *vasovagal reflex*. It may occur during tracheobronchial suctioning, intubation of the airway, or bronchoscopy.

Unmyelinated slow-conducting *C-fiber endings* (also known as *juxtacapillary* or *J receptors*), are present in the walls of the bronchial and terminal airway region and have been linked to a breathing reflex pattern associated with mechanical stretch, pulmonary congestion, and exposure to various chemicals.[59] When C-fibers become activated, signals are sent back to the brainstem via the vagus nerve, resulting in rapid, shallow breathing. C-fiber activation also has been shown to cause bradycardia, hypotension, bronchoconstriction, mucus production, and apnea in experimental animals.[60] Stimulation of these receptors may contribute to the sensation of dyspnea and, in severe cases, the vasovagal reflex, which can accompany pulmonary edema, pulmonary embolism, and pneumonia (see Table 9.10).

ANATOMY OF THE RESPIRATORY TRACT

Upper Respiratory Tract

The *upper respiratory tract* is defined as the airways that start at the nose and mouth and extend down to the trachea (Fig. 9.38).[55] The upper airway is open to the outside environment through the **external nares**, or nostrils, and the mouth opening of the oral cavity. Most of the air moved through the respiratory tract during resting breathing enters through the nares and nasal cavity. Mouth breathing is used during exercise to reduce the resistance to gas flow at higher ventilation rates. The functions of the upper airway are summarized in Box 9.4.

Nasal Cavity and Sinuses

There are two flared openings called **alae** that form the external nares. The alae enclose a space on each side called the *vestibule.* The vestibules have hairs that act as a gross filter. Located posterior to the vestibules are the openings to the internal nose or the **anterior nares**. The left and right nasal cavities are formed by cartilage and numerous skull bones. The roof is formed by the nasal, frontal, sphenoid, and ethmoid bones. The septum separating the two cavities is formed by cartilage and the ethmoid and vomer bones (Fig. 9.39). The lateral walls are created by the maxilla, lacrimal, and palatine bones. The floor of the cavity, or **palate**, is primarily formed by the maxilla. Three shelf-like bones protrude into the cavity from the lateral walls. These bony shelves are called the superior, middle, and inferior *conchae,* or **turbinates**.

The role of the conchae is to increase the surface area and complexity of the nasal cavity, enabling the nasal cavity to work as a passageway, filter, humidifier, and heater of the inhaled gas. The posterior openings of the nasal cavity are called the *internal or posterior nares* and are formed in part by the flexible soft palate.

The surface of the nasal cavity is covered with epithelia. The anterior portion is covered with *stratified squamous* cells and possesses hair follicles and hair. This is the same type of tissue that forms the epidermis of the skin. The middle portion of the cavity is covered with a mucous membrane composed of *ciliated pseudostratified* epithelia and goblet cells. The mucous membrane functions to secrete mucus, humidify the inhaled air, and trap inhaled particles. Just below the mucous membrane is an extensive network of veins forming a venous plexus. Inflammation of this mucous membrane is caused by irritation or infection and leads to vasodilation and increased vessel leakage. The consequence

BOX 9.4 Functions of the Upper Airway

- Passageway for gas flow
- Filter
- Heater
- Humidification
- Sense of smell and taste
- Phonation
- Protection of the lower airways

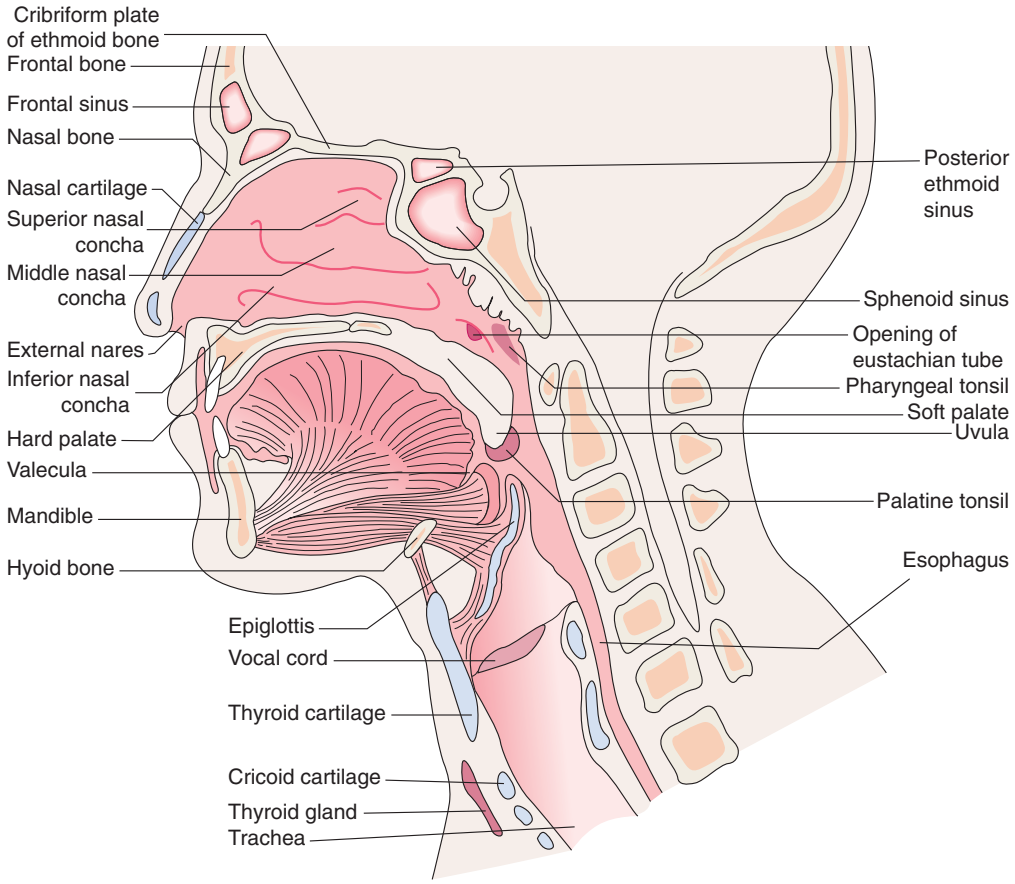


Fig. 9.38 Midsagittal section through the upper airway. (From Hicks GH: *Cardiopulmonary anatomy and physiology*, Philadelphia, 2000, WB Saunders.)

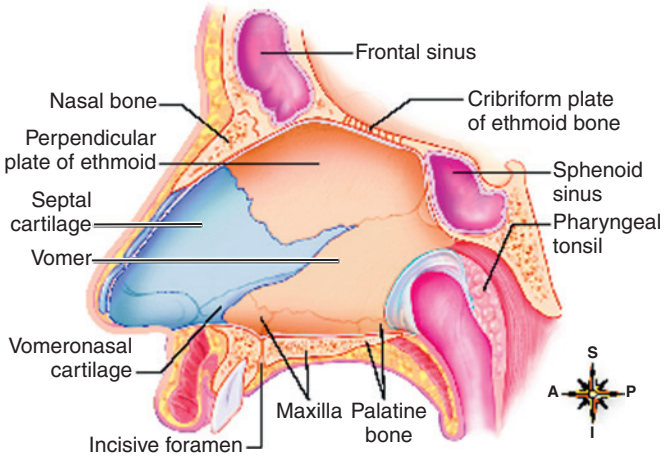


Fig. 9.39 The bony nasal septum. (From Patton KT, Thibodeau GA: *Anatomy and physiology*, ed 7, St. Louis, 2010, Mosby.)

of nasal cavity inflammation is a partial or complete blockage of the air passages. The vessels of the venous plexus can rupture as a result of breathing dry air or the passage of foreign bodies through the nose. Rupture of these vessels can cause considerable nasal bleeding (**epistaxis**). The posterior portion of the nasal cavity is covered with stratified squamous epithelium similar to the tissue covering of the nearby oral cavity.

Within the skull bones and around the nasal cavity are the *sinuses* (Fig. 9.40). These hollow spaces are named for the bones in which they are found.[61] The sinuses are lined with a mucous membrane and drain into the nasal cavity through numerous ducts. They function to reduce the weight of the skull, strengthen the skull, and modify the voice during phonation.

The nasal cavity conducts air to and from the respiratory tract, conditions inhaled gas, acts as the sinus and eye fluid drain, and contains olfactory sensors for the sensation of smell. Conditioning inhaled gas helps defend the respiratory tract and involves filtering, heating, and humidifying the air (see Chapter 39). Filtration of inhaled air is carried out by the hair in the anterior portion of the cavity and the sticky mucous membrane that covers the complex surface of the cavity. Filtration is enhanced by the flow pattern through the nasal cavity. Inhaled gas is accelerated to a high velocity through the anterior nares. It changes direction sharply as it enters the internal nasal cavity. This pattern causes particles larger than 10 μm in diameter to impact on the nasal mucosa. Ciliary action or nose blowing clear these particles. Past the external nares, the cross-sectional area increases resulting in a decrease in gas velocity. Turbulence increases because of the narrow convolutions of the passages and the turbinates. Low velocity and turbulence combine to remove any remaining particles. Filtration is based on impaction, sedimentation, and diffusion of various-sized particles.

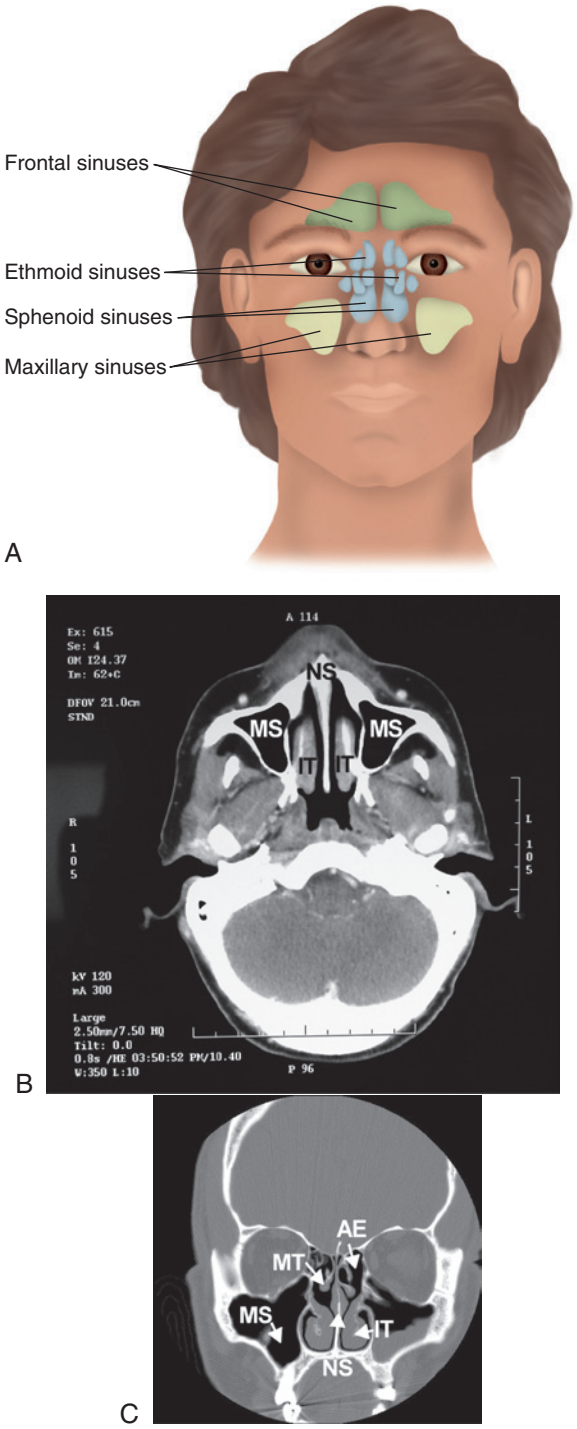


Fig. 9.40 (A) Positions of the frontal, maxillary, sphenoid, and ethmoid sinuses; the nasal sinuses are named for the bones in which they occur. (B) Axial computed tomography (CT) scan at the approximate level of the inferior turbinates *(IT)* and maxillary sinuses *(MS)*. The nasal septum *(NS)* is also well defined. (C) Coronal CT scan showing the anterior ethmoid sinuses *(AE)* and the middle turbinates *(MT)* in addition to the structures seen in (B).

Surface fluids originate from the goblet cells and submucosal glands. This fluid lining has mild antibacterial properties. Ciliary activity in the nasal mucous membranes helps transport the mucus produced so it can be cleared. Foreign matter is typically cleared from the nasal cavity by sniffing and swallowing. During exhalation, the heated and moist exhaled gas passes over the concha and is cooled. The excess moisture deposits on the concha as condensation to help retain and recycle humidity. These defense/conditioning mechanisms help ensure inspired gas is free from particulate and bacterial contamination and is heated and humidified to 37°C and 100% relative humidity by the time it reaches the trachea (see Chapter 39). In addition, the mucous membrane contains chemoreceptors that send signals to the olfactory nerve for the sensation of smell.

MINI CLINI

Exercise-Induced Asthma (EIA)

The upper airway, along with the trachea and mainstem bronchi, plays crucial roles in conditioning the air being breathed. These airways not only conduct gas from the atmosphere to the lower airways but also warm, humidify, and filter it.

Problem

Some asthmatics develop shortness of breath, wheezing, and coughing when they exercise outdoors. What could be causing their asthma attack? Is there an alternative form of exercise that could reduce the symptoms and allow them to receive an aerobic workout?

Discussion

In many cases, exercise-induced asthma (EIA) or exercise-induced bronchospasm (EIB) appears to be triggered by reflexes from the large airways (upper airway, trachea, bronchi). These airways warm and humidify inspired gas. Water vapor is absorbed from the fluid lining of the airways and replenished from the cells lining the airways. As gas is exhaled, it cools, and some of the water vapor is reabsorbed. Only a small amount of water is lost from the body via this mechanism. Exercise (with its increased ventilatory demands) causes an increase in heat and water loss from the airways. The airways in some individuals are especially sensitive (hyperresponsive) to a wide variety of triggering agents. When these individuals exercise and increase their ventilation, the loss of heat or water from the large airways can trigger an asthmatic reaction (i.e., coughing, wheezing, and shortness of breath).

Oral Cavity

Air also can enter and exit from the respiratory tract through the oral cavity (Fig. 9.41). The oral cavity is defined as the space from the lips to the end of the hard palate. The anterior roof of the oral cavity is the ***hard palate*** and is formed by the maxillary bone. The posterior portion is known as the ***soft palate***. Its soft tissue composition has the ability to move upward and seal off the nasal cavity. The end of the soft palate hangs down into the posterior portion of the oral cavity. This part of the soft palate is called the **uvula**. The walls of the oral cavity are formed by the cheeks, and the floor is dominated by the tongue.

The uvula and the surrounding walls control the flow of air, fluid, and food during eating, drinking, sneezing, coughing, and vomiting. The tongue is involved in mechanical digestion, taste, and phonation. The posterior surface of the tongue is supplied with many sensory nerve endings. These nerves produce a vagal gag reflex when stimulated, protecting the lungs from aspiration. This reflex must be considered when passing tubes or instruments through the mouth in conscious or semiconscious patients.[62]

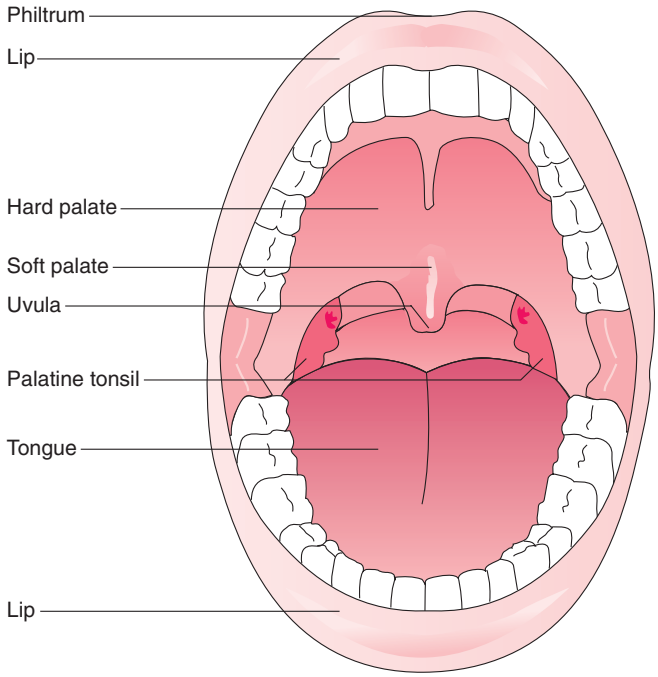


Fig. 9.41 Frontal view into the open mouth showing the major structures within. (From Hicks GH: *Cardiopulmonary anatomy and physiology*, Philadelphia, 2000, WB Saunders.)

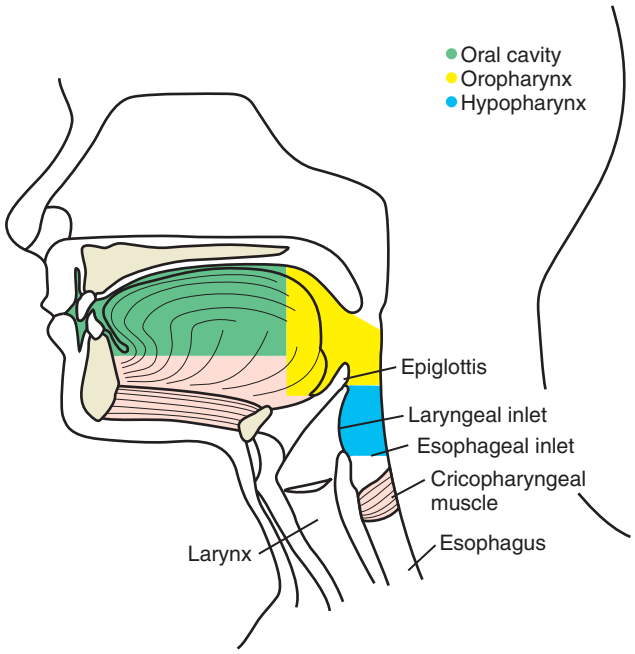


Fig. 9.42 Schematic of the oral cavity (*green*), oropharynx (*yellow*), and hypopharynx (*blue*) along with the esophageal inlet, cricopharyngeal muscle, and upper esophageal sphincter. (From Broaddus VC: *Murray & Nadel's Textbook of Respiratory Medicine*, ed 6, St. Louis, 2013, Mosby.)

The mucosal surfaces of the oral cavity also provide humidification and warming of the inspired air. These surfaces are much less efficient than the nose. Saliva is produced by major and minor salivary glands. Saliva functions primarily as a wetting and digestive agent for food but provides some humidification of inspired gas. The oral cavity ends at a double web on each side, called the ***palatine folds***. The palatine tonsils sit between these folds on each side (see Fig. 9.41). The palatine tonsils are vascularized lymphoid tissues that play an immunologic role, especially in childhood.

Reflexes of the mouth, pharynx, and larynx help protect the lower respiratory tract during swallowing.[63] These protective functions can be severely compromised during anesthesia or unconsciousness. Loss or compromise of these important reflexes can result in aspiration of bacteria-colonized saliva or food causing pulmonary infection and asphyxiation in severe cases.

Pharynx

The posterior portion of the nasal and oral cavities opens into a region called the **pharynx**. The entire pharynx is lined with stratified squamous epithelium. The pharynx is subdivided into the nasopharynx, oropharynx, and hypopharynx, or laryngopharynx. The **nasopharynx** lies at the posterior end of the nasal cavity and extends to the tip of the uvula. Numerous foreign particles impact the surface of the nasopharynx. Located in this region are two pharyngeal tonsils (also called the *adenoids*) on either side of the lateral and posterior walls of the pharynx. They monitor and interact with the particles inhaled through the actions of the lymphoid cells located there. In the same region are two openings into the left and right **eustachian tubes** that link the upper airway with the middle ear (see Fig. 9.38). The eustachian tubes drain fluid out of the middle ear and allow gas to move in or out, equalizing pressure on either side of the tympanic membrane (eardrum).

The **oropharynx** is located in the posterior region of the oral cavity that spans the space between the uvula and the upper rim of the epiglottis. This region is also equipped with a pair of palatine tonsils that are located on the lateral walls of the oropharynx. These tonsils can become chronically swollen causing partial airway obstruction. If the swelling is excessive and the individual has numerous repeat throat and ear infections, the tonsils can be surgically removed via a ***tonsillectomy***.[64]

The region below the oropharynx is known as the **hypopharynx** *or* **laryngopharynx**. It extends from the upper rim of the epiglottis to the opening between the vocal cords. The tissues of the nasopharynx and hypopharynx can move and undergo large changes of shape during speech and swallowing. Immediately below the hypopharynx the digestive and respiratory tracts separate (Fig. 9.42).

During unconsciousness, the muscles of the tongue and hypopharynx can relax and allow the tongue and other soft tissues to collapse and occlude the opening of the hypopharynx. This condition can result in partial to complete blockage of the upper airway and limit air movement to and from the respiratory tract. This condition is a primary cause of obstructive sleep apnea (OSA), discussed later in this text.

Larynx

The larynx lies below the hypopharynx and is formed by a complex arrangement of nine cartilages and numerous muscles (Fig. 9.43).[65] It protects the respiratory tract during eating and drinking and in phonation. The ***thyroid cartilage*** forms most

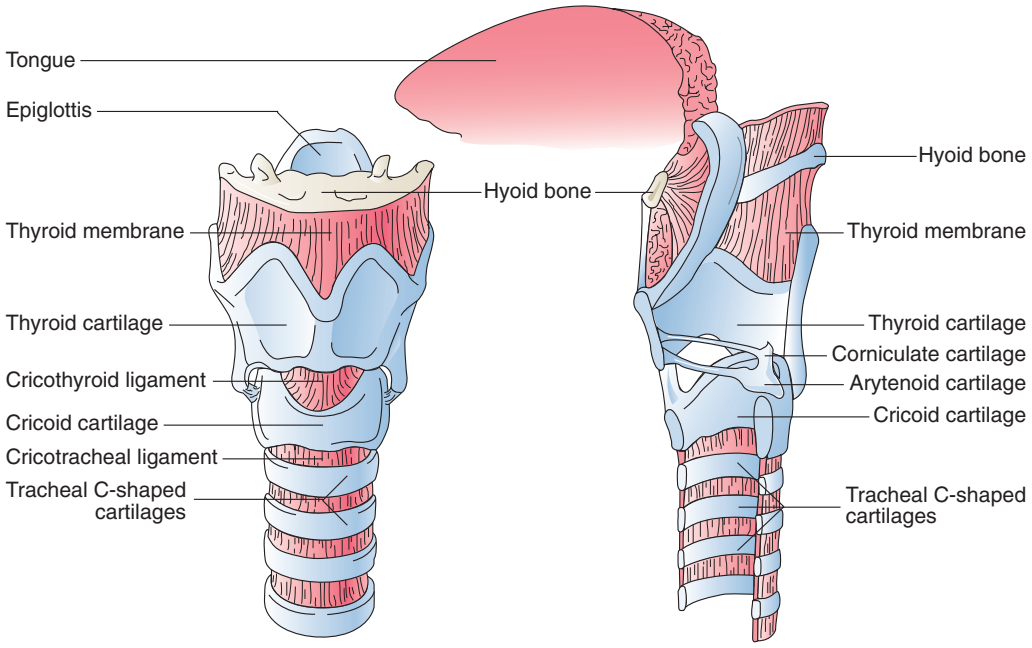


Fig. 9.43 Anterior and lateral views of the larynx. (From Hicks GH: *Cardiopulmonary anatomy and physiology*, Philadelphia, 2000, WB Saunders.)

of the upper portion of the larynx and is generally referred to as *Adam's apple*. This cartilage is named for the thyroid gland that lies over its outer surface. Just below the thyroid cartilage is the ***cricoid cartilage***. It is the only laryngeal structure that forms a complete ring of cartilage around the airway and is the narrowest region of the upper airway in infants. A membrane of connective tissue called the *cricothyroid ligament* spans the space between the thyroid and cricoid cartilage. This membrane is occasionally used as the location for placement of an emergency artificial airway in patients who have a life-threatening blockage of the upper airway (cricothyrotomy).

The cartilaginous and leaf-shaped *epiglottis* lies within and is attached to the thyroid cartilage by a flexible joint. In adults, it is 2 to 4 cm long, 2 to 3 cm wide, and 2 to 5 mm deep. It is not easily visualized in adults, but it can be seen in small children and crying infants because of its higher position. During breathing, the thyroid cartilage slides down and remains apart from the epiglottis, allowing air to move in and out of the respiratory tract. The epiglottis helps prevent liquids and food from entering the respiratory tract by forming a tight seal with the thyroid cartilage during swallowing. The act of swallowing is a complex series of muscular contractions. It results in early closure of the vocal cords, upward motion of the thyroid cartilage, and movement of the epiglottis down and back to form a tight seal as food is propelled to the back of the mouth and toward the esophagus.[66]

The inlet to the larynx lies below and behind the base of the tongue. Fig. 9.44 shows the inlet as it appears when viewed with a laryngoscope. The base of the tongue is attached to the epiglottis by three folds. These folds form a space between the tongue and the epiglottis called the **vallecula**, which is a key landmark in oral intubation (see Fig. 9.38).

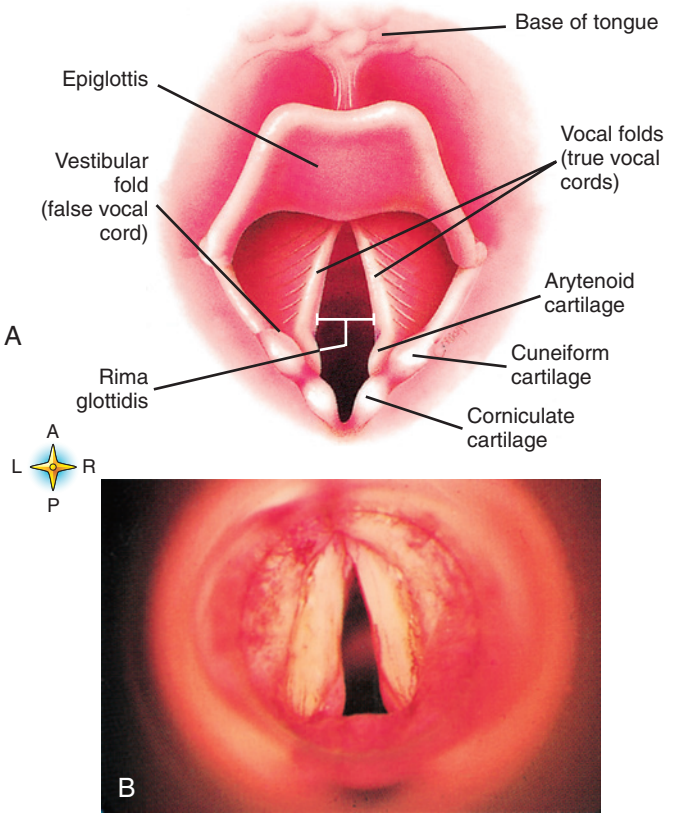


Fig. 9.44 (A) Superior view of true vocal cords, glottis (rima glottidis), epiglottis, and other structures within the larynx. (B) An endoscopic photograph showing vocal cords in the open position. (From Thibodeau GA, Patton KT: *Anatomy and physiology*, ed 7, St Louis, 2011, Mosby.)

Within the thyroid cartilage and just above the cricoid cartilage are the *arytenoid cartilages*. The vocal ligaments or true cords span the opening in the larynx by attachments to the thyroid and movable arytenoid cartilages that lie posteriorly. Above and laterally are the vestibular folds or false cords. The true vocal cords are composed of connective tissue and muscle and covered with a mucous membrane. They have poor lymphatic drainage and are susceptible to inflammation, which can result in airway obstruction. In the same region are the *corniculate* and *cuneiform cartilages* that function to support the soft tissue on either side of the vocal cords. The opening formed between the vocal cords is called the ***glottis*** (Rima glottidis). During swallowing, the vocal cords close to help protect the lower airways. Damage to the cricoarytenoid joint, which allows the *arytenoid cartilages* to rotate, can result in an inability to open the vocal cords properly and cause difficulties in speaking and breathing. Laryngeal spasm and resultant partial or total temporary airway closure are brought about by laryngeal stimulation and reflex spasm of various laryngeal muscles that cause closure of the false and true vocal cords.

The muscles of the larynx are innervated by the *inferior laryngeal nerve,* also known as the *recurrent laryngeal nerve.* It is a motor nerve that branches from the vagus nerve.[53] Impulses carried by this nerve are important in phonation and swallowing. Injuries to this nerve can cause partial or complete paralysis of the vocal cords and inability to swallow correctly. This nerve injury results in difficulty with speech and in severe cases can cause airway obstruction as a result of vocal cord closure.

Speech. The laryngeal component of speech is called *phonation*. It requires the adjustment of vocal cord tension and position relative to one another.[67] The action of the posterior cricoarytenoid muscles causes the arytenoid cartilages to rotate and opens the vocal cords. Closure of the vocal cords is accomplished by rotating the arytenoids in the opposite direction through the action of the lateral cricoarytenoid and oblique arytenoid muscles. On closure of the vocal cords, the expiratory muscles of breathing (e.g., abdominal wall muscle group) compress the thoracic cavity and can increase intrapulmonary pressures to 35 cm H_2O during forceful speech. To form sound, the cricothyroid muscles tilt the cricoid and arytenoid cartilages posteriorly with respect to the thyroid cartilage, elongating and tensing the vocal cords. Simultaneously, this action is opposed by the thyroarytenoid muscles, which pull the arytenoid cartilages anteriorly and relax vocal cord tension. The release of pressurized airflow through the tensed vocal cords causes vocal cord vibration and the production of audible sound waves, which resonate in the upper airway and sinuses. By careful adjustment of thyroarytenoid muscle tension and mandible and tongue position, fine control over sound production or speaking is achieved. Swelling of the vocal cords or the adjacent tissues increases their mass and disturbs their ability to vibrate; this can result in hoarseness and the inability to speak.

Breath hold, effort closure, and cough. Tight closure of the larynx and the buildup of intrapulmonary pressure through muscular effort are called *effort closure.* Effort closure of the larynx is necessary to generate loud sounds and for effective coughing and sneezing. It is generated by closure of the false and true vocal cords of the larynx. This action effectively "clamps" the airway closed and enables the intra-airway pressures to increase to more than 100 cm H_2O when the various expiratory muscles compress the thorax. The sudden opening of the larynx results in the immediate release of high-flow gas that is necessary for coughing and sneezing.[68] Patients who have artificial airways have difficulty producing an effective cough because the artificial airway prevents the closure of the larynx (see Chapter 44).

Patent Upper Airway

The relative positions of the oral cavity, pharynx, and larynx are crucial to the patency of the upper airway in an unconscious patient. In upright subjects, the head and neck form a 90-degree angle with the axis of the pharynx and larynx (Fig. 9.45B). With the loss of consciousness, the head flexes forward and decreases this angle (see Fig. 9.45A). This positional change can partially or completely obstruct the upper airway. Extension of the head and lower jaw into the "sniff" position alleviates this obstruction (see Fig. 9.45C). Extension of the head moves the tongue away from the rear of the pharynx. This technique is used to maintain the airway in unconscious patients and facilitates placement of artificial airways.

RULE OF THUMB When a cervical spinal injury is suspected, the airway must be opened by using the jaw-thrust maneuver. This maneuver is performed by placing the index and middle fingers behind the jaw angle to physically push the posterior aspects of the mandible upwards while the thumbs push down on the chin to open the mouth. This movement will move the tongue forward relieving the obstruction.

Lower Respiratory Tract

The airways of the tracheobronchial tree extend from the larynx down to the airways participating in the gas exchange. Each branching of an airway produces subsequent generations of smaller airways. The first 15 generations are known as *conducting airways* because they transport gas from the upper airway to the structures that participate in the gas exchange with the blood. The microscopic airways beyond the conducting airways that carry out gas exchange with blood are classified as the *respiratory airways.*

Trachea and Bronchi

The ***trachea*** extends from its connection to the cricoid cartilage down through the neck and into the thorax to the articulation point between the manubrium and body of the sternum (angle of Louis). At this point, it divides into two main stem bronchi (Fig. 9.46). The adult trachea is approximately 12 cm long and has an inner diameter of about 2 cm.[55] Fig. 9.47 shows the different layers of tissue that form the trachea. The outermost layer is a thin connective tissue sheath. Below this sheath are numerous C-shaped cartilaginous rings that provide support and maintain the trachea as an open tube. The typical adult trachea has 16 to 20 of these rings. The inner surface of the trachea is covered with a mucous membrane. In the posterior wall of the trachea is a thin band of tissue called the *trachealis muscle* that supports the open ends of the tracheal rings. The esophagus lies just behind the trachea.

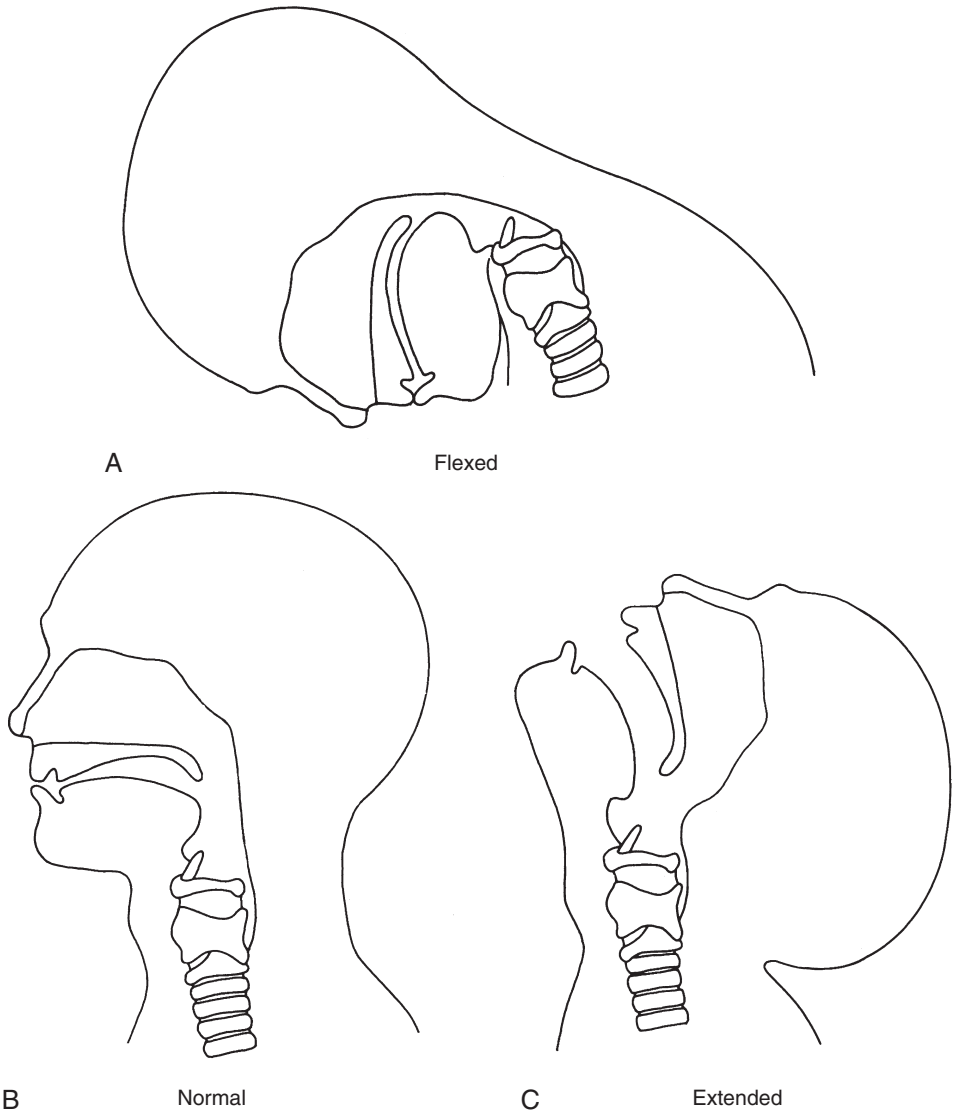


Fig. 9.45 The Position of the Head Affects the Patency of the Airway. (A) With the head flexed, the airway may be kinked, making breathing or intubation difficult. (B) The normal upright relationship of the head and neck to the chest. (C) Extension of the head straightens the airway, making breathing, clearance of material, or intubation easier.

The cartilaginous rings support the trachea so it does not collapse during exhalation. Some compression occurs when the pressure around the trachea becomes positive. During a strong cough, the trachea is capable of some compression and even collapse. The negative pressure generated around the trachea during inhalation causes it to expand and lengthen slightly.

The trachea is positioned midline in the upper mediastinum and branches into right and left main stem bronchi (see Fig. 9.46). As mentioned before, at the base of the trachea, the last cartilaginous ring that forms the bifurcation for the two bronchi is called the ***carina***. The carina is an important landmark used to identify the level where the two mainstem bronchi branch off from the trachea; this is normally at the base of the aortic arch. The right bronchus branches off from the trachea at an angle of approximately 20 to 30 degrees, and the left bronchus branches with an angle of about 45 to 55 degrees (Fig. 9.48). The lower angle branching (closer to mid-line) of the right bronchus results in a greater frequency of right-mainstem intubation and the foreign body aspiration into the right lung because of the more direct pathway.

Each bronchus carries gas to and from one lung. It enters the lung with the pulmonary vessels, lymph vessels, and nerves through the hilum. The bronchus repeatedly branches within each lung to supply gas to separate regions of each lung.

Lobar and Segmental Pulmonary Anatomy

The lungs have an apex and a base and are subdivided by fissures into lobes.[44] The lobes are divided further into bronchopulmonary segments (Table 9.11 and Fig. 9.49). Each segment is supplied with gas from a single *segmental bronchus*. Controversy exists over the exact number of segments; some anatomists accept that each lung has ten segments, whereas others maintain that the right has 10 and the left has 8. Knowledge of segmental anatomy is important in the physical examination of a patient

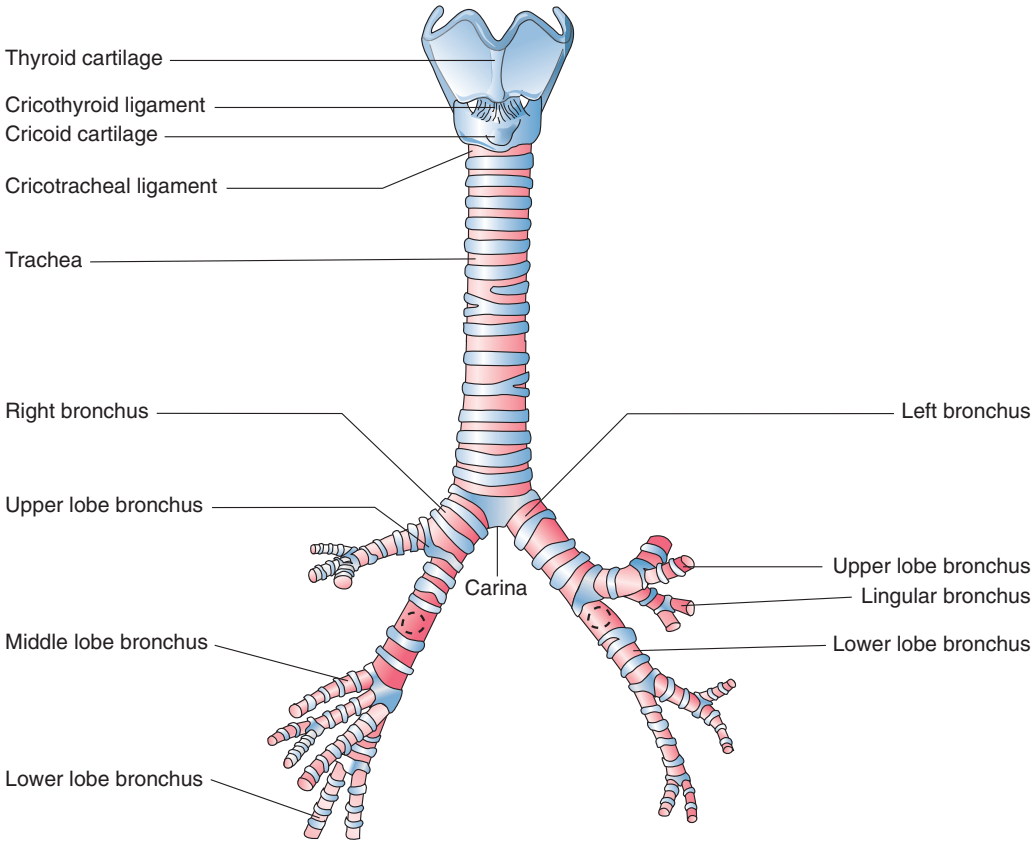


Fig. 9.46 Major airways of the tracheobronchial tree. (From Hicks GH: *Cardiopulmonary anatomy and physiology*, Philadelphia, 2000, WB Saunders.)

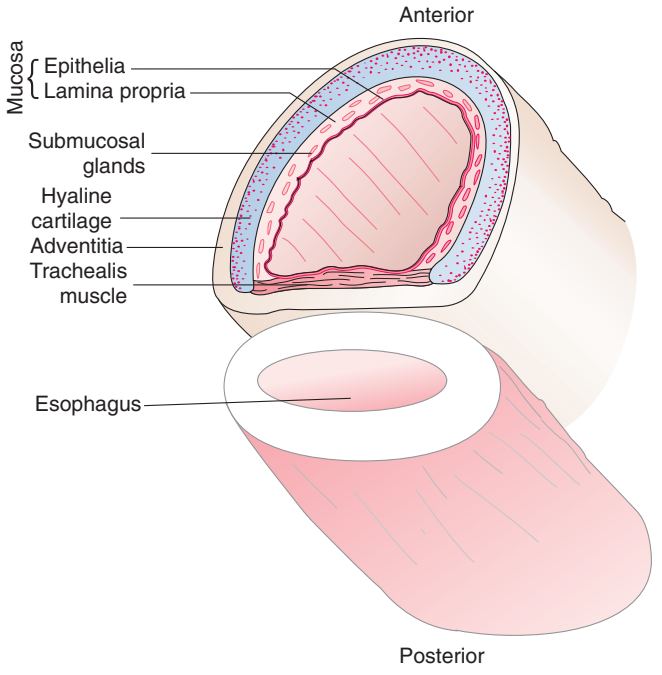


Fig. 9.47 Cross-sectional view through the trachea and esophagus. (From Hicks GH: *Cardiopulmonary anatomy and physiology*, Philadelphia, 2000, WB Saunders.)

MINI CLINI

Right Mainstem Intubation

The placement of an endotracheal tube (ET) through the upper airway and into the trachea is a common airway management technique to facilitate artificial airway placement.

Problem

After placement of an ET in a patient with a 70-kg predicted body weight (PBW), it is noted that breath sounds are heard in the right chest only, it is somewhat difficult to ventilate, and the oxygenation is deteriorating. Is the airway placement the cause of the problem? How can this problem be avoided?

Discussion

An ET of proper diameter should be placed in the trachea, so the tip is 3 to 5 cm above the carina. If the ET is advanced too far, it often enters the right mainstem bronchus because of the straighter path this bronchus offers. Right mainstem intubation results in right lung ventilation only. The left lung continues to receive pulmonary blood flow but does not ventilate and oxygenate adequately and eventually collapses. Neck movement (flexion and extension) can also displace the ET into a mainstem bronchus. To help avoid this problem, the ET tube generally should not be advanced more than 24 cm past the lips in an average 70-kg PBW patient. At this point, auscultation is done with a stethoscope to confirm bilateral breath sounds. Symmetrical chest rising should also be checked. A chest radiograph should always be taken shortly after the ET tube is inserted to confirm proper position inside the trachea.

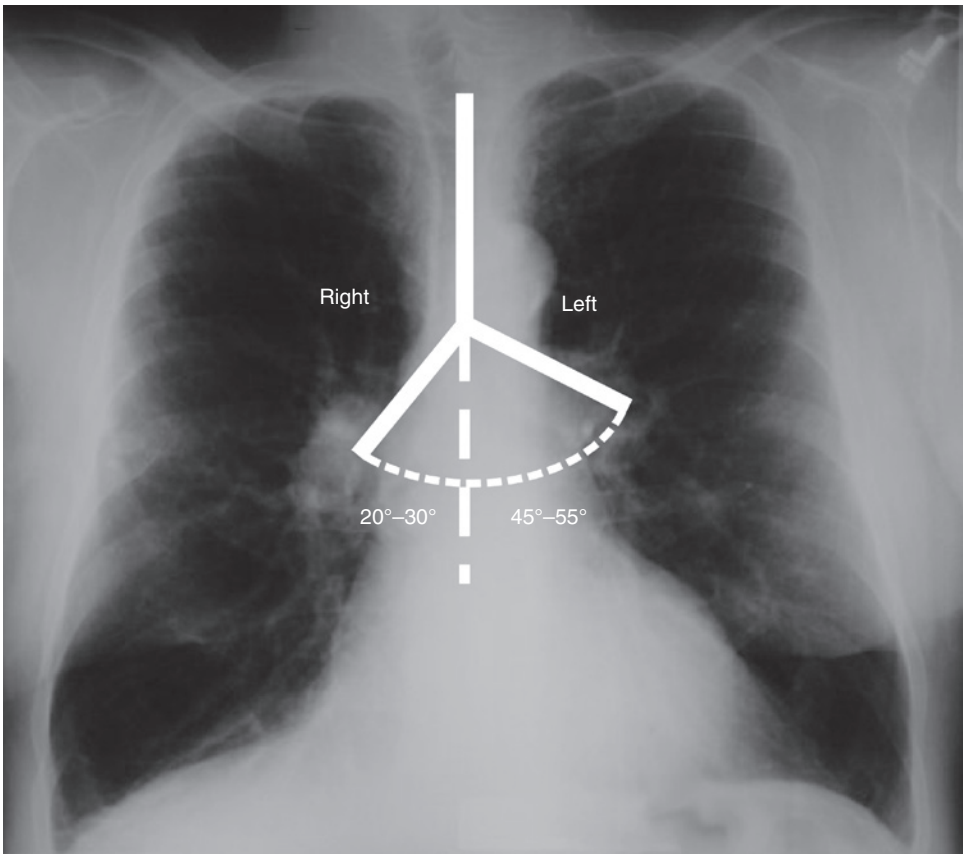


Fig. 9.48 Course of trachea and right and left main stem bronchi, superimposed on a standard chest radiograph. The right mainstem bronchus has a straighter course from midline than the left main stem bronchus.

TABLE 9.11 Bronchopulmonary Segments

Segment	Number	Segment	Number
Right Upper Lobe		**Left Upper Lobe**	
Apical	1	Upper division	
Posterior	2	Apical-posterior	1 and 2[a]
Anterior	3	Anterior	3
Right Middle Lobe		**Lower Division (Lingula)**	
Lateral	4	Superior lingula	4
Medial	5	Inferior lingula	5
Right Lower Lobe		**Left Lower Lobe**	
Superior	6	Superior	6
Medial basal	7	Anterior basal or antero-medial	7 and 8
Anterior basal	8	Lateral basal	9
Lateral basal	9	Posterior basal	10
Posterior basal	10		

The subdivisions of the lung and bronchial tree are fairly constant. Slight variations between right and left sides are noted by combined names and numbers.

[a]Some authors believe that the left lung should be numbered so that there are eight segments, where the apical-posterior is numbered 1, and the anteromedial is numbered 6.

to identify the location of a defect such as an infection site or a tumor mass in the lungs.

RULE OF THUMB: The 60-to-40 Rule The right lung is slightly larger than the left lung because of the location of the heart. The right lung has a sizable middle lobe, and the left lung has a smaller lingular segment in the left upper lobe. For purposes of estimating the contribution of the right and left lungs to ventilation and gas exchange, the 60-to-40 rule is sometimes used. The right lung is assumed to provide 60% of the ventilation/gas–exchange capacity, and the left lung is assumed to provide the remaining 40%. If a patient requires removal of the entire left lung (pneumonectomy), a 40% decrease in lung volume would be expected and vice-versa.

The airways continue to divide as they penetrate deeper into the lungs. The segmental bronchi bifurcate into approximately 40 subsegmental bronchi, and these divide into hundreds of smaller bronchi. Thousands of bronchioles branch from the smaller bronchi. Bronchioles do not possess cartilage in their walls. Tens of thousands of terminal bronchioles arise from the bronchioles. *Terminal bronchioles* are the smallest conducting airways and function to supply gas to the respiratory zone of the lung.

With further divisions, the number of airways increases tremendously. The cross-sectional area of the conducting system increases exponentially to facilitate and enhance gas exchange

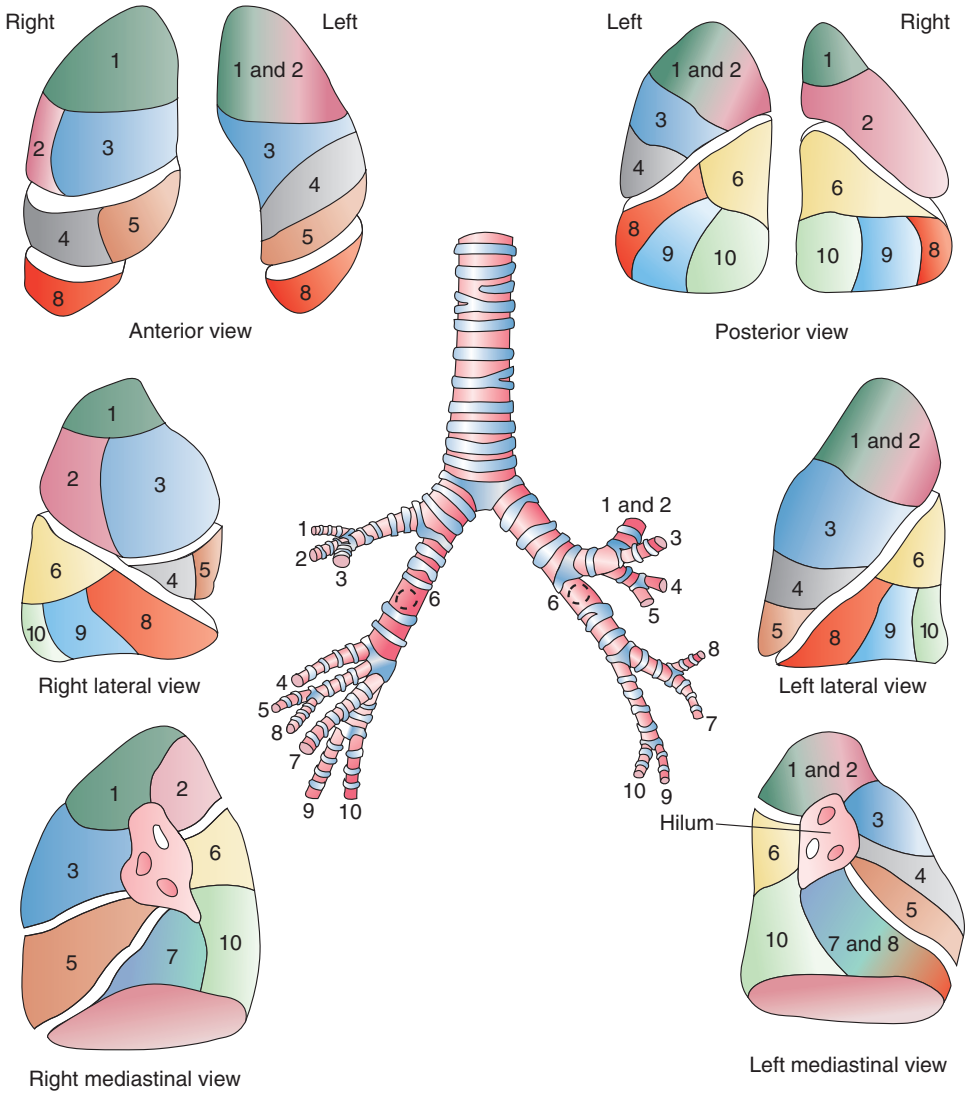


Fig. 9.49 Bronchopulmonary segmental divisions of the lungs (see Table 9.11). (From Hicks GH: *Cardiopulmonary anatomy and physiology*, Philadelphia, 2000, WB Saunders.)

as explained later. At the level of the terminal bronchioles, the cross-sectional area is approximately 20 times greater than at the level of the trachea (Fig. 9.50). Gas flow in these airways conforms to the laws of fluid physics. Increased cross-sectional area reduces the velocity of gas flow during inspiration. When inspired gas reaches the level of the terminal bronchiole, its average velocity has fallen to about the same rate as the speed of diffusing gas molecules.[69] Low-velocity gas movement at the level of the terminal bronchiole and beyond is physiologically important for two reasons. First, laminar flow develops minimizing resistance in the small airways and decreases the work associated with inspiration. Second, low gas velocity facilitates rapid mixing of alveolar gases. This mixing provides a stable partial pressure of O_2 and CO_2 in the alveolar environment that supports stable diffusion and gas exchange.[70]

Histology of the Airway Wall

All of the conducting airways, from the trachea to the bronchioles, have walls that are constructed of three layers: an inner layer, a submucosa middle layer, and outer layer. The inner layer forms a mucous membrane called the *mucosa,* which is primarily composed of epithelia. The submucosa middle layer is composed of connective tissue, bronchial glands, and smooth fibers that wrap around the airway. The outer covering of connective tissue is called the *adventitia* (Figs. 9.51 and 9.52).[71] The cartilaginous rings and plates found in larger airways are located in the adventitia.

The mucosa is composed of many different types of specialized epithelial cells that sit on top of a basement membrane. The most common type of epithelia are the numerous pseudostratified, ciliated, columnar epithelia.[71] The pseudostratified epithelial cells are held together toward their surface, or apical end through three types of junctions—tight apical junctions, zonal adherens junctions, and desmosome-type junctions—and they are anchored in place to the basement membrane.[72] The junctions, especially the tight junctions, play an important role in the maintenance of fluid and electrolyte (e.g., chloride ions) transport across the mucous membrane. These junctions prevent

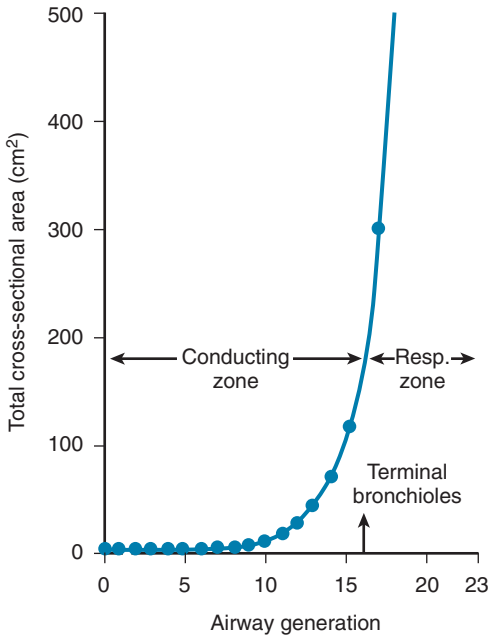


Fig. 9.50 Diagram showing the extremely rapid increase in total cross-sectional area of the airways in the respiratory zone. (From Broaddus: Murray & Nadel's Textbook of Respiratory Medicine, 6th Edition, ed 6, St. Louis, 2013, Mosby.)

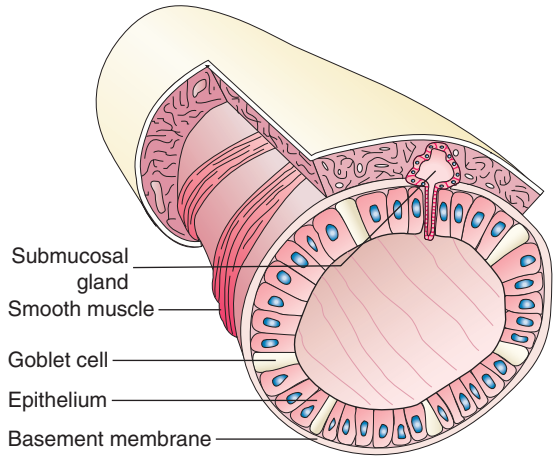


Fig. 9.51 Cross-sectional view through a bronchiole. (From Hicks GH: *Cardiopulmonary anatomy and physiology*, Philadelphia, 2000, WB Saunders.)

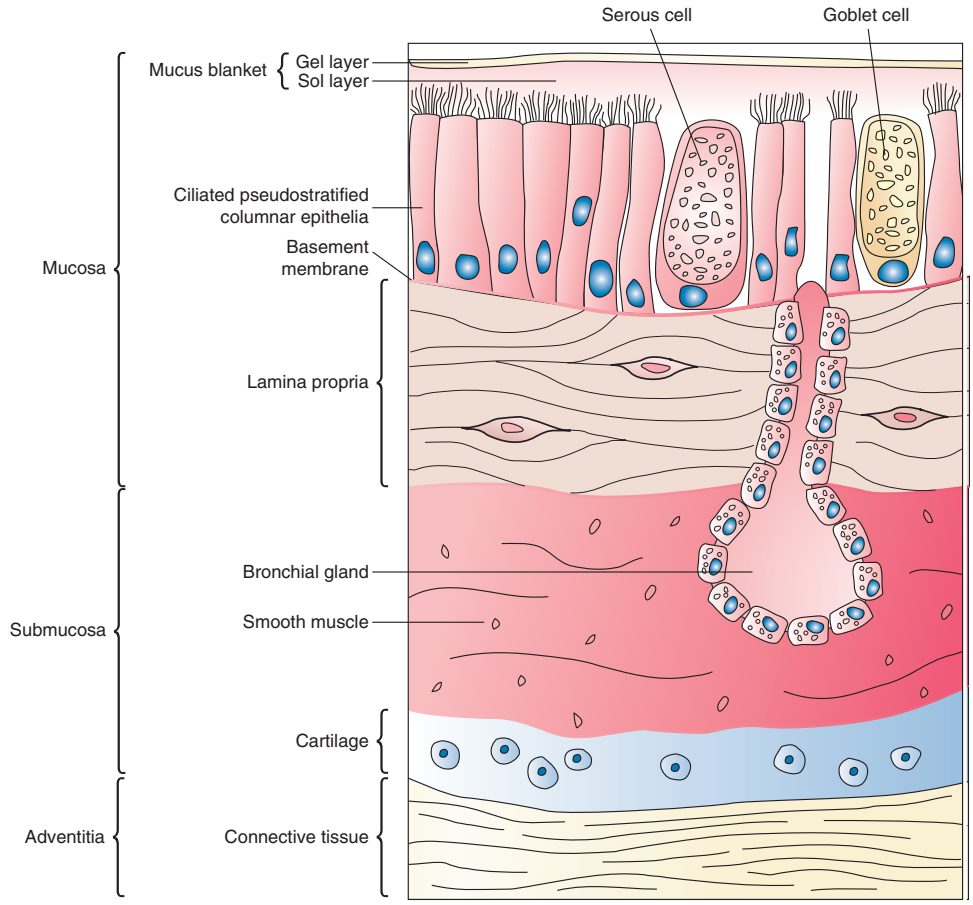


Fig. 9.52 Microscopic view of the mucous membrane. (From Hicks GH: *Cardiopulmonary anatomy and physiology*, Philadelphia, 2000, WB Saunders.)

the movement of fluids and electrolytes between the apical surface and basal surfaces of the airway. Disturbances in this transport (e.g., Cl^- transport malfunction in cystic fibrosis) lead to mucus and mucus transport abnormalities.

Near the base of the pseudostratified cells are large numbers of basal cells. The basal cells contribute to the appearance of a "pseudostratified" cellular layer. Basal cells mature into pseudostratified cells and are thought to play an important role in the repair of the mucous membrane after diseases and injury. Dispersed between the pseudostratified epithelia are mucus-producing *goblet cells* and *serous cells* (in newborns) and the openings of submucosal bronchial glands. The *bronchial glands* are exocrine glands formed by secretory epithelial cells that sit on the basement membrane, extending down into the lamina propria and the submucosa. In this region are also neuroendocrine cells (also known as *Kulchitsky cells*), which often are organized into small clusters called *neuroepithelial bodies*.[73] Neuroendocrine cells are connected to the vagus nerve and are thought to function during lung development, are hypoxia and stress-strain sensors, and secrete various bioactive chemicals (e.g., serotonin, calcitonin, and gastrin-releasing peptide). Lymphocytes are found intermixed with these cells, and it is thought they may be migratory.

Below the epithelial and basement membrane of the mucosa is the *lamina propria*.[72] It is composed of loose fibro-elastic connective tissue, lymphoid tissue, and a dense layer of elastic fibers. Below the lamina propria lies the submucosa. The submucosa of large airways contains bronchial glands, a capillary network, smooth muscle, some elastic tissue, and cartilage in larger airways. Bronchial glands vary in size up to 1 mm in length and connect to the bronchial surface via long, narrow ducts. The number of these glands increases significantly in diseases such as chronic bronchitis. Mast cells are also found in the submucosa and release numerous and potent vasoactive and bronchoactive substances such as histamine.[74] Histamine causes vasodilation and bronchoconstriction, acting directly on smooth muscle. The triggering of mast cell release of its various substances and the resultant inflammation and bronchospasm of the airway are characteristic of asthma.

The various secretory cells (primarily goblet cells) of the mucosa and bronchial glands of the submucosa contribute to the production of mucus.[75] Normally, the respiratory tract produces approximately 100 mL of mucus per day. Most of the mucus formed in the larger airways is produced by the bronchial glands. Goblet cells contribute more in the smaller airways. The amount and composition of mucus produced can increase and change with airway irritation and diseases such as chronic bronchitis and asthma.[76] Mucus is spread over the surface of the mucus membrane to a depth of approximately 7 µm and is propelled by the ciliated epithelia toward the pharynx. The outer layer of mucus is more gelatinous and is called the ***gel layer***. The inner layer is much more fluid-like and is referred to as the ***sol layer***. The mucus normally produced is a nearly clear fluid with greater viscosity than water. It is a mixture of 97% water and 3% solute.[75] The solute portion is produced primarily by goblet cells and bronchial glands; it is called *mucin* and is composed of protein and minerals. The glycoprotein, lipid, and water content of mucus provide its viscoelastic gel properties. *Viscoelastic* refers to the ability of mucus to deform and spread when force is applied.

Mucus functions to protect the underlying tissue. It helps prevent excessive amounts of water moving into and out of the epithelia.[75] It shields the epithelia from direct contact with potentially toxic materials and microorganisms. It acts like sticky flypaper to trap particles. This makes mucus an important part of the pulmonary defenses. The production of mucus is stimulated by local mechanical and chemical irritation, the release of proinflammatory mediators (e.g., cytokines), and parasympathetic (vagal) stimulation.

The ciliated pseudostratified epithelia play a crucial role in the defense of the respiratory tract by propelling mucus toward the pharynx (the mucociliary escalator). Ciliated cells are found in the nasal cavity and all the airways from the larynx to the terminal bronchioles. Each of the pseudostratified cells possesses approximately 200 **cilia** on its luminal surface.[72] Under the electron microscope, the surface of the mucous membrane looks like a "shag carpet" of cilia with approximately 1 to 2 billion cilia per cm^2. Each cilium is an extension of the cell with an average length of about 6 µm and a diameter of about 0.2 µm. A cross-sectional view through the cilium reveals it to be constructed of one inner and nine outer pairs of microtubules that are encased in the cell membrane (Fig. 9.53). The outer pairs of microtubules are interlinked by a filamentous protein called *nexin*. From each of the outer pairs of microtubules, protein filaments called *dynein* extend toward the adjacent pair of microtubules. Each of the outer pairs also extends a protein spoke toward the central pair of microtubules. The presence of magnesium ions and adenosine triphosphate within the cilium causes the dynein arms and spokes to attach and slide along the outer and inner microtubules, similar to the action of actin and myosin. This action results in rapid bending of the cilium resembling a whipping motion (Fig. 9.54).

The cilia "stroke" at a rate of approximately 15 times per second, producing a sequential motion of the cilia called a *metachronal wave*.[77] The metachronal "wavelength" is approximately 20 µm and propels surface material in a specific direction. In the nose, this motion propels material back to the pharynx. From the bronchioles up to the larynx, it moves material toward the pharynx. The stroking action of millions of cilia propels the surrounding mucus at a speed of approximately 2 cm/min. This action is commonly referred to as the **mucociliary escalator**. In healthy lungs, this mechanism allows inhaled particles to be removed within 24 hours. The control and coordination of ciliary motion are not fully understood and represent some of the many fascinating properties of the pulmonary epithelium.

The production of mucus and the rate of ciliary beating are sensitive to various conditions and chemicals. Mucus production increases when the respiratory tract is irritated by particles and by various chemicals and during increased parasympathetic nervous stimulation.[76] Ciliary beating can be effectively slowed or stopped if the viscosity of the sol layer is increased by exposure to dry gas. Ciliary motion is also slowed or stopped after exposure to smoke, high concentrations of inhaled O_2, and drugs such as atropine.

The smooth muscle of the airways varies in location and structure. In the large airways (e.g., the trachea), smooth muscle

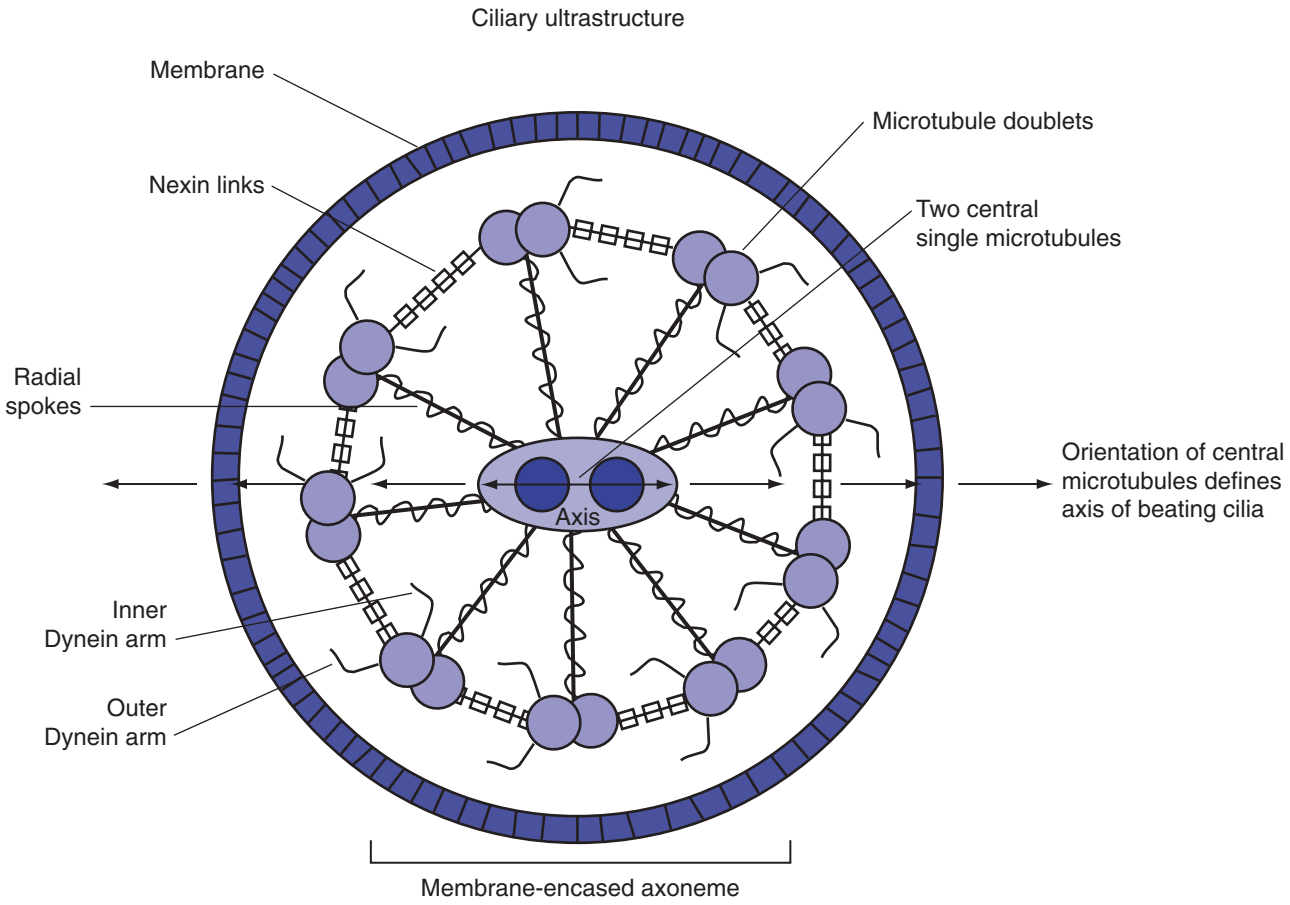


Fig. 9.53 The Structure and Function of Cilia are Elegant and Complex. Each ciliated epithelial cell possesses approximately 200 cilia. The direction of ciliary beating is determined by the orientation of the central pair of microtubules. Dysfunction of the ciliary apparatus may involve a variety of structural abnormalities in the cilia or disorganization of the ciliary axes. The cilia beat in a relatively fluidic periciliary medium; above that, adherent by a thin physicochemical junction, is a gelatinous layer of mucus (not shown). (From Broaddus VC: *Murray & Nadel's Textbook of Respiratory Medicine*, ed 6, St. Louis, 2013, Mosby.)

is bundled in sheets. In smaller airways, smooth muscle forms a helical pattern that wraps the airway in bundles in decreasing quantities as the airways branch and become smaller. Muscle fibers crisscross and spiral around the airway walls. This placement reduces the diameter of the airway and shortens it when the muscle contracts. This pattern of smooth muscle continues but thins out on reaching the smallest bronchioles. The tone of the smooth muscle is increased and results in bronchospasm by the activity of the parasympathetic nervous system (release of acetylcholine) and proinflammatory mediator release from mast and other cells.

The adventitia is a sheath of connective tissue that surrounds the airways. It is interspersed with bronchial arteries, veins, nerves, lymph vessels, and adipose tissue. Between the submucosa and adventitia of the large airways are incomplete rings or plates of hyaline cartilage, providing structural support for the larger airways. However, the small airways depend on transmural pressure gradients and the "traction" of surrounding elastic tissues to remain open. During a forced exhalation, pressures across the walls of the small airways exceed the supporting forces of the elastic tissues. As a result, the small airways can collapse. The cartilage in the larger airways prevents their collapse during such maneuvers.

The type of cell of the respiratory mucosa changes toward the smaller airways (Fig. 9.55). As the thickness of the airway walls decreases, bronchial glands become fewer in number. At the bronchiolar level, the number of ciliated cells decreases. Simple columnar and cuboidal epithelial cells begin to predominate and are interspersed with goblet cells. In this region, large numbers of ***Clara cells***, non-ciliated cuboidal cells with apical granules, are found. It is thought that these cells play a role in degrading various oxidants, contribute proteins for surfactant production, synthesize various lipids, and play a role in lung repair by being able to differentiate into other important epithelial cells in the mucosa after injury.[78]

Respiratory Zone Airways

The terminal bronchioles begin about 12 to 15 generations beyond the trachea (Fig. 9.56).[79] There are about 16,000 terminal bronchioles with airway opening diameters of approximately 700 μm. This yields a combined cross-sectional area opening that is almost 100 times that of the mainstem bronchi. All the

airways down to and including the terminal bronchioles carry or conduct gas flow to and from the airways participating in gas exchange with the blood. As described before, the airways from the nares to and including the terminal bronchioles constitute the *conducting zone airways*, which do not participate in gas exchange (Fig. 9.57). These airways constitute the **anatomic deadspace** (V_D) of the respiratory system, which is rebreathed with each breath. In an adult human, the volume filling the airways of the V_D is approximately 2.2 mL/kg (1 mL/lb) of PBW, or about 150 mL in an average adult. Unless the patient has a tracheostomy (which lowers V_D), V_D will range between 30% to 45% of the tidal volume.[80]

Branching of the terminal bronchioles gives rise to unique airways called ***respiratory bronchioles***. Respiratory bronchioles are approximately 0.4 mm in diameter and have walls formed largely from flattened squamous epithelia and a thin outer layer of connective tissue. They have some ciliated cells at the

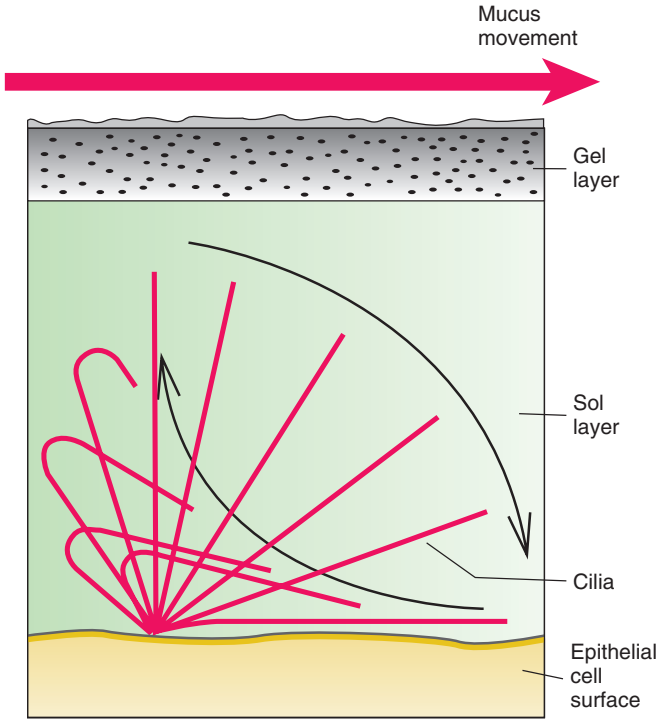


Fig. 9.54 Whipping action of the cilium within the sol layer of mucus produces a metachronal wave motion (mucociliary escalator). (From Hicks GH: Cardiopulmonary anatomy and physiology, Philadelphia, 2000, WB Saunders.)

MINI CLINI

Deadspace to Tidal Volume Ratio

The deadspace (V_D)/tidal volume (V_T) ratio is an indirect indicator of ventilation/perfusion matching. Therefore, it can be used in patients with congestive heart failure to detect the organ system limiting the exercise tolerance (lung or heart) by using it to calculate the actual deadspace.

Problem

A 5-foot tall, 105-lb patient has a deadspace to tidal volume ratio of 0.40 and a tidal volume of 500 mL. What is her deadspace volume?

Discussion

$$V_D = V_D/V_T \quad V_T$$
$$V_D = 0.40 \times 500\ \text{mL}$$
$$V_D = 200\ \text{mL}$$

In healthy subjects, the V_D/V_T ratio ranges between 0.33 and 0.45. Ventilation is efficient when the V_D/V_T falls within this range. However, since positive pressure ventilation increases deadspace, this normal range will seldom be observed in patients receiving ventilatory support. For this reason, V_D/V_T ratios in the 0.4 to 0.6 range are clinically acceptable. V_D/V_T ratios above 0.6 indicate grossly inefficient ventilation that may impair a patient's ability to maintain normal CO_2 levels.

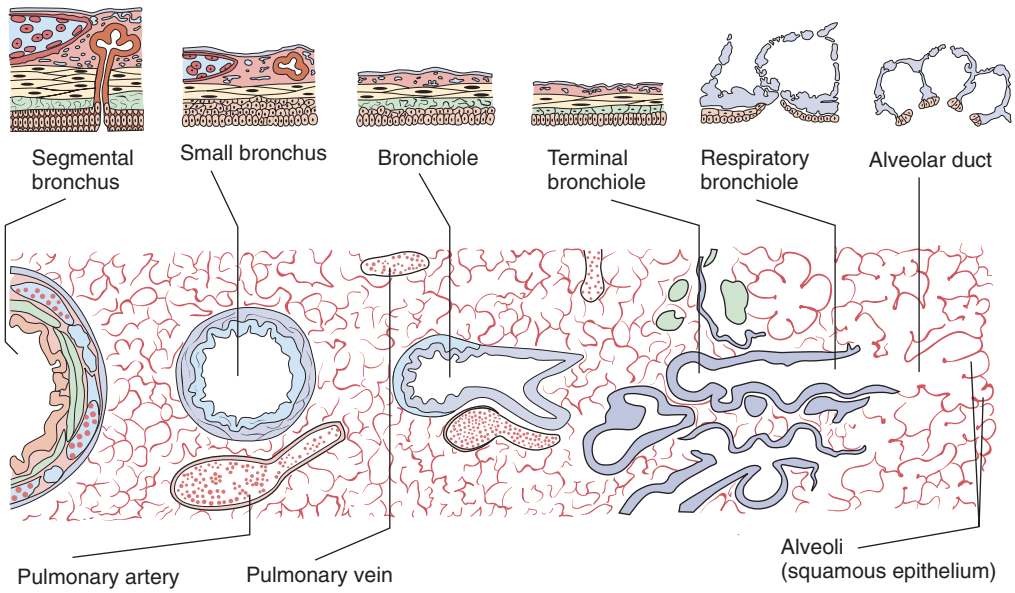


Fig. 9.55 Histologic diagram of airways from the segmental bronchus to the alveolus. (Modified from Freeman WH, Bracegridle B: *An atlas of histology*, London, 1966, Heinemann Educational.)

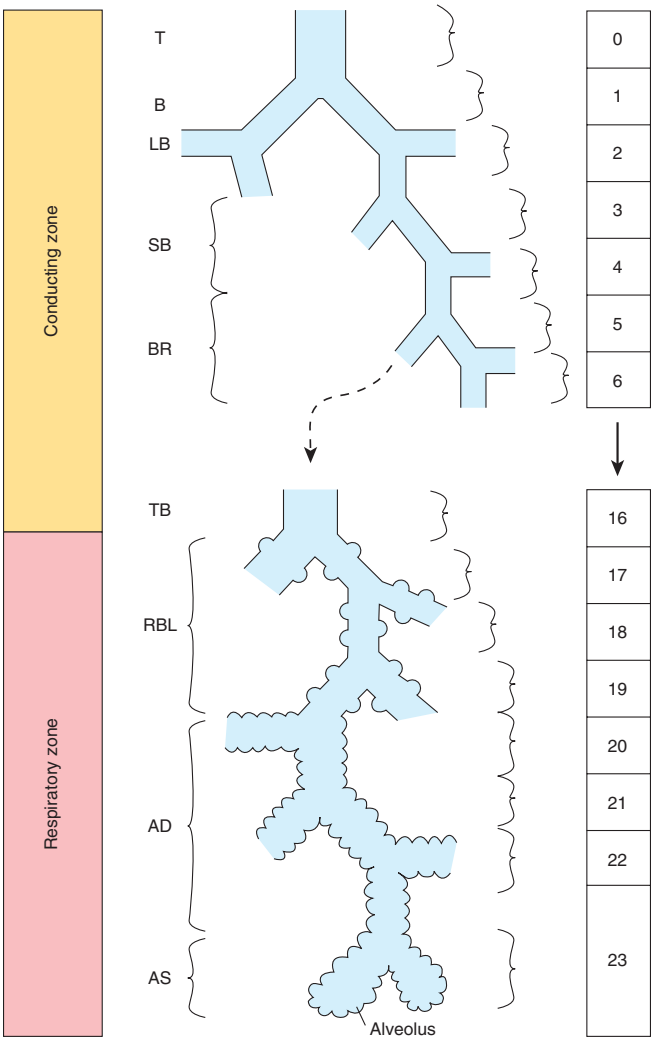


Fig. 9.56 Airways of the conducting (generation *0* through *16*) and respiratory (generation *17* through *23*) zones: *T,* trachea; *B,* right and left bronchi; *LB,* lobar bronchi; *SB,* segmental and subsegmental bronchi; *BR,* bronchioles; *TB,* terminal bronchioles; *RBL,* respiratory bronchioles; *AD,* alveolar ducts; and *AS,* alveolar sacs. (From Hicks GH: *Cardiopulmonary anatomy and physiology*, Philadelphia, 2000, WB Saunders.)

connection with the terminal bronchiole, generally lack mucus-producing cells, and have rings of smooth muscles where they branch to form alveolar ducts. Respiratory bronchioles have a dual function. Similar to conducting airways, they not only conduct gas flow but also have small outpouchings known as *alveoli* in their walls. The alveoli and their pulmonary capillary bed enable the respiratory bronchioles to carry out gas exchange. The respiratory bronchioles constitute a transitional zone type of airway.

A single terminal bronchiole supplies a cluster of respiratory bronchioles. Collectively, this unit is referred to as the *acinus,* or **primary lobule**. Each acinus comprises numerous respiratory bronchioles, alveolar ducts, and approximately 10,000 alveoli (Fig. 9.58). The adult lung is thought to contain more than 30,000 acini. Each acinus is supplied with pulmonary blood flow from a pulmonary arteriole, and blood is drained away from several acini through a pulmonary venule. In addition, each acinus is equipped with a lymphatic drainage vessel and nerve fibers. These features make the primary lobule *the functional unit of the lungs.*[72] Gas molecule movement in this region is mainly via diffusion rather than by convective flow, which occurs in larger airways.

Millions of alveolar ducts branch off the respiratory bronchioles (Fig. 9.59). Alveolar ducts are tiny airways only 0.3 mm in diameter, and their walls are composed entirely of alveoli. Each alveolar duct ends in a cluster of alveoli, which is frequently referred to as an *alveolar sac.* Each alveolar sac opens into about 16 or 17 alveoli, and about one-half the total number of alveoli are found in this region.

Alveoli

More recent estimates suggest the number of alveoli in adult lungs range from 270 to 790 million, with an average of about 480 million.[25] The number of alveoli increases with an individual's height. Fig. 9.60 shows alveoli in a normal rat lung at different states of inflation and how their shapes change. When inflated at and beyond the functional residual volume (see Fig. 9.60A to C), alveoli have a polyhedral shape resulting from numerous flat walls rather than a curved spherical structure. Alveoli found in the apical regions of the vertical lung have greater diameters than alveoli in the basal regions as a result of the gravitational effects. Alveoli in the basal regions are partially collapsed because of the weight of the organ.

The alveolar walls, or septa, are formed by various cell types that are arranged to provide a thin surface for gas exchange and strength.[81] The alveolar septa are covered with the extremely flat squamous epithelia of the ***type I pneumocytes*** (Fig. 9.61). Although they represent only approximately 8% of all the cells found in the alveolar region, type I cells cover about 93% of the alveolar surface.[82] These cells form a "patchwork"-like surface that covers the alveolar capillaries and forms the gas-exchange surface of the alveolus. At the edges where they meet one another, they form tight junctions. These tight junctions help to limit the movement of material into the alveolar airspace from the interstitial space. They are held in place and supported from below by a network of collagen and elastin fibers. They are susceptible to injury and apoptosis (programmed cell death) from inhaled particles (e.g., cigarette smoke), bacterial infection, and high concentrations of inhaled O_2.

Interspersed on the alveolar surface and concentrated in the corners of the alveolar septa are ***type II pneumocytes***, which are cuboidal epithelia with apical microvilli (Fig. 9.62). These cells are twice as numerous as the type I cells, but they occupy only 7% of the alveolar surface.[82] As indicated earlier in this chapter, Type II cells do not function as gas-exchange membranes as the type I cells do. They (along with the Clara cells) manufacture surfactant, store it in vesicles called *lamellated bodies,* and secrete it onto the alveolar surface.[83] As mentioned earlier in the chapter, surfactant reduces the surface tension of the alveolus, sheds water from the alveolar surface, helps prevent alveolar surface tension-driven collapse, improves lung compliance, reduces the work of breathing, and protects the alveolar surface. Normally, the surfactant is removed from the alveolar space continuously by type II cells and macrophages. The type II cells recycle approximately

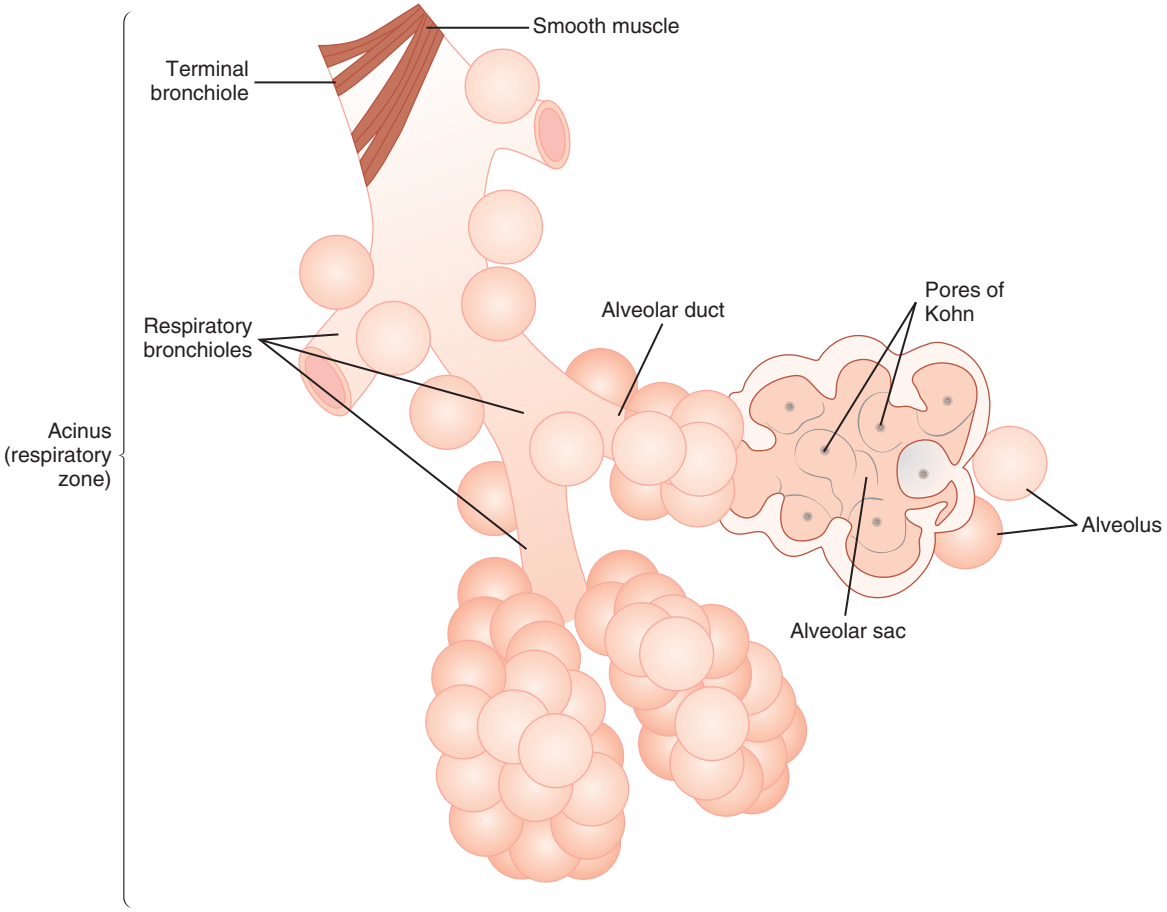


Fig. 9.57 Gas Exchange Portion of the Lungs. These subdivisions of the terminal bronchioles form the acinus. (From Beachey W: *Respiratory care anatomy and physiology foundations for clinical practice*, ed 3, St. Louis, 2013)

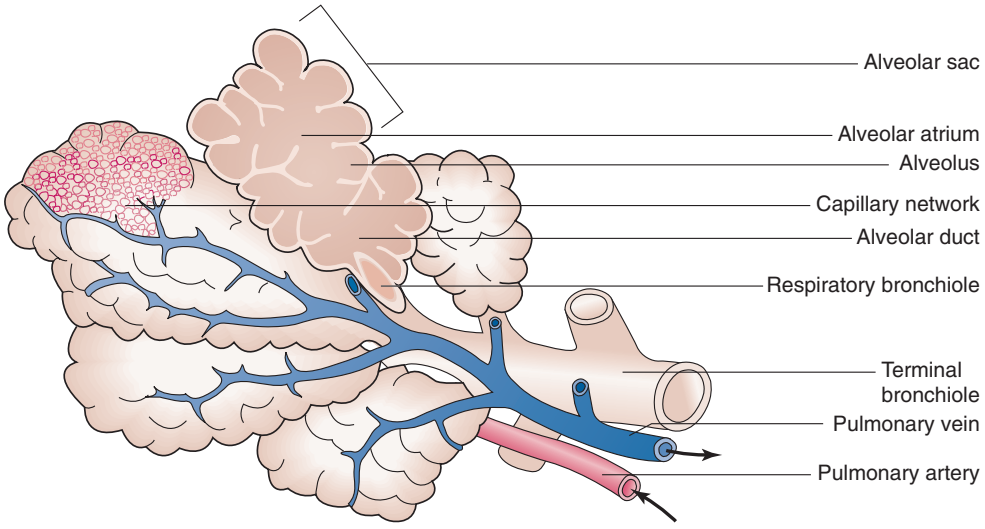


Fig. 9.58 The acinus (primary lobule) of the lung is composed of a single terminal bronchiole, numerous respiratory bronchioles, alveolar ducts, sacs of alveoli, and about 10,000 alveoli. Pulmonary blood flow is delivered to the acinus by a pulmonary arteriole and drained from it by a pulmonary venule. (From Hicks GH: *Cardiopulmonary anatomy and physiology*, Philadelphia, 2000, WB Saunders.)

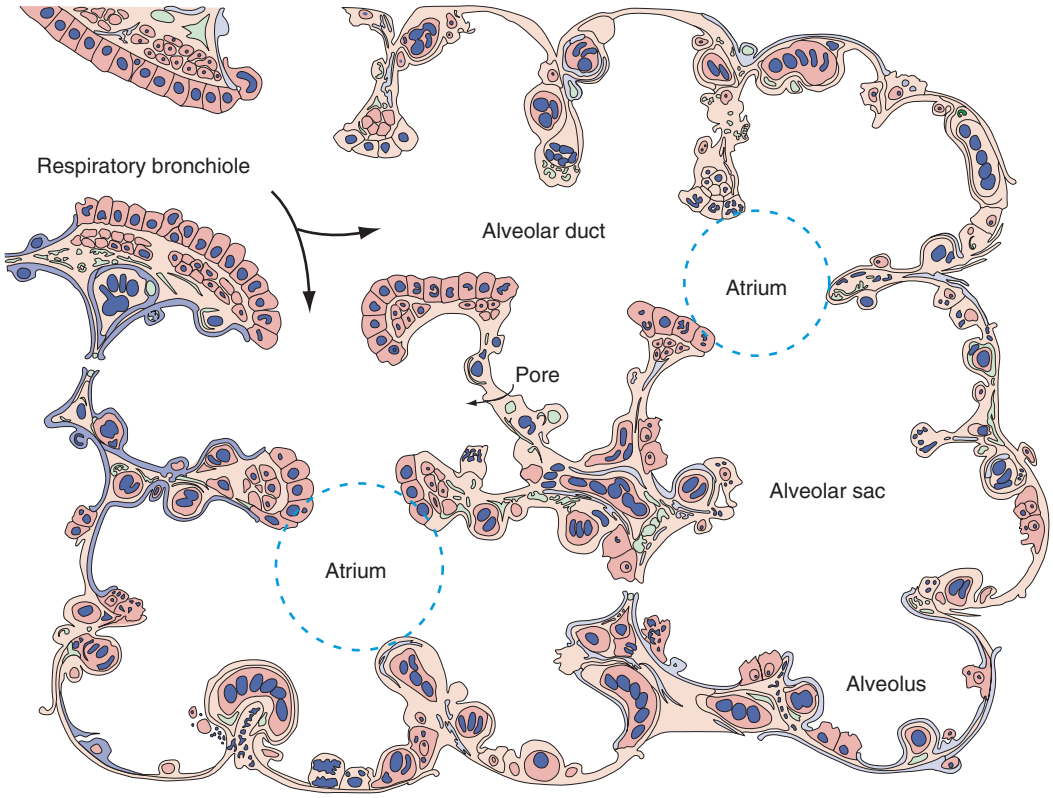


Fig. 9.59 Microscopic view of respiratory zone airways. (Modified from Sorokin SP: *The respiratory system.* In Greep RO, Weiss L, editors: Histology, New York, 1973, McGraw-Hill.)

50% of it, whereas the macrophages primarily remove it through catabolism.[84]

Although the lungs do not have stem cells in the classic sense, the type II cells do have a "stem cell"—like action. They can proliferate and differentiate into type I cells to repopulate and repair the alveolar surface after injury.[85] They are also involved in alveolar defense through surfactant production and the release of some cytokines that trigger inflammation.

Macrophages are another common cell found in the alveolar region.[82] They can move from the pulmonary capillary circulation by squeezing through openings in the alveolar septa and then move out onto the alveolar surface. They are defensive cells that patrol the alveolar region and phagocytize foreign particles and cells (e.g., bacteria). They can present portions of the foreign particles and bacteria to lymphocytes as part of the immune response and contain various digestive enzymes (e.g., trypsin) that break down the material they engulf.

Within the inter-alveolar septum is an interstitial space that contains matrix material and the pulmonary capillaries. Also found in the interstitial space are bands of elastin fibers and a collagen fiber matrix.[47] These fibers support the alveolar cells and the shape of the alveolus. Small openings are found in the alveolar septa. Some of the openings allow gas to move from one alveolus to another. These are called the ***pores of Kohn***. Other openings connect alveoli with secondary respiratory bronchioles. These passageways are called the ***canals of Lambert***. All of these alveolar openings and passageways facilitate the collateral movement of gas (called "collateral ventilation") and help maintain alveolar volume.[81]

Blood-Gas Barrier

Gas exchange between alveolar gas and pulmonary capillary blood occurs across the ***alveolar-capillary membrane***. In a typical adult, this blood-gas barrier stretches over a surface area of approximately 140 m^2 and is less than 1 µm thick.[86] This makes the membrane more than 50 times larger than the area covered by skin and more than 2000 times thinner.

The blood-gas barrier is composed of many different layers through which O_2 and CO_2 diffuse (Fig. 9.63). The outermost layer is a very thin film of a fluid composed primarily of surfactant that forms into a tubular myelin matrix. Below the surfactant fluid layer is the thinly stretched type I cell. The delicate structure of type I cells makes them highly susceptible to injury from toxins carried to them by either airborne or blood-borne routes. The interstitial space and its contents lie below. Within this space are basement membranes, matrix material connective tissue fibers, and the alveolar capillary.[47] The capillary wall is formed from thin, flat squamous epithelia called *endothelial cells* that form a thin tube by connecting at their edges with tight junctions. Within the capillary lie the plasma and, finally, the erythrocytes. Both O_2 and CO_2 cross through the membrane via partial pressure-driven diffusion.

The blood-gas barrier is not equal in thickness and chemical content from side to side (see Fig. 9.63). On one side of the alveolar wall, the type I cells and capillary endothelial cells lie close together, with a thin interstitial space. This part of the blood-gas barrier is, on average, 0.2 to 0.3 µm thick, and it is where the alveolar capillary bulges into the alveolar space.[86] On

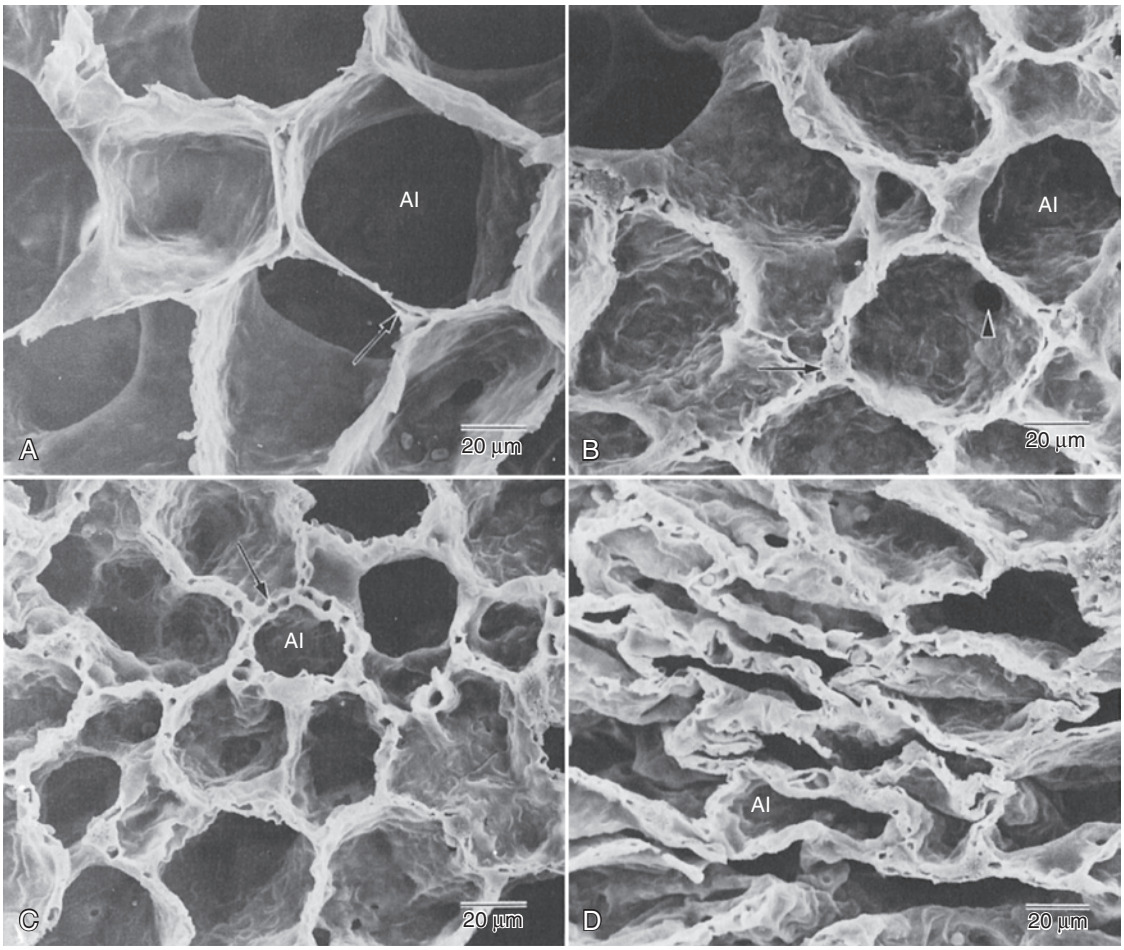


Fig. 9.60 Scanning electron photomicrographs at the same magnification of perfusion-fixed normal rat lung at different degrees of inflation pressure. (A) 30 cm H_2O (total lung capacity [TLC]). (B) 8 cm H_2O (approximately 50% TLC). (C) 4 cm H_2O (near resting inflation or functional residual capacity [FRC]). (D) 0 cm H_2O (minimum volume). Pulmonary artery pressure was held constant at 25 cm H_2O, and left atrial pressure was held at 6 cm H_2O. Intrinsic shape of alveoli *(Al)* is maintained from FRC to TLC (A–C). Alveolar walls are flat with sharp corners where the adjacent walls meet. Note the flat shape of the alveolar capillaries *(arrow)* at TLC (A, lung zone 1 conditions, air pressure > blood pressure) compared with their round shape *(arrow)* at FRC (C, lung zone 3 conditions, blood pressure > air pressure). The alveolar walls are folded, and the alveolar shape is distorted at the minimum lung volume (D). The *arrow* in B identifies a type II pneumocyte at an alveolar corner. The *arrowhead* in B identifies a pore of Kohn through an alveolar wall. (From Mason RJ, Broaddus VC, Martin T, et al., editors: *Murray and Nadel's textbook of respiratory medicine*, ed 4, Philadelphia, 2011, WB Saunders.)

the other side, where there is a thicker interstitial space with greater fiber, matrix, and nuclear material content, the barrier can be more than 3 to 10 times thicker. This difference between the two sides functionally results in "faster-weaker" and "slower-stronger" diffusion sides of the blood-gas barrier.

The interstitial space within the alveolar septum contains a network of fibers that form a kind of connective tissue skeleton holding the alveolar structures in place and together.[87] These fibers within the alveolar septum are part of the continuum of connective tissue fibers found in the pleural surface and in the airway walls. They extend all the way to the root of the lung in the hilar region. Fibroblasts from elastin and collagen fiber bands form into a network within the interstitial space into which the capillaries are woven. Also, around the fibers and capillaries is a non-living matrix of fluid and solutes. The weaving path taken by the capillaries passes them from the thick to the thin sides of the blood-gas barrier as they extend through the septum. On the thin side, the basement membranes of the endothelial and type I cells fuse into a structure called the *lamina densa,* which is formed from collagen.[86] On the thick side, bands of collagen and elastin are found. The collagen and endothelial cells are attached to either side of the *lamina densa* by a series of protein fibers collectively known as *laminins.* Laminins effectively bind together the blood-gas barrier into a three-part laminate that results in a relatively strong and thin structure that can normally, with the additional support offered by the capillary network, withstand the everyday stress of alveolar and capillary stretch.[88]

However, conditions of pulmonary hypertension, excessive tidal volume, and high airway pressures during positive pressure ventilation (e.g., tidal volume > 6 to 8 mL/kg and airway plateau

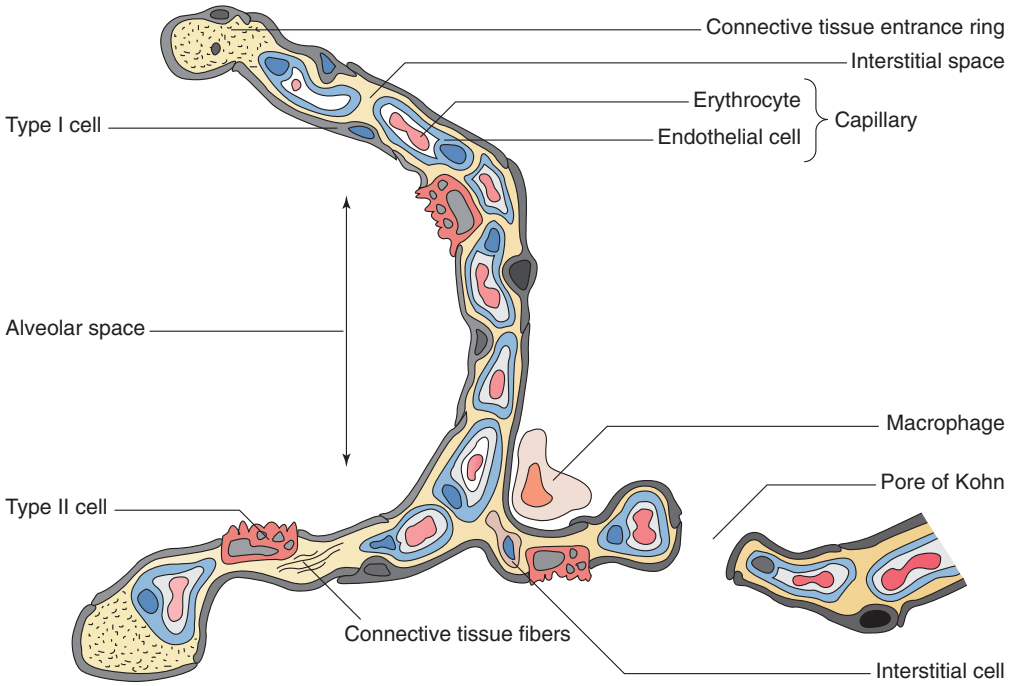
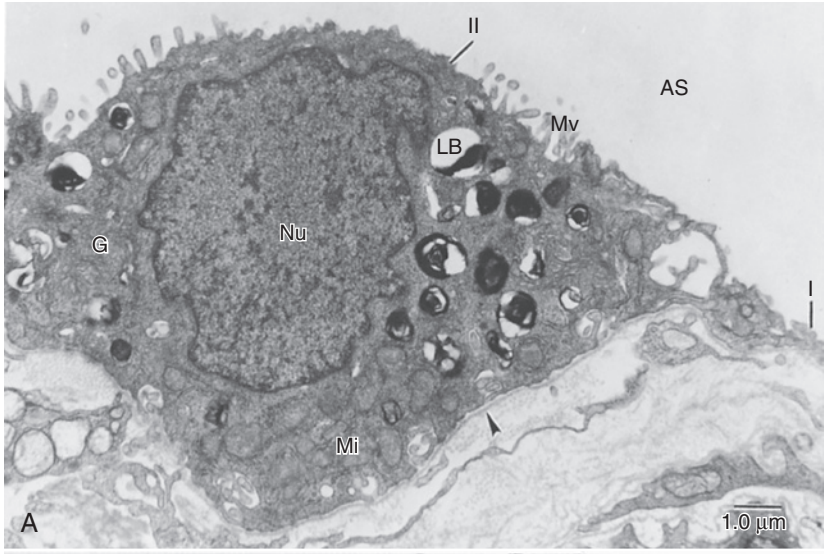


Fig. 9.61 Highly magnified cross-sectional sketch of the cells and organization of the alveolar septa. (From Hicks GH: *Cardiopulmonary anatomy and physiology*, Philadelphia, 2000, WB Saunders.)



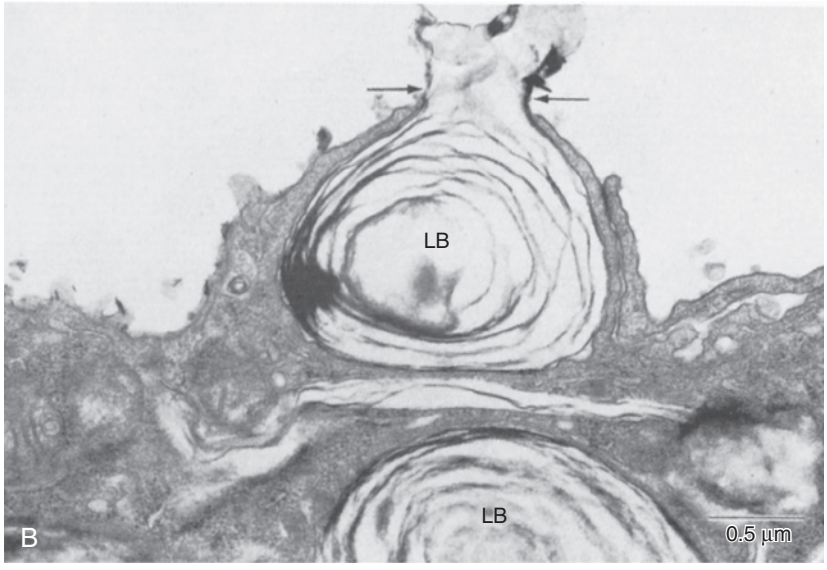


Fig. 9.62 Transmission Electron Photomicrograph of Human Lungs at High Magnification. (A) Type II pneumocytes are cuboidal epithelial cells that contain characteristic lamellar bodies *(LB)* in their cytoplasm and have stubby microvilli *(Mv)* that extend from their apical surface into the alveolar airspace *(AS)*. Other prominent organelles within the type II cells are mitochondria *(Mi),* a single nucleus *(Nu),* and a Golgi apparatus *(G),* which forms the lamellar bodies. Adjacent to the type II cell is a portion of a type I pneumocyte (I). The abluminal side of the epithelial cells of the alveolus rests on a continuous basal lamina *(arrowhead).* (B) Apical region of a type II cell contains two lamellar bodies *(LB),* one of which has been fixed in the process of secreting its contents *(arrows).* The lamellar bodies are believed to be the source of surfactant. Type II cells are more often found in the corners of the alveolar walls. (From Mason RJ, Broaddus VC, Martin, T, et al., editors: *Murray and Nadel's textbook of respiratory medicine*, ed 4, Philadelphia, 2011, WB Saunders.)

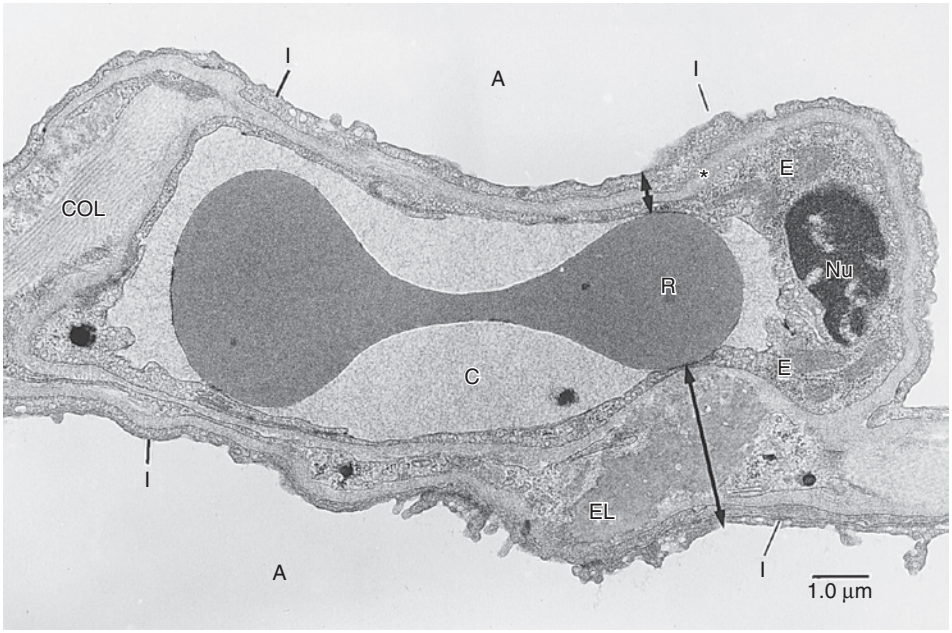


Fig. 9.63 High-magnification transmission electron photomicrograph of a human lung showing a cross-section of an alveolar wall through which O_2 and CO_2 diffuse. Air *(A)* in the alveolar space is seen on either side of the wall. The thin side of the alveolar-capillary membrane *(short double arrow)* consists of type I pneumocytes *(I),* interstitium *(*)* formed by the fused basement membranes of the type I cell and the endothelial cells *(E),* and its nucleus *(Nu)* that forms the pulmonary capillary wall. Within the capillary *(C)* is the erythrocyte *(R).* The thick side of the membrane *(long double arrows)* has an accumulation of elastin *(EL),* collagen *(COL),* and matrix material that jointly separates the type I cell from the capillary endothelial cell. Greater diffusion occurs across the thin side. (From Mason RJ, Broaddus VC, Martin T, et al., editors: *Murray and Nadel's textbook of respiratory medicine*, ed 4, Philadelphia, 2011, WB Saunders.)

pressures > 30 cm H_2O) can result in stress failure of the blood-gas membrane. Stress failure results in endothelial or type I cell stretching and shearing injuries.

SUMMARY CHECKLIST

- Gas exchange between the atmosphere and blood is termed external respiration. This process supports the internal respiration, which is the exchange of gases between blood and tissues.
- The respiratory system humidifies and warms inspired air while removing inhaled contaminants and filtering out chemicals and small blood clots deposited or formed in the blood.
- Many different genes regulate the development of the respiratory system from conception through adult life. Many pulmonary diseases are caused by genetic abnormalities.
- Injury to the embryo or genetic damage during the embryonic phase of development can lead to many congenital anomalies, including tracheoesophageal fistulas, esophageal atresia, choanal atresia, pulmonary hypoplasia, and complex heart and vascular anomalies.
- The development of the respiratory system follows a well-defined schedule; interruptions or insults during development can result in respiratory disease at birth and in adulthood.
- Premature infants younger than 32 weeks are at greater risk for developing respiratory distress due, among other reasons, to the lack of mature alveoli in their lungs.
- Human pulmonary surfactant, which promotes lung inflation and protects the alveolar surface, begins to be produced around 24 to 25 weeks of development by type II pneumocytes.
- The maternal placenta is the actual gas-exchange organ for the fetus.
- Three important bypass pathways (shunts) function in the developing fetus to enhance the flow of blood to the developing organs: ductus venosus, ductus arteriosus, and foramen ovale.
- Before birth, 90% of the fetal blood bypasses the pulmonary circulation through the foramen ovale and the ductus arteriosus (right-to-left shunting). Any additional shunting after birth is considered an anomaly.
- Fetal circulation and respiration differ markedly from circulation and respiration in the postnatal period.
- The transition from intrauterine to extra-uterine life involves a non-aerated, fluid-filled lung converting to an efficient air-filled organ of gas exchange.
- Closure of the foramen ovale and ductus arteriosus are important events in the transition to extra-uterine life.
- During neonatal or infant resuscitation, the baby's head and neck should be neutral or slightly extended in the sniffing position to avoid airway obstruction and collapse and provide effective ventilation.
- Most infants breathe preferentially through the nose. However, most term newborn infants can shift to oral breathing in response to nasal occlusion and hypoxia.

- Despite the presence of cartilage in the central airways of an infant, the trachea and larger bronchi of a neonate lack the rigidity of adult central airways. The compliant nature of these airways makes them prone to collapse and airway obstruction.
- Chest retractions, evident by the use of accessory muscles in the neck, rib cage, sternum, or abdomen, occur when lung compliance is poor, or airway resistance is high in a neonate or infant.
- Visceral control of the smooth muscle of the respiratory system is carried out by branches of the sympathetic and parasympathetic nervous systems and mediators transported to the lungs via the pulmonary circulation.
- The lymphatic circulation plays a central role in the control of fluid and protein balance within the lung and houses various defensive cells.
- Grunting is an expiratory sound caused by the sudden closure of the glottis during exhalation to maintain FRC and prevent alveolar atelectasis.
- Because lung compliance is worse at very low or very high FRC, achieving and maintaining physiologic FRC is essential in the management of respiratory disorders with poor compliance in neonates and infants, such as RDS or TTN.
- The thorax houses and protects the lungs; it is also a movable shell that makes ventilation possible.
- The diaphragm is the primary muscle of ventilation; together with the accessory muscles and thoracic structures, it provides the ability to move large volumes of gas into and out of the lungs.
- Because exhalation is passive, the diaphragm normally does not actively participate in exhalation.
- The accessory muscles of respiration assist the diaphragm and intercostal muscles when ventilatory demand increases.
- The scalene, sternocleidomastoid, pectoral, and abdominal wall muscles are the predominant accessory muscles.
- Patients with advanced COPD often use accessory muscles to assist the flattened diaphragm, helping relieve their work of breathing.
- Abnormal excess of fluids between the visceral and parietal pleura tend to pool in the costophrenic angle in an upright individual. This pooling of fluid causes the angle to appear blunted or flattened to 90 degrees when viewed in the chest radiograph.
- The lungs receive blood flow from the pulmonary circulation for gas exchange and the bronchial circulation to support the airway and pleural tissue metabolism.
- The pulmonary circulation is capable of acting as a reservoir, removing blood clots and numerous mediators, as well as activating important vasoactive agents.
- The low vascular pressures of the pulmonary circulation result in regional blood flow within the lungs that is highly influenced by gravity, airway pressure, and gas exchange.
- The bronchial circulation is a branch of the systemic circuit and is supplied with blood from the aorta via minor thoracic branches. Blood flow through the bronchial circulation constitutes approximately 1% to 2% of the total cardiac output.
- The primary function of the lymphatic system in the lungs is to clear fluid from the interstitial and pleural spaces to help maintain the fluid balance in the lungs. The lymphatic system also plays an important role in the specific defenses of the immune system.
- All of the major structures of the respiratory system are innervated by branches of the peripheral nervous system: the autonomic and somatic branches.
- The somatic system provides voluntary and automatic motor control and sensory innervation to the chest wall and respiratory muscles.
- Autonomic neurons conduct motor and sensory signaling to control various tissues and sense various activities.
- The upper respiratory tract heats and humidifies inspired air. Its various structures also protect the lungs against foreign substances.
- Reflexes of the mouth, pharynx, and larynx help protect the lower respiratory tract during swallowing. These protective functions can be severely compromised during anesthesia or unconsciousness.
- The lower respiratory tract conducts inhaled gases from the upper airway to the respiratory zones of the lung. It contains many structures that help clear and defend the lung.
- During unconsciousness, the muscles of the tongue and hypopharynx can relax and allow the tongue and other soft tissues to collapse and occlude the opening of the hypopharynx.
- The airways branch into lobes in both the right and the left lungs; these lobes consist of various segments.
- The right bronchus branches off from the trachea at an angle of approximately 20 to 30 degrees, and the left bronchus branches with an angle of about 45 to 55 degrees.
- The lower angle branching (closer to mid-line) of the right bronchus results in a greater frequency of right-mainstem intubation and the foreign body aspiration into the right lung because of the more direct pathway.
- The right lung is assumed to provide 60% of the ventilation/gas–exchange capacity, and the left lung is assumed to provide the remaining 40%.
- In an adult human, the volume filling the airways of the anatomic deadspace is approximately 2.2 mL/kg (1 mL/lb) of PBW, or about 150 mL in an average adult.
- Gas exchange between alveolar gas and pulmonary capillary blood occurs across the alveolar-capillary membrane. In a typical adult, this blood-gas barrier stretches over a surface area of approximately 140 m^2 and is less than 1 µm thick.
- The respiratory bronchioles, alveolar ducts, and alveoli provide a large, yet extremely thin, membrane for the exchange of O_2 and CO_2 between air and blood. Disruption of the blood-gas barrier can occur from excessive capillary pressures, lung inflation, and exposure to various toxins (e.g., 100% O_2).

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10

The Cardiovascular System

Narciso E. Rodriguez

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Describe the anatomy of the heart and vascular systems.
- State the key characteristics of the cardiac tissue.
- Describe the local and central control mechanisms of the heart and vascular systems.
- Describe how the cardiovascular system functions under normal and abnormal conditions.
- Calculate cardiac output given stroke volume and heart rate.
- Calculate ejection fraction given stroke volume and end-diastolic volume.
- Identify the electrical and mechanical events related to the normal cardiac cycle.

CHAPTER OUTLINE

KEY TERMS

acute coronary syndrome (ACS)
afterload
angina pectoris
arteriovenous anastomosis
atria
atrial kick
atrioventricular (AV) rings
atrioventricular (AV) valves
automaticity
***a* waves**
baroreceptors
cardiac output (CO)
cardiac tamponade
central venous pressure (CVP)
chemoreceptors
chordae tendineae cordis
conductivity
congestive heart failure (CHF)
contractility
coronary artery diseases (CAD)
coronary circulation
coronary sinus
***c* wave**
dicrotic notch
ejection fraction (EF)
end-diastolic volume (EDV)
end-systolic volume (ESV)
epicardium
excitability
fibrous pericardium
Frank-Starling law
foramen ovale (FO)
heart failure
heart rate (HR)
interatrial septum
interventricular septum
ischemia
left ventricular aid
negative feedback loop
negative inotropism
Non-ST segment elevation myocardial infarction (NSTEMI)
mitral valve
myocardial infarction (MI)
myogenic control
pericardial effusion
pericardial fluid
pericarditis
pericardium
positive inotropism
preload
pulmonary vascular resistance (PVR)
pulseless electrical activity (PEA)
***P* wave**
refractory period
regurgitation
semilunar valves
serous pericardium
ST-segment elevation myocardial infarction (STEMI)
stenosis
stroke volume (SV)
sulci
systemic vascular resistance (SVR)
thebesian veins
thoracic pump
tricuspid valve
***T* wave**
vasoconstriction
vasodilation
***v* wave**

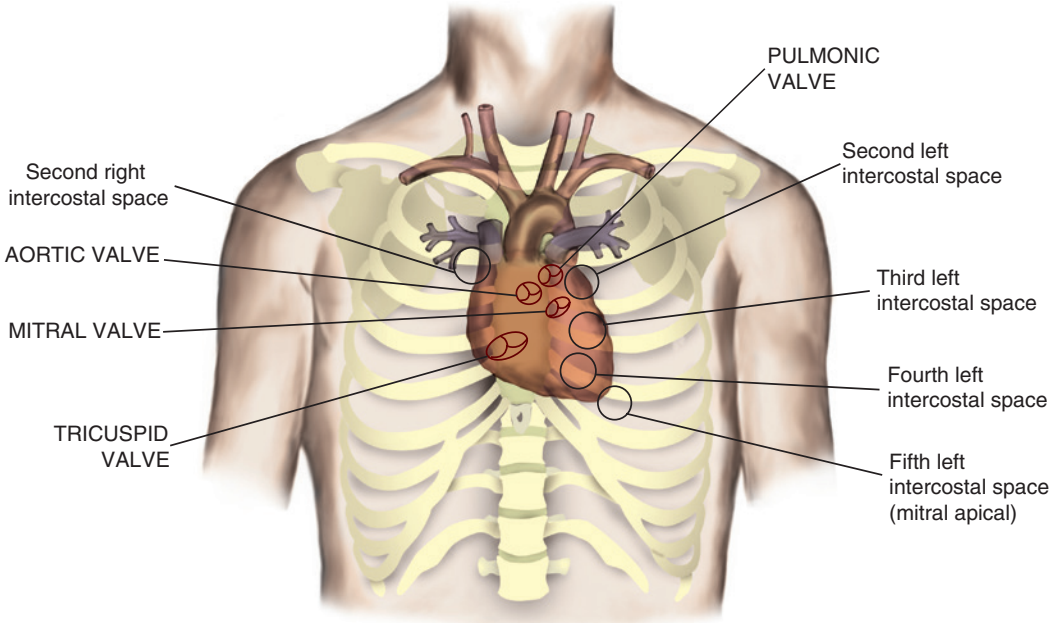


Fig. 10.1 Anterior view of the thorax showing the position of the heart in relation to the ribs, sternum, diaphragm and position of the heart valves. (From Seidel HM, Ball JW, Dains JE, et al: *Mosby's guide to physical examination*, ed 2, St Louis, 1991, Mosby.)

FUNCTIONAL ANATOMY

Heart

Anatomy of the Heart

The heart is a four-chambered muscular organ approximately the size of a fist. It is positioned in the mid-mediastinum of the chest, behind the sternum (Fig. 10.1). Approximately two-thirds of the heart lies to the left of the midline of the sternum between the 2nd and the 6th ribs. The apex of the heart is formed by the tip of the left ventricle and lies above the diaphragm at the level of the 5th intercostal space to the left. The base of the heart is formed by the **atria** and projects to the right, lying below the 2nd rib. Posteriorly, the heart rests at the level of the 5th to the 8th thoracic vertebrae.[1] As a result of its position between the sternum and the spine, compression of the heart maintains blood flow during cardiopulmonary resuscitation (CPR).[2]

RULE OF THUMB High-quality chest compressions improve survival from cardiac arrest. High-quality compressions include ensuring adequate rate, adequate depth, allowing full-chest recoil between compressions and minimizing interruptions.

RULE OF THUMB During cardiopulmonary resuscitation, the heel of one hand should be placed on the center of the chest on the lower half of the sternum while performing chest compressions. Compressions must be done at a depth of at least 2 inches (5 cm) for an average adult, avoiding excessive chest-compression depths.

Externally, surface grooves called ***sulci*** mark the boundaries of the heart chambers.

The heart is enclosed in a sac called the **pericardium**.[3] The structure of the pericardium can be summarized as follows:

1. ***Fibrous pericardium:*** Tough, loose-fitting and inelastic sac surrounding the heart
2. ***Serous pericardium:*** Consisting of two layers:
   a. *Parietal layer:* Inner lining of the fibrous pericardium
   b. *Visceral layer or* ***epicardium:*** Covering the outer surface of the heart and great vessels

A thin layer of fluid called the ***pericardial fluid*** separates the two layers of the serous pericardium. Inflammation of the pericardium results in a clinical condition called ***pericarditis***. An abnormal amount of fluid can accumulate between the layers, resulting in a ***pericardial effusion***. A large pericardial effusion may lessen the pumping function of the heart, resulting in a ***cardiac tamponade***, which compresses the heart muscle, leading to a serious decrease in blood flow to the body. This, ultimately, may lead to shock and death.[1,4]

RULE OF THUMB A cardiac tamponade should be suspected in patients presenting with hypotension, jugular venous distension, pulsus paradoxus, tachycardia, tachypnea, narrowing pulse pressures and/or severe dyspnea.

The heart wall consists of three layers: (1) outer epicardium, (2) middle myocardium, and (3) inner endocardium. The myocardium composes the bulk of the heart muscle and consists of bands of involuntary striated muscle fibers. The contraction of these muscle fibers creates the pump-like action needed to move blood throughout the body.

Support for the four interior chambers and valves of the heart is provided by four **atrioventricular (AV) rings**, which form a fibrous "skeleton." Each ring is composed of dense connective tissue termed *annulus fibrosus cordis*, which encircles the bases of the pulmonary trunk, aorta and heart valves and electrically isolates the atria from the ventricles. No electrical impulses can

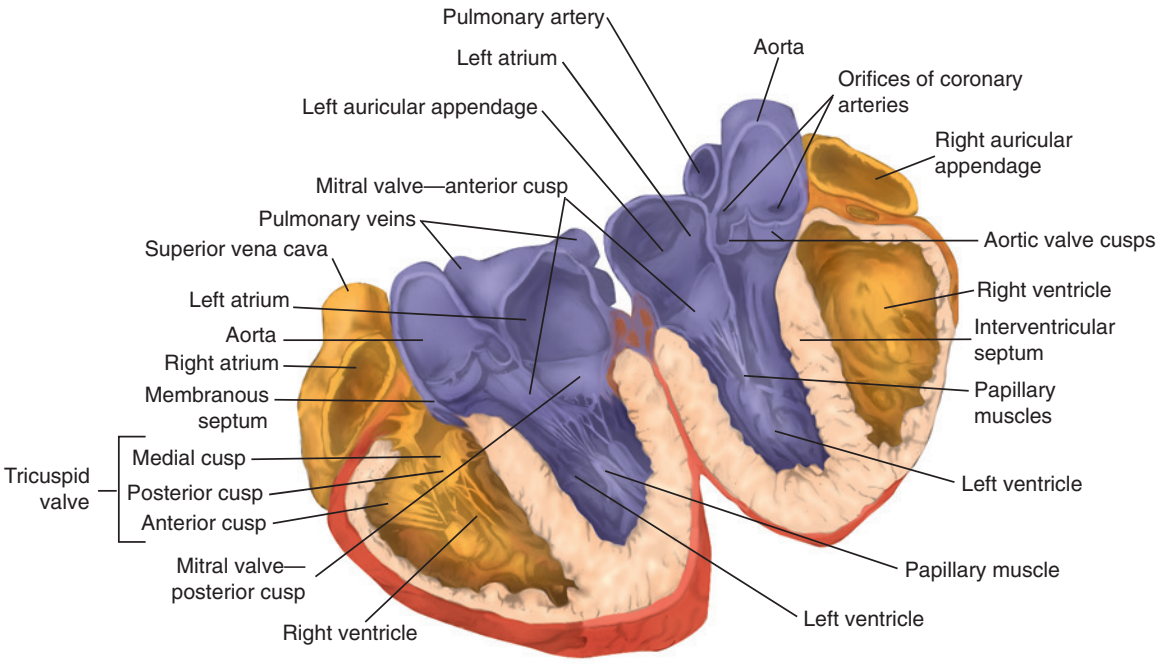


Fig. 10.2 Drawing of the heart split perpendicular to the interventricular septum to illustrate anatomic relationships of the heart. (From Berne RM, Levy MN, editors: *Physiology*, ed 5, St Louis, 2004, Mosby.)

be transmitted through the heart muscle and connective tissue from the atria to the ventricles.[1,3]

The two atrial chambers are thin-walled "cups" of myocardial tissue that contribute little to the total pumping activity of the heart. They are separated by an interatrial wall or septum. On the right side of the **interatrial septum** is an oval depression called the *fossa ovalis cordis,* the remnant of the fetal **foramen ovale (FO)**. Each atrium has an appendage, or auricle, the function of which is unknown. In the presence of cardiac dysrhythmias (e.g., atrial fibrillation), blood flow can pool on these appendages, leading to the formation of thrombi.

The two lower-heart chambers, or ventricles, make up the bulk of the heart's muscle mass and do most of the pumping that circulates the blood (Fig. 10.2). The mass of the left ventricle is approximately two-thirds larger than the mass of the right ventricle and has a spherical appearance when viewed across anteriorly.[5] The right ventricle has a thinner wall than the left and forms a pocket-like attachment to the left ventricle. Because of this relationship, the left ventricle pulls in and pushes the right ventricular wall, aiding to its filling and contraction. This effect, termed ***left ventricular aid,*** explains why some forms of right ventricular failure are less harmful than might be expected. The right and left ventricles are separated by a muscle wall termed the ***interventricular septum*** (see Fig. 10.2).[5]

The valves of the heart are flaps of fibrous tissue firmly anchored to the *annulus fibrosus cordis* (Fig. 10.3) and because they are located between the atria and ventricles, they are called ***atrioventricular (AV) valves*** or AV valves. The valve on the right side is called the ***tricuspid valve*** and the valve on the left is called the *bicuspid* or ***mitral valve.*** The AV valves close during systole (contraction of the ventricles), preventing backflow of blood into the atria. The free ends of the AV valves are anchored to papillary muscles of the endocardium by the ***chordae tendineae cordis*** (see Fig. 10.2). During systole, papillary muscle contraction prevents the AV valves from swinging upward into the atria. Damage to either the chordae tendineae cordis or the papillary muscles can impair the function of the AV valves and cause leakage upward into the atria.[1]

Common valve problems include regurgitation and stenosis. **Regurgitation** is the backflow of blood through a malfunctioning leaky valve and **stenosis** is a pathologic narrowing or constriction of a valve outlet, which causes blood to back up and increased pressure in the proximal chamber and vessels. Both conditions can affect cardiac performance. In mitral stenosis, high pressures in the left atrium back up into the pulmonary circulation and these high pressures can cause pulmonary edema and a diastolic murmur (see Chapter 16).[4,6]

A set of **semilunar valves** separates the ventricles from their arterial outflow tracts, the pulmonary artery (in the right) and the aorta (in the left) (Fig. 10.3). Consisting of three half-moon-shaped cusps attached to the arterial wall, these valves prevent backflow of blood into the ventricles during diastole (or when the chambers of the heart fill with blood). Like the AV valves, the semilunar valves can leak (regurgitation) or become partially obstructed (stenosis).[1]

Similar to the lungs, the heart has its own circulatory system, which is called the ***coronary circulation***; however, in contrast to the lungs, the heart has a high metabolic rate that requires more blood flow per gram of tissue weight than any other organ except the kidneys. To meet these needs, the coronary circulation provides an extensive network of branches to all myocardial tissue (Fig. 10.4).

Two main coronary arteries, one in the left and one in the right, arise from the root of the aorta right underneath the semilunar valves. Blood flows through the coronary arteries only during diastole when the semilunar valves are closed. Partial

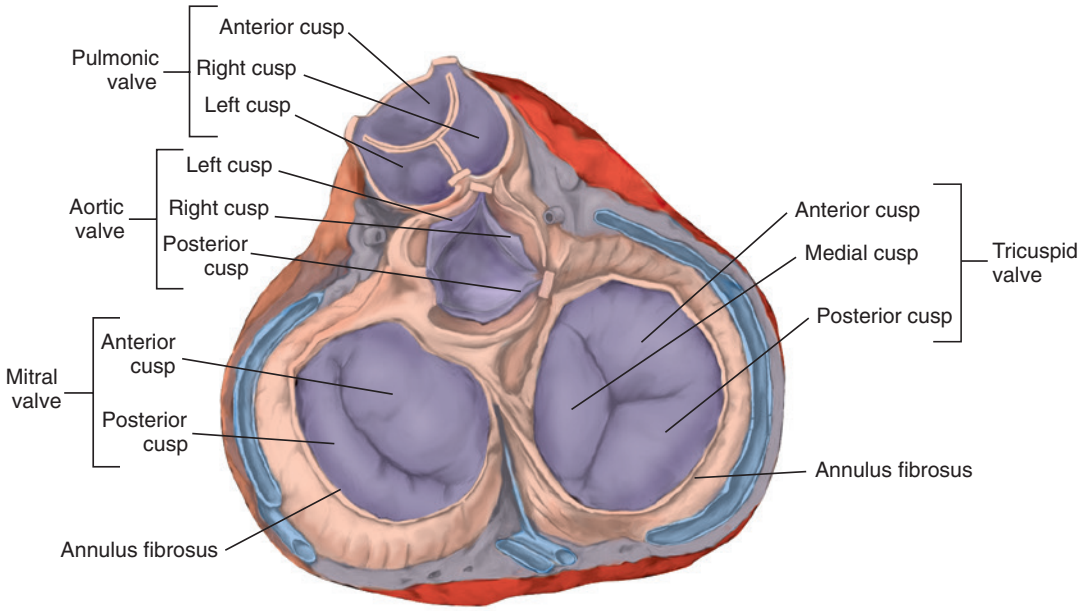


Fig. 10.3 Four Cardiac Valves as Viewed from the Base of the Heart. Note how the leaflets overlap in the closed valves.

MINI CLINI

Mitral Stenosis, Poor Oxygenation, and Increased Work of Breathing

The mitral valve lies between the left atrium and left ventricle. Mitral stenosis causes high resistance to the blood flow into the left ventricle from the left atrium. This increased resistance causes a backflow into the pulmonary circulation, leading to pulmonary edema with fluid collecting in the alveoli and *interstitial spaces* in the lungs, impairing oxygenation and breathing.

Problem

Why does a patient with mitral stenosis have poor oxygenation of the blood and increased work of breathing?

Discussion

Blood flows from the lungs into the left atrium, where it may encounter high resistance through a narrowed, stenotic mitral valve; this causes high pressure to build in the left atrium. The pressure in the pulmonary veins and, eventually, in the pulmonary capillaries also increases. This high pressure within the capillaries engorges them and forces fluid components of the blood plasma out of the vessels and into the interstitial spaces of the lungs and inside the alveoli, creating pulmonary edema. This collection of fluid interferes with oxygen diffusion from the lung into the blood. Engorged capillaries surrounding the alveoli create a stiff "web" around each alveolus, which makes expanding the lungs difficult; thus, mitral stenosis, a cardiac problem, often has significant pulmonary consequences.

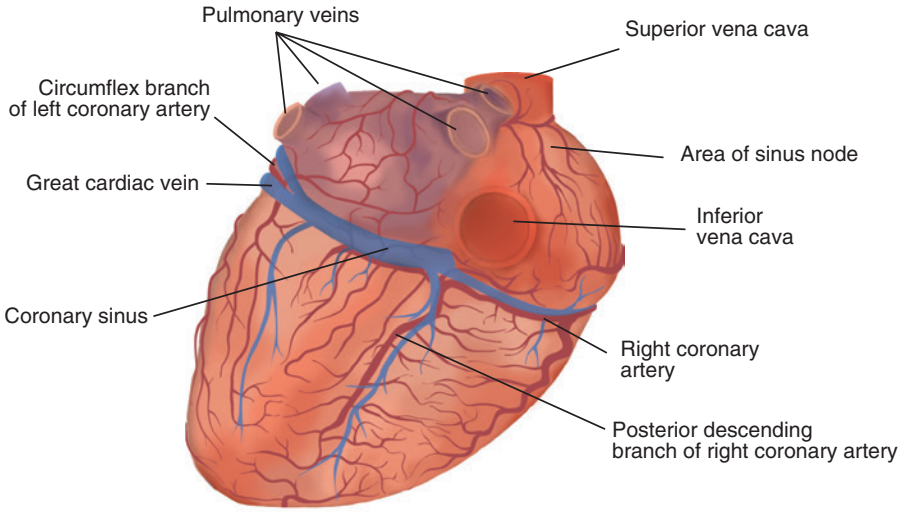
obstruction of a coronary artery may lead to tissue **ischemia** (decreased oxygen supply). Complete obstruction of a coronary artery may cause tissue death or infarct, a condition called ***myocardial infarction (MI)***.[4]

Acute Coronary Syndrome (ACS) is the name given to three types of ***coronary artery diseases (CAD)*** that are associated with gradual and/or sudden obstruction of the coronary arteries. These are (1) unstable angina or ***angina pectoris***, (2) ***Non-ST segment elevation myocardial infarction (NSTEMI)*** and (3) ***ST-segment elevation myocardial infarction (STEMI)***.

Although heart disease mortality rates have declined over the past four decades in western countries, this condition remains responsible for approximately one third of all deaths in individuals over the age of 35.[7] Nearly one-half of all middle-aged men and one-third of middle-aged women in the USA will develop some manifestation of a coronary heart disease (CHD). The 2016 Heart Disease and Stroke Statistics update of the American Heart Association (AHA) reported that 15.5 million people in the USA have CHD. The reported prevalence increases with age for both women and men. In the US the lifetime risk of developing CHD with ≥2 major risk factors is 37.5% for men and 18.3% for women.[8]

RULE OF THUMB Classic signs of *tissue ischemia* (decreased oxygen supply) are chest pain and shortness of breath resulting in a clinical condition called ***angina pectoris***. Symptoms of a *myocardial infarction* include tightness or pain in the chest, neck, back or arms, as well as fatigue, lightheadedness, abnormal heartbeat and anxiety. Women are more likely to have atypical symptoms than men.

After passing through the capillary beds of the myocardium, the venous blood is collected by the coronary veins that closely parallel the arteries (see Fig. 10.4). These veins gather together into a large vessel called the ***coronary sinus***, which passes left to right across the posterior surface of the heart. The coronary sinus empties into the right atrium between the opening of the inferior vena cava (IVC) and the tricuspid valve.[1] In addition, some coronary venous blood flows back into the heart through the ***thebesian veins***.[1] The thebesian veins empty directly into all the heart chambers. Any deoxygenated blood coming from the thebesian veins that enters the left atrium or ventricle lowers



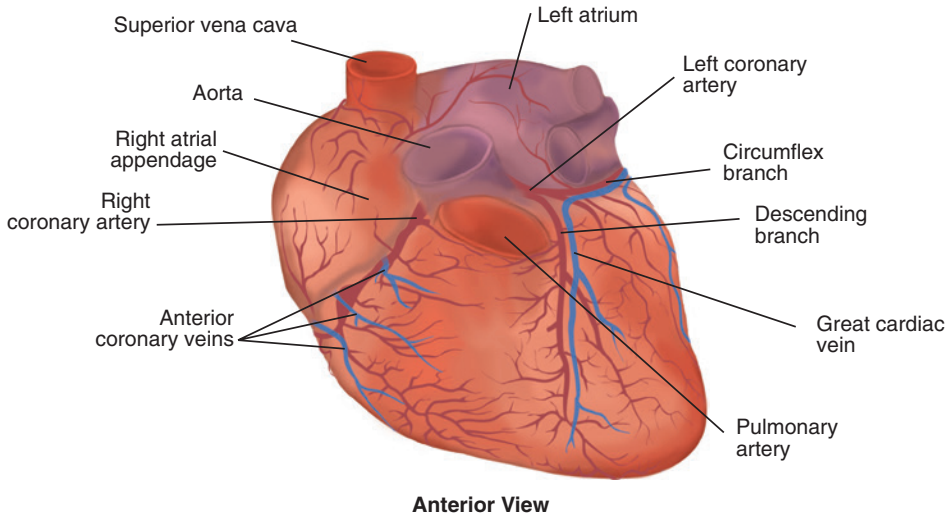


Fig. 10.4 Coronary circulation as seen on anterior and posterior surfaces of the heart, illustrating the location and distribution of the principal coronary vessels.

the overall oxygen content of the systemic circulation. Because the thebesian veins bypass or shunt around the pulmonary circulation as part of the normal anatomy, this phenomenon is called an *anatomic shunt.* When combined with a similar bypass in the bronchial circulation (see Chapter 9), these normal anatomic shunts account for approximately 2% to 3% of the total cardiac output.[1,5]

Properties of the Heart Muscle

The performance of the heart as a pump depends on its ability to (1) initiate and conduct electrical impulses and to (2) synchronously contract the heart's muscle quickly and efficiently.[5] These actions are only possible because myocardial tissue possesses the following four key properties:

- Excitability
- Inherent rhythmicity or automaticity
- Conductivity
- Contractility

Excitability is the ability of cells to respond to electrical, chemical or mechanical stimulation. Electrolyte imbalances, congenital cardiac anomalies and certain drugs can increase myocardial excitability and produce abnormalities in electrical conduction that may lead to cardiac arrhythmias.

Inherent rhythmicity, or **automaticity**, is the unique ability of the cardiac muscle to initiate a spontaneous electrical impulse (depolarization and repolarization). Although such impulses can arise from anywhere in the cardiac tissue. This ability is highly developed in specialized areas called the *heart pacemaker* or *nodal tissues.* The sinoatrial (SA) node and the atrioventricular (AV) node are the heart's primary pacemakers. An electrical impulse from any source other than a normal heart pacemaker is considered abnormal (or ectopic) and represents one of the many causes of abnormal heart rhythms or *cardiac arrhythmias* (see Chapter 18).

Conductivity is the ability of the myocardial tissue to spread and conduct electrical impulses. This property allows the myocardium to contract without direct neural innervation (as required

MINI CLINI

Heart Rate and Coronary Perfusion

Problem

Why might an extremely high heart rate decrease blood flow through the coronary arteries?

Discussion

Blood flow through the coronary arteries occurs only during ventricular diastole when the aortic semilunar valves close and the heart relaxes. During systole, the myocardium contracts with such force that coronary artery pressures increase to values greater than aortic pressures. As the **heart rate (HR)** increases, both systolic and diastolic times must decrease. As diastolic time decreases, increasingly less time is available for coronary artery perfusion that occurs during diastole and, therefore, coronary blood flow is significantly reduced. This reduction in flow is critically important for an individual who already has reduced coronary circulation caused by arteriosclerotic heart disease. Not only is coronary artery perfusion decreased with severe tachycardia but also the shortened ventricular filling time causes decreased **stroke volume (SV)** and decreased **cardiac output (CO)** leading to decreased systemic and coronary perfusion.

MINI CLINI

Pulseless Electrical Activity and Cardiopulmonary Resuscitation

Problem

Why should pulmonary resuscitation should continue even in the presence of a normal sinus rhythm (NSR) in the monitor during a resuscitation attempt?

Discussion

Pulseless electrical activity (PEA), also known as electromechanical dissociation, refers to cardiac arrest in which the electrocardiogram (ECG) shows a heart rhythm that should produce a pulse, but does not.[9] In this case there is an 'electrical' signal but the heart muscle does not respond accordingly to generate a palpable pulse. In the absence of a pulse (non-perfusion state), even in the presence of a "normal" ECG cardiac rhythm, chest compressions must continue to guarantee adequate perfusion to central organs during the arrest. Troubleshooting of the possible causes of PEA must ensue immediately (see Chapter 18).

by skeletal muscle). When the electrical signals of a *depolarization* wave reach the contractile cells they contract (systole). When the *repolarization* signals reach the myocardial cells they relax (diastole) and thus the electrical signals cause the mechanical pumping action of the heart; mechanical events always follow the electrical events.

The rate at which electrical impulses spread throughout the myocardium is variable. These differences in conduction rates are needed to ensure synchronous contraction of the cardiac chambers. Abnormal conductivity can affect the timing of chamber contractions and decrease cardiac efficiency.

Contractility, in response to an electrical impulse, is the primary function of the myocardium. Contrary to the contractions of other muscle tissues, cardiac contractions cannot be sustained or tetanized because myocardial tissue exhibits a prolonged period of inexcitability after contraction. The period during which the myocardium cannot be stimulated is called the ***refractory period*** and lasts approximately 250 ms, nearly as long as the heart contraction or systole.

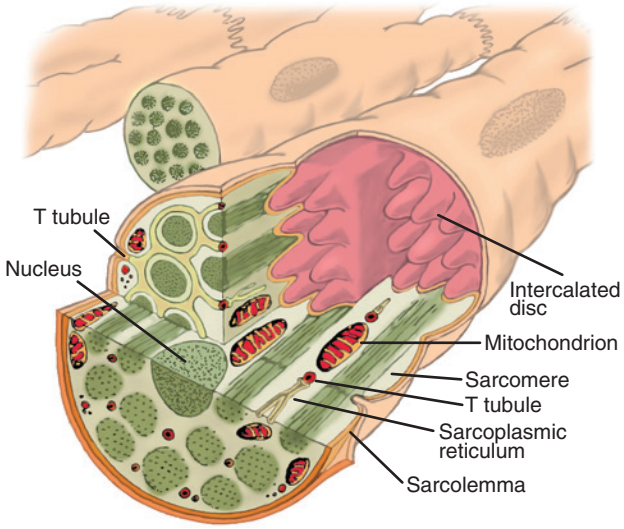


Fig. 10.5 Major Structural Features of Cardiac Muscle Fibers. Note the presence of intercalated discs connecting successive sarcomeres. (Modified from Moffett DF, Moffett SB, Schauf CL: *Human physiology: foundations and frontiers*, ed 2, St Louis, 1993, Mosby.)

Microanatomy of the Heart Muscle

Understanding how cardiac muscle contracts requires knowledge of the microanatomy of the heart. Cardiac cells are short, fat, branched and interconnected. Individual cardiac fibers are enclosed in a membrane called the *sarcolemma*, which is surrounded by a rich capillary network (Fig. 10.5).

Cardiac fibers are separated by irregular transverse thickenings of the sarcolemma called *intercalated discs*. These discs provide structural support and aid in electrical conduction between fibers. Each fiber consists of many smaller units called *myofibrils*, which contain repeated structures approximately 2 µm in size termed *sarcomeres*. Within the sarcomeres are contractile protein filaments responsible for shortening the myocardium during systole. These proteins are of two types: thick filaments composed mainly of myosin and thin filaments composed mostly of actin. Myocardial cells contract when actin and myosin combine to form reversible bridges between these thick and thin filaments.[3,6]

The tensions developed during myocardial contraction are directly proportional to the number of cross-bridges between the actin and myosin filaments. This principle underlies Starling's law of the heart, also known as the **Frank-Starling law**, which is discussed later in this chapter. According to this law, the more a cardiac fiber is stretched (up to a point), the greater the tension it generates when contracted. This relationship is extremely important and is explored later in the discussion of the heart as a pump.[10]

Vascular System

The vascular system has two major subdivisions: the *systemic circulation* and the *pulmonary circulation*. The systemic circulation begins with the aorta on the left ventricle and ends in the right atrium. The pulmonary circulation begins with the pulmonary artery out of the right ventricle and ends in the left atrium. The blood flow to and from the heart is shown in Fig. 10.6.[3]

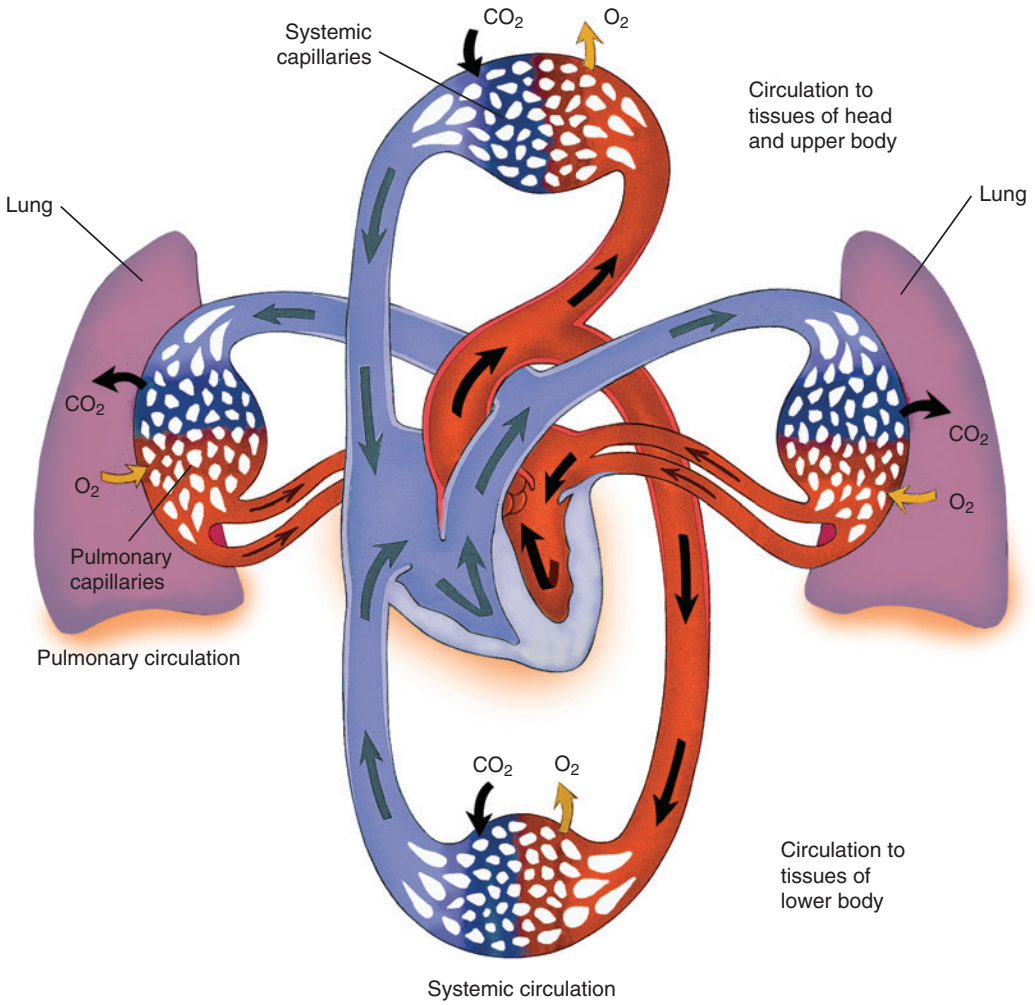


Fig. 10.6 Generalized circulatory and gas exchange pathways between the heart, lung, and systemic circulation.

Venous, or deoxygenated, blood from the head and upper extremities enters the right atrium from the superior vena cava (SVC), and venous blood from the abdomen and lower body enters from the inferior vena cava (IVC). From the right atrium, blood flows into the right ventricle. The right ventricle pumps the blood into the pulmonary arteries, which are the only arteries in the body that carry deoxygenated or venous blood. From there, this venous blood participates in gas exchange in the lungs, picking up oxygen and eliminating carbon dioxide through the alveolar-capillary membrane of the lungs.

RULE OF THUMB When performing hemodynamic calculations requiring the use of mixed-venous blood samples, these blood samples must always be drawn *slowly* from a line inserted in the pulmonary artery vessel. This is commonly called a Swan-Ganz catheter or Pulmonary Artery catheter (PAC). A PAC can also help determine whether any hemodynamic, or blood-flow-related, abnormalities exist in the heart and lungs.[10]

Arterial, or oxygenated, blood returns to the left atrium through the pulmonary veins. The left atrium pumps blood into the left ventricle and the blood is then pumped to the body through the aorta. After gas exchange at the tissue level, from the capillary network of the various body tissues, the deoxygenated venous blood returns to the right ventricle through the SVC and IVC.[1]

Systemic Circulation

The systemic circulation has three major components: (1) the arterial system, (2) the capillary system, and (3) the venous system. These vessels regulate not only the amount of blood flow per minute (CO) but also the distribution of blood to organs and tissues (perfusion). To achieve these functions, each component has a unique structure and plays a different role in the circulatory system as a whole.[3]

The *arterial system* consists of large, highly elastic, low-resistance arteries and small, muscular arterioles of varying resistance. With their elasticity, the large arteries help transmit and maintain the head of pressure generated by the heart. Together, the large arteries are called *conductance vessels*. Just as faucets control the flow of water into a sink, the smaller arterioles control blood flow into the capillaries. Arterioles provide this control by varying their flow resistance; they play a major role in the distribution and regulation of blood pressure and are referred to as *resistance vessels*.

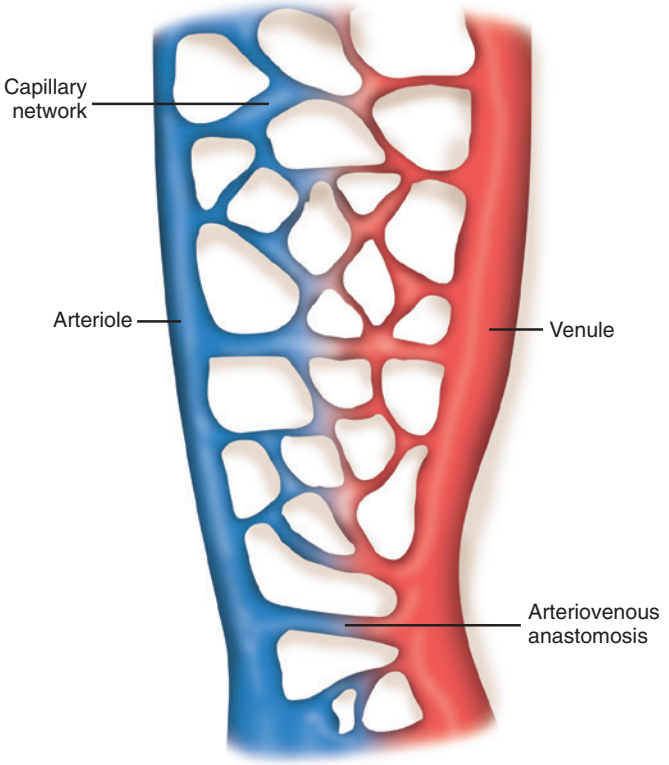


Fig. 10.7 Components of a Microcirculatory Network. Blood flows from arteriolar to venular vessels through a network of capillaries. The opening of the arteriovenous anastomosis directs blood flow out of the capillary network. (Modified from Stevens A, Lowe J: *Human histology*, ed 2, St Louis, 1997, Mosby.)

The vast *capillary system,* or microcirculation, maintains a constant exchange of nutrients and waste products for the cells and tissues of the body. For this reason, the capillaries are commonly referred to as *exchange vessels*. Fig. 10.7 shows the structure of a typical capillary network. Blood flows into the network by an arteriole and out through a venule. Direct communication between these vessels is called an **arteriovenous anastomosis**. When open, these anastomoses allow arterial blood to shunt around the capillary bed and flow directly into the venules. Downstream, the arteriole divides into terminal arterioles, which branch further into thoroughfare channels and true capillaries.

Capillaries have smooth muscle rings at their proximal ends, called *precapillary sphincters.* Contraction of these sphincters decreases blood flow locally, whereas relaxation increases local perfusion. In combination, these various channels, sphincters and bypasses allow precise control over the direction and amount of blood flow to a given organ or area of tissue.

The *venous system* consists of small, expandable venules and veins and larger, more elastic veins. Besides conducting blood back to the heart, these vessels act as a reservoir for the circulatory system. At any given time, the veins and venules hold approximately three-quarters of the body's total blood volume. The volume of blood held in this reservoir can be rapidly changed as needed simply by altering the tone of these vessels. By quickly changing its holding capacity, the venous system can match the volume of circulating blood to that needed to maintain adequate tissue perfusion. The components of the venous system, especially the small, expandable venules and veins, are termed *capacitance vessels.*

The venous system must overcome gravity to return blood to the heart. The following four mechanisms aid the venous return to the heart: (1) sympathetic venous tone; (2) skeletal muscle pumping or "milking" (combined with one-way venous valves); (3) cardiac suction; and (4) thoracic pressure differences caused by respiratory efforts.[5]

The last mechanism is often called the ***thoracic pump***. This is particularly important to respiratory therapists (RTs) because artificial ventilation with positive pressure reverses normal thoracic pressure gradients. Positive pressure ventilation (PPV) impedes, rather than assists, venous return. As long as blood volume, cardiac function and vasomotor tone are adequate, PPV generally has a minimal effect on venous return; however, patients who are hypovolemic or in cardiac failure are vulnerable to a reduction in cardiac output when PPV is applied to the lungs.[10]

Although the heart is a single organ, it functions as two separate pumps. The right side of the heart generates a systolic pressure of approximately 25 mm Hg to drive blood through the low-resistance, low-pressure pulmonary circulation. The left side of the heart generates systolic pressures of approximately 120 mm Hg to propel blood through the higher pressure, high-resistance systemic circulation. This pressure gradient helps the cardiac suction effect in returning the venous blood to the right side of the heart.

Vascular Resistance

Similar to the movement of any fluid through tubes, blood flow through the vascular system is opposed by frictional forces. The sum of all frictional forces opposing blood flow through the systemic circulation is called ***systemic vascular resistance (SVR)***. SVR must equal the difference in pressure between the beginning and the end of the circuit, divided by the flow. The beginning pressure for the systemic circulation is the mean aortic pressure; ending pressure equals right atrial pressure or ***central venous pressure (CVP)***. Flow for the system in its entirety equals the cardiac output (CO). SVR can be calculated by the following formula:

$$\text{SVR} = \frac{\text{Mean aortic pressure} - \text{Right atrial pressure}}{\text{Cardiac output}}$$

Given a normal mean aortic pressure of 90 mm Hg, a mean right atrial pressure of approximately 4 mm Hg and a normal CO of 5 L/min, normal SVR is computed as follows:

$$\text{SVR} = \frac{90\ \text{mm Hg} - 4\ \text{mm Hg}}{5\ \text{L/min}}$$
$$= 17.2\ \text{mm Hg/L/min}$$

The same concepts can be used to compute resistance in the pulmonary circulation. Beginning pressure for the pulmonary circulation is the mean PA pressure; ending pressure equals left atrial pressure. Flow for the pulmonary circulation is the same as it is for the systemic system, which equals the CO; hence,

RULE OF THUMB Changes in resistance are the primary means by which blood flow is regulated within organs because control mechanisms in the body generally maintain arterial and venous blood pressures within a narrow range.

When applying Ohm's law for the flow of blood in a blood vessel (Blood Flow = ΔP/Resistance or MAP = CO/SVR), the ΔP is the pressure difference between any two points along a given length of the vessel. When describing the flow of blood for an organ, the pressure difference is generally expressed as the difference between the arterial pressure (PA) and venous pressure (PV). For example, the blood flow for the kidney is determined by the renal artery pressure, renal vein pressure, and renal vascular resistance.

pulmonary vascular resistance (PVR) can be calculated by using the following formula:

$$\text{PVR} = \frac{\text{Mean PA pressure} - \text{Left atrial pressure}}{\text{Cardiac output}}$$

Given a normal mean PA pressure of approximately 16 mm Hg and a normal mean left atrial pressure of 8 mm Hg, normal PVR is computed as follows:

$$\text{PVR} = \frac{16\,\text{mm Hg} - 8\,\text{mm Hg}}{5\,\text{L/min}}$$
$$= 1.6\,\text{mm Hg/L/min}$$

Resistance to blood flow in the pulmonary circulation is approximately *one-tenth* of that of the systemic circulation. The pulmonary circulation is characterized as a *low-pressure, low-resistance system* and the systemic circulation as a *high-pressure, high-resistance system*.

Determinants of Blood Pressure

A healthy cardiovascular system maintains sufficient pressure to propel blood throughout the body.[6] The priority of the cardiovascular system is to maintain perfusion pressures to tissues and organs at functional levels, even under changing conditions. If the equation for computing SVR is rearranged by deleting the normally low atrial pressure, the average blood pressure in the circulation is directly related to both CO and flow resistance, as follows:

$$\text{Mean arterial pressure (MAP)} = (\text{CO} \times \text{SVR}) + \text{CVP}$$

Some MAP formulas disregard the CVP contribution because the CVP levels are generally negligible under normal circumstances (0 to 6 mm Hg). It is important to note that under many conditions, vascular resistance tends to vary inversely with the size of the blood vessels (i.e., the capacity of the vascular system).

All else being constant, MAP is directly related to the volume of blood in the vascular system and inversely related to its capacity:

$$\text{MAP} = \frac{\text{Volume}}{\text{Capacity}}$$

Based on this relationship, MAP is regulated by either changing the volume of circulating blood, changing the capacity of the vascular system or changing both. Volume changes can reflect absolute changes in total blood volume, such as changes resulting from hemorrhagic shock or blood transfusion. Alternatively, changes in "relative" volume can occur when vascular space increases or decreases. Vascular space decreases when **vasoconstriction** (constriction of the smooth muscles in the peripheral blood vessels) occurs, which causes blood pressure to increase even though blood volume is the same. Vascular space increases when **vasodilation** (relaxation of the smooth muscles in the arterioles) occurs, which causes blood pressure to decrease even though blood volume has not changed (e.g., during septic shock).

In a normal adult, MAP ranges from 80 to 100 mm Hg. When MAP decreases below 60 mm Hg, which may accompany some forms of untreated shock, perfusion to the brain and the kidney is severely compromised and organ failure may occur in minutes.[4]

The blood pressure value that should be targeted during the management of septic shock is an important clinical issue. The MAP is one of the first variables that is monitored in septic patients.[11] Prolonged hypotension, defined as a MAP of less than 60 to 65 mm Hg, is associated with poor outcome in general.

RULE OF THUMB The results of the SEPSISPAM (Sepsis and Mean Arterial Pressure) study suggest that a MAP target of 65 to 75 mm Hg is usually sufficient in patients with septic shock, but a higher MAP (around 75 to 85 mm Hg) may be preferable in patients with chronic arterial hypertension.[12]

To avoid organ and tissue damage and maintain adequate perfusion pressures under changing conditions, the cardiovascular system attempts to balance relative volume and resistance. When a person exercises, the circulating blood volume undergoes a relative increase, but blood pressure remains near normal, because the skeletal muscle vascular beds dilate, causing a large increase in system capacity; however, when blood loss occurs, as with hemorrhage, the system capacity is decreased by constriction of the peripheral vessels. Perfusion pressures may be kept near normal unless the volume loss is extreme.

Regulation of blood flow and pressure is much more complex than is suggested by these simplified equations. Cardiovascular control is achieved by a complex array of integrated functions, some of which are explained subsequently.

CONTROL OF THE CARDIOVASCULAR SYSTEM

The cardiovascular system is responsible for transporting metabolites to and from the tissues under various conditions and demands. It must act in a highly coordinated fashion achieved by integrating the functions of the heart and vascular system. The goal is to maintain adequate perfusion to all tissues according to their needs.[10]

The cardiovascular system regulates blood flow mainly by altering the capacity of the vasculature and the volume of blood it holds. The heart plays only a secondary role in regulating blood flow; the vascular system tells the heart how much blood it needs, rather than the heart dictating what volume of blood the vascular system will receive.

These integrated functions involve local and central neural control mechanisms. Local, or *intrinsic,* controls operate independently without central nervous system control. Intrinsic control alters perfusion under normal conditions to meet metabolic needs. Central or *extrinsic* control involves both the central nervous system and circulating *humoral agents.* Extrinsic control mechanisms maintain a normal level of vascular tone; however, central control mechanisms take over when the competing needs of local vascular beds must be coordinated. Basic knowledge of vascular regulatory mechanisms and factors controlling CO is essential to understand how the cardiovascular system responds under both normal and abnormal conditions.[3]

Regulation of Peripheral Vasculature

A normal level of vascular muscle tone is normally maintained throughout the vascular system at all times. Normal vascular muscle tone must be present to allow for effective regulation. If blood vessels remained completely relaxed, further dilation would be impossible and local increases in perfusion could not occur.

Local vascular tone is maintained by the smooth muscle of the precapillary sphincters of the microcirculation and can function independently of neural control at the local tissue level according to metabolic needs. Central control of vasomotor tone involves either direct central nervous system innervation or circulation hormones. Central control mainly affects the high-resistance arterioles and capacitance veins.

Local Control

Local regulation of tissue blood flow includes both myogenic and metabolic control mechanisms. ***Myogenic control*** involves the relationship between vascular, smooth-muscle tone and perfusion pressure. Myogenic control ensures relatively constant flows to the capillary beds despite changes in perfusion pressures.

Metabolic control involves the relationship between vascular, smooth-muscle tone and the level of local cellular metabolites. High amounts of carbon dioxide (CO_2) or lactic acid, low pH levels, low partial pressures of O_2 levels, histamines (released during an inflammatory response), endothelium-derived relaxing factor, and some prostaglandins all cause relaxation of the smooth muscle and vasodilation, increasing blood flow to the affected area.

The influence of myogenic and metabolic control mechanisms varies in different organ systems, with the brain being the most sensitive to changes in the local metabolite levels, particularly CO_2 and pH.[3]

Central Control

Central control of blood flow is primarily achieved by the sympathetic division of the autonomic nervous system. Smooth-muscle contraction and increased flow resistance are mostly caused by adrenergic stimulation and the release of norepinephrine. Smooth-muscle relaxation and vessel dilation is caused by stimulation of either *cholinergic* or specialized *β-adrenergic* receptors. Although the contractile response is distributed throughout the entire vascular system, the dilation response appears to be limited to the precapillary vessels. In addition to the sympathetic control, blood flow through the large veins can also be affected by abdominal and intrathoracic pressure changes.

MINI CLINI

Calculating Cardiac Output

Problem

How to calculate the CO of a patient with a resting HR of 70 beats/min and a measured stroke volume (SV) of 75 mL/beat?

Discussion

A normal resting CO of approximately 5 L/min can be calculated by substituting a normal HR (70 beats/min) and SV (75 mL, or 0.075 L, per contraction):

$$CO = 70\,\text{beats/min} \times 0.075\,\text{L/beat} = 5.25\,\text{L/min}$$

This calculation is a hypothetical average because actual CO normally varies according to a person's gender, height and weight, as well as being impacted by various diseases.

Regulation of Cardiac Output

The heart, similar to the vascular system, is regulated by both intrinsic and extrinsic factors. These mechanisms act together, along with vascular control, to ensure that the output of the heart matches the different needs of the tissues.

As previously discussed, the total amount of blood pumped by the heart per minute is called the *cardiac output* (CO). CO is simply the product of the HR and the volume ejected by the left ventricle on each contraction, or stroke volume (SV):

$$CO = HR \times SV$$

Regardless of an individual's state of health or illness, a change in CO must involve a change in SV, a change in HR or both. SV is affected primarily by intrinsic control of three factors: (1) preload, (2) afterload, and (3) contractility (all three factors are discussed subsequently). HR is affected primarily by extrinsic or central control mechanisms.[4,10]

Changes in Stroke Volume

The heart does not eject all of the blood it contains during systole. Instead, a small volume, called the **end-systolic volume (ESV)**, remains inside the ventricles. During the resting phase or diastole, the ventricles fill to a volume called the **end-diastolic volume (EDV)**. SV equals the difference between the EDV and the ESV, as follows:

$$SV = EDV - ESV$$

In a healthy person at rest, the EDV ranges from 110 to 120 mL. Given a normal SV of approximately 70 mL, a normal **ejection fraction** (EF), or proportion of the EDV ejected on each stroke, can be calculated as follows:

$$EF = \frac{SV}{EDV} \times 100$$
$$= \frac{70\,\text{mL}}{110\,\text{mL}} \times 100$$
$$= 64\%$$

As shown in Fig. 10.8, an increase in SV occurs when either the EDV increases or the ESV decreases. Conversely, a decrease

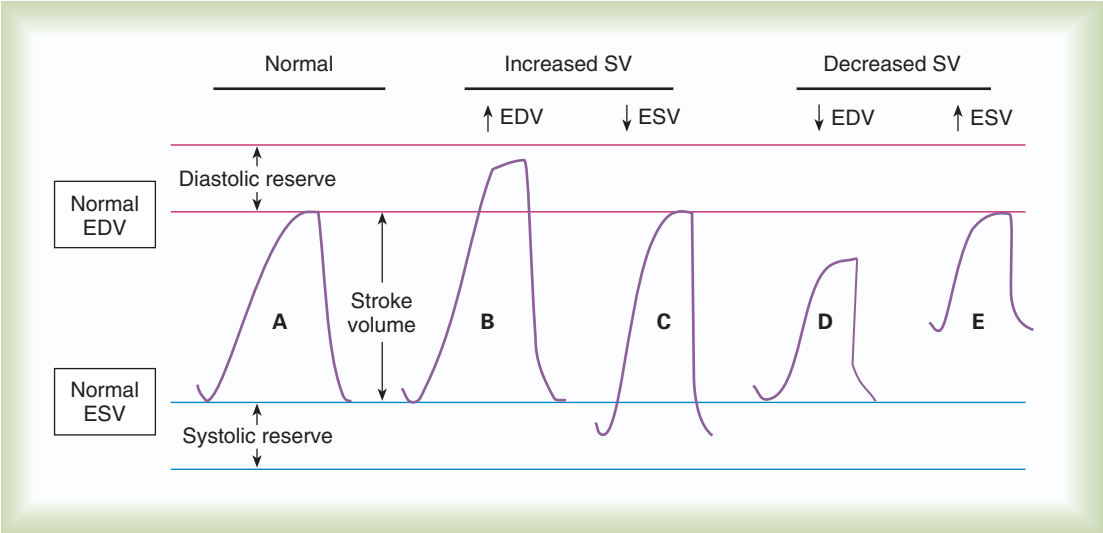


Fig. 10.8 Relationship between stroke volume *(SV),* end-diastolic volume *(EDV),* and end-systolic volume *(ESV).* (A) Normal relationship between EDV, ESV and SV; (B) increased SV resulting from increased EDV; (C) increased SV resulting from decreased ESV; (D) decreased SV resulting from decreased EDV (hypovolemia); and (E) decreased SV resulting from increased ESV (poor contractility).

MINI CLINI

Heart Failure and Cardiomyopathy

On each contraction, a healthy heart ejects approximately two-thirds of its stored volume (60% to 66%). Decreases in EF are normally associated with a weakened myocardium (**heart failure**), decreased contractility or both. When the EF decreases below 30%, a person's exercise tolerance becomes severely limited.[10]

Problem

Why does a patient with heart failure and low EF develop generalized weakness and difficulty breathing?

Discussion

A healthy heart beats about 60 to 100 times per minute to pump oxygenated blood throughout the body. Heart failure, also known as ***congestive heart failure (CHF),*** occurs when a person's heart is weakened and not able to pump blood the way it should, therefore the EF falls below normal, healthy levels. As a result, the body does not get enough blood—and the oxygen that blood cells carry—to maintain the body and its normal functions.

Low EF can be caused by many cardiac and vascular conditions such as cardiomyopathy, CAD, MI, heart valve disease and systolic heart failure (see Chapter 31).

in SV occurs when either the EDV decreases or the ESV increases. This relationship is key to understanding regulation of CO.

The heart's ability to change SV solely according to the EDV is an intrinsic regulatory mechanism. As mentioned before, according to the Frank-Starling law, the force the ventricle can generate results from the length (or stretch) of the myocardial fibers just before contraction. As the ventricle fills with blood, the myocardial fibers are stretched and as the stretch increases, the tension (force) within the walls of the heart increases (analogous to stretching a rubber band).[10]

The concepts of tension or force and filling volume are often described in terms of **preload** and **afterload** and as with many

TABLE 10.1 Factors Affecting Preload

Factor	Affect
End-diastolic filling pressure	Total blood volume
	Blood volume distribution
	Atrial contraction
	Venous compliance
	Total peripheral resistance
	Venous return
End-diastolic stretch	End-diastolic filling pressure
	Compliance of ventricle and pericardium
Myocardial wall thickness	Normal physiology
	Compensatory hypertrophy

Data from Chiumello D, Carlesso E, Cadringher P, et al: Lung stress and strain during mechanical ventilation for acute respiratory distress syndrome, *Am J Respir Crit Care Med* 15;178:346, 2008.

terms in medicine, the definitions of preload and afterload vary considerably in the literature.[13] This variability seems to be related to the term *load,* which in general means "a force against which something that causes motion (a pump or motor) acts." In the context of the cardiovascular system, the heart is analogous to a pump and force, in this sense, is related to stretch of the cardiac muscle according to the Frank-Starling Law.

Using this description of load and preload therefore represents the combined force of all the factors that contribute to ventricular wall stretch at the end of diastole. Preload may be calculated in a manner that recognizes the forces that stretch the resting cardiac muscle to a given length before contraction. Many factors determine preload, including venous return, total blood volume and distribution and atrial activity. These and the other factors that influence preload are summarized in Table 10.1.[13]

In a similar fashion, afterload can be described as the combined force of all the factors that the left ventricle encounters and must overcome when stimulated to contract and achieve the end of systole. Several factors determine afterload, most

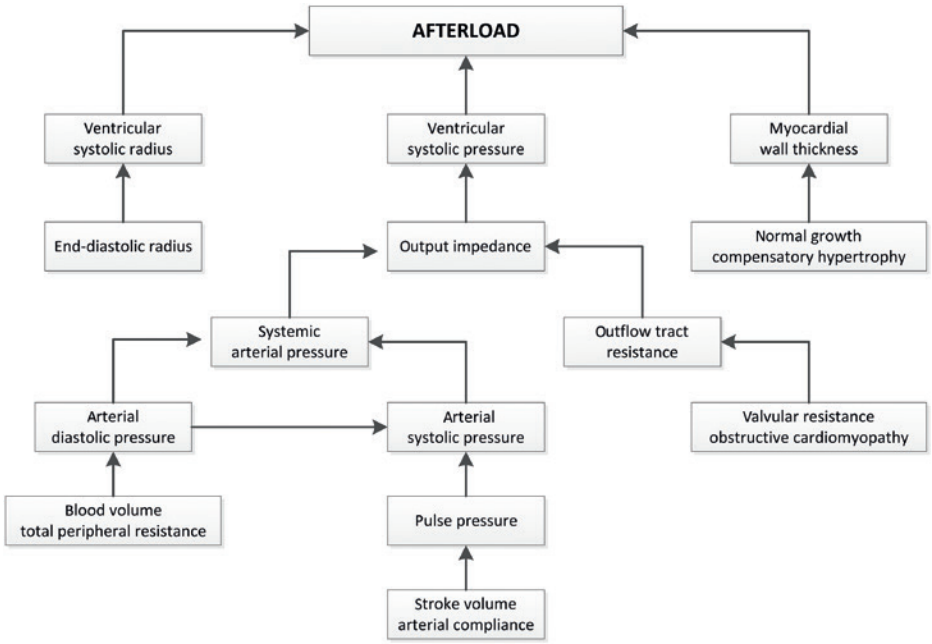


Fig. 10.9 Factors determining afterload within the cardiovascular system during systole. (From Norton JM: Toward consistent definitions for preload and afterload, *Adv Physiol Educ* 25:53, 2001.)

notably peripheral vascular resistance and the physical characteristics of arterial blood. These and the other factors that determine afterload are shown in Fig. 10.9.[13]

It should be noted that an increased preload or afterload caused by an abnormal increased downstream resistance over time can be "normalized" (up to a point) by increasing the wall thickness of the heart, which the body attempts to do by increasing muscle mass (hypertrophy), leading to cardiomyopathy and heart failure.[13]

RULE OF THUMB Increases in preload (EDV) and decreases in ESV result in increased SV in the healthy heart.

All else being constant, the greater the afterload on the ventricles the harder it is for the ventricles to eject their volume. For a given EDV, an increase in afterload means the ESV increased. If the EDV remains constant while the ESV increases, the SV (EDV-ESV) decreases (see Fig. 10.8). Normally, however, the healthy heart muscle responds to increased afterload by altering its contractility.

RULE OF THUMB Increases in afterload can decrease SV, especially in the failing heart by increasing the ESV.

Contractility represents the amount of systolic force exerted by the heart muscle at any given preload. At a given preload (or EDV), an increase in contractility results in an increased EF, a decreased ESV and an increased SV. Conversely, a decrease in contractility results in a decreased EF, an increased ESV and a decreased SV.

Changes in contractility affect the slope of the ventricular function curve (Figs. 10.10 and 10.11). A higher SV for a given preload (increased slope) indicates a state of increased contractility, often

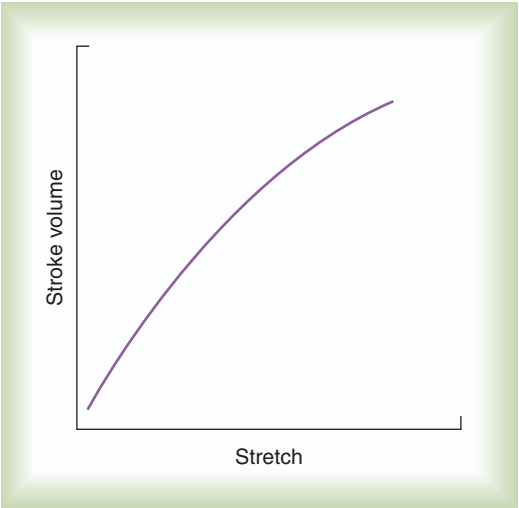


Fig. 10.10 The Frank-Starling law: stroke volume (SV) as a function of ventricular end-diastolic stretch. An increase in the stretch of the ventricles immediately before contraction (end-diastole) results in an increase in end-diastolic volume and SV. Ventricular end-diastolic stretch is synonymous with the concept of preload.

referred to as **positive inotropism**. The opposite is also true. A lower SV for a given preload indicates decreased contractility, referred to as **negative inotropism**. Drugs that increase contractility of the heart muscle are called *positive inotropes* and drugs that decrease contractility are *negative inotropes*.[10]

In addition to local mechanisms, cardiac contractility is influenced by neural control, circulating hormonal factors, and certain medications. Typically, neural or drug-mediated *sympathetic* stimulation has a positive inotropic effect. Conversely, *parasympathetic* stimulation exerts a negative inotropic effect. *Profound hypoxia* and *acidosis* impair myocardial function and decrease cardiac contractility.

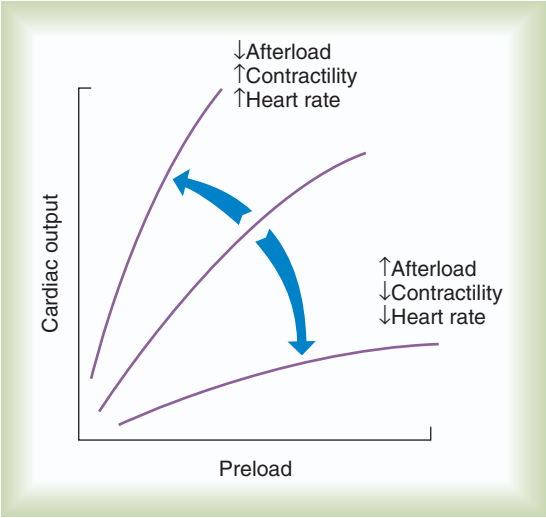


Fig. 10.11 Effects of preload, afterload, contractility and heart rate on cardiac output function curve. (Modified from Green JF: *Fundamental cardiovascular and pulmonary physiology*, ed 2, Philadelphia, 1987, Lea & Febiger.)

RULE OF THUMB Hypoxia and acidosis decrease cardiac contractility and output.

Changes in Heart Rate

The last factor influencing CO is HR. In contrast to the factors controlling SV, the factors affecting HR are mainly of central origin (i.e., neural or hormonal). Factors that increase HR are called *positive chronotropic* factors. Likewise, factors that decrease HR are called *negative chronotropic* factors.

RULE OF THUMB Increase in HR increases CO in a healthy heart up to a rate of 160 to 180 beats/min.

The combined effects of preload, afterload, contractility and HR on cardiac performance are graphically portrayed in Fig. 10.11. The middle curve represents the normal state and the upper, steeper curve represents a hyperdynamic heart. In the hyperdynamic heart, a given preload results in a greater than normal CO. Factors contributing to this state include decreased afterload, increased contractility (decreased ESV), and increased HR. The bottom curve has a lower slope than normal, indicating a hypodynamic heart. Factors contributing to this state include increased afterload, decreased contractility (increased ESV), and decreased rate. When the pumping efficiency of the heart is so low that CO is inadequate to meet tissues needs, the heart is said to be in CHF as discussed before.[4,10]

Cardiovascular Control Mechanisms

Cardiovascular control is achieved by integrating local and central regulatory mechanisms that affect both the heart and the vasculature. The goal is to ensure that all tissues receive sufficient blood flow to meet their metabolic needs; however, when demands are increased or abnormal, such as during exercise or massive bleeding, central mechanisms take over primary control.

MINI CLINI

Effect of Increased Afterload on Cardiac Output in a Normal Heart

Afterload is the resistance the ventricle must overcome or the forces that oppose ejection of blood pressure generated as the heart works to eject its SV. As afterload increases, the SV ejected by the ventricle decreases, assuming that the contractility of the heart (force with which the heart contracts) remains constant.

Problem

During exercise, a healthy person's blood pressure increases considerably, indicating that the afterload has increased. Yet the SV and CO in a healthy heart do not decrease. Why is this so?

Discussion

When afterload increases, the initial ventricular contractions that experience the increased afterload produce smaller SVs, which causes more blood to remain in the ventricle at the end of systole (i.e., ESV is increased). During the subsequent diastole, blood rushes in from the atria to fill the ventricles, and because of the higher-than-normal ESV, the ventricles become more distended and stretched. Healthy heart muscle responds to increased stretch in a way described by the Frank-Starling law; that is, the heart now contracts with greater force than before, ejecting a greater SV. By increasing contractility in this fashion, SV and CO are not compromised by increased afterload in a healthy heart.

As expected, CO increases and decreases with similar changes in HR; however, this relationship is only maintained up to approximately 160 to 180 beats/min in a healthy heart. At higher HRs, there is not enough time for the ventricles to fill completely between each heartbeat, causing a decrease in EDV, SV, and CO. Even worse, as the HR exceeds this level, oxygen consumption of the heart increases and coronary perfusion decreases, further comprising the patient. This phenomenon often occurs at significantly less than 160 beats/min in the failing heart.

RULE OF THUMB Under normal conditions, blood flow to a specific vascular bed is primarily regulated by local mechanisms.

Central control of cardiovascular function occurs by the interaction between the brainstem and selected peripheral receptors (Fig. 10.12). The brainstem constantly receives feedback from these receptors about the pressure, volume and chemical status of the blood. The brainstem also receives input from higher brain centers, such as the hypothalamus and cerebral cortex. These inputs are integrated with the inputs coming from the heart and blood vessels to maintain adequate blood flow and pressure in all but the most abnormal conditions.[4]

Cardiovascular Control Centers

Fig. 10.12 is a simplified diagram of the cardiovascular regulatory centers. Areas in the medulla receive input from higher brain centers, peripheral pressure and chemical receptors. Stimulation of the vasoconstrictor area within the medulla causes vasoconstriction and increased vascular resistance.

Closely associated with the vasoconstrictor center is a cardioaccelerator area. Stimulation of this center increases HR by increasing sympathetic discharge to the SA and AV nodes of the heart. A cardioinhibitory area plays the opposite role. Stimulation

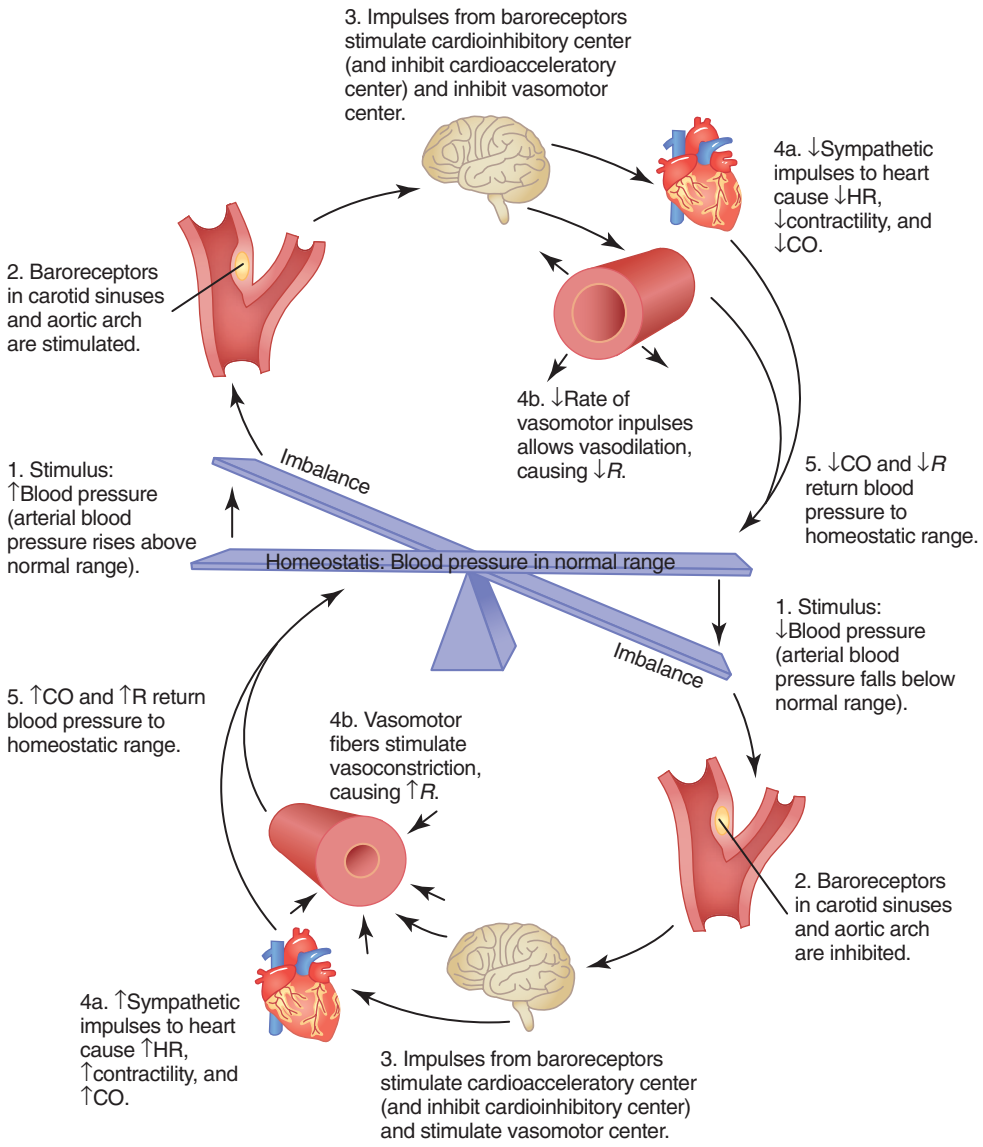


Fig. 10.12 Simplified diagram of cardiovascular regulatory centers. *CO,* Cardiac output; *HR,* heart rate; *R,* resistance. (Modified from Marieb EN, Hoehn KN: *Anatomy and physiology*, ed 4, San Francisco, 2011, Pearson Benjamin Cummings.)

MINI CLINI

Heart Rate and the Administration of Bronchodilator Drugs

Problem

You are giving a bronchodilator-aerosolized drug to a patient and you notice a significant increase in the patient's HR. Would you expect increased HR to be a common side effect of pulmonary bronchodilators?

Discussion

The discharge rate of the sinus node and the HR are increased by sympathetic nervous stimulation and decreased by parasympathetic nervous stimulation. The airways of the lung are dilated by sympathetic nervous stimulation and constricted by parasympathetic stimulation. Drugs that cause bronchodilation either mimic sympathetic stimulation (sympathomimetic) or block parasympathetic stimulation (parasympatholytic). Both of these drug actions can also cause the HR to increase (see Chapter 36).

of this center decreases HR by increasing vagal (parasympathetic) stimulation to the heart.

Higher brain centers also influence the cardiovascular system, both directly and through the medulla. Signals coming from the cerebral cortex in response to exercise, pain or anxiety pass directly through the cholinergic fibers to the vascular smooth muscle, causing vasodilation. Signals from the hypothalamus, in particular its heat-regulating areas, indirectly affect HR and vasomotor tone through the cardiovascular centers.

The cardiovascular centers are also affected by local chemical changes in the surrounding blood and cerebrospinal fluid. Decreased levels of CO_2 tend to inhibit the medullary centers and general inhibition of these centers causes a decrease in vascular tone and a decrease in blood pressure. A local decrease in O_2 tension has the opposite effect. Mild hypoxia in this area increases sympathetic discharge rates, which tends to elevate both HR and blood pressure; however, severe hypoxia has a depressant effect.

Peripheral Receptors

In addition to high-level and local input, the cardiovascular centers receive signals from peripheral receptors (see Fig. 10.12). There are two types of peripheral cardiovascular receptors: **baroreceptors**, or stretch receptors, and **chemoreceptors**. Baroreceptors respond to pressure changes, whereas chemoreceptors respond to changes in blood chemistry.[4]

The cardiovascular system has two different sets of baroreceptors. The first set is located in the aortic arch and carotid sinuses and these receptors monitor arterial pressures generated by the left ventricle. The second set is located in the walls of the atria and the large thoracic and pulmonary veins and these low-pressure sensors respond mainly to changes in vascular volumes. Baroreceptor output is directly proportional to the stretch on the vessel wall. The greater the blood pressure, the greater is the stretch and the higher the rate of neural discharge to the medulla.

Together with the cardiovascular regulatory centers, these receptors form a **negative feedback loop**, where stimulation of a receptor causes an opposite response by the effector. In the case of the arterial receptors, an increase in blood pressure increases aortic and carotid receptor stretch and their neuronal discharge rates. The increased discharge rates cause an opposite response by the medullary centers (i.e., depressor response decreasing blood pressure). Decreased blood pressure (decreased baroreceptor output) has the opposite effect, causing peripheral vessel constriction and increased HR and contractility. This mechanism usually restores blood pressure to normal (see Fig. 10.12).[3,4]

Although the high-pressure arterial receptors constantly control blood pressure, the low-pressure sensors are responsible for long-term regulation of plasma volume. The low-pressure atrial and venous baroreceptors regulate plasma volume mainly by activating several chemical and hormonal mechanisms. Table 10.2 provides a detailed description of some of these mechanisms.

The major pathways for plasma-volume control are outlined in Fig. 10.13. Combined with a central nervous system-mediated increase in renal filtration, these humoral mechanisms decrease the overall plasma volume. A decrease in blood volume has the

TABLE 10.2 Hormonal Control Mechanisms Affecting Blood Pressure

Hormone	Place of Action	Effect
Angiotensin II	Arterioles	↑ SVR (vasoconstriction)
Antidiuretic hormone	Kidneys	↑ Blood volume (↑water retention)
	Arterioles	↑ SVR (vasoconstriction)
Atrial natriuretic peptide	Arterioles	↓ SVR (vasodilation)
Aldosterone	Kidneys	↑ Blood volume (↑water and salt retention)
Cortisol	Kidneys	↑ Blood volume (↑water and salt retention)
Norepinephrine	Heart (β-1 receptors)	↑ Cardiac output (HR and contractility)
	Arterioles (α receptors)	↑ SVR (vasoconstriction)

HR, Heart rate; *SVR,* systemic vascular resistance.

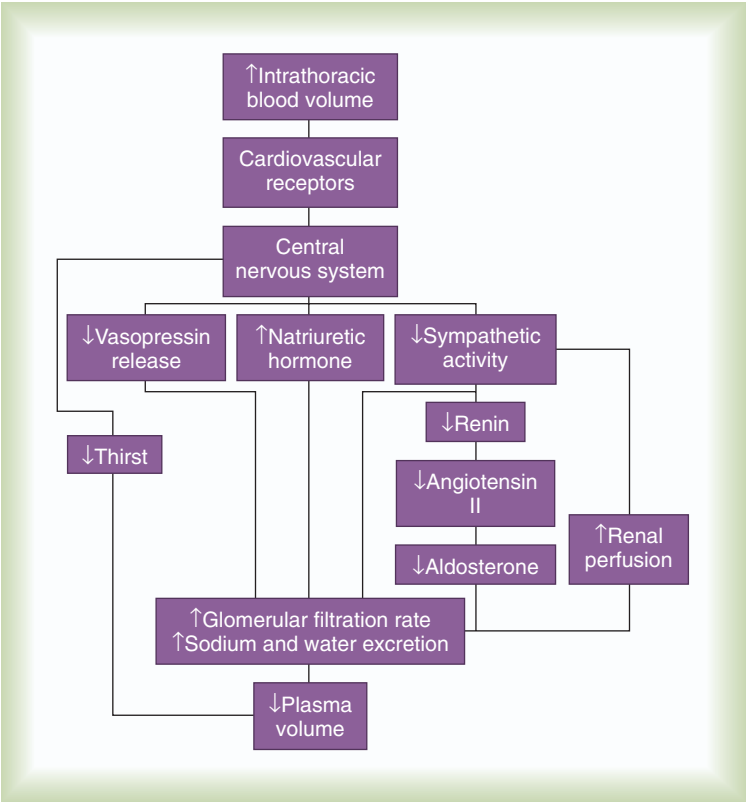


Fig. 10.13 Major Pathways for Plasma Volume Control. See text for details. (Modified from Smith JJ, Kampine JP: *Circulatory physiology: the essentials*, ed 3, Baltimore, 1990, Williams & Wilkins.)

opposite effect (i.e., sodium and water retention and an increase in plasma volume).

Chemoreceptors are small, highly vascularized tissues located near the high-pressure sensors in the aortic arch and carotid sinus that are sensitive to changes in blood chemistry. They are strongly stimulated by decreased O_2 tensions, low pH or high levels of CO_2. Simply put, the major cardiovascular effects of chemoreceptor stimulation are vasoconstriction and increased HR.

RULE OF THUMB As the arterial oxygen content or the pH drops, chemoreceptors will cause an increased in the HR and systemic vasoconstriction.

These changes occur only when the cardiopulmonary system is overtaxed and so the chemoreceptors probably have little influence under normal conditions; however, their influence on respiration is clinically important and therefore discussed in greater detail in Chapter 9.

Blood Volume Regulation

The coordinated response of the cardiovascular system is best shown under abnormal or stressful conditions. Among the most common clinical conditions in which all essential regulatory mechanisms come into play is the large blood loss that occurs with hemorrhage. Fig. 10.14 illustrates changes in these key factors during progressive blood loss in an animal model.

With 10% blood loss, the immediate decline in the CVP causes a 50% decrease in the discharge rate of the low-pressure (atrial) baroreceptors; however, there is little change in the activity of the high-pressure (arterial) receptors. The initial response, mediated through the medullary centers, is an increase in sympathetic discharge to the sinus node, which causes a progressive increase in HR. At the same time, plasma levels of antidiuretic hormone (vasopressin) begin to increase and thus maintaining normal arterial blood pressure.

As the blood loss becomes more severe (20%), atrial receptor activity decreases further, which increases the intensity of sympathetic discharge from the cardiovascular centers. Plasma antidiuretic hormone and HR continue to increase, as does peripheral vasculature tone. An increase in vascular tone occurs through the constriction of the capacitance vessels in the venous system, slowing the decrease in CVP.[4]

The arterial pressure does not start to decrease until blood loss approaches 30%. At this point, arterial receptor activity begins to decrease, resulting in a marked increase in systemic vascular tone. Despite the magnitude of blood loss, CVP levels off. If no further hemorrhage occurs, blood pressure and tissue perfusion can be maintained at adequate levels.

If blood loss continues, however, central control mechanisms begin to take over, causing massive peripheral vasoconstriction, shunting blood away from skeletal muscle to maintain blood flow to the brain and heart. Increasing levels of local metabolites such as CO_2 and other acids override central control and cause further vessel dilation and increased blood flow to these vital organs; however, as these metabolites build up, tissues become hypoxic, cardiac function becomes impaired and vasodilation occurs throughout the body. In such an instance, this vasodilation signals the onset of late stage and irreversible hypovolemic shock, after which death often occurs. Similar events can occur in the presence of severe dehydration and volume depletion by other means such as severe vomiting and diarrhea.

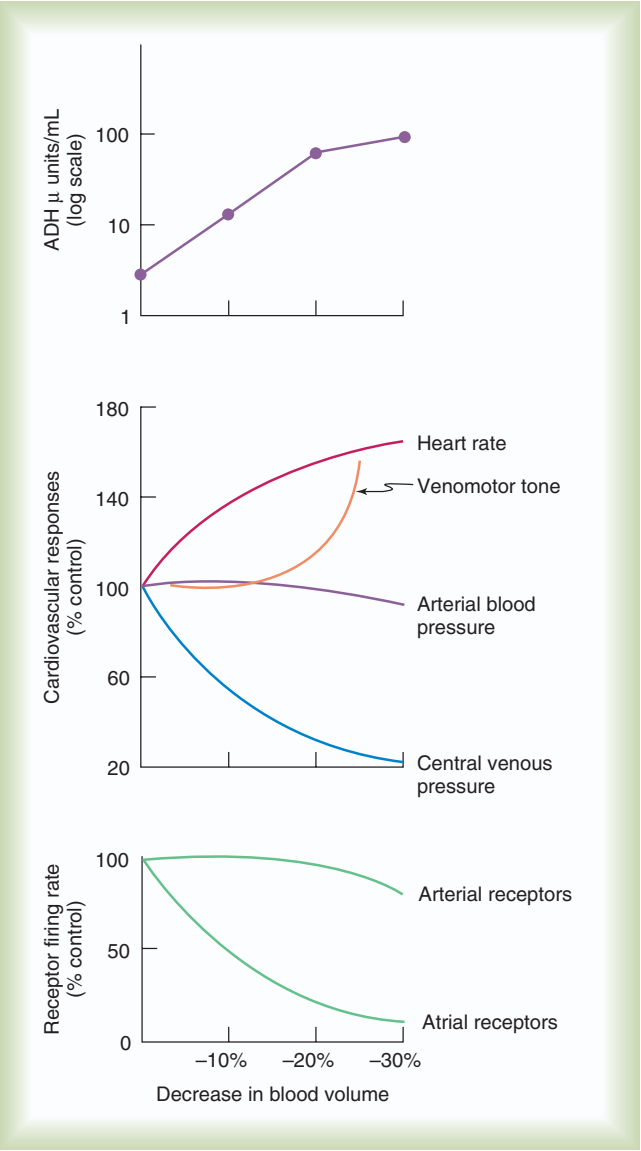


Fig. 10.14 Plasma levels of antidiuretic hormone *(ADH),* cardiovascular responses and receptor firing rates in response to graded hemorrhage in the dog. See text for details. (From Richardson DR: *Basic circulatory physiology*, Boston, 1976, Little, Brown; venomotor tone data are those of W. Sears J, as cited in Gauer OH, Henry JP, Behn C: The regulation of extracellular fluid volume, *Annu Rev Physiol* 32:547, 1970. All other data are from Henry JP, et al: *Can J Physiol Pharmacol* 46:287, 1968.)

EVENTS OF THE CARDIAC CYCLE

This chapter has emphasized the mechanical properties of the heart; the electrical activities of the heart are discussed in Chapter 18. Although they are discussed separately, the mechanical and electrical events are interdependent. Given the role of RTs in dealing with cardiovascular problems, in-depth knowledge of how these events relate is quite useful.[3]

The events of the cardiac cycle are depicted in Fig. 10.15. The top of the figure shows a time axis scaled in tenths of a second;

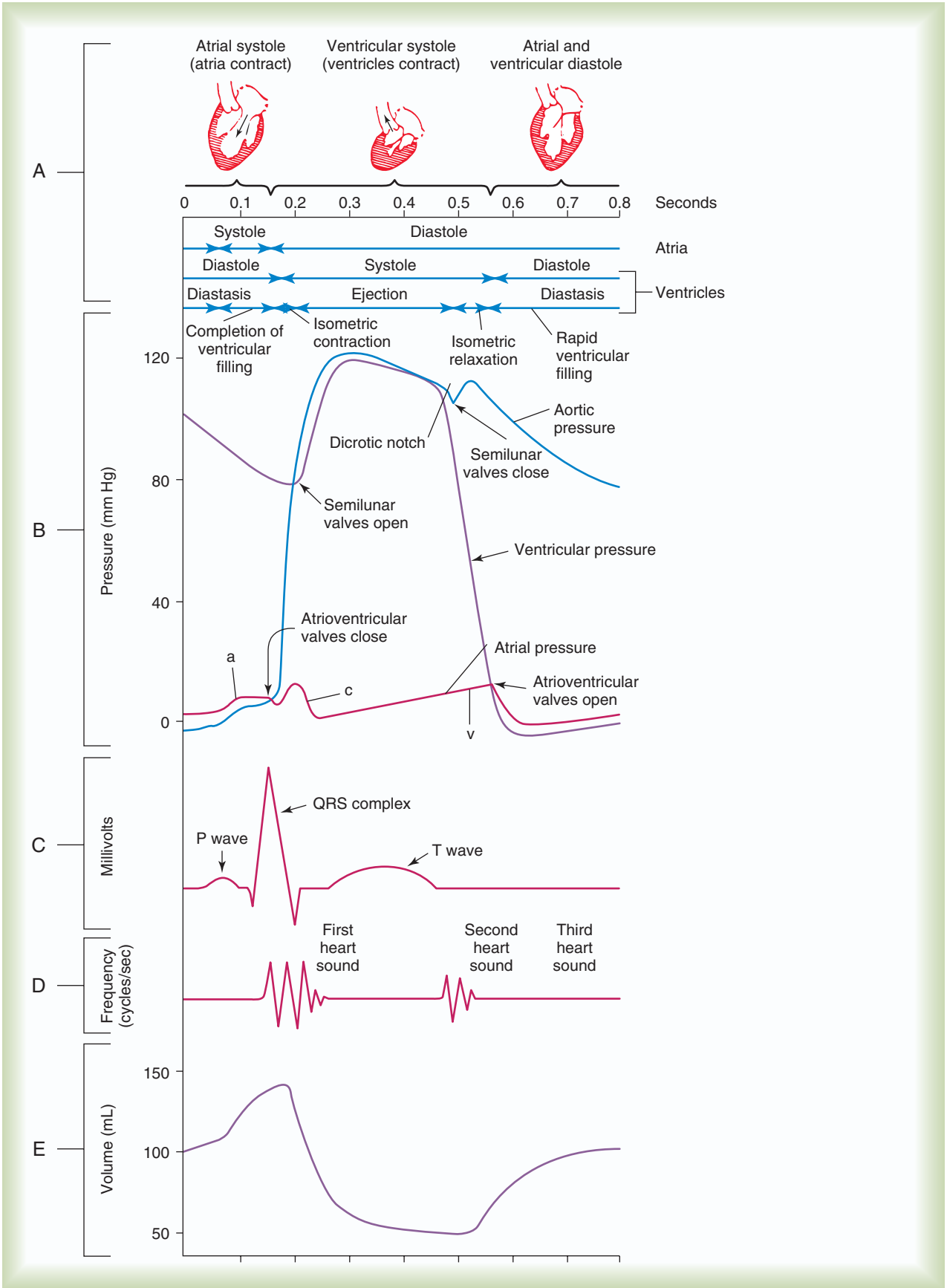


Fig. 10.15 Cardiac Cycle. (A) Timing of cardiac events. (B) Simultaneous pressures created in the aorta, left ventricle and right atrium during the cardiac cycle. (C) Electrical activity during the cardiac cycle. (D) Heart sounds corresponding to the cardiac cycle. (E) Ventricular blood volume during the cardiac cycle. (Modified from Moffett DF, Moffett SB, Schauf CL: *Human physiology: foundations and frontiers*, ed 2, St Louis, 1993, Mosby.)

next are the timing bars for ventricular systole and diastole and pressure events in the atria, ventricles and aorta; these are followed by an ECG, heart sounds, and ventricular flow (see Chapter 18 for an explanation of the ECG waves).

Going from left to right, the **P wave** (atrial depolarization) begins the ECG. Earlier, the ventricles have been passively filling with blood through the open AV valves. Within 0.1 seconds, the atria contract, causing a slight increase in both atrial and ventricular pressures *(**a waves**)*. This atrial contraction helps preload the ventricles, increasing their volume by 25%. This help from the atria to ventricular filling is called the ***atrial kick***. Toward the end of diastole, the electrical impulses from the atria reach the AV node and bundle branches and ventricular depolarization (QRS complex) is initiated. Within a few hundredths of a second after depolarization, the ventricles begin to contract. As soon as ventricular pressures exceed pressures in the atria, the AV valves close, with closure of the mitral valve occurring first, followed immediately by the closure of the tricuspid valve. This closure marks the end of ventricular diastole, producing the first heart sound on the phonocardiogram.[3]

Immediately after AV valve closure, the ventricles become closed chambers. During this short isovolemic phase of contraction, ventricular pressures increase rapidly. Upward bulging of the AV valves during this phase causes a slight upswing in atrial pressure graphs, called the ***c wave***. Within 0.05 seconds, ventricular pressures increase to exceed the pressures in the aorta and pulmonary artery and open the semilunar valves.

Toward the end of systole, as repolarization starts (indicated by the **T wave**), the ventricles begin to relax. Consequently, ventricular pressures decrease rapidly. When arterial pressures exceed pressures in the relaxing ventricles, the semilunar valves shut. Closure of the semilunar valves generates the second heart sound. Rather than immediately dropping off, aortic and pulmonary pressures increase again after the semilunar valves close. The ***dicrotic notch*** is caused by the elastic recoil of the arteries. This recoil provides the extra "push" that helps maintain the pressure created by the ventricles.

As the ventricles continue to relax, their pressures decrease to less than the pressures in the atria and this decline in pressure reopens the AV valves. As soon as the AV valves open, the blood collected in the atria rushes to fill the ventricles, causing a rapid decrease in atrial pressures (the ***v wave***). Subsequently, ventricular filling slows as the heart prepares for a new cycle.

Knowledge of these events can help in understanding many of the diagnostic and monitoring procedures used for patients with cardiopulmonary disorders, including balloon-directed pulmonary artery catheterization and direct arterial pressure monitoring.

SUMMARY CHECKLIST

- The heart is a four-chambered muscular organ approximately the size of a fist. It is positioned in the mid mediastinum of the chest, behind the sternum.
- The cardiovascular system consists of the heart and a vascular network that accounts for normal distribution and regulation of blood flow throughout the body to ensure tissue perfusion.
- Inflammation of the pericardium results in a clinical condition called pericarditis.
- An abnormal amount of fluid can accumulate between the pericardial layers, resulting in a pericardial effusion. A large pericardial effusion may lessen the pumping function of the heart, resulting in cardiac tamponade.
- The two lower-heart chambers, or ventricles, make up the bulk of the heart''s muscle mass and do most of the pumping that circulates the blood.
- Common valve problems include regurgitation and stenosis. Regurgitation is the backflow of blood through a malfunctioning valve. Stenosis is a pathologic narrowing or constriction of a valve outlet, which causes blood to back up and results in increased pressure in the proximal chamber and vessels. Both conditions affect cardiac performance.
- The heart's circulatory system is called the coronary circulation. To meet the heart's needs, the coronary circulation provides an extensive network of branches to all myocardial tissue.
- Complete obstruction of a coronary artery may cause tissue death or infarct, a condition called myocardial infarction (MI).
- ACS is the name given to three types of CAD that are associated with gradual and/or sudden obstruction of the coronary arteries: (1) unstable angina or angina pectoris, (2) NSTEMI, and (3) STEMI.
- Heart diseases remain responsible for approximately one third of all deaths in individuals over the age of 35.7 years. Nearly one-half of all middle-aged men and one-third of middle-aged women in the USA will develop some manifestation of a CHD.
- Symptoms of a MI include tightness or pain in the chest, neck, back or arms, as well as fatigue, lightheadedness, abnormal heartbeat and anxiety. Women are more likely to have atypical symptoms than men.
- The thebesian veins bypass or shunt around the pulmonary circulation as part of the normal anatomy, this phenomenon is called an anatomic shunt. When combined with a similar bypass in the bronchial circulation, these normal anatomic shunts account for approximately 2% to 3% of the total CO.
- Myocardial tissue possesses the following four key properties: excitability, inherent rhythmicity or automaticity, conductivity and contractility.
- During a resuscitation attempt even in the presence of a "normal" cardiac rhythm in a monitor but with an absent pulse, chest compressions must continue to guarantee adequate perfusion to central organs.
- Mechanical and electrical properties of cardiac tissue, combined with internal and external control mechanisms, provide the basis for coordinated cardiac function.
- According to the Frank-Starling law, the more a cardiac fiber is stretched (up to a point), the greater the tension it generates when contracted.
- The systemic circulation has three major components: (1) arterial system, (2) capillary system, and (3) venous system. These vessels regulate not only the amount of blood flow per minute (CO) but also the distribution of blood to organs and tissues (perfusion).

- The venous system consists of small, expandable venules and veins and larger, more elastic veins. Besides conducting blood back to the heart, these vessels act as a reservoir for the circulatory system.
- The heart is a single organ, but it functions as two separate pumps. The right side of the heart generates a systolic pressure of approximately 25 mm Hg to drive blood through the *low-resistance, low-pressure* pulmonary circulation. The left side of the heart generates systolic pressures of approximately 120 mm Hg to propel blood through *the higher pressure, high-resistance* systemic circulation.
- The sum of all frictional forces opposing blood flow through the systemic circulation is called systemic vascular resistance (SVR).
- According to Ohm's law, changes in resistance are the primary means by which blood flow is regulated within organs because control mechanisms in the body generally maintain arterial and venous blood pressures within a narrow range.
- Resistance to blood flow in the pulmonary circulation is approximately *one-tenth* of the systemic circulation.
- The vascular system is regulated by local and central control mechanisms.
- CO is primarily determined by four factors: preload, afterload, contractility and HR and is equivalent to the product of the SV × HR.
- Increased HR decreases CO by decreasing filling times (decreasing EDV) and decreasing contraction times, hence increasing ESV.
- To avoid organ and tissue damage and maintain adequate perfusion pressures under changing conditions, the cardiovascular system attempts to balance relative volume and resistance.
- The cardiovascular system regulates blood flow mainly by altering the capacity of the vasculature and the volume of blood it holds.
- Central control of blood flow is primarily achieved by the sympathetic division of the autonomic nervous system.
- Blood pressure is regulated by changing the volume of circulating blood, changing the capacity of the vascular system, or both.
- The body can generally maintain adequate blood (and perfusing) pressures until blood loss reaches or exceeds approximately 30%, at which point hypovolemic shock is likely, and death may even occur. During increased demand, special compensatory mechanisms are called on to maintain stable blood flow.
- SV is affected primarily by intrinsic control of three factors: (1) preload, (2) afterload, and (3) contractility.
- Preload represents the combined force of all the factors that contribute to ventricular wall stretch at the end of diastole. Many factors determine preload, including venous return, total blood volume and distribution and atrial activity.
- Afterload can be described as the combined force of all the factors the ventricles encounter and must overcome when stimulated to contract and achieve the end of systole.
- Several factors determine afterload; most notably peripheral vascular resistance and the physical characteristics of arterial blood.
- All else being constant, the greater the afterload on the ventricles, the harder it is for the ventricles to eject their volume.
- EF is the proportion of the EDV ejected on each stroke (SV/EDV).
- Low EF can be caused by many cardiac and vascular conditions such as cardiomyopathy, CAD, MI, heart valve disease and systolic heart failure.
- Heart failure, also known as CHF, occurs when a person's heart is weakened and not able to pump blood the way it should, therefore the EF falls below normal, healthy levels.
- Factors that increase HR are called positive chronotropic factors. Likewise, factors that decrease HR are called negative chronotropic factors.
- Failure of cardiovascular control mechanisms often requires clinical intervention to help restore normal function.

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11

Ventilation

Eduardo Mireles-Cabodevila

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Describe the physiologic functions provided by ventilation.
- Describe the pressure gradients responsible for gas flow, diffusion, and lung inflation.
- Identify the forces that oppose gas movement into and out of the lungs.
- Describe how surface tension contributes to lung recoil.
- Describe how lung, chest wall, and total compliance are related.
- State the factors that affect resistance to breathing.
- Describe how various lung diseases affect the work of breathing.
- State why ventilation is not evenly distributed throughout the lung.
- Describe how the time constants affect alveolar filling and emptying.
- Identify the factors that affect alveolar ventilation.
- State how to calculate alveolar ventilation, dead space, and the V_D/V_T ratio.

CHAPTER OUTLINE

KEY TERMS

airway resistance
alveolar dead space
compliance
dynamic compression
dynamic hyperinflation (air trapping)
elastance
elasticity
equal pressure point (EPP)
hyperventilation
hypoventilation
hysteresis
minute ventilation
physiologic dead space
plethysmograph
pneumotachometer
pressure gradient
sub-atmospheric
surface tension
tidal volume (V_T)
transairway pressure gradient
transairway pressure (P_{TAW})
transalveolar pressure (P_{TA})
trans–chest wall pressure (P_{TCW})
transmural pressure
transpulmonary pressure difference (P_{TP})
transpulmonary pressure gradient
transrespiratory pressure (P_{TR})
transthoracic pressure difference (P_{TT})
ventilation

The main functions of the lungs are to supply the body with oxygen and to remove carbon dioxide. To perform these functions, an adequate amount of gas must move from the trachea to the alveoli and then out of the lung.

Ventilation is the process of moving gas (usually air) in and out of the lungs. Ventilation is to be distinguished from respiration, which refers to the physiologic processes of using O_2 by the tissues at the cellular level.

The amount of air movement (ventilation) is regulated to meet the body's needs under a wide range of conditions (e.g., exercise). In disease, this process can be markedly disrupted and often results in inadequate ventilation and/or increased work of

breathing. Respiratory care is directed toward restoring and supporting adequate and efficient ventilation. To provide effective respiratory care, the respiratory therapist (RT) must have a solid understanding of the normal ventilation processes and of how diseases may affect it.

MECHANICS OF VENTILATION

Ventilation occurs in a cycle with two phases: inspiration and expiration. During each cycle, a volume of gas moves in and out of the respiratory tract. This volume, measured during either inspiration or expiration, is called the **tidal volume (V_T)**. The V_T refreshes the gas present in the lung, removing CO_2 and supplying O_2 to meet metabolic needs. The V_T must be able to meet changing metabolic demands, such as during exercise or sleep. To achieve ventilation, the respiratory muscles (and/or a mechanical ventilator) have to generate changes in pressure (a pressure gradient, see later discussion) so that gas will flow in or out of the lungs. To better understand the forces that the muscles (or/and the machine) have to overcome to generate ventilation, we use a formula. This formula is a simplified version of the so-called "equation of motion" for the respiratory system:

$$\Delta\text{Pressure} = (\text{Elastance} \times \Delta\text{Volume}) + (\text{Resistance} \times \Delta\text{Flow})$$

where:

ΔPressure = Force generated by the respiratory muscles or a mechanical ventilator, or both, during inspiration. This "pressure" is actually a pressure difference or gradient, that is, the difference in pressure (see next section).

Volume = Change in volume (e.g., V_T, amount of air inspired in a usual breath)

Elastance = Distensibility of the lungs and thorax (Δpressure/Δvolume); elastance is the reciprocal of compliance (Δvolume/Δpressure)

Resistance = Airflow and tissue resistance (Δpressure/Δflow)

Flow = Volume change per unit of time

In this equation, the terms *(elastance × volume)* and *(resistance × flow)* represent the loads (elastic and resistive) against which the respiratory muscles or ventilator must work to achieve gas movement. Thus, you can now see that in patients with high elastance or/and high resistance, the pressure needed to move gas and achieve ventilation will be high. In healthy lungs, this work is minimal and is performed only during the inspiratory phase. Normally, expiration is passive (i.e., no muscle force is involved) as energy stored from the work of inspiration is released (i.e., through the elastic recoil of the lung and chest wall, which will return to their resting volume).

In discussing ventilation, it may be helpful to review some details about the equation of motion. First, remember that it is a mathematical model. This model simplifies the respiratory system into a single resistance and a single elastance. That is, it combines all the resistances of the many airways into a single flow-conducting tube and lumps *all* the elastances of the alveoli and airways into a single elastic compartment (see later discussions about elastance, compliance, and resistance). The graphic model is shown in Fig. 11.1.[1] Surrounding the "lungs" is another elastic compartment representing the chest wall. This graphic depiction of the respiratory system allows us to define points in space where pressures may be measured (or inferred) as defined in Table 11.1.

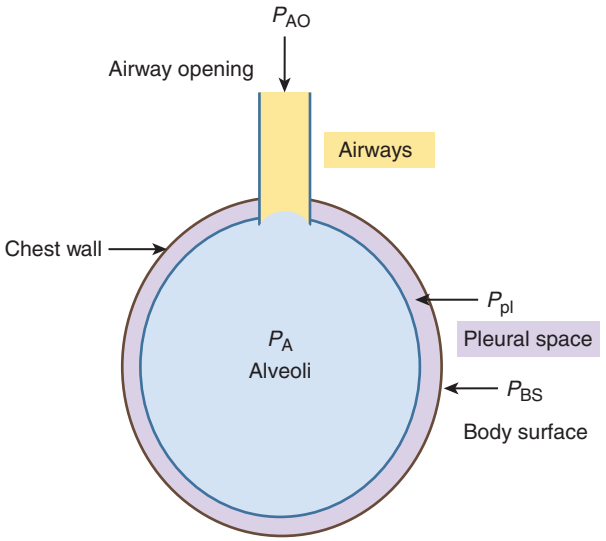

Fig. 11.1 Schematic diagram of the respiratory system consisting of an airway connected to a single alveoli (representing the lungs) surrounded by the chest wall. P_A, Alveolar pressure; P_{AO}, pressure at the airway opening; P_{BS}, pressure on the body surface; P_{pl}, pressure in the intrapleural space.

TABLE 11.1 Measurable Pressures Used in Describing Respiratory System Mechanics

Name	Symbol	Definition
Pressure at the airway opening	P_{AO}	Pressure measured at the opening of the respiratory system airway (e.g., mouth and nose, tracheostomy opening, and endotracheal tube opening)
Pleural pressure	P_{pl}	Pressure measured in the pleural space, changes that are often estimated by measuring pressure changes in the esophagus
Alveolar pressure	P_A	Pressure in the alveolar (gas space) region of the lungs
Body surface pressure	P_{BS}	Pressure measured at the body surface

Pressure Differences During Breathing

A pressure gradient is needed to achieve gas flow from one place to another. Air rushing out of a punctured tire moves from higher pressure inside the tire to a lower pressure outside the tire (i.e., down a pressure gradient). Using the equation of motion, we can recognize the pressure gradients or differences in pressure between two points in space in each of the components of the model. The discussion that follows will focus on various compartments or individual components of the total respiratory system. The individual components of the model (airways, lungs, and chest wall) are *defined as everything that exists between these points in space*. Let's define each of these pressure gradients across different compartments.

Starting with the whole system, the *respiratory system* is everything that exists between the pressure measured at the airway opening (P_{AO}) and the pressure measured at the body surface (P_{BS}). The pressure difference is called the **transrespiratory pressure (P_{TR})**:

$$P_{TR} = P_{AO} - P_{BS}$$

The term P_{AO} comes before the term P_{BS} in the equation. This order is dictated by the direction of flow; at end inspiration, air pressure inside the lung exceeds the pressure outside the lung, so that gas flows out of the lung when expiration begins. During mechanical ventilation, at the end of inspiration, P_{AO} is higher than P_{BS}, and P_{TR} is calculated by subtracting P_{BS} from P_{AO}. The same general principle applies to all the other pressure differences described subsequently. The components of transrespiratory pressure correspond to all the components of the graphic model (i.e., airways, lungs, and chest wall). We can further divide these components and their pressure gradients. Starting at the airways in this model, the pressure gradient across the airways is whatever exists between P_{AO} and pressure measured in the alveoli of the lungs (P_A). The graphic model makes the lungs look like one giant alveolus, which means that alveolar pressure represents an average pressure over all alveoli in real lungs. This pressure difference is called the **transairway pressure (P_{TAW})**:

$$P_{TAW} = P_{AO} - P_A$$

Thus, P_{TAW} represents all the airways (physiological and artificial).

The alveolar region is whatever exists between pressure measured in the alveolus and pressure measured in the pleural space (P_{pl}). This associated pressure difference is **transalveolar pressure (P_{TA})**:

$$P_{TA} = P_A - P_{pl}$$

The P_{TA} represents all the alveoli as if they were one single alveolus.

We also take into account the chest wall. The pressure across the chest wall is the difference between the pressure measured in the pleural space and the pressure on the body surface. The pressure difference is called **trans–chest wall pressure (P_{TCW})**:

$$P_{TCW} = P_{pl} - P_{BS}$$

Some of these components can be combined to encompass structures that are clinically important. One of the most useful combinations bundles together the airways (P_{TAW}) and the alveolar region (P_{TA}) to assess the whole pulmonary system (airways and alveoli), and this is called the **transpulmonary pressure difference (P_{TP})**:

$$P_{TP} = P_{AO} - P_{pl}$$

What may be confusing is that there are other definitions of transpulmonary pressure in the literature. Some authors define P_{TP} as $P_A - P_{pl}$ (i.e., the difference between the pressure in the alveoli and the pleura). The confusion arises from the fact that $P_{TA} = P_{TP} = P_A - P_{pl}$, *but only under static conditions* (i.e., when there is no movement of air occurring). Static conditions can be imposed during mechanical ventilation by using an inspiratory or expiratory hold maneuver which stops air from flowing. This situation should be considered a special case of P_{TP}; however, the general case is $P_{TP} = P_{AO} - P_{pl}$, which shows what pressures must be measured to derive the mechanical properties of the pulmonary system under either static or dynamic (active breathing when air is moving) conditions. If we want to evaluate the elastance and resistance of *the pulmonary system,* we substitute P_{TP} for P in the equation of motion. Alternatively, if we want to evaluate the *total respiratory system* elastance and resistance, we substitute P_{TR} for P.

TABLE 11.2 Pressure Differences Used in Describing Respiratory System Mechanics

Definition	Name	Symbol
$P_{AO} - P_{BS}$	Transrespiratory pressure difference	ΔP_{TR}
$P_{AO} - P_A$	Transairway pressure difference	ΔP_{TAW}
$P_{AO} - P_{pl}$	Transpulmonary pressure difference	ΔP_{TP}
$P_A - P_{pl}$	Transalveolar pressure difference	ΔP_{TA}
$P_A - P_{BS}$	Transthoracic pressure difference	ΔP_{TT}
$P_{pl} - P_{BS}$	Trans–chest wall pressure difference	ΔP_{TCW}
	Global muscle pressure difference	ΔP_{mus}

Sometimes, it may be useful to define the pressure required to expand the lung and chest wall components; to do this, we use the **transthoracic pressure difference (P_{TT})**, which is defined as:

$$P_{TT} = P_A - P_{BS}$$

We use the transrespiratory **pressure gradient** and the other gradients to understand the gas flow into and out of the alveoli during breathing. Table 11.2 summarizes these equations. For a spontaneously breathing person, P_A is **sub-atmospheric** in the beginning of inspiration compared with P_{AO}. Because "nature hates a vacuum," and pressure differences want to equalize, air flows into the alveoli when pressure at the airway opening is higher than pressure in the alveoli. The opposite happens when exhalation begins; here, P_A is higher than P_{AO}, causing air to flow out of the airway opening as pressure in the alveoli is higher than pressure at the airway opening. During a normal breathing cycle, the glottis remains open. The P_{BS} and P_{AO} remain at zero (i.e., atmospheric) throughout the cycle; only changes in P_A and P_{pl} are of interest. It is often helpful to use these to describe the changes in pressures during a breathing cycle.

Before inspiration, pleural pressure is approximately −5 cm H_2O (i.e., 5 cm H_2O below atmospheric pressure), and alveolar pressure is 0 cm H_2O. The **transpulmonary pressure gradient** is also approximately 5 cm H_2O in the resting state, that is, $P_{TP} = P_{AO} - P_{pl} = 0 - (-5) = 5$. This positive end-expiratory P_{TP} maintains the lung at its resting volume which is the functional residual capacity (FRC). The definition of functional residual capacity is the volume of the lung at the end of expiration with the glottis open. Airway opening and alveolar pressures are both zero at FRC, so the **transairway pressure gradient** also is zero. No gas moves into or out of the respiratory tract at FRC.

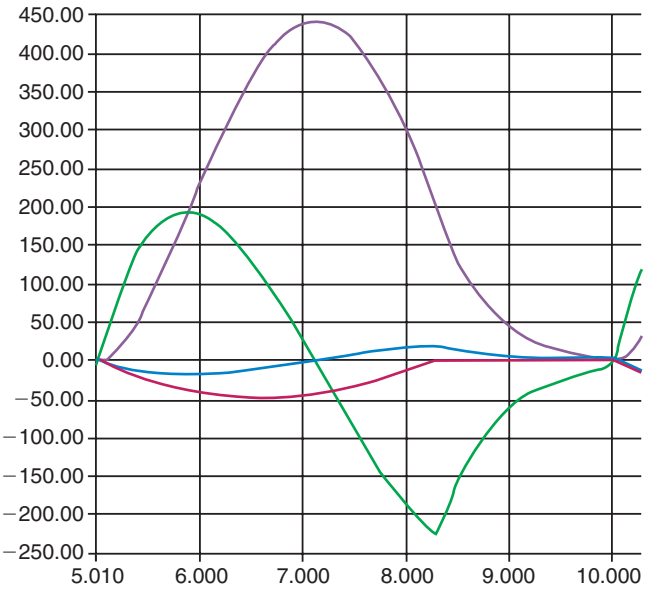

Fig. 11.2 Waveforms for Normal Breathing. *Red,* Change in pleural pressure relative to end-expiratory value (cm H_2O, scaled times 10); *blue,* alveolar pressure (cm H_2O, scaled times 10); *green,* flow (L/min, scaled times 10); *purple,* volume (mL).

RULE OF THUMB A way to imagine FRC is to think of a dead patient's lung volume (or a paralyzed patient). where the glottis is open and there is no muscle activity, then the volume of air in the lungs (the FRC) is the result of a balance of forces; on one side the elastic lungs wanting to shrink and on the other, the recoil of the chest wall trying to expand.

Inspiration begins when muscular effort expands the thorax. Thoracic expansion causes a *decrease* in pleural pressure. This decrease in pleural pressure causes a positive change to P_{TP} and P_{TA}, which induces air to flow into the lungs down the resulting pressure gradient. The inspiratory flow (i.e., the rate at which air is moving) is proportional to the positive change in trans-airway pressure difference; the higher the change in P_{TA}, the higher is the flow.

Pleural pressure continues to decrease until the end of inspiration. Alveolar filling slows when alveolar pressure approaches equilibrium with the atmosphere, and inspiratory flow decreases to zero (Fig. 11.2). At this point, called *end-inspiration,* alveolar pressure has returned to zero, and the intrapleural pressure is maximally negative—and hence transpulmonary pressure gradient reaches the maximal value (for a normal breath) of approximately 10 cm H_2O.

At end inspiration, the muscle pressure relaxes, and the chest wall recoil and lung elastance will lead to an alveolar pressure higher than the pressure at the airway opening, driving flow out of the lung (for expiration). The equation of motion shows this, setting the driving pressure, P_{mus}, to zero:

$$P_{mus} = 0 = (\text{Elastance} \times \text{Volume}) + (\text{Resistance} \times \text{Flow})$$

Rearranging the formula, we get:

$$(\text{Elastance} \times \text{Volume}) = -(\text{Resistance} \times \text{Flow})$$
$$= \text{Resistance} \times (-\text{Flow})$$

This equation says two important things: (1) Flow is negative (i.e., going out of the lung), indicating expiration, and (2) the driving force (transthoracic pressure, equal to elastance × volume) for expiratory flow is the energy stored in the combined elastances of lungs and chest wall (the total elastance is the sum of the chest wall and lung elastances).

These events occur during normal tidal volume excursions. Similar pressure changes accompany deeper inspiration and expiration. The pressure change is greater with deeper breathing. Pleural pressures are always negative (sub-atmospheric) during normal inspiration and exhalation. During forced inspiration with a big downward movement of the diaphragm, the pleural pressure can decrease to −50 cm H_2O, whereas during a forced expiration, pleural pressure may increase above atmospheric pressure to 50 to 100 cm H_2O.

Forces Opposing Inflation of the Lung

The lungs have a tendency to recoil inward, whereas the chest wall tends to move outward; these opposing forces keep the lung at its resting end-expiratory volume (i.e., FRC). To generate the previously described pressure gradients, the lungs must be distended. This distention requires several opposing forces to be overcome for inspiration to occur. As indicated in the equation of motion, the forces opposing lung inflation may be grouped into two categories: *elastic forces* and *frictional forces.* Elastic forces involve the tissues of the lungs, thorax, and abdomen, along with surface tension in the alveoli. Frictional forces include resistance caused by gas flow through the airways (natural and artificial) and tissues moving past each other during breathing.

Surface Tension Forces

Hysteresis is defined as the dependence of a system on its history or past state. When we apply it to the lungs, hysteresis refers to the difference between inspiratory and expiratory pressure-volume curves exhibited by the lung. That is, for the same pressure, the volume in the lungs in inspiration and expiration are different. The difference in expiratory pressure-volume curve is a result of **surface tension** forces in the alveoli. To understand this better it is good to review what happens to the lung in the saline versus air-filled state. In Fig. 11.3, you can see that if a lung is filled with fluid such as saline (fluid-filled), then less pressure is needed to a given volume (higher compliance) and minimal hysteresis than an air-filled lung. This phenomenon indicates that a gas-fluid *interface* in the air-filled lung changes its inflation-deflation characteristics.

The recoil of the lung, its tendency to collapse, is a combination of tissue elasticity and the surface tension forces in the alveoli. During inflation, additional pressure is needed to overcome surface tension forces. During deflation, surface tension forces are reduced, resulting in altered pressure-volume characteristics (i.e., the leftward shift seen in Fig. 11.3). In the intact lung (i.e., within the chest), the volume history also affects the degree of hysteresis that occurs. Factors such as the initial volume, the tidal excursion, and whether the lungs have been previously inflated or deflated help determine the volume history and the shape of the pressure-volume curves of the lung.

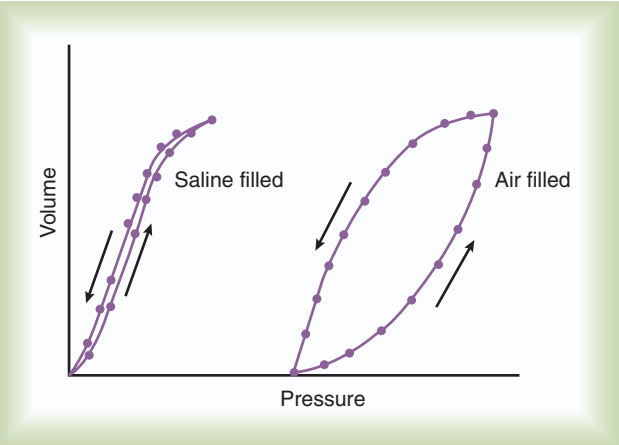

Fig. 11.3 Static Pressure-Volume Curves of Saline-Filled and Air-Filled Excised Lungs. In the saline-filled lung, the distending pressure is the same during inflation and deflation. The air-filled lung shows hysteresis (i.e., higher pressure for a given volume on inflation compared with deflation). The hysteresis results in part from the effects of surface tension forces caused by the air-liquid interface in the alveoli. (Modified from Slonim NB, Hamilton LH: *Respiratory physiology*, ed 5, St Louis, 1987, Mosby.)

RULE OF THUMB Patients with severe lung disease and requiring mechanical ventilation may be subject to a recruitment maneuver. These maneuvers (several techniques exist) consist of increasing the pressure in the airway to regain inflation of the lung. The goal is to open alveoli that are closed, minimize the surface tension, and regain ventilated lung tissue to decrease the pressures needed to provide mechanical ventilation.

This phenomenon is dependent on the surface tension of the lung. Surface tension is the tendency of a fluid surface to become as small as possible (think of a water drop, which is as small as it can be based on the attraction of its molecules). In the alveoli, the alveoli wall is covered with fluid, which is trying to reduce its size (collapse). Thanks to pulmonary surfactant it does not. The lung surface tension is dependent on the presence and function of pulmonary surfactant. A surfactant is any substance that reduces the surface tension.

The mechanism of action of pulmonary surfactant molecules is based on their weak intra-molecular attractive forces. When surfactant molecules are mixed with other liquid molecules that have higher intra-molecular attraction, the surfactant molecules are pushed to the surface of the liquid, where they form the air-liquid interface. Because of the weak intra-molecular attraction between these surfactant molecules at the surface, the liquid lining of the alveoli exhibits much less surface tension than it would in the absence of pulmonary surfactant. In a premature infant with inadequate surfactant, the intra-alveolar surface tension is abnormally high; this produces a collapsing force that increases lung recoil and reduces lung compliance. Greater muscular effort is required to overcome increased recoil during inspiration and the work of breathing is increased. The infant's inspiratory muscles may eventually become fatigued, leading to ventilatory failure. Instillation of artificial surfactant into the lungs reduces surface tension to its normal level. Lung compliance is increased, elastic recoil is reduced, and the muscular work required to inflate the lung is reduced.

MINI CLINI

Surfactant Replacement Therapy and Lung Mechanics

Problem

If an infant is born prematurely, the lungs may be unable to produce adequate amounts of pulmonary surfactant. How does this condition affect lung mechanics and what effect does surfactant replacement therapy have on lung compliance and the work of breathing?

Discussion

The liquid molecules that line each alveolus attract one another. This attraction creates a force called *surface tension,* which tends to shrink the alveolus. A phospholipid called *pulmonary surfactant* reduces surface tension in the lung. Alveolar type II cells produce pulmonary surfactant. In contrast to typical surface-active agents, pulmonary surfactant changes surface tension according to its area.[2] The ability of pulmonary surfactant to reduce surface tension decreases as surface area (i.e., lung volume) increases. Conversely, when surface area decreases, the ability of pulmonary surfactant to reduce surface tension increases. This property of changing surface tension to match lung volume helps stabilize the alveoli. Any disorder that alters this can cause significant changes in the work of breathing.

RULE OF THUMB Surfactant is essential for lung function. When the patient exhales, the size of the alveoli decreases, thus there is "more" surfactant in relation to the size of the alveoli, therefore less tension surface (less pressure needed to expand). As the lung expands, the alveoli is larger, so there is "less" surfactant in relation to the size of the alveoli, therefore more tension surface (this homogenizes lung inflation and deflation).

Elastic Forces Opposing Lung Inflation

Elastin and *collagen* fibers are found in the lung parenchyma. These fibers give the lung the property of elasticity. **Elasticity** is the physical tendency of an object to return to an initial state after deformation. Like a balloon when stretched, an elastic body tends to return to its original shape. The tension developed when an elastic structure is stretched is proportional to the degree of deformation produced (Hooke's law). An example is a simple spring (Fig. 11.4). When tension on a spring is increased, the spring lengthens. However, the ability of the spring to stretch is limited. When the point of maximal stretch is reached, further tension produces little or no increase in length. Additional tension may break the spring.

In the respiratory system, inflation stretches tissue. The elastic properties of the lungs and chest wall oppose inflation. To increase lung volume, pressure must be applied. This property may be shown by subjecting an excised lung to changes in transpulmonary pressure and measuring the associated changes in volume (Fig. 11.5). To simulate the pressures during breathing, the lung is placed in an airtight jar. The force to inflate the lung is provided by a pump that creates a vacuum around the lung inside the jar, simulating the negative P_{pl}. This action mimics the pleural pressure changes associated with thoracic expansion and contraction. The changes in transpulmonary pressure allow the lungs to come to rest in between, so that all of the applied pressure opposes elastic forces and none of it opposes resistive forces (i.e., flow is zero when the measurements are made). The amount of

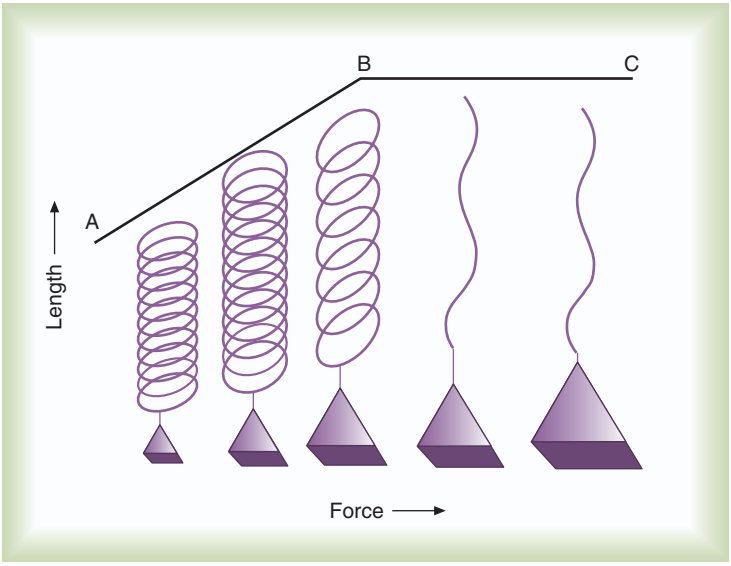

Fig. 11.4 Graphic representation of the force-length relationship applied to a simple spring (increase in length with increase in force). With increasing force, or weight in this example, the spring lengthens from *A* to *B,* but at the point of maximal stretch, further force produces no additional increase in length (*B* to *C*).

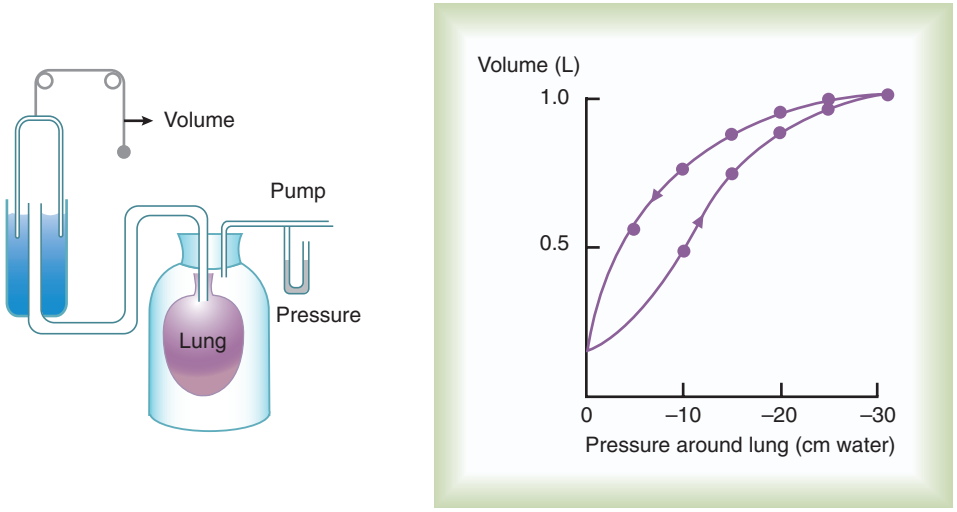

Fig. 11.5 Measurement of the Pressure-Volume Curve of an Excised Lung. The lung is placed in a sealed jar and connected to a spirometer (to measure volume). A pump generates sub-atmospheric pressure around the lung while its volume is measured. The curve plotting the relationship between pressure and volume is nonlinear and flattens at high expanding pressures (sub-atmospheric). The inflation and deflation curves are not the same. This difference is called *hysteresis*.

stretch (inflation) is measured as volume by a spirometer. Changes in volume resulting from changes in transpulmonary pressure are plotted on a graph.

During inspiration in this model, increasingly greater negative pleural pressures are required to stretch the lung to a larger volume. As the lung is stretched to its maximum (total lung capacity [TLC]), the inflation curve becomes flat. This flattening indicates *increasing* opposition to expansion (i.e., for the same change in transpulmonary pressure, there is less change in volume).[3]

As with a spring when tension is removed, deflation occurs passively as pressure in the jar is allowed to return toward atmospheric pressure. Deflation of the lung does not follow the inflation curve exactly. During deflation, lung volume at any given pressure is slightly greater than it is during inflation. This difference between the inflation and deflation curves is called **hysteresis**.[3] In other words, the pressure needed to inflate the lung from its empty state is not the same (and greater, in fact) as the pressure gradient associated with deflating the lung from its full state. Hysteresis indicates that factors other than simple elastic tissue forces are present. The major factor contributing to the increased pressure needed to inflate the lung, particularly in sick lungs, is the opening of collapsed alveoli during inspiration that tend to stay open during expiration until very low lung volumes are reached.

Compliance

Compliance (*C*, the reciprocal of elastance, *E*) is caused by the tissue elastic forces and surface tension that oppose lung inflation. Compliance is defined as the ratio between volume (*V*) and pressure (*P*) in an elastic system and is usually expressed in units of mL/cm H_2O:

$$C = \frac{\Delta V}{\Delta P} = \frac{1}{E}$$

RULE OF THUMB A more intuitive way to think about the compliance of the respiratory system is to ask: How much pressure across the whole respiratory system is needed to inflate the lung maximally (to TLC)? The more compliant the lung, the less the pressure needed to inflate it and the less compliant (i.e., stiffer) the lung, the more pressure needed.

To calculate lung compliance, ΔP_{TP} is substituted for ΔP. To calculate respiratory system compliance, use ΔP_{TR}. To calculate chest wall compliance, use ΔP_{TCW}.

A graph of change in lung volume versus change in transpulmonary pressure (Fig. 11.6A) is called the *compliance curve of the lungs*. Fig. 11.6B compares a normal lung compliance curve with curves that might be observed in patients who have emphysema (obstructive lung disease) or pulmonary fibrosis (restrictive lung disease). The curve from a patient with emphysema is steeper and displaced to the left. The shape and position of this curve represent large changes in volume for small pressure changes (increased compliance). Increased compliance results primarily from loss of elasticity due to breakdown of elastic fibers in the alveolar walls, which occurs in emphysema. The lungs become more distensible (i.e., more compliant) so that a normal transpulmonary pressure results in a larger lung volume. The term *hyperinflation* is used to describe an abnormally increased lung volume. A distinctly opposite pattern is seen in pulmonary fibrosis, where the lung becomes less compliant, or stiffer. Interstitial fibrosis is characterized by an increase in connective tissue in the lung and increased stiffness of the lung. The compliance curve of a patient with pulmonary fibrosis is therefore flatter than the normal curve (i.e., shifted down and to the right), indicating that more pressure is needed to produce the same degree of lung inflation. As a result, there is a smaller volume change for any given pressure change (decreased compliance).

Inflation and deflation of the lung occur with changes in the dimensions of the chest wall. The relationship between the lungs and the chest wall can be illustrated by plotting their relaxation pressure curves separately and combined (see Fig. 11.7). In the intact thorax, the lungs and chest wall recoil against each other. The point at which these opposing forces balance determines the resting end-expiratory volume of the lungs, or FRC. This is also the point at which alveolar pressure equals atmospheric pressure. The normal FRC is approximately 40% of the TLC. The opposing forces between the chest wall and lungs are partially responsible for the sub-atmospheric pressure in the intrapleural space. Diseases that alter the compliance of either the chest wall or the lung often disrupt the balance point, usually with a change in lung volume. With stiffer lungs, FRC is reduced and with more compliant lungs, FRC increases.

Combined Compliances

The two lungs have their own (usually different) compliances. However, the muscles (or ventilator) see the net effect of all the combined compliances. Because the lungs have the same driving

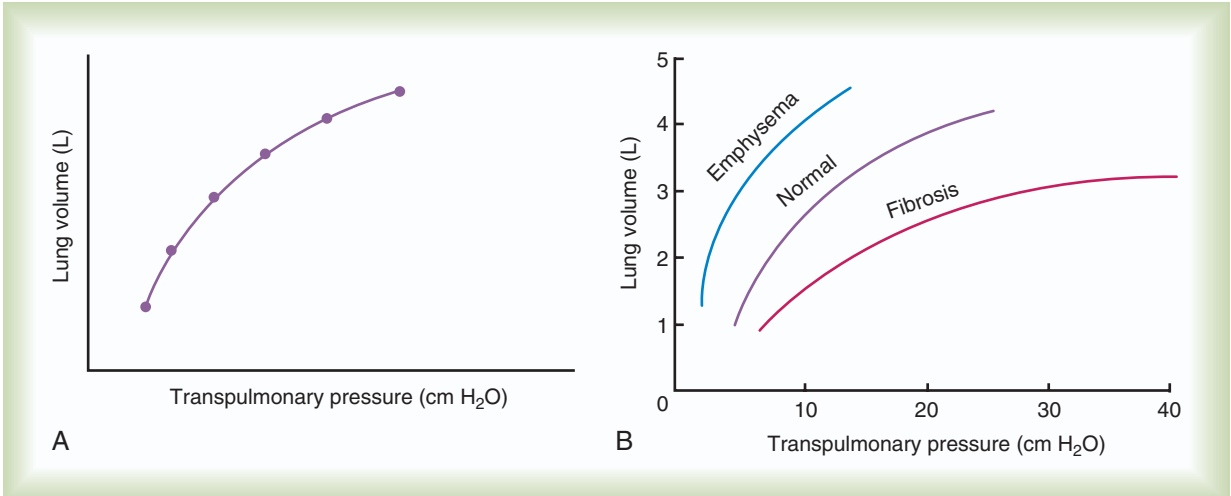

Fig. 11.6 (A) Compliance measurement (deflation curve). After swallowing an esophageal balloon, the person inhales a full breath and then exhales slowly. At specific lung volumes, he holds his breath with the glottis open, ensuring an alveolar pressure of zero. Lung volume is plotted against transpulmonary pressure (esophageal pressure is assumed to reflect pleural pressure) generating a compliance curve. (B) Compliance curves. Normal lung compliance is approximately 0.2 L/cm H_2O (measured from the lower portion of the curve, near resting lung volume). Compliance is increased in emphysema because of the destruction of elastic tissue; conversely, it is decreased in pulmonary fibrosis because of increased elastic recoil. (Modified from Martin L: *Pulmonary physiology in clinical practice: the essentials for patient care and evaluation*, St Louis, 1987, Mosby.)

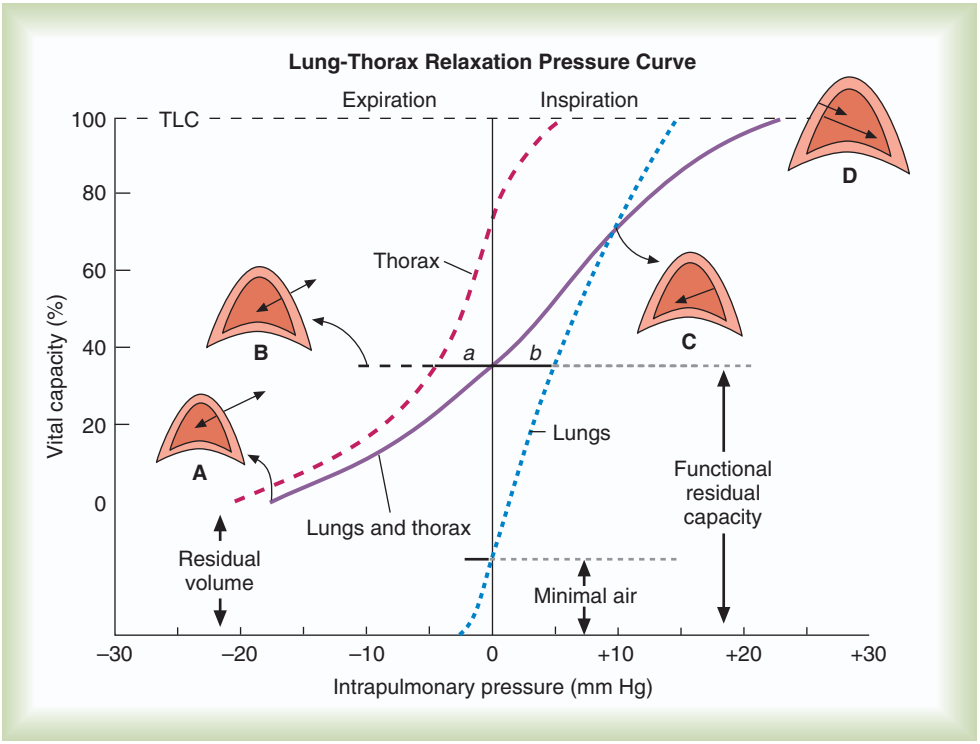

Fig. 11.7 Relationship Between the Lungs and Chest Wall. Volumes of the lungs, thorax, and lungs and thorax combined are plotted as a percentage of vital capacity against intrapulmonary pressure (recoil pressure). The combined lung-thorax relaxation curve *(solid line)* is the sum of the individual lung and thorax curves. Equilibrium (zero pressure) occurs where the lung and thoracic recoil forces balance ($a + b = 0$). This point determines the functional residual capacity (lung *B*). Lung *A* represents low lung volume with greater recoil pressure exerted by the chest wall. Lung *C* shows a chest wall recoil of zero at approximately 70% of total lung capacity *(TLC)*. When lung volume is greater than 70% of TLC, greater pressures are required to distend both the lungs and the thorax (lung *D*). (Modified from Beachey W: *Respiratory care anatomy and physiology*, ed 2, St Louis, 2007, Mosby.)

pressure but different flows in the right versus the left lung, they are said to be connected in parallel. Parallel compliances combine by simple addition:

$$\text{Parallel compliances}: C_{total} = C_{right} + C_{left}$$

The total compliance of a parallel connection is more than any of the components.

The total lung compliance is connected in series with the chest wall compliance, meaning they have different driving pressures but the same flow. Series compliances combine as follows:

$$\text{Series compliances}: C_{total} = \frac{C_{chestwall} \times C_{lungs}}{C_{chestwall} + C_{lungs}}$$

The total compliance of a series connection is less than any of the components.

RULE OF THUMB The lungs and chest wall each have their own compliance, or distensibility. In healthy adults, the compliance of the lungs and chest wall are each equal to approximately 0.2 L/cm H_2O. However, because the lungs are contained within the thorax, the two systems act as springs pulling against the driving force. This reduces the compliance of the system to approximately half that of the individual components, or 0.1 L/cm H_2O. Obesity, kyphoscoliosis, ankylosing spondylitis, and many other abnormalities can reduce chest wall compliance and lung volumes.

Inhalation occurs when the balance of forces between the lungs and chest wall shifts. Energy from the respiratory muscles (primarily the diaphragm) overcomes the tendency of the lungs to contract. At the beginning of the breath, the tendency of the chest wall to expand facilitates lung expansion. When lung volume nears 70% of the TLC, the chest wall reaches its natural resting level. To inspire to a lung volume greater than approximately 70% of TLC, the inspiratory muscles must overcome the recoil of both the lungs and the chest wall (see Fig. 11.7).

For exhalation, potential energy "stored" in the stretched lung (and chest wall at high volumes) during the preceding inspiration allows the lungs to empty passively (i.e., without forcing air out). Still, to exhale below the resting level of the lung (FRC), muscular effort is required to overcome the tendency of the chest wall to expand.

Resistive Forces Opposing Lung Inflation

Frictional forces also oppose ventilation. Frictional opposition forces differ from the elastic properties of the lungs and thorax. Frictional opposition occurs only when the system is in motion; there is no friction when there is no motion. Frictional opposition to ventilation has two components—tissue viscous resistance and airway resistance.

Tissue viscous resistance. Tissue viscous resistance is the impedance of motion (opposition to flow) caused by displacement

of tissues during ventilation. Displaced tissues include the lungs, rib cage, diaphragm, and abdominal organs. The frictional resistance is generated by the movement of each organ surface sliding against the other (e.g., the lung lobes sliding against each other and against the chest wall). Tissue resistance accounts for only approximately 20% of the total resistance to lung inflation. However, in conditions such as obesity, pleural fibrosis, and ascites, the tissue viscous resistance will increase the total impedance to ventilation.

Airway resistance. Gas flow through the airways also causes frictional impedance, called *flow resistance*. Resistance to ventilation by the movement of gas through the airways is called ***airway resistance***. Airway resistance accounts for approximately 80% of the frictional resistance to ventilation.

Resistance is defined as the ratio between pressure (P) and flow ($\dot{V}$) in a flow-conducting system and is usually expressed in units of cm H_2O/L per second:

$$R = \frac{\Delta P}{\Delta \dot{V}}$$

To calculate airway resistance, R_{aw}, use ΔP_{TA} instead of ΔP. To calculate respiratory system resistance, use ΔP_{TR}.

Airway resistance in healthy adults ranges from approximately 0.5 to 2.5 cm H_2O/L per second. To cause gas to flow into or out of the lungs at 1 L/s, a healthy person needs to lower his or her alveolar pressure only 0.5 to 2.5 cm H_2O below atmospheric pressure.

R_{aw} in spontaneously breathing patients is usually measured in a pulmonary function laboratory. Flow is measured with a **pneumotachometer**. Alveolar pressures are determined in a body **plethysmograph**, an airtight box in which the patient sits. By momentarily occluding the patient's airway and measuring the pressure at the mouth, alveolar pressure can be estimated (i.e., mouth pressure equals alveolar pressure under conditions of no flow). By relating flow and alveolar pressure to changes in plethysmograph pressure, airway resistance can be calculated.

Combined Resistances

The right and left main stem bronchi have their own (usually different) resistances. However, the muscles (or ventilator) see a combined resistance from both the right and left lungs together. Because these airways have the same driving pressure but different flows, they are said to be connected in parallel. Parallel compliances combine like compliances in series, as follows:

$$\text{Parallel resistances}: R_{total} = \frac{R_{right} \times R_{left}}{R_{right} + R_{left}}$$

The total resistance of a parallel connection is less than that of any of the components.

The bronchial airway resistance is connected in series with upper airway (and artificial airway, if any), meaning that they have different driving pressures but the same flow. Series resistances combine like compliances in parallel:

$$\text{Series resistance}: R_{total} = R_{upper\ airway} + R_{bronchi}$$

MINI CLINI

Helium and Oxygen Therapy for Large Airway Obstruction

Problem

Patients with significant obstruction in the upper airway, trachea, or main stem bronchi expend a large amount of energy overcoming the resistance to breathing. What type of gas therapy would be most advantageous in this situation?

Discussion

Because most (approximately 80%) of the resistance to breathing occurs in the upper and large airways, disease processes that increase resistance in these airways cause tremendous increases in the work of breathing. Vocal cord edema, tumors in the trachea, and foreign bodies in main stem bronchi are examples of the types of clinical conditions that can markedly increase the work of breathing. Patients who must breathe against high levels of resistance are prone to respiratory muscle fatigue and failure. Gas flow in the upper and large airways is predominantly turbulent. Turbulent flow is highly influenced by gas density. Patients with large airway obstruction often can be treated with a mixture of helium and O_2 (heliox or HeO_2) because helium is approximately 6 times less dense than air. The lower density allows helium to flow more rapidly under conditions of turbulent flow. Thus, HeO_2, usually an 80/20 or 70/30 mixture, can be administered to reduce the work of breathing until the obstructive process can be treated (see Chapter 42). A HeO_2 mixture does little for patients with small airway obstruction, as occurs in emphysema or asthma, because flow in the small airways is mainly laminar and largely independent of the density of the gas breathed. However, heliox therapy can be used for patients with small airway obstruction to allow them to exercise longer and more strenuously with less dyspnea and dynamic hyperinflation.

The total resistance of a series connection is more than that any of the components.

Factors affecting resistance. The two main patterns that characterize the flow of gas through the respiratory tract are *laminar flow* and *turbulent flow* (see Chapter 6). A third pattern, *tracheobronchial flow,* is a combination of laminar and turbulent flow. Laminar flow requires less driving pressure than turbulent flow.

Poiseuille's equation (see Chapter 6) describes laminar flow through a smooth, unbranched tube of fixed dimensions (i.e., length and radius). This equation says that for gas flow to remain constant, the pressure is *inversely proportional* to the fourth power of the airway's radius. That is, by reducing the radius of a tube by half requires a 16-fold pressure increase to maintain a constant flow ($2^4 = 16$)! Clinically, this means that to maintain ventilation in the presence of narrowing airways, large increases in driving pressure may be needed, resulting in marked increases in the work of breathing.

RULE OF THUMB A change in the radius of an airway by a factor of 2 causes a 16-fold change in resistance. If the size of a patient's airway is reduced from 2 to 1 mm, airway resistance increases by a factor of 16. Similarly, increasing the size of an endotracheal tube from 4.5 to 9 decreases 16-fold the pressure needed to achieve the same flow.

Distribution of resistance. Approximately 80% of the resistance to gas flow occurs in the nose, mouth, and large airways,

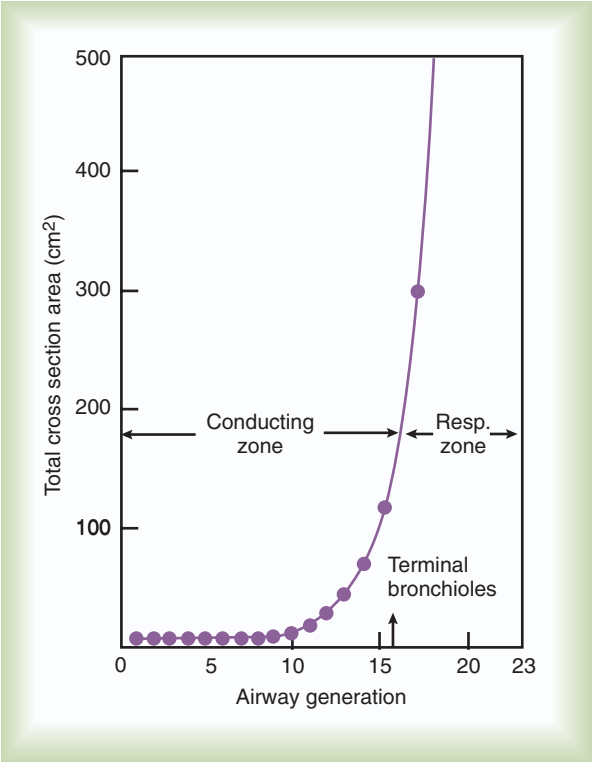

Fig. 11.8 Cross-Sectional Area of the Airways Plotted Against Airway Generation. The first 15 or 16 airway generations represent a conducting zone in which gas moves primarily by bulk flow, and no gas exchange takes place. These airways make up the anatomic dead space (see Chapter 9). The gas-exchange surface increases markedly at the level of the terminal bronchiole.

TABLE 11.3 Distribution of Airway Resistance

Location	Total Resistance (%)
Nose, mouth, upper airway	50
Trachea and bronchi	30
Small airways (<2 mm)	20

where flow is mainly turbulent. Only approximately 20% of the total resistance to flow is attributable to airways smaller than 2 mm in diameter, where flow is mainly laminar. This fact seems to contradict the fact that resistance is inversely related to the radius of the conducting tube.

Branching of the tracheobronchial tree increases the cross-sectional area with each airway generation (Fig. 11.8). As gas moves from the mouth to the alveoli, the combined cross-sectional area of the airways increases exponentially. Gas velocity is high in the bigger airways, favoring turbulent flow patterns. Thus, turbulent flow predominates in the mouth, trachea, and primary bronchi (Table 11.3). As we move deeper into the lung segments, the airways branch into smaller, but many more, airways and more cross-sectional area. At the level of the terminal bronchioles, the cross-sectional area increases more than 30-fold compared with the trachea. The arrangement of the branches at the same bronchial generation is in parallel (compared to in series), thus

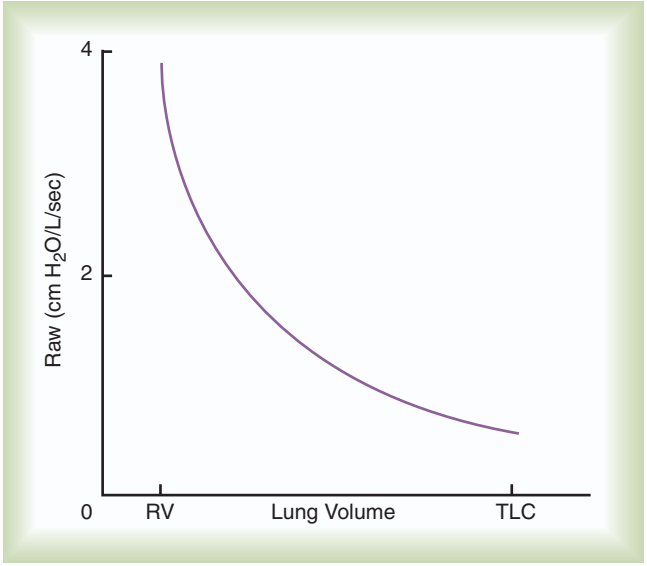

Fig. 11.9 Change in Airway Resistance (R_{aw}) Related to Lung Volume. Resistance to airflow is highly dependent on lung volume. At low lung volumes, near residual volume *(RV)*, the airways are compressed and resistance increases markedly. At high lung volumes, near total lung capacity *(TLC)*, the airways are distended and resistance decreases. See text for discussion.

decreasing the total resistance. This increase in cross-sectional area causes a decrease in gas velocity. The velocity of gas flow and resistance in a branching system arranged in parallel is inversely related to the cross-sectional area of the airways. The decrease in gas velocity promotes a laminar flow pattern, particularly in smaller (i.e., <2 mm) airways. The resistance to flow in these small airways is then very low. The driving pressure across these airways is less than 1% of the total driving pressure for the system.

We must remember that the diameter of the airways is not constant during the ventilatory cycle. During inspiration, the stretch of surrounding lung tissue and widening transpulmonary pressure gradient increase the diameter of the airways. The increase in airway diameter with increasing lung volume decreases airway resistance (Fig. 11.9). As lung volume decreases toward residual volume, airway diameters also decrease and airway resistance dramatically increases; this explains why wheezing is most often heard during exhalation.

STATIC VERSUS DYNAMIC MECHANICS

Resistance and compliance can be evaluated under static or dynamic conditions.[4] The term *static* implies that flow throughout the respiratory system has stopped and all ventilatory muscle activity is absent ($P_{mus} = 0$). In patients on mechanical ventilation, static conditions can be imposed with an inspiratory pause when a patient is sedated. In contrast, the term *dynamic* (in this context) means that flow at the airway opening is not zero. Mechanics are evaluated under dynamic conditions, for example, when a non-intubated patient breathes spontaneously. In this case, the pressure difference used to calculate lung resistance and elastance is P_{TP} and the driving pressure is P_{mus} instead of the ventilator.

In a single-compartment model (see Fig. 11.1), estimation of resistance and compliance under static and dynamic conditions yields the same values. However, in a real respiratory system, composed of multiple compartments with different time constants (each compartment being a resistance in series with a compliance), mechanics estimated during static conditions yield different values than when evaluated during dynamic conditions. For a multiple-compartment system, when flow is zero at the airway opening, there may still be flow between compartments (pendelluft). As a result, dynamic mechanics become dependent on the respiratory frequency.[5,6] Typically, both compliance and resistance decrease as frequency increases.

MECHANICS OF EXHALATION

Airway caliber is determined by several factors, including anatomic (i.e., physical) support provided to the airways and pressure differences across their walls. Anatomic support comes from cartilage in the wall of the airway and from "traction" provided by surrounding tissues. The larger airways depend mainly on cartilaginous support. Because smaller airways lack cartilage, they depend on support provided by surrounding lung parenchyma.[7]

The airways are also supported by the pressure difference across their walls. This transpulmonary pressure gradient helps stabilize the airways, particularly the small ones. During quiet breathing, pleural pressure is normally subatmospheric. Airway pressure varies minimally and is usually close to zero (atmospheric pressure). The **transmural pressure** gradient (the pressure difference between inside and outside the airway wall) during normal quiet breathing is negative, even during exhalation. It ranges from −5 to −10 cm H_2O. This negative transmural pressure gradient helps keep the small airways open.

During a forced exhalation, contraction of expiratory muscles can increase pleural pressure above atmospheric pressure; this reverses the transmural pressure gradient, making it positive. If the positive transmural pressure gradient exceeds the force provided by the lung to keep the airways open, then the small airways may collapse. Alveolar pressure during forced exhalation equals the sum of pleural pressure and the elastic recoil pressure of the lung.[8]

During exhalation, the pressure along the airway decreases as gas flows from the alveoli toward the mouth. Moving "downstream" (toward the mouth), transmural pressure decreases continually. At some point along the airway, the pressure inside the airway equals the pressure outside in the pleural space (i.e., transmural pressure equals zero). This point is referred to as the **equal pressure point (EPP)** (Fig. 11.10). Downstream from this point, pleural pressure exceeds the airway pressure. The resulting increase in transmural pressure gradient causes airway compression and can lead to airway collapse. Airway compression increases expiratory airway resistance and decreases flow. At the EPP, greater expiratory effort increases pleural pressure, restricting flow further.[9] Once the transmural pressure has increased sufficiently to cause this flow limitation (at the EPP), airflow becomes effort independent with airway caliber and elastic recoil pressure determining flow. **Dynamic compression** of the airways (narrowing of the airways owing to an increase in surrounding pressures) is responsible for the characteristic flow patterns observed in forced expiratory tests of pulmonary function. Excessive Dynamic Collapse is the extreme of dynamic compression, it is a pathological condition where the airway lacks enough support (e.g., Mounier-Kuhn syndrome) or the pleural pressure excursions are high (very severe chronic obstructive pulmonary disease [COPD]) where even normal tidal excursions in breathing leads to marked reduction in the size of the airway during exhalation.

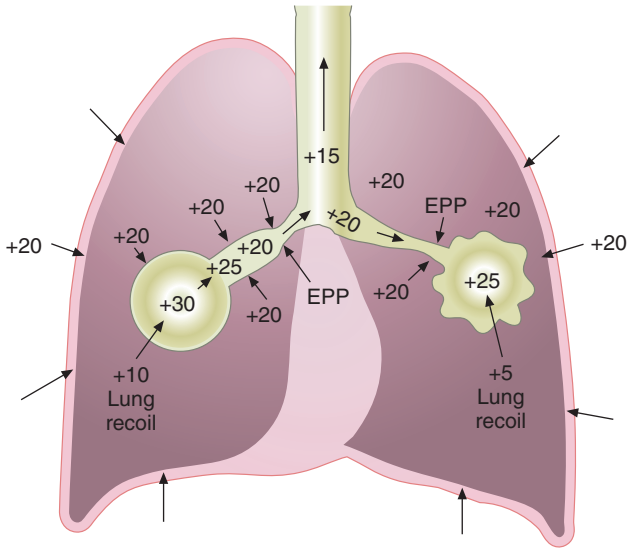

Fig. 11.10 Generation of Equal Pressure Point *(EPP)* in Normal and Diseased Lungs During a Forceful Exhalation. In a normal lung *(left)*, pleural pressure (P_{pl}) increases to approximately +20 cm H_2O when a maximal expiratory effort is performed. Alveolar pressure is the sum of P_{pl} (+20 cm H_2O) and lung elastic recoil pressure (+10 cm H_2O), or +30 cm H_2O. Airway pressure falls along the airway from the alveolus to the mouth from +30 to 0 cm H_2O. At some point along the airway, pressure within the airway equals P_{pl}; this is the EPP. Further toward the mouth (downstream), airway pressure falls below P_{pl}, resulting in a narrowed airway and limitation of airflow. This narrowed airway normally occurs in healthy individuals only during forced exhalation. The EPP moves upstream from larger airways toward smaller airways as the lung empties. In lung diseases such as emphysema *(right)*, the same forces come into play. P_{pl} is still +20 cm H_2O, but lung elastic recoil pressure is only +5 cm H_2O. As a result, driving pressure is only +25 cm H_2O. This causes the EPP to occur in smaller airways (i.e., farther upstream) than normal; airways narrow or collapse at a higher lung volume than in healthy lungs. In patients with emphysema, airway collapse is complicated further by loss of support for the small airways. (Modified from Martin L: *Pulmonary physiology in clinical practice: the essentials for patient care and evaluation*, St Louis, 1987, Mosby.)

In the airways of healthy persons, airway collapse occurs only with forced exhalation and at low lung volumes. Tissue support to keep the airways open opposes the collapsing force created by negative transmural pressure gradients. In pulmonary emphysema, the elastic tissue supporting the small airways is destroyed.[9] Destruction of elastic tissue, such as occurs in emphysema, impacts both compliance and resistance of the lung. It increases the compliance of the lung (i.e., elastic recoil decreases). The combination of decreased elastic recoil and loss of support for the small airways allows the airways to collapse during exhalation. Airway collapse causes increased expiratory resistance leading

to air trapping and increase in the resting volume of the lung. Expiratory flow is reduced by airway collapse during exhalation (called *flow limitation*) and can occur during tidal breathing when emphysematous changes in the lung are severe.[10,11] Also, airway collapse in emphysema is worsened during exercise when the respiratory rate increases and there is inadequate time for the lungs to empty. The resulting progressive air trapping during exercise is a main contributor to exercise limitation and shortness of breath in patients with emphysema.

RULE OF THUMB Patients who have emphysema can directly influence the EPP in their airways to reduce airway collapse and closure. By exhaling through "pursed lips," a patient with emphysema changes the pressure at the airway opening. The gentle back pressure created counters the tendency for small airways to collapse by moving the EPP toward larger airways.

WORK OF BREATHING

The respiratory muscles do the work of breathing. This work requires energy to overcome the elastic and frictional forces opposing inflation. Assessing mechanical work involves measuring the physical parameters of force and distance as they relate to moving air into and out of the lung. Assessing metabolic work involves measuring the O_2 cost of breathing.

During normal quiet breathing, inhalation is active and exhalation is passive. The work of exhaling is obtained from potential energy "stored" in the expanded lung and thorax during inhalation. However, forced exhalation requires additional work by the expiratory muscles. The actual work of forced expiration depends on the mechanical properties of the lungs and thorax.

Mechanical Work

Work done on an object is the product of the force exerted on the object times the distance it is moved.

Work may be expressed in units of either dyne • centimeters (dyne • cm) or joules (J). For a constant applied force, the equation for work is:

$$\text{Work} = \text{Force} \times \text{Distance}$$

In physiology, work is expressed in terms of pressure difference across a structure (P) and the volume change of the structure (V). The product of force times distance can be converted into the product of pressure times volume, because pressure is equal to force/area and volume is equal to area multiplied by distance; thus, work can have the dimensions of $P \times V$:

$$\begin{aligned}\text{Pressure} \times \text{Volume} &= \frac{\text{Force}}{\text{Area}} \times (\text{Area} \times \text{Distance}) \\ &= \text{Force} \times \text{Distance} \\ &= \text{Work}\end{aligned}$$

Graphically, the work is expressed as the area between the pressure-volume curve and the volume axis (Fig. 11.11). Pressure, of course, is actually a pressure difference across a structure (i.e., inside pressure minus outside pressure), and the pressure difference *defines the structure* for which work is evaluated. For example, if we want to evaluate the work that the muscles do to inflate the pulmonary system, we use the transpulmonary pressure, P_{TP}. Similarly, if we want to evaluate the work done by a ventilator to inflate the respiratory system we use the transrespiratory system pressure (P_{TR}).

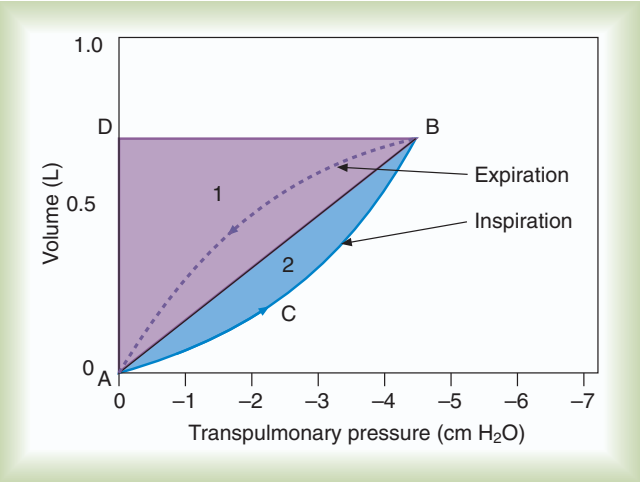

Fig. 11.11 Factors Involved in the Work of Breathing. Point *A* is the resting lung volume (functional residual capacity), and *B* is end-inspiration. The *straight solid line A-B* represents the pressure required to overcome simple elastic forces, and the *curved line A-C-B* represents the additional pressure required to overcome frictional resistance (airway and tissue). At *B,* where airflow momentarily ceases, frictional resistance is inactive. Area 1 represents the work ($P \times V$) required to overcome elastic forces; area 2 represents the work required to overcome frictional forces. The work of breathing (inspiration) is the sum of these two areas. The *curved dashed line* within area 1 represents the pressure-volume curve of passive exhalation using energy stored during inspiration.

Also, because of the equivalence of work and energy, the energy stored in a rigid wall container holding compressed gas is simply the product of the volume of the container and the pressure inside the container (relative to the outside). The higher the pressure, the more energy is stored in the container. When the pressure is released, useful work can be recovered. This is the principle used in air rifles.

Fig. 11.11 shows a graph of transpulmonary pressure versus lung volume derived from measurements taken during dynamic conditions (e.g., during a normal inspiration). The line *AB* connects two points in time when flow is zero. The work done overcoming purely elastic forces opposing inflation is represented by the triangular area 1 in Fig. 11.11. The work required to overcome flow resistive forces is represented by area 2. The total mechanical work for one breath is the sum of the work overcoming both the elastic and the resistive forces opposing inflation; this is represented as the sum of areas 1 and 2. In healthy adults, approximately two-thirds of the work of breathing can be attributed to elastic forces opposing ventilation. The remaining one-third is a result of frictional resistance to gas and tissue movement.

Traditionally, static pressure-volume curves have been created by inflating the lungs with discreet volume steps using a large calibrated syringe ("super syringe").[12] Alternatively, the line *AB* can be approximated under clinical conditions using a very slow inspiratory flow (with the patient heavily sedated) producing

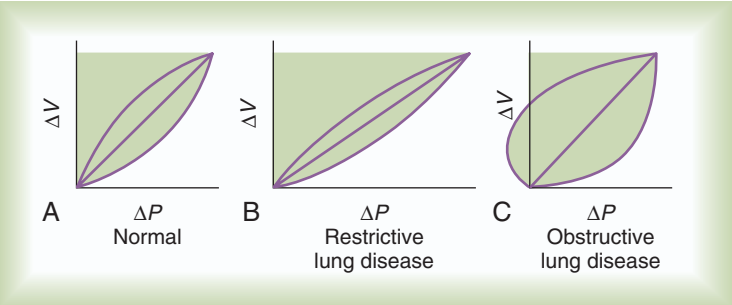

Fig. 11.12 Comparison of the work of breathing *(shaded areas)* for a healthy person (A), a patient with restrictive ventilatory impairment (e.g., pulmonary fibrosis) (B), and a patient with airway obstruction (e.g., emphysema) (C).

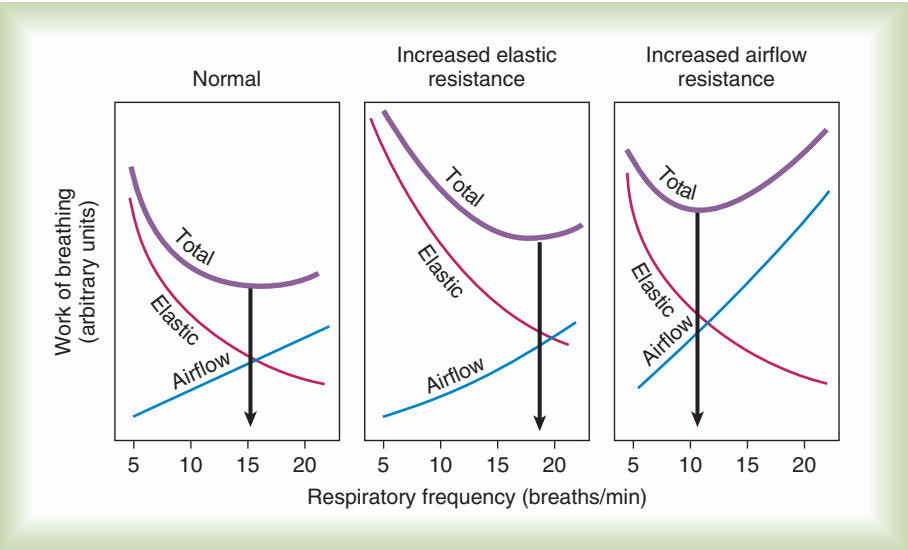

Fig. 11.13 Work Required to Overcome Airflow Plus Elastic Resistance Equals Total Work. In normal lungs, total work of breathing is minimal at approximately 15 breaths/min *(left)*. To achieve the same minute volume with stiff lungs (increased elastic resistance), minimum work is performed at higher frequencies *(middle)*. However, with increased airflow resistance (obstructive lung disease), minimum work requires lower rates of breathing *(right)*.

what is called a *quasistatic* pressure-volume curve.[13] Evaluation of this type of pressure-volume curve can be useful for setting optimal positive end-expiratory pressure (PEEP).[14] Some ventilators generate a quasistatic pressure-volume curve using a slow pressure ramp rather than a slow inspiratory flow. This method allows evaluation of both compliance and lung recruitability.[15]

In the presence of pulmonary disease, the work of breathing can increase dramatically (Fig. 11.12). The areas of the volume-pressure curves for patients with obstruction or restriction are greater than in healthy persons.[16] The reasons for these increases in the mechanical work are quite different in obstructive versus restrictive lung disease. In restrictive lung disease, the area of the volume-pressure curve is greater because the slope of the static component (compliance) is less than normal. In obstructive lung disease, the area of the volume-pressure curve is increased because the portion associated with resistance is markedly widened. The leftward "bulge" of the loop indicates positive pleural pressure that can occur during expiration, notably when lung compliance is increased (see Fig. 11.12C).

In healthy individuals, the mechanical work of breathing depends on the pattern of ventilation. Large V_T increases the elastic component of work. High breathing rates (and high flows) increase frictional work. When changing from quiet breathing to exercise ventilation, a healthy person adjusts V_T and breathing frequency to minimize the work of breathing.[5] Similar adjustments occur in individuals who have lung disease (Fig. 11.13). Patients with "stiff lungs" (i.e., increased elastic work of breathing), such as in pulmonary fibrosis, often assume a rapid, shallow breathing pattern. While this shallow breathing pattern minimizes the mechanical work of distending the lungs, it comes at the expense of spending more energy to increase breathing rate. In contrast, patients who have airway obstruction breathe deeply and slowly. This ventilatory pattern reduces the frictional work of breathing. Breathing slowly and using pursed-lip breathing during exhalation minimize airway resistance.

Increased work of breathing is often complicated by *respiratory muscle weakness,* which may result from electrolyte imbalance, *acidemia,* shock, *sepsis,* or diseases affecting the muscles themselves.[17,18] When increased work of breathing occurs along with respiratory muscle weakness, inspiratory muscles can fatigue. V_T decreases and respiratory rate increases as the muscles fatigue and fail.

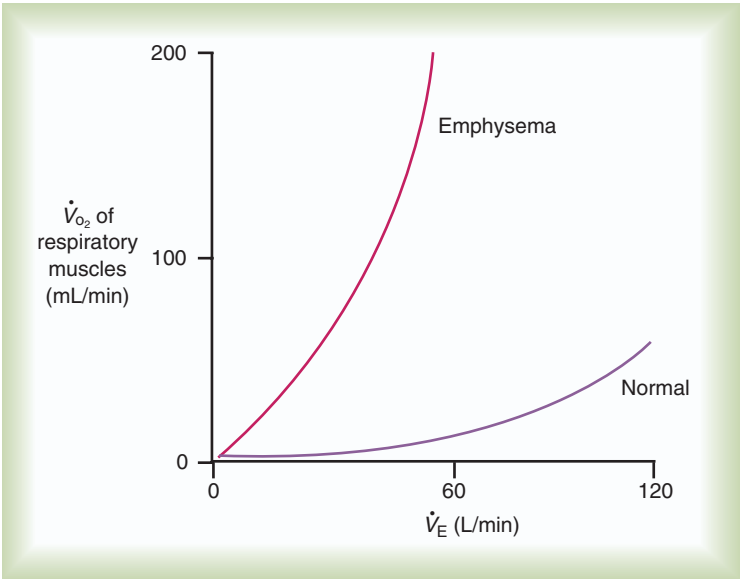

Fig. 11.14 Relationship of oxygen cost of breathing to minute ventilation during maximum exercise for a healthy person and for a patient with emphysema. O_2 consumption ($\dot{V}_{O_2}$) of the respiratory muscles is minimal at levels of ventilation up to approximately 100 L/min in normal persons. The metabolic demand is significantly higher in obstructive lung disease (e.g., emphysema), even at low and moderate levels of ventilation.

Metabolic Work

To perform work, the respiratory muscles consume O_2. The rate of O_2 consumption ($\dot{V}_{O_2}$) by the respiratory muscles reflects their energy requirements. It also provides an indirect measure of the work of breathing.

The O_2 cost of breathing is assessed by measuring $\dot{V}_{O_2}$ at rest and at increased levels of ventilation. If no other factors increase O_2 consumption, the additional O_2 uptake at higher ventilation is a result of respiratory muscle metabolism. The O_2 cost of breathing in healthy individuals averages 0.5 to 1 mL of O_2 per liter of increased ventilation. This range represents less than 5% of the total O_2 consumption of the body. At high levels of ventilation (i.e., >120 L/min), the O_2 cost of breathing increases tremendously and may exceed 30% of the O_2 consumption of the body.

The $\dot{V}_{O_2}$ of the respiratory muscles is closely related to the inspiratory pressures generated by the diaphragm. This transdiaphragmatic pressure can be measured by a technique similar to that used for measuring intrapleural pressure. A thin catheter with two small balloons is advanced into the esophagus. One balloon remains in the esophagus (above the diaphragm), and the balloon at the tip is placed in the stomach. The pressure difference between the balloons measures the pressure across the diaphragm. During normal inspiration, the pressure in the balloon in the chest may decrease whereas the pressure in the balloon in the stomach increases, so the pressure gradient between the abdomen and the chest cavity increases. The greater the pressure required to inflate the lungs, the higher is the O_2 consumption of the respiratory muscles.

In the presence of pulmonary disease (either obstructive or restrictive), the O_2 cost of breathing may increase dramatically with increasing ventilation (Fig. 11.14). In an obstructive disease such as emphysema, increased ventilation needs cause the O_2 consumption of the respiratory muscles to increase. This abnormally high O_2 cost of breathing is another factor that limits exercise in such patients, and also causes weight loss (remember the image of the "pink puffer"). Increased O_2 consumption or inability to increase the oxygen consumption by the respiratory muscles may also contribute to the failure to wean patients from mechanical ventilation.[19] Intubation and mechanical ventilation in cases of shock may be indicated to decrease the excess O_2 consumption of the respiratory muscles and preserve the limited O_2 delivery (DO_2) for other vital body organs.

There are several methods (Table 11.4) to measure mechanical and metabolic work of breathing (see Chapter 52). Their applicability at bedside remains limited, and for the most part the clinician's evaluation of the patient remains the main source of assessment of work of breathing.[20]

DISTRIBUTION OF VENTILATION

Neither ventilation nor perfusion is distributed evenly in healthy lungs. The result is an uneven ventilation-perfusion ($\dot{V}/\dot{Q}$) ratio (0.8). This means that some areas have more or less perfusion in relation to the amount of ventilation. Regional and local factors account for this unevenness in the distribution of ventilation. In disease, the distribution of ventilation can worsen dramatically and can cause serious impairment of O_2 and CO_2 exchange.

RULE OF THUMB Gravity, to a large extent, determines where ventilation goes in the lungs. In an upright lung, the weight of the lung tissues causes alveoli at the bases to be smaller but more easily distended. Alveoli at the top of the lung are larger but distend less easily. Gravity also causes most blood flow through pulmonary capillaries to go to the bases.

TABLE 11.4 Methods to Measure Work of Breathing

Method	Characteristics
Clinical exam	Subjective, nonquantifiable, more reliable when severe
Metabolic cart to measure work of breathing	Measures changes in oxygen consumption. Compares baseline to a clinical change (e.g., weaning).
Trans-diaphragmatic pressure measurement	Allows measurement of the difference in pressure between the thorax and abdomen, which is generated by the diaphragm.
Esophageal balloon placement	Allows measurement of the esophageal pressure, a surrogate of pressure generated by respiratory muscles (P_{musc}).
Calculation by ventilator	Multiple ventilators and devices can display a work of breathing measurement. They use the equation of motion to estimate the values.
Diaphragmatic electromyogram	Esophageal catheter placement, special software required. The electrical activity can be used as a surrogate of effort, especially the changes to maneuvers (e.g., weaning).
Ultrasonography of diaphragm	Observation of diaphragm motion and the quantification of thickening are used as surrogates of work of breathing.
P 0.1	Some ventilators allow the measurement of the airway pressure drop in first 100 ms against an occluded airway. This is a reflection of work of breathing.

MINI CLINI

Oxygen Cost of Breathing During Weaning From Mechanical Ventilation

Problem

During weaning from mechanical ventilation, the O_2 cost of breathing may predict weaning failure. How can you simply detect O_2 cost of breathing at the bedside?

Discussion

O_2 cost of breathing is the difference in O_2 consumption ($\dot{V}_{O_2}$) between unassisted breathing and passive assisted breathing during mechanical ventilation. Although O_2 consumption requires complicated equipment (indirect calorimetry or a metabolic cart), simply looking at the mixed venous O_2 saturation (S_vO_2) before and after initiation of weaning may be a good surrogate for O_2 cost of breathing. If the S_vO_2 was 75% (normal) before initiation of weaning, and after 30 minutes of spontaneous breathing trial the value is 60% without other reason for increased O_2 consumption, it is fair to assume that the O_2 cost of breathing has increased significantly, and failure of weaning or extubation is possible. However, remember that a drop in S_vO_2 also may point toward cardiac dysfunction; clinical examination may help clarify this as the cause.

Regional Factors Affecting Distribution

Two factors interact with the effects of gravity to affect regional distribution of gas in the healthy lung: (1) relative differences in thoracic expansion and (2) regional transpulmonary pressure gradients. In upright individuals, these factors direct more ventilation to the bases and periphery of the lungs than to the apices and central zones.

MINI CLINI

Altering Patient Position to Improve Oxygenation

Altering patient position can improve oxygenation in some pulmonary diseases.[21]

Problem

In patients with severe pulmonary disease causing hypoxemia, how can altering body position improve such hypoxemia?

Discussion

In patients with unilateral lung disease (e.g., pneumonia), having the patient lie on his or her side with the good lung down may improve hypoxemia by altering the gravity-dependent ventilation distribution and the gravity-dependent perfusion distribution. Similarly in patients with severe bilateral pulmonary disease (e.g., acute respiratory distress syndrome [ARDS]), placing the patient in the prone position alters the ventilation and perfusion, favoring the anterior areas of the lungs and may improve the hypoxemia.

Differences in Thoracic Expansion

The conical configuration of the thorax and the action of the respiratory muscles cause proportionately greater expansion at the lung bases than at the apexes. Expansion of the lower chest is approximately 50% greater than expansion of the upper chest.[16] The action of the diaphragm preferentially inflates the lower lobes of the lung.

Transpulmonary Pressure Gradients

The transpulmonary pressure gradient is not uniform throughout the thorax. It varies substantially within the lung and from the top to the bottom of the lung. At a given level of alveolar inflation, the transpulmonary pressure gradient is directly related to the pleural pressure. Pleural pressure represents the pressure on the outer surface of the lung. Its effect lessens toward more centrally located alveoli. Changes in the transpulmonary pressure gradient are greatest in peripheral alveoli (i.e., near the surface of the lung). The changes are least in the alveoli of the central zones. Peripheral alveoli expand proportionately more than their more central counterparts.

Top-to-bottom differences in pleural pressure have an even greater effect on the distribution of ventilation, especially in the upright lung.[3] Pleural pressure increases by approximately 0.25 cm H_2O for each 1 cm from the lung apex to its base for the average-sized adult lung. This increase in pressure results from the weight of the lung itself and the effect of gravity. In an adult-sized lung (approximately 30 cm from apex to base), pleural pressure at the apex is approximately −10 cm H_2O. At the base, pleural pressure is only approximately −2.5 cm H_2O. Because of these differences, the transpulmonary pressure gradient at the top of the upright lung is greater than it is at the bottom. As a result, alveoli at the apexes have a larger resting volume than do alveoli at the bases.

Because of their larger volume, alveoli at the apices expand less during inspiration than alveoli at the bases. Apical alveoli rest on the upper portion of the lung's pressure-volume curve (Fig. 11.15). This part of the curve is relatively flat. Each unit of

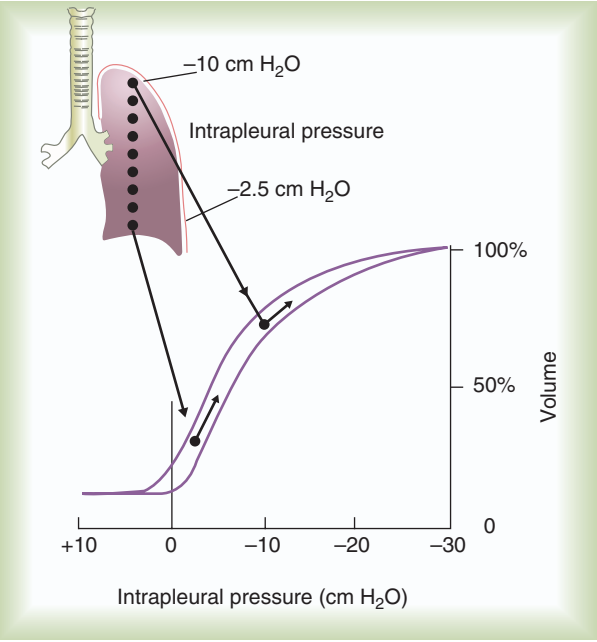

Fig. 11.15 Causes of Regional Differences in Ventilation From the Apex to the Base of an Upright Lung. Because of the weight of the lung and the influence of gravity, intrapleural pressure at the apex is more negative (sub-atmospheric) than at the base. Alveoli at the apex are maintained at a higher resting inflation volume than are alveoli at the base. However, alveoli at the apex reside on the flatter upper portion of the pressure-volume curve. Alveoli at the base are positioned on the lower, steeper portion. For an equal change in intrapleural pressure, alveoli at the base expand more during inspiration than alveoli at the apex. This causes more ventilation to go to the bases in the upright lung.

pressure change causes only a small change in volume. Alveoli at the lung bases are positioned on the steeper middle portion of the pressure-volume curve. For each unit of pressure change, there is a larger change in volume (greater compliance). For a given transpulmonary pressure gradient, alveoli at the bases expand more than alveoli at the apices. The bases of the upright lung receive approximately four times as much ventilation as the apices.

These gravity-dependent differences also are observed in individuals lying down. The magnitude of the differences is less than in the upright lung because the top-to-bottom distance is less. Ventilation is still greatest in the dependent zones of the lung. In recumbent persons, the posterior regions are dependent. Lying on the side causes more ventilation to go to whichever lung is lower.

Local Factors Affecting Distribution

Alveolar filling and emptying are affected by each alveoli compliance and resistance factors. Individual respiratory units and their associated airways may differ from each other. These individual unit differences contribute to uneven ventilation in healthy lungs. Their influence on gas distribution becomes particularly important in disease.

In terms of compliance, the higher the compliance (distensible, less elastic recoil) of the lung unit, the greater is the volume change at a given transpulmonary pressure. These units fill and empty more slowly than normal units. Lung units with low compliance (stiffer, high elastic recoil) tend to fill more slowly and empty faster than normal units. Low compliance units also get lower volume for the same pressure change.

Airway resistance also affects emptying and filling. In healthy airways, the pressure decrease between the airway opening (i.e., the mouth) and the alveolus is minimal. If the airway has high resistance, then the pressure decrease across the obstruction may be substantial, leading to less driving pressure available for alveolar inflation and less alveolar volume increase.

TABLE 11.5 Time Constant in Health and Disease

Time Constant	% of Initial Volume Left	TIME CONSTANT (S) Normal Lung	ARDS	COPD
0	100.0	—	—	—
1	36.8	0.78	0.51	1.1
2	13.5	1.56	1.02	2.2
3	**5.0**	**2.34**	**1.53**	**3.3**
4	1.8	3.12	2.04	4.4
5	0.7	3.9	2.55	5.5

Time Constants

As discussed previously, compliance and resistance determine local rates of alveolar filling and emptying. The time constant helps us understand how both resistance and compliance affect these rates. The time constant is calculated as the product of resistance and compliance and is expressed in units of time (seconds). It is referred to as a "constant" because for any value of resistance and compliance, the time constant always equals the time necessary for the lungs to fill or empty by 63% in response to a change in pressure (up or down). So when there is a change in pressure, after 1 unit of time constant (Table 11.5) the lung volume changes by 63%. After two time constants, lung volume has changed 86% (i.e., 63% further drop); after three time constants, it has changed 95% (another 63% drop, and so on). Units with long time constants take longer to fill and to empty than units with normal compliance and resistance. Lung units have a short time constant when resistance or compliance is low. Lung units with short time constants fill and empty more rapidly than lung units with normal compliance and resistance (Fig. 11.16).

Time constants affect local distribution of ventilation within the lung. Areas having different time constants will have different volumes and pressures. Furthermore, the effects of unequal time constants within the lung are different for volume-control ventilation (with constant inspiratory flow) compared with pressure-controlled ventilation (with constant inspiratory pressure).[22]

RULE OF THUMB Understanding of the time constant is essential when setting mechanical ventilators (discussed later in this text). In pressure-control modes, inspiratory time must be at least three time constants long to deliver 95% of the volume that is possible with the given pressure settings and lung mechanics. For any mode, expiratory time must be set to at least three time constants for the lungs to empty passively to 95% (i.e., 5% of inspired volume still remains).

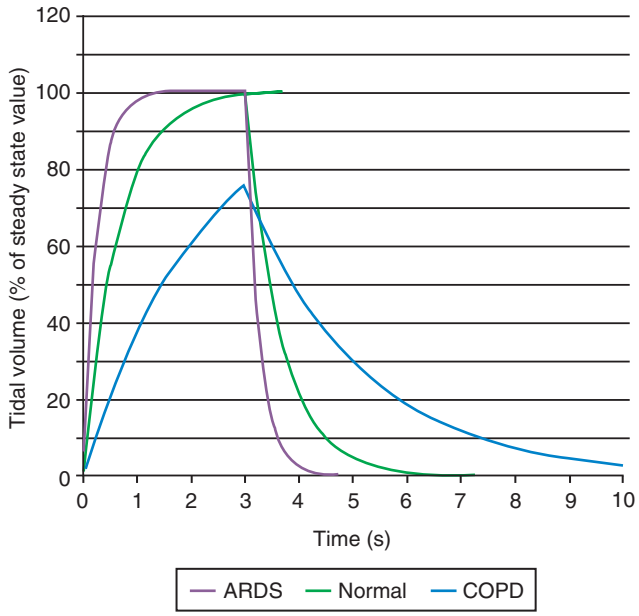

Fig. 11.16 Graph illustrates the effect of the time constant on volume change in the lungs during passive ventilation with constant inspiratory pressure. The time constant for a ventilated patient with acute respiratory distress syndrome *(ARDS)* is short (in this example, 0.26 second) owing to normal resistance but low compliance. A person with normal lungs has a longer time constant (e.g., 0.65 second) owing to normal resistance and normal compliance. A patient with chronic obstructive pulmonary disease *(COPD)* has the longest time constant (e.g., 2.13 seconds) owing to high resistance and high compliance. The horizontal axis shows the expiratory time, and the vertical axis shows the percent of the V_T that remains at each moment. The curve representing the COPD time constant indicates significant gas trapping even after an expiratory time of 5 seconds.

MINI CLINI

Breathlessness and Dynamic Hyperinflation in Obstructive Airway Disease

Problem

Patients who have obstructive airway disease often complain of breathlessness (dyspnea). This breathlessness cannot be easily predicted from simple tests of lung function. Some patients with mild obstruction have debilitating dyspnea, whereas other patients with severe obstruction often have little sensation of breathlessness. Why does expiratory flow limitation cause dyspnea of varying degrees in patients who have obstructive lung disease?

Discussion

Dynamic hyperinflation is an acute increase in the end-expiratory lung volume (EELV) as a result of insufficient expiratory time. This increase in EELV occurs because the rate of lung emptying, which is determined by the time constant, is prolonged while the expiratory time is shortened by the increase in ventilatory frequency. As a result, the inspiratory capacity decreases. Breathing at higher EELV increases the load on the respiratory muscles and restricts the normal tidal volume expansion during exercise. There is a strong correlation between the sensation of dyspnea and the EELV. Patients with obstructive lung disease describe the sensation of dyspnea differently than normal exercising persons. Terms such as "difficulty inspiring" and "can't get the air in" are commonly used to identify the breathlessness associated with dynamic hyperinflation. These specific sensations suggest that patients with airway obstruction receive discordant sensory information from the receptors in the lungs and chest wall. The intensity of these sensations depends on the degree of dynamic hyperinflation that occurs. The use of bronchodilators and lung volume reduction surgery both relieve dyspnea by decreasing the abnormal lung units (bronchodilation or removal of those units) leading to "deflating" the lungs and reducing hyperinflation. Both therapies improve dynamic airway function by improving lung emptying (more normal time constants). Patients are able to achieve the required ventilation at a lower operating lung volume with a lower O_2 cost of breathing.

Frequency Dependence of Compliance

Variations in time constants can affect ventilation. This is characteristic of obstruction in the small airways. Examples are emphysema, asthma, and chronic bronchitis.[23] The time constants of many lung units are increased in obstructive lung disease. These long time constants are mainly caused by increased resistance in the small airways. However, loss of normal tissue elastic recoil (e.g., in emphysema) contributes to slow alveolar filling and emptying.

At increased breathing rates, units with long time constants fill less and empty more slowly than units with normal compliance and resistance. Increasingly more inspired gas goes to lung units with relatively normal time constants. When more inspired volume goes to a smaller number of lung units, higher transpulmonary pressures must be generated to maintain alveolar ventilation. Compliance of the lung *seems* to decrease as breathing frequency increases. This phenomenon is called *frequency dependence of compliance*.[5] If dynamic compliance decreases as the respiratory rate increases, some lung units must have abnormal time constants. In patients with enough abnormal alveolar units, any stimulus to increase ventilation (such as exercise) may lead to redistribution of gas and a mismatching of ventilation and perfusion, which can result in hypoxemia, severely limiting an individual's ability to perform daily activities.

Abnormal time constants in lung units and frequency dependence of compliance can have significant effects on patients requiring mechanical ventilation. When ventilation is controlled in terms of volume or inspiratory-expiratory times, **dynamic hyperinflation (air trapping)** can result. Lung volume can increase with mechanical ventilation in a manner similar to that occurring during exercise. Increased ventilation (i.e., breathing rates, flows, or both) exaggerates the differences between lung units with long or short time constants. A manner to detect is to measure auto PEEP (see Chapter 52).

EFFICIENCY AND EFFECTIVENESS OF VENTILATION

To be effective, ventilation must meet the body's needs for O_2 uptake and CO_2 removal. To be efficient, ventilation should consume little O_2 and should produce the minimum amount of CO_2.

Efficiency

Even in healthy lungs, ventilation is not entirely efficient. A substantial volume of inspired gas is wasted with each breath; this wasted ventilation is referred to as *dead space*. Gases must move

in and out through the airways that lead to the gas-exchange units (alveoli). Not all the gas gets to the alveoli (as it stays in the airways) and, thus, it does not participate in gas exchange. For each inspiration, this gas left in the conducting airways is called *anatomic dead space*. The work to bring this gas into the lung is, in effect, wasted. Gas that reaches the alveoli can also be wasted if the alveoli are not perfused by the pulmonary arteries or their branches. Such gas in alveoli that are ventilated but have no perfusion contribute what is called *alveolar dead space*. The sum of anatomic and alveolar dead space is called ***physiologic dead space***. The relationship between tidal volume (V_T), dead space volume (V_D), and alveolar volume (V_A) is expressed as:

$$V_T = V_A + V_D$$

Because only alveolar volume participates in gas exchange, this equation shows that the larger the dead space, the less efficient the V_T would be in eliminating CO_2. That is, if efficiency is defined as output/input, CO_2 output would be less for a given input V_T as dead space increases.

Minute Ventilation

Ventilation is usually expressed in liters per minute of fresh gas entering the lungs. The total volume moving in or out of the lungs per minute is called ***minute ventilation***. Minute ventilation (exhaled) is denoted by $\dot{V}_E$, which is calculated as the product of frequency of breathing (f_B) times the expired tidal volume (V_T):

$$\dot{V}_E = f_B \times V_T$$

For a healthy adult breathing 12 breaths/min and having a V_T of 500 mL:

$$\dot{V}_E = \left(12\frac{\text{breaths}}{\text{min}}\right) \times \left(500\frac{\text{mL}}{\text{breath}}\right) = 6000\ \text{mL/min} = 6\ \text{L/min}$$

Minute ventilation is normally driven by the production of CO_2 and depends on the size of the person and his or her metabolic rate. Minute ventilation values range from 5 to 10 L/min in healthy adults at rest.

Alveolar Ventilation

The efficiency of ventilation depends on the volume of fresh gas reaching the alveoli (V_A):

$$V_A = V_T - V_D$$

Alveolar ventilation, $\dot{V}_A$, is the product of breathing frequency (f_B) and alveolar volume per breath (V_A):

$$\dot{V}_E = f_B \times V_A$$

In a healthy adult with a respiratory rate of 12, V_T of 500 mL, and dead space (V_D) of 150 mL, alveolar ventilation is calculated as follows:

$$\dot{V}_A = \left(12\frac{\text{breaths}}{\text{min}}\right) \times \left(500\frac{\text{mL}}{\text{breath}} - 150\frac{\text{mL}}{\text{breath}}\right)$$
$$= 4200\ \text{mL/min} = 4.2\ \text{L/min}$$

Compare this volume with that described for minute ventilation. $\dot{V}_A$ is always less than $\dot{V}_E$ because of the effect of dead space.

Anatomic Dead Space

The volume of the conducting airways (including the nasopharynx and oropharynx) is called the *anatomic dead space,* or $V_{D\,anat}$. $V_{D\,anat}$ averages approximately 1 mL/lb of ideal body weight (2.2 mL/kg). For a person who weighs 150 lb (68 kg), $V_{D\,anat}$ is approximately 150 mL. $V_{D\,anat}$ does not participate in gas exchange. During exhalation of a 500-mL tidal breath, the first 150 mL of gas exhaled comes from the $V_{D\,anat}$. The remaining 350 mL is alveolar gas. At the end of exhalation, the airways contain 150 mL of alveolar gas. During the next inhalation, this 150-mL volume is rebreathed. Only approximately 350 mL of fresh gas reaches the alveoli per breath.

RULE OF THUMB In patients on mechanical ventilation, the dead space can be increased by equipment (heat moisture exchangers, connectors, tubing) placed between the ventilator circuit and the endotracheal tube. This type of dead space is called instrumental or mechanical dead space. It becomes relevant in patients that have very small tidal volumes (e.g., neonates) and those on volume-controlled ventilation.

Alveolar Dead Space

Any gas that ventilates alveoli with no blood flow (poorly or not perfused) is also wasted *(dead space)* because gas exchange cannot occur without perfusion of the alveoli. Also, some alveoli have ventilation out of proportion to their perfusion (high $\dot{V}/\dot{Q}$ ratios). These alveoli also contribute to the inefficiency of ventilation because ventilation in excess of what is needed to arterialize the blood in an alveolus is also wasted.

The volume of gas ventilating poorly or not perfused alveoli is called **alveolar dead space**, or $V_{D\,alv}$. $V_{D\,alv}$ is usually related to defects in the pulmonary circulation. A common clinical example of such a defect is a pulmonary embolism. A pulmonary embolism blocks a portion of the pulmonary circulation; this obstructs perfusion to ventilated alveoli, creating alveolar dead space. Alveolar dead space occurs in addition to the anatomic dead space (in the non-gas exchanging conducting airways). In a normal upright person at rest, alveoli at the apices of the lungs have minimal or no perfusion and contribute to the total volume of dead space ventilation.

Physiologic Dead Space

As noted above, the total volume of wasted ventilation, or physiologic dead space, equals the sum of the conducting airways and the alveoli that are ventilated but not perfused (Fig. 11.17).

Physiologic dead space includes both the normal and the abnormal components of wasted ventilation. $V_{D\,phy}$ is the preferred clinical measure of ventilation efficiency. Measuring $V_{D\,phy}$ more accurately assesses alveolar ventilation:

$$\dot{V}_A = f_B(V_T - V_{Dphys})$$

or

$$\dot{V}_A = \dot{V}T_E - \dot{V}_{Dphys}$$

Physiologic dead space is measured clinically by using a modified form of the Bohr equation which requires measuring the exhaled CO_2[24]. The dead space to tidal volume ratio (V_D/V_T) can also be estimated for mechanically ventilated adult patients using more data available at the bedside [24,25]:

$$V_D/V_T = 0.32 + 0.0106\,(PaCO_2 - P_{ET}CO_2) + 0.003\,(RR) + 0.0015\,(age)$$

where $PaCO_2$ is arterial O_2 tension (mm Hg), $P_{ET}CO_2$ is end-tidal CO_2 tension (mm Hg), RR is respiratory rate (breaths/min), and age is in years.

Ratio of Dead Space to Tidal Volume

In clinical practice, $V_{D\,phy}$ is often expressed as a ratio to V_T. This ratio (V_D/V_T) provides an index of the wasted ventilation (anatomic plus alveolar dead space) per breath. Measurement of the V_D/V_T ratio requires measurement (or estimation) of the arterial CO_2 (P_aCO_2) and the *mixed expired* CO_2 ($P_E - CO_2$). P_aCO_2 is usually measured by obtaining an arterial blood gas specimen but can be estimated from an end-tidal gas sample ($P_{ET}CO_2$). Exhaled CO_2 may be collected in a sampling bag or balloon or estimated by means of capnography. The ratio of V_D/V_T is calculated using a modified form of the Bohr equation, which assumes that there is no CO_2 in inspired gas:

$$V_D/V_T \approx (P_aCO_2 - \bar{P}_ECO_2)/P_aCO_2$$

where P_aCO_2 is arterial CO_2 tension and $\bar{P}_ECO_2$ is the average CO_2 tension in exhaled gas.

In a normal adult who has a P_aCO_2 of 40 mm Hg and an average expired (mixed expired) CO_2 of 28 mm Hg,

$$V_D/V_T = (40 - 28)/40 = 0.30$$

The equation indicates that the normal dead space ratio is approximately 30%. This equation assumes that all of the CO_2 in expired gas comes from ventilated alveoli. If all lung units contributed CO_2 equally to the expired gas and there was no anatomic dead space, P_ECO_2 would equal P_aCO_2, and the V_D/V_T ratio would be zero. Because of anatomic and alveolar dead space, the P_ECO_2 is always less than P_aCO_2. In a healthy adult, physiologic dead space is approximately one-third of the V_T, with a normal range of 0.2 to 0.4. The V_D/V_T ratio normally decreases with exercise. Both V_T and V_D increase with increased ventilation during exertion, but the V_T normally increases to a greater degree so the ratio decreases (in healthy persons). V_D/V_T increases with diseases that cause significant dead space, such as pulmonary embolism.

Table 11.6 lists the effects of changes in the parameters that determine alveolar ventilation ($\dot{V}_A$). In healthy individuals, $\dot{V}_A$ changes with breathing rate and V_T because dead space is relatively fixed. High respiratory rate and low V_T result in a high proportion of wasted ventilation per minute (low $\dot{V}_A$). Generally, the most efficient breathing pattern is slow, deep breathing.

In pulmonary disease, increased $V_{D\,phy}$ causes a decrease in $\dot{V}_A$, unless compensation occurs. An increased breathing rate by itself worsens the problem. Effective compensation for increased $V_{D\,phy}$ requires an increased V_T. Elevating V_T increases the elastic work of breathing; however, this increases O_2 consumption by the respiratory muscles. In some patients, these increased demands cannot be met. In such cases, $\dot{V}_A$ may be inadequate to meet body needs, and CO_2 is not removed as rapidly as it is produced. CO_2 retention causes respiratory acidosis, often requiring mechanical ventilation.

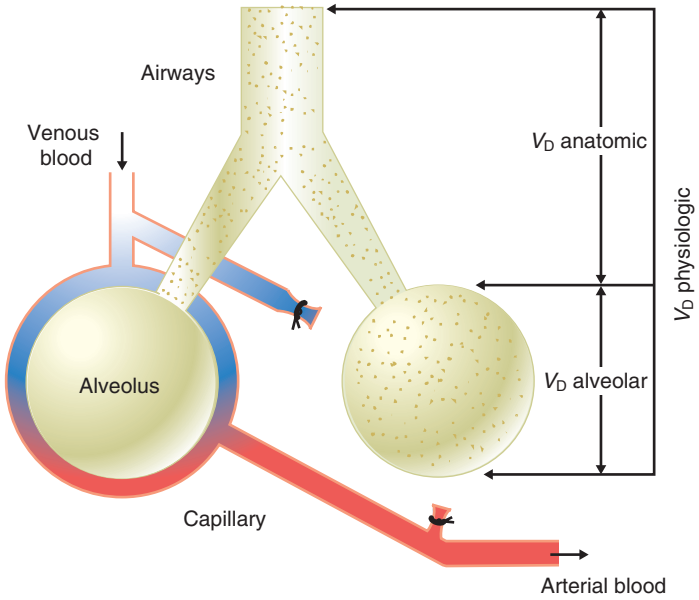

Fig. 11.17 Three Types of Dead Space. Anatomic dead space is composed of the conducting tubes leading to both alveoli. *Left,* Alveolus is normally perfused and ventilated. *Right,* Alveolus is ventilated but not perfused. The volume represents alveolar dead space. Physiologic dead space is the sum of the two components.

TABLE 11.6 Changes in Alveolar Ventilation Associated With Changes in Rate, Volume, and Physiologic Dead Space

Ventilatory Pattern	Rate of Breathing (breaths/min)	Tidal Volume (mL)	Minute Ventilation (mL)	Physiologic Dead Space (mL)	Alveolar Ventilation (mL)
Normal	12	500	6000	150	4200
High rate, low volume	24	250	6000	150	2400
Low rate, high volume	6	1000	6000	150	5100
Increased dead space	12	500	6000	300	2400
Compensation for increased dead space	12	650	7800	300	4200

MINI CLINI

Minute Ventilation, Dead Space, and P_aCO_2

Problem

A patient breathing at a rate of 12 breaths/min has a V_T of 600 mL and a measured physiologic dead space ($V_{D\ phy}$) of 200 mL. This ventilatory pattern produces a P_aCO_2 of 40 mm Hg with a pH of 7.39. Several hours later, the patient has a breathing rate of 24 breaths/min, but the minute ventilation ($\dot{V}_E$) has remained the same as before. Arterial blood gas analysis reveals a P_aCO_2 of 72 mm Hg with a pH of 7.20. Why has the P_aCO_2 increased even though the $\dot{V}_E$ remained constant?

Discussion

The initial $\dot{V}_E$ and alveolar ventilation ($\dot{V}_A$) were as follows:

$$\dot{V}_E = 600 \times 12$$
$$= 7200\ mL/min$$

$$\dot{V}_A = (600 - 200) \times 12$$
$$= 4800\ mL/min$$

The $\dot{V}_A$ of 4800 mL/min was responsible for maintaining a P_aCO_2 of 40 mm Hg. When respiratory rate increased to 24 breaths/min and $\dot{V}_E$ remained at 7200 mL/min, V_T must have decreased:

$$\dot{V}_T = 7200 \div 24$$
$$= 300\ mL$$

However, if dead space remained at 200 mL, $\dot{V}_A$ subsequently decreased:

$$\dot{V}_A = (300 - 200) \times 24$$
$$= 2400\ mL/min$$

The reduction from 4800 mL/min to 2400 mL/min explains the increase in $PaCO_2$ from 40 to 72 mm Hg. $PaCO_2$ is inversely proportional to $\dot{V}_A$. Because $\dot{V}_A$ was reduced by half, P_aCO_2 should have doubled. This approximates the data actually observed. Normally, increased CO_2 tension in the blood resulting in acidemia causes an increase in $\dot{V}_A$. This patient, although tachypneic, is hypoventilating.

Effectiveness of Ventilation

Ventilation is effective when it removes CO_2 at a rate that maintains a normal pH. Under resting metabolic conditions, a healthy adult produces approximately 200 mL of CO_2 per minute. Alveolar ventilation must match CO_2 production per minute to ensure acid-base balance.

The equilibrium between CO_2 production ($\dot{V}CO_2$) and $\dot{V}_A$ determines the PCO_2 in the lungs and arterial blood. This balance also plays a key role in determining the pH of arterial blood. The partial pressure of CO_2 in the alveoli and blood is directly proportional to its production ($\dot{V}CO_2$) and inversely proportional to its rate of removal by alveolar ventilation:

$$P_ACO_2 = \frac{\dot{V}CO_2 \times (P_B - P_{H_2O})}{\dot{V}_A} \approx P_aCO_2$$

where P_ACO_2 is alveolar CO_2 tension, $\dot{V}CO_2$ is CO_2 production, $\dot{V}_A$ is alveolar ventilation, P_B is barometric pressure, P_{H_2O} is the water vapor tension in the alveoli, and P_aCO_2 is arterial CO_2 tension.

Alveolar and arterial partial pressures of CO_2 are normally in equilibrium at approximately 40 mm Hg. If $\dot{V}_A$ decreases, $\dot{V}CO_2$ exceeds the rate at which the lungs are removing it. The P_aCO_2 increases to greater than its normal value of 40 mm Hg, and the arterial pH level decreases. Ventilation that does not meet metabolic needs (resulting in respiratory acidosis [see Chapter 14]) is termed **hypoventilation**. Hypoventilation is indicated by the presence of an elevated P_aCO_2 and a pH level below the normal range (7.35 to 7.45).

If alveolar ventilation increases, the lungs may remove CO_2 faster than it is being produced. In this case, P_aCO_2 decreases to less than its normal value of 40 mm Hg, and pH increases (i.e., respiratory alkalosis). Ventilation that exceeds metabolic needs is termed **hyperventilation**. Hyperventilation is indicated by a lower than normal P_aCO_2 and a pH above the normal range.

Hyperventilation is often confused with the increased ventilation that occurs in response to increased metabolism. The changes observed during low or moderate levels of exercise are an example. Ventilation increases in proportion to the increased $\dot{V}CO_2$ from exercise. The P_aCO_2 remains in the normal range of 35 to 45 mm Hg, and the pH level remains near 7.4. The increase in ventilation that occurs with increased metabolic rates is termed *hyperpnea*.

Effectiveness of ventilation is determined by the partial pressure of CO_2 and the resulting pH, specifically in arterial blood. Ventilation is effective when the $PaCO_2$ is maintained at a level that keeps the pH within normal limits.

SUMMARY CHECKLIST

- Ventilation occurs because of pressure differences across the lung during breathing. Gas flows into the lung when the diaphragm creates a sub-atmospheric pressure in the lung; gas flows out of the lung when the recoil properties of the lung create a slight positive pressure.
- The forces that oppose lung inflation may be grouped into two categories: elastic forces and frictional forces.
- Resting lung volume is determined by the opposing elastic forces of the lungs and chest wall.
- Frictional forces opposing ventilation include airway and tissue resistance.
- Airway resistance accounts for 80% of the frictional resistance to ventilation in a healthy adult lung.
- Exhalation is normally passive but may become active when airway resistance is abnormally high.
- The work of breathing is performed by the muscles of breathing.
- Obstructive lung disease increases the frictional work of breathing, whereas restrictive lung disease increases the elastic work of breathing.
- Respiratory muscle fatigue causes a decrease in the tidal volume and an increase in the respiratory rate.
- Even a healthy lung does not distribute ventilation evenly throughout the lungs; greater ventilation normally occurs in the bases.
- The total volume of gas moving in and out of the lungs each minute is called the *minute volume or minute ventilation.* It

is determined by multiplying the V_T times the breathing frequency.
- Homeostasis is present when the alveolar ventilation matches CO_2 production.
- The portion of the V_T that does not come into contact with pulmonary blood flow is called *dead space ventilation.*
- Normally, approximately 30% of the V_T is dead space. Most of this is called *anatomic dead space* because it is made up of the larger airways that serve to conduct gas to the alveolar sacs.
- Alveoli that are ventilated but have no blood perfusion are called *alveolar dead space.* Normally, alveolar dead space is minimal.
- The combination of anatomic and alveolar dead space is called ***physiologic dead space***.

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12

Gas Exchange and Transport

Zaza Cohen

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Describe how oxygen and carbon dioxide move between the atmosphere and tissues.
- Identify what determines alveolar oxygen and carbon dioxide pressures.
- Calculate the alveolar partial pressure of oxygen.
- State the effects that normal regional variations in ventilation and perfusion have on gas exchange.
- Describe how to compute total oxygen content for arterial blood.
- State the factors that cause the arteriovenous oxygen content difference to change.
- Identify the factors that affect oxygen loading and unloading from hemoglobin.
- Describe how carbon dioxide is carried in the blood.
- Describe how oxygen and carbon dioxide transport are interrelated.
- Describe the factors that impair oxygen delivery to the tissues and how to distinguish among them.
- State the factors that impair carbon dioxide removal.

CHAPTER OUTLINE

KEY TERMS

acute chest syndrome
alveolar dead space
alveolar shunts
anatomic dead space
Bohr effect
carboxyhemoglobin (HbCO)
dead space
dysoxia
fetal hemoglobin (HbF)
Fick equation
Fick first law of diffusion
gaseous diffusion
Haldane effect
Hamburger phenomenon
hypoxemia
hypoxia
methemoglobin
methemoglobinemia
oxyhemoglobin
right-to-left anatomic shunts
sickle cell hemoglobin
venous admixture
ventilation/perfusion (V/Q) ratio

Respiration is the process of oxygen (O_2) movement into the body for tissue use and carbon dioxide (CO_2) removal into the atmosphere. This complex process involves both gas exchange (at the lungs and at the cellular level) and transport of the gases. O_2 must be moved into the lungs, where it diffuses into the pulmonary circulation and is transported in the blood to the tissues. CO_2 builds up in the tissues because of metabolism and diffuses into the capillary blood before being carried to the lungs for exchange with alveolar gases. Normally these processes are well integrated. However, in disease states, impaired gas exchange or transport

can cause physiologic imbalances, which can alter function or threaten survival. At such times, respiratory care intervention may be the only way to maintain or restore a level of function consistent with life. This chapter provides the background knowledge that respiratory therapists (RTs) need to understand and treat patients with diseases that affect gas exchange.

DIFFUSION

Whole-Body Diffusion Gradients

Gas movement between the lungs and tissues occurs via simple diffusion (see Chapters 6 and 9). Fig. 12.1 shows the normal diffusion gradients for O_2 and CO_2. For O_2, there is a gradual downward "cascade" of partial pressures from the normal inspired partial pressure of oxygen (PiO_2) of 159 mm Hg to a low point of 40 mm Hg or less in the capillaries. The intracellular PO_2 (approximately 5 mm Hg) provides the final gradient for O_2 diffusion into the cell.

The diffusion gradient for CO_2 is the opposite of the diffusion gradient for O_2. The partial pressure of CO_2 (PCO_2) is highest in the cells (approximately 60 mm Hg) and lowest in room air (1 mm Hg). This reverse cascade causes CO_2 movement from the tissues into the venous blood, which is transported to the lungs and then exhaled.[1]

Determinants of Alveolar Gas Tensions

Alveolar Carbon Dioxide

The alveolar partial pressure of CO_2 (P_ACO_2) varies directly with the body's production of CO_2 ($\dot{V}_{CO_2}$) and inversely with alveolar ventilation ($\dot{V}_A$). The relationship is expressed by the following formula:

$$P_ACO_2 = \frac{\dot{V}_{CO_2}}{\dot{V}_A} \times K$$

where P_ACO_2 = alveolar CO_2 tension (mm Hg)
$\dot{V}_{CO_2}$ production (in mL/min standard temperature and pressure, dry [STPD])
$\dot{V}_{CO_2}$ = alveolar ventilation (L/min body temperature and pressure, saturated [BTPS])

Note that $\dot{V}_A$, not $\dot{V}_E$ (minute ventilation), is used in this calculation. **Dead space** is the difference between these two variables and is discussed later in this chapter. Because $\dot{V}_{CO_2}$ and $\dot{V}_A$ are measured under different conditions (STPD and BTPS, respectively), a correction factor of K is used. When conventional units are used for $\dot{V}_{CO_2}$ (mL/min) and $\dot{V}_A$ (L/min), $K = 0.863$.

As an example, given $\dot{V}_{CO_2}$ of 200 mL/min and alveolar ventilation of 4.315 L/min, application of this formula yields a P_ACO_2 of approximately 40 mm Hg:

$$P_ACO_2 = 0.863 \times 200 \div 4.315 = 40 (mmHg)$$

P_ACO_2 increases above this level if CO_2 production increases while alveolar ventilation remains constant or if alveolar ventilation decreases while $\dot{V}_{CO_2}$ remains constant. Likewise, P_ACO_2 decreases if CO_2 production decreases or alveolar ventilation increases. Normally, complex respiratory control mechanisms maintain P_ACO_2 within a range of 35 to 45 mm Hg. If CO_2 production increases, as with exercise or fever, ventilation automatically increases to maintain P_ACO_2 within the normal range.

Alveolar Oxygen Tensions

Many factors determine the alveolar partial pressure of O_2 (P_AO_2). The mathematical model relating these factors and applied here is called the *alveolar air equation*. One version of it is

$$P_AO_2 = FiO_2 \times (P_B - P_{H_2O}) - (P_ACO_2 \div RQ)$$

where FiO_2 = fraction of inspired O_2 (expressed in decimals)
P_B = barometric pressure (mm Hg)
P_{H_2O} = water vapor tension (At BTPS, a value of 47 mm Hg is usually used.)
P_ACO_2 = alveolar PCO_2 (mm Hg)
RQ = respiratory quotient, usually estimated at 0.8

$FiO_2 \times (P_B - P_{H_2O})$ represents the partial pressure of O_2 in the inspired air (PiO_2) and is the most important determinant of P_AO_2. The expression ($P_ACO_2 \div RQ$) accounts for the alveolar

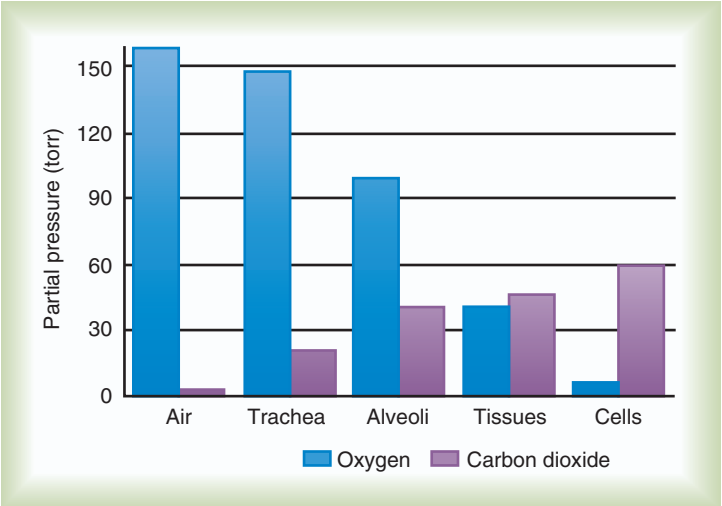

Fig. 12.1 Normal Diffusion Gradients for O_2 and CO_2. There is a downward cascade for O_2 from air to cells, with a reverse gradient for CO_2.

CO_2. However, P_ACO_2 cannot simply be subtracted, as was done for water vapor. Instead, the equation must be corrected for the difference between O_2 and CO_2 movement into and out of the alveoli, which is done by dividing the P_ACO_2 by RQ. RQ is the ratio of CO_2 excretion to O_2 uptake, which normally averages 0.8 throughout the lung. In addition, because P_aCO_2 nearly equals P_ACO_2, P_aCO_2 can be substituted for P_ACO_2. For patients at room air, sea level ($FiO_2 = 0.21$, $P_B = 760$), using $P_{H_2O} = 47$, the equation can be simplified as:

$$P_AO_2 = 0.21 \times (760 - 47) - (P_aCO_2 \div 0.8) = 150 - (P_aCO_2 \div 0.8)$$

Assuming the normal value for P_aCO_2, normal P_AO_2 can be estimated as follows:

$$P_AO_2 = 150 - (40 \div 0.8) = 100 \text{ (mm Hg)}$$

The accompanying Mini Clini provides an example of how to use the alveolar air equation.

Changes in Alveolar Gas Partial Tensions

In addition to CO_2, O_2, and water vapor, alveoli normally contain nitrogen. Nitrogen is inert and plays no role in gas exchange; however, nitrogen occupies space and exerts pressure. According to the Dalton law, the partial pressure of alveolar nitrogen (P_AN_2) must equal the pressure it would exert if it alone were present. To compute P_AN_2, subtract the pressures exerted by all the other alveolar gases, as follows:

$$P_AN_2 = P_B - (P_AO_2 + P_ACO_2 + P_{H_2O})$$

$$P_AN_2 = 760 \text{ mm Hg} - (100 \text{ mm Hg} + 40 \text{ mm Hg} + 47 \text{ mm Hg})$$

$$P_AN_2 = 760 \text{ mm Hg} - 187 \text{ mm Hg}$$

$$P_AN_2 = 573 \text{ mm Hg}$$

Because both water vapor tension and P_AN_2 remain constant, the only partial pressures that change in the alveolus are O_2 and CO_2. Based on the alveolar air equation, if FiO_2 remains constant, P_AO_2 must vary inversely with P_ACO_2.[2–4]

Mechanism of Diffusion

Gaseous diffusion is the process whereby gas molecules move from an area of high partial pressure to an area of low partial pressure. To diffuse into and out of the lung and tissues, O_2 and CO_2 must move through significant barriers.

Barriers to Gaseous Diffusion

The barrier to gaseous diffusion in the lung is the alveolar-capillary membrane. For CO_2 or O_2 to move between the alveoli and the pulmonary capillary blood, the following three barriers must be penetrated: (1) alveolar epithelium, (2) interstitial space, and (3) capillary endothelium. In addition, to pass into and out of the red blood cells (RBCs), these gases must also traverse the RBC membrane.[5,6]

The Fick First Law of Diffusion

The bulk movement of a gas through a biologic membrane ($\dot{V}_{gas}$) is described by **Fick's first law of diffusion**:

MINI CLINI

Alveolar-Arterial PO_2 *Difference and* P/F *Ratio*

Not all of the O_2 from the alveoli gets into the blood. Why this occurs is discussed later in this chapter. This Mini Clini considers how the efficiency of O_2 transfer from the alveoli to the blood can be computed.

Several bedside computations can be used to estimate the efficiency of pulmonary O_2 transfer. The most common computation is the difference between the alveolar and arterial PO_2, called the *A–a gradient* ($D_{A-a}O_2$). Normally this difference is small—only 5 to 10 mm Hg. The reason for this slight difference in normal individuals is discussed later in this chapter. An increase in the A–a gradient is often an indicator of pulmonary parenchymal disease.

Another common bedside computation is the ratio of P_aO_2 to FiO_2, sometimes simplified to *P/F* (pronounced "PF") ratio. The *P/F* ratio has units of millimeters of mercury (because P_aO_2 has units of millimeters of mercury and FiO_2 is dimensionless). It is frequently used for ventilated patients as a measure of oxygenation abnormality and is one of the main criteria for diagnosing acute respiratory distress syndrome (ARDS).

Problem

Compute and interpret the $D_{A-a}O_2$ and *P/F* ratio for a 45-year-old woman breathing 70% O_2 at sea level with the following blood gas values: P_aO_2, 50 mm Hg; P_aCO_2, 40 mm Hg.

Solution

1. Compute P_AO_2 using one form of the alveolar O_2 equation, as follows:

$$P_AO_2 = FiO_2 \times (P_B - 47) - (P_aCO_2 \div 0.8)$$

$$P_AO_2 = 0.7 \times (760 - 47) - (40 \div 0.8)$$

$$P_AO_2 = 449 \text{ mm Hg}$$

2. Compute $D_{A-a}O_2$ as follows:

$$D_{A-a}O_2 = P_AO_2 - PaO_2$$

$$D_{A-a}O_2 = 449 - 50$$

$$D_{A-a}O_2 = 399 \text{ mm Hg}$$

3. Compute *P/F* ratio as follows:

$$P_aO_2/FiO_2 = 50/0.7 = 71.4 \text{ mm Hg}$$

Discussion

Both the $D_{A-a}O_2$ and the *P/F* ratio are abnormal. Compared with a normal value, the $D_{A-a}O_2$ of nearly 400 mm Hg is very high. This $D_{A-a}O_2$ indicates a large difference between the alveolar and arterial PO_2 values (i.e., inefficient O_2 transfer). Likewise, the *P/F* ratio of 71.4 indicates severe **hypoxemia.** Although the patient is receiving a high FiO_2 (0.70), she has a severe problem getting O_2 into her blood and needs immediate evaluation for transfer to the intensive care unit (ICU).

RULE OF THUMB When the patient is breathing room air, the sum of P_AO_2 and P_ACO_2 is approximately 140 mm Hg (100 mm Hg + 40 mm Hg). This equation assumes a constant value for RQ. Changes in ventilation that affect P_ACO_2 will also alter P_AO_2 to keep the total at 140 mm Hg. If the P_ACO_2 of a patient breathing room air decreases from 40 to 20 mm Hg (a decrease of 20 mm Hg), P_AO_2 should increase by approximately 20 mm Hg. It is important to note that although hyperventilation will allow halving the P_ACO_2 (from 40 to 20), it will result in only modest increase of P_AO_2 (from 100 to 120; see Fig. 12.2).

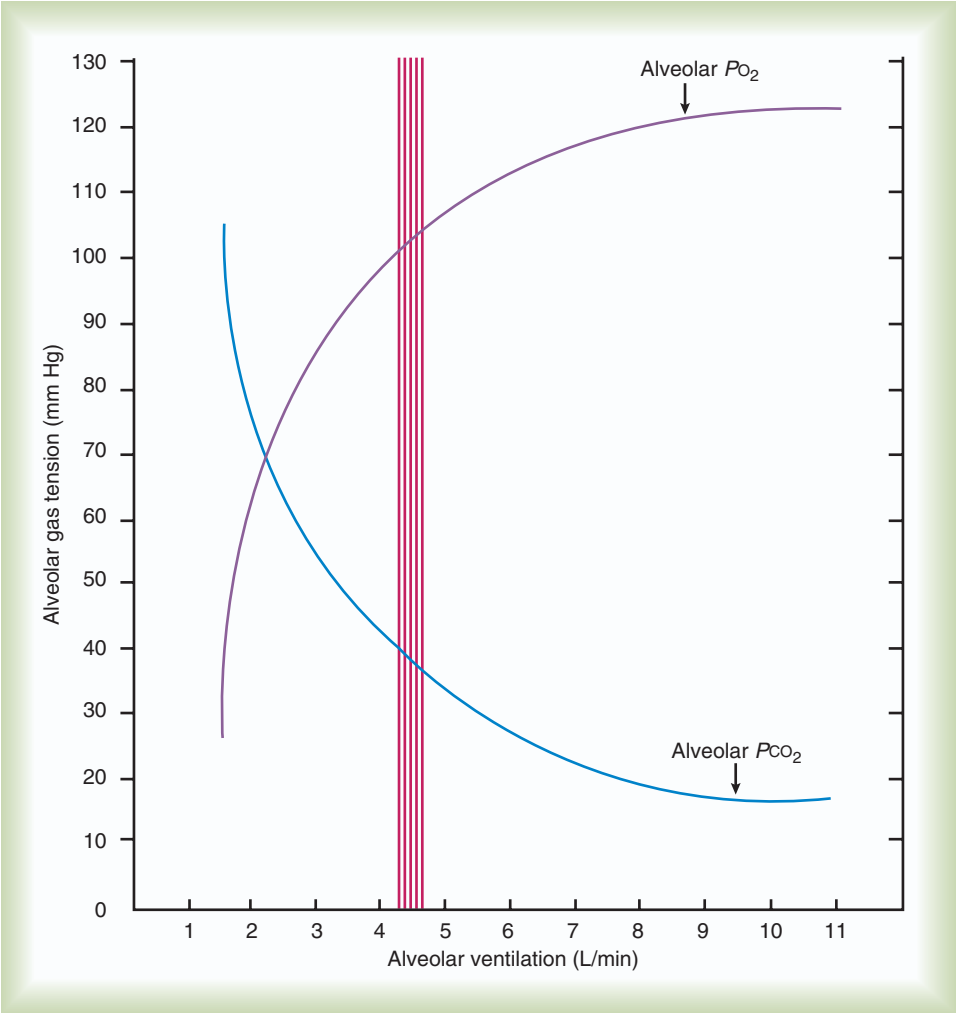

Fig. 12.2 Effect of alveolar ventilation on alveolar gases. (Modified from Pilbeam SP: *Mechanical ventilation*, ed 4, St Louis, 2006, Mosby.)

$$\dot{V}_{gas} = \frac{A \times D \times (P_1 - P_2)}{T}$$

In this formula, A is the cross-sectional area available for diffusion, D is the diffusion coefficient of the gas, T is the thickness of the membrane, and $(P_1 - P_2)$ is the partial pressure gradient across the membrane. Given that the surface area and thickness of the alveolar-capillary membrane are constant in healthy people, diffusion in the normal lung mainly depends on gas pressure gradients. In clinical practice, it is impossible to measure the area and the thickness of the membrane, so the formula is often rewritten as:

$$\dot{V}_{gas} = D_L \times (P_1 - P_2)$$

where D_L (the diffusing capacity of the lungs) combines the area, thickness, and diffusion properties of the gas and the membrane and can be helpful in evaluating certain diseases. Chapter 20 provides details on the technique for measuring D_L and its diagnostic use.

Pulmonary Diffusion Gradients

For gas exchange to occur between the alveoli and pulmonary capillaries, a difference in partial pressures $(P_1 - P_2)$ must exist. Fig. 12.3 shows the size and direction of these gradients for O_2 and CO_2. In the normal lung, the alveolar PO_2 averages approximately 100 mm Hg, whereas the mean PCO_2 is approximately 40 mm Hg. Venous blood returning to the lungs has a lower PO_2 (40 mm Hg) than alveolar gas. The pressure gradient for O_2 diffusion into the blood is approximately 60 mm Hg (100 mm Hg – 40 mm Hg). As blood flows past the alveolus, it takes up O_2 and moves to the left atrium with a PO_2 close to 100 mm Hg in healthy people.

Because venous blood has a higher PCO_2 than alveolar gas (46 vs. 40 mm Hg), the pressure gradient for CO_2 causes it to diffuse in the opposite direction, from the blood into the alveolus. This diffusion continues until capillary PCO_2 equilibrates with the alveolar level at approximately 40 mm Hg.

RULE OF THUMB Alveolar membrane permeability is approximately 20 times greater for CO_2 than that for O_2. Despite such difference, approximately same amount of these gases is diffused across the membrane during normal breathing. This is achieved by having a much larger pressure gradient for O_2 diffusion than for CO_2 diffusion.

Time Limits to Diffusion

For blood leaving the pulmonary capillary to be adequately oxygenated, it must spend sufficient time in contact with the alveolus

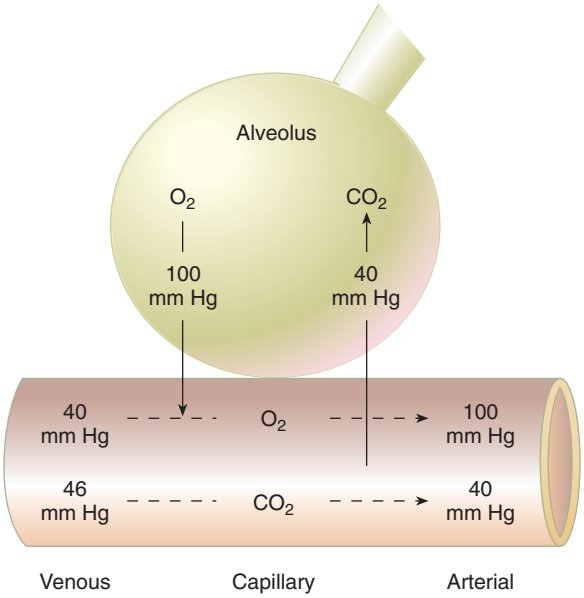

Fig. 12.3 Ventilation maintains mean alveolar gas pressures for O_2 and CO_2 at approximately 100 and 40 mm Hg. As blood enters the venous end of the capillary, it gives up CO_2 and loads O_2 until these two gases are in equilibrium with alveolar pressures. At this point, the blood is "arterialized."

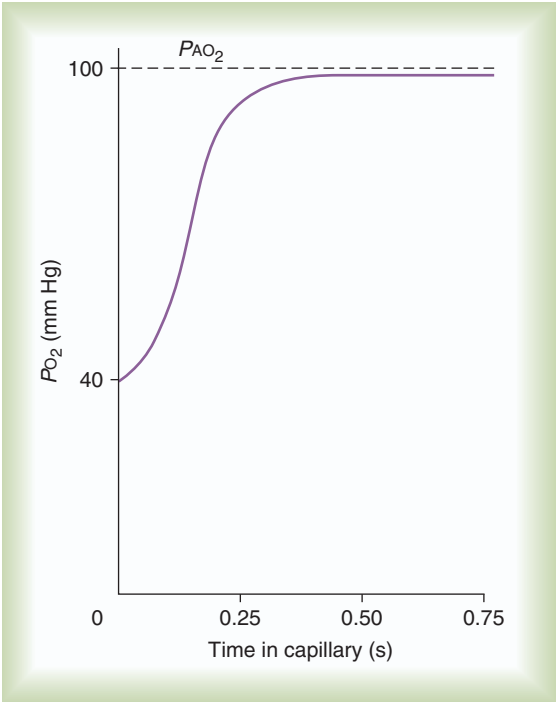

Fig. 12.4 Alveolar-capillary PO_2 Gradient. Normal transit time for red blood cells in the pulmonary capillary is approximately 0.75 second. Normally, blood PO_2 equilibrates with the alveolar PO_2 well before it reaches the end of the capillary.

to allow equilibration.[5,7,8] If the time available for diffusion is inadequate, blood leaving the lungs may not be fully oxygenated. As depicted in Fig. 12.4, blood normally takes only a fraction of the time it spends in the capillary to be fully oxygenated. The shape of the graph is S-like rather than linear. If blood flow increases, as during heavy exercise, capillary transit time decreases, but this short period is still adequate to ensure that equilibration occurs as long as no other factors impair diffusion. However, in the presence of a diffusion limitation, the relationship becomes more linear and the O_2 diffusion across the membrane may occur throughout the entire time that blood spends in the pulmonary capillary. In these patients, rapid blood flow through the pulmonary circulation can result in inadequate oxygenation. For this reason, many patients with certain types of lung disease will have normal O_2 saturation at rest but will quickly desaturate even on minimal exertion.

MINI CLINI

Desaturation With Exercise

Many patients with advanced lung disease will have normal O_2 saturation at rest but would complain of dyspnea on exertion. In these patients it is important to perform exercise oximetry—that is, to measure O_2 saturation during moderate exercise, such as walking in the hallway. At rest, the impairment of O_2 diffusion across the membrane is compensated by allowing a longer diffusion time ("slow" blood flow, therefore longer transit time across the pulmonary capillary). During exercise, cardiac output increases, capillary transit time decreases, and blood does not spend enough time in the pulmonary capillary to be fully oxygenated. If there is significant desaturation during exercise, the patient may be a candidate for supplemental O_2.

Systemic Diffusion Gradients

Partial pressure gradients in the tissues are the opposite of the partial pressure gradients in the lung. As cellular metabolism depletes its O_2, intracellular PO_2 decreases below PaO_2. O_2 diffuses from the tissue capillary blood (PO_2 = 100 mm Hg) to the cells (PO_2 <40 mm Hg). Simultaneously, CO_2 diffuses from the cells (PCO_2 = 60 mm Hg) into the capillary blood (PCO_2 = 40 mm Hg). After equilibration, blood leaves the tissue capillaries with a PO_2 of approximately 40 mm Hg and PCO_2 of approximately 46 mm Hg.

Just as arterial blood reflects pulmonary gas exchange, venous blood reflects events occurring in the tissues. The use of venous blood to assess tissue oxygenation is discussed in Chapter 52.

VARIATIONS FROM IDEAL GAS EXCHANGE

As discussed previously in this chapter, there is a slight difference between alveolar and arterial PO_2 (normally 5–10 mm Hg). Two factors account for this difference: (1) right-to-left shunts in the pulmonary and cardiac circulation and (2) regional differences in pulmonary ventilation and blood flow.

Anatomic Shunts

A shunt is the portion of the cardiac output that returns to the left heart without being oxygenated by exposure to ventilated alveoli. There are two types of **right-to-left anatomic shunts** in normal humans: (1) bronchial venous drainage and (2) thebesian venous drainage (see Chapters 9 and 10). In healthy individuals, it is estimated that approximately 5% of the cardiac output bypasses the pulmonary circulation because of these anatomic shunts. A right-to-left shunt causes poorly oxygenated venous

blood to move directly into the arterial circulation, thus reducing the O_2 content of arterial blood. Together, these normal shunts account for approximately three-fourths of the normal difference between P_AO_2 and P_aO_2. The remaining difference is a result of normal inequalities in pulmonary ventilation and perfusion.[5]

Inequalities in Ventilation and Perfusion

The normal respiratory exchange ratio of 0.8 assumes that ventilation and perfusion in the lung are in balance, with every liter of alveolar ventilation ($\dot{V}_A$) matched by approximately 1 L of pulmonary capillary blood flow ($\dot{Q}_c$). Any variation from this perfect balance alters gas tensions in the affected alveoli. The **ventilation/perfusion ratio** ($\dot{V}_A/\dot{Q}_c$, **or simply *V/Q***) is one of the key concepts in pulmonary physiology because it plays a major role in gas exchange in health and disease.

Ventilation/Perfusion Ratio

An ideal ratio of 1 indicates that ventilation and perfusion are in perfect balance. A high *V/Q* indicates that ventilation is greater than normal, perfusion is less than normal, or both. This can occur when pulmonary blood flow is decreased but ventilation is normal, an example of which occurs with a pulmonary embolism. Conversely, a low *V/Q* indicates that ventilation is less than normal, perfusion is greater than normal, or both. This can occur when alveoli collapse, as when a patient develops atelectasis.

Effect of Alterations in Ventilation/Perfusion Ratio

Fig. 12.5 shows graphs of the effect of *V/Q* changes on the respiratory exchange ratio *(R)*, plotting possible values of P_AO_2 and P_ACO_2. When ventilation and perfusion are in perfect balance (*V/Q* = 1), *R* equals 0.8. At this point, P_AO_2 and P_ACO_2 values equal the ideal values of 100 and 40 mm Hg.

As the *V/Q* decreases below 1.0 (see Fig. 12.5, following the *curve to the left*), proportionally more O_2-poor, CO_2-rich blood reaches alveolar air. The result is a lower P_AO_2 and higher P_ACO_2. At the extreme left of the graph, there is perfusion but no ventilation (*V/Q* = 0). With no ventilation to remove CO_2 and restore O_2, the makeup of gases in these areas is similar to that of mixed venous blood (P_VO_2 = 40 mm Hg; P_VO_2 = 46 mm Hg).

Venous blood entering areas with *V/Q* values of zero cannot pick up O_2 or unload CO_2; therefore it leaves the lungs unchanged. As this venous blood returns to the left side of the heart, it mixes with well-oxygenated arterial blood, diluting its O_2 contents in a manner similar to that described for a right-to-left anatomic shunt. To distinguish such areas from true anatomic shunts, exchange units with *V/Q* values of zero are called **alveolar shunts.** Anatomic and alveolar shunts together cause venous blood to mix with the arterial blood, a phenomenon called **venous admixture.** Alveolar shunts can be caused by chronic obstructive pulmonary disease (COPD), restrictive disorders, or any condition resulting in hypoventilation.

In addition to anatomic and alveolar shunts, a portion of venous blood travels from the right heart to the left heart without being involved in adequate gas exchange with ventilated portions of the lung. Together, they are called a *physiologic shunt.* The shunt equation quantifies the portion of blood included in the *V/Q* mismatch, in which *V/Q* is less than 1. It is usually expressed as a percentage of the total cardiac output, thus:

$$\frac{Q_s}{Q_t} = \frac{C_cO_2 - C_aO_2}{C_cO_2 - C_{\bar{v}}O_2}$$

where Q_s = shunt flow; blood entering systemic blood without being oxygenated in the lungs
Q_t = total cardiac output
C_cO_2 = O_2 content at the end of the ventilated and perfused pulmonary capillaries
C_aO_2 = arterial O_2 content
$C_{\bar{v}}O_2$ = mixed venous O_2 content

Although arterial O_2 content can be directly measured from a systemic artery and mixed venous O_2 content can be directly measured from the pulmonary artery, the end capillary content must be derived from an additional calculation requiring use of

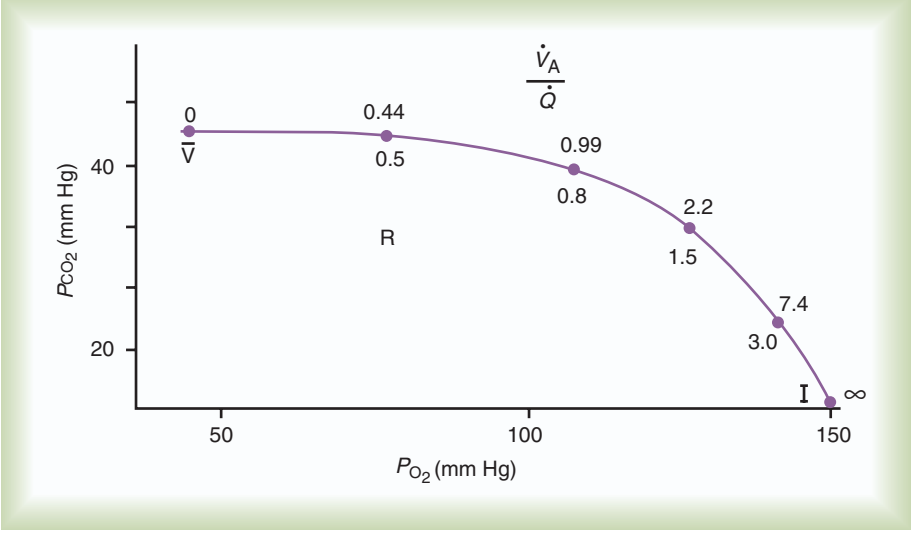

Fig. 12.5 Relationship between alveolar PO_2 and PCO_2 with changes in $\dot{V}_A/\dot{Q}$ and respiratory exchange ratio. (From Cherniak RM, Cherniak L: *Respiration in health and disease*, ed 3, Philadelphia, 1983, Saunders.)

the alveolar air equation and the hemoglobin (Hb) concentration. A more practical *estimation* of the shunt fraction is as follows: each increase of $D_{A-a}O_2$ by 100 mm Hg corresponds to 5% increase in shunt fraction.

RULE OF THUMB *V/Q* imbalance is the most common cause of hypoxemia in patients with respiratory diseases. Shunting can also occur commonly, especially in patients who are critically ill. To differentiate between hypoxemia caused by a simple *V/Q* imbalance from hypoxemia caused by shunting, apply the following 50/50 rule: If FiO_2 is greater than 50 (%) and P_aO_2 is less than 50 (mm Hg), significant shunting is present; otherwise the hypoxemia is mainly caused by a *V/Q* imbalance.

Dead Space

As the *V/Q* increases above 1 (see Fig. 12.5, following the curve to the right), less blood reaches O_2-rich, CO_2-poor inspired gas. The result is a higher P_AO_2 and lower P_ACO_2. At the extreme right of the graph, perfusion is zero ($V/Q = \infty$). Areas with ventilation but no blood flow essentially represent dead space. The makeup of gases in these areas is similar to that of inspired air (PO_2 = 150 mm Hg; PCO_2 = 0 mm Hg).

Dead space, mentioned earlier, has two components: **Anatomic dead space** is the portion of the tidal volume that never reaches the alveoli for gas exchange (upper airways, trachea, bronchi, and so on until the respiratory bronchiole). **Alveolar dead space** is the portion of the tidal volume that enters into alveoli that are without any perfusion or without adequate perfusion. Conditions that can lead to alveolar dead space include pulmonary emboli, partial obstruction of the pulmonary vasculature, destroyed pulmonary vasculature (as can occur in COPD), and reduced cardiac output. The sum of alveolar and anatomic dead space is often referred to as physiologic dead space (V_D). The dead space/tidal volume ratio (V_D/V_T) affects alveolar ventilation:

$$\dot{V}_A = \dot{V}_E\left(1 - \frac{V_D}{V_T}\right)$$

where $\dot{V}_A$ = alveolar ventilation (L/min)
$\dot{V}_E$ = minute ventilation (L/min)
V_D = dead space volume (mL)
V_T = tidal volume (mL)

The clinical significance of increased dead space, or V_D/V_T ratio, is that it decreases alveolar ventilation and hence increases P_aCO_2. This can happen by the addition of extra tubing to the ventilator (exogenous V_D), lung disease (increased alveolar V_D), or shallow breathing (decreased V_T that leads to increased V_D/V_T ratio). In the face of increased dead space, minute ventilation must increase to achieve normal $\dot{V}_A$ and P_aCO_2. This additional ventilation comes at a cost with an increase in the work of breathing, which consumes additional O_2 and further adds to the burden of external ventilation. Similarly, patients with rapid shallow breathing will often have ineffective ventilation with increased P_aCO_2 despite elevated minute ventilation.

Regional Differences in Ventilation/Perfusion Ratio

Regional variations in *V/Q* for a normal lung are mainly caused by gravity and are most evident in the upright posture. Because the pulmonary circulation is a low-pressure system, blood flow in the upright lung varies considerably from top to bottom (see Chapter 9). Farther down the lung, perfusion increases linearly in proportion to the hydrostatic pressure, so that the lung bases receive nearly 20 times as much blood flow as the apexes.

Regional differences in ventilation throughout the lung also occur, but they are less drastic than the differences in perfusion. Similar to perfusion, ventilation also is increased in the lung bases, with approximately four times as much ventilation going to the bases than to the apexes of the upright lung. These regional differences in ventilation are caused by the effect of gravity on pleural pressures (see Chapter 11).

Table 12.1 summarizes the relationships between ventilation and perfusion by lung region.[8] At the lung apexes, ventilation exceeds blood flow, resulting in a high *V/Q* (approximately 3.3), high PO_2 (132 mm Hg), and low PCO_2 (32 mm Hg). Farther down the lung, blood flow increases more than ventilation because of gravity. Toward the middle, the two are approximately equal (V/Q = 1.0). At the bottom of the lung, blood flow is greater than ventilation, resulting in a low *V/Q* (approximately 0.66), low PO_2 (89 mm Hg), and slightly higher PCO_2 (42 mm Hg).

As shown in Table 12.1, because of gravity, most blood flows to the lung bases, PO_2 is less than normal, and PCO_2 is greater than normal. After leaving the lung, this large volume of blood combines with the smaller volume coming from the middle and apical regions. The result is a mixture of blood with less O_2 and more CO_2 than would come from an ideal gas-exchange unit.

TABLE 12.1 Summary of Variations in Gas Exchange in the Upright Lung by Region

Lung Region	*V/Q* Ratio	Mean P_AO_2 (mm Hg)	Mean P_ACO_2 (mm Hg)	Blood Flow
Apexes	3.3	132	32	Low
Middle	1.0	100	40	Moderate
Bases	0.66	89	42	High

MINI CLINI

In patients with normal lungs, the regional differences in ventilation are matched with the regional differences in perfusion, thus keeping the *V/Q* ratio as close to 1 as possible. Patients with adult respiratory distress syndrome (ARDS) have significant gas exchange abnormalities due to the accumulation of exudative fluid in the alveoli, requiring mechanical ventilation with high levels of FiO_2 and positive end-expiratory pressure (PEEP). In addition, the distribution of lung disease is such that it affects gravity-dependent areas more severely. As a result, gravity-dependent areas receive a greater portion of perfusion (as in healthy individuals) but much less ventilation, further compounding the *V/Q* mismatch. One way to offset this imbalance is to place these patients in prone position to improve *V/Q* matching. Unfortunately the actual clinical effect of prone positioning is often small and transient. Placing critically ill patients with endotracheal tubes and various other catheters in prone position must be carried out with extreme caution, and the risks of such a dramatic intervention must be carefully weighed against the proposed benefits.

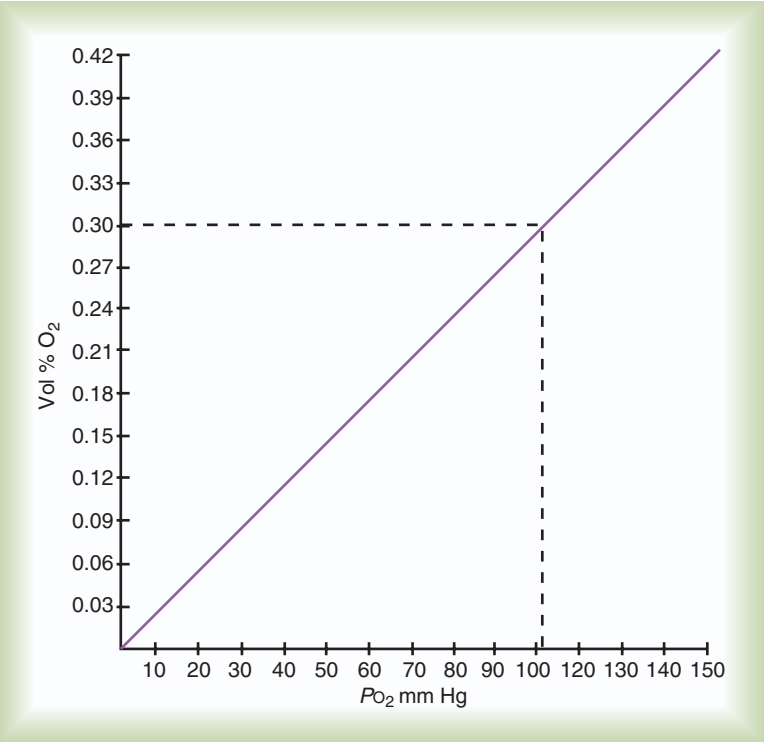

Fig. 12.6 Relationship Between PO_2 and Dissolved O_2 Contents of Plasma at 37°C. The *dashed line* emphasizes the fact that arterial blood, with average PO_2 of 100 mm Hg, has 0.3 mL of O_2 dissolved in each deciliter (100 mL).

OXYGEN TRANSPORT

Blood carries O_2 in two forms. A small amount of O_2 exists in a simple physical solution, dissolved in the plasma and erythrocyte intracellular fluid. However, most O_2 is bound to Hb inside the RBC. As gaseous O_2 diffuses into the blood, it immediately dissolves in the plasma and erythrocyte fluid. By applying Henry's law (see Chapter 6), the amount of dissolved O_2 in the blood (at 37°C) can be computed with the following simple formula:

$$\text{Dissolved } O_2 \text{ (mL/dL)} = PO_2 \text{ (mm Hg)} \times 0.003$$

This equation is plotted in Fig. 12.6, which shows that the relationship between partial pressure and dissolved O_2 is direct and linear. In normal arterial blood with PaO_2 of approximately 100 mm Hg, there is approximately 0.3 mL/dL of dissolved O_2. However, if an individual with normal gas exchange breathes pure O_2, PaO_2 increases to approximately 670 mm Hg. In this case, the dissolved O_2 would increase to approximately 2.0 mL/dL. The blood of someone breathing pure O_2 in a hyperbaric chamber at 3 atmospheres (2280 mm Hg) would carry nearly 6.5 mL/dL dissolved O_2 in the plasma. Despite such extreme conditions (FiO_2 = 100%, P_B = 3 atm), the amount of dissolved O_2 is still much less than the amount carried by Hb (see further on).

Chemically Combined Oxygen (Oxyhemoglobin)

Hemoglobin and Oxygen Transport

Most blood O_2 is transported in chemical combination with Hb in the erythrocytes. Hb is a conjugated protein, consisting of four linked polypeptide chains (the *globin* portion), each of which is combined with a porphyrin complex called *heme*. The four polypeptide chains of Hb are coiled together into a ball-like structure, the shape of which determines its affinity for O_2.[5,8]

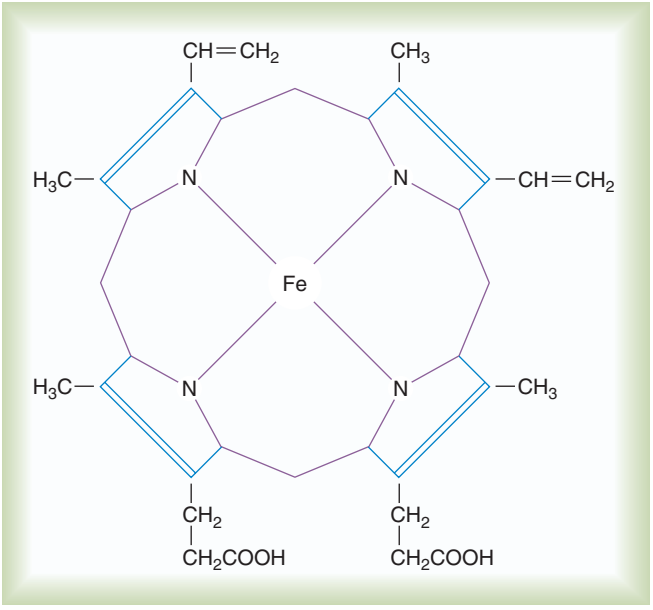

Fig. 12.7 Structure of heme.

As shown in Fig. 12.7, each heme complex contains a centrally located ferrous iron ion. When Hb is not carrying O_2, this ion has four unpaired electrons. In this deoxygenated state, the molecule exhibits the characteristics of a weak acid. Deoxygenated

Hb serves as an important blood buffer for H+, a crucial factor in CO_2 transport.

When fully saturated, four O_2 molecules bind to the iron ion of Hb, one for each protein chain. With complete O_2 binding, all electrons become paired, and Hb is converted to its oxygenated state (**oxyhemoglobin** [HbO_2]).

In whole blood, 1 g of normal Hb can carry approximately 1.34 mL of O_2. Given an average blood Hb content of 15 g/dL, the O_2-carrying capacity of the blood can be calculated as follows:

$$1.34\ \text{mL/g} \times 15\ \text{g/dL} = 20.1\ \text{mL/dL}$$

The addition of Hb increases the O_2-carrying capacity of the blood nearly 70-fold compared with plasma alone. The amount of O_2 bound to Hb depends on its level of saturation with O_2.

Hemoglobin Saturation

Saturation is a measure of the proportion of available Hb that is carrying O_2. Saturation is computed as the ratio of HbO_2 (content) to total Hb (capacity). Hb arterial O_2 saturation (SaO_2) is usually expressed as a percentage of this ratio and calculated according to the following formula:

$$SaO_2 = (HbO_2 \div \text{Total Hb}) \times 100$$

where HbO_2 equals the oxyhemoglobin content. In clinical practice, both SaO_2 and total Hb content are measured directly to derive the HbO_2. Normal SaO_2 is 95% to 100% depending on the age of the patient.

Total Oxygen Content of the Blood

Total O_2 content of the blood equals the sum of O_2 dissolved in the plasma and chemically combined with Hb.[2,7] For total O_2 content to be calculated, the following three values must be known: (1) P_aO_2, (2) total Hb content (g/dL), and (3) % Hb saturation. Given these values, the following equation can be applied:

$$CaO_2 = (0.003 \times PaO_2) + (1.34 \times Hb \times SaO_2)$$

where CaO_2 = total O_2 content (mL/dL)
PaO_2 = partial pressure of O_2 in the blood
Hb = Hb content (in g/dL)
SaO_2 = percent Hb saturation with O_2 (expressed as a decimal, e.g., 70% saturation = 0.7)

The ($0.003 \times PO_2$) component of the equation represents dissolved O_2, whereas the ($1.34 \times Hb \times SaO_2$) component represents the chemically combined oxyhemoglobin. For example, the total O_2 content of normal arterial blood (assuming PaO_2 = 100, Hb = 15g/dL, SaO_2 = 0.97) can be computed as follows:

$$CaO_2 = (0.003 \times PaO_2) + (1.34 \times Hb \times SaO_2)$$

$$CaO_2 = (0.003 \times 100) + (1.34 \times 15 \times 0.97)$$

$$CaO_2 = 0.3 + 19.5$$

$$CaO_2 = 19.8\ (\text{mL/dL})$$

The normal CaO_2 concentration is 16 to 20 mL/dL. As previously noted, O_2 dissolved in the plasma constitutes a small fraction of the blood's total O_2 content (0.3/19.8 = 1.5%) and is sometimes omitted from such calculations because it is so relatively small.

Oxyhemoglobin Dissociation Curve

Hemoglobin saturation with O_2 varies with changes in PO_2. Plotting the saturation (*y*-axis) against PO_2 (*x*-axis) yields the HbO_2 dissociation curve (see Fig. 12.8). The relationship between Hb saturation and PO_2 is not linear[4]; instead, it forms an S-shaped curve. The flatter upper part of this curve represents the normal operating range for arterial blood. Because the slope is minimal in this area, major changes in PaO_2 have little effect on SaO_2, indicating a strong affinity of Hb for O_2. With a normal PaO_2 of 100 mm Hg, SaO_2 is approximately 97%. If a disease process results in a substantial reduction in PaO_2 to 65 mm Hg, SaO_2 would not drop as drastically and will be approximately 90%.

However, with PO_2 less than 60 mm Hg, the curve steepens dramatically and the SaO_2 drops significantly. This is why it is important to keep PaO_2 greater than 60 mm Hg in clinical practice. With PO_2 less than 60 mm Hg, a small decrease in PO_2 causes a large decrease in SaO_2, indicating a lessening affinity for O_2. This normal decrease in the affinity of Hb for O_2 is one way in which the body compensates for hypoxemia by helping to release large amounts of O_2 to the tissues. In other words, when there is less total O_2 available, making the little that is available easier to offload to tissues is an appropriate physiologic adjustment.

MINI CLINI

Relating Hemoglobin Saturation and PaO_2

Problem

Pulse oximeters are simple bedside devices that estimate Hb saturation by way of a noninvasive probe that is generally connected to the patient's finger, earlobe, or forehead. Although oximeters measure Hb saturation percentage, blood oxygenation still tends to be quantified according to PaO_2. Is there a simple way to relate these two measures without carrying around an HbO_2 dissociation curve?

Discussion

First, although extremely useful, pulse oximeters can be somewhat inaccurate compared with other types of clinical measurement devices. This limitation should be understood. Prior to interpreting the O_2 saturation value, the waveform should be examined and deemed accurate. In addition, the actual measurement may be 2%–3% off compared with more accurate measurements, such as arterial blood gas co-oximetry. For example, a patient with a pulse oximetry display of 90% may have co-oximetry values anywhere in the range of 87%–93%. The value of pulse oximetry is in its ability to noninvasively and continuously display trends and provide warning of significant changes in oxyhemoglobin saturation.

Even so, RTs must often estimate PaO_2 from oximeter readings. The following simple rule, called the *40–50–60/70–80–90 rule,* should be helpful. Assuming normal pH, PCO_2, and Hb values, saturations of 70%, 80%, and 90% are roughly equivalent to PO_2 values of 40, 50, and 60 mm Hg, as follows:

Hb Saturation (%)	Approximate PaO_2 (mm Hg)
70	40
80	50
90	60

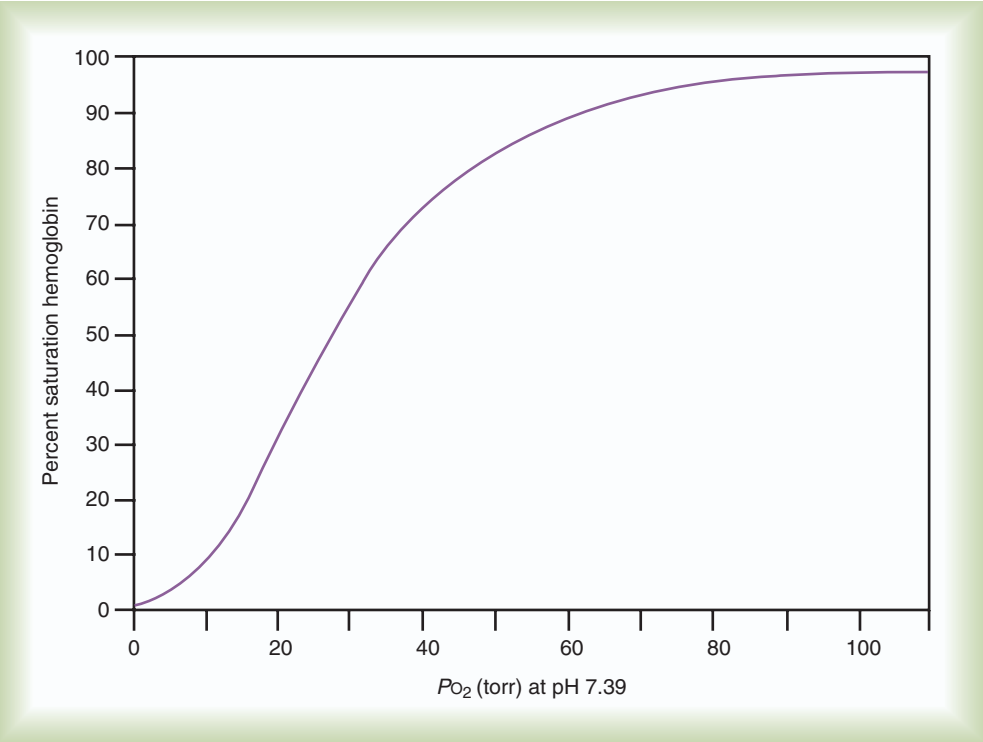

Fig. 12.8 O_2 dissociation curve plots the relationship between plasma PO_2 (*x*-axis) and Hb saturation (*y*-axis).

A patient with a pulse oximetry reading of 90% has a PaO_2 of approximately 60 mm Hg. If the saturation decreased to 80%, the PaO_2 would decrease to approximately 50 mm Hg. This rule works only in the middle range of PO_2 values, where the curve is most linear; it should not be applied with Hb saturations greater than 90% or less than 70%.

Although SaO_2 plays a greater part in total blood O_2 content than PaO_2, it is often important to consider both when a patient's oxygenation is being evaluated. First, PaO_2 is a more accurate measurement than SaO_2, which is usually derived from pulse oximetry. In addition, a patient with an SaO_2 of 100% may have a PaO_2 between 100 and 600 mm Hg, and the knowledge of exact PaO_2 value gives a clinician a better understanding of the patient's gas-exchange status.

Normal Loading and Unloading of Oxygen (Arteriovenous Differences)

Fig. 12.9 uses the HbO_2 dissociation curve to show the effects of O_2 loading and unloading in the lungs and tissues. *Point A* represents freshly arterialized blood leaving the pulmonary capillaries with a PO_2 of approximately 100 mm Hg and Hb saturation of approximately 97%. As blood perfuses body tissues, O_2 uptake causes a decrease in both PO_2 and saturation such that venous blood leaving the tissues *(point V)* has a PO_2 of approximately 40 mm Hg, with Hb saturation of approximately 75%.

Using a normal Hb content of 15 g/dL and knowing the saturation at each possible PO_2, the total O_2 content can be calculated at any PO_2 in the manner previously described. The *y*-axis of Fig. 12.9 provides this information in SaO_2 increments of 10%.

TABLE 12.2 Oxygen Content of Arterial and Venous Blood

O_2 Content	Arterial O_2 (mL/dL)	Venous O_2 (mL/dL)
Combined O_2 ($1.34 \times 15 \times SO_2$)	19.5	14.7
Dissolved O_2 ($PO_2 \times 0.003$)	0.3	0.1
Total O_2 content	19.8	14.8

Table 12.2 summarizes the difference between the O_2 content of these normal arterial and venous points.

As indicated in Table 12.2, the difference between the arterial and venous O_2 contents is normally approximately 5 mL/dL. This is the arterial-to-venous O_2 content difference ($C_{a-v}O_2$). It is the amount of O_2 given up by every 100 mL of blood on each pass through the tissues.

Fick Equation

The Fick principle states that the total O_2 uptake by the peripheral tissues (O_2 consumption, or $\dot{V}_{O_2}$) is equal to the product of the blood flow to the peripheral tissues and the arterial-to-venous O_2 content difference ($C_{a-v}O_2$). The classic **Fick's equation** is written as follows:

$$\dot{V}_{O_2} = C.O. \times (C_aO_2 - C_{\bar{v}}O_2) \times 10$$

where C.O. = cardiac output (dL/min)
$\dot{V}_{O_2}$ = whole-body O_2 consumption (mL/min)
C_aO_2 = arterial O_2 content (mL/dL)
$C_{\bar{v}}O_2$ = mixed venous O_2 content (mL/dL)

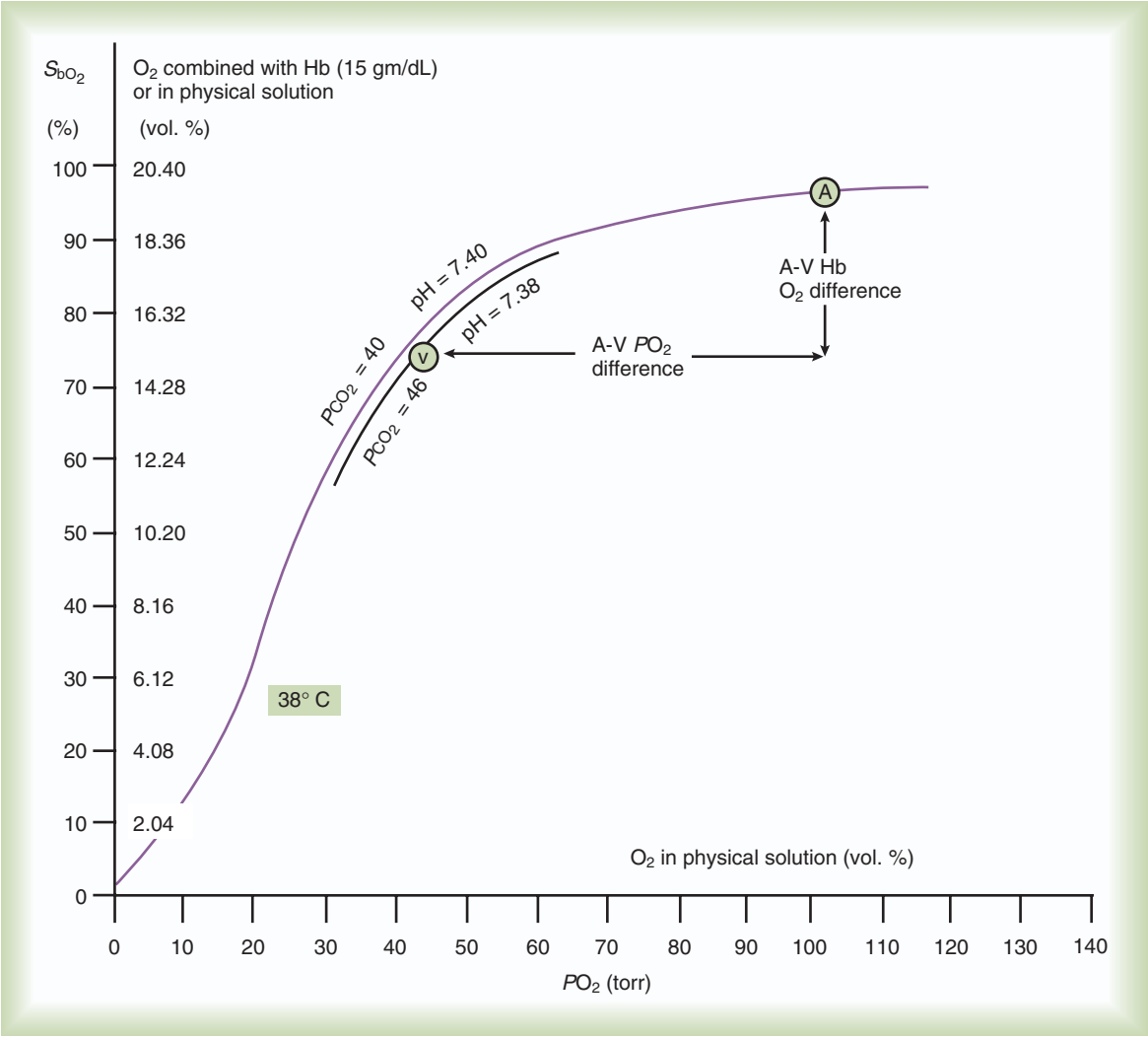

Fig. 12.9 Normal Oxyhemoglobin Dissociation Curve, Showing the Basic Relationship of Blood O_2 Transport. Point *sA* represents normal values for arterial blood leaving the lungs (loading point). Point *sV* represents normal values for venous blood leaving the tissues (unloading point). The slight difference in curve position resulting from pH and CO_2 changes helps O_2 unloading at the tissues. Differences between O_2 content at these two points represent the amount of O_2 taken up by the tissues on one pass through the systemic circulation. (Modified from Slonim NB, Hamilton LH: *Respiratory pysiology*, ed 5, St Louis, 1987, Mosby.)

Note that C.O. is expressed in dL/min, instead of conventional L/min, to maintain the uniformity of values.

According to the Fick equation, if a patient becomes hypoxemic (C_aO_2 falls), total-body O_2 consumption can be maintained by either increasing cardiac output or extracting more O_2 (decreasing $C_{\bar{v}}O_2$). Also, hypoxic tissues compensate by vasodilating (increasing blood flow to the tissues) or increasing O_2 extraction ($C_aO_2 - C_{\bar{v}}O_2$). Owing to the relative difficulty of measuring $\dot{V}_{O_2}$ in clinical situations, an estimated value is often used, making the cardiac output measurement using the Fick equation inaccurate. Nonetheless some of the new methods for monitoring C.O. and tissue oxygenation still employ this concept. More details on these methods are provided in Chapter 52.

MINI CLINI

A patient with septic shock is admitted to the ICU. A central line is placed in her jugular vein with the tip in the superior vena cava and a blood sample is sent for gas analysis. How can the information obtained from venous gas analysis be helpful in managing this patient?

It turns out that central venous blood oxygen saturation ($S_{cv}O_2$) is closely correlated with mixed venous oxygen content ($C_{\bar{v}}O_2$) and can be substituted for it in the Fick equation. Although the actual cardiac output is often not calculated because of the method's inaccuracy, a saturation of 70% is used as a lower limit of "normal." If the $S_{cv}O_2$ falls below that level, it suggests that cardiac output is inadequate for the given situation (even though it may be elevated from "normal" values) and cardiac output augmentation using additional medications may be necessary.

Factors Affecting Oxygen Loading and Unloading

In addition to the shape of the HbO_2 curve, many other factors affect O_2 loading and unloading. Among the most important of

these in clinical practice are blood pH, body temperature, and the erythrocyte concentration of certain organic phosphates.[5] In healthy individuals, the complex interaction of these factors results in maximal loading of Hb (high affinity) with O_2 in the lungs and appropriate unloading of O_2 (low affinity) in the tissues. The cyclic ability to switch from a high- to a low-affinity state and back, based on chemical characteristics of the environment, is the key feature in Hb's ability to transport O_2. Variations in the structure of Hb (as occur in conditions with abnormal Hb molecules, called hemoglobinopathies) also affect O_2 loading and unloading, as can chemical combinations of Hb with substances other than O_2, such as carbon monoxide (CO). These abnormal changes can increase or decrease the Hb affinity for O_2 and interfere with O_2 transport.

RULE OF THUMB O_2 transport from the lungs to the tissues relies on Hb's ability to change its affinity for O_2 from high to low and back to high based on the chemical composition of the blood. Any disease process that permanently changes the affinity of Hb for O_2 in either direction will alter this cyclic process and impair O_2 delivery.

pH (Bohr Effect)

The impact of changes in blood pH on Hb's affinity for O_2 is called the **Bohr effect.** As shown in Fig. 12.10, the Bohr effect alters the position of the HbO_2 dissociation curve. A low pH (acidity) shifts the curve to the right, whereas a high pH (alkalinity) shifts it to the left. These changes are a result of variations in the shape of the Hb molecule caused by fluctuations in pH.

As blood pH decreases and the curve shifts to the right, the Hb saturation for a given PO_2 decreases. This means that the Hb molecule binds the O_2 less avidly, allowing O_2 to offload to the tissues. This is important for tissue O_2 delivery because the acidic environment of the tissues allows O_2 to dissociate from Hb into the tissues. Conversely, as blood pH increases and the curve shifts to the left, the Hb saturation for a given PO_2 increases (i.e., there is increased affinity of Hb for O_2).[4,5,8] Therefore, when venous blood returns to the lungs, the pH increases and higher pH shifts the HbO_2 curve back to the left, increasing the affinity of Hb for O_2 and enhancing its uptake from the alveoli.

Body Temperature

Variations in body temperature also affect the HbO_2 dissociation curve. As shown in Fig. 12.11, a decrease in body temperature shifts the curve to the left, increasing Hb's affinity for O_2. Conversely, as body temperature increases, the curve shifts to the right, and the affinity of Hb for O_2 decreases. As with the Bohr effect, these changes enhance normal O_2 uptake and delivery. At the tissues, metabolic activity increases the temperature, which allows more O_2 to be released into the tissues.

RULE OF THUMB Physiologic signs of increased metabolic activity at the tissue level, such as increased acidity (low pH) and increased temperature, cause changes in oxyhemoglobin dissociation, so that more O_2 is released from Hb into the tissues to allow increased O_2 delivery to the area of increased metabolic activity.

Organic Phosphates (2,3-Diphosphoglycerate)

The organic phosphate 2,3-diphosphoglycerate (2,3-DPG) is found in abundance in the RBCs, where it forms a loose chemical bond with the globin chains of deoxygenated Hb. In this

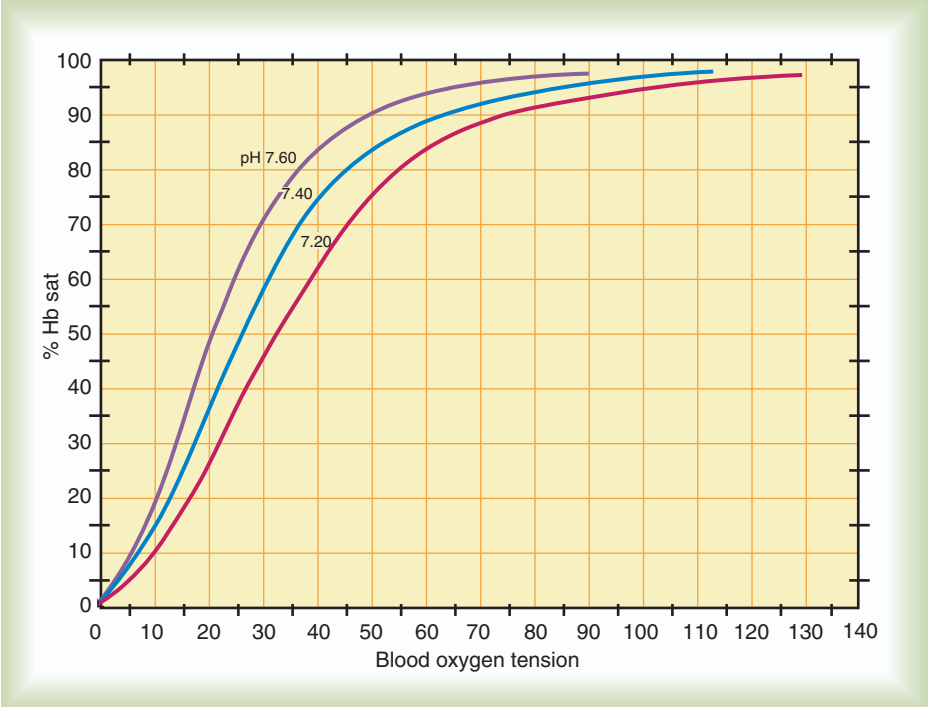

Fig. 12.10 O_2 Dissociation Curve of Blood at 37°C, Showing Variations at Three pH Levels. A right shift (lower pH) decreases Hb affinity for O_2, whereas a left shift (higher pH) increases Hb affinity for O_2.

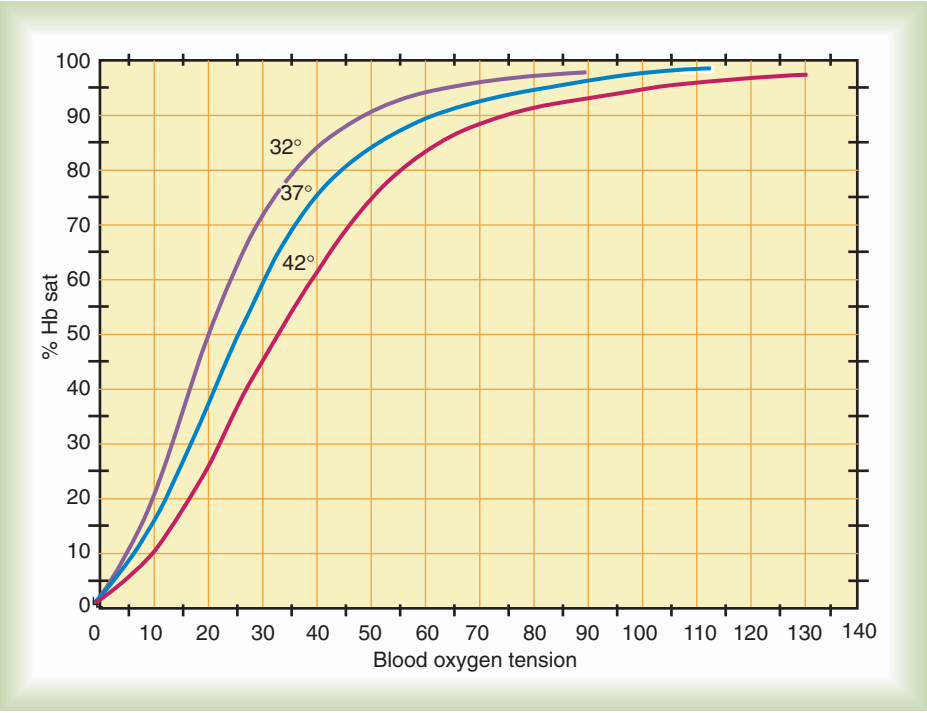

Fig. 12.11 O_2 Dissociation Curve of Blood at pH of 7.40, Showing Variations at Three Temperatures. For a given O_2 tension, the lower the temperature, the more the Hb holds onto O_2, maintaining a higher saturation.

configuration, 2,3-DPG stabilizes the molecule in its deoxygenated state, reducing its affinity for O_2.[5–7] Without 2,3-DPG, Hb affinity for O_2 would be so great that normal O_2 unloading would be impossible. Increased 2,3-DPG concentrations shift the HbO_2 curve to the right, promoting O_2 unloading. Conversely, low 2,3-DPG concentrations shift the curve to the left, increasing Hb affinity for O_2.

Alkalosis, chronic hypoxemia, and anemia all tend to increase 2,3-DPG concentrations and promote O_2 unloading. Conversely, acidosis results in a lower intracellular level of 2,3-DPG and a greater affinity of Hb for O_2.

Erythrocyte concentrations of 2,3-DPG in banked blood decrease over time. After 1 week of storage, the 2,3-DPG level may be less than one-third of the normal value. This change shifts the HbO_2 curve to the left, decreasing the availability of O_2 to the tissues. Large transfusions of banked blood that is more than a few days old can severely impair O_2 delivery even in the presence of normal PO_2. Improved maintenance levels of 2,3-DPG can be achieved with newer blood storage techniques. Fig. 12.12 summarizes how the major factors affect Hb's affinity for O_2.

Abnormal Hemoglobin

Structural or chemical abnormalities within the Hb also affect O_2 affinity. More than 120 abnormal types of the Hb molecule have been identified.

Sickle cell hemoglobin (HbS) is less soluble than normal Hb, which causes it to become susceptible to polymerization and precipitation when deoxygenated. Certain events such as dehydration, hypoxia, and acidosis cause HbS to crystallize and the RBCs to become hardened and curved like a sickle. Erythrocyte fragility is increased (leading to hemolysis), and the risk for clot formation is also increased. Patients with sickle cell disease are prone to vaso-occlusive disease and anemia. Some patients with sickle cell anemia develop **acute chest syndrome.** They usually complain of acute chest pain, cough, and shortness of breath. A new infiltrate is usually seen on the chest x-ray, and the patient often develops worsening anemia and hypoxemia. *Acute chest syndrome* is the most common cause of death in patients with sickle cell anemia.

Methemoglobin (metHb) is an abnormal form of the molecule in which the iron in the heme-complex (Fe^{2+}) loses an electron and is oxidized to its ferric state (Fe^{3+}). In the ferric state, the iron ion cannot combine with O_2. This is called **methemoglobinemia.** As with carboxyhemoglobin (HbCO), clinical abnormalities come from the associated increased affinity for O_2 and loss of O_2-binding capacity. The most common cause of methemoglobinemia is the therapeutic use of oxidant medications such as inhaled nitric oxide, dapsone, nitroglycerin, and lidocaine. When these therapeutic agents are being used, frequent monitoring for metHb is important to weigh the risk against the benefit. The presence of metHb turns the blood brown, which can produce a slate-gray skin coloration that is often confused with cyanosis. The presence of metHb is confirmed by spectrophotometry (see Chapter 19). When the blood level of metHb exceeds 30%, methemoglobinemia is treated with reducing agents such as methylene blue or ascorbic acid.

Carboxyhemoglobin (HbCO) is the chemical combination of Hb with CO. The affinity of Hb for CO is more than 200 times greater than it is for O_2. Extremely low concentrations of CO can quickly displace O_2 from Hb, forming HbCO. A CO partial pressure of 0.12 mm Hg can displace half the O_2 from

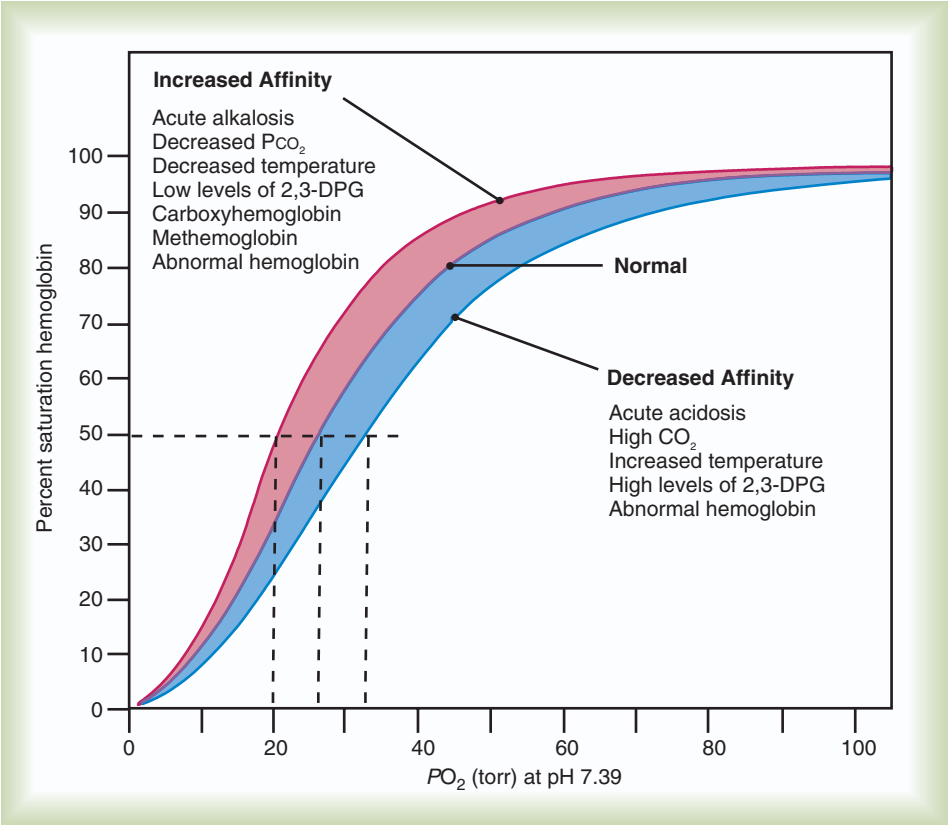

Fig. 12.12 Conditions Associated With Altered Affinity of Hemoglobin for O_2. *2,3-DPG*, 2,3-diphosphoglycerate. (Modified from Lane EE, Walker JF: *Clinical arterial blood gas analysis*, St Louis, 1987, Mosby.)

Hb. Because HbCO cannot carry O_2, each molecule of Hb bound to CO represents a loss in carrying capacity. The combination of CO with Hb shifts the HbO_2 curve to the left, impeding O_2 delivery to the tissues further. Treatment for CO poisoning is detailed in Chapters 30 and 41.

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Patients with CO poisoning present with normal P_aO_2 values despite severe tissue hypoxia. As CO displaces O_2 from Hb, more O_2 is dissolved in blood but less is bound to Hb, resulting in poor O_2 delivery. Typically pulse oximetry values are also low, but the correct diagnosis can be made only by arterial blood gas co-oximetry, which will reliably measure HbCO and HbO_2 levels.

Discussion

During fetal life and for up to 1 year after birth, the blood has a high proportion of an Hb variant called **fetal hemoglobin (HbF).** HbF has a greater affinity for O_2 than normal adult Hb, as manifested by a leftward shift of the HbO_2 curve. Given the low PO_2 values available to the fetus in utero, this leftward shift aids O_2 loading at the placenta. Because of the relatively low pH of the fetal environment, O_2 unloading at the cellular level is not greatly affected. However, after birth, this enhanced O_2 affinity is less advantageous. Over the first year of life, HbF is gradually replaced with normal Hb (see Chapter 35).

CARBON DIOXIDE TRANSPORT

Fig. 12.13 shows the physical and chemical events of gas exchange at the systemic capillaries. In the pulmonary capillaries, all events occur in the opposite direction. Although the primary focus is on CO_2 transport, Fig. 12.13 also includes the basic elements of O_2 exchange. O_2 exchange is included here for completeness and to show that the exchange and transport of these two gases are closely related.

Transport Mechanisms

Approximately 45 to 55 mL/dL of CO_2 is normally carried in the blood in the following three forms: (1) dissolved in physical solution, (2) chemically combined with protein, and (3) ionized as bicarbonate.[5,7]

Dissolved in Physical Solution

As with O_2, CO_2 produced by the tissues dissolves in the plasma and erythrocyte intracellular fluid. However, in contrast to O_2, dissolved CO_2 plays an important role in transport, accounting for approximately 8% of the total released at the lungs; this is because of the higher solubility of CO_2 in plasma.

Chemically Combined With Protein

Molecular CO_2 has the capacity to combine chemically with free amino groups (NH_2) of protein molecules (Prot), forming a carbamino compound, thus:

$$\text{Prot-NH}_2 + \text{CO}_2 = \text{Prot-NHCOO}^- + \text{H}^+$$

A small amount of the CO_2 leaving the tissues combines with plasma proteins to form these carbamino compounds. A larger

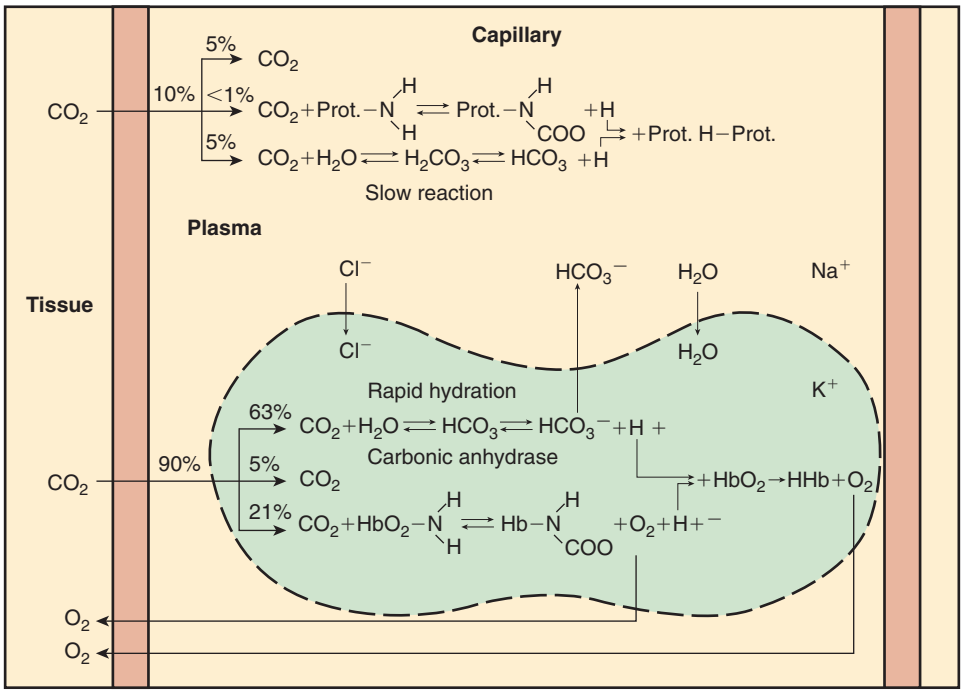

Fig. 12.13 Summary diagram of various fates of CO_2 as it diffuses from the cells and interstitial spaces into the peripheral capillaries before its transport toward the venous circulation. (Modified from Martin DE, Youtsey JW: *Respiratory anatomy and physiology*, St Louis, 1988, Mosby.)

fraction of CO_2 combines with erythrocyte Hb to form a carbamino compound called *carbaminohemoglobin*. As indicated in the previous equation, this reaction produces H^+. These H^+ are buffered by the reduced Hb, which is made available by the concurrent release of O_2.

The availability of additional sites for H^+ buffering increases the affinity of Hb for CO_2. Because reduced Hb is a weaker acid than HbO_2, pH changes associated with the release of the H^+ in the formation of carbaminohemoglobin are minimized. Carbaminohemoglobin constitutes approximately 12% of the total CO_2 transported.

Ionized as Bicarbonate

Approximately 80% of CO_2 in the blood is transported as bicarbonate. Of the CO_2 that dissolves in plasma, a small portion combines chemically with water in the process *hydrolysis*. Hydrolysis of CO_2 initially forms carbonic acid, which quickly ionizes into H^+ and bicarbonate ions:

$$CO_2 + H_2O = H_2CO_3 = HCO_3^- + H^+$$

The H^+ produced in this reaction are buffered by the plasma proteins in much the same way as Hb buffers H^+ in the RBC. However, the rate of this plasma hydrolysis reaction is extremely slow, producing minimal amounts of H^+ and HCO_3^-.

Most CO_2 undergoes hydrolysis inside the erythrocyte. This reaction is greatly enhanced by an enzyme catalyst called *carbonic anhydrase*. The resulting H^+ are buffered by the imidazole group ($R\text{-}NHCOO^-$) of the reduced Hb molecule. The concurrent conversion of HbO_2 to its deoxygenated form helps buffer, enhancing the loading of CO_2 as carbaminohemoglobin.

As the hydrolysis of CO_2 continues, HCO_3^- ions begin to accumulate in the erythrocyte. To maintain a consistent concentration across the cell membrane, some of these anions diffuse outward into the plasma. Because the erythrocyte is not freely permeable by cations, electrolytic equilibrium must be maintained by way of an inward movement of anions. This migration is achieved by the shifting of chloride ions from the plasma into the erythrocyte—a process called the *chloride shift*, or the **Hamburger phenomenon**.

Carbon Dioxide Dissociation Curve

As with O_2, CO_2 has a dissociation curve. The relationship between blood PCO_2 and CO_2 content is depicted in Fig. 12.14. The first point to note is the effect of Hb saturation with O_2 on this curve. As previously discussed, CO_2 levels, through their influence on pH, modify the O_2 dissociation curve (Bohr effect). Fig. 12.14 shows that oxyhemoglobin saturation also affects the position of the CO_2 dissociation curve. The influence of oxyhemoglobin saturation on CO_2 dissociation is called the **Haldane effect.** As previously explained, this phenomenon is a result of changes in the affinity of Hb for CO_2, which occurs as a result of its buffering of H^+.[4–7]

Fig. 12.14A shows CO_2 dissociation curves for three levels of blood O_2 saturation. The first two are physiologic values and the third extreme value is provided for contrast. Fig. 12.14B amplifies selected segments of these curves in the physiologic range of PCO_2. Note first the arterial point *a* lying on the curve, representing SaO_2 of 97.5%. At this point, PCO_2 is 40 mm Hg and CO_2 content is approximately 48 mL/dL. The venous point *v* also falls on the curve, representing SaO_2 of approximately 70%. At this point, PCO_2 is 46 mm Hg and CO_2 content is approximately 52 mL/

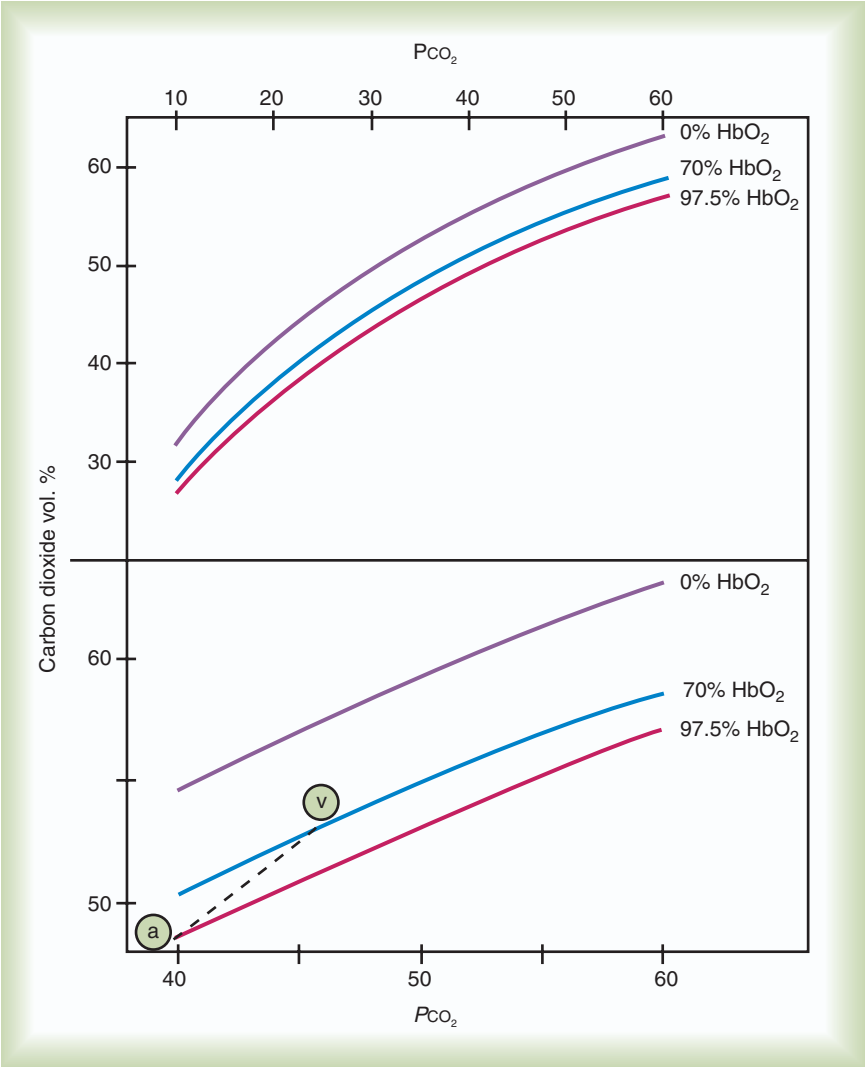

Fig. 12.14 CO_2 Dissociation Curves. (A) Relationship between CO_2 content and tension at three levels of hemoglobin saturation. (B) Closeup of curves between PCO_2 of 40 mm Hg and 60 mm Hg.

dL. Because O_2 saturation changes from arterial to venous blood, the true physiologic CO_2 dissociation curve must lie somewhere between these two points. This physiologic curve is represented as the *dashed line* in Fig. 12.14B. At point *a*, the high SaO_2 decreases the capacity of the blood to hold CO_2, helping unload this gas at the lungs. At point *v*, the lower mixed venous O_2 saturation ($S_{\bar{v}}O_2$) increases the capacity of the blood to hold CO_2, aiding uptake at the tissues.

The total CO_2 content of arterial and venous blood is compared in Table 12.3. The amounts of CO_2 are expressed in gaseous volume equivalents (milliliters per deciliter, or mL/dL) and as millimoles per liter (mmol/L). This latter measure of the chemical combining power of CO_2 in solutions is critical for understanding the role of this gas in acid-base balance.

ABNORMALITIES OF GAS EXCHANGE AND TRANSPORT

Gas exchange is abnormal when either tissue O_2 delivery or CO_2 removal is impaired.

TABLE 12.3 Carbon Dioxide Content of Arterial and Venous Blood

Unit of Measure	Arterial	Venous
mmol/L	21.53	23.21
mL/dL	48.01	51.76

Impaired Oxygen Delivery

O_2 delivery (DO_2) to the tissues is a product of arterial O_2 content (CaO_2) and cardiac output (C.O.).

$$DO_2 = CaO_2 \times C.O.$$

When O_2 delivery is inadequate for cellular needs, **hypoxia** occurs. According to the preceding equation, hypoxia occurs if (1) the arterial blood O_2 content is decreased *(hypoxemia)* or (2) cardiac output or perfusion is decreased (*shock* or *ischemia*). Table 12.4 summarizes causes, common clinical indicators, mechanisms, and examples of hypoxia.

TABLE 12.4 Causes of Hypoxia

Cause	Primary Indicator	Mechanism	Example
Hypoxemia			
Low PiO_2	Low P_AO_2 Low PaO_2	Reduced P_B	Altitude
Hypoventilation	High $PaCO_2$	Decreased $\dot{V}_A$	Drug overdose
V/Q imbalance	Low PaO_2 High $D_{(A-a)}O_2$; resolves with O_2	Decreased $\dot{V}_A$ relative to perfusion	COPD, aging
Anatomic shunt	Low PaO_2 High $D_{(A-a)}O_2$; does not resolve with O_2	Blood flow from right to left side of heart	Congenital heart disease
Physiologic shunt	Low PaO_2 High $D_{(A-a)}O_2$; does not resolve with O_2	Perfusion without ventilation	Atelectasis
Diffusion defect	Low PaO_2 High $D_{(A-a)}O_2$; resolves with O_2	Damage to alveolar-capillary membrane	ARDS
Hb Deficiency			
Absolute	Low Hb content Reduced CaO_2	Loss of Hb	Hemorrhage
Relative	Abnormal SaO_2 Reduced CaO_2	Abnormal Hb	Carboxyhemoglobin
Low blood flow	Increased ($C_{a-v}O_2$)	Decreased perfusion	Shock, ischemia
Dysoxia	Normal CaO_2 Decreased ($C_{a-v}O_2$)	Disruption of cellular enzymes	Cyanide poisoning

ARDS, Acute respiratory distress syndrome; *COPD,* chronic obstructive pulmonary disease; *Hb,* hemoglobin.

Causes of Hypoxemia

Hypoxemia occurs when the partial pressure of O_2 in the arterial blood (PaO_2) is decreased to less than the predicted normal value based on the patient's age. Hypoxia occurs when the tissues have too little O_2. Hypoxemia can cause tissue hypoxia. In addition, impaired O_2 delivery to the tissues also occurs in the presence of abnormalities that prevent saturation of Hb with O_2 (see the subsequent discussion).

Hypoxemia or decreased PaO_2 may be caused by a low ambient PO_2, hypoventilation, impaired diffusion, *V/Q* imbalances, and right-to-left anatomic or physiologic shunting. PaO_2 also decreases normally with aging. The normal predicted PaO_2 decreases steadily with age; the average is approximately 85 mm Hg at age 60 years (see later discussion).

Breathing gases with a low O_2 concentration (hypoxia chamber) or at pressures less than atmospheric (high altitude) lowers PiO_2 (partial pressure of inspired oxygen), thus decreasing P_AO_2 and P_aO_2. A common example of this problem occurs during travel to high altitudes, where the visitor often experiences the ill effects of hypoxia for several days. This condition is called *mountain sickness.* In such cases, although P_aO_2 is reduced, the pressure gradient between the alveoli and the arterial blood for O_2 ($D_{A-a}O_2$) remains normal.

Assuming a constant FiO_2, P_AO_2 varies inversely with P_ACO_2. An increase in P_ACO_2 (hypoventilation) is always accompanied by a proportionate decrease in P_AO_2. $D_{A-a}O_2$ is normal in such cases. Conversely, hyperventilation decreases P_ACO_2 and helps compensate for hypoxemia (but only modestly, as discussed earlier in this chapter).

Even when P_AO_2 is normal, disorders of the alveolar-capillary membrane may limit diffusion of O_2 into the pulmonary capillary blood, thus decreasing P_aO_2. Examples are pulmonary fibrosis, emphysema, and interstitial edema. However, as previously noted, a pure diffusion limitation is an uncommon cause of hypoxemia at rest.

Ventilation/perfusion imbalances are the most common cause of hypoxemia in patients with lung disease. A *V/Q* imbalance is an abnormal deviation in the relationship between ventilation and perfusion in the lung. The normal lung has some *V/Q* mismatch; however, in disease states, the degree of *V/Q* imbalance becomes much greater. To understand how *V/Q* imbalance causes hypoxemia, consider the normal oxyhemoglobin dissociation curve, with PO_2 plotted against O_2 content (Fig. 12.15). The curve is nearly flat in the physiologic range of PaO_2 (>70 mm Hg) but falls steeply when PaO_2 is less than 60 mm Hg. Points representing O_2 content of three separate lung units are also shown. These units have *V/Q*s of 0.1, 1.0, and 10.0.

Blood leaving the normal unit ($V/Q = 1$) has a normal O_2 content (19.5 mL/dL). Blood leaving the unit with poor ventilation ($V/Q = 0.1$) has a low O_2 content (16.0 mL/dL). Because Hb is almost fully saturated at a normal PO_2 of 100 mm Hg, blood leaving the overventilated unit ($V/Q = 10$) has an O_2 content that is just slightly greater than normal (20.0 mL/dL). When the blood from all three units mixes together, the O_2 content is reduced (18.5 mL/dL). The decrease in oxygenation caused by the poorly ventilated unit is not fully compensated for by the high-*V/Q* unit.[9]

A *V/Q* of zero represents a special type of imbalance. When *V/Q* is zero, there is blood flow but no ventilation. The result is equivalent to a right-to-left anatomic shunt, shown at the *bottom* of Fig. 12.16. Here, venous blood bypasses ventilated alveoli and mixes with freshly oxygenated arterial blood, resulting in venous admixture.

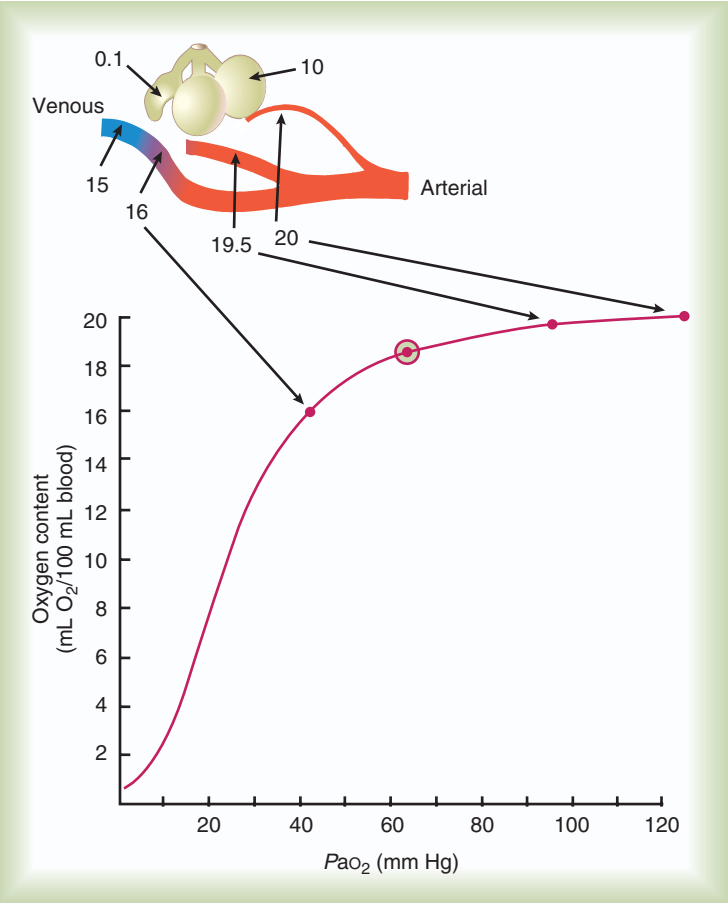

Fig. 12.15 O_2 Dissociation Curve—PaO_2 Versus O_2 Content. O_2 content from alveolar-capillary units with *V/Q* of 0.1, 1; 10 is 16 mL/dL, 19.5 mL/dL, and 20 mL/dL. Lines are drawn for each O_2 content to its point on the dissociation curve. The average O_2 content, 18.5 mL/dL, is represented by a *circle* on the dissociation curve. (Modified from Martin L: *Pulmonary physiology in clinical practice: the essentials for patient care and evaluation*, St Louis, 1987, Mosby.)

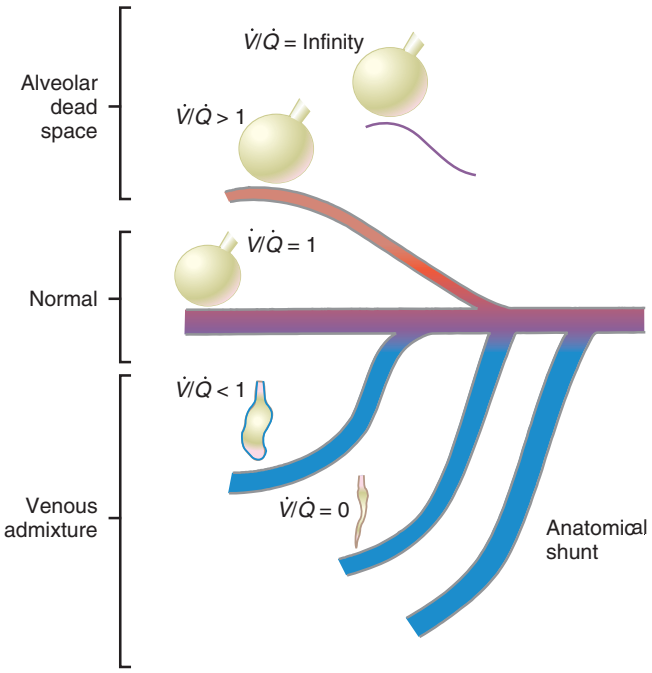

Fig. 12.16 Range of *V/Q* ratios. (Modified from Martin L: *Pulmonary physiology in current practice: the essentials for patient care and evaluation*, St Louis, 1987, Mosby).

RULE OF THUMB Two major causes of hypoxemia are hypoventilation and *V/Q* mismatch (this statement assumes that shunting is the extreme version of *V/Q* mismatch, when the ratio approaches 0). Clinically, $D_{A-a}O_2$ will help to differentiate them. It will be normal in cases of hypoventilation and abnormal in cases of *V/Q* mismatch.

When a low P_aO_2 is observed, the RT must take into account the normal decrease in arterial O_2 tension that occurs with aging. As shown in Fig. 12.17, for an individual breathing air at sea level, the "normal" $D_{A-a}O_2$ increases in a nearly linear fashion with increasing age *(shaded area)*. This increase in $D_{A-a}O_2$ results in a gradual decline in P_aO_2 over time and is probably caused by reduced surface area in the lung for gas exchange and increases in *V/Q* mismatching. A P_aO_2 of 85 mm Hg in a 60-year-old adult would be interpreted as normal, but the same P_aO_2 in a 20-year-old adult would indicate hypoxemia. The expected P_aO_2 in older adults may be estimated by using the following formula:

$$\text{Expected } P_aO_2 = 100 - (0.323 \times \text{Age in years})$$

Hemoglobin deficiencies. Normal P_aO_2 does not guarantee adequate arterial O_2 content or delivery. For arterial O_2 content to be adequate, there also must be enough normal Hb in the blood. If the blood Hb is low—even when PaO_2 is normal—tissue

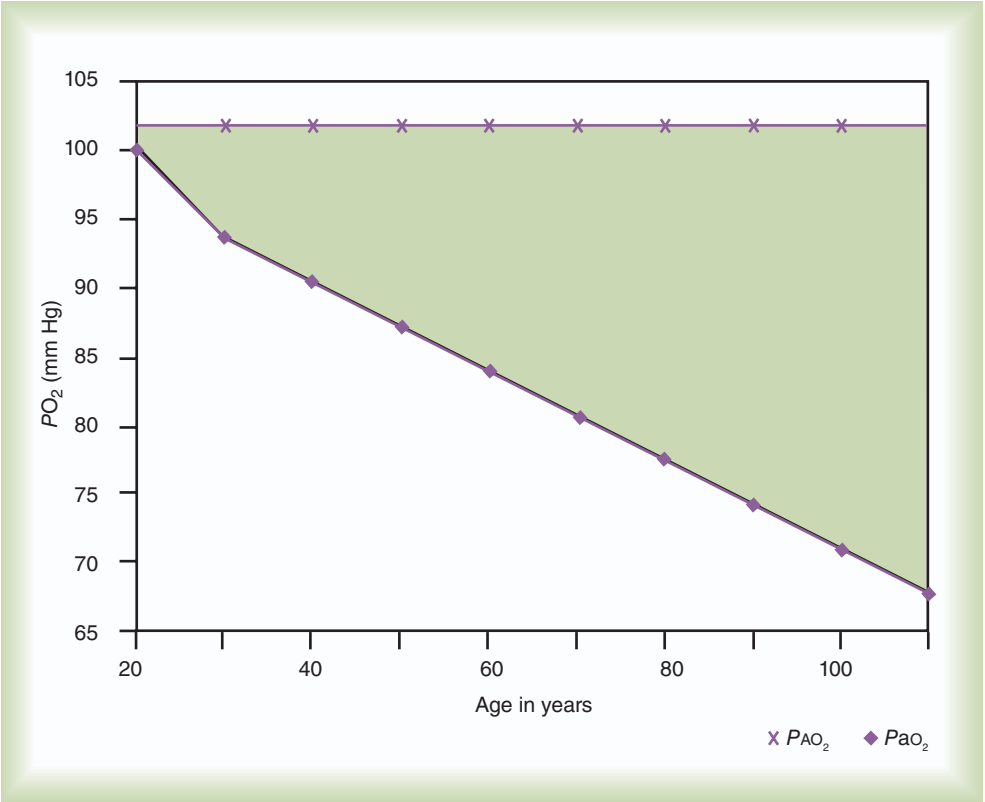

Fig. 12.17 Relationship Between $P_{A-a}O_2$ and aging. As P_aO_2 naturally decreases with age, $P_{A-a}O_2$ increases at the rate of approximately 3 mm Hg each decade beyond 20 years. (Modified from Lane EE, Walker JF: *Clinical arterial blood gas analysis*, St Louis, 1987, Mosby.)

hypoxia can occur because of low O_2 content in the arterial blood. Relative Hb deficiencies are caused by abnormal forms of Hb and were discussed earlier in this chapter.

Hb deficiencies, or anemias, can be either absolute or relative. Absolute Hb deficiency occurs when the Hb concentration is lower than normal. Relative Hb deficiencies are caused by either the displacement of O_2 from normal Hb or the presence of abnormal Hb variants. A low blood Hb concentration may be caused either by a loss of RBCs, as with hemorrhage, or by inadequate erythropoiesis (formation of RBCs in the bone marrow). Regardless of the cause, a low Hb content can seriously impair the O_2-carrying capacity of the blood even in the presence of a normal supply (P_aO_2) and adequate diffusion.[5]

Fig. 12.18 plots the relationship between arterial O_2 content and PaO_2 as a function of Hb concentration. As can be seen, progressive decreases in blood Hb content causes large decreases in arterial O_2 content (CaO_2). A 33% decrease in Hb content (from 15 to 10 g/dL) reduces CaO_2 as much as would a decrease in PaO_2 from 100 to 40 mm Hg.

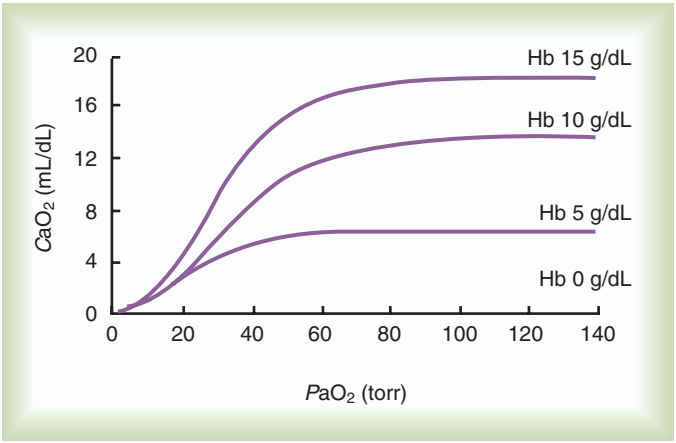

Fig. 12.18 Relationship Between CaO_2 and PaO_2 as a Function of Blood Hb Concentration. Progressive decreases in Hb cause large decreases in CaO_2.

Reduction in Blood Flow (Shock or Ischemia)

Because O_2 delivery depends on both arterial O_2 content and cardiac output, hypoxia can still occur when the CaO_2 is normal and blood flow is reduced. There are two types of reduced blood flow: (1) circulatory failure *(shock)* and (2) local reductions in perfusion *(ischemia)*.

Circulatory failure (shock). In circulatory failure, tissue O_2 deprivation is widespread. Although the body tries to compensate for the lack of O_2 by directing blood flow to vital organs, this response is limited. Prolonged shock ultimately causes irreversible damage to the central nervous system and eventual cardiovascular collapse.

Local reductions in perfusion (ischemia). Even when whole-body perfusion is adequate, local reductions in blood flow can cause localized hypoxia. Ischemia can result in anaerobic metabolism, metabolic acidosis, and eventual death of the affected tissue. Myocardial infarction and stroke are examples of ischemic conditions that can cause hypoxia and tissue death.

MINI CLINI

Effect of Anemia on Oxygen Content

In its most common form, anemia is a clinical disorder in which the number of RBCs is decreased. Because RBCs carry Hb, anemia decreases the amount of this O_2-carrying protein.

Problem

What effect would anemia that causes a progressive decrease in Hb from (a) 15 g/dL, to (b) 12 g/dL, to (c) 8 g/dL, to (d) 4 g/dL have on the amount of O_2 carried in a patient's blood? Assume that PO_2 and saturation stay normal at 100 mm Hg and 97%.

Discussion

1. Calculate dissolved O_2 the same way for all four examples as follows:

$$\text{Dissolved } O_2 = 100 \times 0.003 = 0.30 \text{ mL/dL}$$

2. Compute chemically combined O_2 as follows:

$$\text{Chemically combined } O_2 = \text{Hb (g/dL)} \times 1.34 \text{ mL/g} \times SaO_2$$

   a. 15 g/dL × 1.34 mL/g × 0.97 = 19.50 mL/dL
   b. 12 g/dL × 1.34 mL/g × 0.97 = 15.60 mL/dL
   c. 8 g/dL × 1.34 mL/g × 0.97 = 10.40 mL/dL
   d. 4 g/dL × 1.34 mL/g × 0.97 = 5.20 mL/dL

3. Compute total O_2 content as follows:

$$CaO_2 = \text{Dissolved } O_2 + \text{Chemically combined } O_2$$

   a. 0.30 + 19.50 = 19.80 mL/dL
   b. 0.30 + 15.60 = 15.90 mL/dL
   c. 0.30 + 10.40 = 10.70 mL/dL
   d. 0.30 + 5.20 = 5.50 mL/dL

Loss of Hb decreases the amount of O_2 carried in a patient's blood even though PO_2 and saturation remain normal. With an Hb concentration of 4 g/dL, the amount of O_2 carried in a patient's blood is only approximately one-fourth the normal concentration (5.50 vs. 19.80 mL/dL).

Dysoxia

Dysoxia is a form of hypoxia in which the cellular uptake of O_2 is abnormally decreased. The best example of dysoxia is cyanide poisoning. Cyanide disrupts the intracellular cytochrome oxidase system, preventing cellular use of O_2. Dysoxia also may occur when tissue O_2 consumption becomes dependent on O_2 delivery.

Fig. 12.19 plots tissue O_2 consumption ($\dot{V}_{O_2}$) against O_2 delivery (DO_2) in both normal and pathologic states. Normally, $\dot{V}_{O_2}$ increases along with DO_2, until a critical threshold (dashed line) is reached, after which the line becomes flat and $\dot{V}_{O_2}$ does not change. In certain diseases, such as septic shock, trauma, or ARDS, $\dot{V}_{O_2}$ will become more dependent on DO_2 and will increase proportionally with DO_2. If the demand for $\dot{V}_{O_2}$ is not met with the proportional increase in DO_2, anaerobic metabolism develops, which leads to the accumulation of lactic acid.

RULE OF THUMB Lactic acid level is often used for a quick assessment of circulatory function. In cases of circulatory failure, such as cardiogenic or septic shock, O_2 delivery to the tissues is greatly reduced. Changes in lactic acid level over time can also be used as a measure of the effectiveness of medical interventions in patients with shock.

Calculate (1) O_2 delivery, (2) O_2 extraction ratio, and (3) shunt fraction. Discuss the causes of abnormal values. What would be the potential interventions to increase his O_2 delivery?

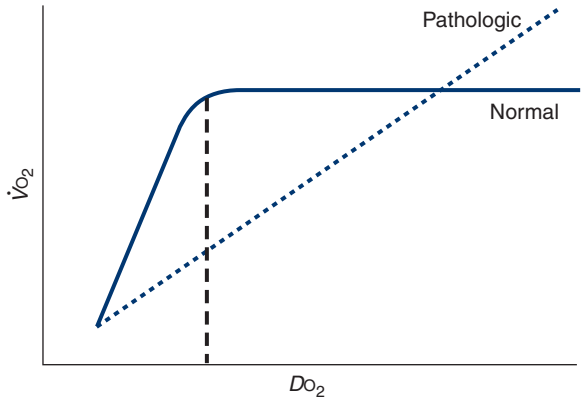

Fig. 12.19 Supply Dependence of Oxygen Consumption ($\dot{V}O_2$). Under normal conditions *(solid line)*, $\dot{V}O_2$ will increase until a critical threshold *(dashed line)* of delivered oxygen (DO_2) is reached. Beyond this critical threshold, $\dot{V}O_2$ remains stable despite the increase in DO_2. In pathologic conditions *(dotted line)*, such as acute respiratory distress syndrome, $\dot{V}O_2$ may not plateau but will continue to rise as DO_2 increases until well past the normal critical threshold. (From Heuer AJ, Scanlan, CL: *Wilkins' clinical assessment in respiratory care*, ed 7, St. Louis, 2018, Elsevier.)

Impaired Carbon Dioxide Removal

Any disorder that decreases alveolar ventilation ($\dot{V}_A$) relative to metabolic need impairs CO_2 removal. Impaired CO_2 removal by the lung causes hypercapnia and respiratory acidosis (see Chapter 14). A decrease in alveolar ventilation occurs when (1) the minute ventilation is inadequate, (2) the dead space ventilation per minute is increased, or (3) a V/Q imbalance exists.[4–8]

Inadequate Minute Ventilation

Clinically, inadequate minute ventilation is caused by decreased tidal volume or respiratory rate. Inadequate minute ventilation occurs in restrictive conditions such as atelectasis, neuromuscular disorders, or impeded thoracic expansion (e.g., kyphoscoliosis). A decrease in respiratory rate is less common but may be present with respiratory center depression, as in drug overdose.

Increased Dead Space Ventilation

An increase in dead space ventilation, or V_D/V_T, is caused by either (1) decreased tidal volume (as with rapid, shallow breathing) or (2) increased physiologic dead space as in various lung diseases. In either case, wasted ventilation increases. Without compensation, alveolar ventilation per minute is decreased and CO_2 removal is impaired.

Ventilation/Perfusion Imbalances

Theoretically any *V/Q* imbalance should cause an increase in P_aCO_2. However, P_aCO_2 does not always increase in these cases. Many patients who are hypoxemic because of a *V/Q* imbalance have a low or normal P_aCO_2. This common clinical finding suggests that *V/Q* imbalances have a greater effect on oxygenation than on CO_2 removal.

Careful inspection of the O_2 and CO_2 dissociation curves supports this finding. The O_2 and CO_2 dissociation curves are plotted on the same scale in Fig. 12.20. The upper CO_2 curve is nearly linear in the physiologic range. The lower O_2 curve is almost flat in the physiologic range. Point *a* on each curve is the

MINI CLINI

Note that this is a comprehensive Mini Clini and will draw on information from the various parts of this chapter.

Problem

A patient is admitted to the ICU with pneumonia. Various devices are placed for monitoring. The following data are obtained:

pH	7.24
PCO_2 (mm Hg)	32
PaO_2 (mm Hg)	60
SaO_2	0.9
FiO_2	0.7
Cardiac output (L/min)	6
Hgb (g/dL)	8
VO_2 (mL/min)	200.00

Discussion

1. Calculate the oxygen delivery:

$$\begin{aligned} DO_2 &= C_aO_2 \times C.O. \\ &= (1.39 \times Hgb \times SaO_2 + 0.003 \times P_aO_2) \times C.O. \\ &= (1.39 \times 8 \times 0.9 + 0.003 \times 60) \times 60 \\ &= 10.18\,(mL/dL) \times 60\,(dL/min) = 610.8\,mL/min \end{aligned}$$

Note that the C.O. of 6 L/min was changed to 60 dL/min to maintain the uniformity of values. Overall, O_2 delivery is reduced mainly due to reduction in Hgb and SaO_2 despite modest increase in C.O.

2. Calculate the oxygen extraction ratio:

$$\dot{V}_{O_2}/D_{O_2} = 200/610.8 = 33\%$$

Extraction fraction is increased to maintain O_2 consumption in the setting of reduced O_2 delivery.

3. Calculate the shunt fraction:

$$\frac{Q_s}{Q_t} = \frac{C_cO_2 - C_aO_2}{C_cO_2 - C_{\bar{v}}O_2}$$

Remember that the actual shunt fraction calculation is deferred in clinical practice because of its complexity. The following estimate (see this chapter's section on shunt fraction) is often used: each increase of $D_{A-a}O_2$ by 100 mm Hg corresponds to a 5% increase in shunt fraction. Now, to calculate $D_{A-a}O_2$,

$$\begin{aligned} D_{A-a}O_2 &= P_AO_2 - P_aO_2 = FiO_2 \times (P_B - P_{H_2O}) - (P_ACO_2 \div RQ) \\ &- PaO_2 = 0.7 \times (760 - 47) - (32/0.8) - 60 = 399 \end{aligned}$$

Shunt fraction is estimated to be increased by 20%. Assuming a "normal" shunt fraction of 5%, the total shunt fraction in this patient can be estimated at 25%. This increase is due to severe *V*/*Q* imbalance caused by pneumonia and possible ARDS.

Potential interventions to increase O_2 delivery would be aimed to improve the components of the following O_2 delivery formula: Hgb (blood transfusion), SaO_2 and/or P_aO_2 (increased PEEP or F_iO_2), and C.O. (administration of vasopressors). In clinical practice, the interrelationships between these variables are very complex and the ultimate decision is often made after consideration of multiple factors. For example, an increase in PEEP will increase SaO_2 but may also decrease cardiac output by decreasing venous return to the heart. The overall impact on DO_2 may be deleterious, as the increase in SaO_2 may be dwarfed by the decrease in C.O.

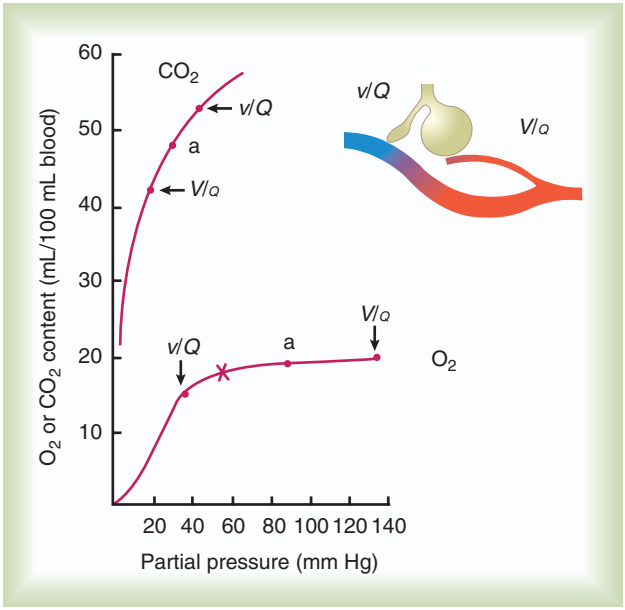

Fig. 12.20 *V*/*Q* Imbalance and Dissociation Curves for CO_2 and O_2. *V*/*Q* represents low *V*/*Q* units, and *V*/*Q* represents high *V*/*Q* units. See text for discussion.

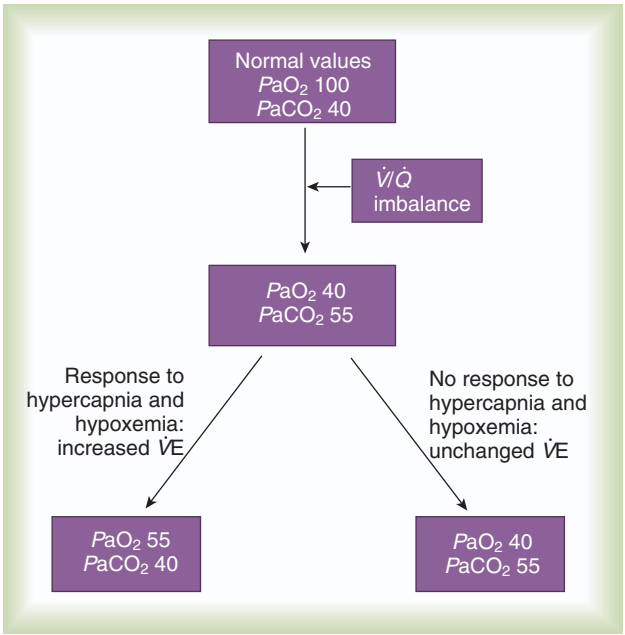

Fig. 12.21 Changes in PaO_2 and $PaCO_2$ Caused by *V*/*Q* Imbalance. All values are given in millimeters of mercury (mm Hg).

normal arterial point for both content and partial pressure. To the right of the graph are two lung units, one with a low *V*/*Q* and the other with a high *V*/*Q*. The blood O_2 and CO_2 contents from each unit are plotted on the curves. The final CO_2 content, arrived at by averaging the high and low *V*/*Q* points, is shown as point *a* on the CO_2 curve. This point is the same as the normal arterial point for CO_2.

Patients with significant *V*/*Q* imbalances must compensate for high PCO_2 coming from underventilated units. To compensate for these high PCO_2 values, the patient's minute ventilation must increase (see Fig. 12.21). Patients who can increase their minute

ventilation tend to have either normal or low P_aCO_2, combined with hypoxemia.

Conversely, patients with *V*/*Q* imbalance who cannot increase their minute ventilation are hypercapnic. Hypercapnia generally occurs only when the *V*/*Q* imbalance is severe and chronic, as in severe COPD. Such patient must sustain a much higher than normal minute ventilation just to maintain normal $PaCO_2$. If the energy costs required to sustain a high minute ventilation are prohibitive, the patient opts for less work—and hence elevated P_aCO_2.

SUMMARY CHECKLIST

- Movement of gases between the lungs and the tissues depends mainly on diffusion.
- P_ACO_2 varies directly with CO_2 production and inversely with alveolar ventilation.
- P_AO_2 is computed using the alveolar air equation.
- With a constant FiO_2, P_AO_2 varies inversely with P_ACO_2.
- Normal P_AO_2 averages 100 mm Hg, with mean P_ACO_2 of approximately 40 mm Hg.
- Normal mixed venous blood has a PO_2 of approximately 40 mm Hg and PCO_2 of approximately 46 mm Hg.
- *V*/*Q* must be in balance for pulmonary gas exchange to be effective. Because of normal anatomic shunts and *V*/*Q* imbalances, pulmonary gas exchange is imperfect.
- In disease, *V*/*Q* can range from zero (perfusion without ventilation or physiologic shunting) to infinity (pure alveolar dead space).
- Blood carries a small amount of O_2 in physical solution, and larger amounts are carried in chemical combination with erythrocyte Hb.
- Hb saturation is the ratio of oxyhemoglobin to total Hb, expressed as a percentage.
- To compute total O_2 contents of the blood, add the dissolved O_2 content ($0.003 \times PO_2$) to the amount of O_2 carried by hemoglobin ($1.34 \times Hb \times SaO_2$)
- The arteriovenous O_2 content difference, $C_{a–v}O_2$, is the amount of O_2 given up by every 100 mL of blood on each pass through the tissues. All else being equal, $C_{a–v}O_2$ varies inversely with cardiac output.
- Hb affinity for O_2 increases with high PO_2, high pH, low temperature, and low levels of 2,3-DPG.
- Hb abnormalities can affect O_2 loading and unloading and can cause hypoxia.
- Most CO_2 (approximately 80%) is transported in the blood as ionized bicarbonate; other forms include carbamino compounds and physical solution.
- Changes in CO_2 levels modify the O_2 dissociation curve (Bohr effect). Changes in Hb saturation affect the CO_2 dissociation curve (Haldane effect). These changes are mutually beneficial, assisting in gas exchange at the lung and the cellular level.
- Hypoxia occurs if (1) the arterial blood O_2 content is decreased, (2) blood flow is decreased, or (3) abnormal cellular function prevents proper uptake of O_2.
- Decreased PaO_2 level may be a result of a low ambient PO_2, hypoventilation, impaired diffusion, *V*/*Q* imbalances, and right-to-left anatomic or physiologic shunting.
- A decrease in alveolar ventilation occurs when (1) the minute ventilation is inadequate, (2) dead space ventilation is increased, or (3) a V/Q imbalance exists.

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13

Solutions, Body Fluids, and Electrolytes

Daniel F. Fisher

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Describe the characteristics of and key terms associated with solutions, colloids, and suspensions.
- Describe the five factors that influence the solubility of a substance in a solution.
- Describe how osmotic pressure functions and what its action is in relation to cell membranes.
- Describe how to calculate the solute content of a solution using ratio, weight/volume, and percent methods.
- State the ionic characteristics of acids, bases, and salts.
- Describe how proteins can function as bases.
- Describe how to calculate the pH of a solution when given the $[H^+]$ in nanomoles per liter.
- Identify where fluid compartments are located in the body and their volumes.
- Describe how water loss and replacement occur.
- Define the roles played by osmotic and hydrostatic pressure in edema.
- Identify clinical findings associated with excess or deficiency of the seven basic electrolytes.

CHAPTER OUTLINE

KEY TERMS

acid
active transport
anions
base
buffering
cations
colloids
diluent
dilute solution
dilution equation
Donnan effect
electrolyte solution
equivalent weight
extracellular
hydrophilic
hydrostatic pressure
hypocalcemia
hypercalcemia
hyperkalemia
hypokalemia
hyponatremia
hyperphosphatemia
hypertonic
hypotonic
ionic
insensible
interstitial fluid
intracellular fluid
isotonic
molal solution
molar solution
nanomole
normal solution
nonpolar covalent
osmolality
osmotic pressure (oncotic pressure)
percent solution
plasma colloid osmotic pressure (oncotic pressure)
polar covalent
ratio solution
saturated solution
sensible
solute
solution
solvent
Starling equilibrium
suspensions
transcellular fluid
weight-per-volume (W/V) solution

Body water and various chemicals are regulated to maintain normal bodily functions. Imbalances in such processes occur in many diseases, including those which affect the respiratory system. Therefore it is important for respiratory therapists (RTs) to have a basic understanding of body fluids, electrolytes, and related physiologic chemistry, as provided in this chapter.

SOLUTIONS, COLLOIDS, AND SUSPENSIONS

Definition of a Solution

The body is based on liquid water chemistry and the interaction of various substances either dissolved or suspended within the fluid. Water itself is a polar (having two sides with one positive and one negative charges) covalent (capable of forming bonds by sharing electrons) molecule and is referred to in chemistry as a *universal solvent*. Water is the primary component of any liquid within the body, and it greatly influences other materials as they are introduced. These substances and particles combine with water in the following three ways: as (1) colloids, (2) suspensions, or (3) solutions.

A **solution** is a stable mixture of two or more substances that cannot be separated using a centrifuge. One substance is evenly distributed between the molecules of the other. The substance that dissolves is called the **solute**. The medium in which it dissolves is called the **solvent**. Gases, liquids, and solids can dissolve to become solutes; for example, carbon dioxide, alcohol, and salt can be dissolved in water. The process of dissolving involves breaking the (relatively weak) bonds between the solute-solute molecules and the solvent-solvent molecules. These intermolecular forces must be broken before a new solute-solvent bond can be formed. A solute dissolves in a solvent if the solute-solvent forces of attraction are great enough to overcome the solute-solute and solvent-solvent forces of attraction. If the solute-solvent force is less than the solute-solute or solvent-solvent force, the solute does not dissolve. When all three sets of forces are approximately equal, the two substances typically are soluble in each other.

In electrochemical terms, there are three basic types of physiologic solutions. Depending on the solute, solutions are **ionic** (electrovalent), ***polar covalent***, or ***nonpolar covalent*** (Table 13.1). In ionic and polar covalent solutions, some of the solute ionizes into separate particles known as *ions*. A solution in which this dissociation occurs is called an ***electrolyte solution***. If an electrode is placed in such a solution, positive ions migrate to the negative pole of the electrode (the cathode). These ions are called **cations**. Negative ions migrate to the positive pole of the electrode (the anode); they are called **anions**. In nonpolar covalent solutions, molecules of solute remain intact and do not carry electrical charges; these solutions are referred to as *nonelectrolytes*. These nonelectrolytes are not attracted to either the positive or the negative pole of an electrode (hence the designation *nonpolar*). All three types of solutions coexist in the body. These solutions also serve as the media in which colloids and simple suspensions are dispersed. Gases such as oxygen and CO_2 are nonpolar molecules (along with nitrogen) and do not dissolve very well in water, which is a polar solvent.

Colloids (sometimes called *dispersions* or *gels*) consist of large molecules that attract and hold water (***hydrophilic:*** "water loving"). These molecules are uniformly distributed throughout the dispersion, and they tend not to settle. The protoplasm inside cells is a common example of a colloid. Physiologically, colloids provide very little free water to the patient's system, and care should be taken not to create a hypotonic (having a lower concentration of electrolytes than body plasma) environment.[1]

Suspensions are composed of larger particles that float within a liquid. Unlike a solution, suspensions can be physically separated by centrifugation. Red blood cells in plasma are an example of a suspension. Dispersion of suspended particles depends on physical agitation. Particles settle because of gravity when the suspension is motionless.

The ease with which a solute dissolves in a solvent is its *solubility,* which is influenced by the following five factors:

1. *Nature of the solute*. The ease with which substances go into a solution (dissociation) in a given solvent depends on the forces of the solute-solute molecules and varies widely.
2. *Nature of the solvent*. The ability of a solvent to dissolve a solute depends on the bonds of the solvent-solvent molecules and varies widely. The electrical properties of the solvent molecules determine how soluble a substance is for a particular solvent. Polar solvents, such as water, dissolve other polar covalent bonds; nonpolar solvents dissolve nonpolar solutes: "Like dissolves like."
3. *Temperature*. The solubility of most solids increases with increased temperature. However, the solubility of gases varies inversely with temperature.
4. *Pressure*. The solubility of solids and liquids is not greatly affected by pressure. However, the solubility of gases in liquids varies directly with pressure.
5. *Concentration.* The concentration of a solute or available solvent affects how much of the substance goes into a solution.

TABLE 13.1 Types of Physiologic Solutions

Type	Characteristics	Physiologic Example
Ionic (electrovalent)	Ionic compounds dissolved from crystalline form, usually in water (hydration); form strong electrolytes with conductivity dependent on concentration of ions	Saline solution (0.9% NaCl)
Polar covalent	Molecular compounds dissolved in water or other solvents to produce ions (ionization); electrolytes may be weak or strong, depending on degree of ionization; solutions polarize and are good conductors	Hydrochloric acid (HCl) (strong electrolyte); acetic acid (CH_3COOH) (weak electrolyte)
Nonpolar covalent	Molecular compounds dissolved into electrically neutral solutions (do not polarize); solutions are not good conductors; nonelectrolytes	Glucose ($C_6H_{12}O_6$)

The effects of temperature and pressure on the solubility of gases are important. More gas dissolves in a liquid at lower temperatures. As the temperature of a liquid increases, gas dissolved in that liquid comes out of solution. Henry's law describes the effect of pressure on solubility of a gas in a liquid. Henry's law states that at a given temperature, the volume of a gas that dissolves in a liquid is proportional to the solubility coefficient of the gas and the partial pressure of gas to which the liquid is exposed. O_2 and CO_2 transport can change significantly with changes in body temperature or atmospheric pressure (see Chapter 6).

Concentration of Solutions

The term *concentration* refers to the amount of solute dissolved into the solvent. Concentration can be described either qualitatively or quantitatively. Calling something a **dilute solution**, suggesting a small amount of solute relative to the solvent or a weak concentration, is an example of a qualitative description. Stating that a specific container holds 50 mL of 0.4 molar solution of sodium hydroxide (NaOH) is a quantitative description (Fig. 13.1A). **Saturated solutions** occur when the solvent can hold no more solute and additional solute added to a saturated solution will settle to the bottom of the container (see Fig. 13.1B). Solute particles precipitate into the solid state at the same rate at which other particles go into solution. This equilibrium characterizes a saturated solution.

MINI CLINI

Solutions and Suspensions

Problem

Respiratory therapists (RTs) work with both solutions and suspensions every day—for example, providing aerosolized medication to a patient with asthma. Many of the medications are solutions of the drug in either water or saline. When the drug is nebulized, small droplets of it are suspended in a gas.

Discussion

The medication to be nebulized is a *solution*. That is, the medication has been dissolved into a solvent of either water or saline. When the medication is placed in the nebulizer chamber, the large volume of liquid is converted to small droplets that can be easily inhaled. The droplets of the aerosol float in the air to be breathed in by the patient. The aerosol is a *suspension* of the droplets of liquid within a gas. Given enough time, the droplets would eventually settle to the floor. For more information on aerosol therapy see Chapter 40.

A solution is characterized as being *supersaturated* when the solvent contains more solute than a saturated solution at the same temperature and pressure. If a saturated solution is heated, the solute equilibrium is disturbed and more solute goes into the solution. This is because of the space between the solvent molecules increases. If undissolved solute is removed and the solution is gradually cooled, there is an excess of dissolved solute (see Fig. 13.1C). The excess solute of supersaturated solutions may be precipitated out (or come out of solution) if the solution is vibrated or if a "seed crystal" is introduced.

Starling Forces

The transport of water across the capillary wall to the tissue was first studied by Ernest Starling, a 19th-century British physiologist. He described that the driving force for fluid filtration across the wall of the capillary is determined by four separate pressures: hydraulic (hydrostatic) and colloid osmotic pressure both within the vessel and in the tissue space.[2] This process can be described mathematically using the following equation:

$$J_v = L_p\,[(P_c - P_i) - s(p_c - p_i)]$$

where:

J_v = Fluid filtration movement across the capillary wall per unit area.

L_p = Permeability of the capillary wall.

s = Oncotic reflection coefficient. Describes how a semipermeable membrane excludes or reflects a specific solute as water moves from one side of the membrane to the other.

P_c, P_i, p_c, p_i = Global values for both the hydrostatic and colloid osmotic pressures in the capillary and interstitial compartments.

Fluid transfer across the membrane is the net result of the aforementioned factors. If the overall result if positive, fluid will move from the capillary to the interstitium. If the overall result is negative, fluid will be reabsorbed from the tissue back into the capillary. A capillary has higher hydrostatic pressure closer to the arteriole and a lower hydrostatic pressure when closer to the venule. Assuming normal transcapillary driving forces (Table 13.2), the net force can be calculated for each end of the capillary.

Osmotic Pressure of Solutions

Most of the solutions of physiologic importance in the body are dilute. Solutes in dilute solution resemble gases. This behavior

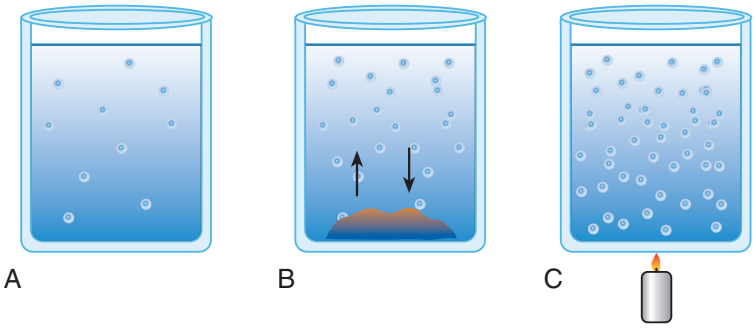

Fig. 13.1 (A) In the dilute solution, there are relatively few solute particles. (B) In the saturated solution, the solvent contains all the solute it can hold in the presence of excess solute. (C) Heating the solution dissolves more solute particles, which may remain in the solution if cooled gently, creating a state of supersaturation.

TABLE 13.2 Typical Values of Transcapillary Pressures

	Capillary Blood Pressure (Pc)	Interstitial Fluid Pressure (Pi)	Effective Capillary Colloid Osmotic Pressure (s pc)	Effective Interstitial Fluid Colloid Osmotic Pressure (s pi)	Net Force
Arteriolar End	+35 mm Hg	–2 mm Hg	+25 mm Hg	+0.1 mm Hg	+12 mm Hg
Venular End	+15 mm Hg	–2 mm Hg	+25 mm Hg	+3 mm Hg	–5 mm Hg

Modified from Boron WF, Boulpaep EL: *Medical physiology: a cellular and molecular approach*, updated edition, Philadelphia, 2003, Elsevier-Saunders.

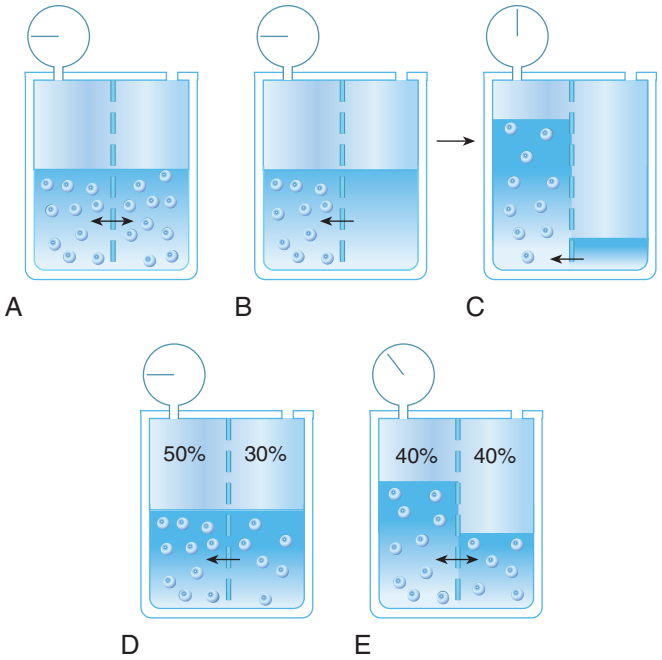

Fig. 13.2 Osmotic Pressure Is Illustrated by the Solutions in the Five Containers. Each container is divided into two compartments by a semipermeable membrane, which permits passage of solvent molecules but not solute *(circles)*. The number of solute particles represents relative concentrations of the solutions. Solute particles are fixed in number and are confined by the membranes. Volume changes are a function of the diffusible solvent. Solvent movement is indicated by arrows through the membranes. Container (A) shows a state of equilibrium, in which solute and solvent are equally distributed on either side of the membrane. Containers (B) and (C) show diffusion of solvent through the membrane as a result of solvent on only one side of the membrane and the resulting pressure change (osmotic pressure indicated by the gauge). Containers (D) and (E) show what happens when different concentrations exist on either side of a semipermeable membrane. Solvent moves from the lower concentration toward the higher concentration to establish an equilibrium because of osmotic pressure.

results from the relatively large distances between the molecules of solute in dilute solutions. The most important physiologic characteristic of solutions is their ability to exert pressure.

Osmotic pressure (oncotic pressure)[3] is the force produced by solvent particles under certain conditions. A membrane that permits passage of solvent molecules but not solute is called a *semipermeable membrane*. If such a membrane divides a solution into two compartments, molecules of solvent can pass (diffuse) through it from one side to the other (Fig. 13.2A). The number of solvent molecules diffusing in one direction must equal the number of solute molecules passing in the opposite direction. An equal ratio of solute to solvent particles (i.e., the concentration of the solution) is maintained on both sides of the membrane. A capillary wall is an example of a semipermeable membranes.[4,5]

If a solution is placed on one side of a semipermeable membrane and pure solvent is placed on the other, solvent molecules move through the membrane into the solution. The force driving solvent molecules through the membrane is called *osmotic pressure*. Osmotic pressure tries to redistribute solvent molecules so that the same concentration exists on both sides of the membrane. Osmotic pressure may be measured by connecting a manometer to the expanding column of the solution (see Fig. 13.2B and C).

Osmotic pressure also can be visualized as an attractive force of solute particles in a concentrated solution. If 100 mL of a 50% solution is placed on one side of a membrane and 100 mL of a 30% solution is placed on the other side, solvent molecules move from the dilute to the concentrated side (see Fig. 13.2D and E). The particles in the concentrated solution attract solvent molecules from the dilute solution until equilibrium occurs. Equilibrium exists when the concentrations (i.e., ratio of solute to solvent) in the two compartments are equal (40% in Fig. 13.2).

Osmolality is defined as the ratio of solute to solvent. In physiology, the solvent is water.[1,4,6] Osmotic pressure depends on the number of particles in solution but not on their charge or identity. A 2% solution has twice the osmotic pressure of a 1% solution under similar conditions. For a given amount of solute, osmotic pressure is inversely proportional to the volume of solvent. Most cell walls are semipermeable membranes. Through osmotic pressure, water is distributed throughout the body within certain physiologic ranges. Tonicity is the relative concentration of solutions that determine the direction and extent of diffusion. Tonicity is a way of describing the response of cells immersed in an external solution. Tonicity is influenced by the concentration of solutes that cannot cross the membrane. Average body cellular fluid has a tonicity equal to a 0.9% solution of sodium chloride (sometimes referred to as *physiologic* or *normal saline*). Solutions with the same tonicity are called **isotonic**. Compared with body fluid, solutions with more tonicity (more oncotic pressure and higher concentration as a result of less water) are **hypertonic**, and solutions with less tonicity (less oncotic pressure and lower concentration as a result of more water) are **hypotonic**. For example, a hypotonic solution has a lower concentration of solutes outside the cell than inside the cell. In an attempt to balance the concentrations of solutes inside and outside the cell, water will move into the cell, causing it to enlarge. Pressure increases inside the cell to counteract osmotic

MINI CLINI

Sputum Induction and Hypertonic Saline

Problem

To obtain samples of respiratory secretions, aerosol therapy is sometimes used to increase the volume of secretions and promote coughing to recover sputum or cells or both from the respiratory tract. Sputum induction combines the effect of hypertonic aerosols on the lining of the respiratory tract and on the normal cough reflex.

Discussion

Sputum induction is usually performed by having the patient inhale a sterile hypertonic saline solution. Isotonic saline is approximately 0.9% (i.e., normal saline); concentrations greater than 0.9% are considered hypertonic. In clinical practice, concentrations of 3% to 10% have been used. When the particles of hypertonic saline are deposited in the airway, osmotic pressure is thought to play a key role. When hypertonic saline comes into contact with the respiratory mucosa, water moves from the cells lining the airway into the sol-gel matrix that lines the airways, increasing its volume. The combination of increased volume of respiratory secretions with irritation of the epithelial cells themselves promotes reflex coughing. The volume of sputum and the rate of clearance from the lungs seem to depend on the osmolarity of the inhaled aerosol. Exposure of mast cells normally present in the airways to hypertonic aerosols results in the release of mediators (e.g., histamine) and bronchospasm. These effects may be related to the stimulation of the cough reflex. For the same reason, hypertonic saline is also sometimes used for bronchial challenge testing.

pressure. This pressure is called *turgor*. Some cells have selective permeability, allowing passage not only of water but also of specific solutes. Through these mechanisms, nutrients and physiologic solutions are distributed throughout the body.

RULE OF THUMB Solutions that have osmotic pressures equal to the average intracellular pressure in the body are called *isotonic*. This is roughly equivalent to a saline (NaCl) solution of 0.9%. Solutions with higher osmotic pressure are called *hypertonic,* whereas solutions with lower osmotic pressure are called *hypotonic*. Administration of isotonic solutions usually causes no net change in cellular water content. Hypertonic solutions draw water out of cells. Hypotonic solutions usually cause water to be absorbed from the solution into cells.

Quantifying Solute Content and Activity

The amount of solute in a solution can be quantified in two ways: (1) by actual weight (grams or milligrams) and (2) by chemical combining power *(electronegativity)*. The weight of a solute is easy to measure and specify. However, it does not indicate chemical combining power. The sodium ion (Na^+) has a gram ionic weight of 23. The bicarbonate ion (HCO_3^-) has a gram ionic weight of 61. Both ions have equal but opposite electronegativities (+1 for Na^+, −1 for HCO_3^-). The number of chemically reactive units is usually more meaningful than their weight.

Equivalent Weights

In medicine, it is customary to refer to physiologic substances in terms of chemical combining power. The measure commonly used is **equivalent weight**. Equivalent weights are amounts of substances that have equal chemical combining power. For example, if chemical *A* reacts with chemical *B,* by definition, 1 equivalent weight of *A* reacts with exactly 1 equivalent weight of *B*. No excess reactants of *A* or *B* remain.

Two magnitudes of equivalent weights are used to calculate chemical combining power: gram equivalent weight (gEq) and milligram equivalent weight, or milliequivalent (mEq). One milliequivalent (1 mEq) is $\frac{1}{1000}$ of 1 gEq.

Gram equivalent weight values. A gram equivalent weight of a substance is calculated as its gram molecular (formula) weight divided by its valence. *Valence* refers to the number of electrons that need to be added or removed to make the substance electrically neutral. The valence signs (+ or −) are disregarded.

$$\text{gEq} = \text{Gram molecular weight/valence}$$

The gram equivalent weight of N^+, with a valence of 1, equals its gram atomic weight of 23 g. The gram equivalent weight of calcium (Ca^{2+}) is its atomic weight (i.e., 40) divided by 2, or 20 g. The gram equivalent weight of ferric iron (Fe^{3+}) is its atomic weight (i.e., 55.8) divided by 3, or approximately 18.6 g.

Gram equivalent weight of an acid. The gram equivalent weight of an acid is the weight of the acid (in grams) that contains 1 mole of replaceable hydrogen (H). The gram equivalent weight of an acid may be calculated by dividing its gram formula weight by the number of H^+ atoms in its formula, as shown in the following reaction:

$$HCl + Na^+ \rightarrow NaCl + H^+$$

The single H^+ of hydrochloric acid (HCl) is replaced by Na^+. In 1 mole of HCl, there is 1 mole of replaceable H^+. By definition, the gram equivalent weight of HCl must be the same as its gram formula weight, or 36.5 g. The two H atoms of H_2SO_4 are both considered to be replaceable. In 1 mole of H_2SO_4, there are 2 moles of replaceable H^+, and the gram equivalent weight of H_2SO_4 is half its gram formula weight, or 48 g.

Acids in which H^+ atoms are not completely replaceable are exceptions to the rule. In some acids, H^+ replacement varies according to specific reactions. Carbonic acid (H_2CO_3) and phosphoric acid (H_3PO_4) are examples of such exceptions. Their equivalent weights are determined by the conditions of their chemical reactions.

For example, H_2CO_3 has two H^+ atoms. In physiologic reactions, only one is considered replaceable:

$$H_2CO_3 + Na^+ \rightarrow NaHCO_3 + H^+$$

Only one H^+ atom is released; the other remains bound. In 1 mole of H_2CO_3, there is only 1 mole of replaceable H^+. The gram equivalent weight of H_2CO_3 is the same as its gram formula weight, or 61 g.

Gram equivalent weight of a base. The equivalent weight of a base is its weight (grams) containing 1 mole of replaceable hydroxyl (OH^-) ions. Similar to acids, the gram equivalent weight of bases is calculated by dividing gram formula weight by the number of OH^- groups in its formula.

Conversion of gram weight to equivalent weight. To determine the number of gram equivalent weights in a substance, the gram weight is divided by its calculated equivalent weight, as shown in the following example:

58.5 g NaCl/gEq 58.5 g = 1 gEq
29.25 g NaCl/gEq 58.5 = 0.5 gEq

Milligram equivalent weights. The concentrations of most chemicals in the body are quite small. The term *milligram equivalent weight (milliequivalent)* is preferred for expressing these minute values; 1 mEq is simply 0.001 gEq:

$$\text{mEq} = \text{gEq}/1000$$

The normal concentration of potassium in plasma ranges from 0.0035 to 0.005 gEq/L. These values may be converted to milliequivalents by multiplying by a factor of 1000. The normal concentration of K^+ in the plasma would be expressed as ranging from 3.5 to 5.0 mEq/L.

Solute Content by Weight

The measurement of many electrolytes is based on actual weight rather than on milliequivalents. This weight is often expressed as milligrams per 100 mL of blood or body fluid. The units for this measurement are abbreviated as mg% (milligram percent) or mg/dL (milligrams per deciliter). This text uses the modern designation *mg/dL*. Some substances present in blood or body fluid are present in extremely small amounts and are expressed in *micrograms* ($\frac{1}{1000}$ of a milligram) per deciliter (µg/dL or mcg/dL).

Values stated in milligrams per deciliter may be converted into their corresponding equivalent weights and reported as milliequivalents per liter. Conversion between mEq/L and mg/dL may be calculated as follows:

$$\text{mEq/L} = \frac{\text{mg/dL} \times 10}{\text{equivalent weight}} \quad (1)$$

$$\text{mEq/L} = \frac{\text{mEq/L} \times \text{equivalent weight}}{10} \quad (2)$$

To convert a serum Na^+ value of 322 mg/dL to mEq/L, the equation is used as follows:

$$\begin{aligned}\text{mEq/L} &= \text{mg/dL} \times 10/\text{equivalent weight} \\ &= 322 \times 10/23 \\ &= 140\ \text{mEq/L}\end{aligned}$$

In clinical practice, electrolyte replacement is common when a laboratory test identifies a significant deficiency. The electrolyte content of intravenous solutions is usually stated in milligrams per deciliter or in milliequivalents per liter. Lactated Ringer (LR) solution is one such infusion used for electrolyte replacement (Table 13.3).

RULE OF THUMB: Volume by Weight Blood is a mixture of substances, including hemoglobin. Hemoglobin is a very large molecule useful in oxygen transport. Because of its relatively large molecular weight, the normal hemoglobin range is approximately 13.5–17.5 mg/dL for males and 12–15.5 mg/dL for females.

TABLE 13.3 Concentration of Ingredients in Lactated Ringer Solution

Substance	mg/dL	Approximate mEq/L
NaCl (sodium chloride)	600 Na	130
	310 Cl	109
$NaC_3H_5O_3$ (sodium lactate)	30 $C_3H_5O_3$	28
KCl (potassium chloride)	30 K	4
$CaCl_2$ (calcium chloride)	20 Ca	27

MINI CLINI

Using Lactated Ringer Solution Over 5% Dextrose in Water

Problem

Patients may have electrolyte imbalances requiring replacement therapy. There are many common solutions that may be used (e.g., lactated Ringer [LR] solution or 5% dextrose in water [D5W]). Both solutions have clinical use but can have different results in fluid distribution.

Discussion

When D5W is given, the body will rapidly metabolize the dextrose sugar, changing the solution from isotonic to hypotonic. The resulting shift in colloid osmotic pressure will cause the water to leave the vascular system and hydrate the surrounding tissue. However, LR solution is isotonic and does not contain sugar, so it remains isotonic within the vascular system. This allows for the fluid to be more evenly distributed throughout the body while replenishing electrolytes and not further adding more fluid to the surrounding tissue.[7,8]

Calculating Solute Content

In addition to gEq, mEq, mg/dL, and µg/dL (mcg/dL), several other methods of calculating solute content exist. These common chemical standards are used to compute solute content and dilution of solutions.

Quantitative Classification of Solutions

The amount of solute in a solution may be quantified by the following six methods:

1. ***Ratio solution.*** The amount of solute to solvent is expressed as a proportion (e.g., 1:100). Ratio solutions are sometimes used in describing concentrations of drugs.
2. ***Weight-per-volume (W/V) solution.*** The W/V solution is commonly used for solids dissolved in liquids. It is defined as weight of solute per volume of solution. This method is sometimes erroneously described as a percent solution. W/V solutions are commonly expressed in grams of solute per 100 mL of solution. For example, 5 g of glucose dissolved in 100 mL of solution is properly called a *5% solution,* according to the W/V scheme. A liquid dissolved in a liquid is measured as volumes of solute to volumes of solution.
3. ***Percent solution.*** A percent solution is weight of solute per weight of solution. For example, 5 g of glucose dissolved in 95 g of water is a true percent solution. The glucose is 5% of the total solution weight of 100 g.

4. ***Molal solution***. A molal solution contains 1 mole of solute per kilogram of solvent, or 1 mmol/g solvent. The concentration of a molal solution is independent of temperature.
5. ***Molar solution***. A molar solution has 1 mole of solute per liter of solution, or 1 mmol/mL of solution. The solute is measured into a container, and solvent is added to produce the solution volume desired.
6. ***Normal solution***. A normal solution has 1 gEq of solute per liter of solution, or 1 mEq/mL of solution. For all monovalent solutes, normal and molar solutions are the same. The equivalent weights of their solutes equal their gram formula weights. Equal volumes of solutions of the same normality contain chemically equivalent amounts of their solutes. If the solutes react chemically with one another, equal volumes of the solutions react completely. Neither substance remains in excess. In the analytic process of titration, normal solutions are often used as standards to determine the concentrations of other solutions.

Dilution Calculations

Dilute solutions are made from a stock preparation. Preparation of medications often involves dilution. Dilution calculations are based on the weight-per-unit volume principle (the aforementioned W/V solution method).

Diluting a solution increases its volume without changing the amount of solute it contains, and this reduces the concentration of the solution. The amount of solute in a solution can be expressed as volume times concentration. For example, 50 mL of a 10% solution (10 g/dL) contains 50 × 0.1, or 5 g. In the dilution of a solution, initial volume (V_1) multiplied by initial concentration (C_1) equals final volume multiplied by final concentration. This can be expressed as follows:

$$V_1C_1 = V_2C_2$$

This equation is sometimes referred to as the **dilution equation**. Whenever three of the variables are known, the fourth can be calculated by isolating the missing variable as in the following examples:

1. Diluting 10 mL of a 2% (0.02) solution to a concentration of 0.5% (0.005) requires finding the new volume (V_2) by rearranging the dilution equation as follows:

$$V_2 = V_1C_1/C_2$$
$$V_2 = 10\ \text{mL} \times 0.02/0.005$$
$$V_2 = 40\ \text{mL}$$

2. If 50 mL of water is added to 150 mL of a 3% (0.03) solution, the new concentration is calculated by rearranging the dilution equation to find C_2 as follows:

$$C_2 = V_1C_1/V_2$$
$$C_2 = 150\ \text{mL} \times 0.02/(50\ \text{mL} + 150\ \text{mL})$$
$$C_2 = 0.0225 \text{ or } (2.25\%)$$

3. To dilute 50 mL of a 0.33 normal (N) solution to a 0.1 N concentration, concentration is given as normality, but it can be used similar to a percentage. The new volume (V_2) can be calculated by rearranging the dilution equation as follows:

$$V_2 = V_1C_1/C_2$$
$$V_2 = 50\ \text{mL} \times 0.33/0.1$$
$$V_2 = 165\ \text{mL}$$

In the last example, the volume needed to produce a 0.1 N solution would be 165 mL to 50 mL (the original volume), or 115 mL. In other words, 115 mL of solvent would have to be added to the original 50 mL of 0.33 N solution to produce the desired concentration. The added solvent is called the **diluent** because it dilutes the original concentration to a lower concentration.

RULE OF THUMB: Isolating Missing Variables When using the dilution equation, separate what is known and what you will need to determine. Look at the side of the equation which has the unknown value. To isolate it, divide both sides by the accompanying known value. This will leave the three known values on one side and the unknown fourth on the other side of the equation. Plug in the numbers, and solve.

ELECTROLYTIC ACTIVITY AND ACID-BASE BALANCE

Acid-base balance depends on the concentration and activity of electrolytic solutes in the body. Clinical application of acid-base homeostasis is discussed in detail in Chapter 14.

Characteristics of Acids, Bases, and Salts

Acids

The term **acid** refers to either compounds that can donate [H^+] (Brönsted-Lowry acid) or any compound that accepts an electron pair (Lewis acid). Although these two theories of acids differ in which is being transferred, both theories attempt to describe how reactive groups perform within an aqueous solution[8,9]:

$$NH_4Cl + NaOH \rightarrow NH_3 + NaCl + HOH$$

In this reaction, Na^+ and Cl^- ions are not involved in the proton transfer. The equation can be rewritten ionically as follows to show the acidity of the ammonium ion:

$$NH_4^+ + OH^- \rightarrow NH_3 + HOH$$

The ammonium ion donates an H^+ ion (proton) to the reaction. The H^+ combines with the hydroxide ion (OH^-), and this converts the former into ammonia gas and the latter into water.

Each of these dilutions uses the same proportions used in the first dilution as determined by the dilution equation. Methacholine is administered by nebulizer to the patient, starting with the lowest concentration (0.0625 mg/mL) and increasing until a change in FEV_1 is observed. (See Chapter 20 for additional information on pulmonary function testing.)

Acids with single ionizable hydrogen. Simple compounds such as hydrochloric acid (HCl) ionize into one cation and one anion:

$$HCl \rightarrow H^+ + Cl^-$$

MINI CLINI

Methacholine Dilution

The dilution equation ($V_1C_1 = V_2C_2$) is commonly used to calculate volumes or concentrations of medications when a specific dosage needs to be administered to a patient. If three of the variables are known, the fourth can be determined.

Problem

Methacholine is a drug used to induce airway constriction in patients suspected of having reactive airway disease. In healthy subjects, only higher doses of methacholine cause bronchospasm. In asthmatics, very low doses can precipitate a 20% decrease in the forced expiratory volume in 1 s (FEV_1). The methacholine challenge test begins with a low dose and increases the concentration (either doubling or quadrupling) until the patient has a significant change in FEV_1 or the highest dose has been given. Methacholine is supplied in vials that contain 100 mg of the active substance to which 6.25 mL of diluent (saline) can be added to produce a concentration of 16 mg/mL. This is the highest dosage administered to the patient. How can you make serial dilutions of the drug so that five different dosages are available and each one is 4 times more concentrated than the previous dose?

Solution

Starting with a 16 mg/mL stock solution of methacholine, how much diluent needs to be added to 3 mL of the stock to make a 4 mg/mL dose (one-fourth of the original concentration)?

Using the dilution equation:

$$C_1V_1 = C_2V_2$$
$$(16)(3.0) = (4)V_2$$
$$48/4 = V_2$$
$$12 = V_1$$

Because there was 3 mL of the stock solution to begin with, the amount of diluent to add is the difference between 12 (V_2) and 3, or 9 mL. Adding 9 mL of diluent to the original 3 mL of stock (16 mg/mL) provides 12 mL of methacholine with a concentration of 4 mg/mL, exactly one-fourth of the highest dose. Additional dilutions can be prepared using 3 mL of solution according to the following:

Start With		To Make
3 mL of 4 mg/mL	9 mL	1 mg/mL
3 mL of 1 mg/mL	9 mL	0.25 mg/mL
3 mL of 0.25 mg/mL	9 mL	0.0625 mg/mL

Acids with multiple ionizable hydrogens. The H^+ ions in an acid may become available in stages. The degree of ionization increases as an electrolyte solution becomes more dilute. Concentrated sulfuric acid ionizes only one of its two H^+ atoms per molecule, as follows:

$$H_2SO_4 \rightarrow H^+ + HSO_4^-$$

With further dilution, second-stage ionization occurs:

$$H_2SO_4 \rightarrow H^+ + H^+ + SO_4^-$$

Bases

A **base** is a compound that yields hydroxyl ions (OH^-) when placed into aqueous solution. A substance capable of inactivating acids is also considered a base. These compounds, called *hydroxides,* consist of a metal that is ionically bound to an OH^- ion or ions. The OH^- may also be bound to an ammonium cation (NH_4^+). An example of this type of base is NaOH. The Brönsted-Lowry definition of a base is any compound that accepts a proton; bases are paired with acids that donate the proton, and these are called *conjugate pairs.* This definition includes substances other than hydroxides, such as ammonia, carbonates, and certain proteins.

Hydroxide bases. In aqueous solution, the following are typical dissociations of hydroxide bases:

$$Na^+OH \rightarrow Na^+ + OH^-$$
$$K^+OH \rightarrow K^+ + OH^-$$
$$Ca^{2+}(OH^-)2 \rightarrow Ca^{2+} + 2(OH^-)$$

Inactivation of an acid is part of the definition of a base. This inactivation is accomplished by OH^- reacting with H^+ to form water:

$$NaOH + HCl \rightarrow NaCl + HOH$$

Nonhydroxide bases. Ammonia and carbonates are examples of nonhydroxide bases. Proteins, with their amino groups, also can serve as nonhydroxide bases.

Ammonia. Ammonia qualifies as a base because it reacts with water to yield OH^-:

$$NH_3 + HOH \rightarrow NH_4^+ + OH^-$$

and neutralizes H^+ directly:

$$NH^3 + H^+ \rightarrow NH_4^+$$

In both instances, NH_3 accepts a proton to become NH_4^+. Ammonia plays an important role in renal excretion of acid (see Chapter 14).

Carbonates. The carbonate ion (CO_3^{2-}), can react with water in the following way to produce OH^-:

$$Na_2CO_3 \rightleftharpoons 2Na^+ + CO_3^{2-} \quad (1)$$
$$CO_3^{2-} + HOH \rightleftharpoons HCO_3^- + OH^- \quad (2)$$

In this reaction, CO_3^{2-} accepts a proton from water, becoming the HCO_3^- ion. It simultaneously produces a hydroxide ion. The CO_3^{2-} ion also can react directly with H^+ to inactivate it:

$$CO_3^{2-} + H^+ \rightleftharpoons HCO_3^-$$

Protein bases. Proteins are composed of amino acids bound together by peptide links. Physiologic reactions in the body occur in a mildly alkaline environment. This environment allows proteins to act as H^+ receptors, or bases. Cellular and blood proteins acting as bases are transcribed as $prot^-$.

The imidazole group of the amino acid histidine is an example of an H^+ acceptor on a protein molecule (Fig. 13.3). The ability of proteins to accept H^+ ions limits H^+ activity in solution, which is called **buffering**. The buffering effect of hemoglobin (Hb) is produced by imidazole groups in the protein. Each Hb molecule contains 38 histidine residues. Each O_2-carrying component (heme group) of Hb is attached to a histidine residue. The ability of Hb to accept (i.e., buffer) H^+ ions depends on its oxygenation state. Deoxygenated (reduced) Hb is a stronger base (i.e., a better

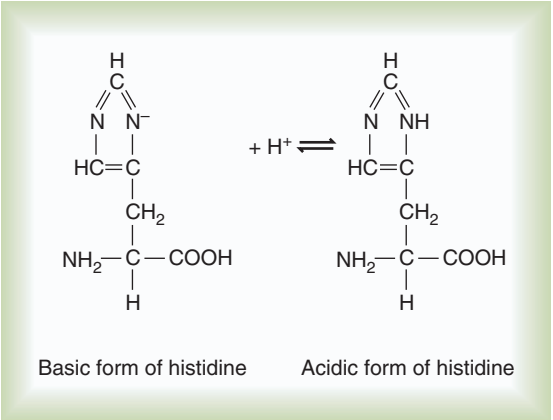

Fig. 13.3 Histidine portion of a protein molecule (at *top*) serving as a proton acceptor (*base*).

H^+ acceptor) than oxygenated Hb. This difference partially accounts for the ability of reduced Hb to buffer more acid than oxygenated Hb can (see Chapter 14). Plasma proteins also act as buffers, although with less buffering power than Hb, which contains more histidine.

Designation of Acidity and Alkalinity

Pure water can be used as a reference point for determining acidity or alkalinity. The concentration of both H^+ and OH^- in pure water is 10^{-7} mol/L. A solution that has a greater H^+ concentration or lower OH^- concentration than water acts as an acid. A solution that has a lower H^+ concentration or a greater OH^- concentration than water is alkaline, or basic.

The H^+ concentration $[H^+]$ of pure water has been adopted as the standard for comparing reactions of other solutions. Electrochemical techniques are used to measure the $[H^+]$ of unknown solutions. Acidity or alkalinity is determined by variation of the $[H^+]$ greater than or less than 1×10^{-7}. For example, a solution with a $[H^+]$ of 89.2×10^{-4} has a higher $[H^+]$ than water and is acidic. A solution with a $[H^+]$ of 3.6×10^{-8} has fewer H^+ ions than water and is by definition alkaline. Two related techniques are used for expressing the acidity or alkalinity of solutions using the $[H^+]$ of water (i.e., 10^{-7}) as a neutral factor: (1) the $[H^+]$ in nanomoles per liter and (2) the logarithmic pH scale.

RULE OF THUMB Pure water is considered to be the reference point for neutral pH. This is because of equilibrium between $[H^+]$ and the hydroxide ion $[-OH^-]$. Because pH reflects the concentration of $[H^+]$, a lower pH on the scale means that the concentration of $[H^+]$ increases relative to $[-OH^-]$. An increase in pH means that there is more $[-OH^-]$ than $[H^+]$. Because pH is an inverse logarithm that means each pH change is a 10-times increase or decrease in $[H^+]$.

Nanomolar Concentrations

The acidity or alkalinity of solutions may be reported using the molar concentration of H^+ compared with that of water. The $[H^+]$ of water is 1×10^{-7} mol/L, or 0.0000001 (one ten-millionth of a mole). The unit for one-billionth of a mole is a **nanomole** (nmol). The $[H^+]$ of water can be expressed as 100 nmol/L. A solution that has a $[H^+]$ of 100 nmol/L is neutral. A solution with an $[H^+]$ greater than 100 nmol/L is acidic; one with an $[H^+]$ less than 100 nmol/L is alkaline. This system is limited because of the wide range of possible $[H^+]$ but is applicable in clinical medicine because the physiologic range of $[H^+]$ is narrow. $[H^+]$ in healthy individuals is usually 30 to 50 nmol/L.

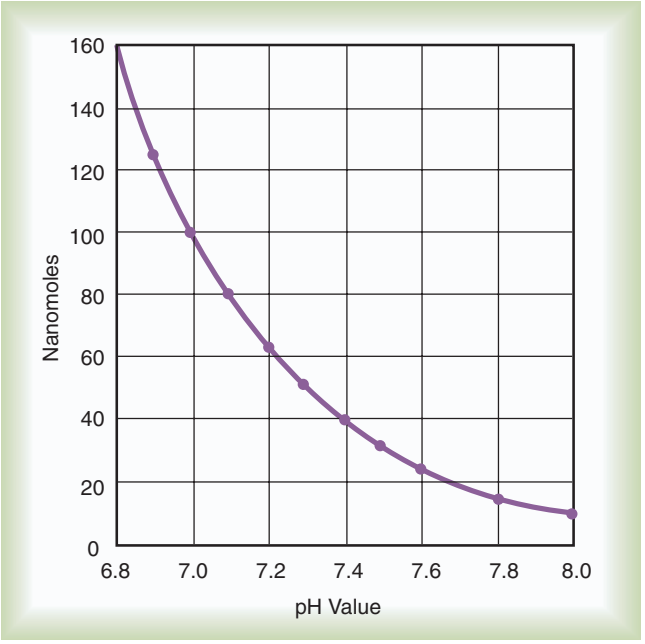

Fig. 13.4 **Relationship between pH scale and $[H^+]$ concentrations in nanomoles per liter (nmol/L).** pH of 7.00 equals 100 nmol/L H^+, whereas the normal human pH (arterial blood) of 7.40 is equal to approximately 40 nmol/L.

pH Scale

The pH scale is used to describe the concentration of H^+, ($[H^+]$), (i.e., Brönsted-Lowry acid) in a solution. Rather than expressing the $[H^+]$ in nanomoles, it is more convenient to describe it in terms of the negative logarithm of the nanomolar $[H^+]$. The equation for calculating pH is:

$$pH = -\log[H^+]$$

The pH of pure water is 7.0: The $[H^+]$ of water is 1×10^{-7} mol/L. The logarithm of 1×10^{-7} is -7, so the negative logarithm of 1×10^{-7} is 7.

Using this scheme, in a solution with a pH of 7.00, the $[H^+]$ is the same as would be seen in pure water, so by convention this is called "neutral." As the pH decreases below 7.00, the solution is termed *acidic*. When the pH increases above 7.00, the solution is considered to be *basic*. With a whole number change in pH (i.e., pH decreasing from 7.00 to 6.00), the $[H^+]$ is a factor of 10 less. With a pH increase from 7.00 to 8.00, the $[H^+]$ is 10 times greater (Fig. 13.4). A pH of 7.00 is equivalent to a $[H^+]$ of 100 nmol. A pH of 8.00 is equivalent to a $[H^+]$ concentration of 10 nmol. Similarly, a change in pH of 0.3 units equals a twofold change in $[H^+]$.

Applying these concepts in an example pertinent to clinical medicine yields the following:

$$[H^+] \text{ in blood} = 4.0 \times 10^{-8} \text{ mol/L}$$
$$pH = -\log(4.0 \times 10^{-8})$$
$$= -\log 4.0 + -\log 10^{-8}$$
$$= -\log 4.0 + \log 10^{8}$$
$$= -0.602 + 8$$
$$= 7.40$$

In this example, the $[H^+]$ in arterial blood of a healthy adult is approximately 4.0×10^{-8} mol/L, or 40 nmol/L.

RULE OF THUMB Logarithms are the opposite of exponents. Consider the exponent:

$$2^3 = 2 \times 2 \times 2$$
$$= 8$$

The exponent tells us how many times to multiply the base to itself. In the previous example, the exponent tells us to multiply 2 by itself 3 times which equals 8. A logarithm is the value of the exponent when the base number is known. Unless otherwise specified, the base is 10.

RULE OF THUMB The pH scale is logarithmic which means that it is the exponent of a base number, usually 10. For example, the logarithm of 100 is 2 ($10^2 = 100$). pH is a positive number representing the negative log of the hydrogen ion concentration $[H^+]$ of a solution. To visualize changes in acidity or alkalinity, the following two rules are helpful:

1. A pH change of 0.3 unit equals a twofold change in $[H^+]$.
2. A pH change of 1 unit equals a tenfold change in $[H^+]$.

For example, if a patient's blood pH decreased from 7.40 (normal) to 7.10, the $[H^+]$ concentration would be twice as high. If a patient's urine pH decreased from 7.00 to 6.00, the $[H^+]$ would have increased by 10 times.

BODY FLUIDS AND ELECTROLYTES

Body Water

Water constitutes 45%–80% of an individual's body mass, depending on the mass, gender, and age of the individual. Obese individuals have a lower percentage of body water (≤30% less) than normal-weight individuals. Men have a slightly higher percentage of total body water than women. The total percentage of body water in infants and children is substantially greater, with water accounting for 80% of a newborn's total body weight (Table 13.4).

Distribution

Body water is divided into the following two major compartments: (1) ***intracellular*** ("within the cells") and (2) ***extracellular*** ("outside the cells"). Intracellular water accounts for approximately two-thirds of the total body water, and extracellular water accounts for the remaining one-third. Extracellular water is found in three subcompartments: (1) intravascular water (plasma), (2) interstitial water, and (3) transcellular fluid. Intravascular water constitutes approximately 5% of the body weight. Interstitial water is water in the tissues between the cells. It constitutes approximately 15% of the body weight. The proportion of ***transcellular fluid*** is quite small in proportion to plasma and **interstitial fluid**. Interstitial fluid is a matrix—a collagen/gel substance that allows the interstitium to provide structural support during times of extracellular volume depletion.[10,11] Examples of transcellular fluid normally occurring in the human body include cerebrospinal fluid, digestive juices, and mucus. However, transcellular fluid can also occur in some disease conditions, such as *ascites* (excess fluid in the peritoneal cavity) or *pleural effusion* (fluid collection in the pleural space).

TABLE 13.4 Distribution of Body Fluids

Body Water	Man (% Body Weight)	Woman (% Body Weight)	Infant (% Body Weight)
Total body Water	60 ± 15	50 ± 15	80
Intracellular	45	40	50
Extracellular	15–20	15–20	30
Interstitial	11–15	11–15	24
Intravascular	4.5	4.5	5.0
Transcellular	<1	<1	<1

Composition

The concentration of ionic solutes in intracellular and extracellular fluids differs significantly. Sodium (Na^+), chloride (Cl^-), and HCO_3^- are predominantly extracellular electrolytes. Potassium (K^+), magnesium (Mg^{2+}), phosphate (PO_4^{3-}), sulfate (SO_4^{2-}), and protein constitute the main intracellular electrolytes. Although protein does not dissociate, ionically, it can create H^+ and other weak bonds and distribute net extra charge within its molecule. Intravascular and interstitial fluids have similar electrolyte compositions. Plasma contains substantially more protein than interstitial fluid. Proteins, chiefly albumin, account for the high osmotic pressure of plasma. Osmotic pressure is an important determinant of fluid distribution between vascular and interstitial compartments.

Regulation

As discussed, movement of certain ions and proteins between body compartments is restricted yet water diffuses freely. Control of total body water occurs through regulation of water intake (thirst) and water excretion (urine production, insensible (nonmeasurable) loss such as sweating, and stool water). The kidneys are mainly responsible for water excretion. If water intake is low, the kidneys reduce urine volume. Solutes in the urine can be concentrated up to 4 times the concentration of solutes in the plasma. If water intake is high, the kidneys normally can excrete large volumes of dilute urine.

The kidneys maintain the volume and composition of body fluids via two related mechanisms. First, filtration and reabsorption of Na^+ adjust urinary Na^+ excretion to match changes in

TABLE 13.5 Daily Water Exchange

Regulation	Average Daily Volume (mL)	Maximum Daily Volume
Water Losses		
Insensible		
Skin	700	1,500 mL
Lung	200	
Sensible		
Urine	1,000–1,200	>2,000 mL/h
Intestinal	200	8,000 mL
Sweat	0	>2,000 mL/h
Water Gain		
Ingestion		
Fluids	1,500–2,000	1,500 mL/h
Solids	500–600	1,500 mL/h
Body Metabolism	250	1,000 mL

MINI CLINI

Insensible Water Loss Through Respiratory System

Problem

The respiratory tract is a source for insensible water loss. Special care must be taken for those people who have artificial airways not to thicken secretions.

Discussion

Artificial airways bypass the natural humidification structures of native, biologic airway. Inspired ambient air has a lower relative humidity than air in the lung at body temperature pressure saturated (BTPS). Without the anatomic structures to help warm and humidify the inspired gas before it gets to the lungs, the air is brought close to BTPS by dehydrating secretions. This humidity deficit can be avoided by placing external heated humidity so the warmed, inspired gas will have a higher relative humidity closer to BTPS as it enters the airways.

dietary intake. Second, water excretion is regulated by osmoreceptors that are located in the hypothalamus and regulate secretion of antidiuretic hormone (ADH, also known as *vasopressin*).[6,12,13] These receptors are exceptionally sensitive, and studies have shown that a single neuron can respond to either an osmotic or a nonosmotic baroreceptor simulus.[13] These mechanisms allow the kidneys to maintain the volume and concentration of body fluid despite variations in salt and water intake. Analysis of the urine (urinalysis) often provides diagnostic clues in disorders of body fluid volume.

Water losses. Water may be lost from the body through the skin, lungs, kidneys, and gastrointestinal (GI) tract. Water loss can be ***insensible*** (nonmeasurable), such as evaporation of water from the skin and lungs (in exhaled gas), or ***sensible*** (measurable), such as losses from urine and the GI tract (Table 13.5).[14] Fluid losses from the body also may occur during vomiting, diarrhea, or suctioning from the stomach. Fever, in conjunction with sweating, as well as severe burns can also cause significant losses.

The GI tract manufactures 8 to 10 L of fluid per day. More than 98% of this volume is reclaimed in the large intestine. In patients who are vomiting or have diarrhea, water losses through the GI tract can be considerable. Individuals with severe burns or open wounds can lose large quantities of water.

Other causes of abnormal fluid loss include certain renal and respiratory disorders. Patients with renal disease may have to excrete larger quantities of urine to get rid of extra nitrogenous wastes. Patients with increased ventilation also have increased insensible water losses through increased evaporation from the respiratory tract. Patients with artificial airways, whose humidifying capabilities of their upper airway are bypassed, are prone to evaporative water loss if inspired air is not adequately humidified. Infants have a greater proportion of body water than adults, particularly in the extracellular compartments (see Table 13.4). Water loss in infants may be twice the water loss in adults. Infants also have a greater body surface area (in proportion to body volume) than adults, making their basal heat production twice as high. Higher metabolic rates in infants necessitate greater urinary excretion. Infants turn over approximately half of their extracellular fluid volume daily versus one-seventh for adults. Fluid loss or lack of intake can rapidly deplete an infant of water.

Water replacement. Water is replenished in two major ways: ingestion and metabolism (see Table 13.5).

Ingestion. Water is replaced mainly by ingestion, through drinking liquids. An average adult drinks 1500 to 2000 mL of water per day. An additional 500 to 600 mL of water is ingested from solid food.

Metabolism. Water also is gained from the oxidation of fats, carbohydrates, and proteins in the body; the destruction of cells also releases some water. During total starvation, 2000 mL of water can be produced daily by the metabolism of 1 kg of fat. Recovery after surgery or trauma may be similar to starvation; under such conditions, approximately 500 mg of protein and a similar amount of fat are metabolized. This metabolism yields approximately 1 L of water per day.

Transport Between Compartments

Homeostasis depends largely on the total volume of body fluids and on fluid transport between body compartments. The first stage of homeostasis is fluid exchange between systemic capillaries and interstitial fluid via passive diffusion. Capillary walls are permeable to crystalline electrolytes. This allows equilibrium between the two extracellular compartments to occur quickly. Except for the large protein molecules, plasma also can move through capillary walls into the tissue spaces. Because water and small molecules can cross the capillary membranes, they produce little or no osmotic effect.

Movement of fluid and solutes from capillary blood to interstitial spaces is enhanced by the difference in **hydrostatic pressure** (pressure exerted by a liquid at rest with respect to adjacent bodies) between compartments. Hydrostatic pressure difference depends on blood pressure, blood volume, and the vertical distance of the capillary from the heart (i.e., the effects of gravity). Hydrostatic pressure tends to cause fluid to leak out of capillaries into the interstitial spaces.

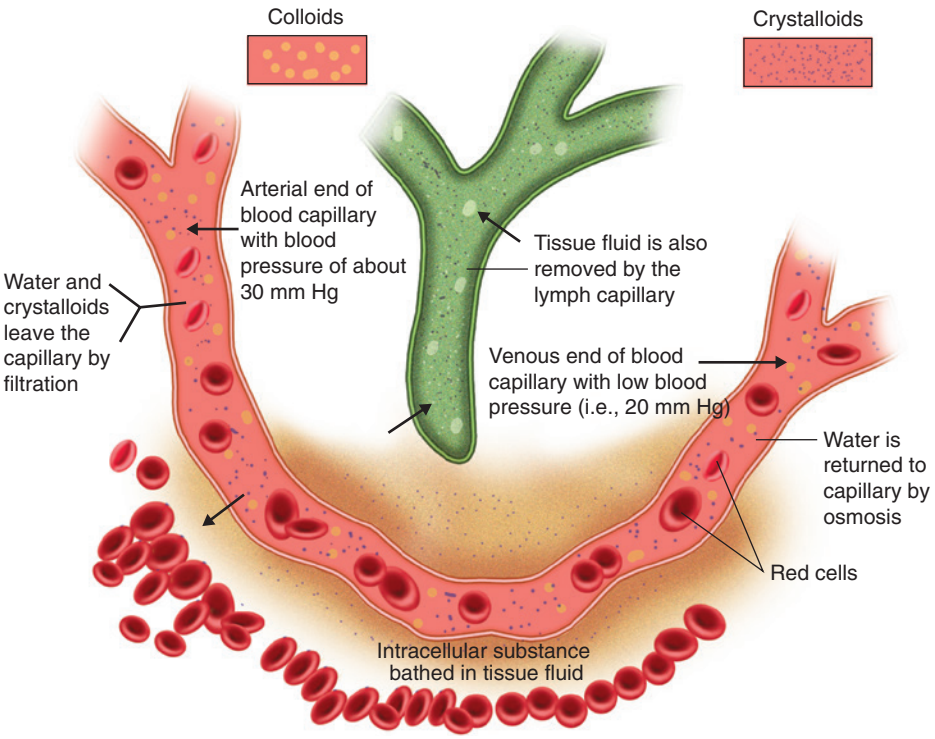

Fig. 13.5 Tissue fluid is formed by a process of filtration at the arterial end of a systemic capillary *(left),* in which blood pressure exceeds colloid osmotic pressure. The fluid is absorbed by the blood capillaries and lymphatic vessels. It returns to the venous end of the capillary *(right)* when colloid osmotic pressure exceeds blood pressure. Fluid is absorbed into the lymphatic capillary system when interstitial fluid pressure is greater than the pressure within the lymphatic capillary. Normally, little colloid escapes from the capillary. Colloid that does escape is returned to the blood circulation by the lymphatic vessels. (Modified from Burke SR: *The composition and function of body fluids*, ed 3, St Louis, 1980, Mosby.)

Osmotic pressure differences between interstitial and intravascular compartments oppose hydrostatic pressure; that is, osmotic pressure tends to keep fluid in the capillaries. Proteins with molecular weights greater than approximately 70,000 in colloidal suspension in the plasma cause this difference in osmotic pressure. Proteins such as albumin are too large to pass through the pores of the capillary. Instead, these proteins remain in the intravascular compartment and exert osmotic pressure, which draws water and small solute molecules back into the capillaries; this is called **plasma colloid osmotic pressure (oncotic pressure)**. Because these large proteins are negatively charged, they attract (but do not bind) an equivalent amount of cations to the intravascular compartment. These cations have the effect of increasing osmotic pressure within the capillary (***Donnan effect***).

In a typical capillary, blood pressure is approximately 35 mm Hg at the arterial end and approximately 15 mm Hg at the venous end (Fig. 13.5). Colloid osmotic pressure of the intravascular fluid remains constant at approximately 25 mm Hg. Hydrostatic pressure along the capillary continually decreases. At the arterial end, hydrostatic pressure normally exceeds osmotic pressure, and water flows out of the vascular space into the interstitial space. At the venous end, colloidal osmotic pressure exceeds hydrostatic forces. Water is pulled back into the vascular compartment.

The outflow of water and electrolytes from the capillary at the arterial end is not completely balanced by the return on the venous end. Slightly more water diffuses out than is reabsorbed.

MINI CLINI

Using Albumin to Limit Third Spacing

Problem

Sometimes patients are given albumin as a treatment for severe edema (third spacing) either before being given a diuretic or in conjunction.

Discussion

If a patient is malnourished or has tissue damage, their serum protein levels may be low. Administration of albumin will increase the plasma colloid osmotic pressure ($p_c - p_i$). This increase in oncotic pressure will draw free water from the surrounding tissues and back into the vascular system, where excess should be excreted by the kidneys.

This slight outward excess is balanced by fluid return through the lymphatic circulation (see Chapter 10). Fluid return via lymphatic channels also depends on pressure differences. The pressure in the interstitial space is determined by the volume of interstitial fluid and its electrolyte content. Interstitial fluid moves from a region of higher pressure (interstitial space) to a region of lower pressure (lymphatic channels). This lymph fluid moves into larger lymphatic spaces, where the pressure is lower.

Three examples of the forces in Starling equation are fluid return from gravity-dependent areas of the body, fluid exchange in the lung, and tissue edema (excess fluid in the interstitial space).

Because of hydrostatic effects, capillary pressure in the feet can reach 100 mm Hg when an individual is standing. Reabsorption of tissue fluid can be accomplished, although hydrostatic pressure greatly exceeds colloidal osmotic pressure. Three factors favor reabsorption under these circumstances:

1. High intravascular hydrostatic pressure is balanced by a proportionally greater interstitial pressure.
2. The "pumping" action of the skeletal muscles surrounding leg veins reduces venous pressures.
3. Lymph flow back to the thorax is enhanced via a similar mechanism; this facilitates clearance of excess interstitial fluid.

However, when an imbalance results from changes in the basic pressures (e.g., arterial hypertension), edema tends to occur in the dependent limbs.

The lungs present a different situation. In systemic tissues, a constant exchange of interstitial fluid is essential. In the lungs, the alveoli must be kept relatively dry. Otherwise, interstitial fluid in the alveolar-capillary spaces would impede the diffusion of gas. Colloid osmotic pressure in pulmonary blood vessels is the same as it is in the systemic circulation. To minimize interstitial fluid in the alveolar-capillary region, the hydrostatic pressure difference must be kept low. The pulmonary circulation is a low-pressure system. The mean pulmonary vascular pressures are approximately one-sixth of those in the systemic circulation. Colloid osmotic pressure exceeds hydrostatic forces across the entire length of the pulmonary capillaries in healthy individuals. The alveoli are relatively free of excess interstitial water.

If hydrostatic pressure increases in the pulmonary circulation, this balance can be upset. This causes fluid movement into the alveolar-capillary spaces. In the lungs, edema caused by increased hydrostatic pressure often is a result of backpressure from a failing left ventricle (e.g., in congestive heart failure [CHF]).

Edema can be caused by other factors. The **Starling equilibrium** equation given earlier shows that edema can be caused by a decrease in colloid osmotic pressure or an increase in capillary permeability. If albumin is depleted in the blood, the balance of forces is upset, favoring increased movement of fluid into the interstitium. Likewise, an increase in capillary permeability results in more fluid leaving the capillaries. Increased capillary permeability is a major factor in certain types of acute lung injuries (see Chapter 29).[15-17]

MINI CLINI

Pulmonary Edema

Problem

In the healthy cardiopulmonary system the colloid osmotic pressure exceeds the hydrostatic pressure in the pulmonary vasculature. With left heart failure, the hydrostatic pressure increases resulting in pulmonary edema.

Discussion

With a failing left heart, the blood backs up in the pulmonary vein resulting in increased hydrostatic pressures within the pulmonary circulation. The pulmonary vasculature system is a low pressure, low resistance system. This increase in hydrostatic force ($P_c - P_i$) is enough to cause fluid to enter the alveoli, decreasing gas exchange and increasing the patient's work of breathing.

MINI CLINI

Pedal Edema

People who work in jobs that require long periods of standing may notice that they have ankle and foot swelling (pedal edema). A common remedy for this is to wear a tight fitting, so-called compression stocking.

Discussion

As mentioned in the text, fluid flow from the vascular space to the tissue is dependent on the net sum of various pressures. The hydrostatic pressure ($P_c - P_i$) in someone who is standing can exceed 100 mm Hg. Applying external compression from the stockings will increase the overall interstitial pressure which balances both the hydrostatic and interstitial forces further reducing the formation of pedal edema. Alternatively, walking tenses the muscles to act as a pumping system that will also balance the pressures and return the fluid to the vascular system.

People with high blood pressure (hypertension) can have hydrostatic pressures even higher so the effect of the external compression stockings will not be as efficient.

Electrolytes

Electrolytes in the various body fluids are not passive solutes. Electrolytes maintain the internal environment while making possible essential chemical and physiologic events. There are seven major electrolytes: sodium, chloride, HCO_3^-, potassium, calcium, magnesium, and phosphorus (phosphate).

Sodium (Na^+)

Na^+ is the major circulating cation within the body.[16,18,19] Regulation of Na^+ concentration in plasma and urine is related to regulation of total body water. Of the total body stores of Na^+, 50% is extracellular. The remaining Na^+ is found in bone (40%) and in cells (10%). The normal serum concentration of Na^+ is 136 to 145 mEq/L. In cells, the Na^+ concentration is much lower, averaging only 4.5 mEq/L.

The average adult ingests and excretes approximately 100 mEq of Na^+ every 24 hours. Children require approximately half this amount, and infants typically exchange 20 mEq of Na^+ per day. Most Na^+ is reabsorbed through the kidney, with approximately 80% of the Na^+ reclaimed passively in the proximal tubules of the kidney. The remainder is actively reabsorbed in the distal tubules. Na^+ reabsorption in the kidneys is governed mainly by the level of aldosterone, which is secreted by the adrenal cortex. Na^+ reabsorption in the distal tubules of the kidney occurs in exchange for other cations. Na^+ balance is involved in acid-base homeostasis (i.e., H^+ exchange) and the regulation of K^+. Abnormal losses of Na^+ can lead to ***hyponatremia*** (low Na^+ concentration in the plasma) and may occur for numerous reasons, as shown in Table 13.6.

Hyponatremia, which is the most common electrolyte imbalance found in hospitalized patients, is defined as having serum Na^+ levels less than 135 mEq/L.[6] Previously considered to be benign, mild hyponatremia has more recently been shown to have a significant impact on a patient's cognitive function and gait stability, and it is thought to be a contributing factor in falls. Hyponatremia can lead to cerebral edema due to a change in

TABLE 13.6 Electrolyte Disorders and Clinical Findings

Electrolyte	Imbalance	Causes	Symptoms
Sodium (Na^+)	Hyponatremia	GI loss, sweating, fever, diuretics, ascites, congestive heart failure, kidney failure	Weakness, lassitude, apathy, headache, orthostatic hypotension, tachycardia
	Hypernatremia	Net sodium gain, net water loss, increased aldosterone, steroid therapy	Tremulousness, irritability, ataxia, confusion, seizures, coma
Chloride (Cl^-)	Hypochloremia	GI loss, diuretics	Metabolic alkalosis, muscle spasm, coma (severe cases)
	Hyperchloremia	Dehydration, metabolic acidosis, respiratory alkalosis	(Minimal)
Potassium (K^+)	Hypokalemia	Diuretics, steroid therapy, renal tubular disease, vomiting, diarrhea, malnutrition, trauma	Muscle weakness, paralysis, ECG abnormalities, supraventricular arrhythmias, circulatory failure, cardiac arrest
	Hyperkalemia	Chronic renal disease, hemorrhage, tissue necrosis, nonsteroidal antiinflammatory drugs, ACE inhibitors, cyclosporine, K^+-sparing diuretics	ECG changes, ventricular arrhythmias, cardiac arrest
Calcium (Ca^{2+})	Hypocalcemia	Hyperparathyroidism, pancreatitis, renal failure, trauma	Hyperactive tendon reflexes, muscle twitching, spasm, abdominal cramps, ECG changes, seizures (rarely)
	Hypercalcemia	Hyperthyroidism, hyperparathyroidism, metastatic bone cancer, sarcoidosis	Fatigue, depression, muscle weakness, anorexia, nausea, vomiting, constipation
Magnesium (Mg^{2+})	Hypomagnesemia	Inadequate intake/impaired absorption of Mg^{2+}, pancreatitis, alcoholism	Muscle weakness, irritability, tetany, ECG changes, arrhythmias, delirium, seizures
	Hypermagnesemia	Dehydration, renal insufficiency, tissue trauma, lupus erythematosus	ECG changes (along with hyperkalemia, cardiac arrest, respiratory muscle paralysis)
Phosphate (HPO_4^{2-})	Hypophosphatemia	Starvation, malabsorption, hyperparathyroidism, hyperthyroidism, uncontrolled diabetes mellitus	Diaphragmatic weakness
	Hyperphosphatemia	Endocrine disorders, acromegaly, chronic renal insufficiency, acute renal failure, tissue trauma	(Minimal)

ACE, Angiotensin-converting enzyme; *ECG,* electrocardiogram; *GI,* gastrointestinal.

osmotic pressure; the two most common causes for acute hyponatremia are postoperative fluid administration and self-induced fluid intake.[16-20] One type of normal-volume (euvolemic) hyponatremia is known as the *syndrome of inappropriate antidiuretic hormone* (SIADH).[15-17]

Treatment of hypovolemic hyponatremia can have dire consequences as well. If fluid is administered too quickly, severe damage to the central nervous system can occur. With significant fluid shifts in Na^+ concentrations, rapid changes in cellular volume can lead to cell damage and cell death (apoptosis).[6] Another hazard is osmotic demyelination syndrome, which occurs when serum Na^+ concentration changes more than 10 Eq/L in chronic hyponatremia or 18 mEq/L over 48 hours.[16-21]

RULE OF THUMB Replenishment of sodium to patients with severe hyponatremia should be given slowly to raise the Na^+ level by 6 mmol/L over a 24-hour period to prevent osmotic demyelination syndrome.

Chloride (Cl^-)

Cl^- is the most prominent anion in the body. Two-thirds of the body's store of Cl^- is extracellular; the remainder is intracellular. Intracellular Cl^- is present in significant amounts in red and white blood cells. It also is present in cells that have excretory functions, such as the GI mucosa.

Normal serum levels of Cl^- are 98 to 106 mEq/L. The concentration of extracellular Cl^- is inversely proportional to the concentration of the other major anion, HCO_3^-. Cl^- is regulated by the kidney in much the same manner as Na^+ (80% reabsorbed in the proximal tubules and 20% reabsorbed in the distal tubules). Cl^- is usually excreted with K^+ in the form of KCl. An imbalance in one of these electrolytes usually affects both. Replacement therapy usually includes both K^+ and Cl^-. The stomach and the small bowel also affect the balance of Cl^-, and sweat contains hypotonic quantities of Cl^-. Abnormal Cl^- levels may occur for various reasons (see Table 13.6).

Bicarbonate

After Cl^-, HCO_3^- is the most important body fluid anion. It plays an important role in acid-base homeostasis and is the strong base in the HCO_3–H_2CO_3 buffer pair (see Chapter 14). HCO_3^- is the primary means for transporting CO_2 from the tissues to the lungs. The ratio of HCO_3^- to H_2CO_3 in healthy individuals is maintained near 20:1; this results in a pH of close to 7.40. HCO_3^- stores are evenly divided between intracellular and extracellular compartments. Normal serum HCO_3^- levels in arterial blood range from 22 to 26 mEq/L. HCO_3^- levels are slightly higher in venous blood as CO_2 is being transported to the lungs.

In acid-base disorders, the kidneys regulate HCO_3^- levels to maintain a near-normal pH. In healthy individuals, more than 80% of blood HCO_3^- is reabsorbed in the proximal tubules of the kidneys. The remainder is reclaimed in the distal tubules. In respiratory acidosis, the kidneys retain or produce HCO_3^- to buffer the additional acid caused by CO_2 retention. In respiratory alkalosis, the opposite occurs. A reciprocal relationship exists

MINI CLINI

Water, Salt, and Congestive Heart Failure

Problem

Why do patients who have congestive heart failure (CHF) need to adhere to a low-salt diet?

Solution

CHF occurs when the left ventricle cannot pump all of the blood presented to it. This situation leads to an increase in pulmonary intravascular pressures, which causes leaking of fluid (transudate) through the alveolar-capillary membrane into the lungs.

between Cl^- and HCO_3^- concentrations. HCO_3^- retention is associated with Cl^- excretion, and vice versa (see Chapter 14).

The left ventricle can fail as a pump either because of intrinsic heart disease, such as infarction or ischemia, or because of elevated distal pressures against which it must pump (systemic hypertension). In addition to pooling of blood in the systemic venous circulation, blood can back up in the lungs, resulting in congestion and edema.

The most important determinant of the extracellular water volume is its Na^+ content. Changes in extracellular water are dictated by the net gain or loss of Na^+, with an accompanying gain or loss of water. To reduce the work of the heart, fluid volume must be carefully regulated. By restricting Na^+ intake, extracellular fluid volume can be reduced, allowing the heart to function more effectively as a pump. Treatment of CHF must address not only excess fluid volume but also the underlying cause.

Diuretics are often used to help reduce fluid volume. Many diuretics cause the kidney to excrete Na^+, causing water to follow and reducing the extracellular fluid load. Because some diuretics also cause K^+ to be excreted, care must be taken in the management of CHF not to cause electrolyte imbalances. K^+ supplements may be used so that diuresis, especially when combined with other therapies such as adrenergic bronchodilators, does not result in hypokalemia. Because of the central role of extracellular water in CHF, weighing the patient is a simple yet sensitive means of detecting excess fluid volume.[22]

Potassium (K^+)

K^+ is the main cation of the intracellular compartment. Most of the K^+ (98%) in the body is found in cells. **Active transport** of K^+ into the cells occurs through an ionic pump mechanism. An electrical differential across the cell membrane also facilitates K^+ movement into the cell. For every three K^+ ions that enter a cell, two Na^+ ions and one H^+ ion must leave. This transfer maintains electrical neutrality in the cell.

The difference in K^+ distribution is evident when comparing concentrations between fluid compartments. Intracellular K^+ concentration is approximately 150 mEq/L, whereas serum K^+ concentration normally ranges from 3.5 to 5.0 mEq/L. Serum K^+ is an indirect indicator only of the total body K^+. Serum K^+ is usually analyzed by assessing both intake and excretion.

The average adult excretes 40 to 75 mEq of K^+ in the urine every 24 hours. An additional 10 mEq is excreted in the stool. The average dietary intake of K^+ ranges from 50 to 85 mEq/d. Patients who have undergone surgery, have sustained trauma, or have renal disease often have greater K^+ losses. Consequently, such patients may need K^+ replacement averaging 100 to 120 mEq/d.

Serum K^+ concentration is determined primarily by the pH of extracellular fluid and the size of the intracellular K^+ pool. In extracellular acidosis, excess H^+ ions are exchanged for intracellular K^+. Movement of K^+ from intracellular to extracellular spaces may produce dangerous levels of *hyperkalemia* (elevated K^+). Alkalosis has the opposite effect. When pH increases, K^+ moves into cells. In the absence of acid-base disturbances, serum K^+ reflects total-body K^+. With excessive loss of K^+ from the GI tract, serum K^+ decreases. A 10% loss of total-body K^+ causes the serum K^+ level to decrease approximately 1 mEq/L.

Renal excretion of K^+ is controlled by aldosterone levels.[19] Aldosterone inhibits the enzyme responsible for K^+ transport in the distal renal tubular cells of the kidney. Metabolic acidosis also inhibits the transport system. Na^+ and H^+ ions enter cells at the expense of increased K^+ excretion. Alkalosis has the reverse effect. It stimulates cellular retention of K^+. Kidney failure results in K^+ retention and hyperkalemia. Serum K^+ has a strong influence on skeletal and cardiac muscle function so it is important to maintain levels in the normal ranges of 3.5 to 5.0 mEq/L.[23]

Hypokalemia (reduced serum K^+) disturbs cellular function in numerous organ systems, including the GI, neuromuscular, renal, and cardiovascular systems (see Table 13.6), and is one of the most common electrolyte abnormalities within the hospital environment.[19] Management of hypokalemia involves replacement of K^+ losses, careful monitoring of therapies which can reduce serum K^+ such as certain diuretics and adrenergic bronchodilators, and treatment of the underlying disorder. To manage the associated Cl^- deficit, K^+ is given with Cl^-. Caution is required in the administration of intravenous K^+ because cardiac muscle is very sensitive to extracellular concentrations of this electrolyte. Infusions of K^+ should be given with caution to avoid immediate hyperkalemia. In general, K^+ infusion should not exceed 20 mEq/h infused.

Hyperkalemia (elevated serum K^+) is most common in patients with renal insufficiency (see Table 13.6). The primary treatment of hyperkalemia is restriction of K^+ intake. The processes that precipitated the hyperkalemia also must be controlled. Temporary measures for reducing serum K^+ levels include administration of insulin, calcium gluconate, Na^+ salts, or large volumes of hypertonic glucose. Cation exchange resins may be given orally or rectally. If these measures fail, peritoneal or renal dialysis can aid in K^+ removal.

Calcium (Ca^{2+})

Ca^{2+} is an important mediator of neuromuscular function and cell enzyme processes. Most of the Ca^{2+} in the body is contained in the bones. The normal serum calcium is 8.7 to 10.4 mg/dL, or approximately 4.5 to 5.25 mEq/L. This concentration is maintained by the interaction of parathyroid hormone, vitamin D (calcitriol), and calcitonin.

Ca^{2+} is present in the blood in the following three forms: ionized, protein bound, and complex. The proportion of Ca^{2+}

in each form is affected by blood pH, concentration of plasma proteins, and presence of Ca^{2+}-combining anions (e.g., HCO_3^- and hydrogen phosphate [HPO_4^{2-}]). Approximately 50% of serum Ca is ionized (Ca^{2+}) and is physiologically active. An additional 10% forms Ca-anion complexes. The remaining 40% is bound to plasma proteins, primarily albumen. Ionized Ca^{2+} is physiologically active in processes such as enzyme activity, blood clotting, neuromuscular irritability, and bone calcification. Acidemia increases the concentration of Ca^{2+} in the serum, and alkalemia decreases the concentration.

Abnormal levels of Ca^{2+} can cause various serious symptoms (see Table 13.6). Treatment of ***hypocalcemia*** (low serum levels of Ca^{2+}) consists of correcting the underlying cause and replacing Ca^{2+} either orally or intravenously. ***Hypercalcemia*** (increased levels of Ca^{2+}) can result from numerous disorders. The most common causes are hyperparathyroidism and malignancies (e.g., multiple myeloma, lung cancer [especially squamous cell type, see Chapter 32]). Acute hypercalcemia requires emergency treatment because death may occur quickly if serum Ca^{2+} increases to more than 17 mg/L (8.5 mEq/L). In such cases, there is usually an associated deficit of extracellular fluid. Volume replacement reduces serum Ca^{2+} by dilution.

Magnesium (Mg^{2+})

Mg^{2+} is the second most abundant intracellular cation after K^+. Mg^{2+} plays an important role in cellular functions, including energy transfer; metabolism of protein, carbohydrate, and fat; and maintenance of normal cell membrane function (see Table 13.6). Systemically, Mg^{2+} decreases blood pressure and alters peripheral vascular resistance. Abnormalities of Mg^{2+} levels can result in disturbances in nearly every organ system and can cause potentially fatal complications (e.g., ventricular arrhythmia, coronary artery vasospasm, sudden death). Hypomagnesemia is also associated with multiple neuromuscular symptoms, such as muscular weakness, tetany, coma, and seizures. There is some evidence that intercellular Mg^{2+} levels may be related to bronchial hyperresponsiveness.

Normal values for serum Mg^{2+} range from 1.7 to 2.1 mg/dL (1.7 to 1.4 mEq/L) in healthy adults. Most (99%) of the Mg^{2+} in the body is intracellular. Of the small portion in extracellular spaces, 80% is ionized or bound to other ions (e.g., phosphate) and the remaining 20% bound to proteins. Extracellular Mg^{2+} is in equilibrium with Mg^{2+} in the bone, kidneys, intestine, and other soft tissues. In contrast to most electrolytes, Mg^{2+} excretion in urine is not regulated hormonally, and circulating Mg^{2+} in the extracellular fluid does not exchange readily with its main repository—the bones. Serum levels of Mg^{2+} may remain normal even if total body stores are depleted by 20%. Conversely, when there is a negative Mg^{2+} balance, most of the losses come from the extracellular spaces.

Phosphorus

An average adult has approximately 1 kg (1000 g) of phosphorus (P), of which 80% to 90% is in bone and teeth in the form of apatite. The remaining P is mostly present in the viscera and skeletal muscle, with a very small amount (<0.1%) in the extracellular fluids.[20] Of this total, 10% to 17% is combined with proteins, carbohydrates, and lipids in muscle tissue and blood, and the remainder is incorporated into complex organic compounds. Only approximately 1% of the total body P is available as free serum compounds, so the serum level (1.2 to 2.3 mEq/L) does not reflect total body content. Serum P levels are influenced by several factors (see Table 13.6), including the serum Ca^{2+} concentration and the pH of blood.

Organic phosphate (HPO_4^{2-}) is the main anion within cells, with 20% present in the mitochondria. Approximately 30% of cellular HPO_4^{2-} is stored in the endoplasmic reticulum and is used in the phosphorylation of various proteins.[20] Inorganic phosphate plays a primary role in the metabolism of cellular energy, being the source from which adenosine triphosphate is synthesized. In acid-base homeostasis, phosphate is the main urinary buffer for titratable acid excretion (see Chapter 14).

Phosphorus homeostasis depends on balance between GI absorption and urinary excretion. The parathyroid hormone provides hormonal regulation. ***Hyperphosphatemia*** (elevated serum levels of P) can occur when the load (e.g., GI absorption, cellular release) exceeds renal excretion and tissue uptake. Hyperphosphatemia precipitates Ca^{2+}, causing hypocalcemia, which can be life threatening if severe. Central nervous system symptoms such as altered mental status, paresthesias (abnormal sensation), and seizures can result from hyperphosphatemia. Prolonged hyperphosphatemia can result in abnormal deposition of calcium phosphate in previously healthy connective tissues, such as cardiac valves, and in solid organs, such as muscles.

SUMMARY CHECKLIST

- The body is a water-based organism in which chemical substances and particles exist in solution, colloids, or suspension.
- There are five factors which affect the ability of a substance to enter into a solution. They are: nature of the solute, nature of the solvent, temperature, pressure, and concentration.
- Solutions commonly involve the action of osmotic pressure. Body cell membranes are semipermeable, and osmotic pressure maintains the distribution of water and solutes in physiologic ranges.
- The concentration of solutes in a solution may be quantified in two ways: (1) by actual weight (grams, milligrams, or micrograms) or (2) by chemical-combining power (equivalents or milliequivalents). The weight of a solute does not give an indication of its chemical-combining power, but gram equivalent weights do.
- Acids are proton donors and bases are proton acceptors. Salts are the end result of acids and bases reacting with one another.
- Proteins made up of amino acids can function as bases in the mildly alkaline environment of the body; this allows Hb and plasma proteins to function as buffers.
- Acidity or alkalinity is determined by variation of [H^+] greater than or less than 1×10^{-7} mol/L. Two methods for recording acidity or alkalinity use H^+ concentration of water as the neutral standard: (1) the actual measured molar concentration of H^+ in nanomoles per liter and (2) the logarithmic pH scale.
- Water makes up 45% to 80% of an individual's body weight. Percentage of total body water depends on weight, gender,

age, and adipose tissue. Total body water is divided into intracellular and extracellular water. Extracellular water is divided further into intravascular and interstitial water, with a small component of transcellular fluids.

- Control of total body water is regulated by water intake and excretion. The kidneys maintain the volume and composition of body fluids by two related mechanisms: (1) filtration and reabsorption of Na^+ and (2) regulation of water excretion in response to changes in secretion of ADH.
- A balance between hydrostatic and osmotic pressure keeps water in the appropriate body compartments. Plasma proteins account for the high colloid osmotic pressure of plasma. Colloid osmotic pressure determines distribution of fluid between vascular and interstitial compartments. Imbalances in osmotic and hydrostatic pressures can result in edema.
- Electrolytes help to maintain the internal environment and make important chemical and physiologic events possible. The concentrations of electrolytes in the intracellular and extracellular fluid compartments differ markedly. Increased or decreased concentrations of any electrolytes can result in disease and sometimes death.

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14

Acid–Base Balance

Will Beachey

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Describe how the lungs and kidneys regulate volatile and fixed acids.
- Describe how the equilibrium constant of an acid is related to its ionization and strength.
- Define open and closed buffer systems.
- Explain why open and closed buffer systems differ in their ability to buffer fixed and volatile acids.
- Explain how to use the Henderson-Hasselbalch equation in hypothetical clinical situations.
- Describe how the kidneys and lungs compensate for each other when the function of one is abnormal.
- Explain how renal absorption and excretion of electrolytes affect acid-base balance.
- Classify and interpret arterial blood acid-base results.
- Explain how to use arterial acid-base information to decide on a clinical course of action.
- Explain why acute changes in the carbon dioxide levels of the blood affect plasma bicarbonate ion concentration.
- Calculate the anion gap and use it to determine the cause of metabolic acidosis.
- Describe how standard bicarbonate and base excess measurements are used to identify the nonrespiratory component of acid-base imbalances.

CHAPTER OUTLINE

KEY TERMS

acid
acidemia
alkalemia
base
base excess (BE)
buffer base
closed buffer system
conjugate base
equilibrium constant
fixed (nonvolatile) acids
Henderson-Hasselbalch (H-H) equation
hypercapnia
hypocapnia
isohydric buffering
metabolic acidosis
metabolic alkalosis
open buffer system
paresthesia
respiratory acidosis
respiratory alkalosis
reabsorption
standard bicarbonate
volatile acid

Normal metabolism continually generates H^+, which means H^+ regulation is extremely important. Even small changes in hydrogen ion concentration $[H^+]$ can produce acid-base abnormalities and cause vital metabolic processes in the body to fail. Several physiologic mechanisms work together to keep $[H^+]$ of body fluids in a range that supports life. This chapter will help respiratory therapists (RTs) understand how these mechanisms work and how to spot abnormalities in their function. This knowledge will help RTs and other members of the patient care team make informed recommendations and decisions about treating the underlying causes of acid-base disturbances.

HYDROGEN ION REGULATION IN BODY FLUIDS

Acid-base balance refers to physiologic mechanisms that keep $[H^+]$ of body fluids in a range that supports life. Hydrogen ions $[H^+]$ react readily with the protein molecules of important cellular catalytic enzymes. These reactions change the physical shape of the protein molecule, which may inactivate enzymes. Body fluids must be kept in a narrow pH range of 7.35 to 7.45 to function normally. This corresponds to $[H^+]$ of 45 to 35 nmol/L.

H^+ formed in the body comes from either *volatile* or *fixed* (nonvolatile) acids. **Volatile acids** are in equilibrium with a dissolved gas. The only volatile **acid** of physiologic importance in the body is carbonic acid (H_2CO_3), which is in equilibrium with dissolved carbon dioxide. Normal aerobic metabolism generates approximately 13,000 mmol/L of CO_2 each day, which produces an equal amount of H^+ as shown by the CO_2 hydration reaction:

$$\begin{array}{l} CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow HCO_3^- + H^+ \\ \quad\uparrow \\ \text{Aerobic metabolism} \end{array}$$

As CO_2 diffuses into the blood at the tissue level, this reaction occurs mostly in the erythrocyte, where it is catalyzed by carbonic anhydrase, an intracellular enzyme. In a process called **isohydric buffering**,[1] most H^+ produced in this way causes no change in pH because hemoglobin (Hb) in the erythrocyte immediately buffers the H^+. When blood reaches the lungs, Hb releases H^+ to form CO_2 as shown:

$$\begin{array}{l} \text{Ventilation} \\ \quad\uparrow \\ CO_2 + H_2O \leftarrow H_2CO_3 \leftarrow HCO_3^- + H^+ \\ \qquad\qquad\qquad\qquad\uparrow \\ \qquad\qquad\qquad\qquad HHb \rightarrow H^+ + Hb^- \end{array}$$

In this way, ventilation gets rid of H_2CO_3 just as fast as it is produced. Isohydric buffering and ventilation are the two major ways the body keeps the blood's pH constant regardless of how much CO_2 is produced.

Catabolism—the breakdown of proteins—continually produces **fixed (nonvolatile) acids**, such as sulfuric and phosphoric acids. In addition, anaerobic metabolism produces lactic acid, another fixed acid. In contrast to H_2CO_3, these nonvolatile acids are not in equilibrium with a gas. However, the H^+ of fixed acids can be buffered by bicarbonate ions (HCO_3^-), which produce CO_2 and water (H_2O; see the previous CO_2 hydration reaction); the CO_2 formed is removed from the body in exhaled gas. Compared with daily CO_2 production, fixed acid production is small, averaging only approximately 50 to 70 mEq/day.[2] Certain diseases, such as untreated diabetes, increase fixed acid production. H^+ produced in this way stimulates respiratory centers in the brain, increasing ventilation; this eliminates more CO_2, which pulls the CO_2 hydration reaction to the left and removes H^+ from the blood (refer to the CO_2 hydration reaction). In this way, the respiratory system *compensates* for increases in fixed acid—that is, it prevents $[H^+]$ from rising as sharply as it otherwise would when fixed acids are produced.

$$\begin{array}{l} \text{Increased ventilation} \\ \quad\uparrow \\ CO_2 + H_2O \leftarrow H_2CO_3 \leftarrow HCO_3^- + H^+ \\ \qquad\qquad\qquad\qquad\uparrow \\ \qquad\qquad\qquad\qquad \text{Fixed acid } H^+ \end{array}$$

Strong and Weak Acids and Bases: Equilibrium Constants

Strong acid and **base** molecules dissociate or ionize almost completely in an aqueous (liquid) solution. Weak acids and bases ionize only to a small extent. An example of a strong acid is hydrochloric acid (HCl). Nearly 100% of the HCl molecules dissociate to form H^+ and Cl^-:

$$HCl \rightarrow H^+ + Cl^- \qquad (1)$$

At *equilibrium*, when all dissociation stops, the concentration of HCl is extremely small compared with either $[H^+]$ or $[Cl^-]$. There is no arrow pointing to the left in Reaction 1, emphasizing that HCl ionizes almost completely in solution. In contrast, H_2CO_3 is an example of a relatively weak acid:

$$H_2CO_3 \rightleftharpoons HCO_3^- + H^+ \qquad (2)$$

The long arrow pointing to the left indicates that at *equilibrium*, the concentration of undissociated H_2CO_3 molecules is far greater than the concentration of either HCO_3^- or H^+.

The **equilibrium constant** of an acid is a measure of the extent to which the acid molecules dissociate (ionize). At equilibrium, the number of dissociating H_2CO_3 molecules in Reaction 2 is equal to the number of associating HCO_3^- and H^+, even though the concentrations of reactants and products are unequal. In this state, no further change occurs in $[H_2CO_3]$, $[HCO_3^-]$, or $[H^+]$. The following reaction expresses the state of affairs at equilibrium:

$$\frac{[H^+] \times [HCO_3^-]}{[H_2CO_3]} = K_A \text{ (Small)} \qquad (3)$$

where K_A is the equilibrium constant for H_2CO_3. (K_A is also known as the acid's *ionization* or *dissociation* constant.)

K_A is a small number because $[H_2CO_3]$ is quite large with respect to the numerator of Reaction 3 ($[H^+] \times [HCO_3^-]$). The value of K_A is always the same for H_2CO_3 at equilibrium, regardless of the initial concentration of H_2CO_3.

A strong acid, such as HCl, has a *large* K_A because the denominator [HCl] is extremely small compared with the numerator ($[H^+] \times [Cl^-]$):

$$\frac{[H^+] \times [Cl^-]}{[HCl]} = K_A \text{ (Large)} \quad \textbf{(4)}$$

As shown by Eqs. (3) and (4), K_A is a measure of the strength of an acid—that is, how much the acid molecule dissociates.

Buffer Solution Characteristics

A buffer solution resists changes in pH when an acid or a base is added to it. Buffer solutions are aqueous mixtures of acids and bases. The acid component is the H^+ cation (positively charged ion), which is formed when a weak acid dissociates in solution. The base component is the remaining anion (negatively charged ion) portion of the acid molecule, known as the **conjugate base**. An important blood buffer system is a solution of carbonic acid and its conjugate base, HCO_3^-:

$$H_2CO_3 \text{(Acid)} \rightleftharpoons HCO_3^- \text{ (Conjugate base)} + H^+$$

In the blood, HCO_3^- combines with sodium ions to form sodium bicarbonate ($NaHCO_3$). If hydrogen chloride, a strong acid, is added to the $H_2CO_3/NaHCO_3$ buffer solution, HCO_3^- reacts with the added H^+ to form weaker H_2CO_3 molecules and a neutral salt:

$$HCl + H_2CO_3/Na^+HCO_3^- \rightarrow 2H_2CO_3 + NaCl$$

The strong acidity of HCl is converted to the relatively weak acidity of H_2CO_3, preventing a large decrease in pH.

Similarly, if sodium hydroxide, a strong base, is added to this buffer solution, it reacts with the H_2CO_3 molecule to form the weak base, $NaHCO_3$, and H_2O:

$$NaOH + H_2CO_3/NaHCO_3 \rightarrow 2NaHCO_3 + H_2O$$

The strong alkalinity of NaOH is changed to the relatively weak alkalinity of $NaHCO_3$. Again, pH change is minimized.

Bicarbonate and Nonbicarbonate Buffer Systems

Blood buffers are classified as bicarbonate or nonbicarbonate buffer systems. The bicarbonate buffer system consists of H_2CO_3 and its conjugate base, HCO_3^-. The nonbicarbonate buffer system consists mainly of phosphate and protein molecules, including the hemoglobin molecule. The blood buffer base is the sum of bicarbonate and nonbicarbonate bases measured in millimoles per liter of blood.

The bicarbonate system is called an **open buffer system** because H_2CO_3 is in equilibrium with dissolved CO_2, which is readily removed by ventilation. That is, when H^+ is buffered by HCO_3^-, the product, H_2CO_3, is broken down into H_2O and CO_2 as long as ventilation removes CO_2. The removal of CO_2 from the reaction prevents the reaction from reaching equilibrium among its reactants. For this reason, buffering activity can continue without being slowed or stopped, as long as ventilation continues:

$$HCO_3^- + H^+ \rightarrow H_2CO_3 \rightarrow H_2O + CO_2 \text{ (Exhaled gas)}$$

BOX 14.1 Classification of Whole Blood Buffers

Open System
Bicarbonate
- Plasma
- Erythrocyte

Closed System
Nonbicarbonate
- Hemoglobin
- Organic phosphates
- Inorganic phosphates
- Plasma proteins

From Beachey W: *Respiratory care anatomy and physiology: foundations for clinical practice*, ed 2, St Louis, 2007, Mosby.

A nonbicarbonate buffer system is called a **closed buffer system** because all the components of acid-base reactions remain in the system. (In the following discussions, all nonbicarbonate buffer systems are grouped together and represented as *Hbuf/Buf*$^-$, where Hbuf is the weak acid, and Buf^- is the conjugate base.) When H^+ is buffered by Buf^-, the product, HBuf, builds up and eventually reaches equilibrium with the reactants, preventing further buffering activity:

$$Buf^- + H^+ \leftrightarrow Hbuf$$

Box 14.1 summarizes the characteristics and components of bicarbonate and nonbicarbonate buffer systems.

Open and closed buffer systems play different roles in buffering fixed and volatile acids, and they differ in their ability to function in wide-ranging pH environments. Volatile acid (H_2CO_3) accumulates in the body only if ventilation cannot eliminate CO_2 fast enough to keep up with the body's CO_2 production. In such a case, CO_2 builds up, continually pushing the hydration reaction (the reaction between CO_2 and H_2O) in the direction that creates more H_2CO_3 and, ultimately, more H^+ and HCO_3^-. In other words, CO_2 buildup renders the bicarbonate buffer system ineffective because it prevents the hydration reaction from moving in the direction necessary for HCO_3^- to react with and buffer H^+. Thus the only system that can buffer the H^+ of volatile acid is the nonbicarbonate buffer system. However, both nonbicarbonate and bicarbonate buffer systems can buffer the H^+ produced by fixed acids; this is true of the bicarbonate buffer system only if ventilation is normal and CO_2 can be adequately eliminated. Both systems are physiologically important, each playing a unique and essential role in maintaining pH homeostasis. Table 14.1 summarizes the approximate contributions of various blood buffers to the total buffer base. Bicarbonate buffers have the greatest buffering capacity because they function in an open system.

Of course, bicarbonate and nonbicarbonate buffer systems do not function in isolation from one another because they are intermingled in the same solution (whole blood) and are in equilibrium with the same $[H^+]$ (Fig. 14.1). Increased ventilation increases the CO_2 removal rate, causing blood $[H^+]$ to fall, which causes nonbicarbonate buffers (Hbuf) to release more H^+. By

the same token, decreased ventilation ultimately causes Hbuf to accept more H^+.

pH of a Buffer System: Henderson-Hasselbalch Equation

Buffer solutions in body fluids consist of mostly undissociated acid molecules and only a small amount of H^+ and conjugate base anions. The $[H^+]$ of a buffer solution can be calculated if the concentrations of the buffer's components and each acid's equilibrium constant are known. Consider the bicarbonate buffer system. As described earlier, the equilibrium constant (K_A) for H_2CO_3 is as follows:

$$K_A = \frac{[H^+] \times [HCO_3^-]}{[H_2CO_3]}$$

$[H^+]$ can be calculated by algebraic rearrangement of this equation, as follows:

TABLE 14.1 Individual Buffer Contributions to Whole Blood Buffering

Buffer Type	Total Buffering (%)
Bicarbonate	
Plasma bicarbonate	35
Erythrocyte bicarbonate	18
Total bicarbonate buffering	53
Nonbicarbonate	
Hemoglobin	35
Organic phosphates	3
Inorganic phosphates	2
Plasma proteins	7
Total nonbicarbonate buffering	47
Total	*100*

From Beachey W: *Respiratory care anatomy and physiology: foundations for clinical practice*, ed 2, St Louis, 2007, Mosby.

$$[H^+] = K_A \times \frac{[H_2CO_3]}{[HCO_3]}$$

This equation shows that $[H^+]$ is determined by the ratio between undissociated acid molecules $[H_2CO_3]$ and base anions $[HCO_3^-]$. This equation is the basis for deriving the **Henderson-Hasselbalch (H-H) equation**:

$$pH = 6.1 + \log \frac{[HCO_3^-]}{PaCO_2 \times 0.03}$$

pH is a logarithmic (nonlinear) expression of $[H^+]$, and the term 6.1 is the logarithmic expression of the H_2CO_3 equilibrium constant. Because dissolved CO_2 ($PCO_2 \times 0.03$) is in equilibrium with and directly proportional to blood $[H_2CO_3]$, and because blood PCO_2 is more easily measured than $[H_2CO_3]$, dissolved CO_2 is used in the denominator of the H-H equation. The H-H equation is specific for calculating the pH of the bicarbonate buffer system of the blood. The calculation of this pH is important because it equals the pH of blood plasma—that is, all buffer systems exist in the same plasma solution and are therefore in equilibrium with its pH (the isohydric principle).[1]

Clinical Use of Henderson-Hasselbalch Equation

The H-H equation allows the pH, $[HCO_3^-]$, or PCO_2 to be computed if two of these three variables are known (shown as follows for PCO_2 and HCO_3^-):

$$[HCO_3^-] = \text{antilog}\,(pH - 6.1) \times (PCO_2 \times 0.03)$$

$$PCO_2 = \frac{[HCO_3^-]}{(\text{antilog}\,[pH - 6.1] \times 0.03)}$$

Blood gas analyzers *measure* pH and PCO_2 but *compute* $[HCO_3^-]$. Assuming a normal arterial pH of 7.40 and a $PaCO_2$ of 40 mm Hg, arterial $[HCO_3^-]$ can be calculated as follows:

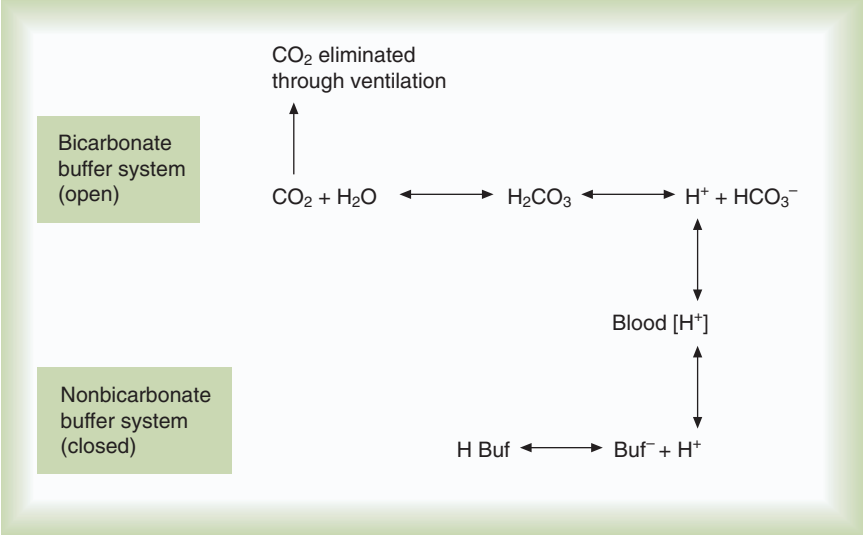

Fig. 14.1 The bicarbonate and nonbicarbonate buffer systems exist in equilibrium in the plasma. (Modified from Beachey W: *Respiratory care anatomy and physiology: foundations for clinical practice*, ed 2, St Louis, 2007, Mosby.)

$$pH = 6.1 + \log\left(\frac{[HCO_3^-]}{PCO_2 \times 0.03}\right)$$

$$7.40 = 6.1 + \log\left(\frac{[HCO_3^-]}{40 \times 0.03}\right)$$

$$7.40 = 6.1 + \log\left(\frac{[HCO_3^-]}{1.2}\right)$$

Solving for $[HCO_3^-]$:

$$\begin{aligned}[HCO_3^-] &= \text{antilog}\,(7.40 - 6.1) \times 1.2\\ &= \text{antilog}\,(1.3) \times 1.2\\ &= 20 \times 1.2\\ &= 24\ \text{mEq/L}\end{aligned}$$

The H-H equation is useful for checking a clinical blood gas report to see if the pH, PCO_2, and $[HCO_3^-]$ values are compatible with one another. In this way, transcription errors and analyzer inaccuracies can be detected. It is also clinically useful to predict what effect changing one H-H equation component will have on the other components. For example, a clinician may want to know how low the arterial blood pH will fall for a given increase in $PaCO_2$.

Physiologic Roles of Bicarbonate and Nonbicarbonate Buffer Systems

The functions of bicarbonate and nonbicarbonate buffer systems are summarized in Table 14.2.

Bicarbonate Buffer System

The bicarbonate buffer system is particularly effective in the body because it is an open system—that is, one of its components (CO_2) is continually removed through ventilation:

$$\text{(Exhaled gas)} \leftarrow CO_2 + H_2O \leftarrow H_2CO_3 \leftarrow HCO_3^- + H^+$$

In this way, HCO_3^- continues to buffer H^+ as long as ventilation continues. Hypothetically, this buffering activity can continue until all body sources of HCO_3^- are used up in binding H^+.

The bicarbonate buffer system can buffer only fixed acid. An increased fixed acid load in the body (e.g., lactic acid) reacts with HCO_3^- of the bicarbonate buffer system:

$$\begin{array}{ccccccc} & & & & & & \text{Ventilation} \\ & & & & & & \uparrow \\ H^+ & + & HCO_3^- & \rightarrow & H_2CO_3 & \rightarrow & H_2O + CO_2 \\ \uparrow & & & & & & \\ \text{Fixed acid} & & & & & & \end{array}$$

As shown, the process of buffering fixed acid produces CO_2, which is eliminated in exhaled gas. Large amounts of acid are normally buffered in this fashion. If ventilation cannot keep up with the body's CO_2 production, this type of buffering cannot occur.

The bicarbonate buffer system cannot buffer carbonic (volatile) acid, which accumulates in the blood whenever ventilation fails to eliminate CO_2 as fast as it is produced (hypoventilation).

TABLE 14.2 Buffering Functions

Buffer	Type of System	Acids Buffered
Bicarbonate	Open	Fixed (nonvolatile)
Nonbicarbonate	Closed	Volatile (carbonic)
		Fixed

From Beachey W: *Respiratory care anatomy and physiology: foundations for clinical practice*, ed 2, St Louis, 2007, Mosby.

MINI CLINI

Applying the Henderson-Hasselbalch Equation in a Clinical Setting

Problem

The RT is caring for a mechanically ventilated patient. The tidal volume (V_T) is set at 400 mL and a breathing frequency of 10/min, yielding a minute ventilation ($\dot{V}_E$) of 4 L/min. The patient's $PaCO_2$ is 55 mm Hg, pH is 7.30, and bicarbonate is 26 mEq/L, and the RT wishes to maintain a pH of 7.35. How much does the RT need to change the $PaCO_2$ to achieve this desired pH, and what change in the patient's V_T does this require?

Solution

First, the therapist needs to calculate the $PaCO_2$ required to achieve a pH of 7.35 using the known values:

$$PaCO_2 = \frac{26\ \text{mEq/L}}{0.03 \times \text{antilog}\,(7.35 - 6.1)}$$

$$PaCO_2 = \frac{26}{0.53}$$

$$PaCO_2 = 49\ \text{mm Hg}$$

Next, the RT must calculate the $\dot{V}_E$ required to produce a $PaCO_2$ of 49 mm Hg. Because $\dot{V}_E$ is inversely proportional to $PaCO_2$ (assuming that tidal volume remains constant), the following can be stated:

$$(\dot{V}_E)_1 \times (PaCO_2)_1 = (\dot{V}_E)_2 \times (PaCO_2)_2,$$

where subscripts 1 and 2 represent current and future values. The RT then solves for $(\dot{V}_E)_2$ as follows:

$$(4\ \text{L/min}) \times 55\ \text{mm Hg} = (\dot{V}_E)_2 \times 49\ \text{mm Hg}$$

$$\frac{(4 \times 55)}{49} = (\dot{V}_E)_2$$

$$4.49\ \text{L/min} = (\dot{V}_E)_2$$

Increasing the patient's $\dot{V}_E$ from 4 L/min to approximately 4.5 L/min yields a $PaCO_2$ of 49 mm Hg and a pH of approximately 7.35. Now the RT divides the new $\dot{V}_E$ of 4.5 L/min by the respiratory frequency to calculate the new V_T required:

$$4.5\ \text{L/min}/10 = 450\ \text{mL}$$

A V_T of 450 mL at a rate of 10 breaths/min should produce an arterial pH of 7.35, according to the H-H equation.

The resulting accumulation of CO_2 drives the hydration reaction in the direction that produces more carbonic acid, H^+, and HCO_3^-, as shown:

$$\begin{array}{ccccccc} \text{Hypoventilation} & & & & & & \\ \downarrow & & & & & & \\ CO_2 & + & H_2O & \rightarrow & H_2CO_3 & \rightarrow & HCO_3^- + H^+ \end{array}$$

The H^+ produced by dissociating H_2CO_3 molecules cannot be buffered by the simultaneously produced HCO_3^- because hypoventilation prevents the reaction from reversing its direction. Thus, the closed nonbicarbonate buffer systems are the only buffers that can buffer H_2CO_3.

Nonbicarbonate Buffer System

Table 14.1 lists the nonbicarbonate buffers in the blood. Of these, Hb is the most important because it is the most abundant. As mentioned, these buffers are the only ones available to buffer H_2CO_3. However, they can buffer H^+ produced by any acid, fixed or volatile. Because nonbicarbonate buffers (Buf^-/HBuf) function in closed systems, the products of their buffering activity eventually accumulate and approach equilibrium, slowing or stopping further buffering activity:

$$H^+ + Buf^- \leftrightarrow HBuf$$

This slowing or stopping of buffering activity means that not all of the Buf^- reserves are available for buffering activity. At equilibrium (denoted by the *double arrow*), Buf^- still exists in solution but cannot combine further with H^+. In contrast, most of the HCO_3^- in the bicarbonate buffer system is available for buffering activity because it functions in an open system in which equilibrium between reactants and products does not occur as long as ventilation continues. Both open and closed systems function in a common fluid compartment (blood plasma), as illustrated in the following equation:

(CO_2 removed by ventilation) (HCO_3^- from body's stores)

↑ ↓

Open system: $CO_2 + H_2O \leftarrow H^+ + HCO_3^-$

↑

Added fixed acid

↓

Closed system: $HBuf \leftrightarrow H^+ + Buf^-$

↑

(Buf^- from body's stores)

Most of the added fixed acid is buffered by HCO_3^- because ventilation continually pulls the reaction to the left. Smaller amounts of H^+ react with Buf^- because equilibrium is approached, slowing the reaction.

ACID EXCRETION

Bicarbonate and nonbicarbonate buffer systems are the immediate defense against the accumulation of H^+. However, if the body fails to eliminate the remaining acids, these buffers are soon exhausted and the pH of body fluids quickly decreases to life-threatening levels.

The lungs and kidneys are the primary acid-excreting organs. The lungs can excrete only volatile acid (i.e., the CO_2 from dissociating H_2CO_3). However, as discussed previously, bicarbonate buffers effectively buffer the H^+ originating from fixed acid, converting it to H_2CO_3 and to CO_2 and H_2O. By eliminating the CO_2, the lungs can rapidly remove large quantities of fixed acid from the blood. The kidneys also remove fixed acids but at a slower pace. In healthy individuals, the acid excretion mechanisms of lungs and kidneys are delicately balanced. In individuals affected by disease, failure of one system can be partially offset by a compensatory response of the other.

Lungs

Because the volatile acid H_2CO_3 is in equilibrium with dissolved CO_2, the lungs can decrease blood H_2CO_3 concentration through ventilation. The elimination of CO_2 is crucial because normal aerobic metabolism produces large quantities of CO_2, which reacts with H_2O to form large quantities of H_2CO_3. The reaction between fixed acids and bicarbonate buffers also produces H_2CO_3. H_2CO_3 generated by both pathways is eliminated as CO_2 through the lungs. Approximately 24,000 mmol/L of CO_2 is removed from the body daily through normal ventilation. CO_2 excretion via the lungs does not remove H^+ from the body. Instead, the chemical reaction that breaks down H_2CO_3 to form CO_2 binds H^+ in the harmless H_2O molecule:

$$H^+ + HCO_3^- \rightarrow H_2CO_3 \rightarrow H_2O + CO_2$$

In this way, increased ventilation lessens the effects of fixed acid accumulation in the body, which is illustrated later in this chapter in the Mini Clini on *Partially Compensated Metabolic Acidosis*.

Kidneys

The kidneys physically remove H^+ from the body. The following terms and their definitions refer to certain kidney functions (Fig. 14.2):

- *Excretion* is the elimination of substances from the body in the urine.
- *Secretion* is the process by which renal tubule cells actively transport substances into the fluid inside the tubule lumen (i.e., the *filtrate*).
- *Reabsorption* is the active or passive transport of filtrate substances that moves them from the tubule lumen back into the tubule cell and into the blood of nearby capillaries.

The amount of H^+ the kidney tubules secrete into the filtrate depends on the blood's pH. Secreted H^+ may originate from H_2CO_3 (when the blood PCO_2 is increased) or from fixed acids. The kidneys excrete less than 100 mEq of fixed acid per day, which is a small amount compared with volatile H_2CO_3 elimination by the lungs.[3] In addition to excreting H^+, the kidneys influence blood pH by reabsorbing or excreting HCO_3^-. If the blood PCO_2 is high, creating high levels of H_2CO_3, the kidneys excrete greater amounts of H^+ and reabsorb all of the tubule filtrate's HCO_3^- back into the blood. The opposite happens when the blood PCO_2 is low. The kidneys excrete less H^+ and more HCO_3^-. Compared with the ability of the lungs to change blood PCO_2 in seconds, the renal process is slow, requiring hours to days to compensate.

Basic Kidney Function

To understand how the kidneys determine whether to excrete acidic or basic urine, some fundamental facts about renal

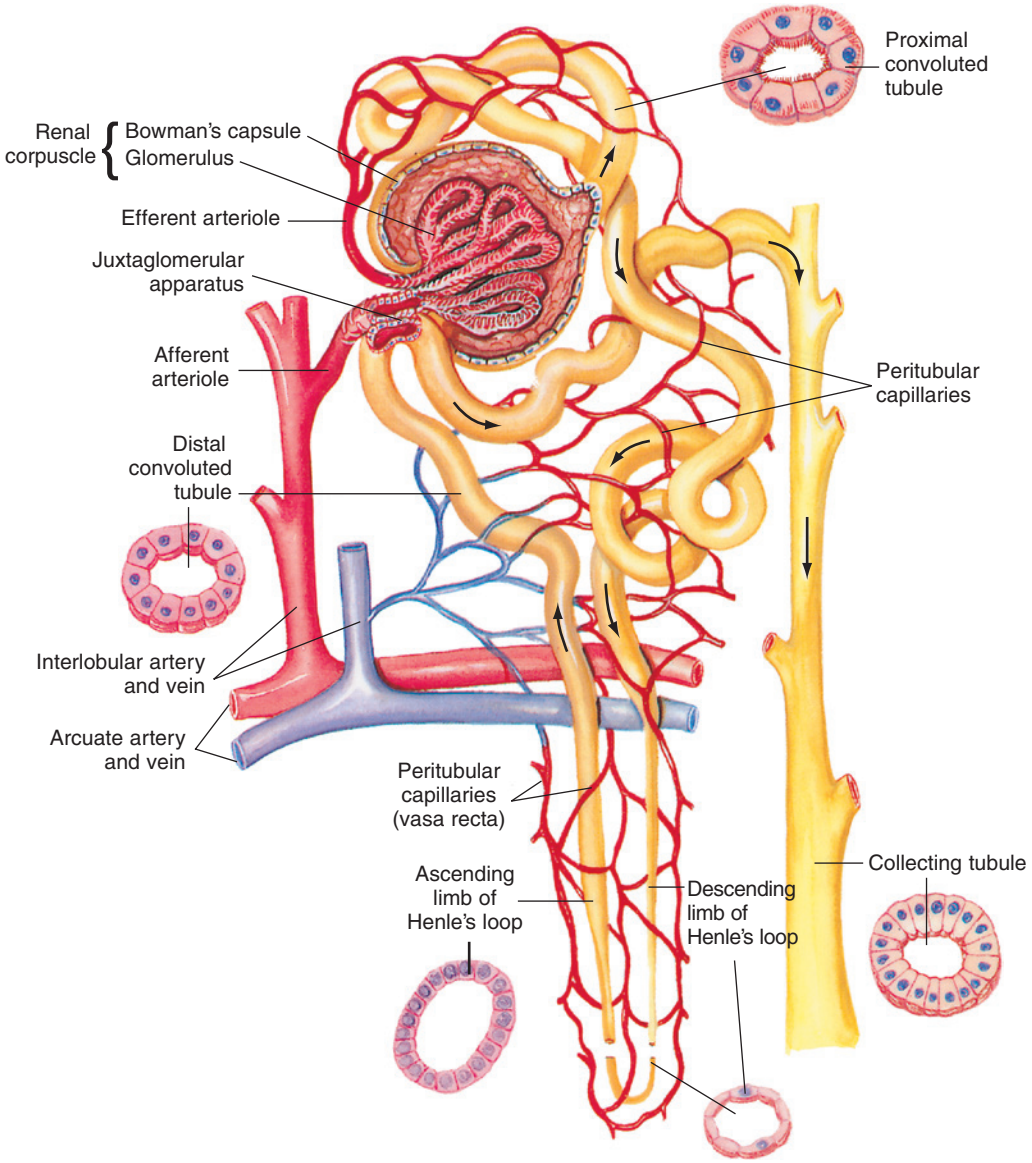

Fig. 14.2 The Nephron—the Functional Unit of the Kidney. The glomerulus filters the blood, forming filtrate in that Bowman capsule, which flows through the nephron's tubules (indicated by *arrows*). Filtrate leaving the collecting tubule is *excreted* as urine. Tubule cells may *secrete* substances into the filtrate, or they may *reabsorb* substances from the filtrate, returning them to the blood. (From Thibodeau GA, Patton KT: *Anatomy & physiology*, ed 3, St Louis, 1996, Mosby.)

function must be understood. The *glomerulus* is the component of the renal nephron responsible for filtering the blood (see Fig. 14.2). Hydrostatic blood pressure forces water, electrolytes, and other non-protein substances through semipermeable glomerular capillary endothelium. The resulting filtrate is greatly modified in volume and composition as it flows through the nephron tubules. Excreted filtrate is called *urine*.

HCO_3^- is one of the electrolytes filtered from the blood at the glomerulus to become part of the tubular filtrate. In this way, base (HCO_3^-) is removed from the blood. This loss of base is offset by the nephron's simultaneous secretion of H^+ into the filtrate of the tubular lumen. Under normal conditions, the rate of H^+ secretion is almost the same as the rate of HCO_3^- filtration.[4] In this way, the kidneys titrate H^+ and HCO_3^- against each other to form CO_2 and H_2O.

H^+ secretion begins with the diffusion of blood CO_2 into the tubule cell (Fig. 14.3). Aided by the enzyme carbonic anhydrase, CO_2 reacts with H_2O to form H_2CO_3, which instantly forms HCO_3^- and H^+. The tubule cell actively secretes H^+ into the filtrate by means of *counter-transport*, in which Na^+ and H^+ are simultaneously transported in opposite directions. That is, Na^+ and H^+ combine with opposite ends of a carrier protein in the luminal border of the tubule cell membrane. Sodium ions move from the filtrate into the cell down its high concentration gradient, providing the energy to secrete H^+ back into the tubular filtrate (see Fig. 14.3).[4]

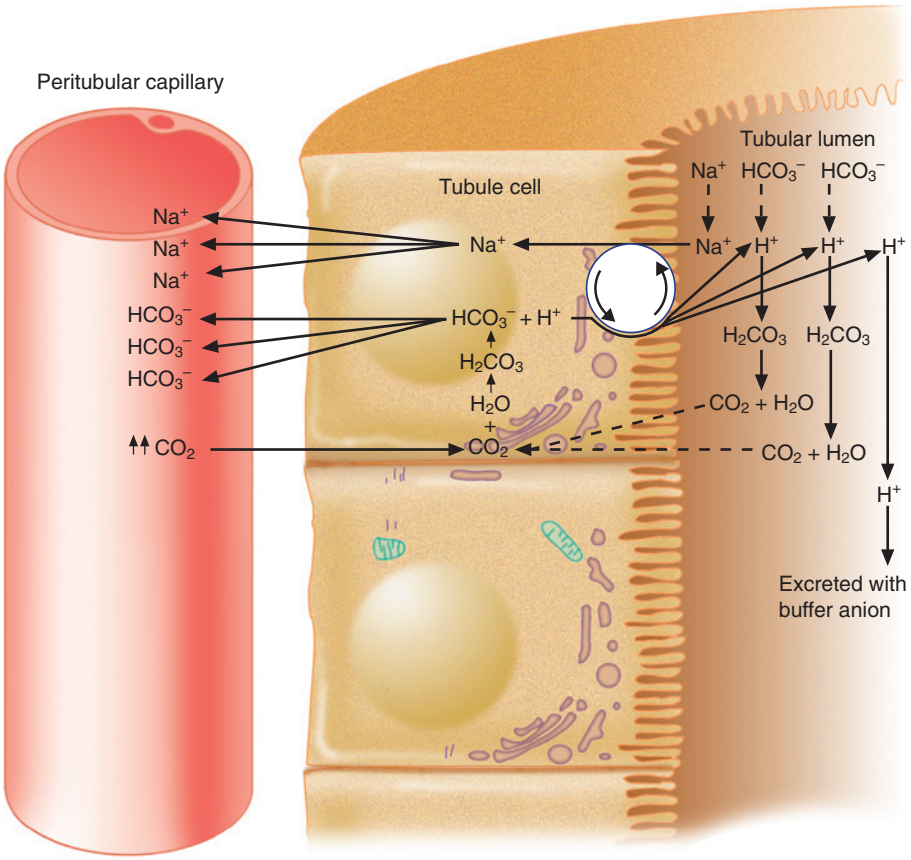

Fig. 14.3 Renal Response to Respiratory Acidosis. Filtrate HCO_3^- is reabsorbed by first reacting with secreted H^+. (Modified from Beachey W: *Respiratory care anatomy and physiology: foundations for clinical practice*, ed 2, St Louis, 2007, Mosby.)

The rate of tubular H^+ secretion increases if the concentration of H^+ in the blood plasma increases. Conversely, the rate of H^+ secretion decreases if blood plasma $[H^+]$ decreases (Fig. 14.4). Any factor that increases $PaCO_2$, such as hypoventilation, increases $[H^+]$ in the blood and thus $[H^+]$ secretion; any factor that decreases $PaCO_2$, such as hyperventilation, decreases H^+ secretion.

HCO_3^- formed in the tubule cell from the reaction between CO_2 and H_2O (see Fig. 14.3) diffuses back into the blood plasma because the luminal side of the tubule cell is relatively impermeable to HCO_3^-. HCO_3^- and Na^+ are reabsorbed whenever H^+ is secreted into the tubular filtrate.

Reabsorption of Bicarbonate Ion

Because the luminal side of the renal tubule cell is relatively impermeable to HCO_3^-, these ions are reabsorbed indirectly, as shown in Fig. 14.3. The HCO_3^- in the tubular filtrate reacts with the H^+ secreted by the tubular cells. The resulting H_2CO_3 breaks down into CO_2 and H_2O. Because CO_2 is extremely diffusible through biologic membranes, it diffuses instantly from the filtrate into the tubule cell. There, CO_2 reacts rapidly with H_2O in the presence of carbonic anhydrase, instantly forming HCO_3^- and H^+. The HCO_3^- thus created diffuses back through the nonluminal side of the tubule cell into the blood. Although the reabsorbed HCO_3^- is not the same HCO_3^- that existed in the tubular fluid, the net result is the same as if HCO_3^- were directly reabsorbed. If the tubule cells secrete sufficient H^+, all HCO_3^- in the tubular fluid is reabsorbed in this manner.

The net effect of secreting H^+ (caused by high blood CO_2 or *hypoventilation*, as shown in Fig. 14.2) is to reabsorb all filtrate HCO_3^-, increasing the quantity of HCO_3^- in the blood. According to the H-H equation, this brings blood pH up toward the normal range.

RULE OF THUMB A rise in arterial CO_2 leads to a rise in HCO_3^- reabsorption from the renal filtrate, which in the long term, buffers the acidic effects of the rise in arterial CO_2.

If blood CO_2 is low, as is the case in a state of *hyperventilation* (see Fig. 14.4), the ratio of HCO_3^- to dissolved CO_2 molecules increases, and the renal filtrate ends up with more HCO_3^- than secreted H^+. Because HCO_3^- cannot be reabsorbed from the filtrate without first reacting with H^+, the extra HCO_3^- is excreted in the urine, which requires positive ions such as Na^+ or K^+ to also be excreted to maintain tubular electrical neutrality. The net effect of secreting less H^+ is to increase the quantity of HCO_3^- (base) lost in the urine. According to the H-H equation, this brings blood pH down toward the normal range. These renal responses to high and low blood PCO_2 are the mechanisms by which the kidneys compensate for or offsets respiratory acid-base disturbances.

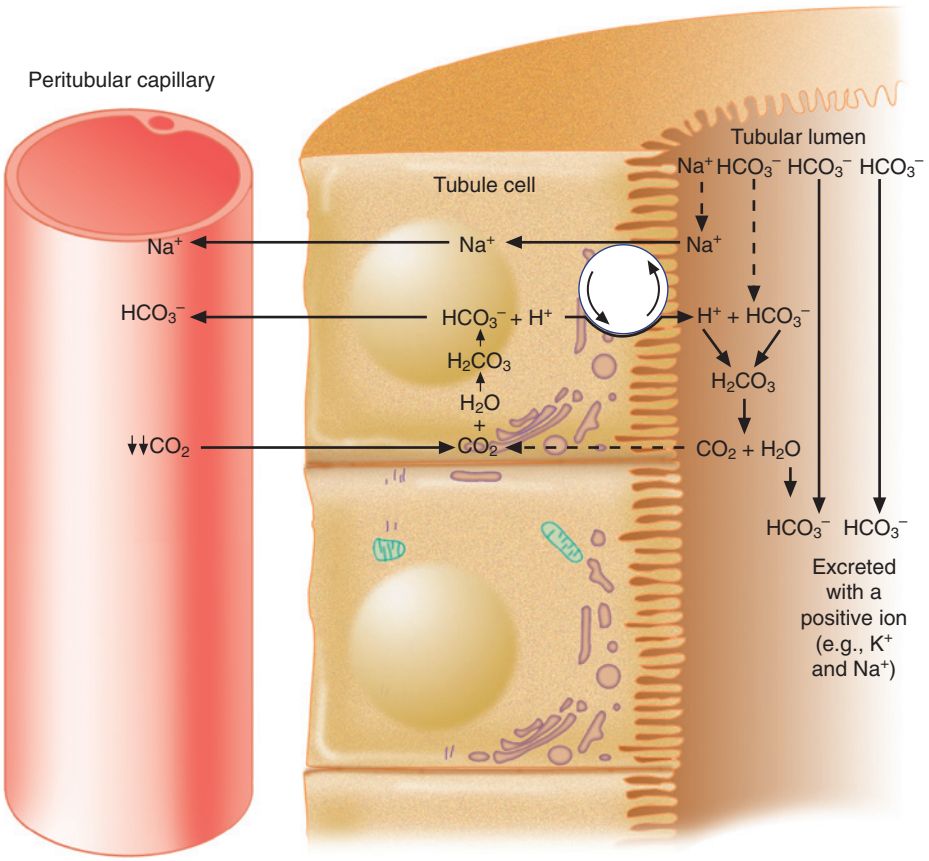

Fig. 14.4 Renal Response to Respiratory Alkalosis. Excess HCO_3^- is excreted in the urine with a positive ion. (Modified from Beachey W: *Respiratory care anatomy and physiology: foundations for clinical practice*, ed 2, St Louis, 2007, Mosby.)

Excess Hydrogen Ion Excretion and Role of Urinary Buffers

If no buffers existed in the filtrate to react with H^+, the H^+-secreting mechanism would soon cease to function because when the filtrate pH decreases to 4.5, H^+ secretion stops.[4] In other words, buffers in the tubular filtrate are essential for the secretion and elimination of excess H^+ in acidotic states.

In Fig. 14.3, more H^+ than HCO_3^- is present in the filtrate. After all available HCO_3^- reacts with H^+, the remaining H^+ reacts with two other filtrate buffers, phosphate and ammonia, as illustrated in Figs. 14.5 and 14.6. In Fig. 14.5, phosphate and H^+ react to form $H_2PO_4^-$, which must be excreted with a positive ion to maintain tubular electrical neutrality (equal exchange of negatively charged and positively charged ions). Fig. 14.6 shows that when urinary buffers are depleted, the resulting fall in filtrate pH stimulates the tubules to secrete ammonia. The NH_3 molecule buffers H^+ by reacting with it to form the positively charged ammonium ion (NH_4^+). To maintain electrical neutrality, the kidney excretes a negatively charged ion to accompany NH_4^+. This negative ion is chloride, the most abundant filtrate anion.

When NH_4^+ reacts with H^+, HCO_3^- diffuses from the tubule cell into the blood (see Fig. 14.6). The net effect of ammonia buffer activity is to cause more HCO_3^- to be reabsorbed into the blood, counteracting the acidic state of the blood. Fig. 14.6 shows that when Cl^- is excreted in combination with NH_4^-, the blood gains HCO_3^-. Blood $[Cl^-]$ and $[HCO_3^-]$ are reciprocally related (i.e., when one is high, the other is low). This relationship explains why people with chronically high blood PCO_2 tend to have low blood $[Cl^-]$ or *hypochloremia*. Activation of the ammonia buffer system enhances Cl^- loss and HCO_3^- gain.

RULE OF THUMB Chronic respiratory acidemia is associated with increased ammonium and chloride ion excretion, resulting in hypochloremia.

ACID-BASE DISTURBANCES

In healthy individuals, the body buffer systems, the lungs, and the kidneys work together to maintain acid-base homeostasis under various conditions.

Normal Acid-Base Balance

Normally, the kidneys keep the arterial $[HCO_3^-]$ in the range of 22 to 26 mEq/L, while lung ventilation keeps the arterial PCO_2 in the range of 35 to 45 mm Hg. These normal values produce an arterial pH range of 7.35 to 7.45; as shown by the H-H equation, when $[HCO_3^-]$ is 24 mEq/L and $PaCO_2$ is 40 mm Hg, the pH is exactly 7.40:

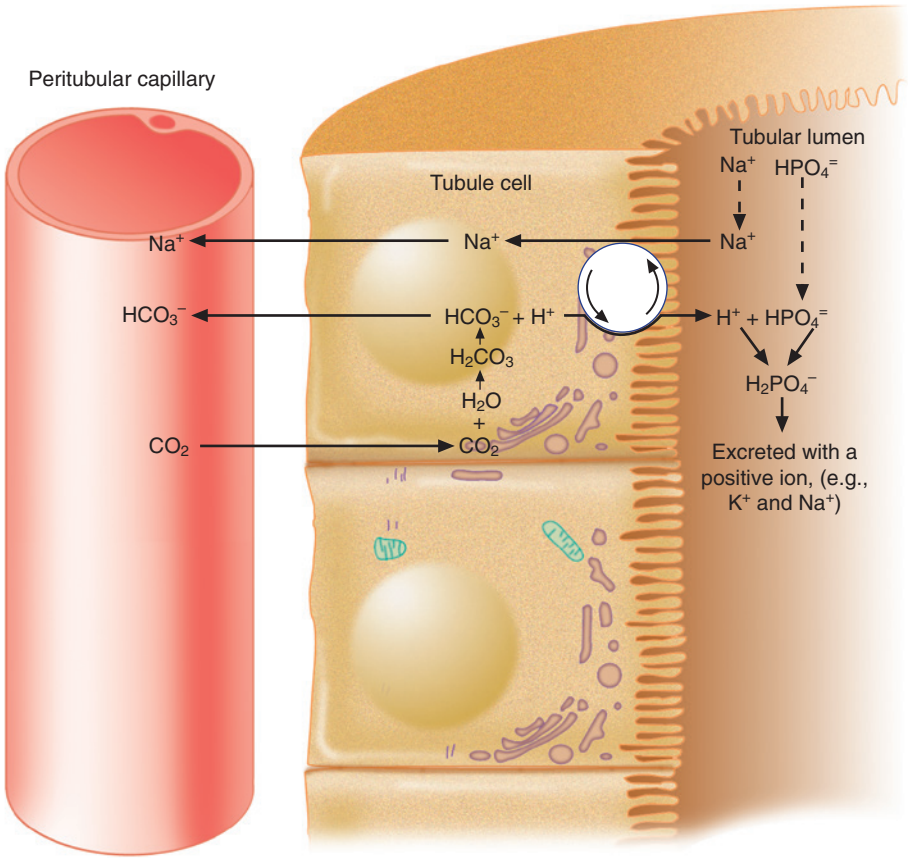

Fig. 14.5 Phosphate Buffer System. After HCO_3^- buffers are exhausted, the remaining H^+ reacts with urinary phosphate buffers. (Modified from Beachey W: *Respiratory care anatomy and physiology: foundations for clinical practice*, ed 2, St Louis, 2007, Mosby.)

$$pH = 6.1 + \log \frac{[HCO_3^-]}{PCO_2 \times 0.03}$$

$$pH = 6.1 + \log \frac{24}{1.2}$$

$$pH = 6.1 + \log[20]$$

$$pH = 7.40$$

The H-H equation shows that plasma pH is determined by the *ratio* of $[HCO_3^-]$ to dissolved CO_2, not the absolute values of these components. As long as the ratio of HCO_3^- buffer to dissolved CO_2 is 20:1, the pH is normal, or 7.40. Because the kidneys control blood $[HCO_3^-]$ and the lungs control blood CO_2 levels, the H-H equation can be conceptually rewritten as follows:

$$pH \propto \frac{\text{Kidney control of } [HCO_3^-]}{\text{Lung control of } PCO_2}$$

An increase in $[HCO_3^-]$ or a decrease in PCO_2 increases the pH, leading to **alkalemia**. This condition produces an $[HCO_3^-]/(PCO_2 \times 0.03)$ ratio greater than 20:1 (e.g., 25:1). A decreased $[HCO_3^-]$ or an increased PCO_2 decreases the pH, leading to **acidemia**. This condition produces an $[HCO_3^-]/(PCO_2 \times 0.03)$ ratio less than 20:1 (e.g., 15:1). The normal ranges for arterial pH, PCO_2, and $[HCO_3^-]$ are as follows:

$$pH = 7.35 \text{ to } 7.45$$

$$PaCO_2 = 35 \text{ to } 45 \text{ mm Hg}$$

$$[HCO_3^-] = 22 \text{ to } 26 \text{ mEq/L}$$

Alkalemia is defined as a blood pH greater than 7.45. *Acidemia* is defined as a blood pH less than 7.35. *Hyperventilation* is defined as $PaCO_2$ less than 35 mm Hg. *Hypoventilation* is defined as $PaCO_2$ greater than 45 mm Hg.

RULE OF THUMB Hypoventilation causes respiratory acidemia; hyperventilation causes respiratory alkalemia.

Primary Respiratory Disturbances

Abnormal arterial pH levels caused by changes in $PaCO_2$ are called *primary respiratory disturbances* because the lungs control $PaCO_2$. Respiratory disturbances affect the denominator of the H-H equation. A high $PaCO_2$ increases dissolved CO_2, decreasing the pH:

$$\downarrow pH \propto \frac{\rightarrow HCO_3^-}{\uparrow PaCO_2}$$

where $\downarrow$ means decreased, $\rightarrow$ means no change, and $\uparrow$ means increased. A respiratory disturbance causing acidemia is called

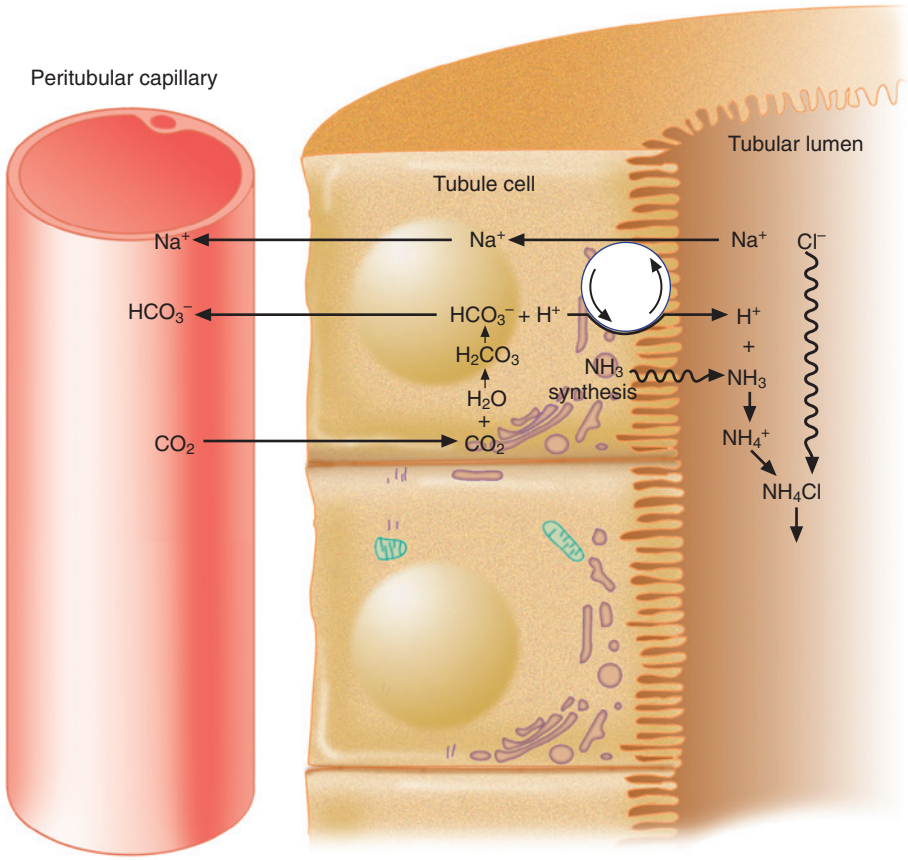

Fig. 14.6 Tubule Cells Secrete Ammonia in Response to Low-Filtrate pH. NH_3 molecules buffer H^+, forming NH_4^+, which is excreted with Cl^-. (Modified from Beachey W: *Respiratory care anatomy and physiology: foundations for clinical practice*, ed 2, St Louis, 2007, Mosby.)

respiratory acidosis. On the other hand, a low $PaCO_2$ decreases dissolved CO_2, raising the pH; this leads to alkalemia and is called **respiratory alkalosis**:

$$\uparrow \text{pH} \propto \frac{\rightarrow HCO_3^-}{\downarrow PaCO_2}$$

*Hypo*ventilation causes respiratory acidosis, whereas *hyper*ventilation causes respiratory alkalosis.

Primary Metabolic (Nonrespiratory) Disturbances

Nonrespiratory processes change arterial pH, manifested by changes in $[HCO_3^-]$. These are called *primary metabolic disturbances*. Although the term *nonrespiratory* is more accurate, the term *metabolic* is, by convention, used to refer to all nonrespiratory acid-base disturbances. These kinds of disturbances involve a gain or loss of fixed acids or HCO_3^-. Such processes affect the numerator of the H-H equation. The build-up of a fixed acid in the body is buffered by HCO_3^-, decreasing the plasma $[HCO_3^-]$ and the pH:

$$\downarrow \text{pH} \propto \frac{\downarrow HCO_3^-}{\rightarrow PaCO_2}$$

The same effect is created by a loss of HCO_3^-. Nonrespiratory processes causing acidemia are traditionally called **metabolic acidosis**.

RULE OF THUMB By convention, in blood gas classification, *metabolic* refers to nonventilatory processes and *respiratory* refers to ventilatory processes.

In contrast, ingesting too much alkali (e.g., $NaHCO_3$ or other antacids) increases $[HCO_3^-]$ and pH:

$$\uparrow \text{pH} \propto \frac{\uparrow HCO_3^-}{\rightarrow PaCO_2}$$

Plasma $[HCO_3^-]$ can be increased by its *addition*, as in the previous example, or by its *generation*, as occurs when fixed acid is lost from the body.[5] An individual may lose HCl from the body by vomiting large amounts of gastric juice. This loss generates HCO_3^-, as discussed later (see Fig. 14.9).

Processes that increase arterial pH by losing fixed acid or gaining HCO_3^- produce a condition called **metabolic alkalosis**. Table 14.3 shows the four primary acid-base disturbances causing alkalemia and acidemia.

Compensation: Restoring pH to Normal

When any primary acid-base defect occurs, the body immediately reacts to make up for the defect—that is, the body initiates a *compensatory* response. If a person hypoventilates (respiratory acidosis), the kidneys bring the pH back toward normal by

TABLE 14.3 Primary Acid-Base Disorders and Compensatory Responses

Acid-Base Disorder	Primary Defect	Compensatory Response
Respiratory acidosis	$\begin{bmatrix}\rightarrow HCO_3^- \\ \uparrow \mathbf{PaCO_2}\end{bmatrix} = \downarrow pH$	$\begin{bmatrix}\uparrow HCO_3^- \\ \uparrow \mathbf{PaCO_2}\end{bmatrix} = \rightarrow pH$
Respiratory alkalosis	$\begin{bmatrix}\rightarrow HCO_3^- \\ \downarrow \mathbf{PaCO_2}\end{bmatrix} = \uparrow pH$	$\begin{bmatrix}\downarrow HCO_3^- \\ \downarrow \mathbf{PaCO_2}\end{bmatrix} = \rightarrow pH$
Metabolic acidosis	$\begin{bmatrix}\downarrow HCO_3^- \\ \rightarrow \mathbf{PaCO_2}\end{bmatrix} = \downarrow pH$	$\begin{bmatrix}\downarrow HCO_3^- \\ \downarrow \mathbf{PaCO_2}\end{bmatrix} = \rightarrow pH$
Metabolic alkalosis	$\begin{bmatrix}\uparrow \mathbf{HCO_3^-} \\ \rightarrow PaCO_2\end{bmatrix} = \uparrow pH$	$\begin{bmatrix}\uparrow HCO_3^- \\ \uparrow \mathbf{PaCO_2}\end{bmatrix} = \rightarrow pH$

Note: Primary defects and compensatory responses appear in boldface type.
→, No change; ↓, decrease; ↑, increase.
From Beachey W: *Respiratory care anatomy and physiology: foundations for clinical practice*, ed 2, St Louis, 2007, Mosby.

returning the filtrate's HCO_3^- ions back to the blood, a process called **reabsorption.** In contrast, the compensatory renal response to hyperventilation (respiratory alkalosis) is urinary elimination of HCO_3^- (bicarbonate diuresis).

Similarly, if a nonrespiratory (metabolic) process decreases or increases $[HCO_3^-]$, the lungs compensate by hyperventilating (eliminating CO_2) or hypoventilating (retaining CO_2), restoring the pH to near normal. Consider the following example of pure (uncompensated) respiratory acidosis in which the PCO_2 level increases to 60 mm Hg:

$$pH = 6.1 + \log \frac{(24\ mEq/L)}{(60\ mm\ Hg \times 0.03)}$$
$$pH = 6.1 + \log(13.3)$$
$$pH = 7.22$$

The kidneys compensate by reabsorbing HCO_3^- from the filtrate into the blood, returning the plasma HCO_3^-/dissolved CO_2 ratio to almost 20:1, as shown:

$$pH = 6.1 + \log \frac{(34\ mEq/L)}{(60\ mm\ Hg \times 0.03)}$$
$$pH = 6.1 + \log(18.9)$$
$$pH = 7.38$$

pH is restored to the normal range of 7.35 to 7.45, although the PCO_2 level remains abnormally high. This compensatory response of the kidney produces a high plasma $[HCO_3^-]$, *not to be confused with primary metabolic alkalosis*; compensatory renal HCO_3^- retention is a normal secondary response to the primary event of respiratory acidosis.

The lungs normally compensate quickly for metabolic acid-base defects because ventilation can change the $PaCO_2$ within seconds. The kidneys require more time to retain or excrete significant amounts of HCO_3^- and compensate for respiratory defects at a much slower pace. Table 14.3 summarizes the four primary acid-base disturbances and the body's compensatory responses.

RULE OF THUMB Compensatory responses of the lungs (ventilation) to acid-base disturbances normally occur within seconds; compensatory responses of the kidneys occur within hours or days.

Effect of the Carbon Dioxide Hydration Reaction on $[HCO_3^-]$

In the previous examples of pure (uncompensated) respiratory acidosis and alkalosis, it was assumed that $[HCO_3^-]$ did not change when the $PaCO_2$ level increased or decreased. However, arterial $[HCO_3^-]$ does increase slightly as the $PaCO_2$ increases because the CO_2 hydration reaction generates HCO_3^-. This reaction occurs primarily in the red blood cell because the catalytic enzyme, carbonic anhydrase, is present:

$$CO_2 + H_2O - (\text{Carbonic anhydrase}) \rightarrow H_2CO_3 \rightarrow H^+ + HCO_3^-$$

As H^+ and HCO_3^- are rapidly produced in the erythrocyte, Hb immediately buffers H^+, pulling the reaction to the right, generating more plasma HCO_3^-.

The amount of HCO_3^- generated by this buffering action depends on the amount of buffer available to accept the H^+ produced by the hydration reaction. In general, when the nonbicarbonate buffer concentration is normal, and the PCO_2 increase is acute, the hydration reaction increases the plasma $[HCO_3^-]$ approximately 1 mEq/L for every 10 mm Hg increase in PCO_2 higher than 40 mm Hg. Fig. 14.7 illustrates this hydration reaction effect. Normal status is represented by point *A:* $PaCO_2$ of 40 mm Hg, pH of 7.40, and plasma HCO_3^- of 24 mEq/L. An acute increase in $PaCO_2$ from 40 to 80 mm Hg proceeds from point *A*, moving to the left, up the normal blood buffer line (line *BAC*) to point *D*, where the buffer line intersects the $PaCO_2$ = 80 mm Hg isopleth. Point *D* indicates an HCO_3^- of approximately 28.5 mEq/L and a pH of approximately 7.18. This small change in $[HCO_3^-]$ is a natural result of the Hb buffering action and should not be wrongly interpreted as early renal compensation.

RULE OF THUMB For an acute increase in PCO_2, the plasma $[HCO_3^-]$ increases by approximately 1 mEq/L for every 10 mm Hg PCO_2 rise above 40 mm Hg.

CLINICAL ACID-BASE STATES

Systematic Acid-Base Classification

In analyzing an acid-base problem, it is helpful to use a series of systematic steps. Consistently applying them to all acid-base disturbances helps one avoid the tendency to jump to conclusions. Four steps in arterial blood acid-base classification are outlined in Box 14.2. After the pH is categorized, the order of the steps is not as important as following the same procedure for each situation.

Step 1: Categorize pH

If the arterial pH is greater than 7.45, a state of alkalemia exists. If the pH is less than 7.35, a state of acidemia exists. Steps 2 through 4 help the clinician determine whether an acid-base abnormality is of respiratory or metabolic (nonrespiratory) origin.

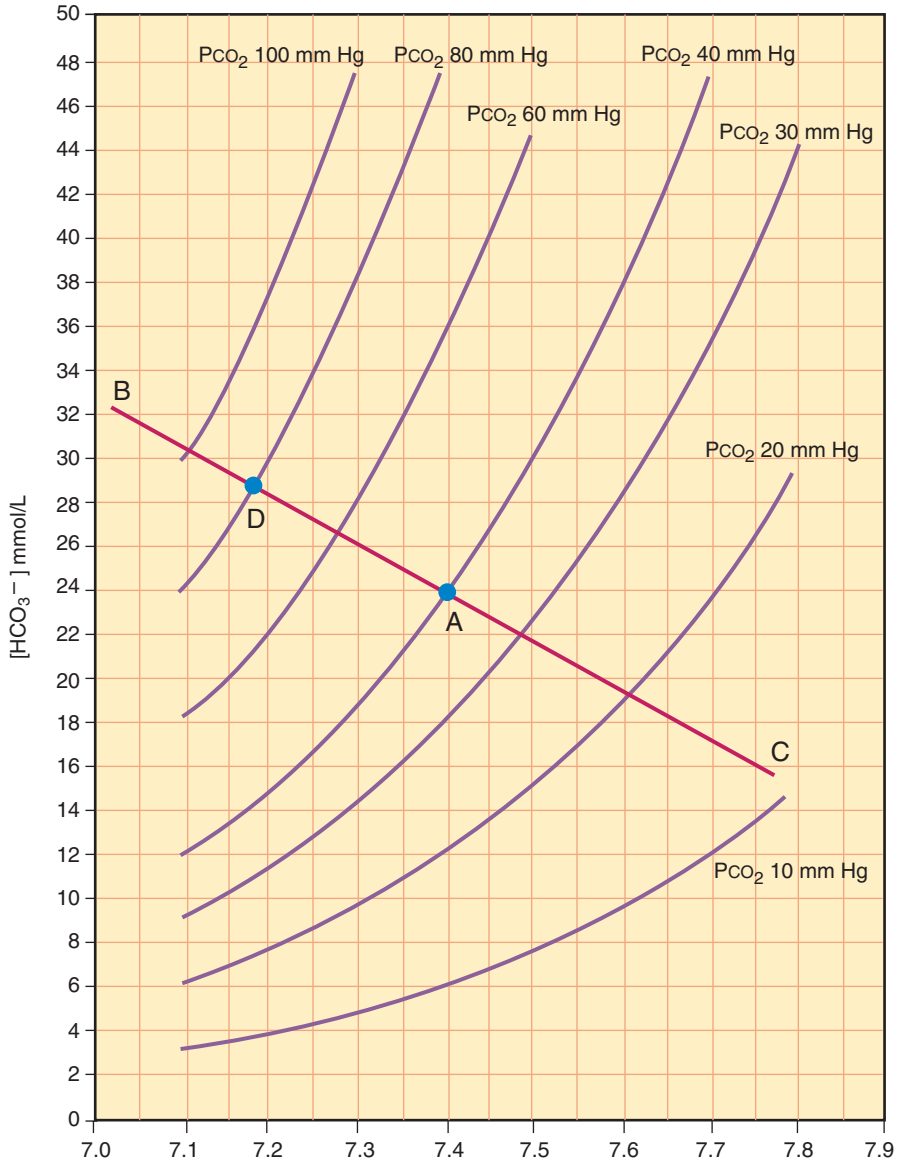

Fig. 14.7 pH-PCO_2 Diagram. Because of the hydration reaction between CO_2 and H_2O, acute increases in PCO_2 increase the plasma HCO_3^- concentration along line *CADB*. An acute increase in PCO_2 from 40 mm Hg to 80 mm Hg (point *A* to point *D*) increases [HCO_3^-] from 24 mEq/L to approximately 29 mEq/L. (Modified from Masoro EJ, Siegel PD: *Acid-base regulation: its physiology and pathophysiology*, Philadelphia, 1971, Saunders.)

BOX 14.2 Systematic Acid-Base Classification

- Inspect the pH (acidemia, alkalemia, or normal).
- Inspect $PaCO_2$ (respiratory component). Can it explain the pH?
- Inspect HCO_3^- (metabolic component). Can it explain the pH?
- Check for compensation. Did the noncausative component respond appropriately?

From Beachey W: *Respiratory care anatomy and physiology: foundations for clinical practice*, ed 2, St Louis, 2007, Mosby.

Step 2: Determine Respiratory Involvement

$PaCO_2$ is the marker for respiratory involvement because the lungs control the level of CO_2 in the arterial blood. (The normal range for $PaCO_2$ is 35 to 45 mm Hg.) If the arterial pH is abnormal, the clinician should determine whether the observed $PaCO_2$ could cause the abnormality by itself. If the pH was less than 7.35 (denoting an acidosis) and $PaCO_2$ was greater than 45 mm Hg, according to the H-H equation, the high $PaCO_2$ would lower the pH (i.e., produce an acidosis). In this case, the respiratory system would be at least partly, if not entirely, responsible for the acidemia. If the pH is less than 7.35 and $PaCO_2$ is in the normal range, the acidemia is of nonrespiratory or metabolic origin.

Step 3: Determine Metabolic (Nonrespiratory) Involvement

Plasma [HCO_3^-] is the marker for metabolic involvement because [HCO_3^-] is controlled by nonrespiratory factors. (The normal plasma [HCO_3^-] of arterial blood is 22 to 26 mEq/L.) If the arterial pH is abnormal, the clinician must determine whether

the observed [HCO_3^-] could cause the abnormality by itself. If the pH was less than 7.35 (denoting an acidemia) and the [HCO_3^-] was less than 22 mEq/L, according to the H-H equation, the low [HCO_3^-] would produce an acidosis. Nonrespiratory (metabolic) factors would be partly, if not entirely, responsible for the acidemia. If [HCO_3^-] is in the normal range in the presence of this acidemia, the acidemia is of respiratory origin.

Step 4: Assess for Compensation

The system (respiratory or nonrespiratory) that is not primarily responsible for the acid-base imbalance usually attempts to return the pH to the normal range. Compensation may be complete (pH is brought into the normal range) or partial (pH is still out of the normal range but is in the process of moving toward the normal range). In a pure respiratory acidosis, the kidneys compensate by reabsorbing more [HCO_3^-], restoring the pH to normal. Similarly, respiratory alkalosis elicits a compensatory loss of [HCO_3^-], decreasing its plasma concentration. A pure metabolic acidosis normally stimulates a compensatory increase in ventilation, decreasing the $PaCO_2$. A pure metabolic alkalosis causes a compensatory decrease in ventilation, increasing the $PaCO_2$. All compensatory responses work to restore the pH to the normal range.

In cases in which compensation has occurred, if the pH is on the acidemic side of the normal range (7.35 to 7.39), the event that would cause an acidosis (either increased $PaCO_2$ or decreased plasma HCO_3^-) is generally the primary cause of the original acid-base imbalance. If compensation is present but pH is on the alkalemic side of the normal range (7.41 to 7.45), the component that would cause an alkalosis (either decreased $PaCO_2$ or increased HCO_3^-) is generally the primary cause of the original acid-base disturbance.

Complete compensation refers to any case in which the compensatory response returns the pH to the normal range (7.35 to 7.45). *Partial compensation* refers to instances in which the expected compensatory response has begun but has not had sufficient time to return the pH into the normal range. For example, suppose a patient has a partially compensated respiratory acidosis. This condition is characterized by high $PaCO_2$ (>45 mm Hg), pH less than 7.35, and plasma [HCO_3^-] greater than 26 mEq/L. The compensatory response (increased HCO_3^-) is not yet sufficient to return the pH into the normal range, although the expected compensatory activity has begun. By comparison, a completely compensated respiratory acidosis might be shown by the same patient several hours later, when the kidneys have had enough time to retain sufficient plasma HCO_3^- to bring the pH into the normal range. This completely compensated respiratory acidosis is characterized by the same originally observed high $PaCO_2$, pH that is in the 7.35 to 7.39 range, and plasma [HCO_3^-] that is greater than it was before *complete compensation* took place. The pH remains on the acidemic side of 7.40 because the primary disturbance (high $PaCO_2$) originally created an acidotic environment. In general, the body does not overcompensate for an acid-base disturbance. Table 14.4 summarizes acid-base and ventilatory classification. Table 14.5 classifies the degree of compensation for acid-base disturbances.

TABLE 14.4 Acid-Base and Ventilatory Classification

Component	Classification	Range
pH (arterial)	Normal status	7.35–7.45
	Acidemia	<7.35
	Alkalemia	>7.45
$PaCO_2$ (mm Hg)	Normal ventilatory status	35–45
	Respiratory acidosis (hypoventilation)	>45
	Respiratory alkalosis (hyperventilation)	<35
HCO_3^- (mEq/L)	Normal metabolic status	22–26
	Metabolic acidosis	<22
	Metabolic alkalosis	>26

From Beachey W: *Respiratory care anatomy and physiology: foundations for clinical practice*, ed 2, St Louis, 2007, Mosby.

TABLE 14.5 Degrees of Acid-Base Compensation

Compensating (Noncausative Component)	pH	Classification
Within normal range	Abnormal	Noncompensated (acute)
Out of normal range in the expected direction	Abnormal	Partially compensated
Out of normal range in the expected direction	Normal	Compensated (chronic)

From Beachey W: *Respiratory care anatomy and physiology: foundations for clinical practice*, ed 2, St Louis, 2007, Mosby.

Respiratory Acidosis

Any physiologic process that increases $PaCO_2$ (>45 mm Hg) with an accompanying decreased arterial pH (<7.35) produces respiratory acidosis. Increased $PaCO_2$ (**hypercapnia**) lowers the arterial pH because dissolved CO_2 produces H_2CO_3:

$$CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow HCO_3^- + H^+$$

Causes

Any process in which alveolar ventilation fails to eliminate CO_2 as rapidly as the body produces it causes respiratory acidosis. This acidosis could occur in two different ways: (1) a drug may depress the central nervous system, preventing the person from ventilating adequately or (2) a preexisting lung disease may limit ventilatory reserve such that the person cannot increase ventilation enough to eliminate the CO_2 produced by increased physical activity. Box 14.3 summarizes causes of respiratory acidosis.

If hypercapnia is uncompensated, respiratory acidosis occurs with decreased pH, increased $PaCO_2$, and normal or slightly increased [HCO_3^-].

Compensation

Renal compensation for respiratory acidosis begins as soon as $PaCO_2$ increases. The kidney reabsorbs HCO_3^- from the renal tubular filtrate, bringing the arterial pH into the normal range (see Fig. 14.3). However, this process is slow and cannot keep

BOX 14.3 Common Causes of Respiratory Acidosis

Normal Lungs

Central Nervous System Depression ("Won't Breathe")

- Anesthesia
- Sedative drugs
- Narcotic analgesics

Neuromuscular Disease

- Poliomyelitis
- Myasthenia gravis
- Guillain-Barré syndrome

Trauma

- Spinal cord
- Brain
- Chest wall
- Severe restrictive disorders
- Obesity (Pickwickian syndrome)
- Kyphoscoliosis

Abnormal Lungs ("Can't Breathe")

- Chronic obstructive pulmonary disease
- Acute airway obstruction (late phase)

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Acute (Uncompensated) Respiratory Acidosis

Problem

A 35-year-old woman was admitted to the emergency department with a diagnosis of heroin overdose. Her breathing was shallow and slow. Arterial blood gas analysis showed a pH of 7.30, PCO_2 of 55 mm Hg, and HCO_3^- of 26 mEq/L. How would the RT assess this patient's respiratory condition?

Solution

The RT should follow these steps:

1. Categorize the pH. The pH is below normal, indicating the presence of acidemia.
2. Determine respiratory involvement. $PaCO_2$ is elevated above normal (hypercapnia), consistent with a low pH, indicating hypoventilation as a contributing factor to acidemia (respiratory acidosis).
3. Determine metabolic involvement. HCO_3^- is elevated slightly above normal. However, this is in the expected range for acute respiratory acidosis (1 mEq for each 10-mm Hg increase in PCO_2).
4. Assess for compensation. As explained in step 3, HCO_3^- is within the expected range for acute respiratory acidosis. There is no evidence of metabolic compensation. Therefore, the condition is interpreted as an uncompensated respiratory acidosis.

pace with an acutely increasing $PaCO_2$. Full compensation may take several days.

Partly compensated respiratory acidosis is characterized by increased $PaCO_2$, increased $[HCO_3^-]$, and an acid pH—still not quite up in the normal range. *Fully compensated* respiratory acidosis is characterized by a pH on the acidic side of the normal (<7.40 but >7.35), increased $PaCO_2$, and increased $[HCO_3^-]$. Increased $[HCO_3^-]$ in the presence of increased $PaCO_2$ is a sign that the $PaCO_2$ has been elevated for a considerable time (i.e., the kidneys have had sufficient time to compensate). The underlying pathologic process that produced hypercapnia is still present; the kidneys simply mask the problem by maintaining a normal-range pH. Because hypercapnia is still present, the term *acidosis* is retained in classifying this condition (fully compensated respiratory *acidosis*). This terminology emphasizes that lung function is still abnormal, and, if it were unopposed by the renal compensatory mechanism, it would still produce an acidosis.

TABLE 14.6 Expected Effect of Acute Changes in $PaCO_2$ on Arterial pH

$PaCO_2$ Change	pH Change
Decrease	*Increase*
1 mm Hg	0.01
10 mm Hg	0.10
Increase	*Decrease*
1 mm Hg	0.006
10 mm Hg	0.06
Expected pH when measured $PaCO_2$ < 40 mm Hg	
Expected pH = 7.40 + (40 mm Hg − Measured $PaCO_2$)0.01	
Expected pH when measured $PaCO_2$ > 40 mm Hg	
Expected pH = 7.40 − (Measured $PaCO_2$ − 40 mm Hg)0.006	

Correction

The main goal in correcting respiratory acidosis is to treat the underlying problem—to improve alveolar ventilation. Various respiratory care modalities may be used, ranging from bronchial hygiene and lung expansion techniques to mechanical ventilation. If hypoventilation is chronic and compensation has restored pH to the normal range, action aimed at decreasing $PaCO_2$ to the normal range is inappropriate and possibly harmful, because the high level of $[HCO_3^-]$ in the blood created by the kidney's compensation would produce an alkalemia (Table 14.6).

Respiratory Alkalosis

Any physiologic process that decreases $PaCO_2$ (<35 mm Hg) and increases arterial pH (>7.45) produces respiratory alkalosis. A low $PaCO_2$ (**hypocapnia**) forces the hydration reaction to the left, decreasing H_2CO_3 concentration and increasing the pH:

$$CO_2 + H_2O \leftarrow H_2CO_3 \leftarrow HCO_3^- + H^+$$

Causes

Any process in which ventilatory elimination of CO_2 exceeds the body's production of CO_2 causes respiratory alkalosis. The most common cause of hyperventilation in patients with pulmonary disease is decreased PaO_2 (hypoxemia). Hypoxemia causes specialized neural structures to signal the brain, increasing ventilation (see Chapter 15). Anxiety, fever, stimulatory drugs, pain, and central nervous system injuries are possible causes of hyperventilation. Other possible causes include stimulation of irritant receptors in the lung parenchyma, which may occur in pneumonia or pulmonary edema.

Hyperventilation and respiratory alkalosis also may be *iatrogenically* induced (caused by medical treatment). Iatrogenic hyperventilation is most commonly associated with overly aggressive mechanical ventilation. It may also be associated with aggressive

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Chronic (Compensated) Respiratory Acidosis

Problem

A 73-year-old man is being treated on an outpatient basis for pulmonary emphysema, which was diagnosed 7 years earlier. His breathing is labored at rest, with marked use of accessory muscles. Arterial blood gas analysis showed a pH of 7.36, PCO_2 of 64 mm Hg, and HCO_3^- of 35 mEq/L. How would the RT assess this patient's arterial blood gas results?

Solution

The RT should follow these steps:

1. Categorize the pH. The pH is on the acidemic side of the normal range, but it is still normal.
2. Determine respiratory involvement. $PaCO_2$ is higher than normal, indicating hypoventilation as a contributing factor to the low-normal pH (respiratory acidosis).
3. Determine metabolic involvement. HCO_3^- is substantially elevated. By itself, this would cause alkalemia, but because pH is on the acidemic side of normal, primary metabolic alkalosis is ruled out. Compensation for the respiratory acidosis has occurred.
4. Assess for compensation. HCO_3^- is approximately 8 to 10 mEq higher than normal. This is consistent with a compensatory response by the kidneys to offset the acidosis. In addition, the expected pH for a $PaCO_2$ of 64 mm Hg is [7.40 − (64 mm Hg − 40 mm Hg) × 0.006], or 7.26 (see Table 14.6). Because the actual pH is 7.36, metabolic compensation (retention of HCO_3^-) must have occurred. Therefore, the interpretation is a fully compensated respiratory acidosis.

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Acute (Uncompensated) Respiratory Alkalosis

Problem

A distraught 77-year-old man experiencing anxiety of apparent psychosomatic origin was brought to the hospital by his wife. The patient exhibited rapid and deep breathing, had slurred speech, and complained about tingling in his extremities. Arterial blood gas analysis showed a pH of 7.57, PCO_2 of 23 mm Hg, and HCO_3^- of 22 mEq/L. How would the RT interpret this patient's acid-base condition?

Solution

The RT should follow these steps:

1. Categorize the pH. The pH is substantially higher than normal, indicating the presence of an alkalemia.
2. Determine respiratory involvement. $PaCO_2$ is well below normal, which is consistent with the high pH, indicating hyperventilation as a contributing factor in alkalemia (respiratory alkalosis).
3. Determine metabolic involvement. HCO_3^- is slightly lower than normal. However, this is within the expected range for acute respiratory alkalosis (CO_2 hydration reaction's effect).
4. Assess for compensation. The decrease in HCO_3^- is within the expected range for acute respiratory alkalosis (1 mEq for each 5-mm Hg decline in PCO_2). Therefore, the interpretation is an uncompensated respiratory alkalosis.

Hypocapnia is synonymous with respiratory alkalosis.

deep breathing and lung expansion respiratory care procedures. Decreased $PaCO_2$, increased pH, and normal-range [HCO_3^-] characterize acute respiratory alkalosis. A slight decrease in [HCO_3^-] is expected from the effect of the hydration reaction. Box 14.4 summarizes causes of respiratory alkalosis.

BOX 14.4 Common Causes of Respiratory Alkalosis

Normal Lungs

- Anxiety
- Fever
- Stimulant drugs
- Central nervous system lesion
- Pain
- Sepsis

Abnormal Lungs

- Hypoxemia-causing conditions
- Acute asthma
- Pneumonia
- Stimulation of vagal lung receptors
- Pulmonary edema
- Pulmonary vascular disease

Either Normal or Abnormal Lungs

- Iatrogenic hyperventilation

Clinical Signs

An early sign of respiratory alkalosis is **paresthesia** (numbness or a tingling sensation in the extremities). Severe hyperventilation is associated with hyperactive reflexes and possibly tetany (intermittent muscle spasms). The low $PaCO_2$ may constrict the brain's cerebral vessels enough to reduce cerebral circulation, causing light-headedness and dizziness.

Compensation

The kidneys compensate for respiratory alkalosis by excreting more HCO_3^- in the urine (HCO_3^- diuresis; see Fig. 14.4). This activity brings arterial pH down toward the normal range. As with respiratory acidosis, renal compensation is a slow process. Complete compensation may take days.

Partly compensated respiratory alkalosis is characterized by decreased $PaCO_2$, decreased [HCO_3^-], and a high pH—still not quite down to the normal range. Fully compensated respiratory alkalosis is characterized by decreased $PaCO_2$, decreased [HCO_3^-], and pH on the alkalemic side of normal (pH > 7.40 but ≤ 7.45). Compensated respiratory alkalosis is sometimes called *chronic respiratory alkalosis* or *chronic alveolar hyperventilation*. The underlying hyperventilation and hypocapnia are still present. The terminology *respiratory alkalosis* is retained in classifying this condition, because although the pH is within the normal range, the $PaCO_2$ is still below normal.

Correction

Correcting respiratory alkalosis involves removing the stimulus that caused the hyperventilation. If hypoxemia is the stimulus, oxygen therapy is needed.

Alveolar Hyperventilation Superimposed on Compensated Respiratory Acidosis

Consider a patient with a compensated respiratory acidosis who has an arterial pH of 7.38, $PaCO_2$ of 58 mm Hg, and HCO_3^- of

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Compensated (Chronic) Respiratory Alkalosis

Problem

A 27-year-old man was admitted to the hospital with a persistent case of bacterial pneumonia, which had not responded to 6 days of ambulatory care with antimicrobial drugs. He exhibited mild cyanosis and labored breathing. Arterial blood gas analysis (with the patient breathing room air) showed a pH of 7.44, $PaCO_2$ of 26 mm Hg, HCO_3^- of 17 mEq/L, and PaO_2 of 53 mm Hg. How would the RT interpret this patient's acid-base condition?

Solution

The RT should follow these steps:

1. Categorize the pH. The pH is on the alkalemic side of the normal range, but it is still normal.
2. Determine respiratory involvement. PCO_2 is well below normal, indicating hyperventilation as a contributing factor to the high-normal pH (respiratory alkalosis).
3. Determine metabolic involvement. HCO_3^- is substantially lower than normal, but because the pH is on the alkalemic side of normal, primary metabolic acidosis is ruled out. Compensation for the respiratory alkalosis has occurred.
4. Assess for compensation. HCO_3^- is approximately 7 mEq below normal. This is consistent with a compensatory response by the kidneys. In addition, the expected pH for $PaCO_2$ of 26 mm Hg is [7.40 + (40 mm Hg − 26 mm Hg) × 0.01], or 7.54 (see Table 14.6). Because the actual pH is 7.44, metabolic compensation (excretion of HCO_3^-) must have occurred. Therefore, the interpretation is a fully compensated respiratory alkalosis.

33 mEq/L. If this patient becomes severely hypoxemic, the hypoxemia may stimulate increased alveolar ventilation if lung mechanics are not too severely impaired. If increased alveolar ventilation acutely lowers the $PaCO_2$ from 58 to 50 mm Hg, the pH could possibly increase to the alkalemic side of the normal range. For example, the patient's blood gas values might now be: pH 7.44, $PaCO_2$ 50 mm Hg, and HCO_3^- 33 mEq/L.

The inexperienced clinician might wrongly interpret these values as compensated metabolic alkalosis. This example shows that blood gas data alone are not enough to make an accurate acid-base assessment. Knowledge of the patient's medical history and the nature of the current problem are essential to evaluate this problem accurately. The blood gas values in this example would be properly classified as acute alveolar hyperventilation (even though the $PaCO_2$ is >45 mm Hg) superimposed on chronic alveolar hypoventilation (i.e., compensated respiratory acidosis).

Metabolic (Nonrespiratory) Acidosis

Any nonrespiratory process that decreases plasma [HCO_3^-] causes metabolic acidosis. A reduction in [HCO_3^-] decreases blood pH because it decreases the amount of base compared with the amount of acid in the blood.

Causes

Metabolic acidosis can occur in one of the following two ways: (1) fixed (nonvolatile) acid build-up in the blood, or (2) an excessive loss of HCO_3^- from the body. An example of fixed acid build-up is a state of low blood flow in which tissue hypoxia and anaerobic metabolism produce lactic acid. The resulting H^+ accumulates and reacts with HCO_3^-, which reduces blood [HCO_3]. On the other hand, an example of HCO_3^- loss is severe diarrhea, in which large stores of HCO_3^- are eliminated from the body, also producing a nonrespiratory (metabolic) acidosis.

Because these two kinds of metabolic acidosis are treated differently, it is important to identify the underlying cause. Analysis of the plasma electrolytes is helpful in distinguishing between these two types of metabolic acidosis. Specifically, measuring the anion gap is helpful in making this distinction.

Anion Gap

The *law of electroneutrality* states that the total number of positive charges must equal the total number of negative charges in the body's fluids. *Cations* (positively charged ions) in the plasma produce a charge exactly balanced by plasma *anions* (negatively charged ions). Plasma electrolytes (cations and anions) *routinely* measured in clinical medicine are Na^+, potassium, Cl^-, and HCO_3^-. Normal plasma concentrations of these electrolytes are such that the cations (Na^+ and K^+) outnumber the anions (Cl^- and HCO_3^-), which leads to what seems to be an *anion gap*. Generally, K^+ is ignored in calculating this apparent anion gap:

$$\text{Anion gap} = [Na^+] - ([Cl^-] + [HCO_3^-])$$

Fig. 14.8A shows that normal concentrations of these ions in the plasma are as follows: 140 mEq/L for Na^+, 105 mEq/L for Cl^-, and 24 mEq/L for HCO_3^-, yielding an "anion gap" of 11 mEq/L (140 mEq/L − [105 mEq/L + 24 mEq/L] = 11 mEq/L). The normal anion gap range is 9 to 14 mEq/L.[6]

An increased anion gap (>14 mEq/L) is caused by a metabolic acidosis in which abnormal fixed acids accumulate in the body. The H^+ of these acids reacts with plasma HCO_3^-, lowering its concentration; this leads to a further increase in the anion gap (i.e., an increase in *unmeasured anions*; see Fig. 14.8B). (When the H^+ of fixed acids is buffered by HCO_3^-, the anion portion of the fixed acid remains in the plasma, increasing unmeasured anion concentration.) A high anion gap indicates that fixed acid concentration in the body has increased.

Metabolic acidosis caused by HCO_3^- loss from the body does not cause a further increase in the anion gap. HCO_3^- loss is accompanied by Cl^- gain, which keeps the anion gap within normal limits (see Fig. 14.8C). The law of electroneutrality helps explain the reciprocal nature of [HCO_3^-] and [Cl^-] in this instance. With a constant cation concentration, losing HCO_3^- means that another anion must be gained to maintain electroneutrality. In this case, the kidney increases its reabsorption of the most abundant anion in the tubular filtrate, the Cl^-. The kind of metabolic acidosis in which HCO_3^- is lost from the body is sometimes called *hyperchloremic acidosis* because of the characteristic increase in plasma [Cl^-]. Box 14.5 summarizes causes of anion gap and non–anion gap metabolic acidosis.

RULE OF THUMB Metabolic acidosis accompanied by a higher than normal anion gap means that the body has accumulated an unusual fixed acid. A metabolic acidosis accompanied by a normal anion gap means that the body has lost a greater than normal amount of base.

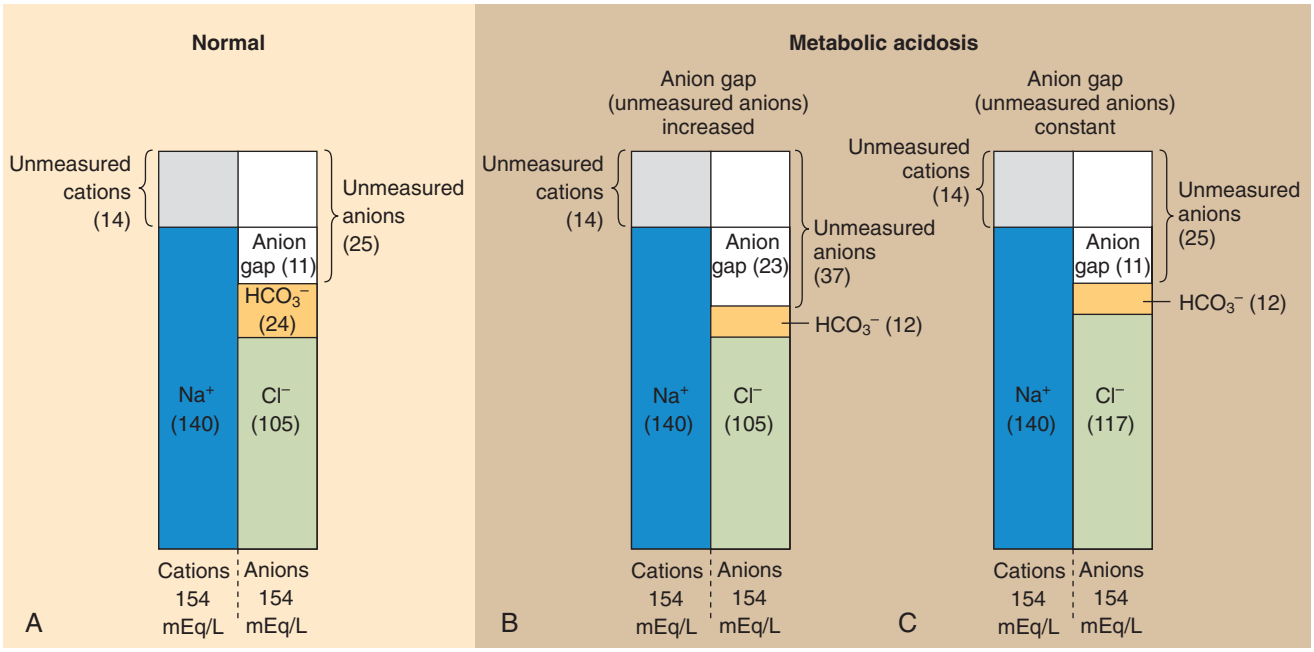

Fig. 14.8 The anion gap in normal (A) and metabolic acidosis (B and C). Fixed acid accumulation increases the anion gap (B), whereas HCO_3^- loss is accompanied by an equal Cl^- gain, keeping the anion gap within the normal range. (Modified from Beachey W: *Respiratory care anatomy and physiology: foundations for clinical practice*, ed 2, St Louis, 2007, Mosby.)

BOX 14.5 Causes of Anion Gap and Nonanion Gap Metabolic Acidosis

High Anion Gap

Metabolically Produced Acid Gain

- Lactic acidosis
- Ketoacidosis
- Renal failure (e.g., retained sulfuric acid)

Ingestion of Acids

- Salicylate (aspirin) intoxication
- Methanol (formic acid)
- Ethylene glycol (oxalic acid)

Normal Anion Gap (Hyperchloremic Acidosis)

Gastrointestinal Loss of HCO_3^-

- Diarrhea
- Pancreatic fistula

Renal Tubular Loss: Failure to Reabsorb HCO_3^-

- Renal tubular acidosis

Ingestion

- Ammonium chloride
- Hyperalimentation intravenous nutrition

From Beachey W: *Respiratory care anatomy and physiology: foundations for clinical practice*, ed 2, St Louis, 2007, Mosby.

Compensation

Hyperventilation is the main compensatory mechanism for metabolic acidosis. The increased plasma $[H^+]$ of metabolic acidosis is buffered by plasma HCO_3^-, which reduces plasma $[HCO_3^-]$ and pH. The low pH activates sensitive receptors in the brain that signal the respiratory muscles to increase ventilation. This increased ventilation lowers the blood's CO_2 levels, and thus its volatile acid (H_2CO_3), which returns the pH toward the normal range. Uncompensated metabolic acidosis suggests that a ventilatory defect must be present, because ventilation usually responds to this stimulus immediately. Metabolic acidosis accompanied by $PaCO_2$ of 40 mm Hg means that something prevents the lungs from responding appropriately to the brain's stimulation. The defect may lie in nerve impulse transmission, the respiratory muscles, or the lungs themselves.

Symptoms

Respiratory compensation in metabolic acidosis means there is a great increase in minute ventilation, which may cause patients to report dyspnea. Hyperpnea (increased tidal volume depth) is a common finding during physical examination of patients with metabolic acidosis. In patients with severe diabetic ketoacidosis, a very deep, fast breathing develops, called *Kussmaul respiration*. Neurologic symptoms of severe metabolic acidosis range from lethargy to coma.

Correction

The initial goal in severe acidemia is to increase the arterial pH greater than 7.20, a level below which serious cardiac arrhythmias become more likely, and treating them becomes more challenging. If respiratory compensation maintains the pH at or above this level, immediate corrective action is usually not required. Treatment of the underlying cause of acid gain or base loss is the reasonable approach.

MINI CLINI

Partially Compensated Metabolic Acidosis

Problem

A 42-year-old woman in a diabetic coma was taken to the emergency department. She exhibited fast and deep respirations. Arterial blood gas analysis showed a pH of 7.22, PCO_2 of 20 mm Hg, HCO_3^- of 8 mEq/L, and base excess (BE) of –16 mEq/L. How would the RT interpret this patient's acid-base condition?

Solution

The RT should follow these steps:

1. Categorize the pH. The pH is below the normal range, indicating the presence of acidemia.
2. Determine respiratory involvement. $PaCO_2$ is well below normal, indicating severe hyperventilation. By itself, this would cause alkalosis, but the presence of acidemia rules out primary respiratory alkalosis. The low $PaCO_2$ is probably a compensatory response to primary metabolic acidosis, although this response is currently insufficient to restore pH to the normal range.
3. Determine metabolic involvement. HCO_3^- is severely reduced, consistent with the low pH. In the presence of low pH and low $PaCO_2$, a low HCO_3^- signals primary metabolic acidosis. This is confirmed by the large BE.
4. Assess for compensation. The severe hyperventilation represents a compensatory response to primary metabolic acidosis, although compensation is far from complete. Nevertheless, the pH level would be even lower if the $PaCO_2$ were normal. Hence the interpretation is a partially compensated metabolic acidosis.

MINI CLINI

Fully Compensated Metabolic Acidosis

Problem

A 38-year-old man had severe diarrhea for weeks without receiving medical attention. Arterial blood gas analysis showed a pH of 7.36, PCO_2 of 24 mm Hg, HCO_3^- of 13 mEq/L, and BE of –11 mEq/L. How would the RT assess this patient's acid-base condition?

Solution

The RT should follow these steps:

1. Categorize the pH. The pH is on the acidemic side of the normal range, but it is still normal.
2. Determine respiratory involvement. $PaCO_2$ is below normal, indicating hyperventilation. By itself, this would cause alkalemia; however, because the pH is on the acidemic side of normal, the presence of primary respiratory alkalosis is ruled out. The low $PaCO_2$ is likely a compensatory response to a primary metabolic acidosis.
3. Determine metabolic involvement. HCO_3^- level is substantially lower than normal, consistent with a low pH. Given that the pH level is on the acidemic side of normal, the low HCO_3^- level signals a possible metabolic acidosis. This is confirmed by the large BE.
4. Assess for compensation. The hyperventilation previously described must represent a compensatory response to primary metabolic acidosis. The pH is in the normal range. Hence the interpretation is a fully compensated metabolic acidosis.

In cases of severe metabolic acidemia, intravenous infusion of $NaHCO_3$ may be indicated. If respiratory compensation is under way, only small amounts of $NaHCO_3$ are required to attain an arterial pH of 7.20. In any case, rapid correction of an arterial pH to greater than 7.20 by $NaHCO_3$ infusion is undesirable.

MINI CLINI

Metabolic Alkalosis

Problem

An 83-year-old woman with heart disease had been taking a powerful diuretic to remove excess edematous fluid from her legs and help keep her free of pulmonary edema. Blood gas and serum electrolyte analyses showed a pH of 7.58, $PaCO_2$ of 46 mm Hg, HCO_3^- of 44 mEq/L, BE of +19 mEq/L, serum K^+ of 2.5 mEq/L, and serum Cl^- of 95 mEq/L. How would the RT assess this patient's acid-base condition?

Solution

The RT should follow these steps:

1. Categorize the pH. The pH level is substantially above normal, indicating the presence of alkalemia.
2. Determine respiratory involvement. $PaCO_2$ is slightly higher than normal, indicating mild hypoventilation. However, because alkalemia is present, the existence of primary respiratory acidosis is ruled out. The elevated $PaCO_2$ may be a compensatory response to a primary metabolic alkalosis.
3. Determine metabolic involvement. HCO_3^- is substantially higher than normal. Given the high pH, the elevated HCO_3^- signals a metabolic alkalosis. This is confirmed by the large BE. In addition, the low serum K^+ and Cl^- values indicate hypokalemic/hypochloremic metabolic alkalosis.
4. Assess for compensation. Although $PaCO_2$ is slightly elevated, compensation for metabolic alkalosis is minimal and the interpretation would be an uncompensated metabolic alkalosis.

Metabolic Alkalosis

Metabolic alkalosis is characterized by increased plasma [HCO_3^-] or a loss of H^+ and a high pH. One must keep in mind that increased [HCO_3^-] is not always diagnostic of a primary metabolic alkalosis because it may be caused by renal compensation for respiratory acidosis.

Causes

Metabolic alkalosis can occur in one of the following two ways: (1) loss of fixed acids, or (2) gain of blood buffer base. Both processes increase plasma [HCO_3^-]. To explain why losing fixed acid increases the plasma [HCO_3^-], consider a situation in which vomiting removes gastric HCl from the body (Fig. 14.9). In response to HCl loss, H^+ diffuses out of the gastric cell into the gastric fluid, where Cl^- accompanies it; this forces the CO_2 hydration reaction in the gastric cell to the right, which generates HCO_3^-. The HCO_3^- enters the blood in exchange for the Cl^-. The plasma gains an HCO_3^- for each Cl^- (or H^+) that is lost (Fig. 14.9).[6]

The causes of metabolic alkalosis are summarized in Box 14.6. Metabolic alkalosis is common in acutely ill patients and is probably the most complicated acid-base imbalance to treat because it involves fluid and electrolyte imbalances. Metabolic alkalosis is often iatrogenic, resulting from the use of diuretics, low-salt diets, or gastric drainage.

To understand how the loss of Cl^-, K^+, and fluid volume may cause alkalosis, one needs to understand how the kidney regulates Na^+. Approximately 26,000 mEq of Na^+ passes through the glomerular membrane daily, but the body's daily Na^+ intake averages only approximately 150 mEq.[4] The kidney's main job is to

reabsorb Na^+, not to excrete it. For this reason, and because Na^+ has a major role in maintaining fluid balance, the kidney places a greater priority on reabsorbing Na^+ than on maintaining Cl^-, K^+, or acid-base balance.

Normally, Na^+ is reabsorbed through *primary active transport* (Fig. 14.10), in which the sodium-potassium–adenosine triphosphatase (Na^+, K^+-ATPase) pump actively transports Na^+ out of the renal tubule cell into the blood. This process causes Na^+ to diffuse continually from the filtrate into the tubule cell. Cl^- (the most abundant anion in the filtrate) accompanies Na^+ because of electrostatic forces—that is, to maintain electroneutrality in the filtrate. If blood Cl^- concentration is much below normal

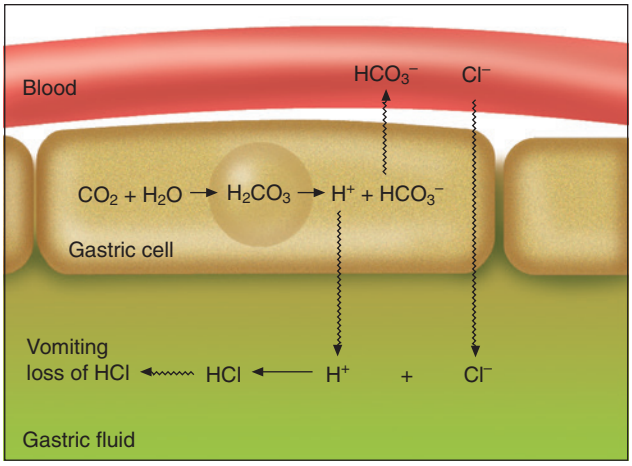

Fig. 14.9 Gastric H^+ loss generates HCO_3^-, creating metabolic alkalosis. (Modified from Beachey W: *Respiratory care anatomy and physiology: foundations for clinical practice*, ed 2, St Louis, 2007, Mosby.)

BOX 14.6 Causes of Metabolic Alkalosis (Increased Plasma HCO_3^-)

Loss of Hydrogen Ions

Gastrointestinal

- Vomiting
- Nasogastric drainage

Renal

- Diuretics (loss of Cl^-, K^+ fluid volume)
- Hypochloremia (increased H^+ secretion and HCO_3^- reabsorption)
- Hypokalemia (increased H^+ secretion and HCO_3^- reabsorption)
- Hypovolemia (increased H^+)

Retention of Bicarbonate Ion

- $NaHCO_3$ infusion or ingestion

From Beachey W: *Respiratory care anatomy and physiology: foundations for clinical practice*, ed 2, St Louis, 2007, Mosby.

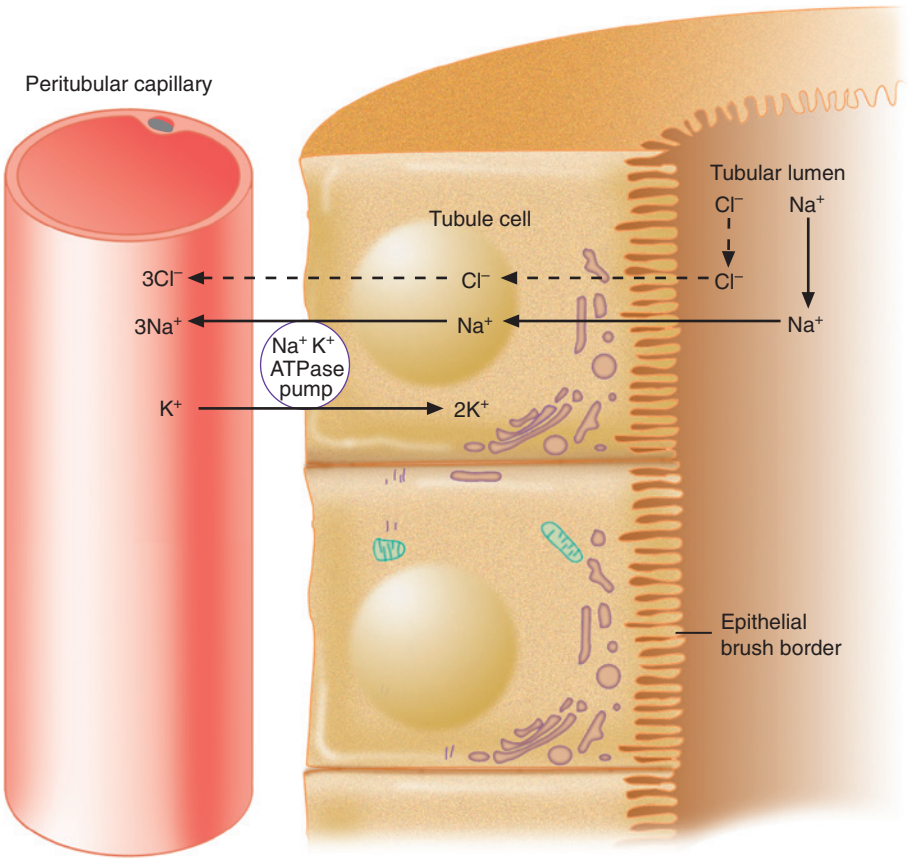

Fig. 14.10 **N^+ Reabsorption Through Primary Active Transport.** The sodium-potassium-adenosine triphosphatase (Na^+,K^+-ATPase) pump generates tubular cell electronegativity by pumping out more Na^+ than it pumps in K^+. This creates both electrostatic and concentration gradients favoring Na^+ diffusion from the filtrate into the tubular cell. Normally, negatively charged Cl^- passively follows Na^+ (cotransport). (Modified from Beachey W: *Respiratory care anatomy and physiology: foundations for clinical practice*, ed 2, St Louis, 2007, Mosby.)

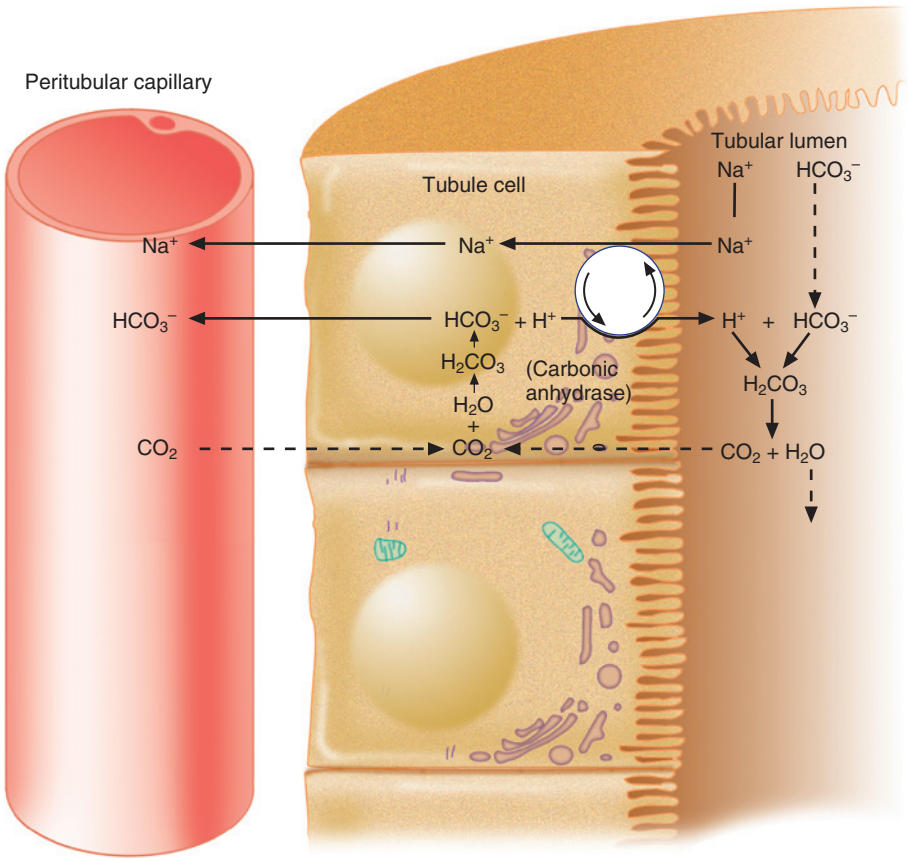

Fig. 14.11 Na^+ Reabsorption Through Secondary Active H^+ Secretion. Through the countertransport process, Na^+ is reabsorbed as H^+ is secreted into the filtrate. HCO_3^- ion is reabsorbed with Na^+ instead of Cl^-. This process becomes more predominant when Cl^- is scarce, and it leads to alkalosis. (Modified from Beachey W: *Respiratory care anatomy and physiology: foundations for clinical practice*, ed 2, St Louis, 2007, Mosby.)

(hypochloremia), less Cl^- is available for reabsorption with Na^+, which means that the kidney relies more on other mechanisms to reabsorb Na^+. These other mechanisms, called *secondary active secretion,* require the kidney to secrete either H^+ or K^+ into the filtrate in exchange for Na^+. In this way, Na^+ is reabsorbed, and filtrate electroneutrality is preserved. Figs. 14.11 and 14.12 illustrate the secondary active secretion process for H^+ and Na^+, which may lead to loss of plasma H^+ (alkalosis) and K^+ (hypokalemia). Preexisting hypokalemia (e.g., from inadequate K^+ intake) in the presence of hypochloremia places an even greater demand on the kidney to secrete H^+ to reabsorb Na^+—that is, hypokalemia leads to alkalosis. Dehydration (fluid volume depletion or hypovolemia) further aggravates alkalosis and hypokalemia because hypovolemia profoundly increases the kidney's stimulus to reabsorb Na^+, which means the kidney depends even more on these secondary mechanisms for Na^+ reabsorption.

Compensation

The expected compensatory response to metabolic alkalosis is hypoventilation (CO_2 retention). Traditionally, it was thought that the hypoxemia accompanying hypoventilation greatly limited respiratory compensation for metabolic alkalosis (i.e., hypoxemia itself stimulates ventilation and should prevent compensatory hypoventilation). However, metabolic alkalosis blunts the hypoxemic stimulus to ventilation—that is, neurologic receptors sensitive to hypoxemia become less sensitive in the presence of alkalemia. Individuals with PaO_2 levels of 50 mm Hg may still hypoventilate to $PaCO_2$ levels of 55 to 60 mm Hg to compensate for metabolic alkalosis.[6] Nevertheless, significant CO_2 retention is not seen often in cases of metabolic alkalosis, probably because metabolic alkalosis commonly coexists with other conditions that may cause hyperventilation, such as anxiety, pain, infection, fever, or pulmonary edema.

Correction

Correction of metabolic alkalosis is aimed at restoring normal fluid volume and electrolyte concentrations, especially K^+ and Cl^- levels. Inadequate fluid volume, especially if coupled with hypochloremia, causes excessive secretion and loss of H^+ and K^+ because of the great need to reabsorb Na^+. In treating this type of alkalosis, it is important to supply adequate fluids containing Cl^-. If hypokalemia is a primary factor, potassium chloride (KCl) is the preferred corrective agent. In rare cases of very severe metabolic alkalosis, acidifying agents, such as dilute HCl may be infused directly into a large central vein.[7]

Metabolic Acid-Base Indicators

Standard Bicarbonate

To eliminate the influence of the hydration reaction on plasma bicarbonate concentration, some laboratories report **standard**

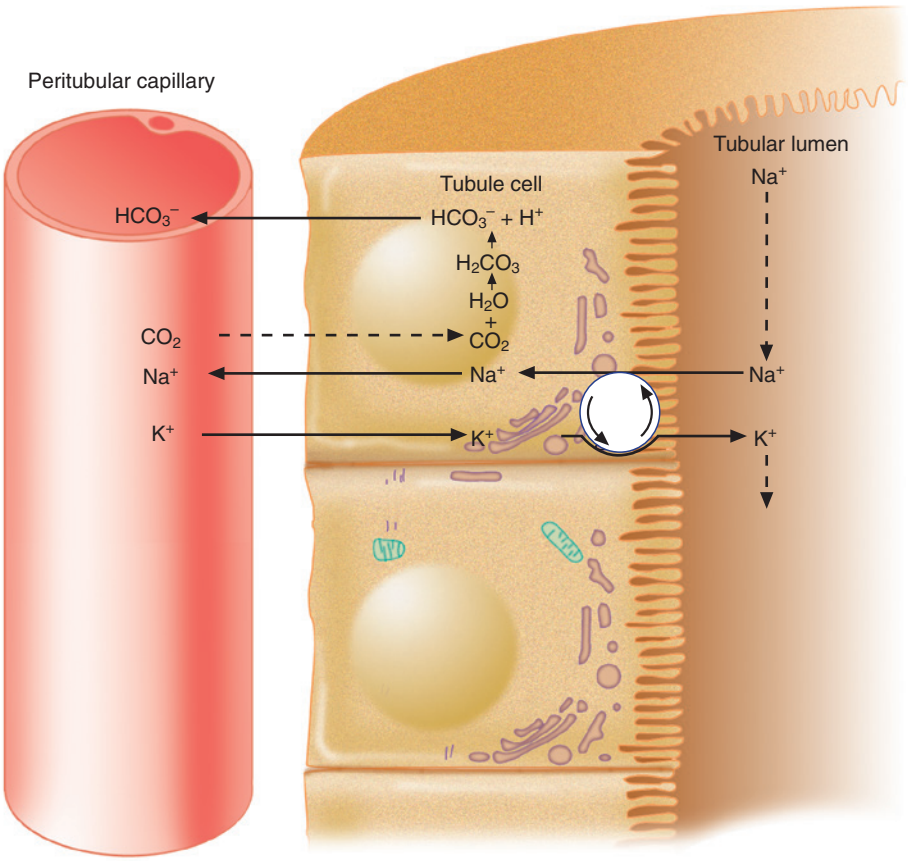

Fig. 14.12 Na^+ Reabsorption Through Secondary Active K^+ Secretion. This mechanism is more likely to occur when Cl^- is scarce and an alkalemia (low H^+) exists. In such instances, hypokalemia develops. (Modified from Beachey W: *Respiratory care anatomy and physiology: foundations for clinical practice*, ed 2, St Louis, 2007, Mosby.)

bicarbonate. The standard bicarbonate is the plasma concentration of HCO_3^- (in mEq/L) obtained from a blood sample that has been equilibrated (at body temperature) with a PCO_2 of 40 mm Hg. This HCO_3^- measurement presumably reflects only the metabolic component of acid-base balance, unhampered by the influence that CO_2 changes have on HCO_3^-. However, the process of standardizing the bicarbonate under in vitro laboratory conditions creates an artificial situation not present in the patient's body. The blood in the patient's vascular system is separated from the extravascular fluid (fluid outside of the vessels) by a thin capillary endothelial membrane, readily permeable to HCO_3^-. When a patient hypoventilates and the blood $PaCO_2$ increases, the plasma HCO_3^- also increases because of the hydration reaction. Consequently, plasma HCO_3^- diffuses out of the capillary into the extravascular fluid until HCO_3^- equilibrium is established between the blood and extravascular fluid. If the patient were now to hyperventilate so that the $PaCO_2$ again was 40 mm Hg, blood HCO_3^- would decrease, and extravascular HCO_3^- would diffuse down its concentration gradient back into the blood until an HCO_3^- equilibrium was established again. This diffusion of HCO_3^- between vascular and extravascular spaces cannot occur in a laboratory blood sample when the blood PCO_2 of a hypercapnic patient is artificially lowered to 40 mm Hg. Thus even the standard bicarbonate is not a perfect measure of purely nonrespiratory factors that influence blood pH.

Base Excess

Base excess (BE) is determined by equilibrating a blood sample in the laboratory to a PCO_2 of 40 mm Hg (at 37°C) and recording the amount of acid or base needed to titrate 1 L of blood to a pH of 7.40. A normal BE is ±2 mEq/L. A positive BE (>+2 mEq/L) indicates a gain of base or loss of acid from nonrespiratory causes. A negative BE (<–2 mEq/L) indicates a loss of base or a gain of acid from nonrespiratory causes. The BE measurement suffers from the same limitation as the standard bicarbonate because it is an in vitro, rather than in vivo, measurement. That is, in hypercapnia, the **buffer base** that diffused into the extravascular fluid in vivo cannot be recovered during laboratory in vitro titrations.

Further, the reliance on BE to quantify metabolic acid-base abnormalities can be misleading. In cases of acute (uncompensated) respiratory acidosis, the BE commonly would be within the normal range, indicating correctly that the disturbance is purely respiratory in origin. However, when renal compensation has occurred to offset chronic hypercapnia, the BE measurement is elevated above the normal range because of the compensatory increase in plasma HCO_3^-.

To illustrate, consider the earlier Mini Clini in which the patient has respiratory acidosis for which the body has compensated by renal retention of HCO_3^-. If this patient's blood were equilibrated in vitro to a $PaCO_2$ of 40 mm Hg, the HCO_3^- would decrease by only 2 to 3 mEq/L to 32 to 33 mEq/L and the pH would increase to much greater than 7.45. This patient's BE would be well above normal. The high BE may lead the clinician to conclude incorrectly that this patient has a primary metabolic alkalosis. However, in this instance, the high BE does not indicate the presence of a pathologic process; it merely reflects the fact that renal compensation has occurred.

Mixed Acid-Base States

Combinations of acid-base disorders may occur in the same patient. A combined disturbance is one in which both respiratory and metabolic disturbances exist and promote the same acid-base disturbance. For example, consider the following arterial blood gas results: a pH of 7.62, $PaCO_2$ of 32 mm Hg, and HCO_3^- of 29 mEq/L. The pH indicates alkalemia, consistent with both the low $PaCO_2$ and the elevated HCO_3^-. This is a combined alkalosis, which means that the patient has two primary acid-base problems (i.e., respiratory and metabolic alkalosis combined); compensation cannot occur in this case. Further, consider the patient in cardiopulmonary arrest whose arterial blood gas results are pH of 7.09, $PaCO_2$ of 77 mm Hg and HCO_3^- of 11 mEq/L, in all likelihood a result of cessation of breathing resulting in hypercapnia, an uncompensated respiratory acidosis, and moderate to severe hypoxemia, which lead to anaerobic metabolism, producing a lactic (metabolic) acidosis and thus a combined respiratory and metabolic acidosis.

SUMMARY CHECKLIST

- The lungs regulate the volatile acid content (CO_2) of the blood, and the kidneys control the fixed acid concentration of the blood.
- The larger the equilibrium constant of an acid, the more the acid molecule dissociates and yields H^+.
- In the *open* bicarbonate buffer system, H^+ is buffered to form the volatile acid, H_2CO_3, which dissociates to form H_2O and CO_2; the CO_2 is exhaled into the atmosphere. In the *closed* nonbicarbonate buffer system, H^+ is buffered to form fixed acids, which accumulate in the body.
- Bicarbonate buffers can buffer only fixed acids, but nonbicarbonate buffers can buffer both fixed and volatile acids.
- The ratio between the plasma $[HCO_3^-]$ and dissolved CO_2 determines the blood pH, according to the H-H equation; a ratio of 20:1 $[HCO_3^-]$ to dissolved CO_2 always yields a normal arterial pH of 7.40.
- The kidneys respond to hypoventilation by reabsorbing HCO_3^-, and they respond to hyperventilation by excreting HCO_3^-.
- The lungs respond to metabolic acidosis by hyperventilating, and they respond to metabolic alkalosis by hypoventilating.
- $PaCO_2$ abnormalities characterize respiratory acid-base disturbances, and $[HCO_3^-]$ abnormalities characterize metabolic acid-base disturbances.
- Hypochloremia forces the kidneys to excrete increased amounts of H^+ and K^+ to reabsorb Na^+, causing alkalosis and hypokalemia.
- Hypokalemia forces the kidneys to excrete increased amounts of H^+ to reabsorb Na^+, causing alkalosis.
- Standard bicarbonate and BE measurements are made under conditions of a normal $PaCO_2$ (40 mm Hg), which means that any abnormality in these measurements reflects only nonrespiratory influences.

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15

Regulation of Breathing

Will Beachey

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Identify where the structures that regulate breathing are located.
- Explain how the inspiratory and expiratory neurons in the medulla establish the basic pattern of breathing.
- Describe the effect that impulses from the pneumotaxic and apneustic centers in the pons have on the medullary centers of breathing.
- Describe the effect of various reflexes on breathing.
- Explain how the central and peripheral chemoreceptors differ in the way they regulate breathing.
- Compare and contrast central chemoreceptors response to respiratory and nonrespiratory acid-base disorders.
- Contrast the regulation of breathing in individuals with chronic hypercapnia with the regulation of breathing in healthy individuals.
- Explain why administering high concentrations of oxygen to patients with chronic hypercapnia poses a special risk that is not present in healthy individuals.
- Describe why ascending to a high altitude has different immediate and long-term effects on ventilation.
- Explain why mechanically ventilated patients with head injuries may benefit from deliberate hyperventilation.

CHAPTER OUTLINE

KEY TERMS

apneustic breathing
apneustic center
blood-brain barrier
chemoreceptors
dorsal respiratory groups (DRGs)
Hering-Breuer inflation reflex
J-receptors
pneumotaxic center
vagovagal reflexes
ventral respiratory groups (VRGs)

Breathing, similar to the heartbeat, is an automatic activity requiring no conscious awareness. In contrast to the heartbeat, breathing patterns can be consciously changed, although powerful neural stimuli overwhelm conscious control soon after one holds the breath. The normal unconscious cycle of breathing is regulated by complex mechanisms that are still not completely understood. The rhythmic cycle of breathing comes from the brainstem, mainly from neurons located in the medulla. Higher brain centers and many systemic receptors and reflexes change the output of the medulla. These different structures function in harmony, precisely controlling ventilatory rate and depth to meet the gas exchange needs of the body. This chapter helps respiratory therapists (RTs) to understand basic physiologic mechanisms that regulate breathing, which allows them and other members of the patient care team to anticipate the effects that various therapies and disease processes have on ventilation.

MEDULLARY RESPIRATORY CENTER

The medulla contains widely scattered groups of respiratory-related neurons, as shown in Fig. 15.1. In the medulla, inspiratory and expiratory neurons are anatomically mixed together where they interact to regulate breathing.[1] The **dorsal respiratory groups (DRGs)** contain mainly inspiratory neurons, whereas the **ventral respiratory groups (VRGs)** contain both inspiratory and expiratory neurons.

Dorsal Respiratory Groups

As shown in Fig. 15.1, DRG neurons are mainly inspiratory neurons located on both sides of the medulla. These neurons send the major inspiratory stimuli to the motor nerves of the diaphragm and external intercostal muscles.[1] Many DRG nerves extend into the VRGs, but few VRG nerve fibers extend into the DRGs.

The vagus and glossopharyngeal nerves transmit many sensory impulses to the DRGs from the lungs, airways, peripheral chemoreceptors, and joint proprioceptors. These impulses change the basic breathing pattern generated in the medulla.

Ventral Respiratory Groups

VRG neurons are located bilaterally in the medulla in two different nuclei and contain inspiratory and expiratory neurons (see Fig. 15.1). Some inspiratory VRG neurons send motor impulses through the vagus nerve to the laryngeal and pharyngeal muscles, abducting the vocal cords and increasing the diameter of the glottis. Other VRG inspiratory neurons transmit impulses to the diaphragm and external intercostal muscles. Still other VRG neurons have mostly expiratory discharge patterns and send impulses to the internal intercostal and abdominal expiratory muscles.

The exact origin of the basic rhythmic pattern of ventilation is unknown. However, two predominant theories of rhythm generation are the *pacemaker hypothesis* and the *network hypothesis*.[2] The pacemaker hypothesis suggests that certain medullary cells have intrinsic pacemaker properties (i.e., rhythmic self-exciting characteristics) and that these cells drive other medullary neurons. The network hypothesis suggests that rhythmic breathing is the result of a particular pattern of interconnections between neurons dispersed throughout the upper part of the VRG, the pre-Bötzinger complex, and the Bötzinger complex. This hypothesis assumes that certain populations of inspiratory and expiratory neurons inhibit one another and that one of the neuron types fires in a self-limiting way, such that it becomes less responsive the longer it fires. There is no definitive proof of either hypothesis.[2]

Inspiratory Ramp Signal

The inspiratory muscles do not receive an instantaneous burst of signals from the dorsal and ventral inspiratory neurons. Rather, the firing rate of DRG and VRG inspiratory neurons increases gradually at the end of the expiratory phase, creating a ramp signal (Fig. 15.2). The inspiratory muscles contract steadily and smoothly, gradually expanding the lungs rather than filling them in an abrupt inspiratory gasp. During exercise, various reflexes and receptors influence the medullary neurons, making the ramp signal much steeper, filling the lungs more rapidly.

During quiet breathing, inspiratory neurons fire with an increasing rate for approximately 2 seconds and then abruptly switch off, allowing expiration to proceed for approximately 3 seconds.[3] At the start of expiration, inspiratory neurons again fire briefly, holding back the early phase of expiration (see Fig. 15.2). The inhibitory neurons that switch off the inspiratory ramp signal are controlled by the pneumotaxic center and

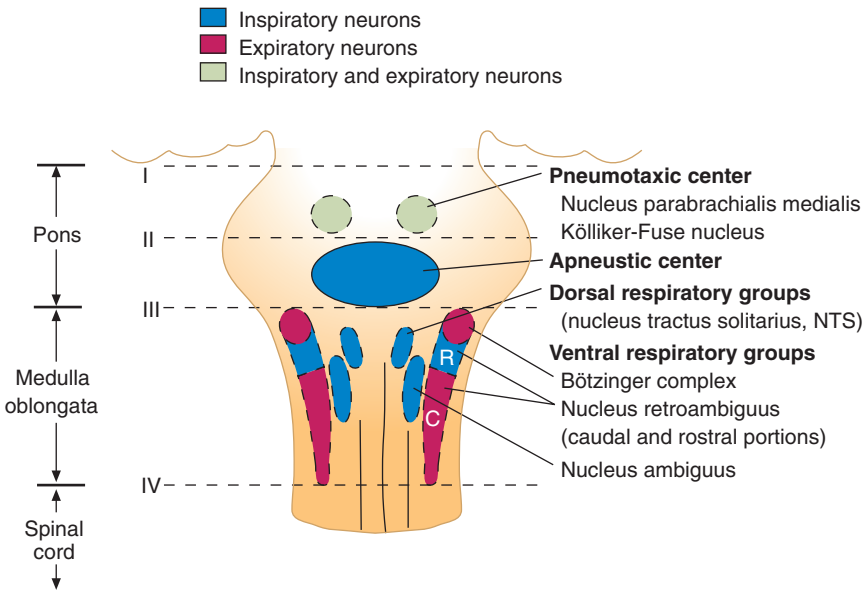

Fig. 15.1 Dorsal View of the Brainstem. Dashed lines *I* to *IV* refer to transections at different levels. (Modified from Beachey W: *Respiratory care anatomy and physiology: foundations for clinical practice,* ed 2, St Louis, 2007, Mosby.)

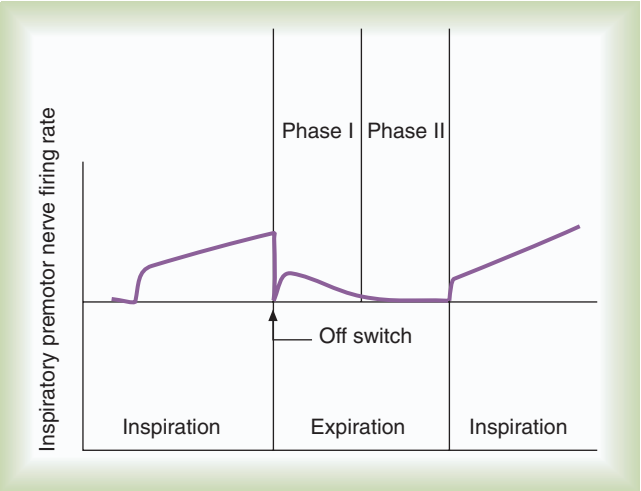

Fig. 15.2 Inspiratory Neural Activity During Breathing Note the inspiratory ramp signal *(left)* and the braking action of inspiratory signals in the early part *(phase I)* of expiration. (Redrawn from Leff AR, Shumacher PT: *Respiratory physiology: basics and applications*, Philadelphia, 1993, Saunders.)

pulmonary stretch receptors, which are discussed later in this chapter.

PONTINE RESPIRATORY CENTERS

If the brainstem is cut above the medulla (see Fig. 15.1, *level III*), spontaneous respiration continues, although in an irregular pattern. The pons does not make breathing rhythmic; rather, it modifies the output of the medullary centers. Fig. 15.1 shows two groups of neurons in the pons: (1) the apneustic center and (2) the pneumotaxic center.

Apneustic Center

The **apneustic center** does not occupy a well-defined anatomic location; its existence and function can be shown only if its connections to the higher pneumotaxic center and vagus nerves are severed. Under such circumstances, the DRG inspiratory neurons fail to switch off, causing prolonged inspiratory gasps interrupted by occasional expirations (**apneustic breathing**). Vagal and pneumotaxic center impulses hold the apneustic center's stimulatory effect on DRG neurons in check.

RULE OF THUMB Apneustic breathing is a sign of damage to the pontine center and is characterized by deep, gasping inspirations with a pause at full inspiration followed by brief partial expirations.

Pneumotaxic Center

The **pneumotaxic center** is a group of neurons located on both sides of the upper pons (see Fig. 15.1). The pneumotaxic center controls the "off-switch" point of the inspiratory ramp, controlling inspiratory time. Strong pneumotaxic signals increase the respiratory rate, and weak signals prolong inspiration and increase tidal volumes. The exact nature of the interaction between the pneumotaxic and apneustic centers is poorly understood. They apparently work together to control the depth of inspiration.[3]

REFLEX CONTROL OF BREATHING

Hering-Breuer Inflation Reflex

The **Hering-Breuer inflation reflex,** described by Hering and Breuer in 1868, is generated by stretch receptors located in the smooth muscle of both large and small airways. When lung inflation stretches these receptors, they send inhibitory impulses through the vagus nerve to the DRG neurons, stopping further inspiration. In this way the Hering-Breuer reflex has an effect similar to that of the pneumotaxic center. In adults the Hering-Breuer reflex is activated only at large tidal volumes (≥800 to 1000 mL), such as during strenuous exercise and apparently is not an important control mechanism in quiet breathing.[2]

Deflation Reflex

Sudden collapse of the lung stimulates strong inspiratory effort. This inspiratory effort may be the result of decreased stretch receptor activity, or it may be caused by the stimulation of other receptors, such as the irritant receptors and J-receptors (discussed later). Although it is unclear which receptors are involved, it is clear that the vagus nerve is the pathway (as it is for the Hering-Breuer reflex) and that the effect is hyperpnea.[1] The deflation reflex is probably responsible for the hyperpnea observed with pneumothorax (air in the pleural space; see Chapter 21).

Head Paradoxical Reflex

In 1889, Head observed that if the Hering-Breuer reflex is blocked by cooling the vagus nerve, lung hyperinflation causes a further increase in inspiratory effort—the opposite of the Hering-Breuer reflex. The receptors for this reflex are called *rapidly adapting receptors* because they stop firing promptly after a volume change occurs. The Head reflex may help maintain large tidal volumes during exercise and may be involved in periodic deep sighs during quiet breathing, which help prevent alveolar collapse, or atelectasis. The Head reflex also may be responsible for the first breaths of a newborn.[1]

Irritant Receptors

Rapidly adapting irritant receptors in the epithelium of the larger conducting airways have vagal sensory nerve fibers. Their stimulation, whether by inhaled irritants or by mechanical factors, causes reflex bronchoconstriction, coughing, sneezing, tachypnea, and narrowing of the glottis. Some of these reflexes, called **vagovagal reflexes,** have both sensory and motor vagal components; they are responsible for laryngospasm, coughing, and slowing of the heartbeat. Endotracheal intubation, airway suctioning, and bronchoscopy often rouse vagovagal reflexes. Physical stimulation of the conducting airways, as with suctioning or bronchoscopy, may cause bronchospasm, coughing, and laryngospasm.

J-Receptors

C-fibers in the lung parenchyma near the pulmonary capillaries are called *juxtacapillary receptors,* or **J-receptors.** Alveolar inflammatory processes (pneumonia), pulmonary vascular congestion (congestive heart failure), and pulmonary edema stimulate these receptors. This stimulation causes rapid, shallow breathing; a sensation of dyspnea; and expiratory narrowing of the glottis.

MINI CLINI

Vagovagal Reflex Stimulation

Problem

Patients who have artificial airways (endotracheal tubes) in place have impaired coughing ability because they cannot close the glottis, which is necessary to generate the high intrapulmonary pressure needed for an effective cough. The clinician sometimes inserts a suction catheter through the endotracheal tube and into the trachea to remove excess secretions. The tip of the catheter may enter a mainstem bronchus during this procedure.

Consider a situation in which the respiratory therapist (RT) is suctioning the airway of a patient whose lungs are being mechanically ventilated; the cardiac monitoring screen at the patient's bedside shows a sudden decrease in heart rate and blood pressure. Upon withdrawing the catheter and manually ventilating the patient's lungs with 100% oxygen, the RT notes that the heart rate and blood pressure return to their previous levels. What is the explanation for your patient's response?

Discussion

The suction catheter undoubtedly stimulated tracheal and bronchial irritant receptors, eliciting a vagovagal reflex. The heart responds to vagal (parasympathetic) stimulation by slowing its rate (bradycardia). Severe bradycardia decreases the cardiac output. Consequently, blood pressure falls. Irritation from the suction catheter also stimulates cough receptors in the trachea and carina, causing vigorous cough efforts. Such coughing may increase intrathoracic pressure enough to momentarily reduce the venous blood return to the heart, decreasing the blood pressure momentarily. The clinician can diminish the likelihood of this complication by following these guidelines:

1. When the suction catheter meets resistance on insertion, do not force it down farther; instead, withdraw it slightly before applying suction.
2. As you withdraw the catheter, apply suction while twirling the catheter between your thumb and forefinger; do not move it in an up-and-down jabbing motion.

The vagovagal reflex is also often elicited during endotracheal intubation. A local anesthetic sprayed into the pharynx and applied to the endotracheal tube helps curb this reflex.

Peripheral Proprioceptors

Proprioceptors in muscles, tendons, joints, and pain receptors in muscles and skin send stimulatory signals to the medullary respiratory center. Such stimuli increase medullary inspiratory activity and cause hyperpnea.[4] For this reason, moving the limbs, slapping or splashing cold water on the skin, and other painful stimuli stimulate ventilation in patients with respiratory depression. Proprioceptors in joints and tendons may be important in initiating and maintaining increased ventilation at the beginning of exercise.

Muscle Spindles

Muscle spindles in the diaphragm and intercostal muscles are part of a reflex that helps the muscles to compensate for an increased load, which may occur with decreased lung compliance or increased airway resistance. Muscle spindles are sensors located on intrafusal muscle fibers, arranged parallel to the main extrafusal muscle fibers (Fig. 15.3). The extrafusal fibers that elevate the ribs are innervated by motor fibers (α-fibers) different from the fibers that innervate the intrafusal spindle fibers (γ-fibers). When the main extrafusal muscle fiber and the intrafusal fibers

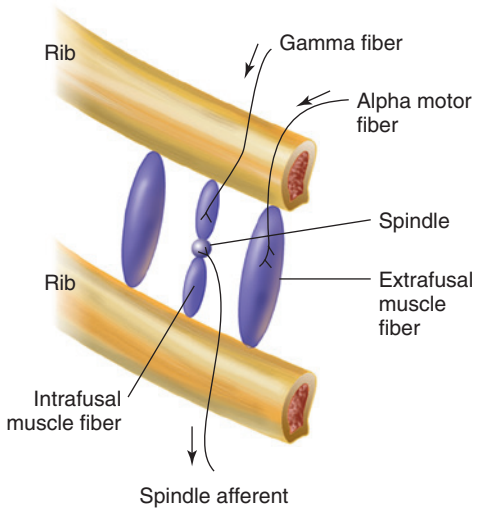

Fig. 15.3 Stretch-Sensitive Muscle Spindle Located on the Intrafusal Fibers of Intercostal Muscles. Motor innervation for intrafusal fibers (γ-nerve fibers) is different than for extrafusal fibers (α-nerve fibers). Spindle afferent nerve fibers synapse with alpha motor neurons in the spinal cord, creating a single synapse reflex arc.

contract simultaneously, the sensing element *(spindle)* of the intrafusal muscle fiber stretches and sends impulses over spindle afferent (sensory) nerves directly to the spinal cord (see Fig. 15.3). The spindle's afferent nerve synapses directly with the α-motor neuron in the spinal cord, sending impulses back to the main extrafusal muscle. α-Motor neuron impulses cause the main extrafusal muscle fibers to contract with greater force, shortening the nearby intrafusal fibers. The stretch-sensitive spindle is thus unloaded, and its impulses cease. In this way, inspiratory muscle force adjusts to the load imposed by decreased lung compliance, as may occur in pulmonary fibrotic diseases, or by increased airway resistance, as would be present in asthma.

CHEMICAL CONTROL OF BREATHING

The body maintains the proper amounts of oxygen (O_2), carbon dioxide (CO_2), and hydrogen ions (H^+) in the blood mainly by regulating ventilation. Physiologic mechanisms that monitor these substances in the blood allow ventilation to respond appropriately to maintain homeostasis. An increase in blood H^+ concentration stimulates specialized nerve structures called **chemoreceptors.** As a result, the chemoreceptors transmit impulses to the medulla, increasing ventilation. Centrally located chemoreceptors in the medulla respond to H^+, which normally arises from dissolved CO_2 in the cerebrospinal fluid (CSF). Peripherally located chemoreceptors in the fork of the common carotid arteries and the aortic arch are also sensitive to H^+ and indirectly to CO_2. These receptors are also indirectly sensitive to hypoxemia because hypoxemia increases the sensitivity of the peripheral chemoreceptors to H^+.[2]

Central Chemoreceptors

H^+, not CO_2 molecules, stimulate highly responsive chemosensitive nerve cells, located on both sides of the medulla. Nevertheless,

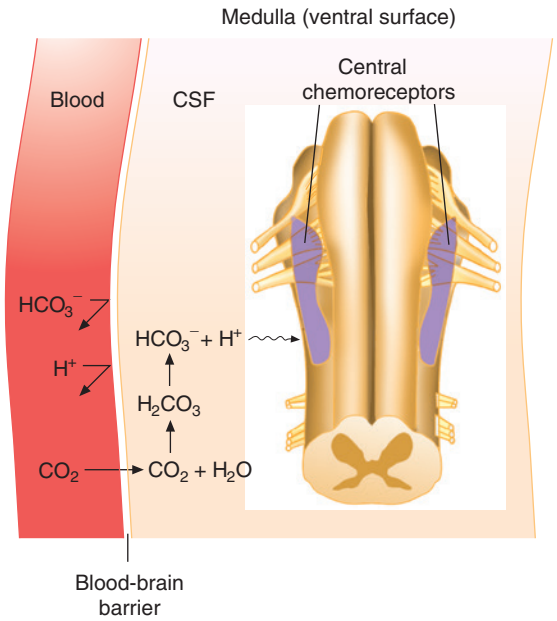

Fig. 15.4 CO_2 Stimulates the Medullary Chemoreceptors by Forming H^+ in the Cerebrospinal Fluid *(CSF)*. The blood-brain barrier is almost impermeable to H^+ and HCO_3^- but is freely permeable to CO_2. (Modified from Beachey W: *Respiratory care anatomy and physiology: foundations for clinical practice,* ed 2, St Louis, 2007, Mosby.)

these central chemoreceptors are extremely sensitive to CO_2 in an indirect fashion. These chemoreceptors are not in direct contact with arterial blood (Fig. 15.4). Instead, they are bathed in the CSF, separated from the blood by a semipermeable membrane called the **blood-brain barrier.** This membrane is almost impermeable to H^+ and HCO_3^-, but it is freely permeable to CO_2. When $PaCO_2$ increases, CO_2 diffuses rapidly through the blood-brain barrier into the CSF. In the CSF, CO_2 reacts with water (H_2O) to form H^+ and HCO_3^- (see Fig. 15.4). The H^+ ions generated in this fashion stimulate the central chemoreceptors, which in turn stimulate the medullary inspiratory neurons. In this way, $PaCO_2$ is indirectly the primary minute-to-minute controller of ventilation. CO_2 diffusing from the blood into the CSF increases $[H^+]$ almost instantly, exciting the chemoreceptors within seconds.

RULE OF THUMB Alveolar ventilation increases by approximately 2–3 L/min for each 1 mm Hg increase in $PaCO_2$.[5]

The stimulatory effect of chronically high CO_2 on the central chemoreceptors gradually declines over 1 or 2 days because the kidneys reabsorb HCO_3^- ions in response to respiratory acidosis, bringing the blood pH level back toward normal. The increased number of HCO_3^- ions in the blood eventually diffuses across the blood-brain barrier into the CSF, where they buffer H^+ and bring the CSF pH level back to normal. This activity removes the stimulus to the chemoreceptors, and ventilation decreases. Thus an acute increase in $PaCO_2$ has a powerful effect on ventilation, which tends to diminish after 1 or 2 days of adaptation.

Peripheral Chemoreceptors

The peripheral chemoreceptors are small, highly vascular structures known as the *carotid* and *aortic bodies*. The carotid bodies are located bilaterally in the bifurcations of the common carotid arteries. The aortic bodies are found in the arch of the aorta. These neural structures increase their firing rates in response to increased arterial $[H^+]$ regardless of its origin (i.e., whether from fixed acid accumulation or increased CO_2). The carotid bodies send their impulses to the respiratory centers in the medulla via the glossopharyngeal nerve, whereas the aortic bodies send their impulses over the vagus nerve. The carotid bodies exert much more influence over the respiratory centers than the aortic bodies do, especially with respect to arterial hypoxemia and acidemia.[1]

Because the carotid bodies receive an extremely high rate of blood flow, they have little time to remove O_2 from the blood. Therefore venous blood leaving the carotid bodies has almost the same O_2 content as the arterial blood entering them. The carotid bodies are exposed at all times to arterial blood, not venous blood, and they sense arterial (not venous) $[H^+]$.

Response to Decreased Arterial Oxygen

The chemosensitive elements of the carotid body are neuron-like *glomus cells* that synapse directly with the glossopharyngeal nerve. Glomus cell membranes have O_2-sensitive potassium (K^+) channels that close when arterial PO_2 falls. Intracellular potassium concentration $[K^+]$ plays an important role in regulating the electrical voltage difference across the cell membrane. At rest, the glomus cell membrane is *polarized* (i.e., its interior is negatively charged with respect to the extracellular environment). Intracellular $[K^+]$ affects the cell membrane's *excitability*, or how easily the cell membrane *depolarizes*. When PaO_2 falls to sufficiently low levels, the glomus cell's O_2-sensitive K^+ channels close, preventing K^+ from diffusing out of the cell; because of the trapped positively charged K^+, the intracellular environment loses some of its electrical negativity, which causes the membrane to depolarize. Depolarization causes voltage sensitive calcium ($Ca+^2$) channels to open, allowing an influx of extracellular Ca^{+2} into the glomus cell; this stimulates the glomus cell to release neurotransmitters that activate the glossopharyngeal nerve, which transmits stimulatory impulses to the medullary DRG neurons. In this way, arterial hypoxemia stimulates an increase in ventilation.[3]

Because of their extremely high blood flow rates, the carotid bodies respond to decreased arterial *partial pressure* of O_2 rather than to an actual decrease in arterial O_2 *content*. That is, the amount of O_2 that the carotid bodies extract from each unit of rapidly flowing blood is so small that their O_2 needs are met entirely by dissolved O_2 in the plasma—which depends on the PaO_2. This is why conditions associated with low arterial O_2 content but normal PaO_2 (e.g., anemia and carbon monoxide poisoning) do not stimulate ventilation.[5]

RULE OF THUMB Abnormally low PaO_2 stimulates the peripheral chemoreceptors, not low arterial O_2 content per se; for example, anemia with a normal range PaO_2 does not activate the peripheral chemoreceptors.

When pH and $PaCO_2$ are normal (pH = 7.40 and $PaCO_2$ = 40 mm Hg), the nerve-impulse transmission rate of the carotid bodies does not increase significantly until the PaO_2 decreases to approximately 60 mm Hg.[5] If PaO_2 decreases further from 60 mm Hg to 30 mm Hg, the rate of impulse transmission increases sharply. A decrease in PaO_2 from 60 to 30 mm Hg corresponds to the sharpest decrease in O_2 content on the O_2-hemoglobin (Hg) equilibrium curve (i.e., the steepest part of the curve). Arterial hypoxemia does not stimulate ventilation greatly until the PaO_2 decreases to less than 60 mm Hg, which is why ventilation increases in healthy people ascending to high altitudes.

Oxygen plays no role in the drive to breathe in healthy individuals at sea level. High altitude causes a healthy person's ventilation to increase because low barometric pressure decreases the inspired and arterial PO_2 values, which stimulate the peripheral chemoreceptors. However, the resulting increase in ventilation is less than expected because hyperventilation decreases $PaCO_2$ and increases arterial pH. The increased pH depresses the medullary respiratory center, counteracting the excitatory effect of a low PaO_2 on peripheral chemoreceptors. Hypoxemia-induced hyperventilation may be impossible in certain conditions, such as severe chronic obstructive pulmonary disease (COPD), in which lung function is so poor that the stimulatory effect of hypoxemia on ventilation fails to decrease $PaCO_2$ regardless of the patient's effort. In such instances, there is no alkalosis to counteract the stimulatory effects of hypoxemia on ventilation.

RULE OF THUMB Hypoxemia is not associated with an increased drive to breathe until PaO_2 is <60 mm Hg, after which the drive to breathe increases in proportion to the decrease in PaO_2.

Response to Increased $PaCO_2$ and Hydrogen Ions

For a given increase in $PaCO_2$ or $[H^+]$, the carotid bodies are less responsive than the central chemoreceptors. The peripheral chemoreceptors account for only 20% to 30% of the ventilatory response to hypercapnia.[5] However, they respond to increased arterial $[H^+]$ more rapidly than the central chemoreceptors. The explanation is that, in contrast to the central chemoreceptors, the carotid bodies are exposed directly to arterial blood. Thus the body's initial ventilatory response to metabolic acidosis is fairly quick, even though H^+ crosses the blood-brain barrier with difficulty.

As stated earlier, hypoxemia increases the sensitivity of the peripheral chemoreceptors to H^+ and indirectly to $PaCO_2$. Conversely, high PaO_2 (hyperoxia) *decreases* the peripheral chemoreceptors' PCO_2 sensitivity to almost zero.[2] This means that when the PaO_2 is high, the ventilatory response to $PaCO_2$ is mainly due to the central chemoreceptors, which are unaffected by hypoxemia.

Because the only effect of hypoxia on the peripheral chemoreceptors is to increase their sensitivity to arterial $[H^+]$—and indirectly to $PaCO_2$—the following statements are true: (1) High PO_2 causes the peripheral chemoreceptors to become almost unresponsive to PCO_2, and (2) low $PaCO_2$ causes peripheral chemoreceptors to become almost unresponsive to hypoxemia.[2] Coexisting arterial hypoxemia, acidemia, and high $PaCO_2$ (i.e., asphyxia) maximally stimulate the peripheral chemoreceptors.

MINI CLINI

Delayed Hyperventilation at High Altitude

Problem

If a person ascends to an elevation of 10,000 feet above sea level, his or her inspired PO_2 decreases because of low barometric pressure. This excites the peripheral chemoreceptors and causes an increase in ventilation. Why must a day or so pass at this altitude before ventilation increases to its maximal level?

Solution

Hypoxia-induced hyperventilation reduces $PaCO_2$ and creates alkalemia. This condition produces an alkalotic cerebrospinal fluid (CSF) because the blood-brain barrier is nearly impermeable to HCO_3^- ions; that is, as CO_2 diffuses out of the CSF in response to the low arterial blood PCO_2, HCO_3^- remains behind in the CSF. The central chemoreceptors are exposed to an alkalotic environment, diminishing the effect of the hypoxic ventilatory stimulus on peripheral chemoreceptors. In other words, the development of respiratory alkalosis limits the degree of hypoxia-induced hyperventilation. Over the first 24 h or so of hyperventilation, HCO_3^- gradually diffuses out of the CSF across the blood-brain barrier, restoring the CSF pH level to normal. In addition, the kidneys excrete HCO_3^- to compensate for the respiratory alkalemia. Consequently, the blood pH level decreases toward normal, and the hypoxic ventilatory stimulus keeps the $PaCO_2$ low. As the CSF pH level returns to normal, the progressively unrestrained hypoxic stimulus increases ventilation further. It takes approximately 24 h of high-altitude exposure before ventilation increases to its maximal level.

Individuals with chronic hypercapnia secondary to advanced COPD have depressed ventilatory responses to acute increases in arterial CO_2, partly because of their altered acid-base status and partly because their impaired lung mechanics prevent them from increasing their ventilation adequately.[1] The altered acid-base status arises from the preexisting high levels of blood buffer base, a compensatory response to chronic respiratory acidosis (see Chapter 14).

RULE OF THUMB The ventilatory response to hypoxemia is greatly enhanced by hypercapnia and acidemia.

Control of Breathing in Chronic Hypercapnia

A sudden increase in arterial PCO_2 causes an immediate increase in ventilation because CO_2 rapidly diffuses from the blood into the CSF, increasing the $[H^+]$ surrounding central chemoreceptors. If $PaCO_2$ increases gradually over many years, as might occur in the development of severe COPD and worsening lung mechanics, the kidneys compensate by increasing the plasma $[HCO_3^-]$, which keeps arterial pH within normal limits. As plasma HCO_3^- levels increase, HCO_3^- ions slowly diffuse across the blood-brain barrier, keeping CSF pH within its normal range. Because the central chemoreceptors respond to $[H^+]$, not the CO_2 molecule, they sense a normal pH environment, even though the $PaCO_2$ is abnormally high.

This adaptation explains why the chronically high $PaCO_2$ of people with severe COPD does not overly stimulate their ventilation. Instead, the hypoxemia that accompanies chronic hypercapnia becomes a major part of the minute-to-minute breathing stimulus, increasing the nerve impulses peripheral chemoreceptors

transmit to the medulla, which stimulates ventilation. Patients with severe COPD are generally hypoxemic when breathing room air because their lungs have severe ventilation and blood flow mismatches. It stands to reason that breathing supplemental O_2 would increase the PaO_2, which would in turn decrease carotid body stimulation, ultimately decreasing ventilation and increasing $PaCO_2$.

Oxygen-Associated Hypercapnia

The $PaCO_2$ of chronically hypercapnic patients with COPD sometimes increases acutely after these patients are given supplemental O_2. The reason for this phenomenon has been a subject of much debate and misunderstanding. The traditional explanation for this phenomenon has been that O_2 breathing removes the hypoxic ventilatory stimulus and induces hypoventilation, but this explanation is probably overly simplified. The reduction in minute ventilation after O_2 breathing in patients with advanced COPD is generally not severe enough to account for the increased $PaCO_2$. The most significant reason for hypercapnia following O_2 breathing in severe COPD is that it worsens the ventilation-perfusion ($\dot{V}/\dot{Q}$) relationships in the lungs.

When patients with severe COPD breathe supplemental O_2, it abolishes the hypoxic pulmonary vasoconstriction present in poorly ventilated lung regions. As a result, vascular resistance of underventilated regions decreases, and these areas receive more blood flow, drawing blood away from well-ventilated regions (Fig. 15.5). At the same time that poorly ventilated regions receive more blood flow, they become even less ventilated as O_2-rich inspired gas washes out resident nitrogen gas, making these alveoli more subject to absorption atelectasis (i.e., O_2 may be absorbed by the pulmonary circulation more rapidly than the slowed ventilation can replenish it—notice the further decreased $\dot{V}$ in Fig. 15.5B). As a result, inspired gas flows preferentially to the compliant, already well-ventilated alveoli (see Fig. 15.5B), increasing their $\dot{V}/\dot{Q}$. To worsen matters, the increased $\dot{V}/\dot{Q}$ in these alveoli is exaggerated further as a greater proportion of the cardiac output than before is redirected to poorly ventilated alveoli, because their vascular resistance was reduced by O_2 breathing.

To summarize, O_2 breathing causes more blood flow to be directed to poorly ventilated alveoli, which takes blood flow away from well-ventilated alveoli. The key point is that already underventilated alveoli receive additional blood flow, which causes blood PCO_2 to increase further. These events can occur without a decrease in overall minute ventilation.

It is important to keep in mind that the diagnosis of COPD on a patient's medical record does not mean the patient has a chronically high $PaCO_2$ or that O_2 administration may be associated with hypercapnia. These characteristics are present only in patients with severe end-stage disease, which includes only a small percentage of patients with a COPD diagnosis. Concern about O_2-associated hypercapnia and acidemia is not justifiable in most patients with a diagnosis of COPD. Oxygen should never be withheld from acutely hypoxemic patients with COPD for fear of inducing hypoventilation and hypercapnia. Tissue oxygenation is the overriding priority; however, the RT must be prepared to support ventilation mechanically if O_2 administration is accompanied by severe hypoventilation.

Central Chemoreceptor Response to Acute Carbon Dioxide Increase in Chronic Hypercapnia

As discussed earlier, the kidneys compensate for the acidic effects of chronic hypercapnia by increasing the plasma HCO_3^- level, keeping the medullary chemoreceptor pH environment in the normal range. This does not mean that the medullary chemoreceptors cannot respond to further *acute* increases in $PaCO_2$. A sudden elevation in $PaCO_2$ immediately crosses the blood-brain barrier into the CSF, generating H^+ that then stimulates the medullary chemoreceptors. However, the resulting ventilatory

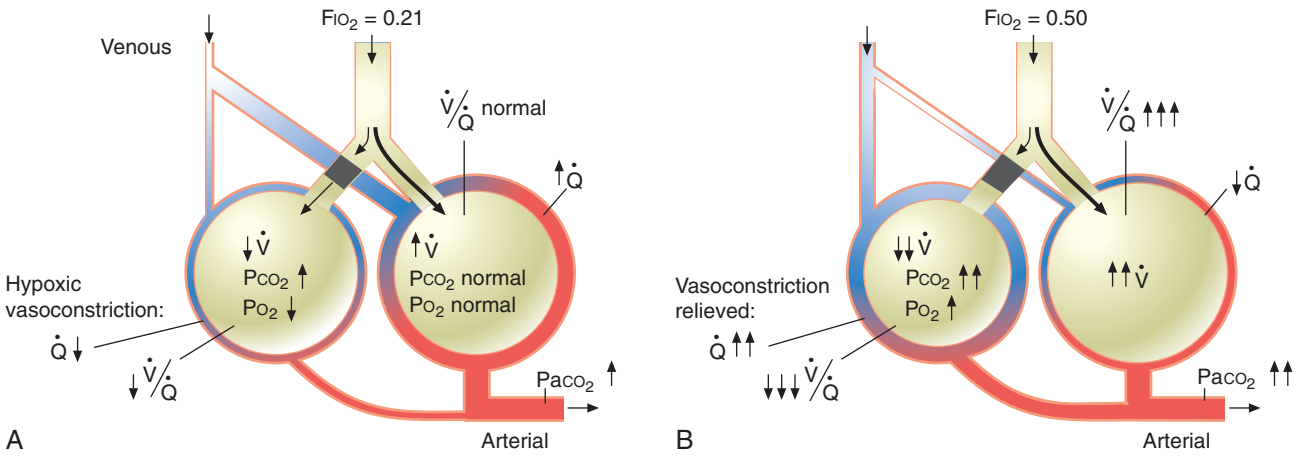

Fig. 15.5 Proposed Mechanism Whereby O_2 Administration in Chronically Hypercapnic Individuals Induces Further Hypercapnia by Creating $\dot{V}/\dot{Q}$ Mismatches. (A) Low $\dot{V}/\dot{Q}$ unit *(left)* is hypoxic and hypercapnic while breathing ambient air; this induces pulmonary vasoconstriction. (B) Breathing 50% O_2 predisposes the poorly ventilated unit to absorption atelectasis, further decreasing its ventilation, and simultaneously relieves hypoxic vasoconstriction, increasing its blood flow. These events (1) lower the poorly ventilated unit's $\dot{V}/\dot{Q}$ ratio further and (2) divert blood flow away from and ventilation toward already well-ventilated units. The latter increases alveolar dead space (high $\dot{V}/\dot{Q}$). (Modified from Beachey W: *Respiratory care anatomy and physiology: foundations for clinical practice,* ed 2, St Louis, 2007, Mosby.)

response is depressed for chemical and mechanical reasons: (1) The blood's increased buffering capacity (high HCO_3^- level) in chronic hypercapnia prevents arterial pH from decreasing as sharply as it would in normal conditions, and (2) abnormal breathing mechanics hamper the lung's ability to increase ventilation appropriately. To illustrate the blood's changed buffering capacity, compare a healthy person (pH = 7.40, $PaCO_2$ = 40 mm Hg, HCO_3^- = 24 mEq/L) with a chronically hypercapnic person (pH = 7.38, $PaCO_2$ = 60 mm Hg, HCO_3^- = 34 mEq/L). A sudden increase of 30 mm Hg in $PaCO_2$ of both individuals causes the healthy person's arterial pH to decrease to 7.21 and the hypercapnic person's pH to decrease to only 7.24. (These values are calculated using the Henderson-Hasselbalch equation, assuming a 1 mEq/L increase in plasma HCO_3^- concentration for each acute increase of 10 mm Hg in $PaCO_2$.)

RULE OF THUMB For the same increase in $PaCO_2$, the central chemoreceptors of a chronically hypercapnic patient experience less stimulation than the central chemoreceptors of normal individuals.

RULE OF THUMB Because maintaining tissue oxygenation is the priority, supplemental oxygen should not be withheld from hypoxemic COPD patients in exacerbation, in spite of concerns that acute hypercapnia and acidemia might develop.

VENTILATORY RESPONSE TO EXERCISE

Strenuous exercise can increase CO_2 production and O_2 consumption by 20-fold.[3] Ventilation normally keeps pace with CO_2 production, keeping $PaCO_2$, PaO_2, and arterial pH constant. Because arterial blood gases do not change during normal exercise, some other mechanism must be responsible for the increased ventilation in healthy individuals during exertion.

The exact mechanism responsible for this increase in ventilation is not well understood. Especially mysterious is the abrupt increase in ventilation at the onset of exercise, long before any chemical or humoral changes can occur in the body. Two leading theories for this phenomenon are: (1) When the cerebral motor cortex sends impulses to exercising muscles, it apparently sends collateral excitatory impulses to the medullary respiratory centers; (2) exercising limbs moving around their joints stimulate proprioceptors, which transmit excitatory impulses to the medullary centers.[1,3] Evidence also suggests that the sudden increase in ventilation at the onset of exercise is a learned response.[1,3] With repeated experience, the brain may learn to anticipate the proper amount of ventilation required to maintain normal blood gases during exercise.

CARBON DIOXIDE AND CEREBRAL BLOOD FLOW

CO_2 plays an important role in regulating cerebral blood flow. Its effect is mediated through the formation of H^+ by CO_2.[6] Increased PCO_2 dilates cerebral vessels, increasing cerebral blood flow, whereas decreased PCO_2 constricts cerebral vessels and reduces cerebral blood flow. In patients with traumatic brain injury (TBI), the brain swells acutely; this increases the intracranial cerebral pressure (ICP) in the rigid skull to such high levels that blood supply to the brain might be severely reduced or cut off, causing cerebral hypoxia *(ischemia)*. That is, high ICP may exceed cerebral arterial pressure and stop blood flow to the brain.

Although controversial, mechanical hyperventilation has been used as a short-term therapy in TBI patients to decrease $PaCO_2$ and reduce the cerebral blood flow and ICP. In patients with TBI, a cerebral blood volume reduction of only 0.5 to 0.7 mL reduces the ICP by 1 mm Hg; for every 1 mm Hg acute reduction in $PaCO_2$ (between 20 and 60 mm Hg), there is a 3% reduction in cerebral blood flow. Although an acute reduction in $PaCO_2$ reduces ICP, it also reduces cerebral blood flow and potentially causes cerebral ischemia. For this reason, the practice of inducing mechanical hyperventilation in patients with TBI is debatable, primarily because it may well reduce blood flow and O_2 to an already injured organ. On the other end of the spectrum, *hypoventilation* in a head trauma patient with an already high ICP is especially dangerous because hypercapnia dilates cerebral vessels and elevates the ICP even more.

The debate centers around the question of whether a hyperventilation-induced decrease in cerebral blood flow creates an additional hypoxic insult to the already ischemic brain and whether patients managed in this way have better clinical outcomes than patients in whom hyperventilation is not instituted. A comprehensive review of the subject published in 2005 concluded that hyperventilation produced no advantage in long-term clinical outcome of TBI compared with ventilation that maintained $PaCO_2$ in the normal range.[6] The authors concluded that

MINI CLINI

Mechanical Hyperventilation of a Patient With Traumatic Brain Injury

Problem

An automobile accident victim, previously healthy, sustained a closed head injury with accompanying high ICP. Mechanical ventilation in the intensive care unit is required, and the physician asks the RT for input regarding ventilator strategies and what $PaCO_2$ should be targeted?

Discussion

More than 40 years ago, clinical investigators showed that the volume of the swollen brain could be reduced by decreasing the $PaCO_2$. Since then, mechanical hyperventilation has been a cornerstone in managing increased ICP associated with TBI.[6] Hyperventilation decreases ICP by causing cerebral vasoconstriction, ultimately reducing cerebral blood volume. This subject is not without controversy because hyperventilation-induced cerebral vasoconstriction has the potential to reduce cerebral blood flow to levels that cause cerebral hypoxia *(ischemia)*. This concern has lessened enthusiasm for hyperventilation in TBI. Both the proponents and the opponents of hyperventilation recognize that TBI poses an ischemic threat to the brain; proponents believe that the reduction of cerebral blood flow ultimately improves cerebral oxygenation by reducing the ICP, which helps to sustain the cerebral perfusion pressure. Opponents point out that no other hypoxic organ in the body is treated by reducing its blood flow and O_2 supply. (Hyperventilation in this context is generally defined as $PaCO_2 < 35$ mm Hg.[6])

in TBI, hyperventilation therapy should be considered only for patients with high ICPs; no benefit can be expected if ICP is normal. They further concluded that hyperventilation is most appropriate in the second or third day after injury because cerebral blood flow is lowest in the first 24 hours after injury, and the risk for inducing ischemia through hyperventilation is greatest during this time. The authors advise against the hyperventilation of patients with TBI to $PaCO_2$ less than 30 mm Hg because of the increased danger of cerebral ischemia. All of these conclusions were affirmed in a more recent review.[7] Finally, hyperventilation is effective for only approximately 24 to 48 hours because compensatory renal elimination of HCO_3^- in the face of alkalemia restores the acid-base balance, negating the vasoconstrictive effect of hypocapnia. In any case, *hypoventilation* in patients with head trauma and increased ICP is especially dangerous because hypercapnia dilates cerebral vessels and increases ICP further. Even opponents of hyperventilation generally maintain $PaCO_2$ of patients with TBI in the low to normal range at approximately 35 mm Hg.[8]

SUMMARY CHECKLIST

- The DRGs and VRGs of neurons in the medulla generate the basic cyclic breathing pattern.
- Apneustic center impulses prevent medullary inspiratory neurons from switching off, creating a prolonged, gasping inspiration.
- Impulses from the pneumotaxic center inhibit the apneustic center and inspiratory neurons of the DRGs, shortening inspiratory time and increasing respiratory rate.
- Various reflexes from peripheral sources affect the breathing pattern by altering the output of the medullary center.
- Central chemoreceptors in the medulla are bathed in the CSF, separated from arterial blood by a semipermeable membrane called the *blood-brain barrier*.
- The blood-brain barrier is almost impermeable to arterial H^+ and HCO_3^- ions, but it is freely permeable to arterial CO_2.
- Central chemoreceptors stimulate increased ventilation in response to the H^+ formed in the CSF by the reaction between arterial CO_2 and H_2O.
- Peripheral chemoreceptors, located mainly in the carotid bodies, respond to arterial $[H^+]$; hypoxemia increases the sensitivity of chemoreceptors to a given arterial pH.
- The peripheral chemoreceptors are indirectly stimulated by arterial CO_2 to the extent that CO_2 reacts with H_2O to form H^+.
- The primary stimulus for breathing in healthy individuals is arterial CO_2, mediated through the central chemoreceptors via H^+ formed by the reaction between H_2O and CO_2 molecules.
- The secondary stimulus for breathing in healthy individuals is arterial hypoxemia, which is not clinically significant until PaO_2 is less than 60 mm Hg.
- Breathing of patients with chronic, compensated hypercapnia is driven more by the hypoxic stimulus than when acid-base status is normal.
- Acute arterial CO_2 retention and acidosis is only associated with oxygen therapy in patients with severe chronic hypercapnia as seen in end-stage COPD.
- O_2 should never be withheld for any reason from patients with severe hypoxemia.
- CO_2 dilates cerebral blood vessels and increases ICP; reducing arterial CO_2 constricts cerebral vessels and decreases ICP.

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16

Bedside Assessment of the Patient

Richard H. Kallet

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Describe why patient interviews are necessary and the appropriate interview techniques.
- Differentiate social from personal space and how these spaces are used during an interview.
- List four influential factors affecting communication between the respiratory therapist (RT) and the patient.
- Differentiate between signs and symptoms.
- List the five neutral questions used to elicit information about a patient's symptoms.
- Differentiate between dyspnea and breathlessness.
- Recall the three factors that generate the perception of breathing.
- List the four interview questions used to assess the degree and context of dyspnea in patients.
- Recall the four factors necessary to generate an effective cough.
- Identify five important cough characteristics that the RT is responsible for monitoring.
- Describe the differences between infected and non-infected sputum.
- Explain the differences between massive and non-massive hemoptysis and their associated clinical conditions.
- Explain the differences between pleuritic and non-pleuritic chest pain and their associated clinical conditions.
- Define the temperature threshold for fever and describe the different sources producing fever.
- Describe the different characteristics of pedal edema and the diseases associated with it.
- List the five major categories of patient information gleaned from reviewing the medical record.
- Calculate smoking history in pack-years.
- Describe the four general steps taken during the physical examination of a patient.
- Define the term sensorium and list the four criteria used to determine its presence.
- List the five elements that constitute basic vital signs and recite the normal parameters for each variable.
- Identify the seven anatomic sites where a pulse pressure can be palpated during a physical exam.
- Define hypertension and describe the three categories used to describe it.
- Define hypotension and explain how it differs from shock.
- Describe the steps required to measure blood pressure using a blood pressure cuff and stethoscope.
- Describe how examination of the head and neck can reveal signs associated with chest diseases such as chronic obstructive pulmonary disease (COPD) and congestive heart failure (CHF).
- Describe common signs of increased work of breathing gleaned from physical exam of the neck and chest.
- Differentiate the two archetypal breathing patterns associated with restrictive versus obstructive lung disease.
- Describe the five abnormal breathing patterns associated with neurological disease and injury.
- Describe how lung hyperinflation and diaphragmatic dysfunction are assessed during physical examination of the chest.
- Identify the three normal breath sounds.
- Differentiate the two main adventitious breath sounds and relate them to common pulmonary disease in which they occur.
- Define the point of maximal impulse (PMI) and describe how it is affected in common cardiopulmonary diseases.
- Define the four common heart sounds and describe the underlying cardiac mechanisms that generate them.
- Explain how abdominal dysfunction can negatively impact breathing and promote lung disease.
- Describe the four signs of cardiopulmonary disease that can be gleaned from examining the extremities.

CHAPTER OUTLINE

KEY TERMS

agonal breathing
apneustic breathing
abdominal compartment syndrome
abdominal paradox
advance directive
adventitious lung sounds
angina
arterial blood pressure
barrel chest
Biot respiration
bradycardia
bradypnea
breathlessness
bronchophony
cachexia
central cyanosis
central neurogenic hyperventilation
central neurogenic hypoventilation
Cheyne-Stokes respiration
chronic cough
clubbing
cough
crackles
cyanosis
diagnosis
differential diagnosis
diaphoresis
diastolic pressure
dyspnea
febrile
fetid
fever
gallop rhythm
heave
hematemesis
hemoptysis
hepatomegaly
Hoover sign
hypertension
hypotension
hypothermia
hypovolemia
jugular venous distension
Kussmaul breathing
Kussmaul sign
loud P_2
lymphadenopathy
mucoid
murmurs
orthodeoxia
orthopnea
pack-years
pedal edema
peripheral cyanosis
phlegm
platypnea
pleural friction rub
pneumothorax
postural hypotension
precordium
pulse pressure
pulsus alternans
pulsus paradoxus
purulent
rales
respiratory alternans
retractions
sensorium
shock
signs
sputum
stridor
subcutaneous emphysema
symptoms
syncope
systolic pressure
tachycardia
tachypnea
thrills
tracheal tugging
trepopnea
tripod sign
wheezes

Decisions regarding when to initiate, change, or discontinue therapy depend upon accurate clinical assessments. Ultimately physicians are responsible for these decisions. However, because respiratory therapists (RTs) often participate in clinical decision-making, they must develop competent bedside assessment skills. To do this effectively, the RT must assume responsibility for gathering and interpreting relevant bedside patient data.

Bedside assessment is the process of interviewing and examining a patient for signs and symptoms of disease, as well as evaluating the effects of treatment. Often, it provides initial evidence that something is wrong. In contrast to some diagnostic tests, bedside assessment techniques have little risk to the patient.

Two key data sources are the patient's medical history and physical examination. This data helps identify the need for subsequent diagnostic tests. After a tentative diagnosis is made, assessment skills are used repeatedly to help the clinician select the best therapy, monitor the patient's response to therapy, and make any necessary adjustments.

The patient initially is assessed to identify the correct diagnosis. **Diagnosis** (from the Greek *to know thoroughly*) is the process of identifying the nature and cause of illness. It is a systematic approach based on careful history taking, physical examination, and testing (e.g., laboratory analysis of blood, radiologic examinations, etc.). **Differential diagnosis** refers to a situation when many diseases share the similar signs and symptoms, making their exact cause unclear. Therefore, differential diagnosis is the list of all possible causes of a symptom or sign. For example, a cough can be a symptom of a common cold, pneumonia, bronchitis, or congestive heart failure (CHF). **Signs** refer to the *objective manifestation* of illness (e.g., increased respiratory rate, heart

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Bedside Assessment of the Postoperative Patient

Problem

The RT is called to see a 54-year-old woman who underwent abdominal surgery 2 days earlier. She is currently afebrile, alert, and oriented but complaining of dyspnea. Her breathing is rapid and shallow (34 breaths/min), with mild tachycardia (110 beats/min). She is 5 feet tall and weighs approximately 185 pounds. During the interview, she reveals her dyspnea has gradually increased over the past 12 h and worsens with exertion. The RT auscultates diminished breath sounds in the bases, with fine, late inspiratory crackles. The remainder of the physical examination is normal. What is the most likely cause of this patient's dyspnea and what should be done?

Solution

The findings indicate lung volume loss as the cause of dyspnea. The rapid, shallow breathing; fine, late inspiratory crackles; and history of recent abdominal surgery suggest atelectasis. Patients undergoing abdominal surgery are susceptible to postoperative atelectasis. The differential diagnosis would include CHF and pulmonary thromboembolism. The RT should ask the physician to order a chest radiograph. If the chest film confirms atelectasis, then lung expansion therapy should be initiated. If pulmonary embolism is suspected, other tests (e.g., a chest computed tomographic scan or an angiogram) would be needed (see Chapter 28).

murmur) whereas **symptoms** refer to the sensation or *subjective experience* of some aspect of an illness (e.g., breathlessness, cough). Symptoms must always be stated by the patient and never inferred from observed signs. Common symptoms and signs associated with cardiopulmonary disease are discussed in this chapter.

Diagnosis is performed primarily by a physician. Exceptions may occur in emergency situations when a physician is unavailable. In such cases, nurses and RTs may evaluate the patient to rapidly implement appropriate lifesaving therapy (e.g., cardiopulmonary resuscitation [CPR]).

The mastery of bedside assessment skills described here requires practice. Initially, students should practice these skills on healthy individuals to improve their technique and appreciate the existence of normal variations. The ability to discriminate abnormal findings from the range of normal findings is important and requires deliberate practice and experience to master.

INTERVIEWING THE PATIENT AND TAKING A MEDICAL HISTORY

Interviewing provides unique information because it represents the patient's perspective, and serves the following purposes:

1. To establish a rapport between the clinician and patient,
2. To obtain information essential for making a diagnosis,
3. To help monitor changes in the patient's symptoms and response to therapy.

Principles of Interviewing

Interviewing is the process of gathering relevant information from a patient, an essential element of which involves establishing rapport. Rapport building requires basic human skills of communicating concern, warmth, and empathy. Illness serious enough to require hospitalization is always stressful. Meaningful human contact lessens a patient's sense of isolation and helps reduce stress. Factors affecting communication between the RT and the patient include the following:

- Sensory and emotional factors
- Environmental factors
- Verbal and nonverbal components of the communication process
- Cultural values, beliefs, feelings, habits, and preoccupations of *both* the RT and the patient.

These factors make every interview unique. Developing interview skills takes practice and experience. It requires adherence to basic techniques and acquiring knowledge about the causes and characteristics of common cardiopulmonary symptoms. The following discussion provides some guidelines for interviewing and discusses common symptoms associated with diseases of the chest.

Structure and Technique for Interviewing

An effective interview makes the patient feel secure enough to talk openly about important personal matters. Each interview should begin with the RT introducing himself or herself to the patient, and stating the purpose of the visit. Introductions are done from a *social space* of 4 to 12 feet from the patient, which is considered "socially appropriate" between strangers and therefore non-threatening. The perception of "appropriate" space varies across individuals and particularly those of different cultural backgrounds. (In some cultures, for example, it is inappropriate for men to shake women's hands, so cultural attentiveness and competence is important.) Creating a sense of privacy (e.g., by pulling the curtain between the beds of a semiprivate room) helps the patient feel more at ease with the interview (Box 16.1).

After an introduction is made it is usually appropriate to begin the interview from what is referred to as *personal space* (2 to 4 feet from the patient). This allows the interview to occur with a normal or soft speaking voice and creates a sense of discretion and intimacy needed for disclosing personal information. Rapport is further established by positioning yourself at an equal level with the patient (e.g., by sitting in a chair). Standing over the patient may cause them to feel intimidated and uneasy. Appropriate eye contact with the patient is essential for a high-quality interview.

Carefully observing nonverbal behavior during an interview (e.g., facial expressions, stiff or relaxed posture, etc.) may hint at a patient's "internal state" such as fear, frustration, or even relief. A related aspect of observing a patient during an interview is their perception of appropriate eye contact. What is considered "appropriate" varies between individuals and across cultures. Direct eye contact may give the patient more confidence in the interviewer. However, prolonged eye contact also can feel intimidating, and in some cultures is considered rude. Therefore, the interviewer must be constantly sensitive to how a patient responds to the interviewer himself/herself.

Avoid asking leading questions and instead inquire using a "nondirectional" neutral style. For example, asking the patient, "Is your breathing better now?" subtly leads the patient toward a desired response (e.g., "my therapy is helping you right?").

BOX 16.1 Guidelines for Effective Patient Interviewing

Project a Sense of Undivided Interest in the Patient

- Provide for privacy and do not permit interruptions.
- Review records and prepare materials before entering the room.
- Listen and observe carefully.
- Use appropriate eye contact.
- Be attentive and respond to the patient's priorities, concerns, feelings, and comfort.

Establish Your Professional Role During the Introduction

- Dress and groom professionally.
- Enter the room with a smile and unhurried manner.
- Make immediate eye contact.
- If the patient is well enough, introduce yourself with a firm handshake.
- State your role and the purpose of your visit, and define the patient's involvement in the interaction.
- Address adult patients by title (e.g., Mr., Mrs., Ms.) and their last name. Using these formal terms of address alerts the patient to the importance of the interaction.

Show Your Respect for the Patient's Beliefs, Attitudes, and Rights

- Ensure the patient is appropriately covered.
- Position yourself so that eye contact is comfortable for the patient. (Ideally, patients should be sitting up, with their eye level at or slightly above yours.)
- Avoid standing at the foot of the bed or with your hand on the door because this may send the nonverbal message that you do not have time for the patient.
- Ask the patient's permission before moving any personal items or making adjustments in the room.
- Remember that the patient's dialogue with you and his or her medical record are confidential. Share this information only with other healthcare providers who need to know about it, and do not share the information in a place where others can overhear the conversation.
- Be honest; never guess at an answer or information that you do not know; do not provide information beyond your scope of practice; providing new information to the patient is the privilege and responsibility of the attending physician.
- Make no moral judgments about the patient; set your values for patient care according to the patient's values, beliefs, and priorities.
- Expect the patient to have an emotional response to illness and the healthcare environment.
- Listen, and then clarify and teach, but never argue.
- Adjust the time, length, and content of the interview to the patient's needs.

Use a Relaxed, Conversational Style

- Ask questions and make statements that communicate empathy.
- Encourage the patient to express his or her concerns.
- Expect and accept some periods of silence.
- Close even the briefest interview by asking whether there is anything the patient needs or wants to discuss.
- Tell the patient when you will return.

Asking the question in a neutral fashion (e.g., "How is your breathing now?") produces more honest and accurate information (Box 16.2).

Common characteristics of symptoms can be identified by asking the following neutral questions during the interview:

- When did the symptom start?
- How severe is it? (This can be rated on a scale of 1 to 10.)
- Where on the body is it? (This is especially important for chest pain.)
- What seems to make it better or worse?
- Has it occurred before? (If so, how long did it last?)

Identifying and characterizing any new symptom may help in identifying its cause and selecting appropriate therapy. Once initiated, further questioning helps evaluate whether symptoms have changed over the course of therapy. For example, the clinician may ask, "Have your symptoms changed in any way since admission?" or "Does the therapy seem to make a difference?"

In essence, the interview is a series of focused questions pursuing specific information related to a tentative or "working" diagnosis. Therefore, beyond developing effective interview techniques the interviewer must have the ability to ask key questions at the right time. This requires both experience and familiarity with the pathophysiology and symptoms of common cardiopulmonary diseases.

BOX 16.2 Types of Questions Used in Patient Interviews

- *Open-ended questions* encourage patients to describe events and priorities as they see them, helping to bring out concerns and attitudes and to promote understanding. Questions such as "What brought you to the hospital?" or "What happened next?" encourage conversational flow and rapport, while giving patients enough direction to know where to start.
- *Closed questions,* such as "When did your cough start?" or "How long did the pain last?" focus on specific information and provide clarification.
- *Direct questions* can be open-ended or closed and always end in a question mark. Although they are used to obtain specific information, a series of direct questions or frequent use of the question "Why?" can be intimidating and cause the patient to minimize his or her responses to questions.
- *Indirect questions* are less threatening than direct questions because they sound like statements (e.g., "I gather your doctor told you to take the treatments every 4 hours"). Inquiries of this type also work well to confront discrepancies in the patient's statements (e.g., "If I understood you correctly, it is harder for you to breathe now than it was before your treatment").
- *Neutral questions* and statements are preferred for all interactions with the patient. "What happened next?" and "Can you tell me more about …?" are neutral, open-ended questions. A neutral, closed question may give the patient a choice of responses, while focusing on the type of information desired (e.g., "Would you say there was a teaspoon, a tablespoon, or a half cup?").
- *Leading questions*, such as "You didn't cough up blood, did you?" should be avoided because they imply an answer.

Common Cardiopulmonary Symptoms

Dyspnea

Dyspnea is a *general term* describing the sensation of breathing discomfort. It is the most important symptom the RT is called upon to assess and treat. Dyspnea is a *subjective experience* and cannot be inferred from observing a patient's breathing pattern. Dyspnea and pain are similar in that both sensations possess qualitatively distinct features of varying intensity. Both pain and dyspnea are processed by the same brain structures.[1] Therefore, both sensations are assumed to produce similar degrees of suffering.

Also the term *dyspnea* specifically refers to *difficulty in the mechanical act of breathing*. In essence, dyspnea occurs when the effort to breathe (i.e., inspiratory muscle pressure) is disproportionately greater than the tidal volume achieved. The perception of breathing is a complex balance among three factors:

1. The neural drive to breathe coming from the respiratory centers in the brainstem
2. The tension developed in the respiratory muscles
3. The corresponding displacement of the lungs and chest wall

When the neuronal signals governing these sensations become unbalanced, breathing is perceived to be abnormal and unpleasant. The technical name for this imbalance is *neuromechanical dissociation*.[2] A normal individual experiences dyspnea only in unusual circumstances, such as trying to breathe through a straw or when wearing a restrictive garment.

Breathlessness. In contrast, **breathlessness** is an *unpleasant urge to breathe*. It is believed to be the conscious perception of intense neural discharge from the brainstem to the respiratory muscles. Breathlessness can be triggered by acute hypercapnia, acidosis, or hypoxemia. A normal experience of breathlessness is the unpleasant "throbbing" sensation induced by breath holding, or feeling "winded" during strenuous exercise. However, it is unknown whether normal encounters with breathlessness resemble the sensation that occurs with cardiopulmonary disease. This is because dyspnea and breathlessness are influenced by other stimuli, including receptors in the lungs and airways, as well as the cardiovascular system. These various stimuli shape both the quality and intensity of the sensation.

The intensity of dyspnea and breathlessness is often magnified by the emotional distress it generates. This is because emotions are partly expressed through alterations in the breathing pattern. Emotional distress arising from dyspnea is influenced by the situation, knowledge, and control. For example, a healthy person can quickly identify the source of breathlessness and arrest the symptom (e.g., stop exercise or breath holding). In patients with cardiopulmonary disease dyspnea often occurs at rest. Therefore, it occurs in an inappropriate context that implies an inability to control the symptom, and often the source of dyspnea is unknown. All these factors have a profound emotional impact that can intensify the sensation.

Positional dyspnea. Dyspnea triggered by reclining is called **orthopnea**. It commonly occurs in patients with CHF, mitral valve disease, bilateral diaphragm paralysis, and superior vena cava syndrome. **Platypnea** is dyspnea triggered by assuming the upright position. It may occur under a variety of conditions: following pneumonectomy, during hypovolemia, in lower cervical spinal injury,[3] and in some patients with chronic liver disease (i.e., who have the hepatopulmonary syndrome). Platypnea may be accompanied by **orthodeoxia,** which is oxygen desaturation on assuming an upright position. **Trepopnea** is dyspnea that occurs when a patient with unilateral lung disease lies with the affected side (e.g., pneumonia, large pleural effusion) in the dependent (down) position.

Language of dyspnea. Because dyspnea is a subjective experience, patients use nuanced language to describe their sensations. RTs should ask patients specific questions about the quality and characteristics of their dyspnea. Such information provides insight into the mechanism provoking dyspnea. Each sensation should be categorized according to specific aspects of breathing: inspiration, expiration, respiratory drive, or lung volume. A remark such as "I feel that my breath stops" reflects a problem with inspiration, whereas the remark "my breath does not go all the way out" suggests a problem with expiration. Statements such as "I can't catch my breath" suggest elevated respiratory drive (i.e., breathlessness).[4]

Different lung diseases often evoke unique sensations. Patients with asthma frequently complain of chest tightness, whereas patients with interstitial lung disease tend to focus on the sensations of increased work of breathing, shallow breathing, and gasping. However, the RT should keep in mind that many lung diseases evoke common sensations.

Cardiopulmonary disease can simultaneously evoke multiple nuanced sensations. Also, a particular sensation may predominate at one moment only to be replaced by another. For example, patients with asthma typically complain first about the sensation of chest tightness. As bronchoconstriction worsens and the lungs become more hyperinflated, patients often begin to focus more on the sensation of excessive work of breathing, air hunger, and the inability to take a deep breath.

Assessing dyspnea in the interview. Dyspnea must be assessed according to the situation encountered by the RT. Foremost is whether the patient can speak in full sentences. Severe dyspnea often limits speech to no more than a few words at a time. In this situation, curtail the interview and initiate treatment as soon as possible. Questions should be brief, structured to elicit a yes or no response, and focused on the quality and intensity of dyspnea. Once dyspnea subsides questions can be asked regarding the circumstances surrounding onset and current duration of dyspnea. Dyspnea should be assessed simultaneously with the physical examination (see later section of this chapter).

In patients with chronic cardiopulmonary disease, a detailed and systematic history should cover four major areas during the initial interview:

1. What activities of daily living trigger dyspnea? For example, is dyspnea triggered by walking on flat surfaces, by climbing stairs, by bathing, by dressing?
2. How much exertion makes the patient stop to catch his or her breath with different activities? Does the patient need to stop after walking up one flight of stairs or one step? Dyspnea provoked by less strenuous activities indicates more advanced disease.
3. Does the quality of dyspnea vary by the type of activity?
4. When did dyspnea first become a common feature of your life? How has it evolved over time? Has dyspnea progressed slowly or rapidly? How long has this progression taken place: over a period of months or years? Has there been a recent change in the intensity of dyspnea?

Beyond the information gleaned, a detailed conversation about patients' dyspnea allows them to share their experience and may decrease their sense of isolation.

Measuring the intensity of dyspnea requires a numeric intensity or visual analogue scale (Fig. 16.1). Such scales provide a way to evaluate the patient's response to treatment over time. These scales are important because objective lung function measurements

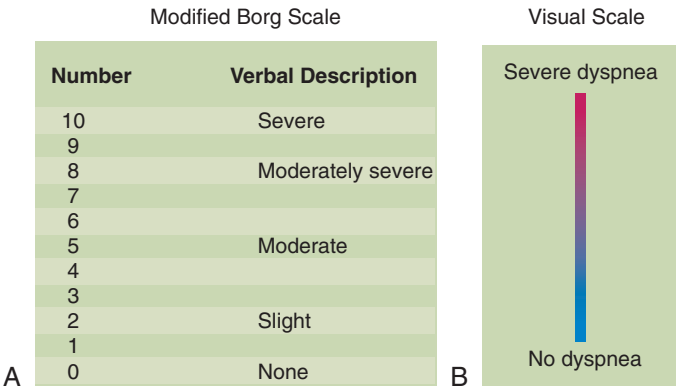

Fig. 16.1 (A) Modified Borg scale. (B) Visual analogue scale for measuring the degree of dyspnea.

(e.g., pulmonary function tests, PaO_2) seldom correlate with the degree of dyspnea.

Psychogenic dyspnea: panic disorders and hyperventilation. A perplexing situation is encountering complaints of dyspnea or suffocation in patients with normal cardiopulmonary function. Known as *psychogenic hyperventilation syndrome* it is associated with panic disorders.[5] Hyperventilation may coincide with other symptoms such as chest pain, anxiety, palpitations, and *paresthesia* (the sensation of tingling and numbness in the extremities that accompanies respiratory alkalosis). This syndrome may be either sporadic or chronic and often is self-perpetuating.

Anxiety often is accompanied by breathlessness and hyperventilation that creates a positive feedback loop. Respiratory alkalosis resulting from hyperventilation amplifies breathlessness, thereby provoking greater anxiety that, in turn, further increases hyperventilation. The classic homespun remedy of slowly rebreathing into a paper bag holds merit, because this arrests respiratory alkalosis and helps break the cycle. However, rebreathing techniques may require formal behavioral therapy and may not be appropriate in the hospital setting. This condition usually is treated clinically by administering judicious amounts of anxiolytic agents.

The first assumption when approaching any situation involving hyperventilation and dyspnea is that there is a physical basis for the symptom. Therefore, the priority is measuring vital signs including SaO_2, and perhaps a 12-lead electrocardiogram and arterial blood gases. A psychogenic source of dyspnea is considered *only* after a physical source for hyperventilation or dyspnea has been ruled out. In other words, psychogenic dyspnea is considered an "exclusionary" diagnosis. Intense pain or fear often provokes anxiety and hyperventilation. The RT must work in concert with nurses and the physician to determine the root cause of any hyperventilation syndrome.

Cough

A **cough** is the most common yet nonspecific symptom observed in patients with pulmonary disease. Coughing is a forceful expiratory maneuver that expels mucus and foreign material from the airways. Coughing usually occurs when irritant receptors are stimulated by inflammation, mucus, foreign materials, or noxious gases. Cough receptors are located primarily in the larynx, trachea, and larger bronchi. The effectiveness of a cough depends on (1) the ability to take a deep breath, (2) lung elastic recoil, (3) expiratory muscle strength, and (4) level of airway resistance. The ability to take a deep breath and exhale forcefully is often impaired in patients with cardiopulmonary, neurologic, or neuromuscular diseases.

Effective coughing also is impaired because of pain in the early postoperative period following upper abdominal or thoracic surgery and after thoracic or abdominal trauma. Often, expiratory flow is limited by factors such as bronchospasm (e.g., asthma), reduced lung elastic recoil (as in emphysema), and muscle weakness. An inadequate cough results in atelectasis, retained secretions, and increased susceptibility for developing pneumonia and/or hypoxemia.

There are several important characteristics of the cough that the RT is responsible for monitoring. These include whether the cough is dry or loose, productive or nonproductive (of sputum), acute or chronic; occurs more frequently at particular times (i.e., day or night); and whether it is provoked by a particular position (e.g., supine). Such knowledge is helpful in determining the source of coughing. A dry, nonproductive cough is typical for restrictive lung diseases such as CHF or pulmonary fibrosis. A loose, productive cough is more often associated with inflammatory obstructive diseases such as bronchitis and asthma. The most common cause of an acute, self-limited cough is a viral infection of the upper airway.

A **chronic cough** is one lasting 8 weeks or longer.[6] It carries with it considerable frustration and anxiety as well as depression. In the absence of specific diseases such as cancer and when the chest radiograph also is normal, more than 90% of chronic cough cases are caused by upper airway cough syndrome (formerly called postnasal drip), asthma, and/or gastroesophageal reflux. However, some medications (i.e., angiotensin-converting enzyme inhibitors like captopril or enalapril) can also cause coughing. Chronic cough has numerous common and uncommon causes that sometimes may have multiple sources (Box 16.3).[6]

Sputum Production

Healthy airways produce minimal mucus that is insufficient to stimulate the cough receptors. Mucus is gradually moved to the hypopharynx by the mucociliary escalator, where it is either swallowed or expectorated. Airway disease (e.g., bronchitis or acute asthma attacks) may cause mucous glands in the airways to produce abnormal amounts of mucus. This stimulates the cough receptors and causes a loose, productive cough.

RULE OF THUMB Ineffective coughing is common in patients with cardiopulmonary, neurologic, or neuromuscular disease, and in the early postoperative period after thoracic and upper abdominal surgery or trauma. An ineffective cough increases the risk for developing atelectasis, retained secretions, pneumonia, and hypoxemia.

RTs must master the terminology associated with sputum. **Phlegm** refers to mucus from the lungs *uncontaminated* by oral secretions, whereas **sputum** refers to mucus expectorated from the mouth. Because most mucus comes from expectorated samples, the term *sputum* is used in this chapter. Sputum

BOX 16.3 Evaluating Chronic Cough in the Adult (>8 Weeks Duration)

Common Sources
- Upper airway cough syndrome (formerly known as "postnasal drip")
- Asthma
- Gastroesophageal reflux
- Chronic bronchitis associated with cigarette smoking
- Angiotensin-converting enzyme–1 cough (caused by the antihypertensive drug angiotensin-converting enzyme inhibitor)
- Non-asthmatic eosinophilic bronchitis

Less Common Sources
- Post-infection (e.g., pertussis, mycoplasma)
- Interstitial lung disease
- Bronchiectasis
- Obstructive sleep apnea
- Primary lung cancer
- Heart failure
- Pulmonary tuberculosis
- Environmental exposures

Uncommon Sources
- Sarcoidosis
- Recurrent aspiration
- Chronic tonsillar enlargement
- Chronic auditory canal irritation
- Foreign body aspiration
- Endemic fungi
- Peritoneal dialysis
- Cystic fibrosis
- Tracheomalacia
- Habit or "tic cough"

From Terasaki G, Paauw DS: Evaluation and treatment of chronic cough. *Med Clin North Am.* 98:391–403, 2014.

containing pus cells is said to be **purulent,** suggesting a bacterial infection. Purulent sputum appears thick, colored, and sticky. Sputum that is foul-smelling is said to be **fetid.** Clear, thick sputum commonly seen in patients with asthma is called **mucoid**. Changes in the color, viscosity, or quantity of sputum often are signs of infection and must be documented and reported to the physician.

Hemoptysis

Coughing up blood (or blood-streaked sputum) is common in patients with pulmonary disease and is called **hemoptysis.** *Frank hemoptysis* is expectorant consisting *primarily* of blood. *Massive hemoptysis* is a medical emergency defined by coughing a variable volume of blood over a defined time period, commonly defined as more than 300 mL within 24 hours. Common causes of hemoptysis include bronchiectasis, lung abscess, and acute or chronic tuberculosis.

Non-massive hemoptysis occurs in many conditions such as airway infections, pneumonia, lung cancer, tuberculosis, blunt or penetrating chest trauma, and pulmonary embolism. Infection-associated hemoptysis usually presents as blood-streaked, purulent sputum. Hemoptysis from bronchogenic carcinoma often is chronic and may be associated with a monophonic wheeze and cough.

Hematemesis refers to blood vomited from the gastrointestinal tract that often occurs in patients with gastrointestinal disease. Because vomiting can stimulate the cough reflex (and vice versa), it is sometimes difficult to differentiate the origin of bleeding. However, whereas blood from the lungs often is mixed with sputum, blood from the stomach may be mixed with food particles and have an acidic pH.

Chest Pain

Chest pain is categorized as either pleuritic or non-pleuritic. *Pleuritic chest pain* usually is located *laterally or posteriorly*. Often it is characterized as a sharp, stabbing pain that worsens with a deep breath. It primarily manifests in chest diseases where the pleura becomes inflamed (such as pneumonia, empyema, pleural effusion), but it is also a common symptom in pulmonary embolism.

Non-pleuritic chest pain typically is located in the *center* of the anterior chest and may *radiate* to the shoulder, neck, or back. It is often characterized as a dull ache or pressure not affected by breathing. **Angina** is a common cause of non-pleuritic chest pain brought on by exertion or stress and is associated with coronary artery occlusion. Other common causes of non-pleuritic chest pain include gastroesophageal reflux, esophageal spasm, chest wall pain (e.g., costochondritis), and gallbladder disease.

Fever

Fever is an elevated body temperature greater than 38.3°C (101°F),[7] with the most common sources being a bacterial, viral, or fungal infection. However, numerous noninfectious causes of fever exist including drug reactions (e.g., sulfa drugs), malignancies (e.g., lymphomas, metastatic cancer), head trauma (e.g., damage to the hypothalamus), burns, alcoholic cirrhosis, thromboembolic disorders (e.g., pulmonary embolism), and noninfectious inflammatory diseases (e.g., rheumatoid arthritis, systemic lupus erythematosus).[7] Therefore, all patients with fever need further assessment to determine the cause. Sustained (e.g., > 3 weeks), unexplained fever despite a comprehensive work-up is called a *fever of unknown origin (FUO)* and is a common finding in patients with HIV disease.[8]

The magnitude of temperature elevation may indicate the type and virulence of the infection. Low-grade fever typically accompanies common upper respiratory tract infections, whereas a high fever occurs with influenza infection. Fever that occurs with a cough suggests a respiratory tract infection, particularly when purulent sputum is produced. Pneumonia is suspected when a high fever (i.e., 38.9°[C102°F]) persists for 2 or more days and is accompanied by chills. However, the absence of coughing or sputum production does not rule out lung infection.

For many years, it was believed that a link existed between fever and atelectasis in postoperative surgical patients. However, we now know that atelectasis does not cause fever.[9]

Patients with a significant fever have an increased metabolic rate that increases both O_2 consumption and carbon dioxide production and may cause tachypnea. Fever is particularly dangerous for patients with severe chronic cardiopulmonary

disease because the increased ventilatory demand may induce acute respiratory failure.

Pedal Edema

Heart failure is often characterized by swelling in the lower extremities referred to as dependent or **pedal edema**, the classic sign being "swollen ankles." It is caused by the heart's inability to pump blood effectively, with blood pooling in the gravity-dependent lower extremities as a consequence. The resulting increase in venous hydrostatic pressure pushes fluid into the interstitial space. It is also common in patients with end-stage liver disease.

Pedal edema has two subtypes. *Pitting edema* is when finger pressure applied on a swollen extremity leaves an indentation mark on the skin. The highest point where pitting edema occurs suggests the severity of heart failure. For example, pitting edema that extends to the knees signifies greater heart failure than edema limited to the ankles. *Weeping edema* occurs when the applied finger pressure causes a small fluid leak.

A standard scale is used to quantify the severity of pitting edema, with "1 plus" equating to trace pitting with rapid refill and "4 plus" meaning severe pitting with refill time in excess of 2 minutes. Any patient who is suspected to have right-sided or left-sided heart failure is examined for pedal edema.

Patients with chronic hypoxemic lung disease are especially prone to right-sided heart failure *(cor pulmonale)* that also causes pedal edema. Chronic hypoxemia causes severe pulmonary vasoconstriction and pulmonary hypertension. Sustained elevated workloads on the thin-walled right ventricle eventually lead to failure and venous congestion.

The Medical Record and Medical History

The first priority of the RT reviewing the medical record is to ensure the presence of a valid physician order for all respiratory care procedures. A valid order is one that is current, clearly written, and complete (i.e., without ambiguity as to what is being administered, the parameters or dosage, and frequency of administration).

All healthcare practitioners must be familiar with the medical history of the patients they are treating regardless of the reason for contact. The medical history familiarizes clinicians with the signs and symptoms that the patient exhibited on admission and the rationale for administered therapies. Afterward, the RT should read the *chief complaint* and *history of present illness* which presents a detailed, systematic account of the patient's major complaints written by a physician after the postadmission interview with the patient.

The next step is to review the patient's *past medical history* describing all past major illnesses, injuries, surgeries, hospitalizations, allergies, and health-related habits. This information is essential to building rapport with the patient as it provides context to whatever the patient shares about their experiences with illness and the healthcare system. The past history also provides context regarding medical decisions made during the current hospitalization.

The *past medical history* also records the patient's smoking history which is extremely important in assessing pulmonary health. Smoking history is recorded in **pack-years** and is determined by *multiplying the number of packs smoked per day by the number of years smoked*. Typically, patients are asked how many cigarettes (on average) they smoke per day. If they state that they have smoked a pack of cigarettes a day for 20 years, then their smoking history is 20 pack-years. If patients describe their smoking in terms of the number of cigarettes, or fractions of a pack, the calculation becomes more difficult. Two examples may be helpful in this situation. There are 20 cigarettes per pack. If a patient states he or she has smoked a pack and a half of cigarettes per day for 20 years, the smoking history is calculated as follows:

$$30 \text{ cigarettes}/20 \text{ cigarettes per pack} = 1.5 \text{ packs} \times 20 \text{ years} = 30 \text{ pack years smoking history}$$

If the patient states that he or she has smoked 15 cigarettes per day for 20 years:

$$15 \text{ cigarettes}/20 \text{ cigarettes per pack} = 0.75 \text{ packs} \times 20 \text{ years} = 15 \text{ pack years smoking history}$$

A review of potential genetic or occupational links to disease and the patient's current life situation are documented in the *family* and *social/environmental history*. Many patients have a genetic predisposition to pulmonary disorders such as asthma, lung cancer, and cystic fibrosis. A detailed occupational history also is important in establishing acquired pulmonary disorders from workplace exposure to inhaled organic (i.e., carbon-based) or non-organic (e.g., asbestos, silica) compounds. A strong link exists between many chronic pulmonary diseases and air pollution which predominantly affects those living in urban poverty.[10]

The *review of systems* uncovers problem areas the patient may have omitted, and is usually obtained in a head-to-toe review of all body systems. For each system, the interviewer obtains information about current symptoms. When reviewing the respiratory system, the interviewer asks about the presence or history of cough, hemoptysis, sputum production, chest pain, shortness of breath, and fever (Box 16.4).

MINI CLINI

Problem

During the interview a patient just diagnosed with chronic obstructive pulmonary disease (COPD) relates a complicated smoking history to the RT. For the first 10 years he smoked roughly 2 packs/day but slowly weaned himself down to 1½ packs/day for 6 years, 1 pack/day for 2 years and then ½ pack per day for 1 year before quitting entirely. About how many pack years did this patient smoke?

Solution

2 packs/day for 10 years is 20 pack-years; 1½ packs/day × 6 years is 9 pack-years, 1 pack/day for 2 years is 2 pack-years, and ½ pack/day for 1 year is ½ pack-years. The estimated smoking history then is 20 + 9 + 2 + 0.5 or approximately 32 pack-years.

BOX 16.4 Outline of a Complete Health History

Demographic data (obtained from admission interview): Name, address, age, birth date, place of birth, race, nationality, marital status, religion, occupation, and source of referral
Date and source of history and estimate of the reliability of the historian
Brief description of the patient's condition at the time the history or patient profile was taken
Chief complaint and reason for seeking treatment
History of present illness: Chronologic description of each symptom
- Onset: Time, type, source, setting
- Frequency and duration of symptoms
- Location and radiation of pain
- Severity (quantity)
- Quality (character)
- Aggravating and alleviating factors
- Associated manifestations

Past medical history
- Childhood diseases and development
- Hospitalizations, surgeries, injuries, accidents, and major illnesses
- Allergies
- Medications

Family history
- Familial disease history
- Marital history
- Family relationships

Social and environmental history
- Education
- Military experience
- Occupational history
- Religious and social activities
- Alcohol and cigarette consumption
- Living arrangements
- Hobbies and recreation
- Satisfaction with and stresses of life situation, finances, and relationships
- Recent travel or other event that might affect health

Review of systems: Respiratory system
- Cough
- Hemoptysis
- Sputum (amount and consistency)
- Chest pain
- Shortness of breath
- Hoarseness or changes in voice
- Dizziness or fainting
- Fever or chills
- Peripheral edema

Patient's printed name and signature

Finally, the medical record should indicate whether any limitations are in place on the extent of care provided in the event of cardiac or respiratory arrest. This information is known as an **advance directive**, whereby the patient (or a legally authorized representative) has formalized his or her wishes for resuscitative efforts. Typically this is referred to as the *DNR status* ("do not resuscitate") or may be expressed as *DNI* ("do not intubate"). A less ambiguous acronym, *AND* ("allow for natural death"), emphasizes that care is focused on patient comfort. This information may be found either in the admission note or within the body of the physician progress notes. In addition to this descriptive note, there must be an order written by the physician clearly specifying how care should be limited in the event of a medical emergency.

BOX 16.5 Typical Format for Recording the Physical Examination

Initial Impression
- Age, height, weight, sensorium, and general appearance

Vital Signs
- Pulse rate, respiratory rate, temperature, and blood pressure

Head, Ears, Eyes, Nose, and Throat
- Inspection findings

Neck
- Inspection and palpation findings

Thorax
- Lungs: Inspection, palpation, percussion, and auscultation findings
- Heart: Inspection, palpation, and auscultation findings

Abdomen
- Inspection, palpation, percussion, and auscultation findings

Extremities
- Inspection and palpation findings

PHYSICAL EXAMINATION

A careful physical examination of the patient is essential for evaluating problem(s) and determining the effects of therapy. The physical examination consists of four general steps: (1) inspection (visually examining), (2) palpation (touching), (3) percussion (tapping), and (4) auscultation (listening with a stethoscope).

General Appearance

The RT's initial impressions when encountering a patient may indicate the severity of the current problem and alter the subsequent assessment course. If the patient's general appearance suggests an acute problem, the examination may be abbreviated and focused upon that singular issue until that condition is stabilized. When the patient appears stable, a more complete assessment can be conducted (Box 16.5). Four important indicators are used when assessing the patient's overall appearance include: (1) their level of consciousness (see later discussion), (2) facial expression, (3) level of anxiety or distress, and (4) positioning.

When observing the patient the RT should look for specific characteristics. Does the patient appear well nourished or emaciated? Weakness and emaciation (**cachexia**) are signs of general ill health and malnutrition that increase susceptibility to infection. Is the patient sweating? **Diaphoresis** (sweating) can indicate fever, pain, severe stress, increased metabolism, or acute anxiety.

Facial expressions communicate a patient's internal state, particularly in regard to stress response. In fact, specific patient facial expression patterns are found to precede clinical deterioration.[11]

By observing facial expressions during encounters with patients the RT might be able to intuit the presence of pain or anxiety, as well as patient alertness and mood.

Body positioning also may be useful in assessing the severity of some pulmonary problems. For example, patients with severe pulmonary hyperinflation tend to sit upright while bracing their elbows on a table. Known as the **tripod sign**, this position gives a mechanical advantage to the accessory breathing muscles of the upper chest and neck.

Level of Consciousness

In medicine the term **sensorium** is used when evaluating a patient's cognitive functioning and level of consciousness. The sensorium is evaluated by asking patients whether they are aware of their current circumstances—namely whether they are oriented to time, place, person (i.e., self), and situation. A normal sensorium is present when the patient can correctly tell the interviewer their name, the current date, their location, and their situation (e.g., "I'm in the hospital because I fell and broke my hip"). This is typically documented as "oriented × 4." The simple rating scale shown in Box 16.6 allows clinicians to describe the patient's level of consciousness objectively.

Depressed consciousness may occur when cerebral blood flow is impaired (e.g., hypotension, neurovascular lesion) or when the brain is perfused with poorly oxygenated blood. Early signs of acutely decreased cerebral oxygenation include restlessness, confusion, or disorientation and may progress to loss of consciousness as hypoxemia worsens. In contrast, patients with severe chronic lung disease have adapted to sustained hypoxemia and often have normal mental status. Other sources of abnormal sensorium include chronic degenerative brain disorders, side effects of certain medications, and drug overdoses (particularly sedatives and narcotics). The Glasgow Coma Scale score is used to assess the level of consciousness and neurologic function and is described in more detail later in this textbook.

Vital Signs

Vital signs include body temperature, pulse rate, respiratory rate, blood pressure, and pulse oximetry and constitute the cornerstone of patient monitoring. They are easy to obtain and provide useful information. Often, abnormal vital signs are the first clue of adverse reactions to treatment. In addition, improvement in a patient's vital signs is strong evidence that a treatment is effective. For example, decreased respiratory and heart rates in response to supplemental O_2 suggest the therapy is beneficial.

Body Temperature

The average adult body temperature is about 37°C (98.6°F), and fluctuates approximately 0.5°C (1°F). Normally it is lowest in the early morning and highest in the late afternoon. Body temperature represents the balancing of heat production with heat loss and is regulated by the hypothalamus. Body temperature is controlled largely through skin perfusion whereby heat dissipates with peripheral vasodilation and sweating *(diaphoresis)* and is conserved by vasoconstriction. Minor dissipation occurs during breathing whereby some of the heat used to warm inspired air is subsequently lost during exhalation.

BOX 16.6 Levels of Consciousness

Confused
The patient
- Exhibits slight decrease of consciousness
- Has slow mental responses
- Has decreased or dulled perception
- Has incoherent thoughts

Delirious
The patient
- Is easily agitated
- Is irritable
- Exhibits hallucinations

Lethargic
The patient
- Is sleepy
- Arouses easily
- Responds appropriately when aroused

Obtunded
The patient
- Awakens only with difficulty
- Responds appropriately when aroused

Stuporous
The patient
- Does not awaken completely
- Has decreased mental and physical activity
- Responds to pain and exhibits deep tendon reflexes
- Responds slowly to verbal stimuli

Comatose
The patient
- Is unconscious
- Does not respond to stimuli
- Does not move voluntarily
- Exhibits possible signs of upper motor neuron dysfunction, such as Babinski reflex or hyperreflexia
- Loses reflexes with deep or prolonged coma

Elevated body temperature (*hyperthermia* or *hyperpyrexia*) can result from disease or from normal strenuous activities. Temperature elevation caused by disease is called *fever,* and the patient is said to be **febrile.** Fever increases metabolism, causing both increased O_2 consumption and CO_2 production. Increased metabolism induces both increased circulation and ventilation to maintain homeostasis. This is why febrile patients often have increased heart and breathing rates. Fever increases the demand placed on the heart and lungs and often complicates clinical management. Patients with limited cardiopulmonary reserve often cannot meet the increased circulatory and ventilatory demand and are vulnerable to respiratory failure.

Hypothermia is a body temperature below normal; the most common source is prolonged exposure to cold. In response the hypothalamus initiates shivering (to generate heat) and vasoconstriction (to conserve heat). Pathological sources of hypothermia include injury to the hypothalamus from trauma or stroke, decreased thyroid activity, and sepsis.

Because hypothermia reduces O_2 consumption and CO_2 production, patients with hypothermia may exhibit slow, shallow respiratory rate and reduced pulse rate.

The most common sites for measuring body temperature are the mouth, axilla, ear (tympanic membrane), and rectum. The oral site typically is used in an alert, adult patient, but cannot be used with infants, comatose, or orally intubated patients. Oral temperature measurement should be delayed for 10 to 15 minutes when patients have recently ingested hot or cold liquid or have been smoking. The axillary site (i.e., in the armpit) is acceptable for infants or small children who do not tolerate rectal thermometers, but less desirable as it may underestimate core temperature by 1° to 2°C. Accurate body temperature also can be measured using a hand-held eardrum (tympanic membrane) thermometer. However, rectal temperatures are closest to actual core body temperature.

Pulse Rate

The peripheral pulse is evaluated for rate, rhythm, and strength (Box 16.7). The normal adult pulse rate is 60 to 100 beats/min, with a regular rhythm. A condition in which the pulse rate is greater than 100 beats/min is called **tachycardia.** Common causes of tachycardia are exercise, fear, anxiety, low blood pressure, anemia, fever, reduced arterial blood O_2 levels *(hypoxemia),* elevated CO_2 *(hypercapnia)*, and certain medications. A condition in which the pulse rate is less than 60 beats/min is called **bradycardia.** Although less common, bradycardia can occur with hypothermia, traumatic brain or cervical spinal cord injury, certain cardiac arrhythmias, and certain medications.

The radial artery is the most common site used to palpate the pulse. The second and third fingertip pads (but not the thumb) are used to palpate the radial pulse. Ideally, the pulse rate is counted for 1 minute, especially if the pulse is irregular. Essential pulse characteristics should be noted and documented Box 16.7.

Spontaneous ventilation influences pulse strength (amplitude) during inspiration with a slight decrease in **pulse pressure** (the difference between the systolic and diastolic systemic blood pressure). This is caused by negative intrathoracic pressure (generated by diaphragmatic contraction) that pools blood in the pulmonary circulation while simultaneously increasing venous return and right ventricular volume. These combined effects (blood pooling in the pulmonary circulation and right ventricular engorgement) limits left ventricular filling during diastole. The end result is a brief reduction in left ventricular stroke volume and decreased systolic blood pressure.

Pulse pressure normally decreases slightly with inspiration (<10 mm Hg) and may not be noticeable with palpation. **Pulsus paradoxus** *("paradoxical pulse")* is a *significant* decrease in pulse strength (>10 mm Hg) during spontaneous inspiration that can be quantified with a blood pressure cuff (see later section). It is a common finding in acute obstructive pulmonary disease, especially in patients experiencing an asthma attack. During respiratory distress, *vigorous* inspiratory efforts decrease stroke volume by impeding the strength of left ventricular contraction.[12] Pulsus paradoxus also may signal a mechanical restriction of the pumping action of the heart, as can occur with constrictive pericarditis or cardiac tamponade. **Pulsus alternans** is an alternating succession of strong and weak pulses that suggests left-sided heart failure rather than pulmonary disease.

BOX 16.7 Key Characteristics of the Pulse

- Is the pulse rate normal, high, or low?
- Is the rhythm regular, consistently irregular, or irregularly irregular?
- Are there any changes in the amplitude (strength) of the pulse in relation to respiration? Are there changes in amplitude from one beat to another?
- Are there any other abnormalities, such as palpable vibrations (thrills or bruits)?

RULE OF THUMB Pulsus paradoxus is an exaggeration of the normal variation in pulse pressure caused by negative intrathoracic pressure during inspiration. During respiratory distress (e.g., COPD exacerbations) large negative intrathoracic pressure swings can greatly magnify pulse pressure swings. In contrast, alternating series of large and small pulse pressures seemingly unrelated to the breathing cycle is more indicative of left heart dysfunction.

The pulse also may be assessed by palpating the carotid, brachial, femoral, temporal, popliteal, posterior tibial, and dorsalis pedis pulses. The more centrally located pulses (e.g., the carotid and femoral) should be used when the blood pressure is abnormally low. If the carotid site is used, great care must be taken to avoid the carotid sinus area. Pressure on the carotid sinus area may cause strong parasympathetic stimulation resulting in bradycardia.

Respiratory Rate

The normal resting adult respiratory rate is 12 to 18 breaths/min. **Tachypnea** is defined as a respiratory rate greater than 20 breaths/min and has multiple sources: exertion, fever, hypoxemia, hypercarbia, metabolic acidosis, pulmonary edema, lung fibrosis, anxiety, and pain. **Bradypnea** is a respiratory rate less than 10 breaths/min and may occur with traumatic brain injury, severe myocardial infarction, hypothermia, anesthetics, opiate narcotics, and recreational drug overdoses.

The respiratory rate is counted by watching the abdomen or chest wall move out and in. Sometimes the respiratory rate may need to be verified by placing a hand on the upper abdomen (i.e., detect diaphragmatic contraction). Ideally, the patient should be unaware that the respiratory rate is being counted (i.e., awareness of having one's breathing being watched generally causes the respiratory rate to increase). One method to accomplish this is to count the respiratory rate immediately after evaluating the patient's pulse, while keeping the fingers on the patient's wrist. This gives the impression that the pulse rate is still being counted.

Arterial Blood Pressure

Arterial blood pressure is the force exerted by the heart against the systemic arteries as the blood moves through them (see Chapter 10). Arterial **systolic pressure** is the peak force exerted in the major arteries during contraction of the left ventricle, whereas **diastolic pressure** is the force in the major arteries

remaining after relaxation of the ventricles. In an adult, normal systolic pressure is 90 to 140 mm Hg, whereas normal diastolic pressure is 60 to 90 mm Hg. Blood pressure tends to increase with age in adulthood. The blood pressure is recorded by listing systolic pressure over diastolic pressure (e.g., 120/80 mm Hg). Pulse pressure is the difference between the systolic and diastolic pressures and is normally 30 to 40 mm Hg. A pulse pressure below 30 mm Hg is difficult to detect.

RULE OF THUMB The pulse pressure is the difference between systolic and diastolic pressure and is normally 30–40 mm Hg. When the pulse pressure falls below 30 mm Hg the pulse can be difficult to palpate.

Systemic **hypertension** is an arterial blood pressure *persistently* greater than 140/90 mm Hg and is a common medical problem in adults. In approximately 90% of cases the cause is unknown ("essential" hypertension). There are three categories of hypertension.[13] *Stage I* is defined as a systolic pressure of 140 to 159 mm Hg or a diastolic pressure of 90 to 99 mm Hg. *Stage II* hypertension occurs when the systolic pressure is 160 mm Hg or greater or the diastolic pressure is 100 mm Hg or greater. A third category ("prehypertension") is used to assess the future risk of developing hypertension. It is defined as systolic pressure between 120 and 139 mm Hg or diastolic pressure between 80 and 89 mm Hg. Prehypertension is not a disease state and does not require treatment.

Hypertension results from increased systemic vascular resistance (e.g., either constriction or stiffening of blood vessels) or an increased force of ventricular contraction. Sustained hypertension can cause central nervous system abnormalities, such as headaches, blurred vision, and confusion. Other potential consequences of hypertension include uremia (renal insufficiency), CHF, and cerebral hemorrhage. Acute, severe elevation of blood pressure can cause acute neurologic, cardiac, and renal failure and is called an *acute hypertensive crisis*.

Hypotension is defined in one of three ways: (1) a systolic arterial pressure less than 90 mm Hg, (2) a mean arterial pressure less than 65 mm Hg, or (3) a decrease in systolic pressure greater than 40 mm Hg from baseline.[14] The last definition acknowledges that patients with baseline hypertension may have inadequate tissue perfusion at blood pressures considered normal for most patients.

The precise definition of **shock** is inadequate delivery of O_2 and nutrients to the vital organs relative to their metabolic demand.[15] Although tissue hypoperfusion often is inferred by the presence of hypotension, the two conditions are not synonymous. In shock, vital body organs are in imminent danger of receiving inadequate blood flow and tissue impaired O_2 delivery (i.e., tissue hypoxia). For this reason, shock is usually treated aggressively with fluids, blood products, or vasoactive drugs, or a combination of these, depending on the cause and severity.

There are two broad categories of hypotension and shock can be broadly characterized as representing either a *hypodynamic* or *hyperdynamic* cardiovascular state.[15] Hypodynamic states include left ventricular failure *(cardiogenic)* and reduced blood volume (**hypovolemia** or *hypovolemic*) from hemorrhage or severe fluid loss. Hyperdynamic states are caused by profound systemic vasodilation *(peripheral vascular failure)* associated with overwhelming infection *(septic shock),* systemic allergic reaction *(anaphylaxis),* or severe liver failure.

In healthy individuals sitting or standing up causes minimal changes in blood pressure. However, similar postural changes in a hypovolemic patient often produce hypotension. This is referred to as **postural hypotension** and is treated with fluid administration. Postural hypotension is confirmed by measuring blood pressure with the patient supine and then measuring with the patient in the sitting (or standing) position. Postural hypotension may reduce cerebral blood flow and lead to **syncope** (fainting).

The most common technique for measuring arterial pressure requires a blood pressure cuff (sphygmomanometer) and a stethoscope (Fig. 16.2). When the cuff is applied to the upper arm and pressurized to exceed systolic blood pressure, brachial arterial blood flow stops. The cuff pressure is then released slowly. Once the cuff pressure falls just below the systolic pressure, blood flows intermittently past the obstruction and creates turbulence and vibrations called *Korotkoff sounds.* These sounds are heard with a stethoscope over the brachial artery distal to the cuff.

To measure the blood pressure, a deflated cuff is wrapped snugly around the patient's upper arm, with the lower edge of the cuff 1 inch above the antecubital fossa. While palpating the brachial pulse, the clinician inflates the cuff approximately 30 mm Hg above the point at which the pulse can no longer be felt. Then, the diaphragm of the stethoscope is placed over the artery and the cuff is slowly deflated (2 to 3 mm Hg/s) while observing the manometer.

The systolic pressure is recorded when the first Korotkoff sounds are heard. The point where cuff pressure equals diastolic pressure turbulence ceases. Therefore the pressure when Korotkoff sounds disappear represents the diastolic pressure.

As mentioned earlier, a paradoxical pulse is when systolic blood pressure decreases more than 10 mm Hg during a resting inhalation and can only be quantified by auscultation. To measure this, inflate the blood pressure cuff until the radial or brachial pulse can no longer be palpated. Then slowly deflate the cuff until sounds are heard only on exhalation (point 1). Next, reduce the cuff pressure until sounds are heard throughout respiration (point 2). The difference between points 1 and 2 indicates the degree of paradoxical pulse.

Most hospitals and clinics now use digital blood pressure measuring devices that do not require clinicians to listen for the Korotkoff sounds. These devices are very accurate and eliminate variances in recorded blood pressures based on human perception. The clinician only needs to apply the blood pressure cuff correctly and press the start button. The device inflates and deflates the cuff automatically and displays the blood pressure and pulse rate on a digital screen.

Examination of the Head and Neck

Head

Respiratory distress produces common facial signs such as nasal flaring, cyanosis, and pursed-lip breathing. *Nasal flaring* occurs when the external nares flare outward during inhalation and is associated with increased work of breathing.

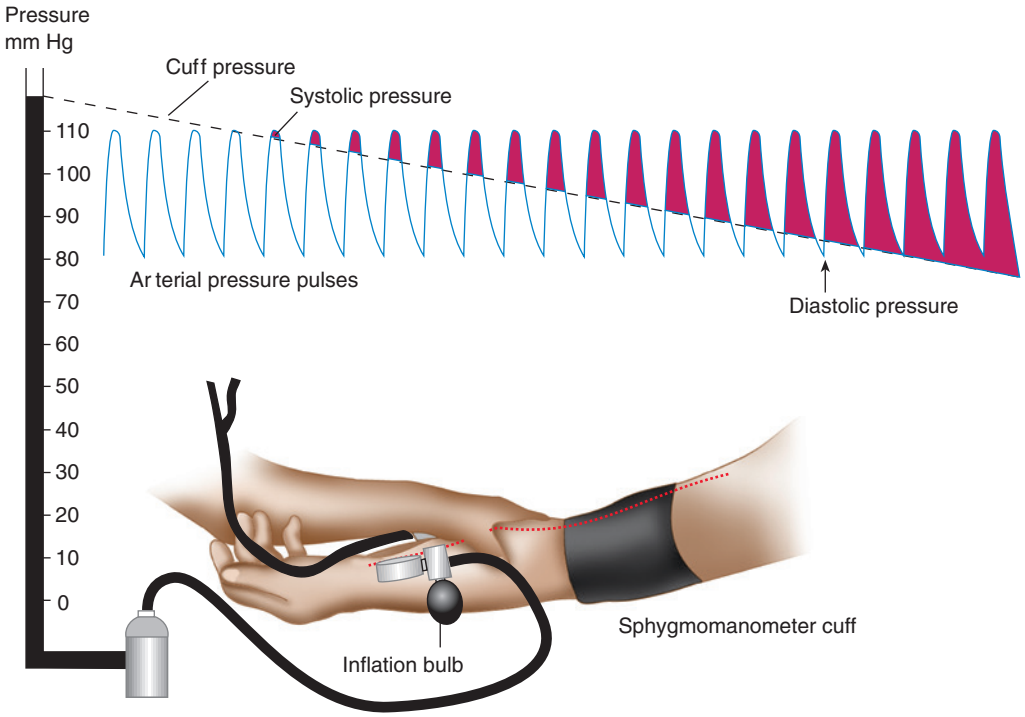

Fig. 16.2 Auscultatory method for measuring arterial blood pressure, using a sphygmomanometer and a stethoscope. (Redrawn from Rushmer RR: *Structure and functions of the cardiovascular system*, ed 2, Philadelphia, 1976, WB Saunders.)

Cyanosis is a bluish discoloration of the skin or oral mucosa resulting from respiratory or cardiac disease (discussed later). Patients with COPD may use pursed-lip breathing during exhalation. Breathing through pursed lips during exhalation creates resistance to flow. The increased resistance creates a slight back pressure in the small airways during exhalation. This back pressure prevents premature airway collapse and allows more complete emptying of the lung.

Neck

Inspection and palpation of the neck help determine the position of the trachea and the jugular venous pressure (JVP). Normally, when the patient faces forward, the trachea is located in the middle of the neck. The midline of the neck can be identified by palpating the suprasternal notch. The midline of the trachea should be directly below the center of the suprasternal notch.

The trachea can shift away from the midline in certain thoracic disorders. Generally, the trachea shifts *toward* an area of collapsed lung and shifts *away* from areas with increased air or fluid (e.g., tension pneumothorax or large pleural effusion).

RULE OF THUMB Volume changes inside the hemithorax often cause the mediastinal contents to shift and are seen on a physical exam by a shift in the position of the trachea. Severe volume loss (i.e., from lobar collapse) will cause the trachea to *shift toward* the affected side. In contrast increased volume and positive pressure in the pleural space (i.e., from large pneumothoraces or pleural effusion) will cause the trachea to shift away from the affected side.

JVP indirectly reflects venous blood volume and pressure of the right heart. A rising JVP (and associated jugular venous distension) typically reflects the heart's inability to adequately pump blood. JVP is estimated by determining how high the jugular vein extends above the level of the sternal angle. Individuals with obese necks may not have visible neck veins, even when the veins are distended.

When lying supine healthy individuals have visible neck veins that extend up the neck. As the head of the bed is elevated (i.e., 45-degree angle) the blood column descends and their visibility diminishes to approximately the clavicular level. With elevated venous pressure, the neck veins may be distended as high as the angle of the jaw, even when the patient is sitting upright.

JVP decreases during inspiration with increasing negative intrathoracic pressure causing the blood column to descend toward the thorax. During passive expiration the blood column returns to its previous position. However, during active expiration (i.e., positive intrathoracic pressure from abdominal muscular contraction) JVP and the position of the neck veins may actually rise higher than the previously observed end-expiratory baseline. Under abnormal conditions (e.g., cardiac tamponade), the JVP may increase during inhalation and is called **Kussmaul sign**.

Jugular venous distension (JVD) is present when the jugular vein is enlarged and can be seen more than 4 cm above the sternal angle. It is common in patients with chronic hypoxemia who develop right heart failure (cor pulmonale) from hypoxemia-induced pulmonary hypertension. Other conditions associated with JVD include left heart failure, cardiac tamponade, tension pneumothoraces, and mediastinal tumors.

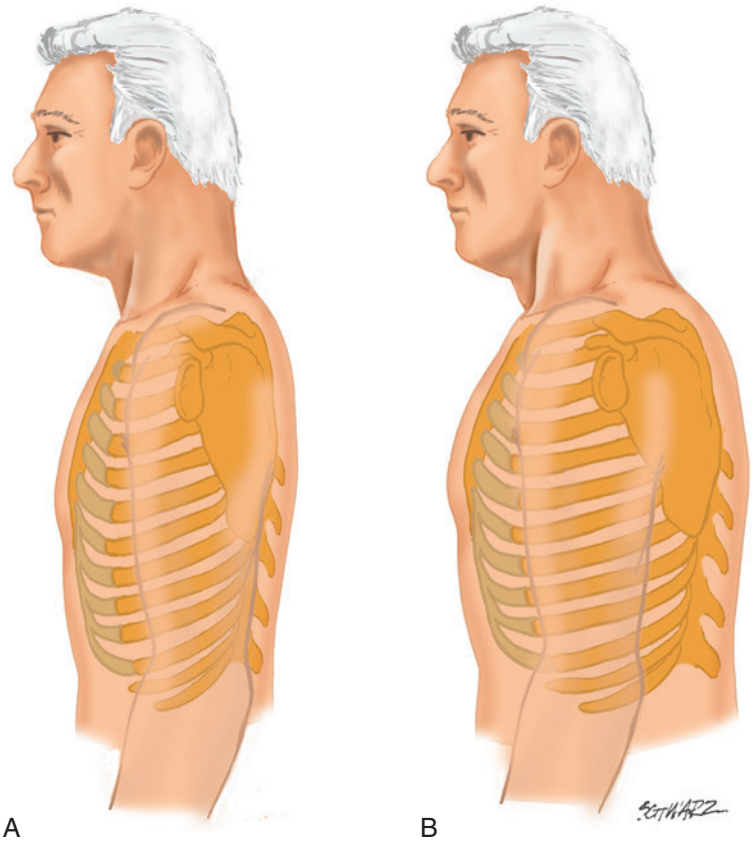

Fig. 16.3 (A) Patient with normal thoracic configuration. (B) Patient with increased anteroposterior diameter. Note contrasts in the angle of slope of the ribs and development of accessory muscles.

The neck also is palpated to detect **lymphadenopathy** (i.e., enlarged lymph nodes) Lymphadenopathy occurs with various medical disorders, including infection, malignancy, and sarcoidosis. Tender lymph nodes in the neck suggest a nearby infection. In contrast malignancy is characterized by enlarged, non-tender lymph nodes.

Examination of the Thorax and Lungs

Inspection

Visual inspection of the chest assesses thoracic configuration, expansion, breathing pattern, and breathing effort. This should occur in a well-lit room with the patient sitting upright. When the patient is unable to sit up, the clinician should carefully roll the patient to one side to examine the posterior chest. Inspection, palpation, percussion, and auscultation require at least partial exposure of the thorax. Therefore, clinicians must be sensitive to issues of privacy and patient modesty (especially for female patients). In a semiprivate room the drapes must be drawn and whenever possible expose as little of the thorax as needed to adequately conduct the examination.

Thoracic configuration. With normal body habitus transverse diameter of the thorax exceeds the anteroposterior (AP) diameter. Normally, the AP diameter increases with age but may prematurely increase in patients with COPD. This abnormal increase in AP diameter is called **barrel chest** and is associated with emphysema. When the AP diameter increases, the normal 45-degree angle of articulation between the ribs and spine is increased, becoming more horizontal (Fig. 16.3). Other abnormalities of the thoracic configuration are listed in Table 16.1.

TABLE 16.1 Abnormalities of Thoracic Configuration

Name	Condition
Pectus carinatum	Abnormal protrusion of sternum
Pectus excavatum	Depression of part or entire sternum, which can produce a restrictive lung defect
Kyphosis	Spinal deformity in which the spine has an abnormal anteroposterior curvature
Scoliosis	Spinal deformity in which the spine has a lateral curvature
Kyphoscoliosis	Combination of kyphosis and scoliosis, which may produce a severe restrictive lung defect as a result of poor lung expansion

Thoracic expansion. The diaphragm is the primary muscle of (and power source for) breathing. Diaphragmatic contraction causes the ribs to distend both outward and upward and the anterior abdominal wall to protrude outward. Therefore, when palpating the chest wall, both the chest and abdomen should expand synchronously during inspiration. However, the relative expansion of the thorax and abdomen depend upon body position. When supine, the primary motion during *normal tidal breathing* is outward abdominal expansion with little noticeable chest

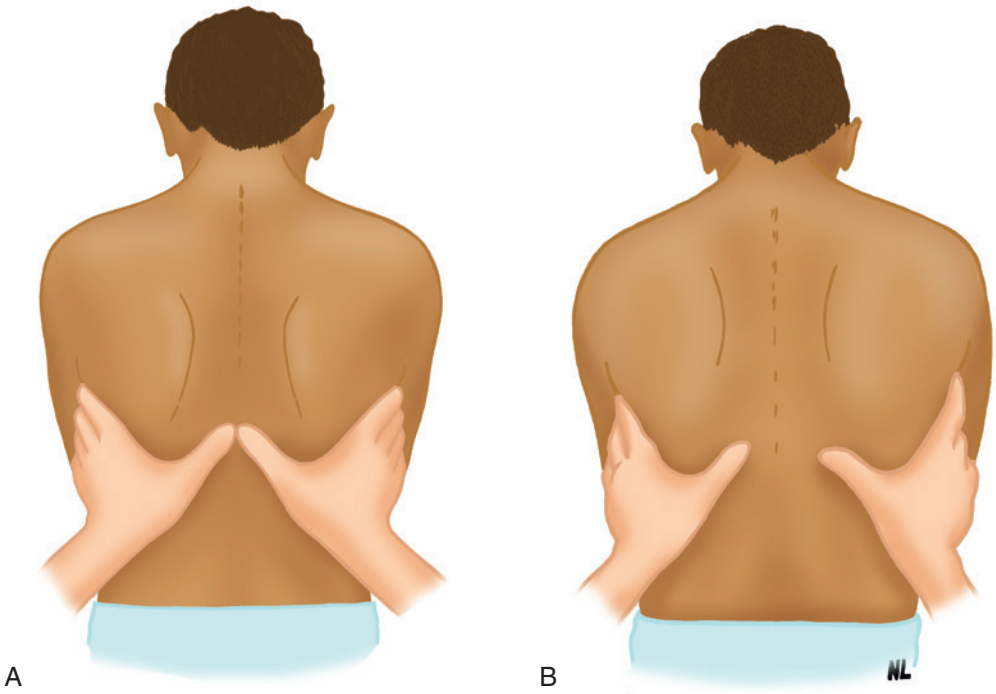

Fig. 16.4 Estimation of Thoracic Expansion. (A) Exhalation. (B) Maximal inhalation.

excursion. In the upright position rib cage motion becomes more pronounced.[16]

The normal chest wall expands symmetrically and can be evaluated anteriorly and posteriorly. Anterior expansion is evaluated by placing the hands over the anterolateral chest, with the thumbs extended along the costal margin toward the xiphoid process. To evaluate posteriorly, position the hands over the posterolateral chest with the thumbs meeting at the T-8 vertebra (Fig. 16.4). Instruct the patient to exhale slowly and completely. At maximal exhalation, gently secure the fingertips against the sides of the patient's chest and extend the thumbs toward the midline until the tip of each thumb meets at the midline. Next instruct the patient to take a full, deep breath. Note the distance the tip of each of the thumbs moves from midline. Normally, each thumb moves an equal distance of approximately 3 to 5 cm.

Diseases that restrict lung expansion also reduce chest expansion on the affected side (i.e., either unilateral or bilateral). Causes of reduced expansion include neuromuscular disorders (from muscular weakness), COPD (from lung hyperinflation), lobar consolidation (non-distensible tissue), pleural effusion, and pneumothorax (loss of pleural space integrity to transmit inspiratory muscle pressure).

Breathing pattern and effort. A healthy resting adult has a consistent breathing rate and rhythm with minimal effort and passive exhalation. There are two broad categories encompassing abnormal patterns: (1) those directly associated with cardiopulmonary or chest wall diseases that increase work of breathing and (2) those associated with neurologic disease (Table 16.2).

The hallmark of increased breathing effort ("work of breathing") is the recruitment of accessory breathing muscles in the neck and thorax to maintain ventilation. The most readily apparent (and palpable) is the sternocleidomastoid or "strap muscles." Common causes of increased work of breathing are airway obstruction (e.g., COPD, asthma), edematous ("heavy") lungs (e.g., acute respiratory distress syndrome [ARDS], cardiogenic pulmonary edema), or a stiff chest wall (e.g., ascites, anasarca, pleural effusions). One sign of severely increased work of breathing is visible distortions in the chest wall called *retractions*. During labored breathing the abdominal muscles also are recruited during expiration to assist subsequent inspiratory efforts (see later: assessing the diaphragm)

Retractions are an inward sinking of the chest wall during inspiration. This occurs when inspiratory muscle contractions generate large negative intrathoracic pressures. The respiratory muscles can generate negative inspiratory pressures of approximately 150 cm H_2O (112 mm Hg) at maximal effort.[17] There are three distinct types of retractions: (1) *intercostal* (seen between the ribs), (2) *supraclavicular* (above the clavicles), and (3) *subcostal* (below the rib cage). Another form of retraction is **tracheal tugging,** which is the downward movement of the thyroid cartilage toward the chest during inspiration in concert with sternocleidomastoid muscle recruitment. Note that retractions are difficult to see in obese patients.

Two archetypal abnormal breathing patterns exist providing clues about the underlying pulmonary disease. The first is characterized by a rapid, shallow breathing pattern and the second is characterized by an abnormally prolonged exhalation with pronounced, sustained abdominal muscular contraction. An additional pattern, **Kussmaul breathing,** is observed during severe metabolic acidosis whereby patients breathe rapidly and deeply, similar to a normal person during strenuous exercise.

Rapid, shallow breathing typically occurs in patients with increased lung inflammation or stiffness (e.g., ARDS, pulmonary fibrosis), whereas lower airway obstruction slows lung emptying

TABLE 16.2 Abnormal Breathing Patterns

Breathing Pattern	Characteristics	Causes
Agonal breathing	Intermittent prolonged gasps	Preterminal brain stem reflex
Apnea	No breathing	Cardiac arrest, narcotic overdose, severe brain trauma
Apneustic breathing	Deep, gasping inspiration with brief, partial expiration	Damage to upper medulla or pons caused by stroke or trauma; sometimes observed with hypoglycemic coma or profound hypoxemia
Ataxic breathing	Completely irregular breathing pattern with variable periods of apnea	Damage to medulla
Asthmatic breathing	Prolonged exhalation with recruitment of abdominal muscles	Obstruction to airflow out of the lungs
Biot respiration	Chaotic breathing pattern characterized by frequent irregularity in both rate and tidal volume that eventually deteriorates to agonal breathing and terminal apnea	Damage to medulla or pons caused by stroke or trauma; severe intracranial hypertension
Cheyne-Stokes respiration	Irregular type of breathing; breaths increase and decrease in depth and rate with periods of apnea; variant of "periodic breathing"	Most often caused by severe damage to bilateral cerebral hemispheres and basal ganglia (usually infarction); also seen in patients with congestive heart failure owing to increased circulation time and in various forms of encephalopathy. Also observed in some elderly patients in the absence of neurologic or cardiac disease.
Central neurogenic hyperventilation	Persistent hyperventilation	Midbrain and upper pons damage associated with head trauma, severe brain hypoxia, or ischemia
Kussmaul breathing	Deep and fast respirations	Metabolic acidosis
Paradoxical breathing	*Abdominal paradox:* Abdominal wall moves inward on inspiration and outward on expiration	*Abdominal paradox:* Diaphragmatic fatigue or paralysis
	Chest paradox: Part or all of the chest wall moves in with inhalation and out with exhalation	*Chest paradox:* Typically observed in chest trauma with multiple rib or sternal fractures Also found in patients with high spinal cord injury with paralysis of intercostal muscles
Periodic breathing	Breathing oscillates between periods of rapid, deep breathing and slow, shallow breathing *without* prolonged periods of apnea	Same causes as Cheyne-Stokes respiration

and prolongs the expiratory phase as patients attempt to minimize gas trapping inside the lungs. This causes the inspiratory-to-expiratory time ratio to decrease from a normal value of 1:2 to 1:4 or greater. In contrast, extrathoracic upper airway obstruction (e.g., epiglottitis or croup) results in a prolonged inspiratory time in an attempt to achieve an adequate tidal volume.

Neurologic and some cardiac diseases also produce abnormal breathing patterns. These include Cheyne-Stokes respiration, Biot respiration, apneustic breathing, central neurogenic hypoventilation, and hyperventilation. **Cheyne-Stokes respiration** is when the respiratory rate and tidal volume gradually increase in intensity and then gradually decrease to complete apnea (absence of ventilation), which may last several seconds. This pattern is associated with coma from severe cerebral lesions, metabolic derangements, or low cardiac output states (e.g., CHF). However, it is not always associated with profound pathology as it sometimes occurs during sleep in the elderly.[18] In comatose states, the regulatory influence of the cerebral cortex on the respiratory centers in the medulla is lost. As a result, the medulla becomes overly sensitive to CO_2 resulting in the waxing and waning breathing pattern. In CHF Cheyne-Stokes respiration is caused by prolonged blood transit time between the lungs and the medulla wherein changes in respiratory center PCO_2 lag behind changes in arterial PCO_2.

Biot respiration occurs with damage to the medulla resulting in a chaotic breathing pattern characterized by frequent irregularity in both rate and tidal volume. The pattern eventually deteriorates to **agonal breathing** (i.e., intermittent prolonged gasps) and then apnea.

Apneustic breathing is characterized by a prolonged inspiratory pause at full inspiration typically lasting for 2 to 3 seconds. It indicates damage to the lower pons (which regulates the transition from the inspiratory to expiratory phase) and is usually caused by basilar artery occlusion.[19] **Central neurogenic hyperventilation** is characterized by persistent hyperventilation driven by abnormal neural stimuli. It is related to midbrain and upper pons damage associated with head trauma, severe brain hypoxia, or lack of blood flow to the brain.[20] Conversely, **central neurogenic hypoventilation** means the respiratory centers do not respond appropriately to ventilatory stimuli, such as CO_2. It also is associated with head trauma and brain hypoxia as well as narcotic suppression of the respiratory center.[19]

RULE OF THUMB Patients with lung diseases that cause lung volume loss and stiffness (e.g., pulmonary fibrosis, ARDS) typically present with a rapid-shallow breathing pattern.

RULE OF THUMB Patients with lung diseases that cause intrathoracic airways to narrow (e.g., asthma, bronchitis) tend to breathe with a prolonged expiratory phase.

RULE OF THUMB Lung diseases that cause the upper airway to narrow (e.g., croup, epiglottitis) also cause the patient to breathe with a prolonged inspiratory phase.

Assessing the diaphragm. The diaphragm may be nonfunctional or severely limited in patients with high cervical spinal cord injury, neuromuscular disease, and COPD. When the diaphragm is nonfunctional or limited, the accessory muscles of ventilation become active to maintain adequate gas exchange. Excluding strenuous exercise, heavy use of accessory muscles is reliable evidence of significant cardiopulmonary disease.

In patients with emphysema, the lungs become hyperinflated, preventing the diaphragm from achieving its relaxed position whereby the muscle fibers lengthen. When the diaphragm must contract from above its relaxed position the force or pressure it can generate decreases. As hyperinflation pushes the diaphragm downward into a flat position its effectiveness in moving air is greatly limited. Contraction of a flat diaphragm tends to draw in the lateral costal margins (**Hoover sign**) instead of normal expansion outward. The accessory muscles therefore must assist the diaphragm. The severity of emphysema is often reflected by the magnitude of accessory muscle activity.

Diaphragmatic fatigue occurs in many chronic and acute pulmonary diseases. Fatigue is the inability of a contracting muscle(s) to achieve a target pressure. In contrast, muscle weakness is the inability to achieve a target pressure in a rested muscle. For the respiratory muscles, the target pressure is that needed to maintain normal ventilation as assessed by the arterial CO_2 partial pressure ($PaCO_2$).

Acute diaphragmatic fatigue often manifests with distinctive breathing patterns; the first sign is tachypnea.[16] Sometimes this evolves into a breathing pattern in which the diaphragm and rib cage muscles alternately power breathing in an attempt to rest each muscle group (**respiratory alternans**). This pattern is noted by the upward motion of the diaphragm during inspiration on a *series of breaths,* followed by diaphragmatic contractions and outward abdominal movement on the following series of breaths. When the diaphragm is inactive, contraction of the rib cage muscles sucks the diaphragm upward and the abdomen moves inward. The opposite motion occurs when the diaphragm is active and the rib cage muscles are inactive: the chest moves inward as the abdomen protrudes, producing a rocking motion appearance to the chest. **Abdominal paradox** occurs with complete diaphragmatic fatigue, as the diaphragm is drawn upward into the thoracic cavity with *each* inspiratory effort of the rib cage muscles.

These patterns are not always associated with impending muscle fatigue. Sometimes they reflect adaptations to high workloads when the respiratory muscle strength is normal.[20] Also, during respiratory distress the expiratory muscles are recruited to increase diaphragmatic strength (i.e., maximizing muscle length).[17] This situation can make it difficult to discern accurately the presence and type of abnormal breathing patterns. The RT must be careful not to offer definitive therapeutic suggestions (e.g., need for mechanical ventilation) based solely on his or her perception of an abnormal breathing pattern.

Palpation

Palpation is the art of touching the chest wall to evaluate underlying structure and function. It is used to confirm or rule out suspected problems suggested by the history and initial examination findings. Palpation is performed to evaluate vocal fremitus, estimate thoracic expansion, and assess the skin and subcutaneous tissues of the chest.

Vocal and tactile fremitus. *Vocal fremitus* are vibrations created by the vocal cords during speech. These vibrations are transmitted down the tracheobronchial tree and through the lung to the chest wall. When these vibrations are felt on the chest wall, it is called *tactile fremitus.* Assessing vocal fremitus requires a conscious, cooperative patient.

Increased intensity of fremitus occurs when the lung becomes consolidated (e.g., filled with inflammatory exudate) as in pneumonia. However, fremitus is absent when consolidated tissue is not in communication with patent airways because speech is not transmitted. In addition, fremitus is reduced in patients who are obese or overly muscular.

Decreased intensity of fremitus occurs when fluid or air collects in the pleural space (e.g., pleural effusion or pneumothoraces). Speech transmission also decreases with hyperinflation (e.g., asthma, emphysema) as lung tissue density is reduced.

Tactile fremitus is assessed by asking the patient to repeat the word "ninety-nine" while the RT systematically palpates the anterior, lateral, and posterior portions of the thorax. The palmar aspect of the fingers or the ulnar aspect of the hand can be used for palpation. If one hand is used, it should be moved from one side of the chest to the corresponding area on the other side.

Skin and subcutaneous tissues. Lung rupture often causes air to leak into the subcutaneous tissues of the chest and neck. Fine air bubbles collecting in subcutaneous tissues produces a crackling sound and sensation when palpated. This is referred to as **subcutaneous emphysema.** The tactile sensation it produces is called *crepitus* which is a classic sign of barotrauma. Two situations when the RT should be vigilant for the presence of subcutaneous emphysema are when high airway pressures and end-inspiratory volumes occur during mechanical ventilation and in patients with blunt or penetrating chest trauma.

Percussion of the Chest

Percussion is the art of tapping on a surface to evaluate the underlying structure. Percussion of the chest wall produces a sound and a palpable vibration useful in evaluating underlying lung tissue. The vibration created by percussion penetrates the lung to a depth of 5 to 7 cm below the chest wall. This assessment technique is not performed routinely on all patients but is reserved for patients with suspected pneumothorax or lung consolidation.

The technique most often used in percussing the chest wall is called *mediate,* or *indirect,* percussion and can be broken down into two steps. First, place the middle finger of the non-dominant hand firmly against the patient's chest wall, parallel to the ribs, with the palm and other fingers held off the chest. Second, the tips of middle and index fingers of the dominant hand are then used to strike the finger pressed against the chest. Alternatively, the lateral aspect of the thumb can be used. A quick, sharp blow

should be placed near the base of the terminal phalanx. Movement of the hand striking the chest is generated at the wrist, not at the elbow or shoulder.

Percussion over lung fields. Percussion of the lung fields is performed systematically by consecutively testing comparable areas on both sides of the chest. Percussion over the bony structures and over the breasts of female patients has no diagnostic value and should not be performed. Asking patients to raise their arms above their shoulders helps move the scapulae laterally and minimizes their interference with percussion on the posterior chest wall.

The sounds generated during chest percussion are evaluated for intensity (loudness). Percussion over normal lung fields produces an easily heard, moderately low-pitched, resonate sound described as *tympanic*. When the percussion note is louder, deeper, and more resonant, it is said to be *hypertympanic*. Percussion may also produce a *damped* or *dull* noise resembling the sound of a heavily muffled drum. Unilateral problems are easier to detect than bilateral problems because the unaffected side provides a normal standard for immediate comparison.

Clinical implications. In modern practice, chest percussion enables rapid bedside assessment of chest abnormalities and may aid in deciding whether to obtain a chest radiograph. Any abnormality that either increases lung tissue density (e.g., pneumonia, tumor, or atelectasis) or increases the density of the pleural space (e.g., pleural effusion, empyema) results in *decreased resonance* or a *dull note* to percussion over the affected area. In contrast, *increased resonance* or a *hyper-resonate note* is detected when the lungs are either hyperinflated (e.g., asthma or emphysema) or when the pleural space contains large amounts of air (**pneumothorax**). Percussion of the chest has important limitations. Abnormalities that are small or deep below the surface are not likely to be detected during percussion of the chest.

RULE OF THUMB Percussing the chest can produce two abnormal resonance sounds related to an imbalance between gas and tissue/fluid inside the chest cavity. Dull resonance is produced by the muffling effects of increased tissue density (e.g., atelectasis or consolidation) or fluid collection (e.g., pleural effusion, hemothorax), whereas hyper-resonance is produced by lung hyperinflation (e.g., COPD or asthma exacerbation) or gas trapped in the pleural space (i.e., pneumothorax).

Auscultation of the Lungs

Auscultation is the process of listening for bodily sounds. The thorax is auscultated to identify normal and abnormal lung sounds and to evaluate the effects of therapy. It is a particularly useful clinical tool because it is noninvasive and can be performed quickly. Auscultation requires a stethoscope to enhance sound transmission from the patient's lungs to the examiner's ears.

Stethoscope. A stethoscope has the following four basic parts: (1) a bell, (2) a diaphragm, (3) tubing, and (4) earpieces (Fig. 16.5). The bell detects a broad spectrum of sounds and is useful for hearing low-pitched sounds (e.g., heart sounds). Proper technique for listening to heart sounds is to place the bell lightly against the chest. This avoids stretching the skin, which inadvertently makes auscultating heart sounds more difficult because it filters out low-frequency sounds.

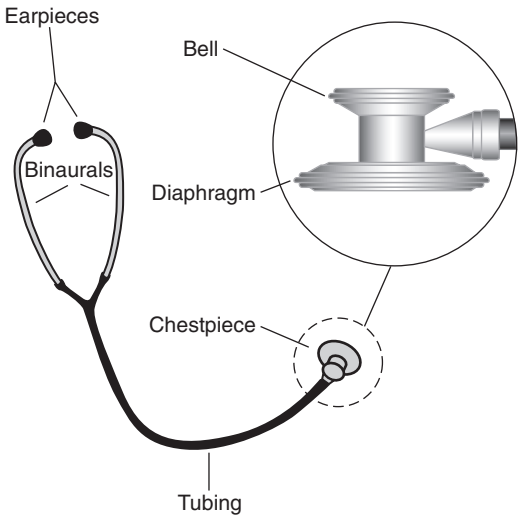

Fig. 16.5 Acoustic stethoscope.

The diaphragm is used to auscultate the lungs as it is better at capturing high-frequency sounds. The ideal tubing is thick enough to exclude external noises and approximately 25 to 35 cm (11 to 16 in) in length. Longer tubing may impair sound transmission.

The stethoscope should be examined regularly for cracks in the diaphragm, wax or dirt in the earpieces, and other defects that may interfere with sound transmission. A hospital-approved disinfectant should be used to clean the stethoscope *after every patient contact* to minimize contamination with microorganisms.[22] Patients requiring either contact or protective isolation must have a dedicated stethoscope in the room to prevent cross infection.

Technique. Ideally the patient should be relaxed, sitting upright, and instructed to breathe through the mouth a little more deeply than normal. Exhalation should be passive. Because clothing may distort lung or heart sounds the bell or diaphragm should be placed directly against the chest wall. Likewise, be careful not to allow objects to rub against the tubing as this may produce artifacts that could be mistaken for adventitious lung sounds (discussed later).

Auscultating the lungs should be systematic including all lobes on the anterior, lateral, and posterior chest. Begin at the bases and compare breath sounds side to side, working upward toward the lung apexes (Fig. 16.6). Beginning at the bases is important because certain abnormal sounds only occur in the lower lobes and quickly resolve with deep breaths. Evaluate one full breath at each stethoscope position and listen to several breaths when abnormal sounds are present to clarify the characteristics.

Breath sounds consist of several key features: pitch (vibration frequency), intensity (loudness), and the duration of inspiratory and expiratory phases. The acoustic characteristics of breath sounds are illustrated in breath sound diagrams (Fig. 16.7), as well as their normal features (Table 16.3). The RT must be familiar with normal breath sounds before acquiring the ability to identify changes that accompany respiratory disease.

Normal lung sound terminology. There are three normal breath sounds referred to as tracheal, bronchovesicular, and vesicular. *Tracheal breath sounds* have a loud, tubular quality and are heard

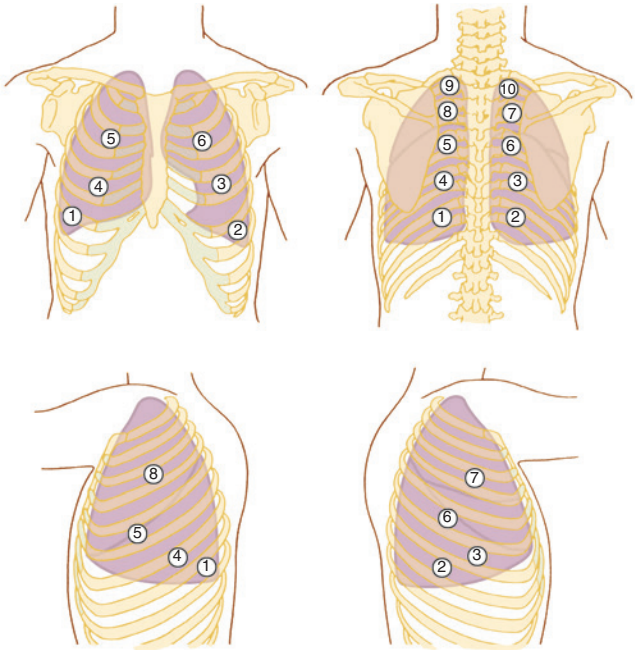

Fig. 16.6 Sequencing for auscultation technique. (Modified from Wilkins RL, Dexter JR, editors: *Respiratory diseases: a case study approach to patient care*, ed 3, Philadelphia, 2007, FA Davis.)

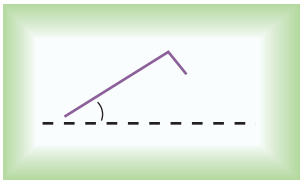

Fig. 16.7 Diagram of Normal Breath Sound. Upstroke represents inhalation, and downstroke represents exhalation; length of upstroke represents duration; thickness of stroke represents intensity; angle between upstroke and horizontal line represents pitch.

TABLE 16.3 Characteristics of Normal Breath Sounds

Breath Sound	Pitch	Intensity	Location	Diagram
Vesicular	Low	Soft	Peripheral lung areas	
Bronchovesicular	Moderate	Moderate	Around upper part of sternum, between the scapulae	
Tracheal	High	Loud	Over the trachea	

when auscultating the trachea and are characterized by approximately equal durations between the inspiratory and expiratory phases. *Bronchovesicular breath sounds*, heard around the upper half of the sternum and between the scapulae, are slightly lower in pitch and also have equal inspiratory and expiratory components. *Vesicular breath sounds* are heard over normal lung parenchyma and are characterized by a soft, muffled sound quality that is lower both in pitch and intensity than bronchovesicular breath sounds. Vesicular sounds are heard primarily during inhalation, with an exhalation component approximately one-third the duration of inhalation (see Table 16.3).

Lung Sounds in Pulmonary Disease

Respiratory diseases often alter breath sounds with descriptors such as *diminished* or even *absent* when the intensity decreases and *harsh* when the intensity increases. Harsh breath sounds of approximately equal duration between inspiration are described as *bronchial breath sounds.*

Adventitious lung sounds are additional sounds or vibrations produced by air movement through diseased airways. These sounds may be loud or faint, scattered or diffuse, and inspiratory or expiratory (or both). Adventitious sounds have two classifications. *Discontinuous* sounds are intermittent, crackling, or bubbling sounds of short duration and are referred to as either **crackles** or **rales** (from the French word for "rattle"). Faint or low-intensity crackles are often referred to as *fine crackles;* more pronounced or more intense crackles are referred to as *coarse crackles.*

In contrast *continuous* adventitious lung sounds are described with the term **wheezes** (i.e., a high or low-pitched quasi-musical sound). However, the RT may encounter the term *rhonchi* (derived from the Latin word for "wheezing"). Although no longer favored, it was used previously to describe low-pitched, continuous sounds associated with secretions in the larger airways (i.e., now synonymous with coarse crackles).[23] It is useful to monitor the pitch and duration of wheezing. Improved expiratory flow is associated with a decrease in the pitch and length of the wheezing.

Another continuous adventitious lung sound, heard primarily over the larynx and trachea during inhalation, is **stridor**, a loud, high-pitched sound associated with upper airway obstruction (i.e., larynx or trachea) and often heard without a stethoscope. It is more common in infants and children. Laryngomalacia is the most common cause of chronic stridor, whereas croup is the most common acute cause. Generally, inspiratory stridor is consistent with narrowing above the glottis, whereas expiratory stridor indicates narrowing of the lower trachea. In adults, stridor most often occurs from laryngeal or subglottic edema secondary to airway trauma or infection (e.g., epiglottitis).

Mechanisms and significance of lung sounds. Lung sounds are audible vibrations primarily generated by turbulent airflow in the larger airways. These sounds are altered as they travel through the lung periphery and chest wall. Normal lung tissue acts as a *low-pass filter* (preferentially passes low-frequency sounds). This explains the characteristic differences between tracheal breath sounds, heard directly over the trachea, and vesicular sounds, heard over the lung periphery.[23] In essence vesicular lung sounds are attenuated tracheal breath sounds. However, when lung tissue density increases because of atelectasis or because it is consolidated (e.g., pneumonia), attenuation is reduced, and breath sounds over the affected area change from vesicular to something resembling that heard over the trachea. When in doubt, the RT should use tracheal sounds as a reference point for assessing lung sounds.

Diminished breath sounds. Diminished breath sounds have two sources: either diminished airflow velocity (i.e., sound intensity) in the larger airways, or when sound transmission through the lung or chest wall is blunted. Shallow and slow breathing patterns reduce sound intensity by creating less

turbulent flow, whereas reduced sound transmission occurs for a variety of other reasons. These include: (1) airways plugged with mucus, (2) hyperinflated lung tissue (e.g., COPD, asthma), (3) air or fluid in the pleural space (e.g., pneumothorax, hemothorax, pleural effusion), (4) anasarca (generalized body edema), and (5) obesity or when chest muscles are highly developed.

Wheezes and stridor. High-velocity airflow through a narrowed airway (e.g., from bronchospasm, airway edema, foreign bodies, etc.) produces vibrations described as wheezes or stridor. Narrowing initially causes airflow velocity to increase which in turn causes lateral wall pressure to decrease, narrowing the airways to the point that airflow ceases. When airflow stops, the lateral wall pressure increases, and the airway opens back to the previous position. This cycle repeats many times per second and causes the airway walls to vibrate and make a musical sound similar to a reed instrument.

RULE OF THUMB Expiratory wheezing indicates intrathoracic airway constriction typical of obstructive lung diseases (e.g., bronchitis, asthma). Wheezing may be monophonic (single note) or polyphonic (multiple notes). A monophonic wheeze indicates that a single airway is partially obstructed. Monophonic wheezing may be heard during inhalation and exhalation or during exhalation only. Polyphonic wheezing suggests that many airways are obstructed, such as with asthma, and is heard only during exhalation. Bronchitis and CHF with pulmonary edema also can cause polyphonic wheezing.

Crackles. Crackles are primarily inspiratory sounds produced when airflow moves secretions or fluid in the airways or when collapsed airways pop open during inspiration. They are differentiated according to sound quality (e.g., course or fine) and timing (e.g., early or late). Coarse crackles, also known as rhonchi, are usually associated with airway secretions and often clear with coughing or when the airways are suctioned. Fine crackles that do not clear with coughing are either indicative of air moving through fluid-filled airways such as that which occurs with CHF, or collapsed smaller airways that re-open ("recruited") during inspiration. When alveoli are recruited in this way, they produce a relatively fine sound quality that may appear early or late in the inspiratory phase depending on their location (depth) in the bronchial tree and the intensity of inspiratory effort (i.e., magnitude of inthoracic pressure generated) (Fig. 16.8). A summary linking adventitious breath sounds with potential mechanisms, characteristics, and associated disease states is presented in Table 16.4.

RULE OF THUMB Fine, late inspiratory crackles suggest either restrictive lung diseases such as pulmonary fibrosis or the opening of collapsed (atelectatic) alveoli.

Pleural friction rub. Inflamed pleural surfaces create friction during breathing that produces a creaking or grating sound referred to as a **pleural friction rub.** It is typically heard during inspiration and usually is localized to a discreet site on the chest wall. Although it sounds similar to coarse crackles it is not affected by coughing. The intensity of pleural rubs may increase with deep breathing.

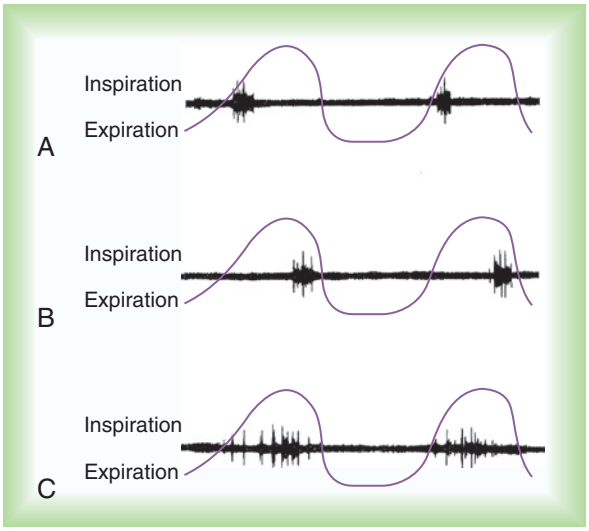

Fig. 16.8 Timing of Inspiratory Crackles. (A) Early inspiratory crackles. (B) Late inspiratory crackles. (C) Pan-inspiratory crackles.

TABLE 16.4 Application of Adventitious Lung Sounds

Lung Sound	Possible Mechanism	Characteristics	Causes
Wheezes	Rapid airflow through obstructed airways	High-pitched, usually expiratory	Asthma, congestive heart failure
Stridor	Rapid airflow through obstructed upper airway	High-pitched, monophonic	Croup, epiglottitis, postextubation laryngeal edema
Coarse crackles	Excess airway secretions moving through airways	Coarse, inspiratory and expiratory	Severe pneumonia, bronchitis
Fine crackles	Sudden opening of peripheral airways	Fine, late inspiratory	Atelectasis, fibrosis, pulmonary edema

Voice sounds. As described above, normal, air-filled lung tissue alters sound transmission ("low pass filter") and reduces the intensity and clarity of spoken words. In contrast, collapsed or consolidated lung tissue increases the transmission of higher-frequency vocal vibrations that enhance the clarity and resonance of spoken words. The terms used for this phenomenon are *egophony* or **bronchophony.** This is evaluated by instructing the patient to repeat the words "one," "two," "three," or "ninety-nine" while auscultating the chest, comparing one side with the other. When listening over consolidated lung tissue, the words will be transmitted louder and clearer. Alternatively, instruct the patient to repeatedly pronounce a long A sound. Consolidated lung will transmit the A sound as an E, which is referred to as *E to A egophony*.

Cardiac Examination

Because of the close relationship between the heart and lungs, chronic lung diseases often cause cardiac problems. The techniques for physical examination of the chest wall overlying the heart

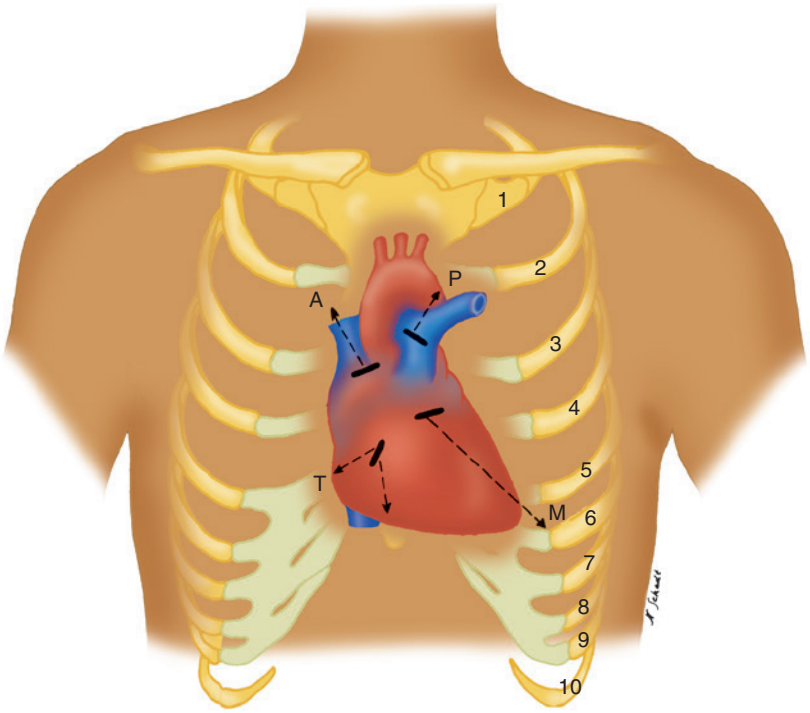

Fig. 16.9 Anatomic and Auscultatory Valve Area. Location of anatomic valve sites is represented by solid bars. Arrows designate transmission of valve sounds to their respective auscultatory valve areas. *A,* Aortic valve; *M,* mitral valve; *P,* pulmonic valve; *T,* tricuspid valve.

(**precordium**) include inspection, palpation, and auscultation. Most clinicians examine the precordium at the same time they assess the lungs.

Inspection and Palpation

Inspection and palpation of the precordium help identify normal or abnormal pulsations. Pulsations on the precordium are created by ventricular contraction. Detection of pulsations depends on the force of ventricular contraction and the thickness of the chest wall through which the vibrations travel.

Normally, left ventricular contraction is the most forceful and generates a palpable pulsation called the *point of maximal impulse* (PMI). To identify the PMI, place the palm of the right hand over the lower left sternal border.

Cardiopulmonary disease often produces changes in PMI. For example, PMI shifts laterally with left ventricular hypertrophy. In contrast, right ventricular hypertrophy produces a systolic **heave** (or thrust) felt near the lower left sternal border. This is a common finding in patients with chronic hypoxemia, pulmonary valvular disease, or primary pulmonary hypertension. The PMI is often difficult to palpate in severe emphysema, because hyperinflated lungs poorly transmit systolic vibrations.

Both pneumothorax and lobar collapse shift the mediastinum and therefore PMI location. The PMI will shift *toward* lobar collapse and *away* from a tension pneumothorax. With severe pulmonary hyperinflation the PMI may shift centrally to the epigastric area.

The second left intercostal space near the sternal border is referred to as the *pulmonic area* and is palpated to identify accentuated pulmonary valve closure. Strong vibrations may be felt in this area with the presence of pulmonary hypertension or valvular abnormalities (Fig. 16.9). Valvular abnormalities may produce palpable vibrations or **thrills** that often are accompanied by a murmur (see later).

Auscultation of Heart Sounds

Heart sounds are auscultated using either the bell or diaphragm of the stethoscope. Optimal auscultation occurs when the patient leans forward or lies on the left side, as this moves the heart closer to the chest wall.

Normal heart sounds are created by closure of the heart valves (see Chapter 10). The first heart sound (S_1) is produced by closure of the mitral and tricuspid (atrioventricular [AV]) valves during ventricular contraction. When systole ends and the ventricles relax, the pulmonic and aortic (semilunar) valves close, creating the second heart sound (S_2). Asynchronous closure of the AV valves and semilunar valves creates a *pronounced* split heart sound. A third, low-pitched heart sound (S_3) is heard over the apex of the heart that, in adults, may signify CHF. A fourth heart sound (S_4) occurs later and may be a sign of heart disease. A patient with heart disease who has S_3 and S_4 is said to have a **gallop rhythm**.

Abnormal Heart Sounds

Both cardiac and extracardiac abnormalities reduce the intensity of heart sounds. Pulmonary hyperinflation, pleural effusion, pneumothorax, and obesity make it difficult to identify S_1 and S_2 as well as poor cardiac contractility or valvular disease. In

contrast, an intense S_2 (**loud P2**) occurs in pulmonary hypertension due to forceful closure of the pulmonic valve.

Cardiac **murmurs** are created by (1) a backflow of blood through an incompetent valve, (2) a forward flow of blood through a stenotic ("narrowed") valve, and (3) rapid blood flow through a normal valve (i.e., strenuous exercise). Cardiac murmurs caused by incompetent or stenotic heart valves are classified as systolic or diastolic.

An incompetent AV valve produces a high-pitched, "whooshing" *systolic murmur* during S_1, whereas restricted blood flow through a stenotic semilunar valve produces a crescendo-decrescendo sound. Blood back-flowing across an incompetent semilunar valve produces an S_2 *diastolic murmur* whereas restricted blood flow across a stenotic AV produces a *turbulent diastolic murmur*.

Abdominal Examination

The RT's focus in abdominal exams is detecting distension and tenderness that impairs diaphragmatic movement and contributes to or causes respiratory insufficiency. Abdominal dysfunction often inhibits deep breathing and coughing thereby promoting atelectasis and secretion retention that increases the risk of pneumonia. For example, **hepatomegaly** (i.e., an enlarged liver) commonly occurs in both patients with liver disease or cor pulmonale and frequently results in right lower lobe atelectasis and pleural effusion.

Of particular concern is intraabdominal hypertension (i.e., intraabdominal pressure >12 mm Hg) that occurs in 20% to 30% of critically ill patients.[24] **Abdominal compartment syndrome** occurs when intraabdominal pressures exceed 20 mm Hg, often requiring emergency decompressive surgery. This syndrome causes profound atelectasis and hypoxemia, hypotension, and renal failure.

Intraabdominal hypertension is characterized by pronounced abdominal distension, and is common in patients with abdominal trauma, ruptured aortic aneurysm, bowel infarction, and end-stage liver failure. Intraabdominal pressure is measured by connecting an intraarterial pressure catheter to the culture port of a Foley urine catheter.

Examination of the Extremities

Respiratory disease may cause abnormalities of the extremities, including digital clubbing, cyanosis, and pedal edema.

Clubbing

Clubbing is the painless enlargement of the terminal phalanges of the fingers and toes associated with numerous cardiopulmonary and other diseases. It is a slow-emerging process whereby the angle of the fingernail to the nail base increases, and the base of the nail feels "spongy." Although a profile view of the digits allows easier recognition (Fig. 16.10), the most important sign is the sponginess of the nail beds. Causes of clubbing include infiltrative or interstitial lung disease, bronchiectasis, various cancers (particularly lung cancer),[25] congenital heart disease, severe liver failure,[26] and inflammatory bowel disease. COPD alone, even when hypoxemia is present, does not lead to clubbing. Clubbing of the digits in a patient with COPD indicates that something other than obstructive lung disease is occurring.

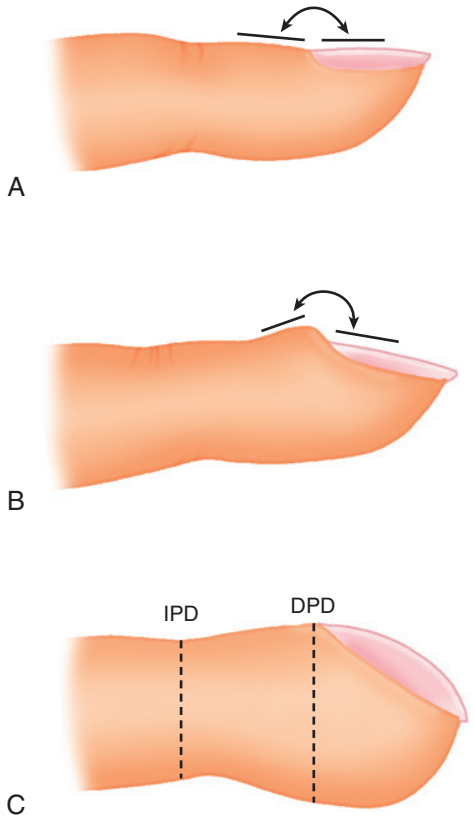

Fig. 16.10 (A) Normal digit configuration. (B) Mild digital clubbing with increased hyponychial angle. (C) Severe digital clubbing; the depth of the finger at the base of the nail *(DPD)* is greater than the depth of the interphalangeal joint *(IPD)* with clubbing.

Cyanosis

Whenever hypoxemia is suspected the digits should be examined for cyanosis. Because the fingernails and skin are relatively translucent cyanosis is readily detectable. Cyanosis becomes visible when the amount of unsaturated hemoglobin in capillary blood exceeds 5 to 6 g/dL. This may be caused by a reduction in arterial or venous O_2 content, or both.

Cyanosis is classified as either peripheral or central. **Peripheral cyanosis** signifies poor perfusion of the extremities (particularly the digits), so that the tissues extract more O_2. This reduces the venous O_2 content, thereby increasing the amount of reduced hemoglobin. The term *acrocyanosis* is used when extensive portions of limbs are involved. The extremities are usually cool to the touch when peripheral cyanosis is present. It should be noted that a brief period of acrocyanosis is a normal finding in certain newborn babies. In contrast, **central cyanosis** is when the mucosa or the torso are involved and may signal severe lung disease, profound hypotension, or the presence of certain congenital heart diseases. Of note, the RT must always be mindful that cyanosis may be masked by several factors, including low room lighting, darker skin pigmentation, and severe anemia.

Pedal Edema

See discussions of common cardiopulmonary symptoms.

MINI CLINI

Evaluation of Acute-Onset Respiratory Distress

Problem

The RT is called to evaluate a 55-year-old woman with acute respiratory distress and worsening hypoxemia. The patient is 3 days post-admission for right-sided rib fractures. This resulted from falling down a flight of stairs during alcohol intoxication with brief loss of consciousness. Since admission her oxygenation has been adequate with pulse oximetry (SpO_2) of 95% on 3 L/min of nasal O_2. Over the past hour she has become febrile (maximum temperature 39.5°C), has developed tachypnea (32 breaths/min), tachycardia (heart rate 130 beats/min), and hypotension (blood pressure 88/50 mm Hg; mean, 63 mm Hg). Her SpO_2 is now 87% on 6 L/min nasal O_2. This also coincides with new-onset altered mental status. Her medical history is significant for alcoholism and a 30 pack-year smoking history. What can the physical examination and history tell us about the potential source of respiratory distress?

Solution

The signs, symptoms, and history suggest bacterial pneumonia possibly from aspiration during her initial loss of consciousness or from a pulmonary contusion. Bacterial pneumonia has an incubation period of 1 to 3 days. The associated high fever, tachycardia, hypotension, and altered mental status also suggest that pneumonia has resulted in sepsis (systemic inflammation). Pulmonary contusion also can result in pneumonia and ARDS (see Chapter 29), with a peak occurrence at approximately 72 h.[27]

Rib fractures are painful and limit deep breathing and effective coughing, leading to atelectasis and retained secretions that increase the risk for pneumonia. When extensive, rib fractures also cause chest wall instability that limits effective ventilation and heightens the risk for respiratory failure. Both alcoholism and cigarette smoking further increase the susceptibility to pneumonia.[28,29] Also, a history of alcohol abuse may be a contributory factor because the onset of acute alcohol withdrawal typically occurs in this time frame.[30]

The first priority is to increase O_2 therapy to achieve adequate oxygenation (SpO_2 ≥90%) while conducting an examination. Worsening oxygenation, despite doubling O_2 therapy, suggests refractory hypoxemia, which is a hallmark of ARDS. This situation indicates the need for high-concentration O_2 therapy, continuous pulse oximetry, and close hemodynamic monitoring.

The RT should be alert for signs suggestive for heightened work of breathing (rapid-shallow breathing, accessory inspiratory muscle use, along with tracheal or intercostal retractions and expiratory muscle recruitment), chest wall instability (paradoxical chest motion), and diminished ventilation (global decrease in breath sound intensity). Breath sounds should be evaluated for evidence suggesting the presence of secretions (coarse, bubbling crackles) or pulmonary edema (fine inspiratory crackles). Another possibility is acute pulmonary embolism, which would become a more prominent consideration if the patient had also suffered pelvic or leg fractures and was immobilized or has redness and swelling of the lower extremities. Although a pneumothorax is unlikely in this situation, the chest should be inspected for signs (e.g., subcutaneous emphysema, JVD, unilateral chest excursion).

Further work-up would include a chest radiograph to confirm the suspicion of pneumonia or chest contusion (and to rule out a pneumothorax), an arterial blood gas to evaluate the severity of hypoxemia and the adequacy of ventilation, and blood samples to evaluate the presence of infection (see Chapter 17). The results of these tests and the patient's response to therapeutic interventions would determine where the patient can be safely and optimally managed.

Capillary Refill

Capillary refill is an expedient method to assess peripheral perfusion by pressing firmly on the patient's fingernail until the nail bed is blanched, and then releasing the pressure. The speed at which the blood flow and color return is noted. Healthy individuals with good cardiac output and digital perfusion have capillary refill times of 3 seconds or less. Poor cardiac output and/or poor digital perfusion results in a slow capillary refill that often exceeds 5 seconds. Capillary refill time should be assessed in the context of whether or not the skin is mottled (i.e., blotched skin shade) and skin temperature.

Peripheral Skin Temperature

When systemic perfusion is poor (as in heart failure or shock), there is a compensatory vasoconstriction in the extremities that diverts blood to the vital organs. This reduction in peripheral perfusion causes the extremities to become cool to the touch. The extent to which coolness extends back toward the torso indicates the degree of circulatory failure. In contrast, patients with high cardiac output and peripheral vascular failure (as occurs in septic shock) may have warm, dry skin.

SUMMARY CHECKLIST

- Bedside assessment is the process of interviewing and examining a patient for signs and symptoms of disease, as well as evaluating the effects of treatment.
- Signs refer to the *objective manifestation* of illness (e.g., increased respiratory rate) whereas symptoms refer the sensation or *subjective experience* of some aspect of an illness (e.g., breathlessness).
- Four factors affecting communication between the RT and the patient are sensory and emotional, environmental, verbal and nonverbal communication process, and cultural-social-personal histories of both the RT and the patient.
- Social space is socially-appropriate space (approximately 4 to 12 feet distance) from where introductions are made. Personal space is 2 to 4 feet and is the distance from which private information is exchanged.
- The five common characteristics of symptoms that can be identified by asking neutral questions are: When did it start? How severe is it? Where on the body is it? What seems to make it better or worse? Has it occurred before?
- Dyspnea specifically refers to the perception that breathing effort is excessive relative to the tidal volume achieved (e.g., "hard to breathe"), whereas breathlessness refers to an unpleasant urge to breathe (e.g., not being able to "catch your breath").
- The perception of breathing is complex and includes the following three major factors: neural drive emanating from the respiratory centers in the brainstem, sensory information regarding tension developed in the respiratory muscles, and the corresponding displacement of the lungs and chest wall.
- The four questions used to assess dyspnea in patients during an interview are: What activities trigger dyspnea? How much activity triggers the sensation? Does the quality of dyspnea change depending upon the activity? How long ago did dyspnea first become noticeable and how rapidly did it progress over time?
- An effective cough depends upon the ability to take a deep breath, the elastic recoil properties of the lungs, expiratory muscle strength, and airways resistance.

- The five characteristics that RTs must monitor are whether a cough is dry or loose, productive or nonproductive, acute or chronic; occurs more frequently at particular times; and whether it is provoked by a certain body positions.
- Infected or purulent sputum typically is thick, colored, sticky, and sometimes foul-smelling, whereas mucoid sputum is clear and may be thick.
- Massive hemoptysis is a medical emergency defined as more than 300 mL within 24 hours and commonly occurs in patients with bronchiectasis, lung abscess, and tuberculosis. In contrast, non-massive hemoptysis produces less blood and is associated with a multitude of conditions such as airway infections, pneumonia, lung cancer, tuberculosis, blunt or penetrating chest trauma, and pulmonary embolism.
- Pleuritic chest pain usually is a sharp, stabbing pain located laterally or posteriorly on the chest that worsens with deep breathing. It is a common symptom in pneumonia, empyema, pleural effusion, and pulmonary embolism. Non-pleuritic chest pain typically is a dull ache or pressure located in the center of the anterior chest and may radiate to the shoulder, neck, or back brought on by exertion or stress and is associated with coronary artery occlusion. It is not affected by breathing.
- Fever is a temperature greater than 38.3°C (101°F) commonly associated with bacterial, viral, or fungal infections. But there are also numerous non-infectious causes including drug reactions, malignancies, head trauma, burns, alcoholic cirrhosis, thromboembolic disorders, and noninfectious inflammatory diseases.
- Pedal edema is either pitting (e.g., leaves a dent when pushing down on the skin) or weeping (e.g., causes fluid to leak when pushing down on the skin) and is a characteristic finding in CHF and cor pulmonale as well as end-stage liver disease.
- The five major categories of patient information documented in the medical record are: chief complaint and history of present illness, past medical history, family and social/environmental history, review of systems, and advance directive (i.e., any limits of care).
- Smoking history is recorded in pack-years and is determined by multiplying the number of packs smoked per day by the number of years smoked.
- The physical examination consists of four general steps: visual inspection, palpation, percussion, and auscultation.
- The four criteria that comprise sensorium (i.e., cognitive functioning) are the patient's orientation to time, place, self, and their current circumstances.
- The basic vital signs are temperature, pulse rate, blood pressure, respiratory rate, and oxygen saturation.
- The eight anatomic locations where a pulse can be palpated are the radial, brachial, femoral, carotid, dorsalis pedis, temporal, popliteal, posterior tibial arteries.
- Arterial hypertension is chronically elevated blood pressure of 140/90 mm Hg or greater that is categorized as Stage I (systolic pressure: 140 to 159 mm Hg or diastolic pressure: 90 to 99 mm Hg), stage II (systolic pressure: ≥160 mm Hg, or the diastolic pressure is ≥100 mm Hg), or prehypertension (systolic pressure of 120 to139 mm Hg or diastolic pressure of 80 to 89 mm Hg), which denotes increased risk of developing hypertension.
- Hypotension is a systolic arterial pressure less than 90 mm Hg, a mean arterial pressure less than 65 mm Hg, or a decrease in systolic pressure greater than 40 mm Hg in patients with established hypertension. Although hypotension often is associated with shock, the distinction is that shock specifically refers to tissue perfusion that fails to meet metabolic demand (i.e., it cannot reliably be determined by measuring blood pressure alone).
- The common signs used to infer increased work of breathing on a physical exam include nasal flaring, recruitment of the sternocleidomastoid and abdominal muscles, tracheal tugging, and chest wall retractions (i.e., intercostal, subcostal, supraclavicular).
- The two archetypal breathing patterns during respiratory distress are rapid shallow breathing (restrictive conditions) and a pattern characterized by a prolonged expiratory phase.
- Abnormal breathing patterns typically associated with neurologic disease or injury include Cheyne-Stokes respiration, Biot respiration, apneustic breathing, central neurogenic hypoventilation, and hyperventilation.
- Lung hyperinflation causes a flattening of the diaphragm that produces a paradoxical inward movement of the lower rib cage during inspiration (Hoover's sign). Without clinical intervention diaphragmatic fatigue can manifest into one of two breathing patterns (respiratory alternans or abdominal paradox).
- The three normal breath sounds are vesicular, bronchovesicular, and tracheal and are related to specific sites of auscultation.
- The two main adventitious breath sounds are discontinuous sounds (rales or crackles) and continuous, quasi-musical sounds (wheezing and stridor). Rales and crackles are associated with pneumonia, bronchitis, atelectasis. Wheezing is associated with asthma and CHF whereas stridor is most frequently associated with upper airway obstruction from laryngeal edema or spasm.
- The PMI is a palpable pulsation over the lower left sternal border created by left ventricular contraction. In the presence of left ventricular hypertrophy the PMI shifts laterally whereas right ventricular hypertrophy produces a systolic heave that can be felt near the lower left sternal border. The PMI is often difficult to palpate in severe emphysema.
- The four common heart sounds are: S_1 (produced by AV valve closure during ventricular contraction), S_2 (closure of the semilunar valves), S_3 (a low-pitched sound heard over the apex of the heart in adults that may signify CHF), and S_4 that occurs later and also is associated with heart disease.
- Abdominal distension and tenderness impair diaphragmatic movement and inhibits deep breathing and coughing thereby promoting atelectasis and secretion retention that increases the risk of pneumonia.
- The four signs gleaned from examination of the extremities that suggest the presence of cardiopulmonary disease are clubbing of the digits, cyanosis, pedal edema, and skin temperature.

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17

Interpreting Clinical and Laboratory Data

Richard H. Kallet

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Describe a critical value and its importance in clinical practice.
- Define leukocytosis, leukopenia, anemia, polycythemia, and thrombocytopenia.
- Identify which electrolyte disturbances interfere with normal respiratory function.
- Describe clinical tests used to identify cardiac stress and myocardial infarction.
- Identify the three main tests used to diagnose coagulation disorders.
- Describe how the sputum Gram stain and culture are used to diagnose pulmonary infections.
  - Discuss the acid-fast test used to identify *Mycobacterium tuberculosis.*
  - Explain the advantages of the Xpert MTB/RIF in diagnosing Mycobacterium tuberculosis infections.
- List the cut-off values of sweat chloride used to diagnose cystic fibrosis and identify borderline cystic fibrosis cases.

CHAPTER OUTLINE

KEY TERMS

acid-fast bacterium
analyte
anemia
anion gap
bands
basic chemistry panel
B-type natriuretic peptide
complete blood count
creatine phosphokinase
critical test value
D-dimer
erythrocytes
glucose
hematocrit
hematology
hemolysis
homeostasis
hyperglycemia
hyperkalemia
hypernatremia
hypoglycemia
hypokalemia
lactate
leukocytes
leukocytosis
leukopenia
neutropenia
neutrophilia
polycythemia
reference range
segs
sweat chloride
thrombocytes
thrombocytopenia
total bilirubin
troponin
troponin I

INTERPRETING CLINICAL LABORATORY TESTS

This chapter discusses common blood tests performed on patients. These tests evaluate a patient's general health and baseline status, identify organ dysfunction, detect infection, shape the care plan, and monitor its effectiveness. Hence, the respiratory therapist (RT) must be familiar with these tests and their value in helping diagnose and treat respiratory disease. Also, this chapter briefly reviews physiologic concepts related to these tests, contains reference-range values, and explains their significance in patient assessment.

Introduction to Laboratory Medicine

Laboratory medicine studies tissue and fluid specimens from patients and consists of five disciplines. *Clinical biochemistry* analyzes blood, urine, and other bodily fluids for electrolytes and proteins; **hematology** analyzes cellular components of blood. *Clinical microbiology* tests blood and other bodily fluids for infectious agents including bacteria *(bacteriology)*, viruses *(virology)*, fungi *(mycology)*, and parasites *(parasitology)*. *Immunology* is a discipline focusing on autoimmune and immunodeficiency diseases. Finally, *anatomic pathology* assists with diagnosing diseases by analyzing tissue samples.

Reference Range

Laboratory tests help determine a patient's health status and aid medical decisions. Therefore it is important to determine whether test results fall within an expected range of values considered to be "normal." However, the term *normal* is not synonymous with *healthy*. For example, someone can have a normal red blood cell (RBC) count but the cells may not be capable of carrying or unloading oxygen, such as can occur with cyanide poisoning.

In the 1970s,[1] the term *normal ranges* was replaced with more appropriate terms such as *reference ranges, biologic reference intervals,* and *expected value*.[2] This newer terminology acknowledged that what we consider normal must account for variations related to age, gender, race, and ethnicity which change over time. A **reference range** sets the boundaries for, and expected variability of, any **analyte** (the object of a test such as an electrolyte or blood cell) likely to be encountered in healthy patients.

Reference ranges differ from laboratory to laboratory for various reasons. These include differences in measurement techniques, the populations of healthy individuals used to establish the reference intervals, and analytic imprecision. Most differences in reference ranges between laboratories are small.[2] Reference ranges and critical values displayed in this chapter serve as representative examples; however, RTs must become familiar with the reference ranges used at their institutions.

RULE OF THUMB A normal laboratory test value is not synonymous with health. Rather, it is just one clinical finding which must be combined with many others to determine a patient's health status.

Critical Test Value

A **critical test value** is a result *significantly* outside the reference range and represents a pathophysiologic condition. A critical value may signal a *potentially* life-threatening condition and often warrants immediate clinical action to protect patients. Critical values are communicated by the clinical laboratory to the unit where the patient is located. The nurse or RT receiving these results must read back the critical value to the clinical laboratory or point of service to ensure accuracy. The nurse or RT then must communicate the critical value in a timely fashion to the physician, physician assistant, or nurse practitioner caring for the patient. The same read-back procedure is used. All communication of critical test values is documented in the medical record.

RULE OF THUMB A critical lab value is one that may indicate a potentially life-threatening condition. These values must be communicated to the treating physician in a timely fashion.

In this chapter, critical values are listed along with pathophysiologic states in which they commonly occur. Some clinical analytes lack a critical value because none has been established. Other analytes have only a one-sided value that exists below or above a critical threshold. This occurs with substances not normally present in the blood such as intracellular enzymes and proteins released only after extensive damage following injury (see later section on enzyme tests). Normally these proteins or enzymes are virtually undetectable.

When interpreting abnormal test results, clinicians must consider the *context* of the change. For example, a serum creatinine of 3.0 mg/dL (approximately twice the upper limit of normal) generally is not considered urgent in patients with chronic renal disease. However, in a patient with previously normal kidney function who now presents with septic shock, the same creatinine value is critical because it indicates acute kidney injury from both bloodstream infection and insufficient renal perfusion.

Complete Blood Count

The **complete blood count** (CBC) describes the number of circulating white blood cells (WBCs), called **leukocytes**; RBCs, called **erythrocytes**; and platelets, called **thrombocytes**. The WBC count consists of five types of cells and is reported as a *differential*. RBCs are evaluated for size and hemoglobin (Hb) content. Platelets are evaluated by the number present. Table 17.1 lists the normal CBC results for adults.

Leukocytosis refers to an elevated WBC count and has multiple causes including stress, infection, and trauma. The degree of leukocytosis reflects the severity of infection. A significantly elevated WBC count ($>20 \times 10^3$/mcL) raises concern for serious infection and that the patient's immune system is generating a strong response. In contrast, **leukopenia** (or leukocytopenia) is a WBC count below normal often occurring when the immune system is overwhelmed by infection, or with immunosuppressive conditions such as acquired immunodeficiency syndrome (AIDS) and chemotherapy given to cancer patients.

RULE OF THUMB Leukocytosis often represents a vigorous immune response often to either infection or trauma.

RULE OF THUMB Leukocytopenia often signifies that either the immune system has been overwhelmed by infection or there is presence of immunosuppression.

White Blood Cell Count

The WBC differential count determines the number of each type of WBC present in the blood (Table 17.2). Most circulating WBCs are either neutrophils or lymphocytes. Leukocytosis is a significant elevation in the WBC count ($>15 \times 10^3$/mcL) that occurs when either neutrophils or lymphocytes are responding

to an abnormality. Basophils, eosinophils, and monocytes make up a small proportion of the circulating WBCs and rarely cause a major increase in the WBC count.

The WBC count differential is calculated by multiplying the percentage of each WBC subtype by the total WBC count. This prevents misinterpreting the WBC count differential when one cell type changes, causing a *relative change* (percentage) in the other four cell types. For example, if the neutrophil count doubles because of infection, the relative percentage of the other four cell types would decrease, although their absolute number would not change.

Analyzing specific lymphocytes is crucial in identifying human immunodeficiency virus (HIV) infection that causes AIDS. HIV targets and destroys CD4 T lymphocytes. Opportunistic infections such as *Pneumocystis jiroveci* pneumonia generally occur when lymphocytes decrease to less than 200×10^6/L, and this information is used to diagnose AIDS.

Neutrophilia refers to an absolute elevation in neutrophils. Immature neutrophils are called **bands** because of their banded shape nucleus, and are located in the bone marrow, where they mature. Mature neutrophils are known as **segs** because their nucleus has a segmented shape. Severe infection causes the bone marrow to release stores of both mature and immature neutrophils, and both bands and segs into the circulating blood. When bands and segs are elevated in the CBC, the patient is likely experiencing a more severe bacterial infection.

Neutropenia is a reduction in the number of circulating neutrophils observed in patients with bone marrow disease (e.g., lymphoma, leukemia), autoimmune disorders, HIV infection, and those undergoing chemotherapy for cancer. Neutropenia increases the risk for the developing opportunistic infections.

TABLE 17.1 Reference Range Values for Complete Blood Count in an Adult

Test	Reference Range
Red Blood Cell Count	
Men	$4.4–5.9 \times 10^6$/mcL
Women	$3.8–5.2 \times 10^6$/mcL
Hemoglobin	
Men	13.3–17.7 g/dL
Women	11.7–15.7 g/dL
Hematocrit	
Men	40%–52%
Women	35%–47%
White blood cell count	$3.9–11.7 \times 10^3$/mcL
White Blood Cell Differential	
Segmented neutrophils	40%–75%
Bands	0%–6%
Eosinophils	0%–6%
Basophils	0%–1%
Lymphocytes	20%–45%
Monocytes	2%–10%
Platelet count	$150–400 \times 10^3$/mcL

Values for reference ranges and critical test results are from the University of California–San Francisco Moffit-Long Hospital and San Francisco General Hospital.[14] Reference ranges may differ between hospitals and laboratories so the respiratory therapist should be aware of the value in her/his own hospital.

RULE OF THUMB Elevation of the white blood cell count usually is caused by an increase in either neutrophils or lymphocytes in response to infection.

RULE OF THUMB When bands and segs are elevated in the complete blood count, the patient is likely experiencing a more severe bacterial infection.

Red Blood Cell Count

Erythrocytes (i.e., RBCs) supply oxygen to the tissues, so the RBC count helps determine the ability of the blood to carry O_2. An abnormally low RBC count is referred to as **anemia** which has several potential causes: inadequate production of RBCs by the bone marrow, **hemolysis** (RBC destruction), or excessive blood loss (e.g., from hemorrhage).

Regardless of the source, the blood's O_2-carrying capacity is reduced, placing the patient at risk for tissue hypoxia. Causes of anemia include dietary deficiencies in iron or vitamins (e.g., vitamin B_{12} and folate), chronic inflammatory diseases such as Crohn disease, HIV/AIDS, lymphoma, and autoimmune diseases

TABLE 17.2 Reference Range Values for White Blood Cell Count Differential and Common Causes for Abnormalities

Cell Type	Relative Value (%)	Absolute Value	Causes for Abnormalities
Neutrophils	40–75	$1.8–6.8 \times 10^9$/L	Increased with bacterial infection and trauma; reduced with bone marrow diseases (critical value <1.0)
Lymphocytes	20–45	$1.0–3.4 \times 10^9$/L	Increased with viral and other infections; reduced with immunodeficiency problems
CD4 T lymphocytes	31–60[a]	$410–1590 \times 10^6$/L	HIV disease; diagnostic threshold <200
Eosinophils	0–6	$0–0.4 \times 10^6$/L	Increased with allergic reactions and parasitic infections
Basophils	0–1	$0–0.1 \times 10^6$/L	Increased with allergic reactions
Monocytes	2–10	$0.2–0.8 \times 10^6$/L	Increased with invasion of foreign material

[a]Percentage of lymphocyte.

Values for reference ranges and critical test results are from the University of California–San Francisco Moffit-Long Hospital and San Francisco General Hospital. Reference ranges may differ between hospitals and laboratories so the respiratory therapist should be aware of the value in her/his own hospital.

MINI CLINI

White Blood Cell Count Differential

Problem

A patient admitted to the hospital for acute shortness of breath and fever has a chest X-ray revealing pneumonia. The CBC shows an increased WBC count of 15×10^3/mcL with 75% neutrophils but only 10% lymphocytes. Given that the normal lymphocyte differential is 20% to 45%, does the value of 10% suggest a problem with lymphocyte production by the immune system? What type of pneumonia is probably present in this case?

Solution

The 10% differential for the lymphocytes represents a *relative value*. Because the total WBC count is markedly elevated, the 10% in relative terms represents 1500 lymphocytes in absolute value, which is within normal range. If the total WBC count was reduced to less than normal and the differential showed a lymphocyte count of 10%, an abnormal absolute value would be present and would suggest an immunologic problem. This patient probably has bacterial pneumonia, given the elevated number of neutrophils.

that destroy erythrocytes (hemolytic and aplastic anemia). A hereditary cause is sickle cell anemia, which is more common in African Americans. For most forms of anemia, a blood transfusion may be needed if the RBC count is too low, as discussed later in this chapter.

Polycythemia is an abnormally elevated RBC count. It often occurs when the bone marrow is stimulated to produce extra RBCs generally in response to chronic hypoxemia (secondary polycythemia). Polycythemia counteracts reduced PO_2 by increasing the O_2-carrying capacity of the blood. Patients living at high altitudes and those with chronic lung disease are most likely to experience chronic hypoxia and develop secondary polycythemia.

In addition to the RBC count, the clinical laboratory reports Hb and hematocrit (Hct) levels. Hb (sometimes referred to as "Hgb") is a protein substance with the unique ability to bind with O_2. Each healthy RBC contains 200 million to 300 million molecules of Hb, for an Hb level of 12 to 18 g/dL in a healthy adult. Females tend to have a slightly lower Hb than males. Patients with an inadequate Hb concentration have a reduced O_2-carrying capacity. In this condition, the RBCs are smaller than normal *(microcytic anemia)* and lack normal color *(hypochromic anemia)*. The necessity for RBC transfusion depends on the cause of anemia and the patient's overall condition. Transfusions generally are indicated only when the Hb concentration falls to 7.0 g/dL (an Hct of approximately 21%) or below.[3]

The Hct is the ratio of RBC volume to whole blood. It is determined by spinning a blood sample in a centrifuge to separate the blood cells from the plasma. The proportion of the sample represented by the packed cells is the **hematocrit**. A low Hct occurs with anemia and a high Hct with polycythemia. The Hct also reflects the patient's hydration status. Dehydration causes the Hct to increase (hemoconcentration) due to lower blood volume relative to RBC count, whereas overhydration causes it to decrease via hemodilution.

RULE OF THUMB In most circumstances, the recommended threshold for blood transfusion is at or below a Hb of 7.0 g/dL or Hct of 21%.

Electrolyte Tests

Basic Concepts for Understanding Electrolyte Balance

Normal cellular function depends on homeostasis of fluids, electrolytes, and acid-base balance. **Homeostasis** is the ability of complex organisms to maintain a *dynamic balance* or *equilibrium* in their internal environments by making constant adjustments. The guiding principle is that the total amount of water, electrolytes, acid, and base gained each day must be balanced by the total amount lost.

Two important points must be emphasized when interpreting blood tests. First, blood samples provide a one-time "snapshot" of processes that are constantly changing. These "snapshots" provide the clinician with valuable but time-limited insight. Often, the most important information comes from repeated or serial measurements, whereby the trends can be assessed. Changes over time provide vital information about the severity and progression of disease as well as the need for therapy and its effectiveness.

Second, the intravascular blood compartment is remote from the intracellular environment. Serum electrolyte levels only suggest what might be occurring in the intracellular compartment. This is because the intracellular fluid compartment represents approximately two-thirds of total body fluid. By comparison, the extracellular fluid compartment represents approximately one-third, and the blood plasma is only a small fraction of the extracellular environment. Therefore, monitoring blood plasma abnormalities provides important but limited indirect information about the intracellular environment.

Basic Chemistry Panel

The **basic chemistry panel** (BCP) or *basic metabolic panel* (BMP) includes the predominant electrolytes sodium (Na^+), potassium (K^+), chloride (Cl^-), total carbon dioxide/bicarbonate (CO_2), and **glucose** (Chapter 13). Because the body's electrolyte balance is controlled by the kidneys, excretion of renal-mediated waste products is included: creatinine and blood urea nitrogen. A comprehensive metabolic panel (CMP) includes electrolytes, such as magnesium (Mg^{++}), phosphorus (PO_4^-), and calcium (Ca^{++}). Each electrolyte plays a crucial role in maintaining normal cellular function. Specific information on the reference ranges and physiologic significance of each electrolyte and waste product can be found in Table 17.3. Information regarding the terminology used to describe abnormal test values for electrolytes, diseases associated with these disturbances, and sample critical test results are provided in Table 17.4.

There are subtle differences in how electrolytes are reported, and this may cause confusion. The concentration of electrolytes in solution is reported by either the *number of molecules* (millimoles [mmol]) or their associated valence or *electrical charge* (milliequivalents [mEq]). Although customary practice has been to report electrolytes as mEq/L, many laboratories report electrolytes as mmol/L. In an electrolyte solution, milliequivalents are simply millimoles per liter multiplied by the valence. For example, Na^+ possesses a valence of 1, so that the expression as either mmol/L or mEq/L is the same. For Ca^{++} and Mg^{++}, which both possess a valence of 2, then the mEq value is twice the mmol value.

TABLE 17.3 Components of Basic Metabolic Panel and Common Electrolyte Tests With Sample Reference Ranges and Physiologic Significance

Test	Reference Range[a]	Physiologic Importance
Sodium (Na^+)	136–145 mmol/L	Primary extracellular cation; crucial for maintaining fluid balance and nerve impulse conduction
Potassium (K^+)	3.5–5.1 mmol/L	Primary intracellular cation; crucial for maintaining normal heart and kidney function and acid-base balance
Chloride (Cl^-)	98–109 mmol/L	Primary extracellular anion; crucial for maintaining serum osmolarity and acid-base balance
Total carbon dioxide (CO_2)	22–29 mmol/L	Primary metabolic end product of aerobic metabolism; crucial for maintaining acid-base balance
Calcium (Ca)	8.6–10.5 mg/dL	Most abundant mineral in the body; essential for bone strength, muscular contraction, nerve impulse conduction, and coagulation
Ionized calcium (Ca^{++})	1.12–1.32 mmol/L	The approximately 50% of calcium not bound to circulating proteins; represents the biologically active portion
Glucose (Glu)	70–139 mg/dL	Primary cellular energy source
Creatinine (Cr)	0.7–1.3 mg/dL	Waste product from muscle catabolism excreted by the kidneys; one of the key markers of kidney function because it provides a gross estimation of glomerular filtration rate
Blood urea nitrogen (BUN)	8–23 mg/dL	Waste product from metabolism of amino acids; a key marker of kidney function
Magnesium (Mg^{++})	0.7–0.99 mmol/L	Essential for regulation of most biochemical processes; important for normal muscle and neuronal functioning, regulating heart rate and blood pressure, glucose levels, bone strength, and immune function
Phosphorus (PO_4^-)	0.81–1.45 mmol/L	Main intracellular anion (phosphate), exists as PO_4^- in serum; combined with Ca in teeth and bones; serum levels inversely related to serum Ca
Lactate	0.5–2.2 mmol/L	End product of glucose metabolism under anaerobic conditions; clinically significant levels coincide with regional or systemic tissue hypoxia
Osmolarity	275–295 mOsm/kg	Tonicity or ability to attract water molecules; indicates overall ionic concentration in the serum

[a]Reference ranges vary among clinical laboratories. See text for explanation.
Values for reference ranges and critical test results are from the University of California–San Francisco Moffit-Long Hospital and San Francisco General Hospital.

RULE OF THUMB In reporting electrolytes millimoles (mmol) refers to the *number of molecules* in solution whereas milliequivalents (mEq) refers to their associated valence or *electrical charge*.

Glucose

Carbohydrate degradation produces serum glucose that is metabolized by cells for energy. Insulin, which comes from the pancreas, is necessary for cells to use glucose. **Hyperglycemia** is an abnormally elevated blood glucose level, most often resulting from either diabetes or severe sepsis. **Hypoglycemia** is an abnormally reduced serum glucose level associated with digestive problems, inadequate dietary intake of carbohydrates, or excessive use of insulin in treating diabetes, or it may be drug induced.

Diabetes is diagnosed in one of 3 ways. First is by measuring fasting blood glucose levels (i.e., measured after 12 hours without food). Second is a glycated hemoglobin (hemoglobin A1C) value ≥6.5%. Third is an abnormally elevated serum glucose value after an oral glucose tolerance test (OGTT) whereby a glucose meal is eaten and blood is drawn afterward. Diabetes usually is indicated when one of the following is found: (1) fasting blood glucose level greater than 125 mg/dL on two occasions, (2) hemoglobin A1C ≥6.5%, or (3) 2 glucose values of ≥140 mg/dL after an OGTT.[4] Severe hyperglycemia associated with metabolic acidosis is consistent with *diabetic ketoacidosis* and represents a potentially life-threatening condition if not treated immediately.

In critically ill patients, insulin resistance and severe hyperglycemia (glucose levels >200 mg/dL) are common and are associated with a higher incidence of organ failure and mortality. Insulin therapy is used in critically ill surgical and medical patients to control blood sugar. The practice of maintaining tightly controlled glucose levels (80 to 110 mg/dL) in these patients has been controversial. It now appears that the association between hyperglycemia and mortality is limited to critically ill patients who are *not* diabetic at hospital admission, so that less stringent parameters (glucose levels ≤180 mg/dL) are probably acceptable.[5]

Anion Gap

As discussed in Chapter 14, metabolic acidosis is caused by either the addition of nonvolatile acids or a primary loss of HCO_3^-. The **anion gap** provides a quick method for determining whether a decrease in HCO_3^- is caused by a disruption of normal anion balance or the presence of an abnormal acid anion. A balance normally exists between cations (+ charge) and anions (– charge) in the serum. The normal anion gap occurs because sulfate, phosphate, and organic anions such as lactate are not routinely measured, whereas most cations are measured. The anion gap is calculated by adding the CO_2 and Cl^- values and then subtracting this total from the serum Na^+. The normal anion gap is approximately 8 to 14 mEq/L, and *gap acidosis* usually coincides with an anion gap of 16 mmol/L or greater. However, serum proteins are an important determinant of the anion gap. *Hypoalbuminemia* (decreased serum albumin) is common in critically ill patients and significantly reduces the anion gap. As a rule, for every 1 g reduction in serum albumin below 4 g/dL, the normal value for the anion gap increases (i.e., is corrected upward by 3 mEq/L).

TABLE 17.4 Sample Critical Test Results Reflecting Abnormalities in Electrolyte and Other Common Laboratory Tests

Test	Sample Critical Test Result[a]	Common Pathologic Conditions Associated With *Abnormally High Levels*	Common Pathologic Conditions Associated With *Abnormally Low Levels*
Sodium (Na^+)	>155 mmol/L; <125 mmol/L	***Hypernatremia:*** Dehydration from excessive water loss or fluid restriction; excessive administration of saline fluids or diuretics (usually ≥180 mmol)	*Hyponatremia:* Overhydration or abnormal secretion of antidiuretic hormone; severe vomiting or diarrhea; congestive heart failure, renal or hepatic failure, Addison disease
Potassium (K^+)	>6.0 mmol/L; <3.0 mmol/L	***Hyperkalemia:*** Acute or chronic kidney disease, Addison disease, severe alcoholism, rhabdomyolysis; values ≥ 6 mmol are life-threatening	***Hypokalemia:*** Severe vomiting or diarrhea; chronic renal disease; high-dose beta-agonist therapy
Chloride (Cl^-)	>120 mmol/L; <70 mmol/L	*Hyperchloremia:* Excessive Cl^- administration (usually saline resuscitation during shock); metabolic acidosis, diabetes insipidus	*Hypochloremia:* Severe vomiting or diarrhea; metabolic alkalosis, adrenal insufficiency, severe burns, excessive intravenous dextrose administration
Total carbon dioxide (CO_2)	>40 mmol/L; <15 mmol/L	Ventilatory failure	Metabolic acidosis; hyperventilation syndrome; severe diarrhea
Calcium (Ca)	>13.5 mg/dL; <6.5 mg/dL	*Hypercalcemia:* Hyperparathyroidism, lithium or thiazide diuretic therapy, metastatic cancer, multiple myeloma	*Hypocalcemia:* Hypoparathyroidism, blood transfusions, acute pancreatitis, vitamin D deficiency
Ionized calcium (Ca^{++})	>1.55 mmol/L; <0.8 mmol/L	See above	See above
Glucose (Glu)	>500 mg/dL; <50 mg/dL	*Hyperglycemia:* Diabetes mellitus, severe sepsis	*Hypoglycemia:* Excessive insulin administration, inadequate dietary intake of carbohydrates
Creatinine (Cr)	>10 mg/dL	Acute kidney injury, chronic renal failure	Protein starvation, liver disease
Blood urea nitrogen (BUN)	>100 mg/dL	Acute kidney injury, chronic renal failure, dehydration	Liver disease, malnutrition
Magnesium (Mg^{++})	>1.85 mmol/L; <0.41 mmol/L	*Hypermagnesemia:* Chronic renal failure, Addison disease, diabetic ketoacidosis, dehydration	*Hypomagnesemia:* Cirrhosis, pancreatitis, severe alcoholism, hemodialysis, toxemia of pregnancy, ulcerative colitis
Phosphorus (PO_4^-)	<1.0 mmol/L; >2.5 mmol/L	*Hyperphosphatemia:* Commonly found in patients with renal failure, hepatic failure, bone metastasis, hypocalcemia, hypoparathyroidism	*Hypophosphatemia:* Most often seen in chronic hyperventilation syndrome; also caused by hypercalcemia, hyperparathyroidism, and malnutrition
Lactate	>4 mmol/L	Primary causes of abnormally high lactate: Anaerobic metabolism, hemorrhagic or septic shock, reduced hepatic clearance, dehydration, trauma	N/A
Osmolarity	>320 mOsm/kg; <240 mOsm/kg	Causes for abnorally high osmolarity: Hyperosmolarity: dehydration, uremia, hyperglycemia Hypoosmolarity: diuretic therapy, salt-wasting nephropathy, mineralcorticoid deficiency	Causes for abnormally low osmolarity: Hypoosmolarity: diuretic therapy, salt-wasting nephropathy, mineralcorticoid deficiency

[a]Reference ranges and critical test results vary among clinical laboratories. See text for explanation.
Values for reference ranges and critical test results are from the University of California–San Francisco Moffit-Long Hospital and San Francisco General Hospital.

RULE OF THUMB An anion gap greater than 16 is consistent with the presence of metabolic acidosis.

Lactate

Lactate is the end product of anaerobic glucose metabolism. Blood lactate concentration represents a balance between the rate of lactate production in muscle cells and erythrocytes and the rate of lactate metabolism by the liver. Therefore, lactic acidosis results either from overproduction or its insufficient metabolism. Abnormal lactate levels are found in diverse conditions including liver disease, diabetes mellitus, thiamine deficiency, malignancies, and toxic ingestion (e.g., ethanol, methanol, salicylates). However, the most common cause of lactic acidosis is anaerobic metabolism from tissue hypoxia associated with shock. An initial lactate level above 4 mEq/L signifies the inability to clear excessive lactate and is associated with higher mortality in patients with septic, traumatic, or cardiogenic shock.[6]

RULE OF THUMB In patients with shock, a serum lactate level greater than 4 mEq/L is associated with higher mortality.

Enzyme Tests

Liver Function Tests

The liver is primarily responsible for converting food into substrates essential for cellular metabolism, protein synthesis, and detoxifying substances in the body. Liver damage is assessed by abnormal increases in the hepatic enzymes *alanine*

MINI CLINIC

Anion Gap

Problem 1

A patient is admitted to the intensive care unit for shock and acute renal failure. No arterial blood gas (ABG) samples have been drawn, but the RT suspects the respiratory system is involved because the patient has become increasingly tachypneic over the past 4 h. The electrolyte panel reveals a serum Na^+ of 146 mEq/L, a total CO_2 of 20 mEq/L, and a serum Cl^- of 100 mEq/L. Does the electrolyte panel suggest any problems, and what should be done if there are any?

Solution

The electrolytes are normal except for a decrease in the serum CO_2. The anion gap is calculated by subtracting the sum of CO_2 and Cl^- from Na^+ (146 – [100 + 20]). In this case, the anion gap is elevated (26 mEq/L) and is consistent with a metabolic acidosis. An ABG analysis is needed to evaluate the acid-base status. The patient's rapid breathing probably is related to the metabolic acidosis because hyperventilation decreases PCO_2 and promotes acid-base compensation.

MINI CLINIC

Anion Gap

Problem 2

A patient admitted to the trauma intensive care unit is in hemorrhagic shock after a gunshot wound and is undergoing large fluid volume resuscitation with normal saline. An initial arterial blood gas reveals a pH of 7.25, PCO_2 of 25 mm Hg, and HCO_3^- of 10.6 with a base deficit of –14.9 mEq/L. The trauma surgeon suspects that the volume of normal saline infused is inadequate, and that metabolic acidosis is worsening from continued lactate accumulation. What additional information can be provided by obtaining a basic chemistry panel (BCP) to help guide therapy?

Solution

If the BCP reveals Na^+ of 140 mEq/L, Cl^- of 95 mEq/L, and CO_2 of 20 mEq/L (anion gap of 25 mEq/L), then the surgeon's suspicion that the resuscitation volume is inadequate would be correct. The anion gap of 25 likely represents a worsening lactic acidosis. However, if the BCP reveals Na^+ of 150 mEq/L, CO_2 of 20 mEq/L, and Cl^- of 122 mEq/L, the anion gap would be normal (8 mEq/L). The metabolic acidosis would be caused by an abnormally high serum Cl^- concentration from excessive normal saline administration. This example represents a common problem in emergency and critical care practice: the excessive fluid resuscitation with normal saline of trauma patients with severe shock.

aminotransferase, *aspartate aminotransferase*, and *alkaline phosphatase*. **Total bilirubin** is produced by the liver from the breakdown of destroyed RBCs. It is a crucial component of the liver panel test because it assesses one of the primary functions of the liver. Protein synthesis, another vital aspect of liver function, is assessed by measuring total protein and albumin concentrations. Liver disease is characterized by the inability to remove toxins from the bloodstream. One of the primary toxins associated with altered mental function in patients with liver disease is the accumulation of *ammonia*, which forms from the breakdown of proteins.

Pancreatic and Muscle Enzyme Tests

Other diseases cause abnormal serum enzyme levels. Pancreatitis causes leakage of *lipase* and *amylase* into the circulation. **Creatine phosphokinase** (CPK) or *creatinine kinase* is an enzyme found mainly in heart, brain, and skeletal muscle tissue and ischemic damage to these tissues produce elevated CPK levels. Three types of CPK are associated with each tissue. CPK-1 (CPK-BB) is released primarily from the lungs or brain after injury. Patients with extensive crush injuries and those with muscular dystrophy have elevated CPK due to the skeletal muscle destruction. In addition, those with myositis (i.e., muscle inflammation from infection, trauma, or autoimmune disease) have elevated levels of CPK-3 (CPK-MM). The third type of CPK is associated with cardiac injury and is discussed subsequently.

Lactate dehydrogenase is the enzyme that catalyzes the conversion of pyruvate into lactate. Elevated serum lactate dehydrogenase is associated with tissue breakdown that occurs with many conditions. These include rhabdomyolysis (e.g., skeletal muscle breakdown, typically from traumatic crush injuries that releases myoglobin into the blood), cancer, meningitis, hemolytic anemia, acute pancreatitis, acute myocardial infarction, and HIV disease. Moderate lactate dehydrogenase increases are associated with myocardial infarction or hemolytic anemia (880 units/L), whereas large increases are seen in extensive cancers, rhabdomyolysis, severe shock, and anoxia (8800 units/L).

Cardiac Enzyme and Protein Tests

The most common CPK test is CPK-2 (CPK-MB), an enzyme released from injured heart muscle after myocardial infarction. Levels notably increase 4 to 6 hours and peak 12 to 24 hours after injury. Serial CPK-2 measurements are monitored in patients with suspected myocardial infarction, cardiac contusion from chest trauma, open heart surgery, or myocarditis. **Troponin** is a complex protein regulating skeletal and cardiac muscle contractility. The protein fragment **troponin I** is associated with cardiac muscle damage and is more commonly used than CPK today. Similar to CPK-2, troponin I levels peak 12 to 16 hours after myocardial infarction. Reference values for these enzyme tests are presented in Table 17.5.

B-type natriuretic peptide (BNP) is secreted by the heart in response to increased cardiac muscle stretch. The BNP test primarily is used to evaluate patients for heart failure, particularly those presenting to the emergency department with dyspnea and pulmonary edema.[6] Values greater than 300 pg/mL indicate mild heart failure, above 600 pg/mL moderate heart failure, and greater than 900 pg/mL severe heart failure. Other conditions such as acute respiratory distress syndrome (ARDS) and severe sepsis also cause increased cardiac muscle stretch, often resulting in BNP levels in the range of 300 to 500 pg/mL.[7] BNP cut-off values of ≤200 pg/mL for ARDS and ≥ 1200 pg/mL for acute cardiogenic pulmonary edema are very reliable for discriminating between these two conditions.[8]

Coagulation Studies

Coagulation is the process by which the blood and vascular tree form clots to stop bleeding and repair damage to the injured blood vessels. Damage to the internal vascular wall (endothelium) exposes the blood to tissue factors (i.e., proteins) that attract and activate platelets, which then stimulate clotting. **Thrombocytopenia** (low platelets) and *thrombasthenia* (abnormal platelet

TABLE 17.5 Liver Function and Other Enzymatic Tests

Test	Reference Range	Sample Critical Test Result[a]
Total bilirubin (T Bil)	0.1–1.2 mg/dL	≥19.9 mg/dL
Alanine aminotransferase (ALT)	10–40 units/L (M) 7–35 units/L (F)	[b]
Aspartate aminotransferase (AST)	10–41 units/L	[b]
Alkaline phosphatase (ALK)	53–128 units/L	[b]
Total protein (TP)	6.4–8.3 g/dL	[b]
Albumin (ALB)	3.4–4.8 g/dL	[b]
Ammonia	10–47 μmol/L	≥500 mcg/dL
Amylase (serum)	20–110 units/L	>330 units/L
Lipase	7–58 units/L	>420 units/L
Creatinine phosphokinase (CPK)	20–220 units/L	>10,000 units/L
Troponin I	0 ng/mL	>0.05 ng/mL
B-type natriuretic peptide	<100 pg/mL	[b]
Lactate dehydrogenase (LDH)	110–220 units/L	>880 (moderate); >8800 (severe)

[a]Critical test results vary among clinical laboratories based on instrumentation and calibration procedures. Not all tests have an associated critical result that can be reported.
[b]No critical value established.
Values for reference ranges and critical test results from the University of California–San Francisco Moffit-Long Hospital/San Francisco General Hospital.

MINI CLINIC

Pulmonary Edema and BNP

Problem

A 60-year-old man presents to the Emergency department with altered mental status, hypotension, hypoxemia, and tachypnea. A physical exam is notable for right lower leg cellulitis. Chest radiograph shows diffuse bilateral opacities and a mildly enlarged cardiac silhouette. The physician weighs whether the initial treatment approach should be for possible cardiogenic pulmonary edema (e.g., fluid restriction and diuretics) or severe sepsis and ARDS (fluid resuscitation and vasopressors).

Solution

The initial BNP level is 150 pg/mL indicating sepsis and non-cardiogenic pulmonary edema rather than cardiac failure as the source of hypotension and hypoxemia.

RULE OF THUMB In patients suffering a myocardial infarction, cardiac injury markers (CPK-2, troponin I) tend to reach peak values beginning at 12 h and up to 24 h after the onset of symptoms.

functioning) lead to excessive bleeding, whereas *thrombocytosis* (excessive platelets) causes excessive clotting. In addition to direct platelet measurement, the functionality of the entire process of coagulation is measured by the *prothrombin time* (PT) and *partial thromboplastin time* (PTT). These tests assess two different pathways by which fibrin clots are formed.

PT is the time in seconds required by plasma to form a fibrin clot after exposure to tissue factors. It assesses the *extrinsic coagulation pathway* and reflects the function of clotting factors I, II, V, VII, and X. In contrast, PTT assesses the *intrinsic coagulation pathway* and evaluates abnormalities in blood clotting to monitor the effects of anticoagulation therapy. PTT abnormalities are associated with clotting factors I through VI and VIII through XII. Clinically, abnormal increases in PT and PTT are associated with vitamin K deficiencies and anticoagulation therapies (e.g., warfarin, heparin, enoxaparin). Increased PT and PTT also occur in patients with *disseminated intravascular coagulation* (DIC) and end-stage liver disease.

TABLE 17.6 Coagulation Studies

Test	Reference Range	Critical Test Result
Prothrombin time (PT)	<14.8 s	>30 s
Partial thromboplastin time (PTT)	<37.6 s	>50 s
International normalized ratio (INR)	0.8–1.2	>5 s
Fibrin D-dimer	<400 ng/mL	[a]
Platelet count	150,000–400,000/mm^3	<25,000/mm^3

[a]No critical value established.
Values for reference ranges and critical test results are from the University of California–San Francisco Moffit-Long Hospital and San Francisco General Hospital. Reference ranges may differ between hospitals and laboratories so the RT should be aware of the value in her/his own hospital.

Because PT test results (Table 17.6) depend upon manufactured animal tissue factors, there is unavoidable variability. This is solved by an additional measurement called the *international normalized ratio* (INR). INR expresses PT relative to an established sample value with a reference range of 0.9 to 1.3. INR values of approximately 5.0 indicate a high likelihood for bleeding. Values of 0.5 are associated with a tendency toward increased clotting. Coagulation studies should be reviewed before selected procedures, including bronchoscopy, especially where tissue sample may be taken.

D-dimer is a small protein fragment found in the blood when fibrin clots are dissolving. It belongs to a larger group of substances referred to as *fibrin degradation products*. D-dimer levels help to diagnose deep vein thrombosis (DVT), pulmonary embolism (PE), or DIC. Unless significant clotting has occurred in the body, the D-dimer test is normal. The upper reference range for D-dimer is 240 ng/mL. The D-dimer is very sensitive and generally elevated in the presence of clotting. However, D-dimer cannot determine the specific cause or source of clotting. Besides DVT and PE, other conditions such as surgery and trauma can cause an elevated D-dimer. Therefore, the D-dimer test is more useful in *ruling out* a DVT or PE in a patient with a normal D-dimer than in diagnosing such a condition when a D-dimer is elevated.

Protein C is integral in regulating coagulation. In its activated state (activated protein C), it inhibits coagulation and promotes clot degradation. Protein C levels are reduced in patients with severe sepsis and ARDS.[10] Low protein C promotes abnormal clot formation and damages blood vessels in the microcirculation throughout the body (DIC). Significant protein C deficiencies

MINI CLINIC

Sudden Onset of Severe Hypoxemia and Chest Pain

Problem

A 55-year-old patient is recovering from community acquired pneumonia on the medical ward. After 72 h of complete bed rest she begins to ambulate. Shortly afterward she develops sudden onset of severe dyspnea, pleuritic chest pain, and anxiety. This is accompanied by a decreased SpO_2 from 97% on 4 L/min nasal O_2 to 84%. An acute pulmonary embolism is suspected but an acute myocardial infarction also must be considered.

Solution

As part of a differential diagnosis, a D-dimer test is ordered along with baseline cardiac enzyme tests and ECG. The D-dimer test result is 570 ug/L. The age-adjusted cut-off for the likelihood of acute pulmonary embolism for those 50 years or older is age × 10 (i.e., ≥550 in this patient).[9] The next diagnostic step would be to obtain a computed tomography pulmonary angiography to confirm the diagnosis.

(<40% of normal) are associated with increased mortality risk in severe sepsis. Therefore, protein C levels are sometimes used to assess the severity of inflammation and coagulation disorders in patients with severe sepsis.

Infection Monitoring

Procalcitonin (PCT) is an inactive protein of the hormone calcitonin released in response to bacterial infections (particularly sepsis). PCT levels are directly related to infection severity. Because PCT levels are unaffected by viral infections, it is a unique marker for bacterial infections. PCT levels typically increase within 2 to 4 hours of sepsis with peak levels occurring 24 to 48 hours later. In healthy individuals PCT levels are less than 0.1 ng/mL. A diagnosis of sepsis is confirmed when PCT levels are greater than 0.5 ng/mL and excluded when PCT levels are 0.2 ng/mL or less.[11] Antibiotic therapy often is initiated when PCT levels reach 0.25 to 0.50 ng/mL. Once infection is controlled with appropriate antibiotic therapy, PCT levels promptly decrease. Therefore, PCT is used to titrate antibiotic therapy with measurements repeated every 1 to 2 days. When PCT decreases by approximately 90% from peak values, antibiotic therapy is usually terminated.

C-reactive protein (CRP) is a plasma protein expressed by the liver in response to infection (particularly sepsis) or trauma. The primary role of CRP is activating the complement system that assists antibodies in destroying bacteria. CRP levels begin to increase 6 to 8 hours after the onset of infection or injury and peak between 36 and 50 hours.[12] Normal CRP level is approximately 0.8 mg/L and cutoff values of 80 to 100 mg/L indicate infection; levels of approximately 130 mg/L are associated with severe sepsis.

MICROBIOLOGY TESTS

Sputum Gram Stain

Patients suspected of having a serious lung infection require a sputum sample to identify the microorganism causing the infection, thereby facilitating appropriate antibiotic selection. The Gram stain is the first test used in evaluating sputum samples. A laboratory technician smears the sputum sample onto a glass slide, applies a staining solution, and examines it through a microscope.

The Gram stain determines the quality of the sputum sample. Some patients have difficulty producing adequate sputum and may expectorate only saliva into the sputum cup. In such cases, the Gram stain shows few (<25 per low-power field) or no pus cells and numerous epithelial cells, and the sample must be discarded. A sample with numerous pus cells and few epithelial cells is probably a true lung sample and likely reflects the infection source.

RULE OF THUMB A legitimate sputum sample has few epithelial cells and many pus cells (leukocytes).

After the sample is verified, the laboratory technician identifies the Gram stain reaction (either positive or negative) and the shape of any bacteria present (rods vs. cocci). For example, *Streptococcus pneumoniae,* a common bacterium associated with pneumonia, is characterized as lancet-shaped, gram-positive diplococci. Although a Gram stain can be helpful in identifying an invading organism so antibiotics can be more quickly started, a definitive diagnosis is made only by culture of the specific organism.

Sputum Culture

When the sputum sample is adequate, a portion of the sputum is prepared for culture by placing it in a medium that promotes organism growth. When the organism has matured, it is examined microscopically to determine its exact type and sensitivity to antibiotic therapy. However, antibiotics are sometimes started before the results of the culture are available based on the Gram stain and/or the usual patterns of infection in the specific clinical setting. Culture results allow the physician to adjust appropriate antibiotic therapy. Gram staining and culturing are also applied to samples of blood, pleural fluid, or any other body fluid involved in an infection.

Sputum Testing for Mycobacterium Tuberculosis

Pulmonary tuberculosis is caused by *Mycobacterium tuberculosis (TB)*. The prompt identification, isolation, and treatment of patients with suspected tuberculosis infection is a crucial infection control measure. An effective method for detecting tuberculosis infection is to perform a Gram stain of a slide containing a sputum sample followed by an acid wash. Characteristically, the cell walls of mycobacteria resist weakening to acid so that dye is retained within the cell. This resistance to decolorization classifies the organism as an **acid-fast bacterium**.

With the rise of multi-drug resistant tuberculosis there is a need for rapid testing in order to improve care and prevent transmission. Xpert MTB/RIF assay is an automated genetics test that can detect TB within 2 hours and identify strains that are resistant to Rifampicin (one of the key antibiotics used to treat TB infection). Therefore, the test makes the time-consuming

delays needed to grow TB in a culture medium unnecessary. This test is highly accurate for detecting TB infection both in patients with and without HIV infection.[13]

Sweat Chloride

Measuring **sweat chloride** is the standard test for diagnosing cystic fibrosis (CF). CF is characterized by a genetic defect in cellular chloride channels which prevents normal reabsorption and conservation of Cl^-. Consequently those with CF have increased Cl^- levels in their sweat that is greater than 60 mmol/L. Values between 40 and 60 mmol/L are considered borderline for CF, while levels below 40 mmol/L are unlikely to confirm the diagnosis. Although the sweat electrolyte test is an important tool, a diagnosis of CF requires genetic testing for mutations in the gene that produces the cystic fibrosis transmembrane conductance regulator (CFTR) protein.

RULE OF THUMB A sweat chloride test of greater than 60 mmol/L generally indicates the presence of cystic fibrosis.

CLINICAL APPLICATION OF LABORATORY DATA

RTs are focused primarily on the pulmonary system and not as much on other organ systems. However, many of the laboratory tests previously discussed in this chapter are relevant to the RT's implementation of various aspects of the plan of care.

Coagulation Disorders

In patients requiring ABG testing, bronchoscopy, or nasotracheal suctioning (discussed in subsequent chapters), the RT must evaluate the clotting characteristics of the blood. Patients with an abnormally low platelet count or an elevated PT and INR requiring an ABG sample need to have the puncture site compressed for a longer duration to prevent hematoma development. Because of the extremely high risk for bleeding, patients with an extremely low platelet count should have an arterial puncture performed (or undergo nasotracheal suctioning) *only* when it is essential.

Because RTs help to assess patients with suspected PE, which has some of the same symptoms as patients with myocardial infarction (e.g., dyspnea and chest pain), it is important for the RT to be familiar with tests such as D-dimer, troponin I, CPK-1, and CPK-2, which help establish the diagnosis.

Electrolyte Disorders and Conclusion

Electrolyte disorders are discussed in more detail in Chapter 13. The primary concern of the RT is the effect of electrolyte disorders on respiratory and cardiac muscle function. Many electrolyte disorders cause generalized skeletal muscle weakness. This weakness may limit ambulation and increases the risk for patients developing pneumonia and venous thromboembolism that can lead to PE. In a patient with pulmonary disease, respiratory muscle weakness impairs the ability to sustain spontaneous ventilation and the ability to maintain pulmonary hygiene through deep breathing and adequate cough. Electrolyte disorders can also contribute to cardiac dysrhythmias (see Chapter 18).[14]

SUMMARY CHECKLIST

- Laboratory medicine consists of five disciplines: clinical biochemistry, hematology, clinical microbiology, immunology, and anatomic pathology.
- Reference ranges demarcate the boundaries for, and expected variability of, any analyte and take into consideration variations related to age, gender, race, and ethnicity which changes over time.
- The three formed elements of the blood are the WBCs (leukocytes), RBCs (erythrocytes), and platelets (thrombocytes).
- Elevation of the WBC count is known as *leukocytosis*. It often occurs with infection, stress, or trauma.
- A reduced WBC count is known as *leukopenia*. It puts the patient at risk for serious infection.
- Abnormal elevation of the RBC count is known as *polycythemia,* and an abnormal reduction in the RBC count is known as *anemia*. Anemia reduces the O_2-carrying capacity of the blood and increases the risk for tissue hypoxia.
- Two important points when interpreting serum electrolytes are their value is limited to only a one-time "snapshot" of dynamic processes, and the intravascular blood compartment is remote from the intracellular environment. Serum electrolyte levels only suggest what might be occurring in the intracellular compartment.
- Severe hyperkalemia (>6 mmol/L) greatly increases the risk for cardiac arrhythmias.
- Metabolic acidosis is caused by either the addition of nonvolatile acids or a primary loss of HCO_3^-. The anion gap provides a quick method for determining whether a decrease in HCO_3^- is caused by a disruption of normal anion balance or the presence of an abnormal acid anion (e.g., lactic acidosis, ketoacidosis, etc.).
- Troponin I and CPK-MM tests are used to help diagnose myocardial infarction.
- BNP is secreted by the heart in response to increased cardiac muscle stretch and is used primarily to evaluate patients for heart failure, but also can help differentiate pulmonary edema between cardiogenic and acute lung injury sources.
- Abnormal increases in PT and PTT are indicative of increased bleeding risk and are associated with vitamin K deficiencies, anticoagulation therapy, disseminated intravascular coagulation, and end-stage liver disease.
- To minimize bleeding risk in arterial punctures and nasotracheal suctioning, extreme caution should be used in patients with thrombocytopenia and elevated PT or INR.
- An elevated D-dimer is a very sensitive indicator of increased clotting and is a useful adjunct test in helping to diagnose or rule out the presence of deep vein thrombosis and pulmonary embolism.
- A sputum Gram stain is useful for determining the quality of the sample and the type of organism present. Samples with many epithelial cells and few pus cells suggest oral and not pulmonary secretions.
- Xpert MTB/RIF assay is an automated genetics test that can detect TB within 2 hours and can identify strains that are

resistant to Rifampicin (one of the key antibiotics used to treat TB infection).

- Measuring sweat chloride is the standard test for diagnosing CF. Sweat Cl^- levels greater than 60 mmol/L is indicative of CF.

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18

Interpreting the Electrocardiogram

Albert J. Heuer

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Describe indications for and limitations of the electrocardiogram.
- Discuss the electrophysiology of cardiac cells.
- Describe how the cardiac impulse is conducted.
- Review the electrocardiogram equipment set-up.
- Discuss steps involved in interpreting an ECG.
- Review the features of a normal ECG tracing.
- Compare and contrast the features of various cardiac arrhythmias.
- Review major treatment alternatives of major cardiac arrhythmias.

CHAPTER OUTLINE

KEY TERMS

atrial kick
automaticity
depolarization
dysrhythmias
ectopic beat
ectopic foci
electrocardiogram
impulse-conducting system
repolarization
S-T elevation myocardial infarction (STEMI)

The ***electrocardiogram*** (ECG) is an important diagnostic tool that in some settings is obtained by the respiratory therapist (RT). As a result, this can place the RT in a prime position to recognize and respond to life-threatening cardiac events and arrhythmias. This chapter emphasizes the basics of cardiac physiology, lead placement, ECG interpretation, and the identification and key points in the treatment of ***dysrhythmias***. More details of the cardiopulmonary anatomy and emergency cardiovascular life support are presented in Chapters 10 and 38.

An ECG can be done using either a 12-lead system, which provides more diagnostic value than the alternative approach, or a 3-lead system, which is commonly used for telemetry. A 12-lead ECG provides a complete assessment of the electrical activity of the heart by viewing it from 12 different angles and is the focus of this chapter.

The ECG is a popular evaluation tool because it is inexpensive, noninvasive, and easy to obtain. It is used primarily to help evaluate a patient with signs and/or symptoms of cardiac disease. A physician would order an ECG for most adult patients complaining of certain types of chest pain, shortness of breath, dyspnea with palpitations, weakness, lethargy, or syncope; these are the classic clinical symptoms associated with heart disease. In addition, the ECG is routinely used to detect abnormalities that are occurring or have already occurred, such as a myocardial infarction (MI), or for preoperative screening. However, ECGs done at rest have little or no value as a predictor of future heart problems and they cannot directly identify certain abnormalities, such as valvular defects.[1]

BASIC PRINCIPLES OF ELECTROPHYSIOLOGY

The muscle cells of the heart normally are stimulated and paced by the electrical activity of the cardiac **impulse-conducting system.** The impulse-conducting system cells have the ability to stimulate the heart without the influence of the nervous system. However, the autonomic nervous system normally plays a major role in controlling heart function.[1]

Cardiac muscle cells normally generate an electrical imbalance across the cell membrane, with a positive charge on the outside and a negative charge on the inside. This is the resting or polarized

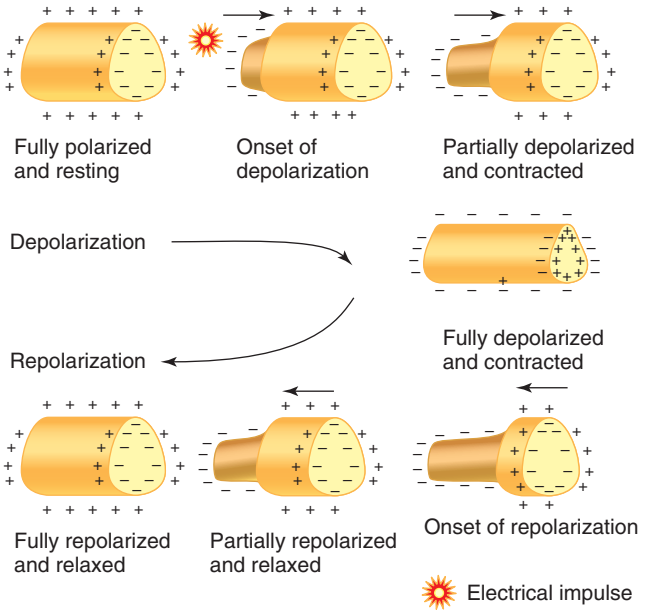

Fig. 18.1 Depolarization and repolarization of a cardiac cell. (Modified from Wesley K: *Huszar's basic dysrhythmias and acute coronary syndromes: interpretation and management*, ed 4, St Louis, 2014, Elsevier.)

MINI CLINI

Acute Chest Pain in the Emergency Room

Problem

A 52-year-old man presents with severe chest pain that radiates to his left shoulder and shortness of breath. The newly graduated resident physician is obtaining a comprehensive history and performing a physical examination; the RT assisting with the evaluation notes that the man is diaphoretic and tachycardic, with pale skin color. After giving an order for O_2, the physician resumes taking the history and performing the physical. What additional tests should the RT recommend be obtained at this time?

Solution

A STAT ECG should be ordered to help differentiate among causes of chest pain, for example, associated with an MI or other cardiac abnormality such as angina versus other noncardiac causes. As discussed later in this chapter, T wave inversion and ST segment elevation suggest cardiac ischemia and perhaps an MI, which would warrant immediate treatment.

state in which there is no electrical activity. Stimulation of the "polarized" cells causes an influx of Na^+ into the interior portion of the cell; this is called **depolarization** (Fig. 18.1). Depolarization causes the cardiac muscle cells to contract momentarily. Depolarization is immediately followed by **repolarization,** which is a rapid return of the cell to the "polarized" position in which the electrical imbalance across the membrane is reestablished.

The impulse-conducting system has three types of cardiac cells capable of electrical excitation: pacemaker cells (e.g., sinoatrial [SA] node, atrioventricular [AV] node), specialized rapidly conducting tissue (e.g., Purkinje fibers), and atrial and ventricular muscle cells. The ability of these cells to depolarize without stimulation is known as **automaticity.** Each of these cardiac cell groups varies in degree of automaticity.[1–3]

Impulse-Conducting System

The impulse-conducting system is responsible for initiating the heartbeat and controlling the heart rate. It also coordinates the contraction of the heart chambers, which is essential to move blood effectively. A defect in the impulse-conducting system may lead to inadequate cardiac output and decreased tissue perfusion. Normally, the SA node, which is located in the upper portion of the right atrium, has the greatest degree of automaticity and paces the heart (Fig. 18.2). Any heartbeat originating outside the SA node is considered an **ectopic beat.**[2] The SA node is innervated by the autonomic nervous system, which allows the sympathetic and parasympathetic nervous systems to influence heart rate. Stimulation of the sympathetic nervous system, such as occurs with the administration of certain medications (e.g., adrenergic bronchodilators), increases the heart rate, whereas activation of the parasympathetic nervous system slows the heart rate by influencing the degree of automaticity within the SA node.

The electrical impulse generated by the SA node travels rapidly across the right atrium, through intraatrial pathways, to the left atrium by way of the Bachmann bundle; this causes a wave of depolarization to occur over the atria, producing atrial contraction. Next, the impulse moves to the AV node, located in the intraventricular septum in the inferior aspect of the right atrium (see Fig. 18.2). The AV node is the "backup" pacemaker because it has the second greatest degree of automaticity in the healthy heart. In most cases, if the SA node fails to function properly such as may occur with ischemia or in response to certain medications, the AV node paces ventricular activity at a lower heart rate of 40 to 60 beats/min, which is generally sufficient to maintain adequate cardiac output.[2]

RULE OF THUMB A patient who suffers myocardial ischemia or other condition which causes the SA node to function improperly may well experience a reduction in heart rate attributable to the AV node taking over as the dominant pacemaker. Such patients who do not respond to pharmacologic therapy may need a pacemaker implanted to ensure an adequate heart rate and cardiac output.

The electrical impulse is temporarily delayed at the AV node to allow the ventricles time to fill with blood. That brief delay also limits the rate of the ventricular stimulation during excessively fast atrial rhythms that, if passed to the ventricles, would lead to a very rapid heart rate that would cause the cardiac output to be inadequate.[3,4]

The impulse exits the AV node, enters the bundle of His, and rapidly moves to the bundle branches. The bundle branches carry the impulse rapidly into the right and left ventricles. The bundle branches terminate in the Purkinje fibers, which are small, finger-like projections that penetrate the myocardium (see Fig. 18.2). These fibers stimulate contraction of the myocardium from the apex of the heart upward toward the base of the heart, causing a coordinated contraction of the ventricles, which normally is effective in moving blood. The impulse travels most rapidly in the Purkinje fibers, which is essential if contraction of the ventricles is to occur in a coordinated fashion. Immediately

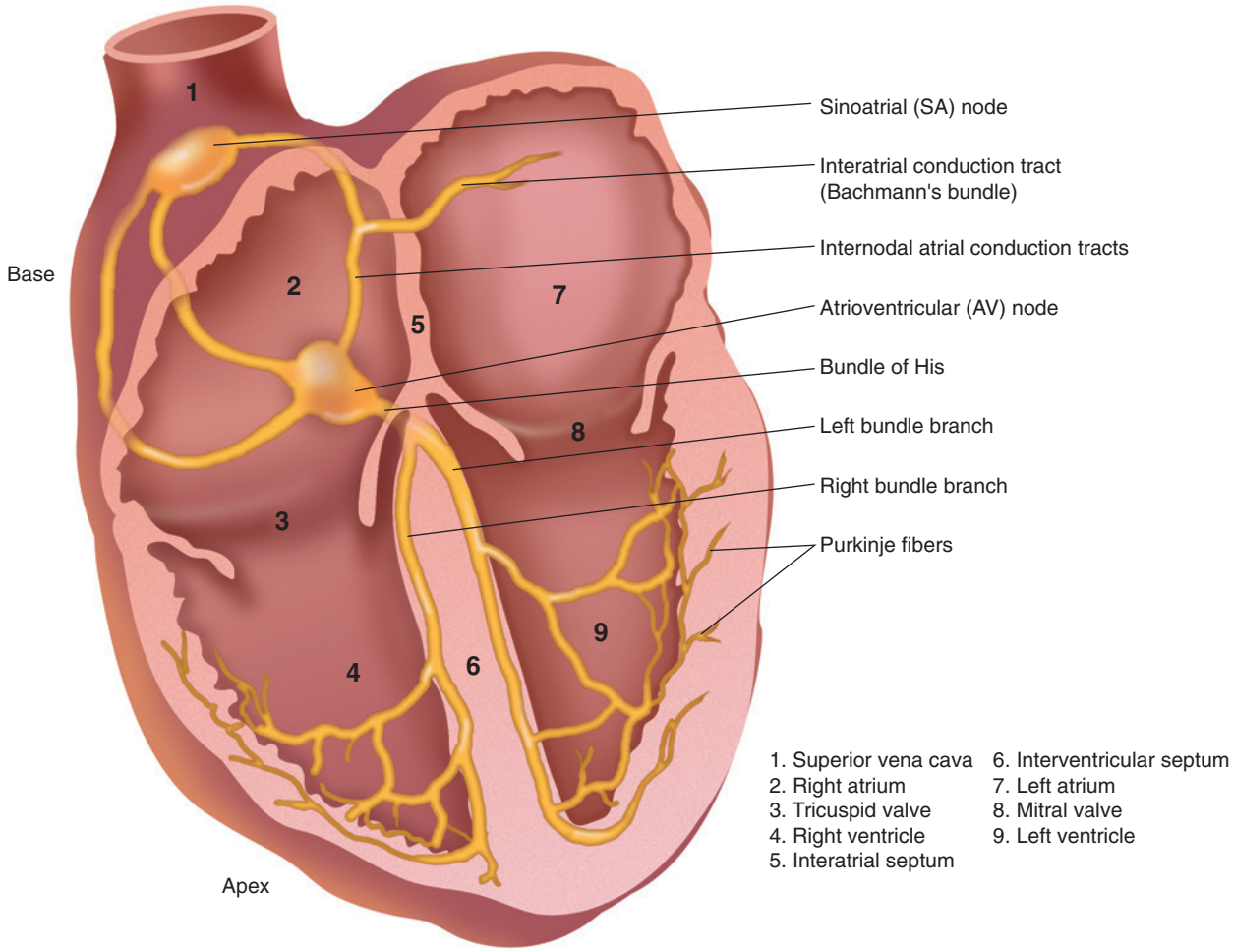

Fig. 18.2 Anatomy of the impulse-conducting system of the human heart.

after depolarization of the ventricles, repolarization occurs in preparation for the next impulse.[3,4]

ELECTROCARDIOGRAM PROCEDURAL SUMMARY

In some healthcare organizations, RTs are responsible for performing or trouble shooting ECGs. As a result of this, RTs should be familiar with how to set up and perform such a test. Once the physician orders a 12-lead ECG, the equipment is gathered, which includes the portable ECG unit, lead wires, and electrodes.

The lead wires permit the connection between the ECG unit and the electrodes, which have adhesive permitting temporary attachment to the skin. Generally, the lead wires should be attached to the electrodes before being placed on the skin, to avoid unnecessary pressure to the skin's surface. The lead wires are often marked to help ensure proper placement on the patient's body.

The American Heart Association (AHA) has published guidelines for lead placement to help ensure consistency and accuracy in how ECGs are performed.[4] Under these guidelines, the 12 leads are subdivided into two groups: 6 extremity (limb) leads and 6 chest (precordial) leads. For the six limb leads, four electrodes are placed on the extremities, one on each wrist and one on each ankle. These leads are bipolar, which permits the measurement of electrical activity in two different directions. Additionally, the ECG unit can vary the orientation of these four electrodes to create six different views. Any electrical activity of the heart that is directed up, down, left, or right is recorded by the limb leads. The limb leads are called leads *I, II, III,* aV_R, aV_L, and aV_F (Table 18.1).

The six chest or precordial leads are called leads V_1, V_2, V_3, V_4, V_5, and V_6. These leads are unipolar, which means that they measure electrical activity in only one direction. These leads are placed in a horizontal plane across the chest, starting with V_1 in the fourth intercostal space to the right of the sternum. The rest of the chest leads are on the left side, starting with V_2, which is placed in the fourth intercostal space just to the left of the sternum, and ending with V_6, which is placed at the fifth intercostal space at the left midaxillary line (V_6). Fig. 18.3 illustrates proper placement of ECG leads. The view from each chest lead provides its own angle of orientation to measure cardiac electrical activity moving anteriorly or posteriorly.

It should be noted certain circumstances may warrant that lead placement vary from that recommended by the AHA. Such situations may include a physical abnormality or injury of the

TABLE 18.1 The 12 Leads of an Electrocardiograph and the Myocardial Wall That Each Set Views

Facing Lead[a]	View
I, aV_L, V_5, V_6	Lateral
II, III, aV_F	Inferior
V_1, V_2	Septal
V_3, V_4	Anterior
Cells and Function	
Pacemaker cells	Specialized cells that have a high degree of automaticity and provide electrical power for the heart
Conducting cells	Cells that conduct the electrical impulse throughout the heart
Myocardial cells	Cells that contract in response to electrical stimuli and pump blood

[a]Excludes aV_R, which faces the interior, endocardial surface of the ventricles.

From Heuer AJ, Scanlan CL: *Clinical assessment in respiratory care*, ed 8, St Louis, 2018, Elsevier.

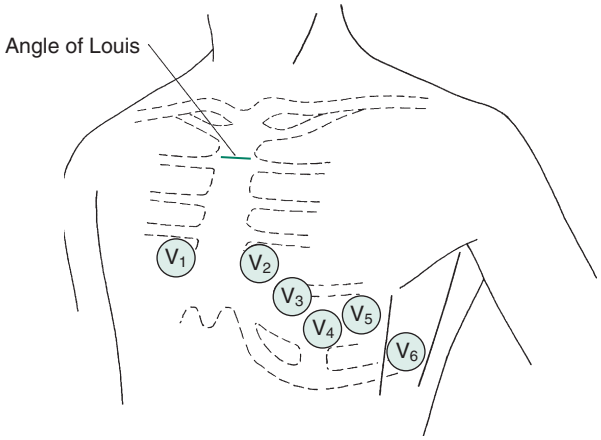

Fig. 18.3 Proper precordial lead placement. (From Heuer AJ, Scanlan CL: *Clinical assessment in respiratory care*, ed 8, St Louis, 2018, Elsevier.)

chest wall or limb where the lead may otherwise have been placed. In such a situation, a notation should be made in the patient's medical record acknowledging the specific nature of the nonstandard lead placement and the rationale for why it was necessary to do so.[2,4]

RULE OF THUMB Certain circumstances, such as a chest wall or limb abnormality or injury may warrant ECG lead placement which varies from that recommended by the AHA. In such instances, the alternate lead placement should be described in the medical record along with the rationale for doing so.

After all leads are properly placed and the ECG unit is activated, all 12 leads together provide a comprehensive view of the electrical activity of the heart. Given that an array of conditions, including cardiac ischemia and acute MI can alter electrical conduction through the heart, the ECG has considerable diagnostic value. The balance of this chapter focuses mainly on how

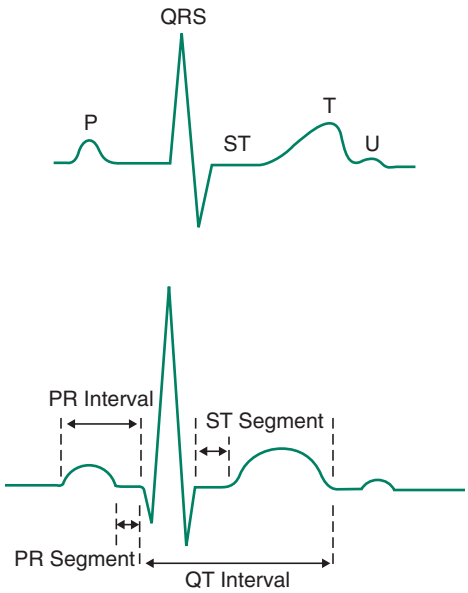

Fig. 18.4 Normal Configuration of Electrocardiographic Waves, Segments, and Intervals. *Note:* Though there is some individual variation, the typical P-R Interval is 0.12 to 0.20 seconds and QRS segment is less than 0.12 seconds. (From Heuer AJ, Scanlan CL: *Clinical assessment in respiratory care*, ed 8, St Louis, 2018, Elsevier.)

electrocardiographic waves are generated, how to interpret ECGs, how to identify abnormal rhythms, and finally on some treatments of conditions detected by the ECG.

Basic Electrocardiographic Waves

The wave of depolarization occurring in the atria is seen as the P wave on the ECG (Fig. 18.4). The normal P wave is no more than 2.5 mm high and 3 mm long. Atrial hypertrophy may cause the P wave to enlarge to a larger height and length. Atrial repolarization is not seen on the electrocardiographic tracing because it is obscured by the electrical activity occurring in the ventricles at the same time.

The wave of depolarization occurring over the ventricles is seen as the QRS complex on the electrocardiographic tracing. The QRS complex is normally larger than the P wave because the muscle mass of the ventricles is much greater than that of the atria. The normal QRS complex is not wider than 3 mm (0.12 s) because of the rapid movement of the impulse through the ventricles by the bundle branches and Purkinje fibers. Abnormalities in the ventricular conduction system may lead to irregular QRS complexes that are wider than normal.

The QRS complex usually consists of several distinct waves, each of which has a letter assigned to it as a label. If the first wave of the complex is negative (downward), it is labeled the *Q wave*. The initial positive (upward) deflection is electrocardiographically referred to as the *R wave*, and the next negative deflection after the R wave is labeled the *S wave*. Not all QRS complexes have all three components present, but the waves making up ventricular depolarization are electrocardiographically referred to as the *QRS complex*, regardless of its exact makeup. The wave of repolarization occurring in the ventricles immediately after depolarization is the *T wave*. Though there is some

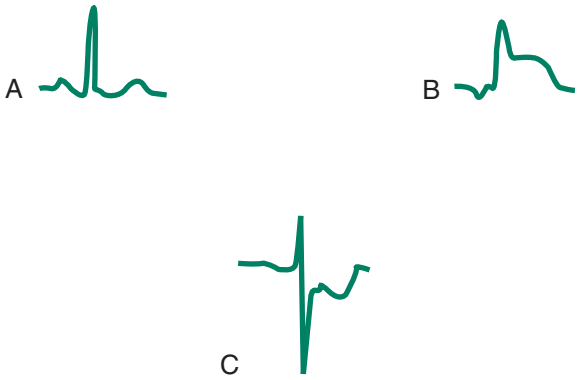

Fig. 18.5 ST Segments. (A) Normal. (B) Abnormal elevation. (C) Abnormal depression. (From Heuer AJ, Scanlan CL: *Clinical assessment in respiratory care*, ed 8, St Louis, 2018, Elsevier.)

individual variation, the typical PR interval is 0.12 to 0.20 seconds and QRS segment is less than 0.12 seconds (see Fig. 18.4).

Two important segments of the electrocardiographic pattern must be observed and measured. The first is the *PR interval*, which refers to the distance (time) between the start of atrial depolarization and the start of ventricular depolarization. The PR interval represents the time in which the impulse begins in the SA node and travels across the atria to the AV node, where it is held briefly before passing on to the ventricles. Normally, the PR interval represents a period no longer than 0.20 second. PR intervals longer than 0.20 second suggest that the impulse is abnormally delayed at the AV node and a "block" is present, often as a result of a defect in the impulse-conducting system.

The next important part of the ECG to evaluate is the *ST segment*, which represents the time from the end of ventricular depolarization to the start of ventricular repolarization. The normal ST segment is isoelectric and is seen as a flat line that is not above or below the neutral baseline. Certain pathologic abnormalities in the myocardium cause the ST segment configuration to become abnormal; this is seen as an elevated or depressed ST segment and is common in cardiac ischemia and MI (Fig. 18.5). Specifically, a depressed ST segment is a common finding with cardiac ischemia such as occurs in angina. On the other hand, an elevated ST segment is associated with certain types of MIs; hence, the origin of the acronym, STEMI which stands for **S-T elevation myocardial infarction**. Because these configurations represent potentially life-threatening changes, abnormal ST segments must be identified as soon as possible.[3–5]

RULE OF THUMB A negative QRS complex in lead I is consistent with right-axis deviation, which is often caused by cor pulmonale.

Electrocardiographic Paper and Measurements

Electrocardiographic paper is made up of gridlike boxes that define time on the horizontal axis and voltage on the vertical axis. Dark lines circumscribe larger boxes that are 5 × 5 mm, and lighter lines define smaller boxes that are 1 × 1 mm (Fig. 18.6). Because the paper normally passes through the electrocardiograph at a set speed of 25 mm/s, each large box represents 0.20 second and each small box represents 0.04 second on the horizontal axis. The standard ECG is calibrated so that 1 mV causes an upward deflection of 10 small boxes or 2 large boxes on the vertical axis; this allows measurement of the exact voltage occurring during depolarization of the cardiac muscle fibers.[1,4,6] Recognizing the times that each box on the ECG tracing represents can speed the interpretation of the ECG. For example, as stated above, the PR interval is normal as long as it is less than 1 large box in width (0.2 seconds) and abnormal if it is longer. A prolonged PR interval is the distinguishing feature of first-degree heart block which is discussed and illustrated later in this chapter.

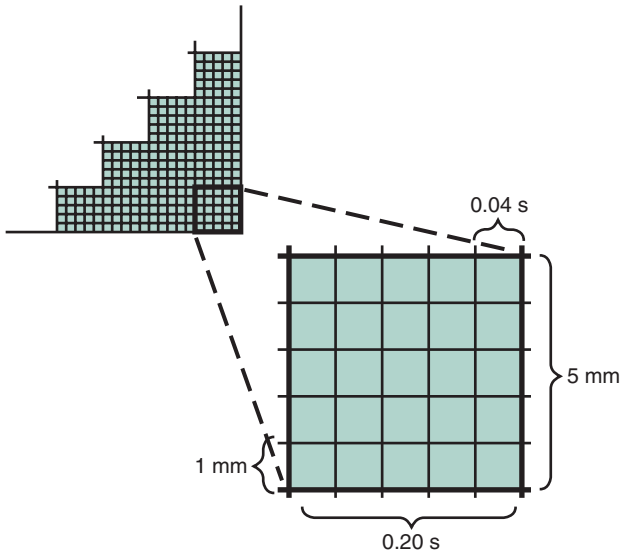

Fig. 18.6 Gridlike boxes of electrocardiographic paper illustrating the 1 × 1 mm and 5 × 5 mm boxes. (From Heuer AJ, Scanlan CL: *Clinical assessment in respiratory care*, ed 8, St Louis, 2018, Elsevier.)

MINI CLINI

Weaning Complications

Problem

The clinician is in the intensive care unit (ICU) attending to a 65-year-old woman who is being weaned from the ventilator after 2 weeks of mechanical ventilation. After 15 minutes of T-piece weaning, the patient complains of mild shortness of breath and the bedside ECG shows an increase in heart rate, inverted T waves, and acute elevation of the ST segment. What do the inverted T waves and ST segment elevation indicate? What should be done?

Solution

The inverted T waves and elevated ST segment suggest that the heart is experiencing acute hypoxia, probably caused by the stress of weaning. T wave inversion and ST segment elevation are serious signs indicating that the patient is not tolerating the weaning. She should be put back on full ventilatory support at an elevated FiO_2 and monitored closely. Weaning should not be attempted again until the patient's clinical condition improves significantly and the heart is evaluated further. The attending physician should be notified.

Interpreting the Electrocardiogram

The following steps should be followed in interpreting the ECG.

Steps to Follow

Step 1. *Identify the atrial and ventricular rates.* Normally, the rate of the atria and ventricles is the same, but rates may differ when a defect in the conduction system is present. The clinician can closely estimate the heart rate by counting the number of QRS complexes (for the ventricular rate) or the number of P waves (for the atrial rate) in 6 seconds (30 large boxes) and multiplying this number by 10. For example, seven P waves/QRS complexes (in a six-second strip) × 10 = HR ~ 70 beats/min. When the rate is regular, the clinician also can count the number of large boxes between two successive complexes and divide this number into 300 to obtain the heart rate. For example:
2 large boxes: 300/2 = HR 150
4 large boxes: 300/4 = HR 75
6 large boxes: 300/6 = HR 50

Step 2. *Measure the PR interval.* This is done by determining the number of small boxes between the *start* of the P wave and the *start* of the QRS complex. Normally, this interval is less than 0.20 second (five small boxes) and is consistently the same for each complex. PR intervals that are longer than 0.20 second or vary from one complex to the next indicate an abnormality in the impulse-conducting system.

Step 3. *Evaluate the QRS complex.* Normally, the QRS complex is shorter than 0.12 second (3 small boxes at a normal ECG paper speed). If the QRS complex is wider than 3 boxes, there is an abnormality in the impulse-conducting system within the ventricles, which can be associated with a decrease in cardiac output and blood pressure.

Step 4. *Evaluate the T wave.* Normally, the T wave is upright and rounded. Inverted T waves can suggest ischemia of the heart muscle, and abnormal configuration of the T wave occurs with electrolyte abnormalities such as hyperkalemia (where the T waves take on a "peaked" or sharper than normal appearance).

Step 5. *Evaluate the ST segment.* The ST segment should be flat or at least no more than 1 mm above or below baseline. As stated earlier, significant elevation or depression of the ST segment may indicate a serious problem with perfusion of the myocardium and must be recognized as soon as possible.

Step 6. *Identify the R-R interval.* The R-R interval is identified to assess regularity of the rhythm. The distance, in millimeters or time, is measured between the R waves of several successive QRS complexes. Normally, there is little variation in the R-R interval between QRS complexes, but if the variation between the different R-R intervals exceeds 0.12 second, abnormal conduction, called a "bundle branch block," exists.

Step 7. *Identify the mean QRS axis.* The limb lead exhibiting the largest amount of voltage is identified. If the lead shows a positive QRS complex, the axis is very close to the position on the hexaxial reference circle where that limb lead is labeled. If the QRS complex with the most voltage is negative, the mean axis is moving in the opposite direction from where that lead is labeled on the hexaxial reference circle.[1–3]

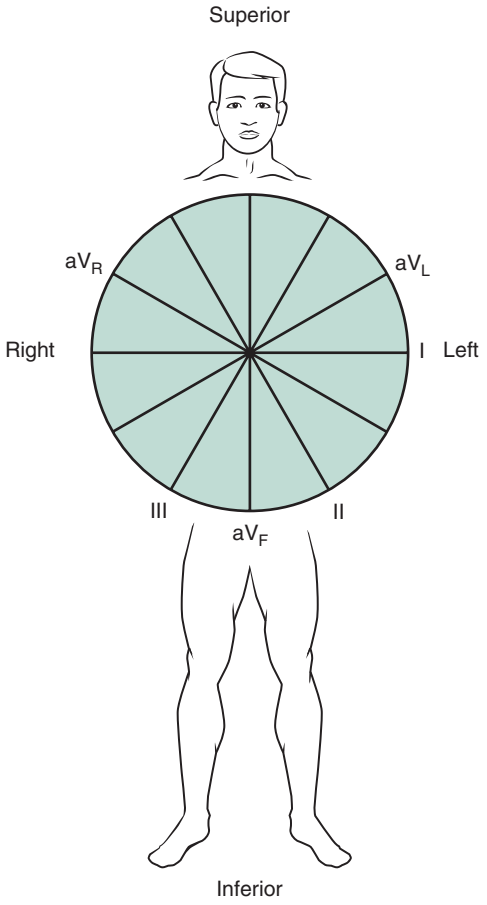

Fig. 18.7 Hexaxial reference circle used for axis evaluation. (From Heuer AJ, Scanlan CL: *Clinical assessment in respiratory care*, ed 8, St Louis, 2018, Elsevier.)

RULE OF THUMB There are two common ways for calculating the heart rate. One involves counting the number of QRS complexes or P waves (for the atrial rate) in 6 seconds (30 large boxes) and multiplying this number by 10. For example, nine P waves/QRS complexes in a six-second strip × 10 = HR ~ 90 beats/min. Alternatively, the clinician also can count the number of large boxes between two successive complexes and divide this number into 300. For example, if there are four large boxes between complexes, the calculation would be as follows: 300/4 = HR 75.

Axis Evaluation

A less understood area of ECG interpretation for RTs is the axis evaluation and the identification of related deviations from normal. Axis evaluation is used to determine the general direction of current flow during ventricular depolarization; this is helpful to know when hypertrophy of one of the ventricles is suspected, which would cause the direction of current flow and the intensity of the voltage to deviate from normal. Normally, the mean QRS axis (vector) points leftward (patient's left) and downward, between 0 and +90 degrees in the frontal plane (Fig. 18.7). The normal position of the QRS axis results from the slight tilt of the heart to the left and from the larger muscle mass of the left ventricle compared with the right ventricle.

The mean QRS axis is identified by using the hexaxial reference circle (see Fig. 18.7) with the position of each limb lead

labeled on the circle. Next, the clinician identifies the limb lead with the most voltage (either positive or negative) from the ECG being evaluated. If the lead with the most voltage is positive (upright), the clinician locates the position of that lead on the hexaxial reference circle. The mean axis must be very close to that position on the circle. If the lead with the most voltage is negative (downward), the mean axis points in the opposite direction from that lead. If the lead with the most voltage is lead II and it is positive, the mean QRS axis must be approximately +60 degrees because this is where lead II is located on the hexaxial reference circle (see Fig. 18.7). This is considered a normal axis because it falls between 0 and +90 degrees.[5,6]

In some situations, the most voltage may be equally present in two leads. When this is the case, the mean axis must fall equally between the two leads if they are both upright QRS complexes. For example, if the QRS complexes are equally positive in voltage in leads II and aV_F, the mean axis must be at approximately +75 degrees (i.e., halfway between +60 and +90 degrees) and is considered normal. This is a common situation. If the mean QRS axis is between +90 degrees and +180 degrees, the patient has what is called a "right-axis deviation"; this is quickly identified by looking at lead I. If lead I is negative, right-axis deviation is present; this is commonly seen in patients with chronic obstructive pulmonary disease (COPD) with cor pulmonale. Left-axis deviation is present when the mean axis is between +90 degrees and −90 degrees on the hexaxial reference circle. This is common in patients with left ventricular hypertrophy.

Recognizing Arrhythmias

Normal sinus rhythm. Recognizing abnormal ECG results is easier if you have an appreciation for the normal tracing. The normal sinus rhythm begins with an upright P wave that is identical from one complex to the next. The PR interval is consistent throughout the rhythm strip and normally lasts from 0.12 to 0.20 second. The QRS complexes are identical and no longer than 0.12 second. The ST segment is flat. The R-R interval is regular and does not vary more than 0.12 second between QRS complexes. The normal adult heart rate is between 60 and 100 beats/min (Fig. 18.8).[2,3]

Sinus tachycardia. Heart rates exceeding 100 beats/min are abnormal in resting adult patients and are electrocardiographically referred to as *sinus tachycardia* when a P wave is appropriately present before each QRS complex (Fig. 18.9). Other than the rate exceeding 100 beats/min, the appearance of the ECG in sinus tachycardia does not differ from a normal sinus rhythm. All intervals and shapes of the waves are normal. Sinus tachycardia is common and can be caused by numerous problems, including anxiety, pain, fever, hypovolemia, or hypoxemia. Sinus tachycardia (sometimes called "sinus tach") may also be a side effect of certain medications, such as beta-adrenergic bronchodilators. Treatment of sinus tachycardia typically involves eliminating the underlying cause, such as pain relievers, fever reducers (antipyretics), fluids, or oxygen.[5,6]

Sinus bradycardia. A heart rate of less than 60 beats/min that is otherwise normal is electrocardiographically referred to as *sinus bradycardia*. Other than the rate being too slow, sinus bradycardia does not differ from a normal sinus rhythm (Fig. 18.10). This abnormal rhythm is not as common as sinus tachycardia, but it represents a significant clinical problem if it causes the patient's blood pressure to decrease significantly or impairs tissue perfusion, causing symptoms such as fatigue, lightheadedness, or

MINI CLINI

Right-Axis Deviation on Electrocardiogram

Problem

A 54-year-old man with COPD has been admitted to the hospital for abdominal surgery. His routine laboratory data are normal, but his heart (cardiac silhouette) appears somewhat enlarged. The ECG shows a normal sinus rhythm with a right-axis deviation. How is the right-axis deviation detected and what does the right-axis deviation suggest?

Solution

Normally, the mean axis (summary of electrical activity) of the heart travels from top to bottom and from right to left. This results in the mean axis of 0 to +90 degrees in the healthy heart. The slight leftward shift of the normal axis results from the angle at which the heart is situated in the chest and the fact that the left ventricle is normally larger than the right ventricle. Right-axis deviation indicates that the electrical activity of the heart has been abnormally shifted to the patient's right side, between +90 degrees and +180 degrees. In this case, right-axis deviation is detected by noting a negative deflection of the QRS in lead I. This is most commonly the result of right ventricle enlargement, such as occurs with cor pulmonale (right heart strain caused by chronic hypoxic lung disease).

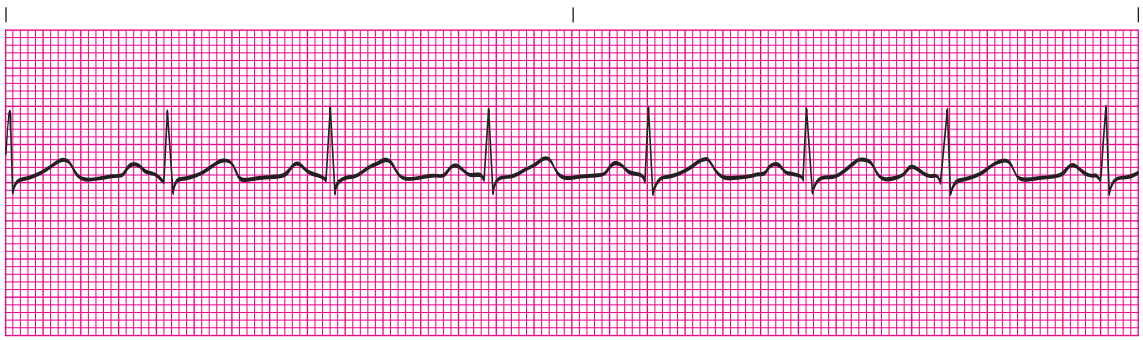

Fig. 18.8 Electrocardiographic tracing showing a normal sinus rhythm. (Modified from Atwood S, Stanton C, Storey Davenport J: *Introduction to basic cardiac dysrhythmias*, ed 4, St Louis, 2009, Mosby/JEMS.)

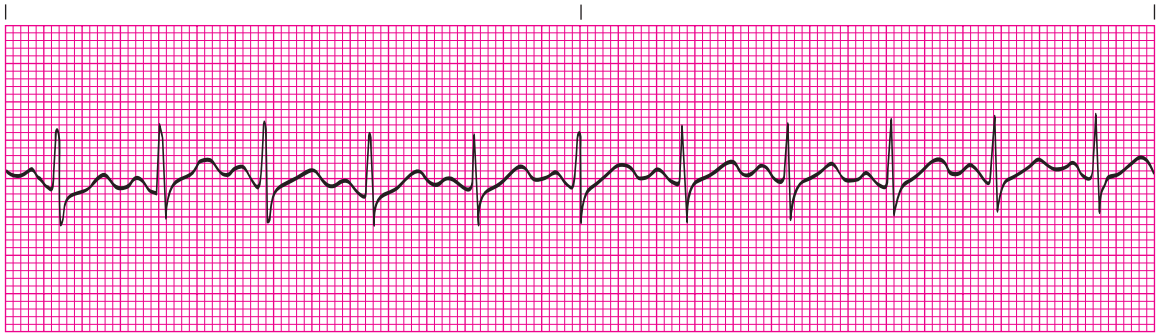

Fig. 18.9 Electrocardiographic tracing showing sinus tachycardia. (Modified from Atwood S, Stanton C, Storey Davenport J: *Introduction to basic cardiac dysrhythmias*, ed 4, St Louis, 2009, Mosby/JEMS.)

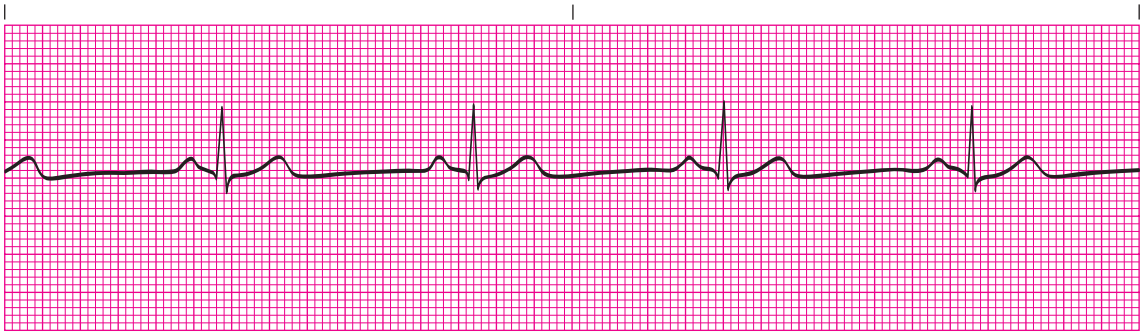

Fig. 18.10 Electrocardiographic tracing showing sinus bradycardia with first-degree heart block. (Modified from Atwood S, Stanton C, Storey Davenport J: *Introduction to basic cardiac dysrhythmias*, ed 4, St Louis, 2009, Mosby/JEMS.)

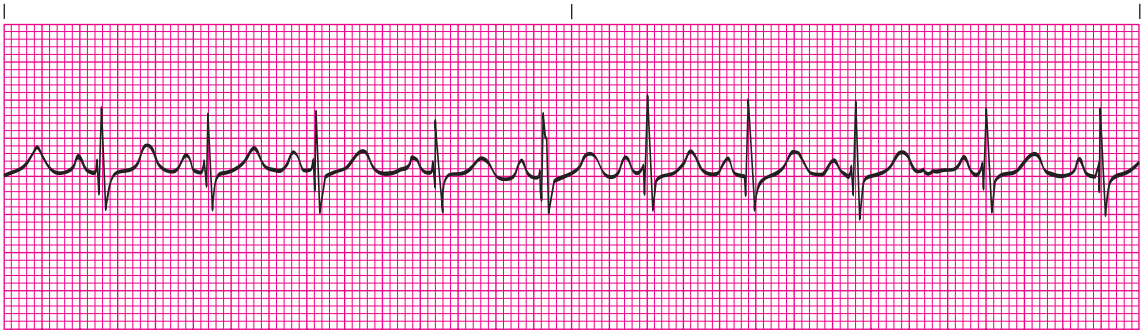

Fig. 18.11 Electrocardiographic tracing showing sinus arrhythmia. (Modified from Atwood S, Stanton C, Storey Davenport J: *Introduction to basic cardiac dysrhythmias*, ed 4, St Louis, 2009, Mosby/JEMS.)

syncope. Sinus bradycardia is most often caused by hypothermia, abnormalities in the SA node, or intense athletic conditioning. Numerous medications, such as atropine, are available to treat symptomatic sinus bradycardia by stimulating the heart rate.[5,6]

Sinus arrhythmia. Sinus arrhythmia is a common arrhythmia and is recognized by the irregular spacing between QRS complexes. The spacing is measured by identifying the intervals between the R waves of successive QRS complexes, which are normally consistent from one beat to the next. When the R-R interval varies more than 0.12 second throughout the rhythm strip and the ECG is otherwise normal, sinus arrhythmia is present (Fig. 18.11). This arrhythmia may occur with the effects of breathing on the heart or as a side effect of medications such as digoxin. Most cases of sinus arrhythmia are benign and do not need treatment.[5,6]

First-degree heart block. In first-degree heart block, the PR interval is longer than 0.20 second and, as is normally the case, each QRS complex is preceded by a P wave with the same PR interval (Fig. 18.12). This tracing indicates that the impulse from the SA node is getting through to the ventricles but is abnormally delayed in passing through the AV node or bundle of His. Typically, the QRS complex has a normal configuration, and the R-R intervals are regular. First-degree heart block is common after an MI that damages the AV node, or it may be a complication of certain medications, such as digoxin or beta blockers. Treatment usually is not needed for first-degree heart block if the patient is able to maintain an adequate blood pressure.[6,7]

Second-degree heart block. Second-degree heart block comes in two different types. Type I (Wenckebach or Mobitz type I) block is a relatively benign and often transient arrhythmia. It

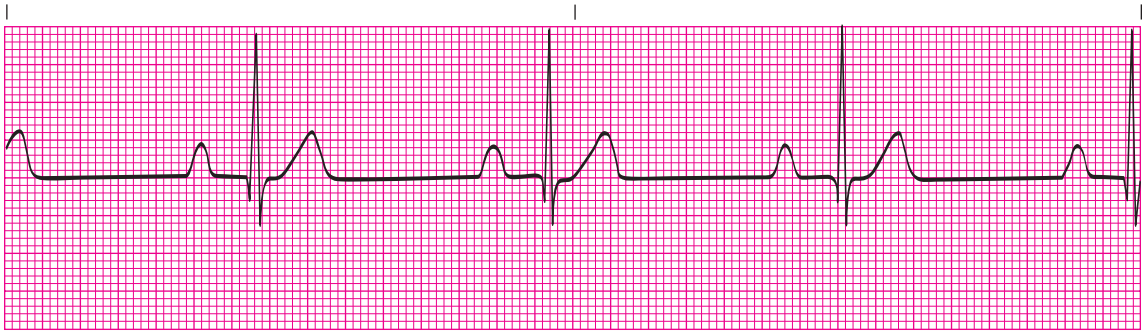

Fig. 18.12 Electrocardiographic tracing showing first-degree heart block. (Modified from Atwood S, Stanton C, Storey Davenport J: *Introduction to basic cardiac dysrhythmias*, ed 4, St Louis, 2009, Mosby/JEMS.)

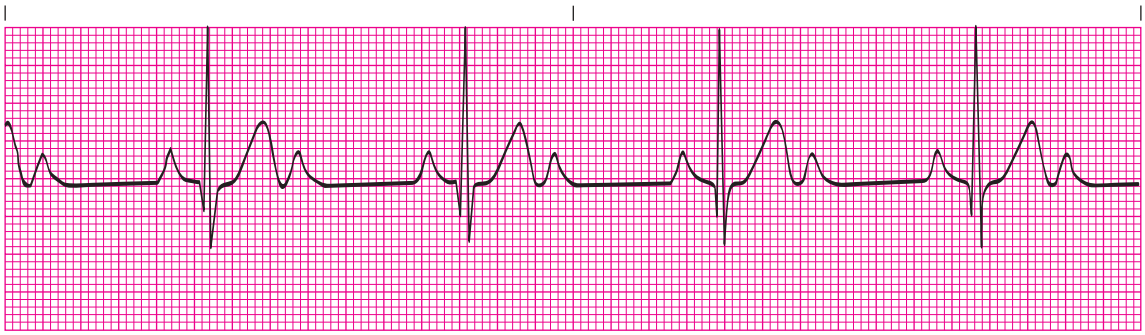

Fig. 18.13 Electrocardiographic tracing showing second-degree heart block type II. (Modified from Atwood S, Stanton C, Storey Davenport J: *Introduction to basic cardiac dysrhythmias*, ed 4, St Louis, 2009, Mosby/JEMS.)

occurs when an abnormality in the AV junction delays or blocks conduction of some of the impulses through the AV node. It can be recognized by a progressively increasing PR interval with consecutive beats until one impulse does not pass on to the ventricles at all; this "dropping" of the QRS complex is recognized by a P wave that is not followed by a QRS complex. The cycle then repeats itself.

Second-degree heart block type II (Mobitz type II) is less common and is more often the result of serious problems such as MI or ischemia. Type II heart block is seen as a series of nonconducted P waves followed by a P wave that is conducted to the ventricles (Fig. 18.13). In other words, in Mobitz II, the P wave may not be followed by a QRS complex and this occurs without progressive prolongation of the PR interval as in Mobitz I block. Sometimes, every other P wave is not followed by a QRS complex, which is a Mobitz II with a 1:1 ratio. (This is difficult to distinguish from Mobitz I block.) In other instances, the ratio of nonconducted to conducted P waves is fixed at 3:1 or 4:1. The PR interval for the conducted impulses is consistent.[6,7]

Treatment for type I second-degree heart block is not needed because it usually does not impair cardiac output or cause symptoms. Mobitz Type II heart block requires treatment in most cases because the resulting reduction in ventricular rate causes a decrease in blood pressure. Medications such as atropine may provide a better cardiac output until a pacemaker can be inserted. Because type II block may progress to third-degree heart block without warning, a pacemaker may be indicated.[8,9]

Third-degree heart block. Third-degree heart block is the most serious of the different types of heart block. It indicates that the conduction system between the atria and ventricles is completely blocked, and impulses generated in the SA node are not conducted to the ventricles. In this circumstance, the atria and ventricles are paced by independent sources. Most commonly, the atria are paced by the SA node, and the ventricles are paced by the AV node. This arrhythmia can be recognized when it is established that there is no relationship between the P waves and the QRS complexes. In other words, P waves occur with no fixed time relationship to the QRS complexes. The P-P intervals are regular and the R-R intervals are regular, but they have no correlation with one another. In addition, the QRS complexes are normal in configuration if the ventricles are paced by the AV node (Fig. 18.14). If the ventricles are paced by an abnormal (so-called ectopic) site in the myocardium, the QRS complexes may be abnormally wide, consistent with a bundle branch block. Typically, the ventricular rate is slower than the atrial rate because the AV node depolarizes at a slower rate than the SA node.[6,7]

Third-degree heart block is a serious arrhythmia because it often is caused by MI or drug toxicity (especially digitalis), and it may render the heart unable to meet the normal metabolic demands of the body. Treatment usually includes addressing the underlying cause (like a MI) as well as medication to speed up the ventricles and possibly a temporary external pacemaker until a permanent one can be placed.[8,9]

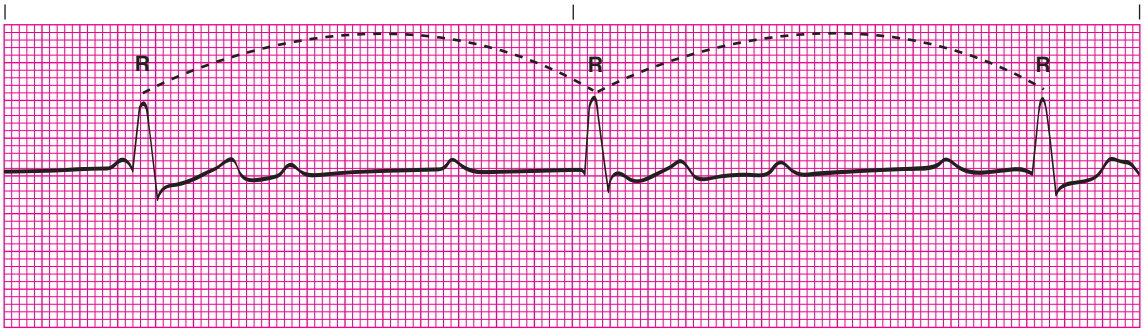

Fig. 18.14 Electrocardiographic tracing showing third-degree heart block. (Modified from Atwood S, Stanton C, Storey Davenport J: *Introduction to basic cardiac dysrhythmias*, ed 4, St Louis, 2009, Mosby/JEMS.)

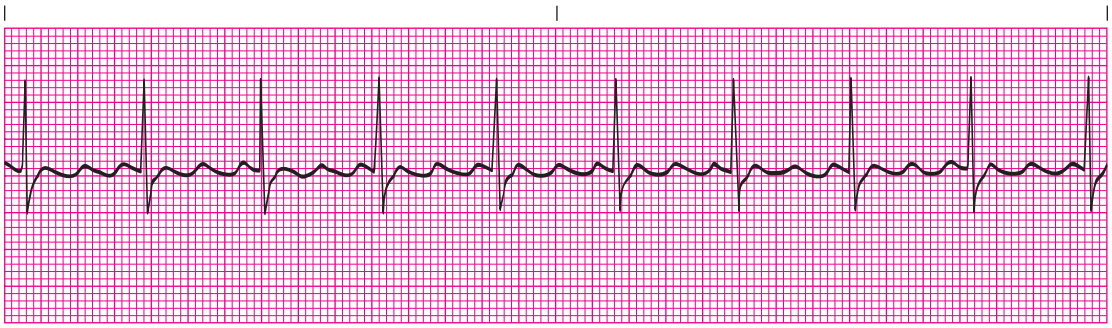

Fig. 18.15 Electrocardiographic tracing showing atrial flutter. (Modified from Atwood S, Stanton C, Storey Davenport J: *Introduction to basic cardiac dysrhythmias*, ed 4, St Louis, 2009, Mosby/JEMS.)

Atrial flutter. Atrial flutter is the rapid depolarization of the atria resulting from an ectopic focus that depolarizes at a rate of 250 to 350 times per minute. Typically, only one ectopic focus is causing the arrhythmia, which causes all each P waves to have the same appearance. The result is a characteristic saw-toothed baseline pattern (Fig. 18.15). Numerous P waves are present for every QRS complex, and the QRS complexes are normal in configuration. The R-R interval may be regular or may vary, depending on the ability of the atrial impulse to pass through the AV node.[1,3,4]

Various conditions can produce atrial flutter, including rheumatic heart disease, coronary heart disease, pulmonary embolism, stress, renal failure, and hypoxemia. This arrhythmia is generally not considered life-threatening but may lead to atrial fibrillation if untreated and can cause hemodynamic instability. Treatment usually includes medications such as digoxin, β blockers, or calcium channel blockers. Occasionally, electrical cardioversion is required. Once the rate is significantly slowed, cardioversion may be attempted to return the heart rhythm back to a normal sinus rhythm.[8,9]

Atrial fibrillation. Atrial fibrillation is present when the atrial muscle quivers in an irregular pattern that does not result in a coordinated contraction. The baseline electrical activity appears erratic, and no true P waves are seen in atrial fibrillation (Fig. 18.16). The AV node determines the ventricular response to the atrial activity by controlling which impulses pass through and which do not. The ventricular rate is often very irregular and results in an abnormal R-R interval.[1,3,4] Atrial fibrillation is referred to as an "irregularly irregular" rhythm, meaning that the QRS complexes occur with no predictable pattern, as determined by how many of the atrial impulses can pass through the AV node.

The causes of atrial fibrillation are similar to the causes of atrial flutter. However, atrial fibrillation is a more serious arrhythmia because it can lead to a significant reduction in cardiac output resulting from the loss of the **atrial kick.** Atrial kick is a feature of normal cardiac activity which results from synchronized contraction of the atria which push blood into the ventricles, helping them to fill before systole. The resulting stagnation of blood in the atria can also lead to formation of blood clots, which can lead to pulmonary emboli or an embolic stroke. Treatment for atrial fibrillation is similar to the treatment for atrial flutter. However, patients with sustained atrial fibrillation are often treated with anticoagulant medications to treat potential blood clot formation. Medications to slow the heart rate including beta blockers and calcium channel blockers. In addition, patients with either atrial fibrillation or atrial flutter who do not respond to drug therapy are often treated with synchronized cardioversion or ablation to try to eliminate the abnormal electrical activity and restore a normal rhythm.[8,9]

RULE OF THUMB Atrial fibrillation generally results in a reduction in cardiac output due to what is known as a loss of *atrial kick* resulting from a lack of coordination between the atria and ventricles. However, an even bigger problem is the potential for blood clot formation from stagnation of blood in the atria. These blood clots can easily travel to the pulmonary artery, causing a pulmonary embolism, or to the aorta, leading to an embolic stroke. As a result, most patients with atrial fibrillation of any duration should receive anticoagulant therapy.

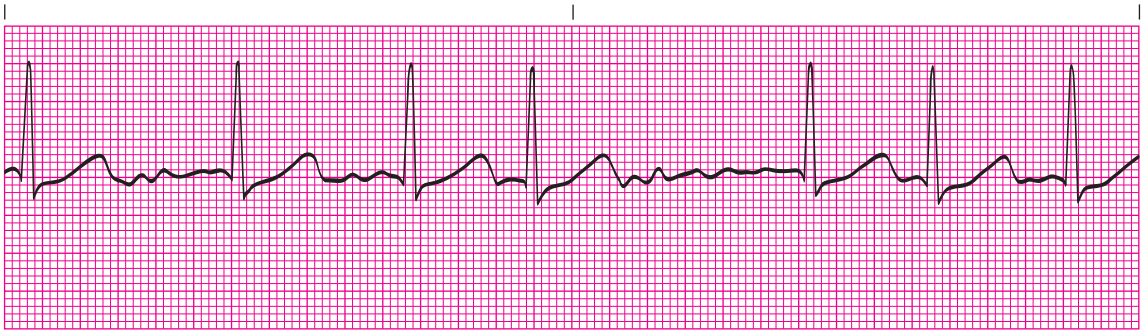

Fig. 18.16 Electrocardiographic tracing showing atrial fibrillation. (Modified from Atwood S, Stanton C, Storey Davenport J: *Introduction to basic cardiac dysrhythmias*, ed 4, St Louis, 2009, Mosby/JEMS.)

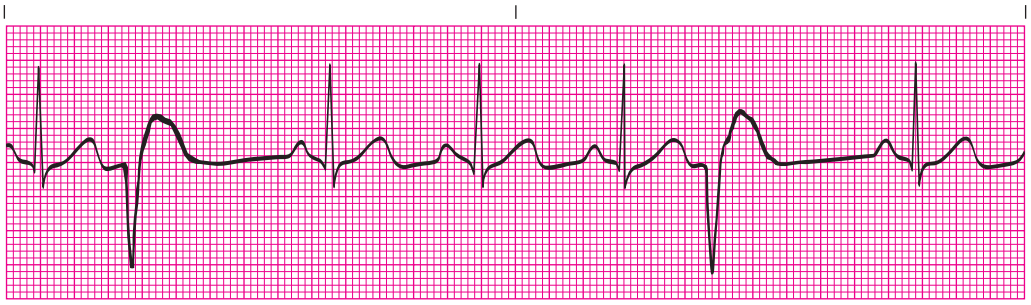

Fig. 18.17 Electrocardiographic tracing showing PVCs. (Modified from Atwood S, Stanton C, Storey Davenport J: *Introduction to basic cardiac dysrhythmias*, ed 4, St Louis, 2009, Mosby/JEMS.)

Premature ventricular contractions. Premature beats can occur when a portion of the impulse-conducting system or myocardium other than the SA node becomes diseased and triggers depolarization of the surrounding cardiac cells. Sources for the impulse outside the SA node are called **ectopic foci.** Ectopic foci occur when tissue hypoxia, acid-base imbalance, or electrolyte abnormalities are present and cause the cardiac cells in the ventricles to become abnormally excited. PVCs are easy to recognize because they cause a unique and bizarre QRS complex that is much wider than normal (Fig. 18.17). The QRS complex of a PVC is wider than normal because the ectopic focus is using channels outside the normal conduction system to move the impulse throughout the myocardium. PVCs have no P wave preceding them and may occur as a singular event or, more commonly, as a temporary sequence or "run" of PVCs. They also may occur at every other beat (called bigeminy) or every third beat (called trigeminy).[1,3,4]

An occasional PVC is common, should not cause major concern, and may occur as a result of stress, caffeine intake, nicotine use, or electrolyte imbalance. However, frequent PVCs are more serious and may result from ischemia of the myocardium. They also are commonly seen as a side effect of some medications. Treatment is based on the frequency and cause of the PVCs and is needed when the PVCs are frequent, paired together, or multifocal (appear differently because they come from more than one ectopic focus) or when they land directly on the T wave *(R on T phenomenon)*. In such cases, treatment must be prompt because the problem may progress rapidly to ventricular tachycardia (VT) and ventricular fibrillation (VF) (see subsequent discussion). Antiarrhythmic medications (e.g., lidocaine) may offer a temporary solution until the underlying cause can be addressed.[8,9]

Ventricular tachycardia. VT is a run of three or more PVCs. It usually is easy to recognize as a series of wide, bizarre QRS complexes that have no preceding P wave. When all the bizarre QRS complexes have the same appearance, the VT is called "monomorphic" and when there is more than one kind of bizarre QRS complex, the VT is called "polymorphic." One of the hallmarks of VT in general is third-degree AV block because the ventricles are beating independently of the atria. The ventricular rate is usually 100 to 250 beats/min (Fig. 18.18). It is considered "sustained VT" if it lasts longer than 30 seconds. A variant of polymorphic VT called "torsade de pointes" has a distinctive pattern in which the axis of the QRS complexes rotate or "twist" around the baseline, Torsade de pointes may result from conditions in which the QT interval is prolonged or as a complication of some medications, including macrolides used for COPD exacerbations.

Sustained or symptomatic VT is a serious and potentially life-threatening arrhythmia because it indicates that an ectopic focus is rapidly firing from the ventricles, which results from increased automaticity. It suggests a significant pathologic defect in the myocardium and often leads to VF, which is an immediately life-threatening arrhythmia, if untreated. MI, coronary artery disease, and hypertensive heart disease are the most common causes. As a result, VT is considered a rhythm for which electrical cardioversion is sometimes recommended in accordance with AHA resuscitation protocols (Chapter 38). [1,3,4]

Treatment must be prompt and specific and usually consists of cardioversion followed by long-term antiarrhythmic drugs

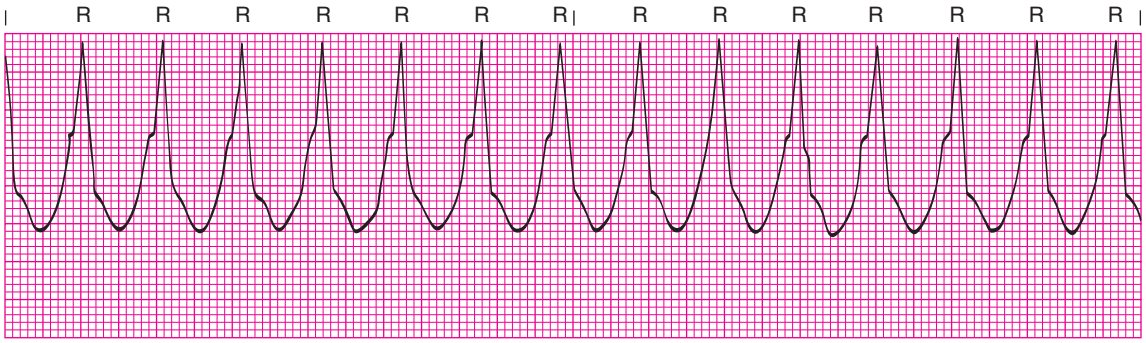

Fig. 18.18 Electrocardiographic tracing showing ventricular tachycardia. (Modified from Atwood S, Stanton C, Storey Davenport J: *Introduction to basic cardiac dysrhythmias*, ed 4, St Louis, 2009, Mosby/JEMS.)

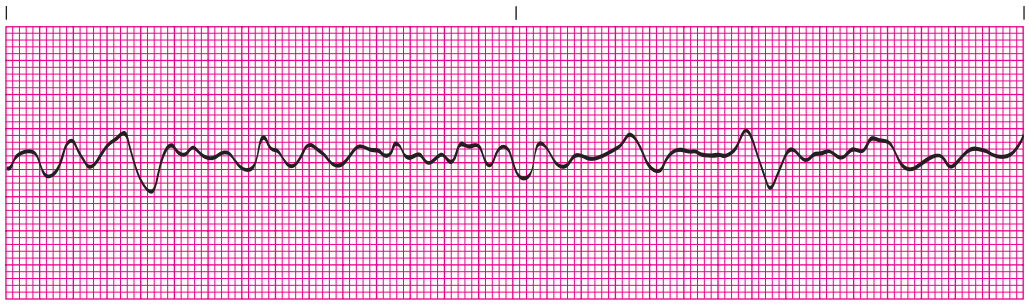

Fig. 18.19 Electrocardiographic tracing showing ventricular fibrillation. (Modified from Atwood S, Stanton C, Storey Davenport J: *Introduction to Basic cardiac dysrhythmias*, ed 4, St Louis, 2009, Mosby/JEMS.)

for long-term suppression. Patients at high risk for recurrent VT may have an internal cardioverter-defibrillator (ICD) placed so that if VT recurs, it can be treated automatically and promptly. Asymptomatic patients with recurrent nonsustained VT and ventricular ectopic beats may be treated with beta blockers to reduce symptoms of non–life-threatening ventricular arrhythmias. Symptomatic or sustained VT is considered a medical emergency, and the patient must be treated and monitored continuously in the ICU until his or her condition is stabilized.[8–12]

RULE OF THUMB VT causes the cardiac output to decrease significantly because the ventricles do not have time to fill between contractions. This places the patient in danger of cardiac arrest and death.

Ventricular fibrillation. VF is the most life-threatening arrhythmia and is defined as erratic quivering of the ventricular muscle mass. It causes the cardiac output to drop to zero; the patient becomes unconscious and VF represents a true medical emergency that results in the need for acute resuscitation. The electrocardiographic tracing of VF shows grossly irregular fluctuations with a zigzag pattern (Fig. 18.19). This pattern is caused by the same problems associated with VT.

Treatment calls for rapid defibrillation, cardiopulmonary resuscitation, and administration of O_2 and antiarrhythmic medications. Treatment of the underlying cause of the ischemia is also warranted (see Chapter 38). Survivors of VF often receive an ICD.[8–12]

MINI CLINI

Ventricular Fibrillation

Problem

A hospitalized 66-year-old woman with a history of congestive heart failure (CHF) and MI becomes unresponsive, pulseless, and apneic. She is quickly successfully resuscitated and transferred to the cardiac ICU. Her treatment plan will likely include which elements?

Solution

Patients who have a cardiac history as described above, especially one which includes a near–life-threatening event which includes VF, should be monitored by their cardiologist on a regular basis. In addition to medication therapy, their treatment plan may well include the insertion of an ICD to both pace the heart at an adequate rate, as well as respond and correct any repeat episodes of VF.

Pulseless Electrical Activity

In addition to the arrhythmias noted throughout this chapter, pulseless electrical activity (PEA) is a serious condition characterized by a disassociation between the electrical and mechanical activity of the heart. In essence, the heart generates an electrical signal that produces an ECG pattern on the monitor but the heart does not mechanically generate a pulse. PEA is relatively rare and generally does not occur without a precipitating event, such as a tension pneumothorax, MI, drug overdose, or severe electrolyte or acid-base disturbance.

MINI CLINI

Pulseless Electrical Activity

Problem

A 68-year-old man with a recent complaint of radiating chest pain is being placed on O_2 therapy with a nasal cannula at 2 L/min. Immediately after being set up on a 12-lead ECG, the patient loses consciousness. The ECG continues to show an apparent sinus bradycardia, but assessment reveals that the patient is pulseless.

Solution

This is an apparent case of PEA, which should be treated as a potentially life-threatening emergency. A "code blue" should be initiated, cardiopulmonary resuscitation should be started immediately, and potential causes, including in this instance MI, should be considered and treated.

Treatment involves resuscitation, emergency life support, and the immediate reversal of the cause. PEA also illustrates why RTs and other clinicians should never "treat the monitor" and underscores the importance of using ECGs as just one of several clinical indicators in assessing patients.[10–12] The prompt recognition and response to VT, VF, and PEA are discussed in detail in Chapter 38, which covers the broader topic of emergency cardiovascular life support.

Table 18.2 summarizes the primary features, causes, and treatment for the cardiac arrhythmias described in this chapter. In addition, Chapter 39 of this textbook, which covers emergency cardiovascular life support, provides more detail on this topic.

TABLE 18.2 Common Arrhythmias, Their Features, Causes, and Treatment

Arrhythmia	Major Distinguishing Feature(s)	Common Causes	Main Treatment Options
Sinus tachycardia	Heart rates exceeding 100 beats/min are abnormal in resting adult patients	Fever, pain, anxiety, hypovolemia, hypoxemia	Addressing the underlying cause by using relievers, fever reducers (antipyretics), fluids, or oxygen
Sinus bradycardia	A heart rate of less than 60 beats/min	Hypothermia, abnormalities in the SA node, or intense athletic conditioning	Medications such as atropine or pacing may be used when this occurs due to pathologic reasons
Sinus arrhythmia	Irregular spacing between QRS complexes. When the R-R interval varies more than 0.12 seconds throughout the rhythm strip and the ECG is otherwise normal	May occur with the effects of breathing on the heart or as a side effect of medications such as digoxin	Most cases of sinus arrhythmia are benign and do not need treatment
First-degree heart block	A PR interval which is longer than 0.20 seconds	Following an MI that damages the AV node, or a complication of certain medications, such as digoxin or beta blockers	Treatment usually is not needed for first-degree heart block if the patient is able to maintain an adequate blood pressure
Second-degree heart block	Second-degree heart block comes in two types. *Type I (Wenckebach or Mobitz type I)* produces a cycle of progressively increasing PR interval until the QRS complex is dropped, as recognized by a P wave that is not followed by a QRS *Second-degree heart block type II (Mobitz type II)* is characterized by some P waves not followed by a QRS complex without progressive prolongation of the PR interval	*Type I (Wenckebach or Mobitz type I)* block is a relatively benign and often transient arrhythmia *Second-degree heart block type II (Mobitz type II)* is less common and is often the result of serious problems such as MI or ischemia	Treatment for *type I second-degree heart block* is generally not needed because it usually does not impair cardiac output or cause symptoms *Mobitz type II heart block* often requires treatment because the resulting reduction in ventricular rate causes a decrease in blood pressure Treatment often consists of temporary pacing until a permanent pacemaker can be inserted
Third-degree heart block	No relationship between the P waves (atrial activity) and QRS complexes (ventricular activity). In other words, P waves occur with no fixed time relationship to the QRS complexes. The P-P intervals are regular and the R-R intervals are regular, but they have no correlation with one another	Often is caused by MI or drug toxicity (especially digitalis), and it may render the heart unable to meet the normal metabolic demands of the body	Addressing the underlying cause (like a myocardial infarction) as well as medications to speed up the ventricles and possibly a temporary external pacemaker until a permanent one can be placed
Atrial flutter	Saw-toothed baseline pattern. Numerous P waves are present for every QRS complex, and the QRS complexes are normal in configuration. The R-R interval may be regular or may vary, depending on the ability of the atrial impulse to pass through the AV node	Rheumatic heart disease, coronary heart disease, pulmonary embolism, stress, renal failure, hypoxemia, and hypertension	Medications such as digoxin, beta blockers, or calcium channel blockers. Occasionally, electrical cardioversion is required. Once the rate is significantly slowed, cardioversion may be attempted to return the heart rhythm back to a normal sinus rhythm

Continued

TABLE 18.2 Common Arrhythmias, Their Features, Causes, and Treatment—*cont'd*

Arrhythmia	Major Distinguishing Feature(s)	Common Causes	Main Treatment Options
Atrial fibrillation	The baseline electrical activity appears erratic, and no true P waves are seen in atrial fibrillation	Similar to atrial flutter (above)	Anticoagulant medications to treat potential blood clot formation, β blockers, calcium channel blockers, or anti-arrhythmia medications. Patients who do not respond to drug therapy are often treated with synchronized cardioversion or ablation
Premature ventricular contractions (PVCs)	A unique and bizarre QRS complex that is much wider than normal	Occasional PVCs are common. They may result from stress, caffeine intake, nicotine use, or electrolyte imbalance. Frequent PVCs are more serious and may result from ischemia, a side effect of some medications	Based on the frequency and cause. When the PVCs are frequent, paired together, multifocal, or when they land directly on the T wave, treatment must be prompt because it may progress rapidly to a more serious arrhythmia (e.g., VT or VF). Anti-arrhythmia medications may be prescribed until the underlying cause is addressed
Ventricular tachycardia	A run of three or more PVCs characterized by a series of wide, bizarre QRS complexes that have no preceding P wave.	Myocardial infarction, coronary artery disease, hypertensive heart disease, and untreated obstructive sleep apnea are the most common causes	Asymptomatic patients with recurrent, nonsustained VT may be treated with β blockers. Cardioversion followed by long-term antiarrhythmic drugs may be used for long-term suppression. Patients at high risk for recurrent VT may have an internal cardioverter-defibrillator (ICD) placed
Ventricular fibrillation	Grossly irregular fluctuations with a zigzag pattern. Erratic quivering of the ventricular muscle causes the cardiac output to drop to zero	Similar to VT	Rapid defibrillation, cardiopulmonary resuscitation, and the immediate reversal of the underlying cause. Administration of O_2 and antiarrhythmic medications. Survivors of VF often receive an ICD
Pulseless electrical activity	Disassociation between the electrical and mechanical activity of the heart. In essence, the heart generates an electrical signal that produces an ECG pattern but the heart does not pump and there is no pulse	Generally does not occur without a precipitating event, such as a tension pneumothorax, MI, drug overdose, or severe electrolyte or acid-base disturbance	Emergency life support, and the immediate reversal of the underlying cause. Illustrates why clinicians should never "treat the monitor" and underscores the importance of using ECGs as just one of several clinical indicators

Chapter 38 of this textbook includes more extensive discussion of the recognition and treatment of arrhythmias.
AV, Atrioventricular; *ECG*, electrocardiogram; *MI*, myocardial infarction; *SA*, sinoatrial; *VF*, ventricular fibrillation; *VT*, ventricular tachycardia.

SUMMARY CHECKLIST

- The ECG is an inexpensive, noninvasive, and easy way to evaluate patients, but it does not predict future heart problems nor identify all abnormalities (i.e., valvular defects).
- The impulse-conducting system has three types of cardiac muscle cells capable of electrical excitation: pacemaker cells (e.g., SA node, AV node), specialized rapid conducting tissue (e.g., Purkinje fibers), and atrial and ventricular muscle cells. Each of these vary in their degree of automaticity.
- An elevated or depressed ST segment is a common ECG finding during a MI and indicates a potentially life-threatening condition.
- Axis evaluation is used to determine the general direction of current flow during ventricular depolarization and is helpful in identifying hypertrophy of one of the ventricles.
- The heart rate can be calculated by counting the number of QRS complexes (for the ventricular rate) or the number of P waves (for the atrial rate) in 6 seconds (30 large boxes) and multiplying this number by 10. When the rate is regular, the number of large boxes between two successive complexes can be counted and divide this number into 300.
- Sinus bradycardia is a significant clinical problem only if it causes the patient's blood pressure to decrease significantly or the patient becomes symptomatic.
- Frequent, paired together, multifocal PVCs or the R on T phenomenon with PVCs is serious because it may be due to ischemia of the myocardium and can progress rapidly to ventricular tachycardia and fibrillation.
- Type II second-degree heart block usually causes a significant decrease in cardiac output and may also progress to third-degree heart block.
- Third-degree heart block is the most serious of the different types of heart block often caused by MI or drug toxicity and may render the heart unable to meet the normal metabolic demands of the body. Treatment usually includes medication to speed up the ventricles and a pacemaker.
- Atrial fibrillation is a serious arrhythmia that can lead to a significant reduction in cardiac output. In addition, if untreated, over time it can potentially cause an embolic event. Treatment entails medications to control the rate, anticoagulants, and potential cardioversion.
- Sustained or symptomatic VT is a serious arrhythmia that often leads to VF if untreated. Prompt treatment usually

consists of cardioversion, antiarrhythmic drugs, and transfer to the ICU.

- VF is a life-threatening arrhythmia, requiring emergent treatment with rapid defibrillation, cardiopulmonary resuscitation, and administration of O_2 and antiarrhythmic medications.
- Always treat the patient, not the ECG pattern on the monitor. Patients with PEA may have a normal-looking ECG pattern but are pulseless and require immediate emergency life support.

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19

Analysis and Monitoring of Gas Exchange

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CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- List the risks involved with invasive and noninvasive monitoring.
- Describe the two types of electrochemical oxygen analyzers.
- Describe calibration and problem-solving techniques for oxygen analyzers.
- State how to obtain, process, and analyze arterial and capillary blood gas samples.
- Describe how to perform a modified Allen test.
- List the quality control procedures applied to blood gas analysis.
- List the potential advantages of point-of-care testing.
- Describe how to obtain and interpret transcutaneous oxygen and carbon dioxide monitoring.
- Describe the basic principles used by an oximeter to monitor oxygen saturation.
- Describe the different types of oximetry used.
- State how to perform and interpret pulse oximetry.
- List the limitations of pulse oximetry.
- Describe the different forms of hemoglobin.
- Describe how to perform capnometry and interpret capnograms.

CHAPTER OUTLINE

KEY TERMS

analyte
analyzer
arterialized blood
calibration media
capnography
capnometry
collateral circulation
cuvette
electrochemical
invasive
modified Allen test
monitor
noninvasive
optical luminescent tissue
optode
oximetry
photoplethysmography
point-of-care testing
pre-analytic error
precision
proficiency testing
pulse co-oximeters
pulse co-oximetry
quality control
random error
spectrophotometry
systematic error
volumetric capnography

Many important and potentially lifesaving clinical decisions are based on a patient's gas exchange information. Gas exchange takes place inside each of the body's cells, where complex metabolic pathways use oxygen (O_2) to create energy and produce carbon dioxide (CO_2) as a waste product. The physiologic mechanisms which facilitate and inhibit gas exchange and transport are detailed in Chapter 12 of this book. The focus of this chapter is on the procedures for monitoring gas exchange, including instrumentation, problem solving and troubleshooting, as well as the clinical use of this information to direct patient care.

Although it is possible (but often not clinically practical) to analyze gas exchange at the cellular level, clinical focus normally is on gas exchange between the lungs and blood or between the blood and tissues. Gas exchange between the lungs and blood is usually analyzed by measuring O_2 and CO_2 levels in the arterial blood. Clinicians, including respiratory therapists (RTs), can also measure CO_2 levels in the expired gas to monitor ventilation. The most common approach to analyzing gas exchange between the blood and tissues is to measure O_2 levels in the mixed venous blood. This chapter focuses on these and other important parameters related to gas exchange.

INVASIVE VERSUS NONINVASIVE PROCEDURES

Invasive procedures require insertion of a sensor or collection device into the body (e.g., an indwelling arterial catheter), whereas **noninvasive** monitoring gathers data externally.[1] Laboratory analysis of gas exchange requires sampling blood, therefore it is considered invasive. In general, invasive procedures provide more accurate data than noninvasive methods, but carry greater risk.

When both invasive and noninvasive approaches are available, the need for measurement accuracy, cost, and risks are key factors for determining whether an invasive or noninvasive approach is chosen. RTs and other clinicians sometimes combine the approaches—using the invasive approach to establish accurate baseline information and applying the noninvasive method for ongoing monitoring of a patient. After the relationship between the results of invasive versus noninvasive methods in a single patient is established, trending changes by noninvasive methods can be useful for making clinical decisions while minimizing risk.

MONITORING FRACTIONAL INSPIRED OXYGEN

Gas exchange analysis begins with knowledge of the system inputs—the inspired O_2 and CO_2 concentrations. Healthy individuals breathe air that contains a fixed O_2 concentration (21%) and negligible amounts of CO_2 (approximately 0.2%). Hypoxemic patients are routinely given supplemental O_2. In most cases, O_2 **analyzers** are used to measure the fractional inspired O_2 concentration (FiO_2).

Instrumentation

Although many methods exist for measuring O_2 concentrations, most bedside systems apply electrochemical principles. There are two common types of **electrochemical** O_2 analyzers—the polarographic (Clark) electrode and the galvanic fuel cell. Under ideal conditions of temperature, pressure, and relative humidity, both types are generally quite accurate and within ± 2% of the actual concentration.[1]

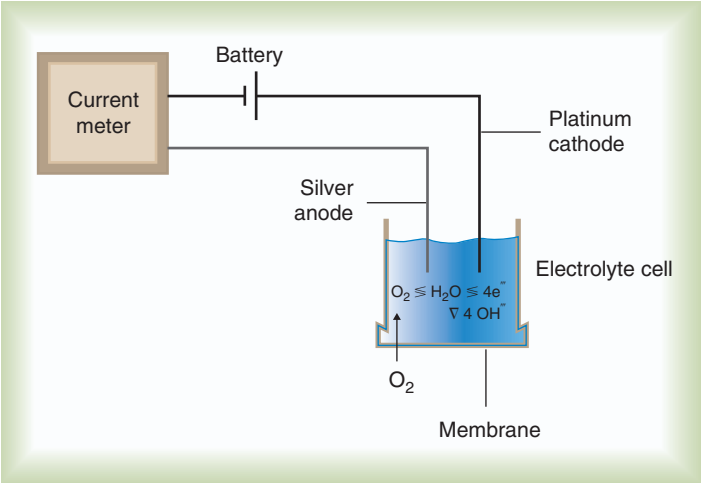

Fig. 19.1 The basic principle underlying the Clark polarographic analyzer. (Modified from Kacmarek RM, Hess D, Stoller JK, editors: *Monitoring in respiratory care,* St Louis, 1993, Mosby.)

The Clark electrode is similar to electrodes used in blood gas analyzers, transcutaneous **monitors**, and tissue O_2 probes discussed later in this chapter. This system typically consists of a platinum cathode and a silver–silver chloride anode (Fig. 19.1). Molecules of O_2 diffuse through the sensor membrane into the electrolyte, where a polarizing voltage causes an electron flow between the anode and cathode. While silver is oxidized at the anode, the flow of electrons reduces O_2 (and H_2O) to hydroxyl ions (OH^-) at the cathode. More O_2 molecules undergoing reduction causes a greater electron flow across the poles (current). The resulting current is proportional to the PaO_2, with its value displayed on a galvanometer calibrated in % O_2. Response times for O_2 analyzers range from 10 to 30 seconds.

Galvanic fuel cells work in a similar fashion. Most galvanic fuel cells use a gold anode and a lead cathode. In contrast to the Clark electrode, current flow across these poles is generated by the chemical reaction itself.

The Clark electrode and galvanic cell are suitable for basic FiO_2 monitoring. When greater accuracy or faster response times are needed (e.g., when performing indirect calorimetry), a paramagnetic, zirconium cell, Raman scattering, or mass spectroscopy analyzer should be selected.

Procedure

To obtain accurate results with an O_2 analyzer, the clinician first must calibrate it. Although procedures differ according to the manufacturer, the basic steps are similar. This requires exposing the sensor to two gases with different O_2 concentrations, usually 100% O_2 and room air (21% O_2). In one common procedure, the sensor is first exposed to 100% O_2. If the analyzer fails to read 100%, the device's *calibration,* or balance control, must be adjusted until it reads 100%. Then the clinician exposes the sensor to room air and confirms a second reading of 21% (±2%). The clinician should use the analyzer to measure a patient's FiO_2 only after confirming both readings.

Problem Solving and Troubleshooting

Because O_2 analyzers include replaceable components that deteriorate over time (batteries, electrodes, membranes, electrolytes), the best way to avoid problems is through preventive maintenance. This should include both scheduled parts replacement and routine operational testing.

Even with the best preventive maintenance, O_2 analyzers may malfunction. The clinician would know that an analyzer is not working if it fails to calibrate or gives an inconsistent reading during use. Common causes of analyzer malfunction are low batteries, sensor depletion, and electronic failure. Because a low battery condition is common, the first step in troubleshooting is to replace the batteries. If the analyzer still does not calibrate, the problem is probably a depleted sensor. With most analyzers, a depleted sensor must be replaced. If an analyzer still fails to calibrate after battery and sensor replacement, the most likely problem is an internal failure of its electrical system. In this case, the device should be taken out of service and repaired.

Inaccurate readings with electrochemical analyzers can also result from condensed water vapor or pressure fluctuations. Galvanic cells are particularly sensitive to condensation. To avoid this problem during continuous use in humidified circuits, the clinician should place the analyzer sensor proximal to any humidification device.

Fuel cell and Clark electrode readings also are affected by ambient pressure changes. Under conditions of low pressure (high altitude), these devices read lower than the actual O_2 concentration. Conversely, higher pressures, such as pressures that occur during positive pressure ventilation, cause these devices to read higher than the actual FiO_2. These observations are consistent with the fact that both devices measure the PO_2 but report on a percent concentration scale.

RULE OF THUMB Three common causes of O_2 analyzer malfunction are low batteries (most common), sensor depletion, and electronic failure.

SAMPLING AND ANALYZING BLOOD GASES

In the clinical setting, it is common for blood specimens to be sampled and analyzed separately. Each procedure involves different knowledge and skill. For these reasons, these topics are covered separately.

Sampling

RTs and other clinicians have been using blood samples to assess gas exchange parameters for more than 50 years.[2] The definition of *respiratory failure* is based largely on blood gas measurements (i.e., PaO_2 and $PaCO_2$). Depending on the need, blood gas samples can be obtained by percutaneous puncture of a peripheral artery, from an indwelling catheter (e.g., arterial, central venous, or pulmonary artery [PA]), or by capillary sampling.

Arterial Puncture and Interpretation

Results obtained from sampling arterial blood gas (ABG) are the foundation for the diagnosis and management of oxygenation and acid-base disturbances. ABGs are considered the "gold standard" of gas exchange analysis, against which all other methods are compared.

Arterial puncture involves drawing blood from a peripheral artery (radial, brachial, femoral, or dorsalis pedis) through a single percutaneous needle puncture (Fig. 19.2). The radial artery

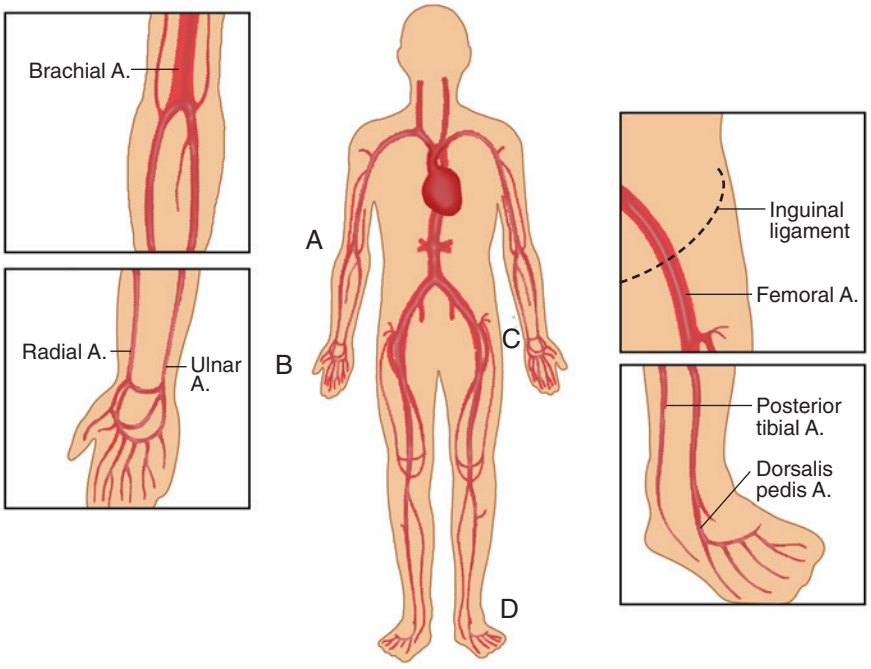

Fig. 19.2 Arteries (A.) Used for Arterial Puncture. (A) Brachial artery. (B) Radial artery (with collateral flow through the ulnar arteries). (C) Femoral artery. (D) Dorsalis pedis (with collateral flow through the posterior tibial artery). The radial artery is the preferred site.

BOX 19.1 Recommended Equipment for Percutaneous Arterial Blood Sampling

- Standard precautions barrier protection (gloves, safety goggles)
- Preheparinized blood gas kit syringe (1–3 mL)
- Short-bevel 20- to 22-gauge needle with a clear hub (23- to 25-gauge for children and infants)
- Patient and sample label
- Isopropyl alcohol (70%), povidone-iodine (Betadine) (check patient for iodine sensitivity), or chlorhexidine swabs
- Sterile gauze squares, tape, bandages
- Puncture-resistant container
- Ice slush, depending upon the analyzer. Note: For most point-of-care (bedside) analyzers, samples should not be chilled and should be run within 1–2 min after being obtained.
- Towels
- Sharps container
- Local anesthetic (optional)
- Hypodermic needle (25- or 26-gauge)
- Needle capping device

BOX 19.2 Procedure for Radial Artery Puncture

- Check the medical record to: (1) confirm the order and indications, and (2) determine the patient's primary diagnosis, history (especially bleeding disorders or blood-borne infections), current status, respiratory care orders (especially oxygen therapy or mechanical ventilation), and anticoagulant or thrombolytic therapy.
- Confirm steady-state conditions (20–30 min after changes).
- Obtain and assemble necessary equipment and supplies.
- Wash hands and don barrier protection (e.g., gloves, eyewear).
- Identify the patient using current patient safety standards.
- Explain the procedure to the patient.
- Position the patient, extending the patient's wrist to approximately 30 degrees.
- Perform a modified Allen test, and confirm collateral circulation.
- Clean site thoroughly with 70% isopropyl alcohol or an equivalent antiseptic.
- Inject a local anesthetic subcutaneously/periarterially, wait 2 min for effect (optional).
- Use a preheparinized blood gas kit syringe or heparinize a syringe and expel the excess (fill dead space only).
- Palpate and secure the artery with one hand.
- Insert the needle, bevel up, through the skin at a 45-degree angle until blood pulsates into the syringe.
- Allow 1 mL of blood to fill syringe (the need to aspirate indicates a venous puncture).
- Apply firm pressure to puncture site with sterile gauze until the bleeding stops.
- Expel any air bubbles from the sample, and cap or plug the syringe.
- Mix the sample by rolling and inverting the syringe.
- Place the sample in a transport container and chill or not, depending on analyzer manufacturer recommendation. Note: For most point-of-care (bedside) analyzers, samples should not be chilled and should be run within 1–2 min after being obtained.
- Dispose of waste materials and sharps properly.
- Document the procedure and patient status in the medical record and on the specimen label.
- Check the site for hematoma and adequacy of distal circulation.

From Malley WJ: *Clinical blood gases: assessment and intervention*, St Louis, 2005, Saunders.

is the preferred site for arterial blood sampling for the following reasons:

- It is near the surface and relatively easy to palpate and stabilize.
- Effective **collateral circulation** normally exists in the ulnar artery.
- The artery is not near any large veins.

The other sites mentioned (brachial, femoral, and dorsalis pedis) are riskier and should be used only by clinicians specifically trained in their use. Likewise, arterial puncture in infants (through either the radial or the temporal artery) requires advanced training. Arterial cannulation sites for indwelling catheters include radial, brachial, femoral, dorsalis pedis, umbilical (in neonates), and axillary arteries. The focus here is on radial artery puncture.

To guide practitioners in providing quality care, the American Association for Respiratory Care (AARC) has published Clinical Practice Guideline: Sampling for Arterial Blood Gas Analysis.[3] Complementary recommendations have been published by the Clinical Laboratory Standards Institute (CLSI).[4]

Equipment. Box 19.1 lists the equipment needed to perform an arterial puncture. Commercial vendors provide kits containing most of the equipment listed.

Procedure. Box 19.2 outlines the basic procedure for radial artery puncture of adults. Before radial artery puncture is performed, a **modified Allen test** (Fig. 19.3) is recommended. The test is normal, also called positive (indicating adequate collateral circulation), if the palm, fingers, and thumb flush pink within 5 to 10 seconds after pressure on the ulnar artery is released. Although a normal test result indicates the presence of collateral circulation in the ulnar artery, it may not predict the development of complications after radial artery puncture or cannulation.

The modified Allen test has been a widely used clinical method to assess adequacy of ulnar artery collateral blood flow despite the lack of evidence that it can predict ischemic complications in the setting of complete radial artery occlusion.[5] The criteria for an abnormal test result are not agreed on, and therefore the significance of an abnormal test is unclear. For example, test results (1) may be inaccurate in predicting post-cannulation hand ischemia, (2) may vary depending on the clinician performing the test, and (3) are known to yield high incidences of both false normal and abnormal results. In addition, prior radial artery cannulation, severe circulatory insufficiency, wrist or hand burns, or jaundice makes interpreting the results difficult. Despite these limitations, an Allen test may reveal gross circulatory abnormalities and therefore should be performed beforehand and then documented in the patient's medical record.

In patients who have undergone previous radial artery cannulation, the modified Allen test can provide documentation of possible arterial thrombosis and should be used to direct catheter placement. If the Allen test is negative (or abnormal) and the hand does not pink-up in 5 to 10 seconds, then it should be tried on the other hand and if positive, the cannulation should be attempted on that hand.[6]

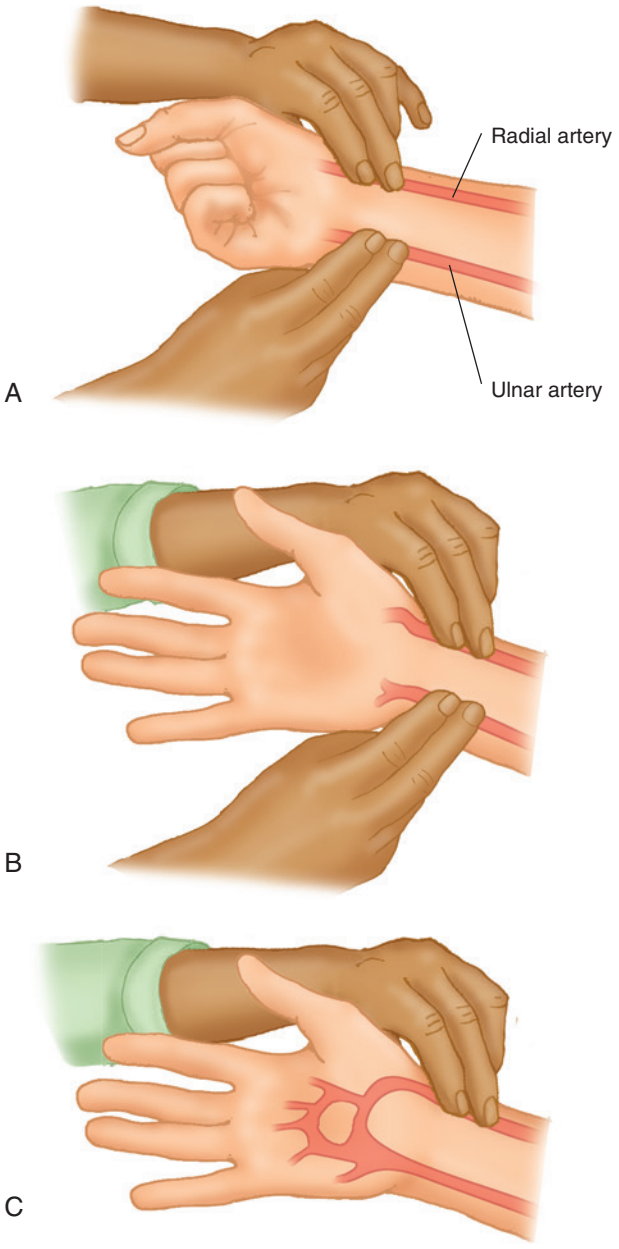

Fig. 19.3 Modified Allen Test. (A) The hand is clenched into a tight fist, and pressure is applied to the radial and ulnar arteries. (B) The hand is opened (but not fully extended); the palm and fingers are blanched. (C) Removal of pressure on the ulnar artery should cause flushing of the entire hand (within 5 to 10 s), indicative of adequate collateral circulation or a normal modified Allen test.

In most cases, a sample volume of 0.5 to 1 mL of blood is adequate. The actual sample volume needed depends on: (1) the anticoagulant used, (2) the requirements of the specific analyzer used, and (3) whether other tests will be performed on the sample. It should be noted that point-of-care (bedside) analyzers tend to require less blood (≤0.5 mL) than laboratory analyzers.

The following rules for careful handling of the needle help avoid transmission of blood-borne diseases:

- Never recap a used needle without a safety device.
- Never handle a used needle using both hands.
- Never point a used needle toward any part of the body.
- Never bend, break, or remove used needles from syringes by hand.
- Always dispose of used syringes, needles, and other sharp items in appropriate puncture-resistant sharps containers.

Indications for blood gas sampling. Knowing when to obtain a blood gas sample is just as important as knowing how to perform the procedure. Box 19.3 lists common clinical situations associated with the need for ABG analysis.

Problem solving and troubleshooting. There are two major problem areas associated with arterial puncture. The first problem involves difficulties in getting a good sample. The second problem involves pre-analytic error.

Getting a good sample. Problems with getting a good sample include an inaccessible artery, absent pulse, deficient sample return, and alteration of test results caused by the patient's response. If the selected artery cannot be located, another site should be considered. Likewise, if an adequate pulse cannot be palpated at the chosen site, another site should be selected or an acceptable noninvasive approach should be considered as an alternative (e.g., pulse oximetry). Ultrasound guidance may be useful in artery identification and sampling success.[7]

BOX 19.3 Clinical Indications for Arterial Blood Gas Analysis

- Sudden, unexplained dyspnea
- Cyanosis
- Abnormal breath sounds
- Severe, unexplained tachypnea
- Heavy use of accessory muscles
- Changes in ventilator settings
- Cardiopulmonary resuscitation
- New appearance of diffuse infiltrates in chest radiograph
- Sudden appearance or progression of cardiac arrhythmias
- Acute hypotension
- Acute deterioration in neurologic function

MINI CLINI

Use of the Modified Allen Test

Problem

A 53-year-old man was hospitalized for pneumonia. An ABG is ordered by the pulmonologist. The RT comes to the patients' bedside to draw an arterial blood sample. The patient has a bounding right radial artery pulse, but it is noted that the patient has a scar on his distal forearm. Upon questioning the patient, the RT discovers that the patient had a motorcycle accident 25 years ago. He had surgery to repair a right wrist injury. A modified Allen test is performed and the patient's entire hand flushes pink in 25 seconds when ulnar artery pressure is released.

What should be done next?

Solution

The patient has an abnormal (negative) modified Allen test indicating inadequate circulation through the ulnar artery. The previous injury and surgery might have affected the ulnar artery of that hand. While this cannot predict complications, the RT should perform the modified Allen test on the patient's other hand and, if normal, perform the radial artery puncture on that hand.

TABLE 19.1 Pre-analytic Errors Associated With Arterial Blood

Error	Effect on Parameters	How to Recognize	How to Avoid
Air in sample	↓ PCO_2 ↑ pH ↑ low PO_2 ↓ high PO_2	Visible bubbles or froth Low PCO_2 inconsistent with patient status	Discard frothy samples Fully expel bubbles Mix only after air is expelled Cap syringe quickly
Venous admixture	↑ PCO_2 ↓ pH Can greatly lower PO_2	Failure of syringe to fill by pulsations Patient has no symptoms of hypoxemia	Avoid brachial and femoral sites Do not aspirate sample Use short-bevel needles Avoid artery "overshoot" Cross-check with SpO_2
Excess anticoagulant (dilution)	↓ PCO_2 ↑ pH ↑ low PO_2 ↓ high PO_2	Visible heparin remains in syringe before sampling	Use premade lyophilized (dry) heparin blood gas kits Fill dead space only Collect >2 mL (adults) and >0.6 mL (infants)
Metabolic effects	↑ PCO_2 ↓ pH ↓ PO_2	Excessive time lag since sample collection Values inconsistent with patient status	Analyze within 15 min Place sample in ice slush

If the clinician gets only a small spurt of blood, the needle has probably passed through or entered near the wall of the artery. In this situation, the needle should be slowly withdrawn and rotated until a pulsatile flow fills the syringe. The tip of the needle is never redirected without it first being withdrawn to the subcutaneous tissue. If the needle must be withdrawn completely and the clinician does not have an adequate sample, the procedure is repeated with a fresh blood gas kit.

Small sample volumes or the need to apply syringe suction also may indicate that venous blood has been obtained. However, when drawing arterial blood from hypotensive patients or when using small needles (<23-gauge), the clinician may need to pull gently on the syringe barrel. If the clinician suspects that pain or anxiety during the procedure may have altered the results (most typically causing hyperventilation, but sometimes breath holding), then the clinician may occasionally consider using a local anesthetic for subsequent sampling attempts.

Pre-analytic error. **Pre-analytic errors** are problems occurring before sample analysis that can alter the accuracy of the blood gas results. Table 19.1 summarizes the most common errors associated with arterial blood sampling, including recommendations on how to recognize and avoid these problems. Clinicians can avoid most pre-analytic errors by ensuring that the sample is obtained anaerobically (with immediate expulsion of air bubbles), properly anticoagulated, and quickly analyzed.

The traditional method used to avoid pre-analytic errors caused by blood cell metabolism is to chill the sample quickly by placing it in ice.[3] However, some studies suggest that results may be altered if samples are stored in certain types of plastic syringes, especially if placed on ice before being analyzed. In addition, chilled samples can result in potassium transport between blood cells and plasma and can result in erroneous elevation in potassium measured from a blood gas sample. Hence, the best ways to minimize such pre-analytic errors is to use low-diffusability syringes which minimize the risk for room air altering the sample, and to analyze the sample as soon as possible after it has been obtained. Furthermore, samples that have been stored for an undetermined time, whether chilled or not, should be discarded.[8,9] Another consideration is that pneumatic tube transport of samples containing small air bubbles can have a noticeable effect on increasing PaO_2.[9] Finally, most point-of-care (bedside) analyzer systems (discussed later in this chapter) require that the sample not be chilled and that it be analyzed within 1 to 2 minutes after being obtained, depending on the manufacturer.

RULE OF THUMB Common methods for avoiding pre-analytic errors in ABG measurements are ensuring that the sample is obtained anaerobically (with immediate expulsion of air bubbles), the sample syringe is made of low-diffusability material and is properly anticoagulated, and the sample is analyzed promptly using properly functioning equipment.

Interpretation of arterial blood gases. Because gas exchange is a dynamic process, looking at results from a single blood sample is akin to looking at a single frame of streaming video, representing a single point in time rather than an ongoing physiologic process. Blood gas results must be interpreted in light of the patient's status at the time the sample was obtained.

Any major change in the patient's condition or therapy disrupts the patient's steady state. However, over time, a new steady state emerges. The time needed to restore steady-state conditions varies with the patient's pulmonary status. Patients with healthy lungs achieve a steady state in only 5 minutes after changes, whereas patients with chronic obstructive pulmonary disease (COPD) may require up to 30 minutes. For example, when FiO_2 is changed, the measured PaO_2 would accurately reflect the patient's gas exchange status within 5 minutes in healthy individuals but may require up to 30 minutes in patients with COPD.

To document the patient's status, the following need to be recorded: (1) date, time, and site of sampling; (2) results of the modified Allen test, when performed; (3) patient's body temperature, position, activity level, and respiratory rate; and (4) FiO_2 concentration or nasal cannula flow and all applicable

TABLE 19.2 Common Sites for Indwelling Vascular Catheters and the Information They Provide

	BLOOD COLLECTION		PRESSURE MONITORING	
Location	**Sample**	**Reflects**	**Pressure**	**Reflects**
Peripheral, umbilical artery	Arterial blood	Pulmonary gas exchange (O_2 uptake/CO_2 removal)	Systemic arterial pressure	LV afterload, vascular tone, blood volume
Central vein	Venous blood (unmixed)	Not useful for assessing gas exchange; can be used for some other laboratory tests	CVP	Fluid volume, vascular tone, RV preload
Pulmonary artery	Mixed venous blood (balloon deflated)	Gas exchange at tissues (O_2 consumption/CO_2 production)	PAP, PCWP	RV afterload, vascular tone, blood volume, LV preload

CVP, Central venous pressure; *LV,* left ventricular; *PAP,* pulmonary artery pressure; *PCWP,* pulmonary capillary wedge pressure; *RV,* right ventricular.

ventilatory support settings. Noting such information may prove useful in interpreting the results.

RULE OF THUMB Waiting up to 30 min after any major change in ventilatory support may be necessary before sampling and analyzing the blood gases of a critically ill patient. This waiting period covers the timeframe to ensure a steady state in an individual with healthy lungs (5 min) or with COPD (30 min).

In the first step of interpreting results, clinicians must ensure they are looking at the results for the correct patient. The name and patient identification number from the blood gas report must match the patient. Interpretation of the results can be divided into two basic steps: interpretation of the oxygenation status and interpretation of the acid-base status (see Chapters 12 and 14).

Indwelling Catheters (Arterial Pressure, Central Venous Pressure, and Pulmonary Artery Lines)

Indwelling catheters provide ready access for blood sampling and allow continuous monitoring of vascular pressures without the traumatic risks associated with repetitive percutaneous punctures. However, infection and thrombosis are more likely with indwelling catheters than with intermittent punctures.

The most common route for an indwelling arterial vascular line is the radial artery; less commonly used sites are the dorsalis pedis, brachial, axillary, and femoral arteries (see Fig. 19.2). Venous blood gases are obtained from either a central venous catheter or a PA catheter, which can access both the superior vena cava and a main branch of the PA. In neonates, the umbilical artery is cannulated for arterial blood sampling. Table 19.2 summarizes the usefulness of these various sites in providing relevant clinical information. Chapter 52 provides details on the use of these systems for hemodynamic pressure and flow monitoring.

Equipment. Fig. 19.4 shows the basic setup used for an indwelling vascular line; in this case a brachial artery catheter. The catheter connects to a disposable continuous flush device. This device keeps the line open by providing a continuous low rate of flow (2 to 4 mL/h) of intravenous (IV) saline solution through the system.

A heparinized saline flush solution may be used with indwelling vascular catheters. However, results of coagulation studies are affected by the anticoagulant in the heparinized flush solution and unnecessary exposure to heparin may increase the risk for heparin-induced thrombocytopenia.[10] Because arterial pressures are much higher than venous pressures, the IV bag supplying these systems must be pressurized, usually by using a hand bulb pump. A strain-gauge pressure transducer connected to the flush device provides an electrical signal to an amplifier or monitor, which displays the corresponding pressure waveform.

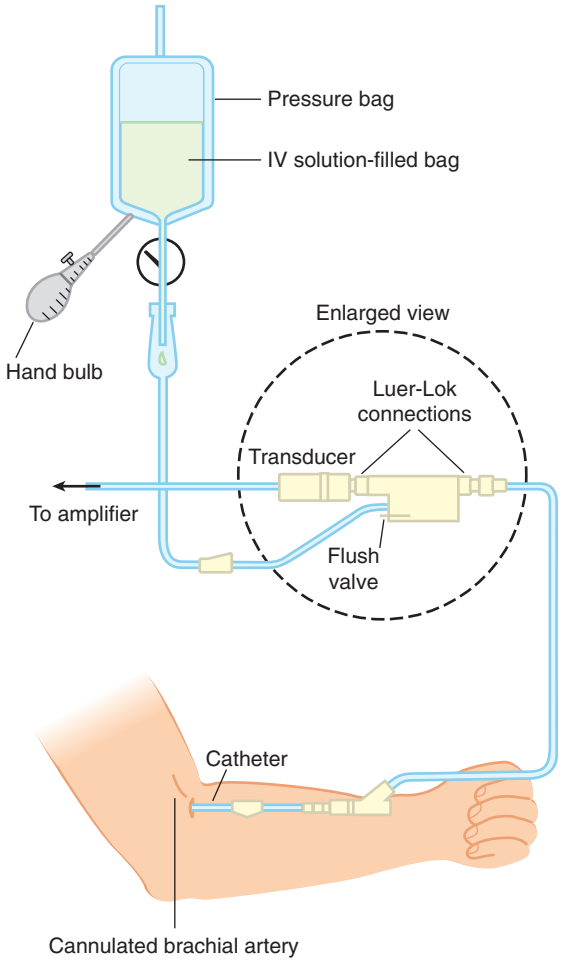

Fig. 19.4 An indwelling vascular line (brachial artery catheter) used to monitor blood pressure and obtain a blood sample.

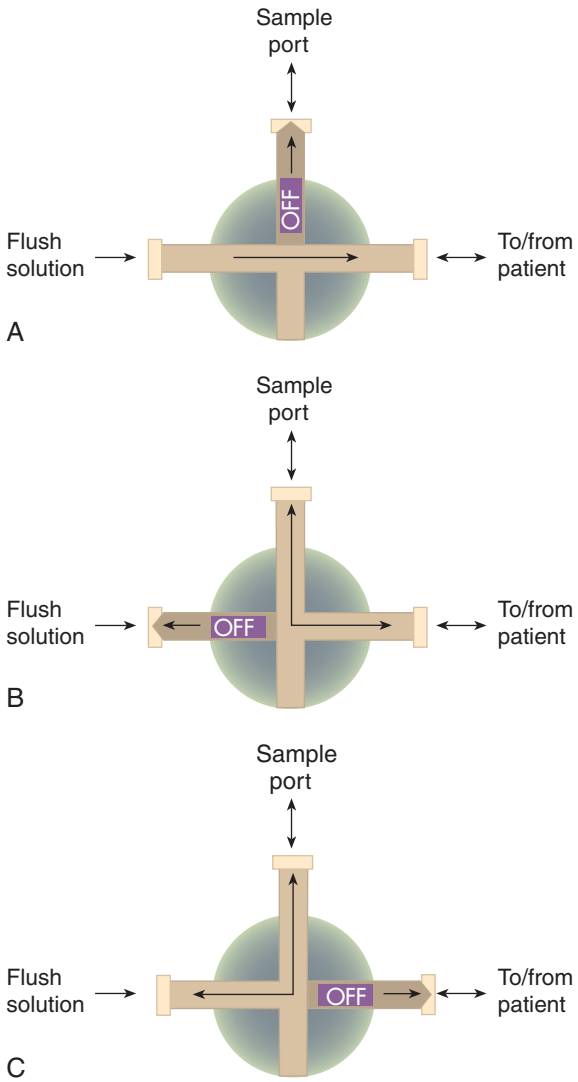

Fig. 19.5 A Three-Way Stopcock in a Vascular Line System Showing the Various Positions Used. (A) Normal operating position, with flush solution going to the patient and the sample port closed. (B) Position to draw a blood sample from the vascular line (closed to flush solution). (C) Position to flush sample port (closed to patient). In any intermediary position, all ports are closed.

Procedure. Access for sampling blood from most intravascular lines is provided by a three-way stopcock (Fig. 19.5). Equipment and supplies are the same as specified for arterial puncture, with the addition of a second "waste" syringe. Box 19.4 outlines the proper procedure for taking an arterial blood sample from a three-way stopcock system.

The procedure is slightly different when obtaining mixed venous blood samples from PA catheters because PA catheters have separate sampling and IV infusion ports. The catheters also have a balloon at the tip which is used to measure pulmonary capillary wedge pressure. The clinician must ensure that the balloon is deflated and withdraw the sample slowly (e.g., approximately 3 mL/min or 1 mL in 20 s). If the clinician fails to deflate the balloon or withdraws the sample too quickly, the venous blood may be "contaminated" with blood from the pulmonary capillaries. The result is always a falsely high O_2 level. In addition, close attention must be paid to the infusion rate through the catheter. Rapid flow of IV fluid can dilute the blood sample and affect O_2 content measurements.

BOX 19.4 Procedure for Sampling Arterial Blood From an Indwelling Catheter

- Check the medical record to affirm order (as per arterial puncture).
- Confirm steady-state conditions (20–30 min after changes).
- Obtain and assemble needed equipment and supplies.
- Wash hands and don barrier protection (e.g., gloves, eyewear).
- Identify the patient using current patient safety standards.
- Explain the procedure to the patient.
- Attach the waste syringe to the stopcock port.
- Position the stopcock so that blood flows into the syringe and the IV bag port is closed.
- Aspirate at least 1–2 mL or 5–6 times the tubing volume of fluid or blood.
- Reposition the stopcock handle to close off all ports.
- Disconnect and properly discard waste syringe.
- Attach new heparinized syringe to the sampling port.
- Position the stopcock so that blood flows into the sample syringe and the IV bag port is closed.
- Fill syringe with 1 mL of blood.
- Reposition the stopcock handle to close off the sampling port and open the IV bag port.
- Disconnect the syringe, expel air bubbles from sample, and cap or plug the syringe.
- Flush the line and stopcock with the IV solution.
- Mix the sample by rolling and inverting the syringe.
- Confirm that the stopcock port is open to the IV bag solution and catheter.
- Confirm undampened pulse pressure waveform on the monitor graphic display.
- Place the sample in a transport container (ice slush) if specimen is not to be analyzed within 10–30 min.
- Dispose of waste materials properly. Note: For most point-of-care (bedside) analyzers, samples should not be chilled and should be run within 1–2 min after being obtained.
- Document the procedure and patient status in the medical record and on the specimen label.

RULE OF THUMB To prevent a falsely elevated O_2 content while sampling blood from a PA catheter, the clinician must deflate the balloon and withdraw the sample slowly (3 mL/min).

Problem solving and troubleshooting. With the exception of venous admixture, the pre-analytic errors that occur when sampling blood from a vascular line are the same as the errors that occur with intermittent puncture, as are the ways to avoid them. For clinicians, the challenge with vascular lines is to maintain their function properly and troubleshoot the many potential problems that can occur. Because these are key components of bedside monitoring skills, they are discussed in the section on hemodynamics in Chapter 52.

Capillary Blood Gases

Capillary blood gas sampling is used as an alternative to direct arterial access in infants and small children. Properly obtained capillary blood from a well-perfused patient can provide clinically

useful estimates of arterial pH and PCO_2 levels. However, capillary PO_2 is of little value in estimating arterial oxygenation. Therefore O_2 saturation by pulse oximetry also must be evaluated when obtaining a capillary blood gas sample. Clinicians must be very cautious when using capillary blood gases to guide clinical decisions. Direct arterial access is still the preferred approach for assessing gas exchange in infants and small children.

Capillary blood values are meaningful only if the sample site is properly warmed. Warming the skin (to approximately 42°C) causes dilation of the underlying blood vessels, which increases capillary flow well above tissue needs. Blood gas values resemble the values in the arterial circulation; this is why a sample obtained from a warmed capillary site is often referred to as **arterialized blood.** It has been shown that capillary blood samples from the earlobe reflect arterial PCO_2 and PO_2 better than samples drawn from a finger stick.[11] The posterior medial or lateral curvature of the heel is the recommended site for capillary puncture specimens in infants younger than 1 month old to avoid nerve and bone damage.

To guide practitioners in providing quality care, the AARC has published Clinical Practice Guideline: Capillary Blood Gas Sampling for Neonatal and Pediatric Patients.[12]

Equipment. Equipment needed for capillary blood sampling includes a lancet, pre-heparinized capillary tubes, small metal stirrer bar (metal flea), magnet, clay or wax sealant or caps, gauze or cotton balls, bandages, ice, gloves, skin antiseptic, warming pads (42°C), sharps container, and labeling materials.

Procedure. Box 19.5 outlines the basic procedure for capillary blood sampling. The most common site for sampling is the heel, specifically the lateral aspect of the plantar surface.

Problem solving and troubleshooting. Sampling of capillary blood is useful for patient management only if the procedure is performed according to an established quality assurance program.

BOX 19.5 Procedure for Capillary Blood Sampling

- Check the medical record (as per arterial puncture).
- Confirm steady-state conditions (20–30 min after changes).
- Obtain and assemble necessary equipment and supplies.
- Wash hands and don barrier protection (e.g., gloves, eyewear).
- Select site (e.g., heel, earlobe, great toe, finger).
- Warm site to 42°C for 10 min using a compress, heat lamp, or commercial hot pack.
- Clean skin with an antiseptic solution.
- Puncture the skin (<2.5 mm) with the lancet.
- Wipe away the first drop of blood and observe free flow (do not squeeze).
- Fill the sample tube from the middle of the blood drop until it is completely full (75–100 mcl).
- Place the metal flea in the capillary tube, and then seal the tube ends.
- Tape sterile cotton or a bandage over the puncture wound.
- Mix the sample by moving the magnet back and forth along the capillary tube.
- Sample should be immediately chilled or analyzed within 10–15 min if left at room temperature.
- Dispose of waste materials properly.
- Document the procedure and patient status in the medical record and on the specimen label.

The most common technical errors in capillary sampling are inadequate warming of the capillary bed and squeezing of the puncture site. Squeezing the puncture site may result in venous and lymphatic contamination of the sample.[12] Both errors invalidate the test results. Other pre-analytic errors are the same as the errors described for arterial puncture. Because of the small sample volume (75 to 100 mcl or 0.075 to 0.1 mL) and collection tube size, the clinician must ensure an adequate sample collection while avoiding air contamination and clotting.

Analyzing

The primary **analytes** or parameters of pH, PCO_2, and PO_2 in a blood sample are measured with a blood gas analyzer. Typically analyzers use these measures to compute several secondary values, such as plasma bicarbonate level, base excess or deficit, and hemoglobin (Hb) saturation. If actual measurement of total Hb saturation (oxyhemoglobin [HbO_2], methemoglobin [metHb], and carboxyhemoglobin [HbCO]) is required, the sample usually must be analyzed separately using hemoximetry, also known as co-oximetry and described in more detail later in this chapter. Some analyzers combine the blood gas and hemoximetry measurements, which may require a larger sample size (usually 100 mcl).

Blood gas analysis and hemoximetry are moderately complex laboratory procedures. Clinicians performing these tests must have documented training and must demonstrate proficiency in performing the procedures, preventive maintenance, troubleshooting, and instrument calibration. In addition, clinicians must be skilled in validating test results using rigorous **quality control** methods that ensure that clinical decisions used to determine patient care are based on accurate information.[13]

To guide practitioners in providing quality care, the AARC has published Clinical Practice Guideline: Blood Gas Analysis and Hemoximetry.[14] Related recommendations have been published by the CLSI.[9]

Instrumentation

Many instrumentation companies manufacture laboratory blood gas analyzers. Although available in a range of designs, these devices typically share the following key components:

- Operator interface (e.g., operating controls, display screen, touch screen keypads, software)
- Measuring chamber incorporating the typical three-electrode system
- Calibrating gas tanks
- Reagent containers (buffers used for calibration, rinse solutions)
- Waste container
- Results display, storage, and transmittal system (e.g., screen, printer, disk storage device, network interface)

Measurement of the three primary parameters—pH, PCO_2, and PO_2—is accomplished using three separate electrodes. To measure PO_2, blood gas analyzers use the Clark polarographic electrode (see Fig. 19.1).

The pH electrode consists of two electrodes or half cells (Fig. 19.6). The measuring half cell contains a silver–silver chloride rod surrounded by a solution of constant pH and enclosed by

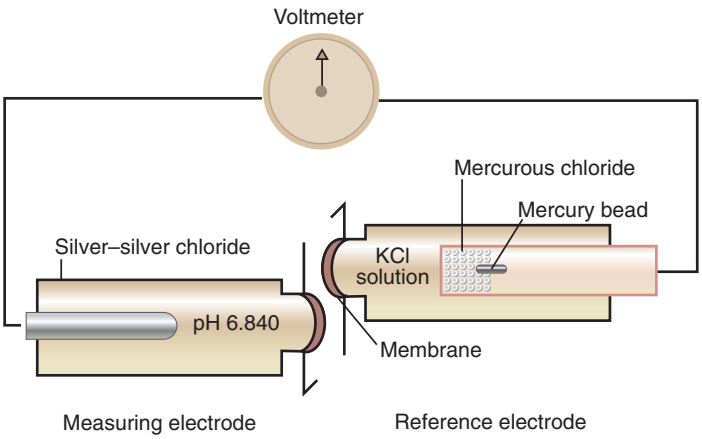

Fig. 19.6 Blood gas analyzer pH electrode system, consisting of both a measurement and a reference electrode. (Modified from Shapiro BA, Peruzzi WT, Kozelowski-Templin R: *Clinical application of blood gases*, ed 5, St Louis, 1994, Mosby.)

BOX 19.6 Basic Procedure for Analyzing a Blood Gas Sample

- Apply standard precautions.
- Confirm that the instrument and its electrodes are operating properly.
- Identify the specimen, and confirm all relevant information provided.
- Note the time at which the sample was obtained (discard sample if >60 min has passed).
- Inspect the sample for obvious signs of pre-analytic errors (e.g., air bubbles, gross dilution, clotting, air exposure).
- Mix the sample (critical for hemoglobin and hematocrit measurements).
- Uncap the syringe and expel and discard a drop or two of blood from the syringe tip.
- Introduce the sample (manually or by automatic aspiration).
- Confirm the readings.
- Remove the syringe and clear the system.
- Dispose of waste materials properly.
- Transmit the results.
- Contact the responsible clinician if the results warrant.

a pH-sensitive glass membrane. As the sample passes this membrane, the difference in hydrogen ion (H^+) concentration on either side of the glass changes the potential of the measuring electrode. The reference half cell (mercury–mercurous chloride) produces a constant potential, regardless of sample pH. The difference in potential between the two electrodes is proportional to the H^+ concentration of the sample, which is displayed on a voltmeter calibrated in pH units.

To measure PCO_2, blood gas analyzers use the Severinghaus electrode, which is essentially a pH electrode exposed to an electrolyte solution in equilibrium with the sample through a CO_2-permeable membrane. As CO_2 diffuses through this membrane into the electrolyte solution, it undergoes the following hydration reaction:

$$CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$$

The greater the partial pressure of CO_2 (PCO_2), the more H^+ that are produced by this reaction and the greater the change in electrolyte solution pH. The measuring electrode detects the pH change as a change in electrical potential, which is proportional to the PCO_2 of the sample.

Procedure

To provide accurate and clinically useful data, blood gas analysis must be performed as follows:

- On a sample free of pre-analytic errors
- With a properly functioning analyzer (validated by quality control procedures)
- Using a procedure that follows the manufacturer's recommendations.

Prior discussion addressed how to avoid pre-analytic errors. The following discussion focuses on blood gas quality control and key elements involved in the analysis procedure.

Box 19.6 outlines the steps commonly used in most established procedures for laboratory blood gas analysis. One should always refer to the manufacturer's literature for the particular steps to use with a specific analyzer.

Rigorous application of the U.S. Centers for Disease Control and Prevention (CDC) standard precautions is essential. In addition, the Occupational Safety and Health Administration (OSHA) requires personnel to wear personal protective equipment when handling all laboratory specimens. Waste fluids are potentially infectious and should be handled as if they were blood samples. In addition, the National Committee for Clinical Laboratory Standards recommends adding a strong disinfectant, such as 2% glutaraldehyde or a 1:4 solution of sodium hypochlorite (bleach) and water, to the waste container of the instrument either during use or before disposal.

Quality Assurance

High-quality patient care depends on consistently accurate blood gas results. Modern laboratory analyzers are often automated, computer-controlled, self-calibrating systems. Likewise, most point-of-care (bedside) analyzer systems are self-calibrating. This sophistication has led to the false assumption that accurate results are "automatic," with clinicians needing only to input the sample properly and record the results. Nothing could be further from the truth. As with all diagnostic laboratory procedures, the accuracy of blood gas testing depends on rigorous quality control.

The CLSI has established guidelines and standards for blood gas analysis and quality assurance. Government regulatory agencies collaborate to update the Clinical Laboratory Improvement Amendments (CLIA) that establish proficiency testing requirements.[15] Although an in-depth review of laboratory quality control is beyond the scope of this text, all clinicians must understand the key elements.[16]

Fig. 19.7 depicts the key components of laboratory quality control. A brief description of each element follows.

Recordkeeping. Meticulous recordkeeping and clearly written, comprehensive policies and procedures are the hallmarks of a quality control program. Applicable laws, professional accreditation requirements, and internal quality standards emphasize this component as the basis for demonstrating and ensuring quality.

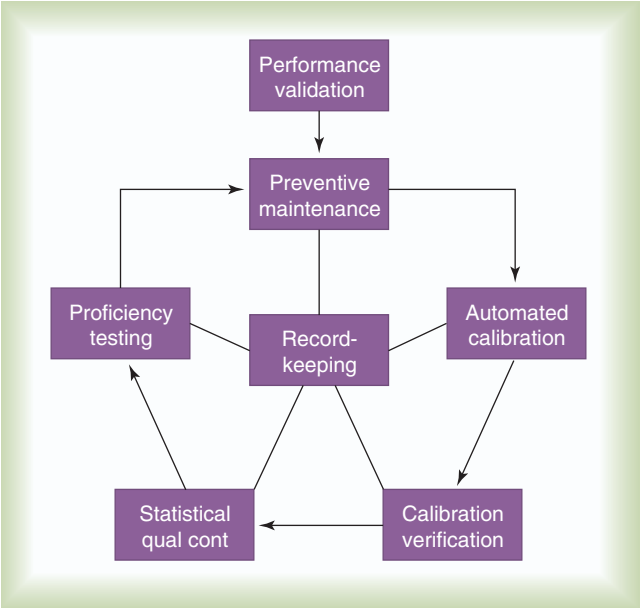

Fig. 19.7 Blood gas analysis quality control program. (Data from Kozelowski-Templin R: Blood gas analyzers. *Respir Care Clin North Am* 1:35–46, 1995.)

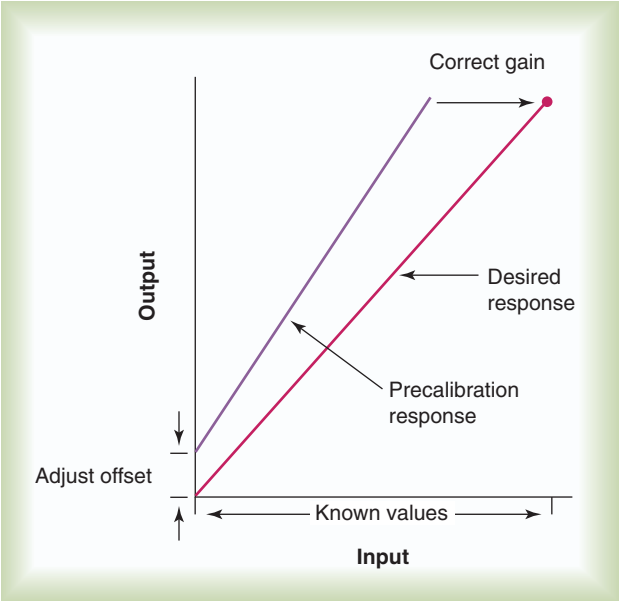

Fig. 19.8 Two-point calibration procedure. (Modified from Chatburn RL: Fundamentals of metrology: evaluation of instrument error and method agreement. In Kacmarek RM, Hess D, Stoller JK, editors: *Monitoring in respiratory care*, St Louis, 1993, Mosby.)

Performance validation. Performance validation is the process of testing a new instrument to confirm accurate measurement. Typically, this process involves using samples with known values to assess both the accuracy (comparing the value from the tested instrument with a known value) and the **precision** (examining the repeatability of results) of the instrument.

Preventive maintenance and function checks. Many blood gas analyzer components (e.g., filters, membranes, electrolyte solution, and single-test and multitest cartridges) have a limited life and deteriorate or fail over time, resulting in faulty analysis. The best way to avoid these problems is to schedule regular preventive maintenance. This should include scheduled parts replacement and routine function tests, as recommended by the manufacturer.

Automated calibration. Calibration is the only fully automated element of blood gas quality control for laboratory analyzers. Blood gas analyzers regularly calibrate themselves by adjusting the output signal of each electrode when exposed to media having known values. In most units, the media used to calibrate the gas electrodes are precision mixtures of O_2 and CO_2. For the pH electrode, standard pH buffer solutions are used. **Calibration media** must meet the requirements set by nationally recognized standards organizations. Users are responsible for ensuring that calibration media are properly stored, and that in-use life and expiration dates are strictly enforced.

Calibration is performed to ensure that the analyzer output is both accurate and linear across the range of measured values. Parameters must be measured with known input values representing at least two points, usually a low and a high value. Fig. 19.8 shows a typical two-point calibration procedure. In this example, the instrument's initial precalibration response indicates that the output readings are consistently higher than the actual input, with this positive bias worsening at higher levels. Calibration is performed first by adjusting the offset (or balance) of the instrument so that the low output equals the low input (in this case zero). Next, the gain (or slope) of the device is adjusted to ensure that the high output equals the high input. When both offset and gain are adjusted against known inputs, the instrument is properly calibrated and can undergo calibration verification with control samples.

Internal statistical quality control. Internal quality control takes calibration verification a step further by applying statistical and rule-based procedures (Westgard rules)[17,18] to help detect, respond to, and correct instrument error. In one common approach, the results of control media analyses are plotted on a graph and compared with statistically derived limits, usually ± 2 standard deviation (SD) ranges (Fig. 19.9). Control results that fall outside these limits indicate analytic error.

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Blood Gas Quality Control

Problem

Using control media for calibration verification, the RT responsible for the quality control of a blood gas analyzer in the intensive care unit (ICU) notes that the "high PCO_2" control readings have increased progressively over the last four quality control analyses from 60 ± 1 mm Hg to 66 ± 1 mm Hg. What is the likely cause and what actions should the RT take?

Solution

The observed problem indicates a trending, or systematic error (bias). If the analyzer solutions and calibrating gases have not been changed during the error period, the likely problem is component failure—probably the PCO_2 electrode. The electrode should be checked, and any faulty components should be replaced.

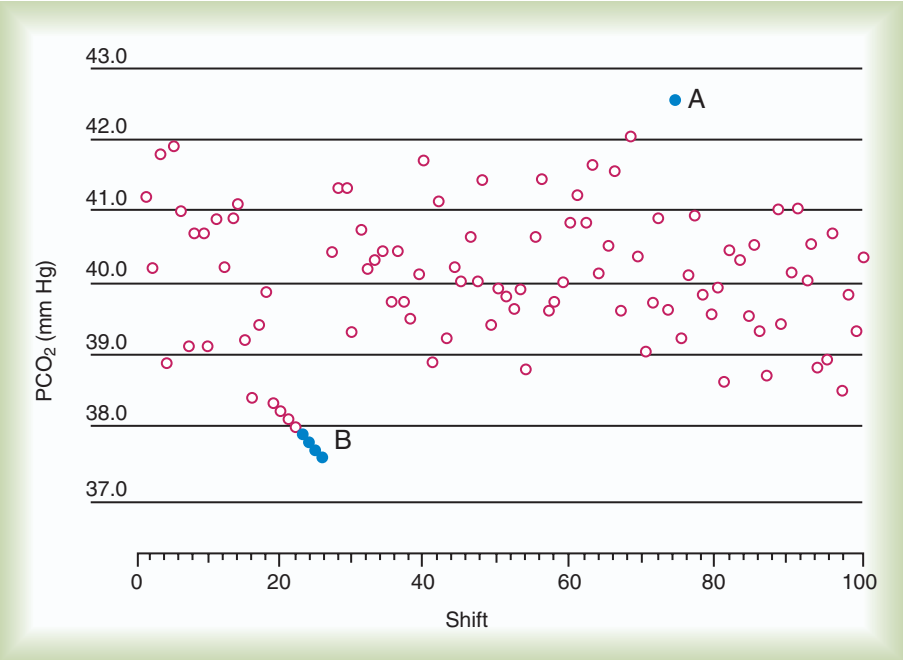

Fig. 19.9 Schematic Representation of a Quality Control Plot for PCO_2. The horizontal axis depicts time. White circles represent values within 2 standard deviations of the mean; blue circles represent values outside 2 standard deviations of the mean. Point *A* represents a random error; point *B* represents systematic errors. (Modified from Shapiro BA, Peruzzi WT, Kozelowski-Templin R: *Clinical application of blood gases*, ed 5, St Louis, 1994, Mosby.)

TABLE 19.3 Correction of Analytic Errors

Error Type	Common Contributing Factors	Common Corrective Actions
Imprecision (random) errors	Statistical probability Sample contamination Sample mishandling	Rerun control Repeat analysis on different instrument
Bias (systematic) errors	Contaminated buffers Incorrect gas concentrations Incorrect procedures Component failure	Perform function check of suspected problem area Repair or replace failed components

There are two categories of analytic error: **random error,** and **systematic error.** Random error is observed when sporadic, out-of-range data points occur (see Fig. 19.9, point *A*). Random errors are errors of precision or, more precisely, imprecision. Conversely, either a trending or an abrupt shift in data points outside the statistical limits (see Fig. 19.9, point *B*) is sometimes observed. This phenomenon is called *systematic error* or sometimes *bias.* Bias plus imprecision equals total instrument error, or *inaccuracy.* Table 19.3 outlines the major factors causing these two types of error and suggests some common corrective actions.

External quality control (proficiency testing). The federal government mandated a rigorous program of external quality control for analytic laboratories. CLIA standards were established in 1988 and updated in 2012. To meet these standards, analytic laboratories must undergo regular proficiency testing designed to evaluate their operating procedures and the competence of their personnel.[19] **Proficiency testing** requires analysis and reporting on externally provided control media with unknown values, usually three times per year, with five samples per test. There are many CLIA-approved proficiency testing providers. A commonly used provider is the College of American Pathologists (CAP) proficiency testing survey. Proficiency testing survey analyses must be performed along with the regular workload by the personnel routinely responsible for testing, following the laboratory's standard testing practices.[20]

Criteria for acceptable performance specify a range around a target value, such as ± 0.04 for pH. A single incident of unsatisfactory performance requires documentation of remedial action. Multiple or recurring incidents of poor performance can result in severe sanctions, including suspension of Medicare and Medicaid reimbursement or the loss of the laboratory's operating license and accreditation.

Remedial action. Remedial action is the ongoing process of applying appropriate measures to correct errors identified through the quality assurance cycle. Analytic errors include calibration and internal quality control failures, actual sample errors, and unsatisfactory proficiency test results. A comprehensive quality assurance program also tries to identify and correct both preanalytic and post-analytic errors, such as clerical misreporting.

Examples of remedial action include procedural changes, staff training and retraining, closer supervision, and more frequent preventive maintenance checks. The remedial action chosen should be appropriate for the identified problem. As with all

Fig. 19.10 *GEM Premier 4000* critical care analyzer for blood gas, electrolyte, metabolite, and integrated co-oximetry testing; the device also performs continuous automated quality assurance. (Courtesy Instrumentation Laboratory, Bedford, MA.)

other components of the process, meticulous documentation is necessary.

Point-of-Care Testing

Point-of-care testing takes blood gas analysis from the specialized laboratory to the patient's bedside. Point-of-care testing reduces turnaround time, which may lead to quicker diagnosis and treatment. Theoretically, cost savings can be achieved by eliminating delays in therapy, and decreasing patient length of stay in the hospital and emergency department (ED). Such systems also often eliminate the need to maintain and staff a blood gas lab as well as associated equipment, resulting in additional savings. For these reasons, point-of-care testing is used increasingly in the hospital and physician office settings.[21, 22]

Instrumentation. Fig. 19.10 shows a typical point-of-care blood gas analyzer (GEM 4000; Instrumentation Laboratory, Bedford, MA). Smaller point-of-care analyzers using similar technology, such as the i-STAT point-of-care system (Abbott Laboratories, Abbott Park, IL), are also gaining popularity. In addition to blood gas analysis, such devices can be used to measure several chemistry and hematology parameters, including serum electrolytes, blood glucose levels, blood urea nitrogen, hematocrit, hemoximetry, lactate, bilirubin, and prothrombin and partial thromboplastin times. It should be noted that unlike conventional analyzers, blood samples for most point-of-care analyzers should *not* be chilled and should be run within 1 to 2 minutes after being obtained.

These devices are portable, and some can perform 900 tests using a disposable cartridge. They typically include a display screen for accessing menu functions and viewing results. Most devices include a simple keypad or touch screen for data and command entry. Analysis occurs using disposable cartridges or inside a chamber in the body of the unit.

Some devices employ single-use sample cartridges that differ according to the array of tests being performed. Each cartridge contains the necessary calibration solution, a sample handling system, a waste chamber, and miniaturized electrochemical or photochemical sensors. The cartridge system requires little to no operator oversight because it is self-calibrating and disposable after a single use. After self-calibration and introduction of the sample into the cartridge, the sensors measure the concentration of the analytes and conduct their output signal through conductive contact pads to the analyzer microprocessor. Test results usually are ready within 60 seconds. Waste management involves simple removal and proper disposal of the analysis cartridge.

Other devices use self-contained multiuse cartridge packs that include all testing components, are maintenance-free, and incorporate automated quality control management systems. Multiuse cartridges are typically replaced every 30 days or when testing components are used up.

Clinical performance. More recent method comparisons indicate that portable point-of-care blood gas analyzers can achieve accuracy and precision levels comparable to those with laboratory-based analyzers.[13,23] Such findings have resulted in the widespread use of these systems.

Clinical laboratories have expanded point-of-care testing solutions to improve operational costs, streamline workflow in the clinical laboratory and critical care setting, and provide blood analysis results more quickly.[24,25] Guidelines for providers who are considering adoption of this new technology have been published in the clinical laboratory literature.[26]

BLOOD GAS MONITORING

A blood gas monitor is a bedside tool (usually dedicated to a single patient) that can provide measurements either continuously or at appropriate intervals without permanently removing blood from the patient. Of the systems which are currently in use, two of the most common ones are transcutaneous blood gas monitoring and tissue O_2 monitoring.

Transcutaneous Blood Gas Monitoring

Transcutaneous blood gas monitoring provides continuous, noninvasive estimates of arterial PO_2 and PCO_2 through a surface skin sensor. Transcutaneous blood gas monitoring has been used for many decades in infants and now is available for use in adults because of advances in technology. As with capillary sampling, the device arterializes the underlying blood by heating the skin. Warming also increases the permeability of the skin to O_2 and CO_2, which enhances diffusion from the capillaries to the sensor, where they are measured as transcutaneous partial pressures ($PtcO_2$ and $PtcCO_2$).

Numerous factors influence the agreement between arterial blood and transcutaneous gas measurements, with O_2 levels being

TABLE 19.4 Ratios Correlating $PtcO_2$ With PaO_2

Age Group	$PtcO_2/PaO_2$ Ratio	Perfusion Status	$PtcO_2/PaO_2$
Premature infants	1.14:1	Stable	0.79:1
Neonates	1.00:1	Moderate shock	0.48:1
Children	0.84:1	Severe shock	0.12:1
Adults	0.79:1		
Older adults	0.68:1		

From Tobin MJ: Respiratory monitoring. *JAMA* 264:244–251, 1990.

affected most. The two most important factors are age and perfusion status (Table 19.4). With regard to perfusion status, PaO_2 and $PtcO_2$ are similar only in patients with normal cardiac output and fluid balance, because accurate transcutaneous measures require adequate skin perfusion. Peripheral vasoconstriction and impaired capillary flow decrease the $PtcO_2$; common causes include low cardiac output, shock, and dehydration. Some clinicians use $PtcO_2$ not to monitor oxygenation as a surrogate for PaO_2, but to assess blood flow changes during procedures such as vascular surgery and resuscitation. Agreement between $PaCO_2$ and $PtcCO_2$ is better because CO_2 is more diffusible than O_2. Heating of the skin increases the metabolic rate at the probe site which causes the $PtcCO_2$ value to be slightly higher than the $PaCO_2$ value. This discrepancy is removed by correction factors embedded in the systems' software. $PaCO_2$ changes of 5 mm Hg can be monitored or "trended" by transcutaneous blood gas analysis. Based on these factors, $PtcCO_2$ monitoring is a reasonable choice when there is a need for continuous, noninvasive analysis of trends in ventilation and $PaCO_2$. In hemodynamically stable infants and children, PaO_2 can be "correlated" with $PtcO_2$, thus decreasing the need for repeated arterial samples. Because pulse oximetry cannot provide accurate estimates of excessive blood O_2, the transcutaneous monitor may be useful for monitoring hyperoxia in neonates. However, prevention of hyperoxia in premature neonates is more often achieved by maintaining pulse oximetry saturation between 85% and 93%, with an upper limit of 95%.[27]

RULE OF THUMB PaO_2 and $PtcO_2$ are only in agreement in patients with adequate skin perfusion. $PaCO_2$ and $PtcCO_2$ are in better agreement because of the diffusability of CO_2, but accuracy is still affected by skin perfusion.

Transcutaneous blood gas monitoring of $PtcCO_2$ can be useful in adult patients during deep sedation and mechanical ventilation in the ED, in the ICU, and during surgery. $PtcCO_2$ is a more accurate reflection of $PaCO_2$ than both $P_{ET}CO_2$ and nasal $ETCO_2$ in intubated and spontaneously breathing adult patients. The use of $PtcCO_2$ in conjunction with pulse oximetry reduces the need for repeated ABG sampling.[28–32]

To guide practitioners in providing high-quality care, the AARC has published Clinical Practice Guideline: Transcutaneous Blood Monitoring of Carbon Dioxide and Oxygen.[33]

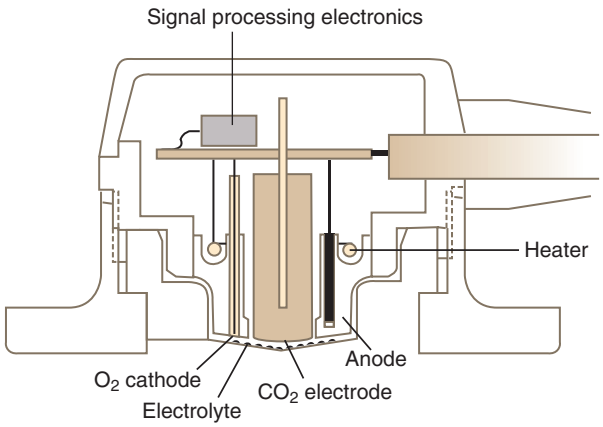

Fig. 19.11 Schematic diagram of transcutaneous O_2-CO_2 sensor. (Modified from Mahutte CK, Michiels TM, Hassell KT, et al: Evaluation of a single transcutaneous PO2-PCO2 sensor in adult patients. *Crit Care Med* 12:1063–1066, 1984.)

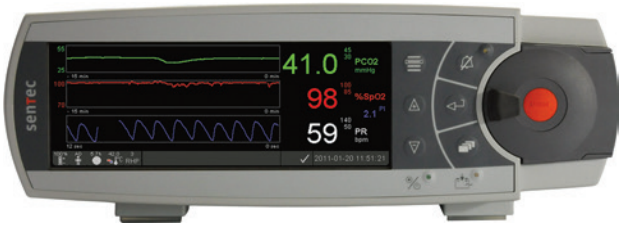

Fig. 19.12 SenTec Digital Monitoring System, combined $PtcCO_2$ and SpO_2 sensor suitable for neonatal, pediatric, and adult patients. (Courtesy SenTec AG, Therwil, Switzerland.)

Instrumentation

Fig. 19.11 shows a simplified diagram of a dual $PtcO_2/PtcCO_2$ transcutaneous blood gas monitor sensor. Included are a heating element and two electrodes, one each for O_2 (Clark type) and CO_2 (Severinghaus type). These electrodes are similar in design to the electrodes found in bench-top analyzers. However, instead of measuring gas tensions in a blood sample, transcutaneous electrodes measure PO_2 and PCO_2 in an electrolyte gel between the sensor and the skin. When properly set up, the response time for these electrodes is 20 to 30 seconds, a bit slower than the response time for pulse oximetry.

Fig. 19.12 shows a transcutaneous monitor with digital signal processing. A Severinghaus-type $PtcCO_2$ electrode and two-wavelength reflectance SpO_2 are combined into a single sensor. The sensor can be applied to the skin surface in neonates and infants, or to the earlobe of pediatric and adult patients for combined noninvasive monitoring of ventilation and oxygenation.

Procedure

Box 19.7 outlines the basic procedure for setting up a transcutaneous blood gas monitor. Once the electrodes are properly set up, the clinician should compare the monitor readings with a concurrent ABG. Consistency between values validates monitor performance under the existing conditions. This validation should be repeated any time the patient's status undergoes a major change. During validation studies of patients with anatomic

BOX 19.7 Procedure for Using a Transcutaneous Monitor

- Place the unit at bedside and provide manufacturer-specified warm-up time.
- Check the membrane to ensure that it is free of bubbles and scratches; change if necessary.
- Select the monitoring site by evaluating perfusion, skin thickness, and absence of bones.
- Prepare the sensor with an adhesive ring and electrolyte gel.
- Set the appropriate probe temperature (per the manufacturer's recommendations).
- Prepare the site by removing excess hair and cleaning the skin.
- Securely attach probe to the patient.
- Schedule site change time (2–12 h, depending on patient/device).
- Set the high and low alarms.
- Monitor and document the results per institutional protocol.
- Change site at appropriate intervals.
- Validate the reading against arterial blood gas values.

From Koff PB, Hess D: Transcutaneous oxygen and carbon dioxide measurements. In: Kacmarek RM, Hess D, Stoller JK, editors: *Monitoring in respiratory care*, St Louis, 1993, Mosby.

MINI CLINI

Selecting a Monitoring System

Problem

With a concern about retinopathy of prematurity, the RT sets up a noninvasive system to monitor a preterm infant for hyperoxia. What type of system should the RT choose and why?

Solution

Since the infant should be monitored for hyperoxia, a system that provides continuous data would be the best choice. Because hyperoxia is best assessed using PO_2 (as opposed to Hb saturation), the RT needs to use a PO_2 electrode system. A transcutaneous PO_2 electrode system would provide the needed measurement noninvasively.

shunts, the electrode site and arterial sampling site should be on the same "side" of the shunt.

Problem Solving and Troubleshooting

Monitoring requires setup and calibration. In terms of technical limitations, transcutaneous blood gas sensors must be calibrated and maintained using methods similar to those described for bench-top analyzers. Improper calibration yields erroneous patient information. Meticulous care of the sensor membranes is also essential for proper maintenance.

Because the sensor is heated, clinicians must take care to avoid thermal injury to the patient's skin. Thermal injury can be avoided by careful monitoring of sensor temperature (the safe upper limit is approximately 42°C) and regularly rotating the sensor site. Proper sensor-electrolyte contact is essential, as is proper application to the skin surface.

When arterial and transcutaneous blood gas values are inconsistent with each other or with the clinical status of the patient, the clinician should explore possible causes before reporting any results. Often, discrepancies can be reduced by switching the monitoring site or recalibrating the instrument. If these steps fail to resolve the inconsistencies, the clinician should recommend an alternative method for assessing gas exchange, such as pulse oximetry or more frequent ABG analysis.

Tissue Oxygen

Tissue O_2 (PtO_2) can be measured by probes inserted directly into organs, tissue, and body fluids. Ease of probe placement and the sensitivity of PtO_2 as an indicator of tissue perfusion make tissue O_2 monitoring attractive for clinical research applications. Clinical indications for measuring PtO_2 include monitoring brain tissue O_2 as an early sign of ischemia, assessing brain blood flow autoregulation, and monitoring the adequacy of brain perfusion in patients with traumatic brain injury. Normal brain PtO_2 values are between 20 and 35 mm Hg. In patients with traumatic brain injury, the critical threshold for ischemic brain damage and poor outcome is suspected to be at a brain PtO_2 of approximately 10 to 15 mm Hg.[34]

Instrumentation

Both electrochemical and **optical luminescent tissue** O_2 probes have been developed for clinical use and research applications. Fig. 19.13 shows a Clarke-type polarographic sensor and its insertion into brain tissue through an intracranial bolt. In the optical luminescent probe, O_2 molecules diffuse into a silicone matrix and change the color of a ruthenium dye. A pulse of light is then sent down a fiber optic filament. The light changes frequency as it passes through the dye. This change in frequency is then converted into a partial pressure of oxygen. **Optode** probes capable of monitoring tissue pH and CO_2 have also been developed.[35]

OXIMETRY

Oximetry is the measurement of blood Hb saturations using **spectrophotometry.** According to the principles of spectrophotometry, every substance has a unique pattern of light absorption, similar to a fingerprint. The pattern of light absorption of a substance varies predictably with the amount present; this is known as the *Lambert-Beer law*. By measuring the light absorbed and transmitted by a substance, scientists can identify its presence and determine its concentration.

The particular pattern of light absorption exhibited by a substance at different wavelengths is called its *absorption spectrum*. As shown in Fig. 19.14, each form of Hb (i.e., reduced Hb, HbO_2, HbCO, metHb) has its own unique pattern. By comparing the amount of light transmitted through (or reflected from) a blood sample at two or more specific wavelengths, the relative concentrations of Hb forms can be measured. For example, oxygenated Hb absorbs less red light (600 to 750 nm) and more infrared light (850 to 1000 nm) than deoxygenated or reduced Hb. Comparing a blood sample's light absorption with red and infrared light yields the $\%HbO_2$ and %Hb. When measuring additional forms of Hb, more than two wavelengths of light must be used.

Several types of oximetry are used in clinical practice, including hemoximetry (also called *co-oximetry*), pulse oximetry, venous oximetry, and tissue oximetry. Hemoximetry is a laboratory analytic procedure requiring invasive sampling of arterial blood. Pulse oximetry is a noninvasive monitoring technique performed

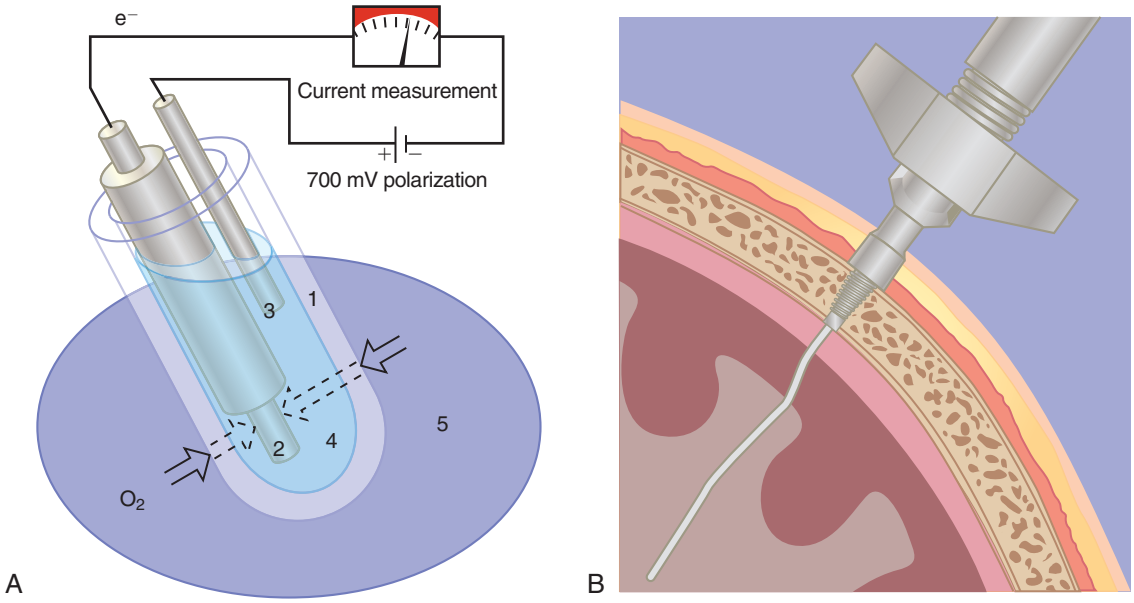

Fig. 19.13 (A) Schematic of Clark-type polarographic tissue oxygen probe. Polyethylene membrane (1), gold cathode (2), silver anode (3), electrolyte solution (4), cerebral tissue (5). (B) Insertion into cerebral tissue. (From Mulvey JM, Dorsch NW, Mudaliar Y, et al: Multimodality monitoring in severe traumatic brain injury: the role of brain tissue oxygenation monitoring. *Neurocrit Care* 1:391–402, 2004.)

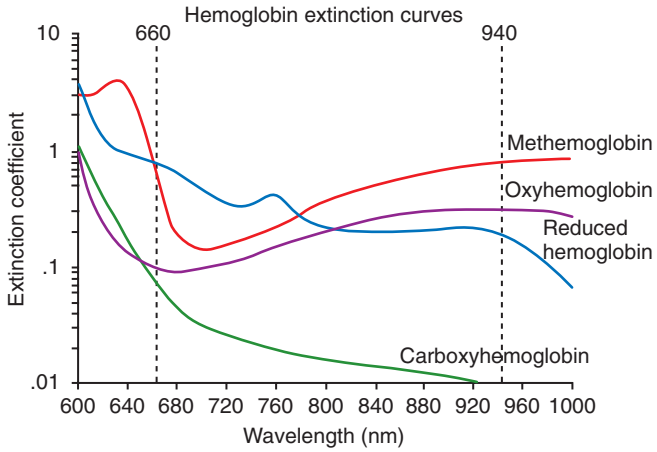

Fig. 19.14 Principle of Spectrophotometric Oximetry. Different forms of hemoglobin (e.g., reduced Hb, HbO_2, HbCO, metHb) absorb light differently at different wavelengths. By comparing points of equal absorbance (isobestic points) between pairs of Hb forms (e.g., Hb vs HbO_2, Hb vs HbCO), the relative proportion of each can be measured.

at the bedside. Venous oximetry requires invasive monitoring through a fiberoptic catheter placed in the vena cava or PA. Tissue oximetry is a noninvasive method of measuring the saturation of Hb at the tissue level.

Methemoglobin

Oxidation of ferrous iron to ferric iron within the Hb molecule results in metHb. The ferric iron causes an allosteric change in the heme portion of Hb. This change in the Hb molecule causes an increase in its O_2 affinity and a functional decrease in its O_2 binding capability. As a result, the O_2 dissociation curve is shifted to the left, causing impaired O_2 delivery to the tissues. The net effect is that patients with acutely increased concentrations of metHb have a functional anemia (i.e., the amount of functional Hb is less than the measured level of total Hb). Methemoglobinemia can cause dyspnea, cyanosis, and even death.

Several congenital forms of methemoglobinemia have been found, but by far the most common cause is an acute drug reaction. Many oxidizing agents have been identified. Local anesthetics, such as benzocaine, lidocaine, and prilocaine, have been correlated with methemoglobinemia.[36]

Carboxyhemoglobin

Carbon monoxide (CO) is a colorless, odorless, and tasteless gas produced by the incomplete combustion of carbon-based matter. It diffuses rapidly across the pulmonary capillary membrane and binds to the iron moiety of heme with approximately 200 to 250 times the affinity of O_2. The degree of carboxyhemoglobinemia is a function of the relative amounts of CO and O_2 in the environment and the duration of exposure.

Nonsmokers may have up to 2% HbCO at baseline; smokers may have levels up to 9%. Rarely the HbCO levels of heavy smokers have been reported above 10%.

The binding of CO competitively prevents O_2 from binding to the hemoglobin. This results in functional anemia because the arterial blood O_2 content is reduced. Furthermore, HbCO results in a leftward shift of the HbO_2 dissociation curve. This causes impairment in tissue O_2 delivery. Even though the CO avidly binds to the Hb, it is reversible.[37]

Hemoximetry

Hemoximetry, also known as co-oximetry, is a method of measuring the O_2 carrying state of Hb in the blood. It uses the unique light absorbing characteristics described above to measure Hb

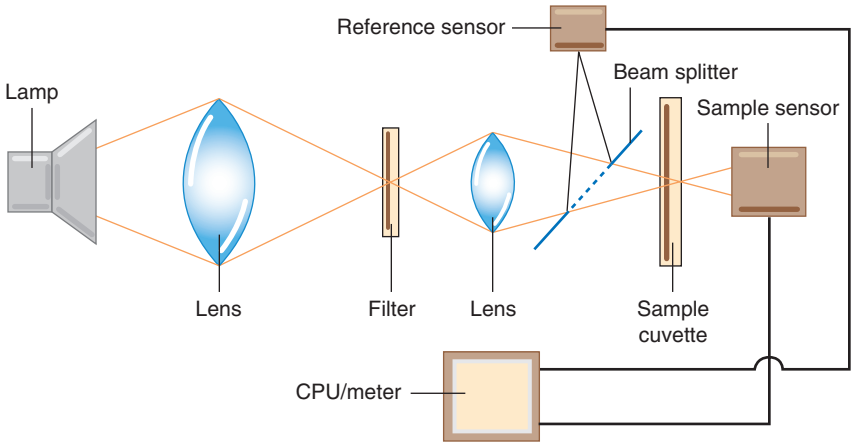

Fig. 19.15 Simplified diagram showing key components of a laboratory hemoximeter. *CPU*, Central processing unit. (Modified from Lane EE: *Clinical arterial blood gas analysis*, St Louis, 1987, Mosby.)

that is carrying O_2, as well as abnormal or dyshemoglobins, such as HbCO and metHb which diminish the O_2 carrying capacity of blood.

Instrumentation

Fig. 19.15 is a simplified diagram showing the key components of a laboratory hemoximeter. Light generated by a thallium cathode lamp passes through a series of lenses and filters, yielding the specific wavelengths needed for analysis. A beam splitter divides the light into two portions, directing one through a reference solution and the other through a sample chamber, or **cuvette.** Photodetection sensors measure the amount of light transmitted through these two sources. By comparing the difference in light transmission through the reference and sample solutions, a microprocessor computes the relative amount of Hb present, with its output sent to the calibrated device meter or display. Because a laboratory hemoximeter uses four or more different wavelengths of light, it can simultaneously compute the relative concentrations of multiple forms of Hb, such as reduced Hb, HbO_2, HbCO, and metHb.

Procedure and Quality Assurance

Similar to modern blood gas analyzers, laboratory hemoximeters are highly automated and simple to use. Some devices now combine both technologies into a single instrument. However, the caveats remain the same. Accurate and clinically useful hemoximetry results can be expected only if an error-free sample is assessed on a calibrated analyzer, using the manufacturer's protocol.

Although variations exist among devices, the basic procedure is similar. First, the blood is introduced into the sampling port of the analyzer, usually by either aspiration or injection. Required sample sizes vary from approximately 200 mcl to 40 mcl (microanalysis). Once introduced, erythrocyte Hb is released into the solution by hemolysis. After hemolysis, the sample is transported to the cuvette for analysis. On completion of the analysis, the sampling system (cuvette and tubing) is flushed and cleaned. As with blood gas analysis, operators must follow CDC standard precautions and ensure proper disposal of syringes and waste materials.

TABLE 19.5 Problems Causing Measurement Errors With Hemoximeters

Problem	Potential Error
Incomplete hemolysis	Falsely low total Hb, HbO_2
Sickle cell anemia (caused by incomplete hemolysis)	Falsely low HbO_2
Presence of vascular dyes (e.g., methylene blue)	Falsely low total Hb, HbO_2
High lipid levels (e.g., from parenteral nutrition)	Falsely low total Hb, HbO_2
Presence of high levels of fetal hemoglobin	Falsely high HbCO
Elevated bilirubin levels (>20 mg/dL)	Falsely high total Hb, HbO_2, metHb
Dirty cuvette chamber	Falsely high total Hb, HbO_2

Quality assurance procedures for hemoximetry are essentially the same as the procedures used for blood gas analysis, differing only with regard to the control materials used. In addition, careful cleaning and maintenance of the cuvette chamber is essential because clouding of its walls decreases absorbance and can cause falsely elevated values.[38]

Problem Solving and Troubleshooting

A major assumption underlying hemoximetry is that the measured changes in light absorbance result only from variations in the relative concentrations of various Hbs. In practice, this assumption does not always hold true. Table 19.5 outlines some of the potential problems and resulting errors that can occur with hemoximetry.

Pulse Oximetry

Pulse oximeters are portable noninvasive monitors that estimate arterial blood HbO_2 saturation levels. So as not to confuse these estimates with actual SaO_2 measures obtained by hemoximetry, the abbreviation SpO_2 is used to refer to pulse oximetry readings. No other device in recent medical history has been so widely and quickly adopted into clinical practice. However, its rapid embracement has been accompanied by equally sweeping misconceptions regarding the appropriate applications and technologic

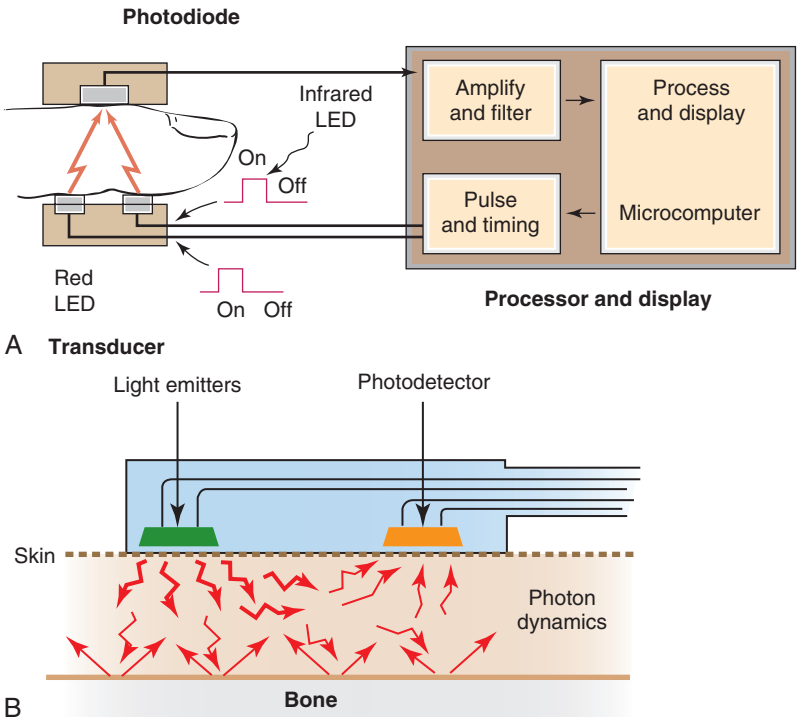

Fig. 19.16 (A) Schematic block diagram of a transmission pulse oximeter sensor and monitor. (B) Schematic of a reflectance pulse oximeter sensor. *LED,* Light-emitting diode. (A, Modified from Gardner R: Pulse oximetry: is it monitoring's "silver bullet"? *J Cardiovasc Nurs* 1:79–83, 1987; B, From Keogh BF, Kopotic RJ: Recent findings in the use of reflectance oximetry: a critical review. *Curr Opin Anaesthesiol* 18:649–654, 2005.)

limitations. Moreover, the true impact of pulse oximetry on patient outcomes is unknown.[39] To guide practitioners in providing quality care, the AARC has published Clinical Practice Guideline: Pulse Oximetry.[40]

Instrumentation

The pulse oximeter combines the principle of spectrophotometry, as used by hemoximeters, with **photoplethysmography.** Photoplethysmography uses light to detect the tiny volume changes that occur in living tissue during pulsatile blood flow. However, compared with a hemoximeter, the pulse oximeter usually uses only two wavelengths of light, one red (approximately 660 nm) and one infrared (approximately 940 nm) (see Fig. 19.14). In addition, rather than measuring light transmission through a blood sample in a glass cuvette, the pulse oximeter measures transmission through living tissue, such as a finger or earlobe, or reflectance through the skin surface. In addition, given significant reductions in cost, size, and relative accuracy, there is a growing popularity of small stand-alone, finger-probe/oximeter combination units.

Fig. 19.16A provides a schematic block diagram of a pulse oximeter consisting of a transmission sensor, processor, and display unit. The sensor has two sides. From one side, separate red and infrared light-emitting diodes (LEDs) alternately transmit light through the tissue. The transmitted light intensity is measured by a photodetector on the other side. The resulting output signal is filtered and amplified by instrument electronics, with processing and display functions controlled by a microprocessor.

Fig. 19.16B shows a schematic of a reflectance pulse oximeter sensor. This type of sensor has only one side, which contains both the LED light sources and the photodetector. The principle of operation is identical to a transmission sensor except that the sensor is placed on the skin surface, usually the forehead, and reflected light from the tissue back to the sensor is used to calculate SpO_2.

Fig. 19.17 shows a typical output signal generated by the photodetector (the pulsatile component can be observed on instruments that have a plethysmographic display). A baseline component represents the stable absorbance of the tissue bed, which mainly represents venous and capillary blood. At the top is the pulsatile component, caused by intermittent arterial flow through the tissues. By comparing light absorbance during the pulsatile phase with the baseline value at each wavelength, a pulse-added measure is obtained. Arterial HbO_2 saturation is computed as the ratio of the pulse-added absorbance at the two different wavelengths.

The accuracy of pulse oximetry readings is usually within ±2% to 4% of invasive hemoximetry readings.[39] Generally the lower the actual SaO_2, the less accurate and reliable is the SpO_2 measurement. Most clinicians consider pulse oximeter readings unreliable at saturations less than 80%. Instrument response times vary by manufacturer, sensor location, and the patient's hemodynamic status from 10 to 60 seconds or longer. Other factors which can affect their accuracy include poor peripheral circulation, motion artifact, ambient light, nail polish, and dark skin pigmentation.

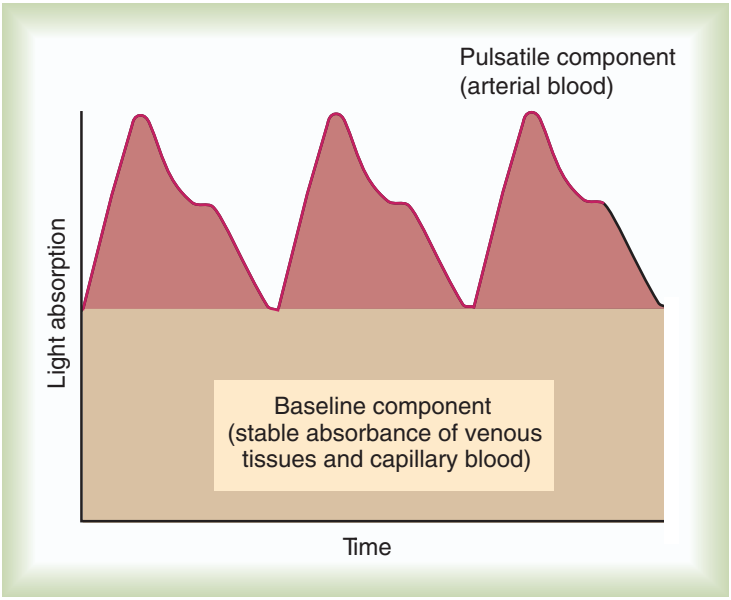

Fig. 19.17 Output Signal Generated by Pulse Oximeter. Saturation is based on the ratio of light absorption between two or more wavelengths during pulsatile and baseline phases.

BOX 19.8 Key Points for Performing Pulse Oximetry

- Always follow manufacturer's recommended protocol.
- Never mix sensors among different devices.
- Ensure the sensor is the correct size for the site chosen.
- Ensure the sensor is properly applied (not too tight or loose).
- Before taking or recording a reading, confirm the adequacy and accuracy of the pulse signal.
- When doing spot checks, allow sufficient response time before taking a reading because response times vary greatly.
- For continuous monitoring of adults and children, set the low alarm at 88% to 92%.
- Whenever possible, validate the initial SpO_2 reading against the actual SaO_2.
- Clean multiuse sensors and disinfect the instrument housing between patients.
- Inspect the sensor site frequently throughout the duration of continuous monitoring and change it as needed.
- Never act on SpO_2 readings alone.
- Pulse oximetry is unreliable at saturations below 80%.
- Accuracy is affected by poor peripheral circulation, form of Hb, dark skin pigmentation, nail polish, motion, and ambient light.
- Avoid using pulse oximetry to monitor hyperoxia in neonates.

Procedure. The actual procedure used to measure SpO_2 varies according to the device used, sensor site selected, and whether a spot check or continuous monitoring is required. Box 19.8 lists key points to be considered when performing pulse oximetry.

Given the limits of this technology, very careful documentation is important. Specifically, all SpO_2 results should be recorded in the patient's medical record. The following details should be documented:

- Date, time of measurement, and reading
- Patient's position, activity level, and location during monitoring
- FiO_2 or O_2 flow and O_2 delivery device
- Probe type and placement site
- Model of device (if more than one device is available for use)
- Results of simultaneously obtained ABGs and hemoximetry (if available)
- Stability of readings (length of observation time and range of fluctuation)
- Patient's clinical appearance, including assessment of perfusion at the measuring site (e.g., cyanosis, skin temperature)
- Agreement between oximeter and actual patient heart rate, as determined by palpation or electrocardiogram

RULE OF THUMB When using a pulse oximeter to detect hypoxemia in an otherwise healthy adult, the low alarm is usually set at 88%. Generally this level ensures that the alarm is activated before true arterial saturation drops below that critical value. It also reduces false positive alarms without negatively affecting patients. The low alarm is patient dependent, and it should be set based on the patients' underlying status.

Problem Solving and Troubleshooting

Problems with pulse oximetry fall into two categories: inherent technology problems, and problems associated with clinical interpretation of the data. Dozens of technical factors may affect the readings, limit the precision, or alter the performance of pulse oximeters. Table 19.6 summarizes the most important of these factors and the types of errors they cause.

RULE OF THUMB To quickly test the functioning of a pulse oximeter, the clinician can place the probe on his or her own finger.

Motion artifact probably is the most common source of error and false alarms. Although new technologies promise to reduce motion artifact, relocation of the sensor to the earlobe, toe, nose, or forehead can minimize the problem.

TABLE 19.6 Factors Affecting Accuracy or Precision of Pulse Oximeters

Factor	Potential Error
Presence of HbCO	Falsely high $\%HbO_2$
Presence of high levels of metHb	Falsely low $\%HbO_2$ if SaO_2 >85% Falsely high $\%HbO_2$ if SaO_2 <85%
Presence of fetal hemoglobin	No effect
Anemia (very low hematocrit, <10%)	Falsely low CaO_2 and high $\%HbO_2$
Vascular dyes (e.g., methylene blue)	Falsely low $\%HbO_2$
Elevated bilirubin levels	No effect
Dark skin pigmentation	Falsely high $\%HbO_2$ (3%–5%)
Nail polish (especially black)	Falsely low $\%HbO_2$
Ambient light	Varies (e.g., falsely high $\%HbO_2$ in sunlight); also may cause falsely high pulse reading
Poor perfusion (vasoconstriction)	Inadequate signal; unpredictable results
Motion artifact	Unpredictable, spurious readings
Electrocautery	Falsely low HbO_2
Magnetic resonance imaging	Falsely low HbO_2

MINI CLINI

Troubleshooting Pulse Oximetry

Problem

The RT draws an ABG sample from a conscious and alert patient in a postsurgical unit who also is being monitored with a pulse oximeter, which reads 80% saturation. The patient is breathing 35% O_2 through an air-entrainment mask. The patient's extremities are pink and warm. After running the blood sample through a calibrated ABG analyzer with a hemoximeter, the RT obtains the following values:

PaO_2 = 90 mm Hg
Hb = 12 g/dL
SaO_2 = 98%
metHb = 0.5%
HbCO = 1%

Explain the difference between the pulse oximeter and hemoximeter readings of this patient's blood O_2 levels and what action the RT should take.

Solution

Given that a calibrated hemoximeter provides more accurate results than a pulse oximeter and that the patient exhibits no signs of hypoxemia, it is likely that the pulse oximeter reading is falsely low. Because the total Hb and metHb levels are not grossly abnormal, potential problems include motion artifact, poor sensor placement, and device malfunction. The oximeter and sensor should be rechecked, and, if found to be malfunctioning, they should be replaced.

RULE OF THUMB To compensate for a falsely elevated O_2 saturation reading in dark skinned individuals, set the oximeter low alarm 3% to 5% higher.

Early studies on the effects of nail polish found significant lower SpO_2 readings with nail polish. More recent studies have found either no effect or small differences that are considered clinically irrelevant; this may be due to improvements in LED light sources.[41,42] The effect of nail polish may be minimized by using a different site or by rotating the sensor so that the light path does not cross the fingernails.

If ambient light interference is creating problems, the sensor can be loosely covered with an opaque towel or cloth. Problems that occur during procedures producing electromagnetic interference (e.g., electrocautery, magnetic resonance imaging) need only be recognized. Careful monitoring of the patient during episodes of false low alarms is essential.

RULE OF THUMB For a properly functioning pulse oximeter that is giving erroneous readings, most potential sources of error are resolvable. Simple solutions include repositioning the probe, alternating the probe site, or removing the ambient light source or nail polish.

Regarding problems with interpreting pulse oximetry data, the most important issue is to treat the patient, not the monitor. The clinician should never interpret or act on monitoring data without first assessing the patient and verifying proper sensor placement and signal quality. A related problem is simple confusion over the relationship between HbO_2 saturation and PO_2. Many clinicians rely solely on PaO_2 readings to assess oxygenation and do not understand HbO_2 saturation. To these clinicians, an SpO_2 reading of 80% might be confused easily with PaO_2 of 80 mm Hg. The latter measure of partial pressure is normal, whereas a saturation of 80% indicates moderate to severe hypoxemia, equivalent to PaO_2 of approximately 45 mm Hg.

A similar interpretation error (PaO_2 vs SpO_2) occurs because of the limited accuracy of most pulse oximeters. It is common practice to set the low alarm of a monitoring oximeter to 88%. In theory, this practice makes sense because an SaO_2 reading of 88% normally corresponds to a PaO_2 reading of approximately 55 mm Hg (the lower limit of clinically acceptable oxygenation). However, with the accuracy of some oximeters being only ± 4%, an SpO_2 reading of 88% could mean an actual SaO_2 reading of 84%, corresponding to a PaO_2 level of 50 mm Hg or less.

At the high end, oximetry data can be even less meaningful. Because of the characteristics of the HbO_2 dissociation curve (see Chapter 12), a patient with an SpO_2 reading of 100% could represent a PaO_2 level between 100 and 600 mm Hg. Therefore pulse oximetry should not be used for monitoring hyperoxia (as is important for all patients but especially neonates).

RULE OF THUMB If the pulse oximeter is reading a critically low value (<87%) but the patient appears in no distress, then it is likely that there is an erroneous pulse oximeter reading. In such situations, it is best to further assess the patient's clinical status and troubleshoot the pulse oximetry equipment setup. If further examination suggests that the patient is stable, it is likely that the problem is related to the equipment; the setup, including the sensor, should be checked.

It is also important to remember that a pulse oximeter does not measure $PaCO_2$. A patient breathing an elevated FiO_2 can have normal SpO_2 readings despite severe hypercarbia. ABG analysis is needed when acute ventilatory failure may be present.

SpO_2 can read falsely high when carbon monoxide poisoning or methemoglobinemia is present. This false reading is due to the fact that the two-wavelength pulse oximeter measures only saturation of the Hb and not specifically saturation with O_2. HbCO and metHb cannot be distinguished from HbO_2 with a

MINI CLINI

Limitations of Pulse Oximetry

Problem

A 40-year-old woman came to the hospital for an elective upper endoscopy. Her throat was sprayed with benzocaine prior to the case. She tolerated the procedure well but shortly after the case she complained of shortness of breath. She was noted to be cyanotic. The RT placed her on a pulse oximeter and treated her with 100% O_2 via a mask. Her O_2 saturation was 85% unresponsive to O_2. Blood was drawn for an ABG. The blood was noted to be chocolate brown in color. Running the blood sample through a calibrated ABG analyzer without a hemoximeter produced the following results:

pH = 7.30

PaO_2 = 104 mm Hg

$PaCO_2$ = 17 mm Hg

SaO_2 = 98%

What other information is needed to diagnose the patients' problem?

Solution

The patient shows signs of methemoglobinemia. The O_2 saturation levels measured with pulse oximetry are substantially lower than ABG O_2 saturation levels. This saturation gap should alert the practitioner that an alternative, nonfunctional species of hemoglobin is present. A sample of blood should be run through a hemoximeter to check the metHb level to confirm the diagnosis.

pulse oximeter. A falsely high SpO_2 reading occurs when significant HbCO is present. When metHb is elevated, the SpO_2 reading is higher than the actual measured SaO_2. As metHb level increases, SpO_2 decreases and plateaus at approximately 85% when the metHb level reaches 30%.[36]

To address these limitations, modified pulse oximeters known as **pulse co-oximeters** use seven or more wavelengths of light to noninvasively distinguish among and measure reduced Hb, HbO_2, HbCO, and metHb. Some studies show that the accuracy of these measurements does not equal that of conventional hemoximetry (co-oximetry). However, **pulse co-oximetry** appears useful for trend monitoring in some clinical situations (e.g., monitoring therapy for acute CO poisoning in the ED).[43]

As with transcutaneous monitoring, if pulse oximetry and blood gas values are inconsistent with each other or with the clinical status of the patient, the RT should explore possible causes before reporting, interpreting, or acting on results. Often, discrepancies can be reduced by switching sites or replacing the sensor probe. If these steps fail to resolve the inconsistencies, the RT should document the problem and recommend obtaining an ABG measurement with hemoximetry, if indicated.

Venous Oximetry

Continuous central venous (vena cava) and mixed venous (PA) O_2 saturation monitoring ($S\bar{v}O_2$) is performed to assess the balance between O_2 delivery and use as an indirect index of global tissue oxygenation and perfusion. Decreased $S\bar{v}O_2$ is indicative of cardiac failure in patients with myocardial infarction and after cardiovascular surgery, as well as in patients with severe cardiopulmonary disease, including those in septic or cardiogenic shock.[44] The rationale for the low mixed venous saturation in shock is that the reduced cardiac output associated with shock leads to low perfusion and higher O_2 unloading at the tissues, causing venous blood to have less O_2. To monitor this phenomenon, regional and organ-specific $S\bar{v}O_2$ monitoring may be performed via catheters placed in the coronary sinus, hepatic vein, or cranial jugular venous bulb for cerebral perfusion monitoring. Normal values for $S\bar{v}O_2$ range from 60% to 80%.

Instrumentation

Fig. 19.18 shows a diagram of an $S\bar{v}O_2$ monitoring system. Venous oximetry is measured through a fiberoptic catheter by reflectance spectrophotometry. Two or three wavelengths of light are emitted from LEDs through fiberoptic filaments into the venous blood. Some of this light is reflected back and received through another fiberoptic channel, which is read by a photodetector. The amount of light that is absorbed by the venous blood and reflected back is determined by the amount of O_2 that is saturated or bound to Hb. This information is processed by the monitor, updated, and displayed as $S\bar{v}O_2$.

Clinical Usefulness

Continuous $S\bar{v}O_2$ can be monitored through an $S\bar{v}O_2$-equipped PA catheter or venous catheter. Mixed venous oximetry from the PA is an indication of global O_2 use. Central venous oximetry is nearly interchangeable with mixed venous oximetry. Both correlate with mixed venous saturation measured by hemoximetry with an accuracy of ±3% to 5%. Accuracy of venous oximetry monitoring depends on several factors, including the frequency of calibration with measured $S\bar{v}O_2$ and Hb, the position of the catheter free floating in the vein, the absence of wall artifact, damage to the fiberoptic filaments, and clot formation at the catheter tip.[44]

Tissue Oximetry

Tissue level O_2 saturation (StO_2) assesses the adequacy of circulation and O_2 delivery. Low StO_2 can be used for early detection of tissue hypoperfusion in patients with traumatic injuries. Unlike pulse oximetry, StO_2 can be used to measure perfusion in a pulseless or hypothermic patient.[45] Cerebral StO_2 monitoring also can be used to monitor brain oxygenation and detect cerebral ischemia during neurosurgical or cardiovascular procedures.[46]

Instrumentation

Tissue oximetry is essentially a reflectance oximeter that uses near-infrared spectroscopy to measure StO_2. It allows continuous noninvasive monitoring. Multi-wavelengths of light in the near-infrared spectrum transilluminate muscle tissue in the hand or brain through the forehead. Because biologic tissue, including the skull, is relatively transparent in the near-infrared range, the absorbance and reflectance characteristics of HbO_2 and reduced Hb concentrations in the tissue being monitored is used to calculate StO_2. Monitoring of StO_2 is used primarily for research purposes but it is starting to see more use in clinical practice, especially to monitor skin flaps.

CAPNOMETRY AND CAPNOGRAPHY

Capnometry is the measurement of CO_2 in respiratory gases. A capnometer is the device that measures CO_2. **Capnography**

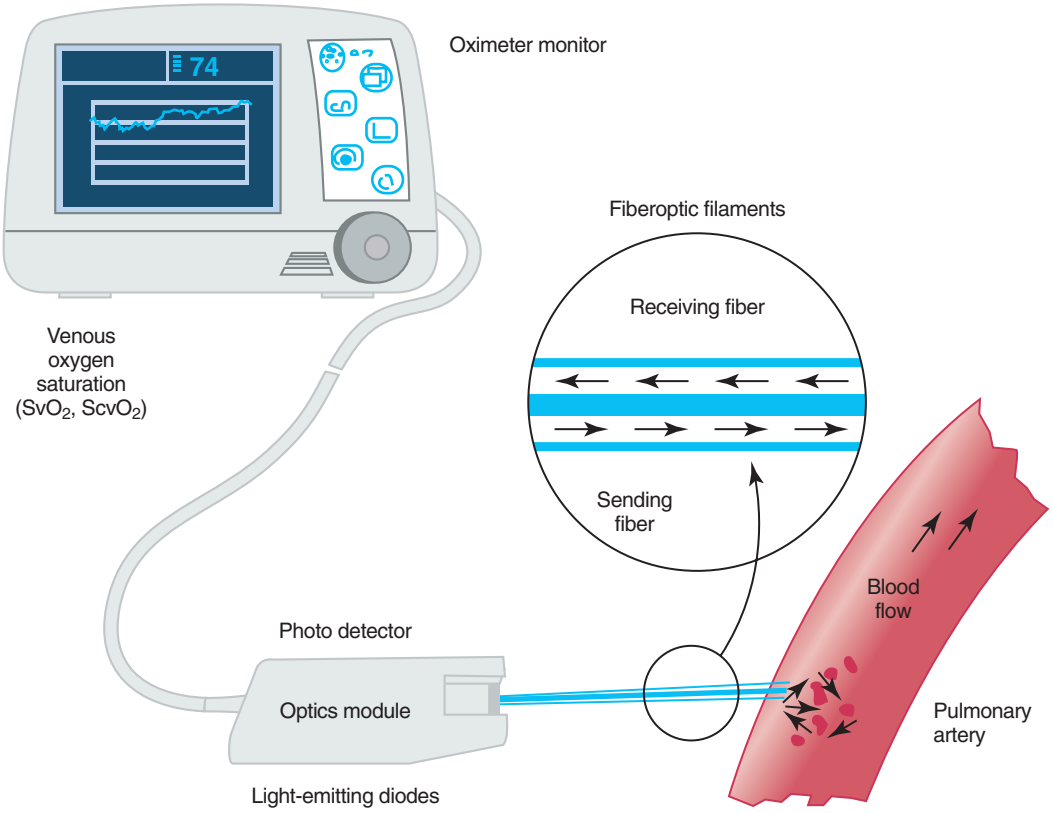

Fig. 19.18 Diagram of a venous oximetry monitoring system using reflectance oximetry. (Courtesy Edwards Life Science, Irvine, CA.)

is the graphic display of CO_2 levels versus time (scalar display) as they change during breathing. **Volumetric capnography** is the graphic displaying of CO_2 versus expired tidal volume that allows for the measurement of physiologic dead-space fraction and volumetric CO_2 excretion.[47,48] Some equipment combines these related but different monitoring techniques.

Although capnography can be applied to any patient, its primary clinical use is for monitoring during either general anesthesia or moderate sedation (where it is a standard of care), as well as mechanical ventilation. Other common indications include use during a cardiopulmonary resuscitation to both identify the proper placement of an artificial airway and to assess the effectiveness in restoring adequate perfusion pressures, which are discussed in Chapter 38 of this book. However, the following section of this chapter focuses mainly on the application of capnography and capnometry during mechanical ventilation. To guide practitioners in providing quality care, the AARC has published the Clinical Practice Guideline: Capnography/Capnometry During Mechanical Ventilation.[49]

Instrumentation

The key component in a capnograph is a rapid-responding CO_2 analyzer. Rapid CO_2 analysis can be achieved using infrared absorption, Raman scattering, mass spectroscopy, or photoacoustic technology, with the infrared capnometer being the most common.

Fig. 19.19 provides a simple schematic of a double-beam infrared capnometer. A filtered infrared light source passes through a sample chamber. (Because glass absorbs infrared radiation, the chamber "windows" usually are constructed with sodium chloride or sodium bromide.) After the infrared light passes through the sample chamber, a lens focuses the remaining, unabsorbed radiation onto an electrical photodetector. Because CO_2 absorbs infrared radiation, the greater the concentration of CO_2 in the sample, the less infrared light that arrives at the detector. Variations in the concentration of CO_2 alter the electrical output signal of the detector. This signal is used either to display the CO_2 concentration (capnometer) or to generate a real-time graphic display (capnogram).

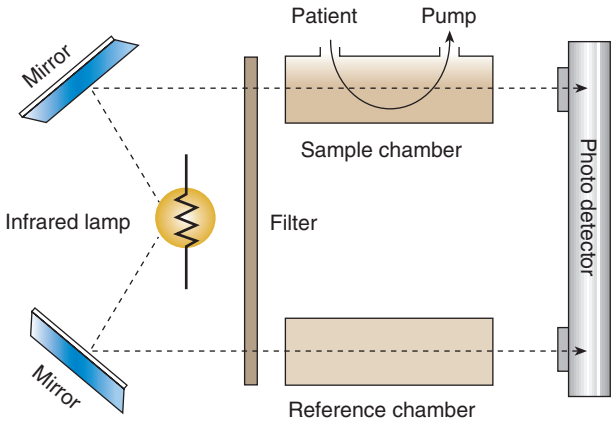

Fig. 19.19 Schematic representation of infrared capnometer.

Capnometers use two different methods to sample the respiratory gases: mainstream sampling and sidestream sampling (Fig. 19.20). The mainstream analyzer places an in-line analysis chamber between the patient's airway and the ventilator circuit.

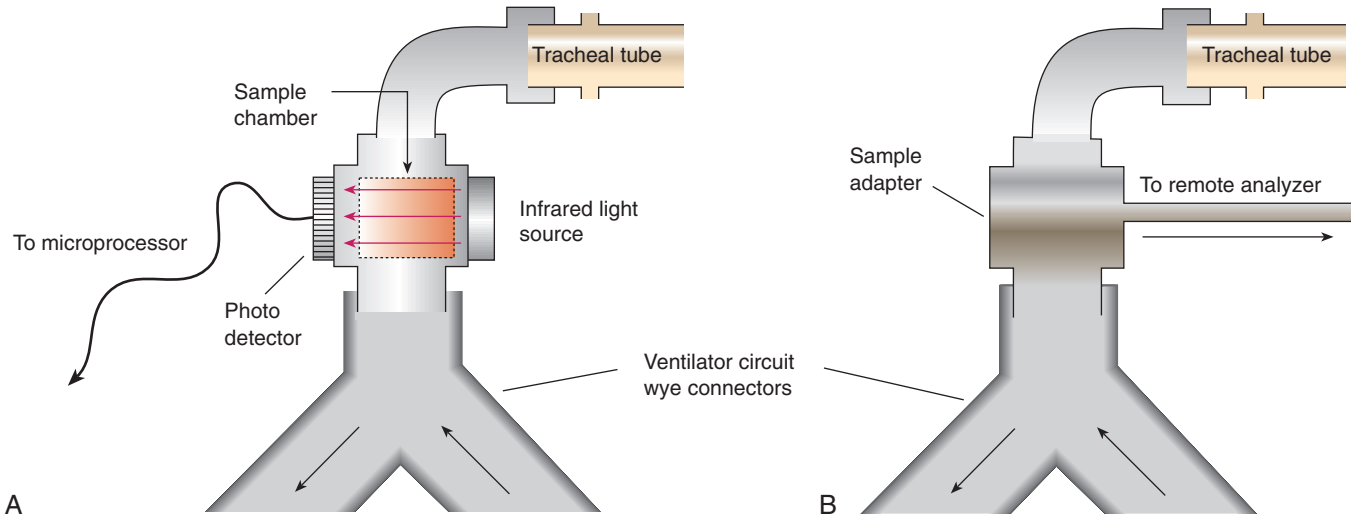

Fig. 19.20 (A) Mainstream CO_2 sampling. The sample chamber, light source, and photodetector are attached to the breathing circuit, with the output signal sent to a microprocessor for analysis and display. (B) Side-stream CO_2 sampling through an in-line sampling adapter with a small-bore connector. A small sample of expired gas is drawn continuously through the tubing and analyzed inside a remote capnometer.

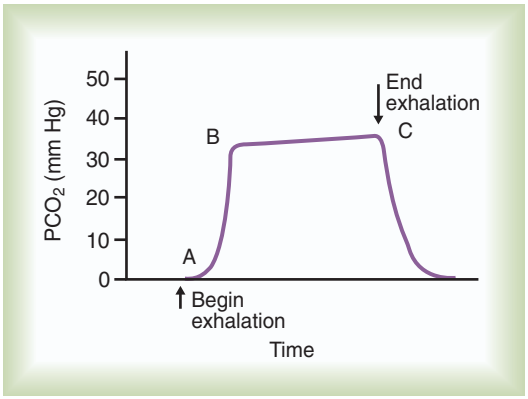

Fig. 19.21 Normal single-breath capnograph tracing.

MINI CLINI

Interpreting Capnometry Data

Problem

The RT is monitoring an intubated, mechanically ventilated patient in the ICU with a capnograph. They notice the expired CO_2 level suddenly drop to near zero. On auscultation, the patient exhibits good bilateral breath sounds, and all connections between the airway and capnograph are tight. What is the likely problem?

Solution

The most common causes of a zero $P_{ET}CO_2$ are extubation and ventilator or monitoring system disconnection. However, a $P_{ET}CO_2$ of zero also can occur with shock or cardiac arrest (no CO_2 returns to the lungs for exhalation). The RT should check this patient's cardiovascular status immediately. If the patient's cardiovascular system is functioning within normal limits, the RT should check the position of the endotracheal tube to assure that it is in the airway.

The sidestream analyzer uses a sampling tube to pump a small volume of gas continually from the ventilator circuit into the analysis chamber within the device. Box 19.9 lists the advantages and disadvantages of these two approaches.

Interpretation

Interpretation of the capnogram can be useful in assessing trends in alveolar ventilation and detecting ventilation/perfusion ratio ($\dot{V}/\dot{Q}$) imbalance caused by either pulmonary disease or cardiovascular disorders. Capnometry also is used to measure physiologic dead space, detect esophageal intubation, assess blood flow during cardiac arrest, and guide setting positive end-expiratory pressure levels. To interpret abnormal events, clinicians first must understand the normal capnogram.

Normal Capnogram

Fig. 19.21 shows a normal single-breath capnogram. Initially, the expired PCO_2 is 0 mm Hg, indicating exhalation of pure dead space gas from the airways (*A*, phase I). Soon after, alveolar gas begins mixing with dead space gas in the airways, causing a rapid increase in expired PCO_2 (*A* to *B*, phase II). The CO_2 concentration then reaches a plateau, indicating exhalation of alveolar gas (*B* to *C*, phase III). Gas sampled at the end of exhalation is called *end-tidal gas,* with its partial pressure of CO_2 abbreviated as $P_{ET}CO_2$. In healthy individuals, $P_{ET}CO_2$ averages 3 to 5 mm Hg less than $PaCO_2$, or 35 to 43 mm Hg (approximately 5% to 6% CO_2). This difference can change dramatically when ventilation-perfusion ratios vary from normal. The sharp downstroke and return to baseline that normally occurs after the end-tidal point indicates inhalation of fresh gas with zero CO_2.

The same phases are also captured during volumetric capnography (Fig. 19.22). The difference is that the area within the V_T-CO_2 curve with each breath is used to calculate the mean expired PCO_2 (P_ECO_2), which in turn is used to calculate physiologic dead space according to the Bohr-Enghoff equation ($V_D/V_T = [PaCO_2 - P_ECO2]/PaCO_2$).[47] The area within the V_T-CO_2 curve (when multiplied by the respiratory rate) calculates CO_2 excretion per minute, which under normal physiologic conditions equals CO_2 production.[48]

BOX 19.9 Advantages and Disadvantages of Mainstream and Sidestream Capnometers

Mainstream

Advantages

- Sensor at patient airway
- Fast response (crisp waveform)
- Short lag time (real-time readings)
- No sample flow to reduce tidal volume

Disadvantages

- Secretions and humidity can block sensor window
- Sensor requires heating to prevent condensation
- Requires frequent calibration
- Bulky sensor at patient airway
- Does not measure N_2O
- Difficult to use with nonintubated patients
- Reusable adapters require cleaning and sterilization

Sidestream

Advantages

- No bulky sensors or heaters at airway
- Ability to measure N_2O
- Disposable sample line
- Ability to use with nonintubated patients

Disadvantages

- Secretions block sample tubing
- Trap required to remove water from sample
- Frequent calibration required
- Slow response to CO_2 changes
- Lag time between CO_2 change and measurement
- Sample flow may decrease tidal volume

From Kacmarek RM, Hess D, Stoller J, editors: *Monitoring in respiratory care*, St Louis, 1993, Mosby.

Abnormal Capnogram

The first step in assessing the capnogram is to determine the actual $P_{ET}CO_2$ and whether it has changed over time. Table 19.7 differentiates between the causes of high and low $P_{ET}CO_2$ readings by the suddenness of the change. A $P_{ET}CO_2$ of zero usually indicates a system leak, endotracheal tube displacement out of the airway, esophageal intubation, or cardiac arrest.

After the capnogram has been assessed for changes in $P_{ET}CO_2$, the waveform and its pattern should be analyzed. A normal capnogram starts with a sharp upstroke, followed by a plateau and then a rapid downstroke. Changes in this normal contour may

TABLE 19.7 Conditions Associated With Changes in $P_{ET}CO_2$

Change	High $P_{ET}CO_2$	Low $P_{ET}CO_2$
Sudden	Sudden increase in cardiac output	Sudden hyperventilation
	Sudden release of a tourniquet	Sudden decrease in cardiac output
	Injection of sodium bicarbonate	Massive pulmonary embolism
		Air embolism
		Disconnection of ventilator
		Obstruction of endotracheal tube
		Leakage in the circuit
Gradual	Hypoventilation	Hyperventilation
	Increase in CO_2 production	Decrease in oxygen consumption
		Decreased pulmonary perfusion

NOTE: A $P_{ET}CO_2$ value of zero means that a system leak, esophageal intubation, or cardiac arrest has occurred.

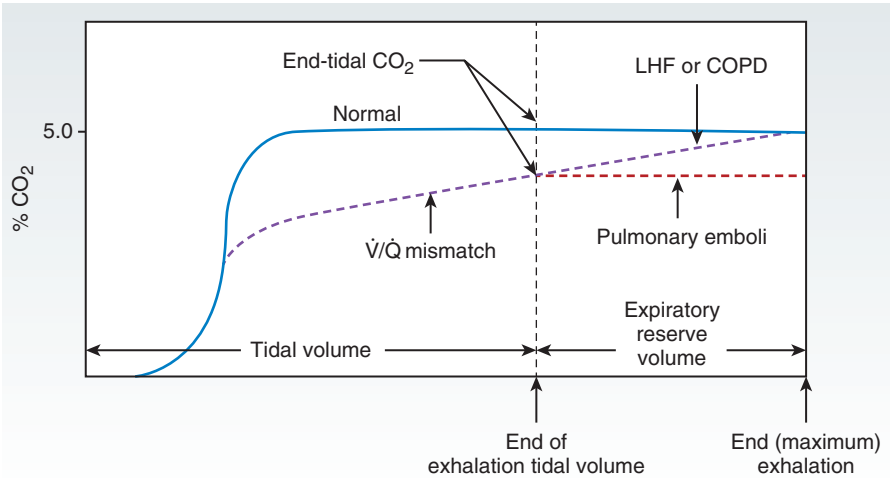

Fig. 19.22 Normal and Abnormal Volumetric Capnogram Waveforms. For a healthy individual (solid line), the end-tidal CO_2 *(ETCO$_2$)* at the completion of normal tidal exhalation is equal to end-tidal CO_2 at maximum exhalation. With shock caused by left ventricular heart failure *(LHF)* or chronic obstructive pulmonary disease *(COPD)*, the CO_2 level increases more slowly and does not reach a true end-tidal plateau. The $ETCO_2$ is less than normal at the completion of a normal exhalation (but may increase slightly with a maximum exhalation). Similar findings can be noted with a pulmonary embolus except that the low $ETCO_2$ does not increase with a maximum exhalation. (Modified from Darin J: Capnography. *Curr Rev Resp Ther* 3:146, 1981; Erickson L, Wollmer P, Olsson CG, et al: Diagnosis of pulmonary embolism based upon alveolar dead space analysis. *Chest* 96:357–362, 1989; Hatte CJ, Rokseth R: The arterial to end-expiratory carbon dioxide tension gradient in acute pulmonary embolism and other cardiopulmonary diseases. *Chest* 66:352–357, 1974. In: Pilbeam SP, Cairo JM: *Mechanical ventilation*, ed 4, St Louis, 2006, Mosby.)

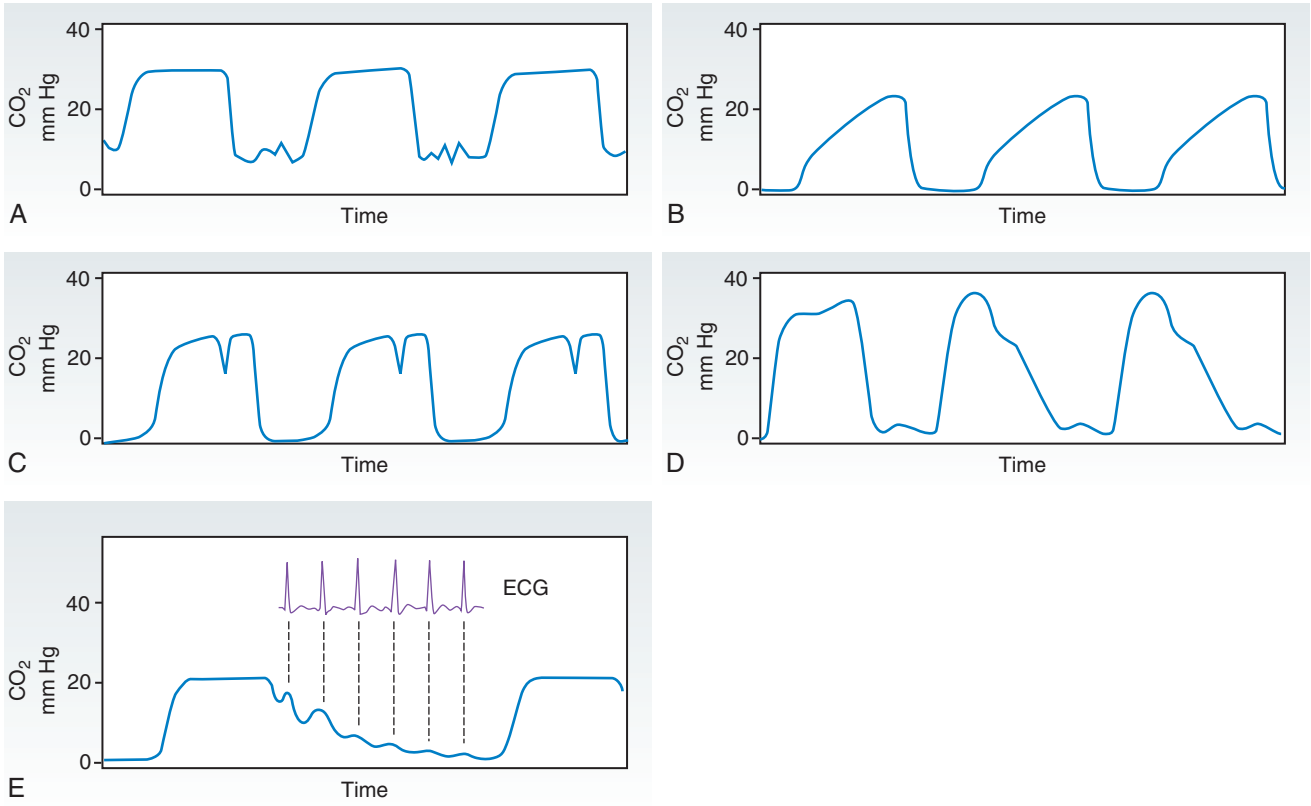

Fig. 19.23 Abnormal Capnograph Tracings. (A) Effect of rebreathing carbon dioxide on the capnogram. Note that the inspiratory level does not return to zero. (B) Sloping alveolar plateau ("Shark Fin") representative of airway obstruction or bronchospasm. (C) Curare cleft in the alveolar plateau may indicate a return in diaphragmatic activity of a paralyzed patient. (D) Unequal and incomplete emptying of the lungs ("Stair Stepping"), and a failure to return to baseline may suggest a pneumothorax. (E) Cardiogenic oscillations may be seen in patients with long expiratory times and slow respiratory rates. (Modified from Walsh BK: *Neonatal and pediatric respiratory care*, ed 4, St Louis, 2015, Elsevier.)

indicate a $\dot{V}/\dot{Q}$ abnormality. Such patterns, although not diagnostic, can indicate the severity of the $\dot{V}/\dot{Q}$ disturbance and warn of developing problems, such as acute pulmonary emboli. Fig. 19.23 shows some common abnormal capnograms.

Waveform changes also may occur with equipment malfunction. Because the normal inspired CO_2 level is zero, the capnogram baseline should also be at zero. An elevated baseline (>0 mm Hg) indicates rebreathing. However, an expired CO_2 level of zero might indicate patient disconnect. (For more information on the use of capnography during mechanical ventilation, see Chapter 52.)

Procedure

Bedside capnography procedures vary according to the type of equipment used and the manufacturer's recommended protocol. In terms of infection control, nondisposable components that contact the patient's airway or ventilator circuit should undergo high-level disinfection between patients. The monitor should be cleaned as needed according to the manufacturer's recommendations.

Problem Solving and Troubleshooting

Monitoring a patient with a capnograph that is properly calibrated and operating according to the manufacturer's specifications presents few major problems. The most significant error is assuming that the end-expired CO_2 levels can substitute for actual $PaCO_2$ measurements. Other than the expected physiologic difference between end expiratory PCO_2 and arterial $PaCO_2$, the most common problem that causes false $P_{ET}CO_2$ readings is contamination or obstruction of the sampling system or monitor by secretions or condensate.[47] Proper use of water traps and regular changing of sample tubing or chambers can help prevent this problem. Other potential problems include the following:

- False reading caused by the presence of gases with infrared absorption spectra similar to CO_2 (e.g., nitrous oxide).
- False readings based on V/Q ratios. Inaccuracy increases as V/Q deviates from 0.8 in either direction.
- Inaccurate readings with high respiratory rates (this is more of a problem with sidestream systems).
- No reading with cable disconnection or condensate in sensor or monitoring tubing.
- Misinterpreting low or absent cardiac output as a disconnect or possible esophageal intubation (all three can cause $P_{ET}CO_2$ to read zero).

SUMMARY CHECKLIST

- To measure the inspired O_2 concentration, a properly calibrated electrochemical O_2 analyzer should be used.

- The most common causes of O_2 analyzer malfunction are low batteries, sensor depletion, and electronic failure.
- As the "gold standard" of gas exchange analysis, ABG results help the clinician assess ventilation, acid–base balance, oxygenation, and the O_2-carrying capacity of blood.
- The radial artery is the preferred site for adult arterial blood sampling. Before radial puncture, a modified Allen test to confirm collateral circulation is performed.
- For critically ill patients, the clinician waits 20 to 30 minutes after a change in treatment before sampling arterial blood.
- Most pre-analytic blood gas errors can be avoided by ensuring that the sample was obtained anaerobically, is properly anticoagulated, and is promptly analyzed.
- Indwelling peripheral artery, central venous, and PA catheters give ready access for blood sampling and allow continuous pressure monitoring but with increased risk for infection and thrombosis.
- Capillary blood pH and PCO_2 are sometimes used to assess acid-base status in infants and children. Capillary PO_2 is of little value in estimating arterial oxygenation.
- To perform blood gas analysis and hemoximetry, the clinician must be proficient in performing procedures, preventive maintenance, troubleshooting, instrument calibration, and quality control.
- A blood gas analyzer measures pH, PCO_2, and PO_2 using three separate electrodes.
- To obtain accurate blood gas results, the clinician ensures that the sample is free of pre-analytic error and follows the manufacturer's recommended analysis protocol.
- Blood gas analysis quality control involves a cycle of performance validation for new instruments, preventive maintenance and function checks, automated calibration, calibration verification with control media, internal statistical quality control, external proficiency testing, and thorough recordkeeping on all processes.
- Portable point-of-care blood gas analyzers can achieve accuracy and precision levels comparable to laboratory-based analyzers.
- Transcutaneous blood gas monitoring provides continuous noninvasive analysis of gas exchange.
- Oximetry is the measurement of blood Hb saturations using spectrophotometry. Hemoximetry is a laboratory procedure that requires an arterial blood sample. Pulse oximetry combines spectrophotometry with photoplethysmography to obtain a noninvasive measure of blood Hb saturations.
- At best, pulse oximetry readings fall within ± 2% to 4% of readings obtained by hemoximetry (co-oximetry).
- Technical factors may affect the readings, limit the precision, or alter the performance of pulse oximeters. To interpret test results properly, clinicians must have in-depth knowledge of these factors.
- Capnometry is the measurement of CO_2 in respiratory gases. A capnometer is the device that measures the CO_2. Capnography is the graphic display of CO_2 levels as they change during breathing.
- A capnogram may be used to assess trends in alveolar ventilation, to identify $\dot{V}/\dot{Q}$ imbalance caused by cardiopulmonary disorders, to estimate physiologic dead space, to detect esophageal intubation, or to determine the effectiveness of a resuscitative effort and the return to spontaneous cardiac activity.

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20

Pulmonary Function Testing

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CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- List the three categories of pulmonary function tests (PFTs).
- State the primary purposes of pulmonary function testing.
- Compare and contrast the four general principles that should be considered for PFTs.
- Describe different physiologic patterns seen on PFTs.
- Discuss general principles of infection control in the PFT laboratory.
- Evaluate various devices used for measurement of pulmonary function and discuss differences and similarities among them.
- Discuss the grading system for PFT quality.
- Describe how reference values are obtained.
- Evaluate various tests based on their characteristics such as sensitivity and specificity, validity, and reliability.
- Define individual tests of pulmonary function and explain how they are obtained.
- Describe bronchodilator responsiveness and discuss its importance.
- Describe the purpose and technique for the bronchoprovocation test.
- Describe the purpose and techniques used to measure diffusing capacity.
- Analyze pulmonary function reports.

CHAPTER OUTLINE

KEY TERMS

accuracy
capacity
compliance
diffusing capacity of the lung
diffusing capacity of the lung for carbon monoxide
diffusing capacity of the lung-to–effective total lung capacity ratio
effective total lung capacity
expiratory reserve volume
extrapolated volume
forced expiratory volume in 1 second (FEV_1)
forced expiratory volume in 1 second-to-vital capacity ratio (FEV_1/FVC)
forced expiratory volume in half of a second ($FEV_{0.5}$)
forced vital capacity
functional residual capacity
inspiratory capacity
inspiratory reserve volume
linearity
maximal voluntary ventilation
minute ventilation
obstructive pulmonary disease
output
peak expiratory flow rate
precision
pneumotachometers
pseudorestriction
reliability
residual volume
restrictive pulmonary disease
sensitivity
specificity
spirometer
spirometry
turbinometers
thoracic gas volume
tidal volume
total lung capacity
validity
vital capacity

The most important function of the lungs is gas exchange. As mixed venous blood passes through the pulmonary circulation, the lungs add oxygen and remove carbon dioxide. The ability of the lungs to perform gas exchange depends on the following four general physiologic functions:

1. The diaphragm and thoracic muscles expand the thorax and lungs.
2. The airway size (radius) is suitable to allow gas to flow into the lungs and reach the alveoli.
3. O_2 and CO_2 diffuse through the alveolar-capillary membrane.
4. The cardiovascular system circulates blood through the lungs and ventilated alveoli.

Pulmonary function tests (PFTs) can provide valuable information about these important individual processes that support gas exchange. Various measurements are available to aid in the diagnosis and assessment of pulmonary diseases, to determine the need for therapy, and to evaluate the effectiveness of respiratory care. For respiratory therapists (RTs), knowledge of these tests and the ability to interpret the measurements are essential for assessing patients objectively and for planning and implementing effective patient care.

The American Thoracic Society (ATS) in collaboration with the European Respiratory Society (ERS) has developed and published a set of guidelines on measurement, reporting, and interpretation of the PFTs.[1-6] These guidelines are currently recognized internationally as the standards for the industry and have been adopted by other government agencies and medical organizations, including the American Association for Respiratory Care (AARC). Although widely accepted as the standard of care, these guidelines are not commonly used by practicing clinicians and laboratories. This chapter will closely follow the most recent ATS/ERS publications on reporting and interpretation of PFT results. However, to keep the reader familiar with all possible scenarios, an alternative (older) method of reporting and interpretation will be occasionally discussed.

PULMONARY FUNCTION TESTING

A complete evaluation of the respiratory system includes a patient history, physical examination, radiographic imaging, arterial blood gas analysis, and tests of pulmonary function. Test results become most meaningful when considered in relation to a complete clinical evaluation. Although diagnostic pulmonary function testing is performed in a laboratory setting and usually only on patients in a stable condition, RTs also perform many of these tests at the bedside on patients who are acutely ill or being evaluated for surgical readiness. There are three categories of PFTs, measuring: (1) dynamic flow rates of gases through the airways, (2) lung volumes and capacities, and (3) the ability of gases to diffuse through the lungs. A combination of these measurements provides a quantitative picture of lung function. Although PFTs do not diagnose specific pulmonary diseases, these tests identify the presence and type of pulmonary impairments, quantify the degree of pulmonary disease present, and when repeated tests are done over time, the progression of respiratory disease. Some basic tests of pulmonary function are often performed at the bedside to provide immediate information about the need for respiratory therapy and its effectiveness.

Purposes

In general, the primary purposes of pulmonary function testing are to identify pulmonary impairment and quantify the severity of pulmonary impairment if present.[3] Pulmonary function testing has diagnostic and therapeutic roles and helps clinicians to answer some general questions about patients with lung disease (Box 20.1).

The indications for pulmonary function testing are as follows[3-5]:

- *To identify and quantify changes in pulmonary function.* The most common purposes of pulmonary function testing are to detect the presence or absence of pulmonary disease, to classify the type of disease as either obstructive, restrictive, or both (mixed), and to quantify the severity of pulmonary impairment as mild, moderate, severe, or very severe. Over time, PFTs help to quantify the progression or the reversibility of the disease.
- *To evaluate need and quantify therapeutic effectiveness.* PFTs may aid clinicians in selecting or modifying a specific treatment or technique (e.g., bronchodilator medication, airway clearance therapy, rehabilitation exercise protocol). Clinicians and researchers use PFTs to measure changes in lung function objectively before and after treatment.
- *To perform epidemiologic surveillance for pulmonary disease.* Screening programs may detect pulmonary abnormalities caused by disease or environmental factors in general populations, in people in occupational settings, in smokers, or in other high-risk groups. In addition, researchers have determined what normal pulmonary function is by measuring the pulmonary function of healthy people.
- *To assess patients for risk for postoperative pulmonary complications.* Preoperative testing can help to identify patients who may have an increased risk for pulmonary complications after surgery. Sometimes, the risk of complications can be reduced by preoperative respiratory care, or in some cases, the risk may be significant enough to rule out surgery. Furthermore, for quality improvement and/or research purposes, preoperative

BOX 20.1 Basic Diagnostic and Therapeutic Questions for Clinical Pulmonary Function Testing

Diagnostic

- Is lung disease present?
- What type of lung impairment is present?
- What is the degree of lung impairment?
  - Is more than one type of lung impairment present?
  - Can multiple lung diseases be separated?

Therapeutic

- Is therapy indicated?
- What treatments are most effective?
- To what degree is the disease reversible?
- Can treatments be evaluated?
- Is rehabilitation feasible?

BOX 20.2 Indications and Contraindications to Pulmonary Function Testing

Indications

- To identify and quantify changes in pulmonary function.
- To evaluate the need for and quantify therapeutic effectiveness.
- To perform epidemiologic surveillance for pulmonary disease.
- To assess patients for postoperative pulmonary complications.

Contraindications

- Hemoptysis
- Pneumothorax
- Acute myocardial infarction or ischemia
- Acute pulmonary embolism
- Acute chest or abdominal pain
- Recent cataract surgery
- Inability to follow instructions

PFTs can permit risk adjustment of patients to facilitate a fair comparison of clinical outcomes between/among surgical teams and facilities.

- *To determine pulmonary disability*. PFTs can also determine the degree of disability caused by lung diseases, such as occupational asthma or coal workers' pneumoconiosis. Some federal entitlement programs and insurance policies rely on PFTs to confirm claims for financial compensation.

There are also contraindications to pulmonary function testing.[3] Patients with acute, unstable cardiopulmonary problems, such as hemoptysis, pneumothorax, myocardial infarction, pulmonary embolism, and patients with acute chest or abdominal pain should not be tested. Patients who have nausea and who have recently vomited should not be tested because there is a risk of aspiration. Testing for patients who have had recent cataract removal surgery should be delayed because changes in ocular pressure may be harmful to the eye. Pulmonary function testing requires patient effort and cooperation. Patients with dementia or confusion may not achieve optimal or repeatable results. Pulmonary function testing should not be performed if valid and reliable results cannot be expected. In patients who are acutely ill or who have recently smoked a cigarette, the test validity of measuring the **forced vital capacity** (FVC) may be hindered. A list of indications and contraindications for performing PFTs is given in Box 20.2.

Pathophysiologic Patterns

Pulmonary function testing provides the basis for classifying pulmonary diseases into two major categories, **obstructive pulmonary disease** and **restrictive pulmonary disease.** These two types of lung diseases sometimes occur together as a mixed impairment. Obstructive and restrictive types of lung diseases differ in several important ways. Fig. 20.1 shows normal lungs with the pathophysiologic aspects of obstructive lung diseases and restrictive lung diseases, and the differences are summarized in Table 20.1. The primary problem in obstructive pulmonary disease is an increased airway resistance (R_{aw}). R_{aw} is the difference in pressure between the ends of the airways divided by the flow rate of gas moving through the airway (see Chapter 6 for a detailed discussion of airway resistance):

$$R_{aw} = \frac{\Delta P}{\dot{V}}$$

According to Poiseuille's law, the major determinant of airway resistance is its radius. Airway radius can be reduced by excessive contraction of the bronchial and bronchiolar muscles

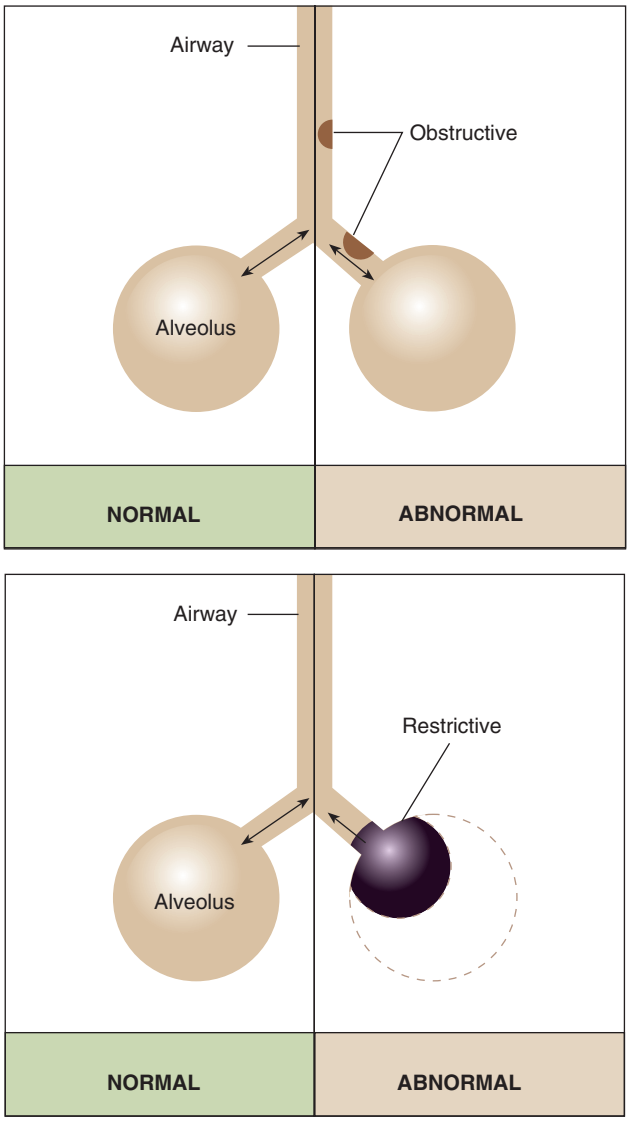

Fig. 20.1 Pathophysiologic aspects of lung disease.

TABLE 20.1 Comparison of Obstructive and Restrictive Types of Pulmonary Diseases

Characteristic	Obstructive Disease	Restrictive Disease
Anatomy affected	Airways	Lung parenchyma, thoracic pump
Breathing phase difficulty	Expiration	Inspiration
Pathophysiology	Increased airway resistance	Decreased lung or thoracic compliance
Useful measurements	Flow rates	Volumes or capacities

(bronchospasm), excessive secretions in the airways, swelling of the airway mucosa, airway tumors, collapse of the bronchioles, and other causes. By measuring flow rates, PFTs indirectly measure R_{aw}, estimate the size of the airways, and indicate the presence of obstructive disease.

The primary problem in restrictive lung disease is reduced lung compliance, thoracic compliance, or both. **Compliance** is the volume of gas inspired per the amount of inspiratory effort. Effort is measured as the amount of pressure created in the lung or in the pleural space when the inspiratory muscles contract. Compliance is calculated according to the following formula:

$$C = \frac{\Delta V}{\Delta P}$$

There is a direct relationship between compliance (*C*) and volume (*V*), in that they tend to change in the same direction. If the pressure difference is constant, a reduced inspiratory volume indicates a reduction in compliance. Reduced lung compliance is usually the result of alveolar inflammation (pneumonia), swelling (pulmonary edema), or scarring (pulmonary fibrosis); a reduced thoracic compliance may be the result of thoracic wall abnormalities, such as kyphoscoliosis, or external pressure exerted on the thoracic cavity, such as ascites, severe obesity, or pregnancy. Neuromuscular diseases such as amyotrophic lateral sclerosis (ALS) or muscular dystrophy also can result in reduced lung volumes and restrictive-type pulmonary impairments, mainly by affecting the function of the inspiratory muscles. In these circumstances, lung compliance and thoracic compliance may be normal, but the patient is unable to generate enough subatmospheric pressure to take a full, deep breath.

Some obstructive diseases and some restrictive diseases also may affect the ability of gases to diffuse in the lung. In some diseases, there is damage to the alveolar-capillary membrane, or less alveolar surface area is accessible for diffusion, such as may occur with advanced emphysema. Measuring the **diffusing capacity of the lung for carbon monoxide** (DLCO) can identify the destruction of alveolar tissue or the loss of functioning alveolar surface area.

Infection Control

Pulmonary function testing is generally regarded as a very low-risk procedure. However, there is potential to transmit infective microorganisms to patients and technologists.[3] Transmission can occur by direct or indirect contact. Standard precautions should be applied because of the potential exposure to saliva, mucus, or blood, which can harbor potentially hazardous microorganisms. Patients with oral lesions or active respiratory infections pose the greatest potential hazard, and patients with compromised immune systems are at the greatest risk. Practitioners should wear gloves when handling potentially contaminated mouthpieces, valves, tubing, and equipment surfaces. When performing procedures on patients with potentially infectious airborne diseases, practitioners should wear a personal respirator or a close-fitting surgical mask, especially if the testing induces coughing. Practitioners should always wash their hands between testing patients and after contact with testing equipment. Although it is unnecessary to clean the interior surfaces of the testing instruments routinely between patients, the mouthpiece, nose clips, tubing, and any parts of the instrument that come into direct contact with a patient should be disposed, sterilized, or disinfected between patients.[3] Any equipment surface showing visible condensation from exhaled air should be discarded, disinfected, or sterilized before reuse. When testing instruments are disassembled for cleaning and disinfecting, manufacturer recommendations should be considered and recalibration may be necessary before testing resumes. The routine use of low-resistance, in-line barrier filters is controversial.[3] Filters may be appropriate when internal surfaces of manifolds and valves proximal to mouthpieces are inaccessible or difficult to disassemble for cleaning and disinfecting. Filters provide visible evidence to reassure patients that their protection has been considered.

Equipment

Pulmonary function testing requires measurement of gas volume or flow, and various instruments and measurement principles are used to make these measurements. There are two general types of measuring instruments: instruments that measure gas volume and instruments that measure gas flow. Both types of instruments simultaneously measure time, and both compute various volumes and flow rates used in pulmonary function testing. The term ***spirometer*** is sometimes used as a generic term for all volume-measuring and flow-measuring devices.

Volume-measuring devices are specifically called *spirometers* and include water-sealed, bellows, and dry rolling seal types. These devices expand as they collect gas volumes. The magnitude of the expansion is the *volume* measured, and the speed of expansion represents the *flow rate*. In the absence of leaks and with low-momentum forces, volume-measuring devices can be extremely accurate for measuring volumes, and with low inertia and friction forces, volume-measuring devices can be extremely accurate when computing flow rates.

Flow-measuring devices are commonly called ***pneumotachometers,*** although some practitioners reserve this term for only the device originally designed by Fleisch. These devices measure flow using a variety of unique principles. The Fleisch-type pneumotachometer measures the change in pressure as gas flows through it. Known as *thermistors* or *mass flowmeters,* another type of flow-measuring device measures the temperature change created by gas flowing through it. There are also ***turbinometers,*** which use rotation of a fan or blades similar to a windmill. Detailed descriptions and examples of each type of device are beyond the scope of this chapter.

Regardless of the type of device or the principle of measurement used, several important characteristics are common to all measuring devices. Having an understanding of these common characteristics provides RTs the ability to select and use these devices properly. Every measuring instrument has **capacity,** accuracy, error, resolution, precision, linearity, and output. The ideal instrument would have unlimited capacity to measure every pulmonary parameter, and it would have perfect accuracy and precision over its entire measurement range. However, in real practice, there are no ideal instruments.

The *capacity* of an instrument refers to the range or limits of how much it can measure. This term should not be confused

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Performance of a Testing Unit Was Measured Over Time

Problem

Using standard calibrated 3-L cylinder as a testing subject, the following measurements were obtained over the 10 separate tests:

Test	#1	#2	#3	#4	#5	#6	#7	#8	#9	#10
Value	2.89 L	2.95 L	3.01 L	3.05 L	3 L	2.95 L	2.86 L	3.11 L	3.04 L	2.96 L

Calculate the accuracy and the error of the test.

Solution

First, calculate the error of each test (absolute value of the difference between actual and measured values). The individual error for tests 1 through 10 would be 0.11, 0.05, 0.01, 0.05, 0, 0.05, 0.14, 0.11, 0.04, and 0.04 L, respectively. The average of these values is 0.06 L. Now we can calculate the error 0.06 L/3 L = 0.02, or 2%. Therefore the error is 2% and the accuracy is 98%.

TABLE 20.2 Spirometer Performance Standards of the American Thoracic Society/European Respiratory Society Task Force

Test	Volume	Flow (L/S)	Accuracy	Time (S)	Back Pressure
VC	0.5–8 L	0–14	≤3% or 0.05 L[a]	30	
FVC	0.5–8 L	0–14	≤3% or 0.05 L[a]	15	<1.5% cm H_2O/L/s at 14 L/sec
FEV_1	0.5–8 L	0–14	≤3% or 0.05 L[a]	1	<1.5% cm H_2O/L/s at 14 L/sec
PEF		0–14	≤10% or 0.3 L/sec[a]		<1.5% cm H_2O/L/s at 14 L/sec
MVV	250 L/min at 2 L/breath		±10% or 15 L/min[a]	12–15	<1.5% cm H_2O/L/s at 14 L/s

[a]Whichever is greater.
FEV_1, Forced vital capacity in 1 second; *FVC*, forced vital capacity; *MVV*, maximal voluntary ventilation; *PEF*, peak expiratory flow; *VC*, vital capacity.

with "capacity" used in describing lung compartments. In that context, capacity is the combination of two or more lung volumes as discussed later in this chapter. Most instruments are designed with capacities to measure volumes and flow rates of all adults. The ***accuracy*** of a measuring instrument is how well it measures a known reference value. For volume measurements, standard reference values are provided by a graduated 3.0-L calibration syringe. No measuring instrument is perfect, and there usually is an arithmetic difference between reference values and measured values. This difference is called the *error*. *Accuracy* and *error* are opposing terms; the greater the accuracy, the smaller is the error. Accuracy and error are commonly expressed as percentages, with their sum always equaling 100%. To determine percent accuracy and percent error, an object of known measurement (e.g., 3-L cylinder) is tested multiple times and the absolute value of the deviation from the known measurement (error) calculated. The average value of the error over multiple tests is then computed. *Resolution* is the smallest detectable measurement; instruments with high resolution can measure the smallest volumes, flows, and times. ***Precision*** is synonymous with reliability (repeatability) of measurements and the opposite of variability. When multiple values are measured for a given test, the standard deviation of these values indicates the extent to which these values vary from the mean and is therefore an indication of the precision of an instrument. A small standard deviation indicates low variability and high precision. ***Linearity*** refers to the accuracy of the instrument over its entire range of measurement, or its ***capacity.*** Some devices may accurately measure large volumes or high flow rates but may be less accurate when measuring small volumes or low flow rates. To determine linearity, accuracy and precision are calculated at different points over the range (capacity) of the device. ***Output*** includes the specific measurements made or computed by the instrument.

Most volume-measuring and flow-measuring devices measure the FVC and **forced expiratory volume in 1 second (FEV_1)**. Others calculate various forced expiratory flow (FEF) rates, and some measure tidal volume (V_T) and **minute ventilation** ($\dot{V}_E$). Diagnostic spirometers usually measure and calculate **vital capacity** (VC), FVC, FEV_1, **peak expiratory flow** (PEF) rate, and FEF rates. Some measure and calculate **maximal voluntary ventilation** (MVV). Some of these instruments may be a component of a laboratory system providing the volume-measuring or flow-measuring capability for other diagnostic tests of pulmonary function. For example, they may be used with gas analyzers to measure **functional residual capacity** (FRC) and **total lung capacity** (TLC) or the inspiratory VC during *single-breath diffusing capacity (DLCO-SB)*. Whether a spirometer or pneumotachometer is used in a diagnostic laboratory, a physician's office, or at the bedside in a hospital, it should meet or exceed the national performance standards for volume-measuring and flow-measuring devices.

The spirometry performance standards are summarized in Table 20.2. In addition, the spirometer standards also require spirometers to have a thermometer or to produce values corrected for body temperature, ambient pressure, and fully saturated with water vapor (BTPS). For quality control, the standards include verifying volume accuracy at least daily, although best practice in many laboratories is to verify accuracy before each test subject.

Grading of Quality

Most modern pulmonary function laboratories use computers for data acquisition and reproduction. Computer-assisted testing decreases the time necessary to complete the tests and enhances the effectiveness of pulmonary function testing by increasing accuracy, increasing patient acceptance, and monitoring patient performance. Although computer-assisted testing and interpretations of test results are often applied by a computer, pulmonary function testing always requires a trained and competent RT to administer the tests, and computer analysis should not replace human analysis. In addition, both technician (RT performing the test) and reviewer (physician interpreting the test) should pay a close attention to grading the quality of PFTs. The grading system recommended by the ATS guidelines includes typical A through F grading scale (A being the highest and F being the lowest quality).

It is recommended that tests achieving grades A through C are clinically useful and should be reported, grades D and E may have limited value, and grade F should not be reported.[1] Unfortunately, many believe that stricter guidelines on grading the quality of tests are still needed. The purpose of quality grading is to provide the reviewer with possible limitations of test interpretation, and evaluate the possibility whether abnormal PFT results are due to underlying disease or suboptimal effort/performance.

REFERENCE VALUES AND INTERPRETATION OF RESULTS

The reference values for PFTs, as for any other physiologic variable, are based for population studies and are, to some extent, arbitrary (see Chapter 17). Unlike other commonly used laboratory values, such as serum sodium level, or white blood cell count, the "normal" values for the PFT measurements are based on height, age, gender, and race/ethnicity. With all else being equal, taller, younger male patients tend to produce greater volumes and flows than their shorter, older female counterparts. Racial and ethnic differences also exist. Large population-based studies[7,8] have established the equations for reference values based on height, age, gender, and race/ethnicity. For individuals of mixed ethnic origin, or not represented by the major ethnic groups, composite equations were developed. Along with the individual patient results, the ATS recommends routine reporting of the following reference values: predicted value, upper and lower limit of normal (ULN, and LLN, respectively), and z score.[1] The predicted value is simply an average value derived from a large population of healthy subjects. ULN and LLN are mathematically derived and encompass the range of "normal" values. It is expected that 95% of healthy individuals fall between these two values. The z score is a statistical measurement that is used to show how much the patient's result deviates from the predicted value. For example, a z score of 0.5 would indicate that the test result is 0.5 standard deviations greater than the predicted value (negative z scores are used to indicate that the test result is less than the predicted value). With the widespread use of computers for the measurement and reporting of PFTs, the reference values for given patient characteristics are the part of the computer software, eliminating the need for manual calculation using cumbersome mathematical formulas.

RULE OF THUMB Normal pulmonary function values are based on the subject's age, height, gender, ethnicity, and sometimes weight. Normal pulmonary function predictably declines with age older than 20 to 25 years.

A brief explanation on interpreting pulmonary function test (PFT) results will be given as follows, and a more detailed discussion can be found elsewhere in the chapter and in the references.[1,6] The presence of pulmonary disease is suspected when the test result falls outside the upper limit of normal (ULN)/lower limit of normal (LLN) range. The severity of pulmonary impairment is assessed by comparison of each patient's actual measurement with the predicted normal value for the patient. A common method of comparison is to compute a percentage of the predicted normal value according to the following equation:

TABLE 20.3 Severity of Pulmonary Impairment Based on a Percentage of Predicted Normal Values

Degree of Impairment	Obstruction Based on FEV_1 (%)	Gas Exchange Based on DLCO (%)
Normal	80–120	80–120
Mild	70–79	61–79
Moderate	60–69	40–60
Moderately severe	50–59	
Severe	35–49	<40
Very severe	<35	

DLCO, Diffusing capacity of the lung for carbon monoxide; *FEV_1,* forced vital capacity in 1 second.

$$\%\ \text{Predicted} = \frac{\text{Measured value}}{\text{Predicted normal value}} \times 100$$

Typical degrees of severity based on percent predicted values are listed in Table 20.3.

Although the most recent ATS guidelines strongly support the use of ULN/LLN range to identify abnormal values, and the use of percent predicted values to quantify the severity of illness, some clinicians and PFT laboratories still use percent predicted values to identify the abnormality. In this approach, arbitrary range of 80% to 120% predicted is used as the "normal" range. Any value less than 80% or greater than 120% predicted is therefore considered abnormal. Although these two methods often produce similar results, the former is considered to be more accurate and is endorsed and recommended by the respiratory societies.

PRINCIPLES OF MEASUREMENT AND SIGNIFICANCE

For tests of pulmonary function, these general principles should be considered: test sensitivity and specificity, validity, and reliability.

Sensitivity and **specificity** address the test's ability to detect disease or absence of it, respectively. Sensitivity is high if the test is abnormal whenever disease is present. Specificity is high if the test is normal whenever disease is absent. Some tests are extremely *sensitive,* so that apparently healthy individuals may have an abnormal test result. However, some tests are not sensitive; individuals must be extremely sick to have an abnormal test result. Most tests of pulmonary function are not *specific* because several different diseases may cause the test result to be abnormal. This limitation of many PFTs explains why these tests identify a pattern of impairment rather than diagnose specific diseases.

Validity of the test relates to its meaningfulness or the ability to accurately measure what it is intended to measure. When performing pulmonary function testing, strictly following testing procedures, ensuring patient effort and performance, and ensuring equipment accuracy and calibration establish test validity.

Reliability of the test is its consistency. A reliable test produces consistent test results with minimal variability, when repeated.

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Sensitivity and Specificity

Problem

In search for a perfect test for disease X, researchers have developed two tests: Test A is very sensitive but not specific, and Test B, which is very specific but not sensitive. How would you use these tests to achieve maximum results for diagnosing disease X in large population of healthy subjects?

Solution

Naturally, we would like to have tests that are 100% sensitive and 100% specific, but no such test exists. In the given scenario, Test A should be used first. That will select all patients with the disease X. Because Test A is not very specific, the group will likely include some healthy subjects who happen to have a positive test, without having the actual disease. Now, everyone positive for Test A should undergo Test B. Because it has high specificity, healthy subjects will be identified by having a negative Test B. Those who are positive for both Test A and B will truly have disease X. Any other combination of tests A and B will result in either unnecessary testing or missing patients with disease.

To be reliable, each test must be performed more than once. Ensuring test validity and reliability is the most important role of the RT. Test results that are invalid or unreliable can lead to misdiagnosis, treatment errors, and poor outcomes.

RULE OF THUMB A sensitive test would be positive in patients with disease, whereas a specific test would be negative in patients without disease. A valid test would give results reflective of the individual's true pulmonary function abilities, regardless of other factors such as effort or equipment faults. A reliable test would give the same, or very similar, results on multiple testing attempts.

INDIVIDUAL TESTS AND MEASUREMENTS

There are three basic tests of pulmonary function: (1) spirometry, (2) lung volumes, and (3) diffusing capacity (DL). When the purpose of the testing is to identify the presence and the degree of pulmonary impairment and the type of pulmonary disease, all three testing components are required. When the purpose of the testing is more limited, such as to assess postoperative pulmonary risk or to evaluate and quantify therapeutic effectiveness, the scope of measurement also is limited.

General indications, contraindications, and potential complications of pulmonary function testing were briefly discussed at the beginning of this chapter. A complete listing of all indications, contraindications (absolute and relative), hazards, and complications, assessment of need and test quality, techniques and different types of equipment that make the measurements, and quality control measures is outside of the scope of this chapter. They are summarized in the ATS/ERS documents included in the references for this chapter.[3] Many pulmonary function laboratories also perform arterial blood gas analysis (see Chapter 19), and some laboratories provide more specialized and advanced tests, such as bronchial challenge tests and exercise stress tests.

Spirometry

Spirometry—the measurement of air entering and leaving the lungs—includes measurement of several values of forced airflow and volume during inspiration and expiration. For the most part, the purpose of spirometry is to assess the ability of the lungs to move large volumes of air quickly through the airways to identify airway obstruction. Some measurements are aimed at large intrathoracic airways, some are aimed at small airways, and some assess obstruction throughout the lungs. Measuring flow rates is a surrogate for measuring airways resistance, as discussed earlier in the chapter. The major values measured during spirometry are discussed later.

Spirometry is an effort-dependent test that requires careful patient instruction, understanding, coordination, and cooperation. Spirometry standards for FVC specify that patients must be instructed in the FVC maneuver, that the appropriate technique be demonstrated, and that enthusiastic coaching occurs.[4] When measuring FVC, the RT needs to coach the preceding **inspiratory capacity** (IC) as enthusiastically as the FVC. According to the standards, nose clips are encouraged but not required and patients may be tested in the sitting or standing position. Although standing usually produces a larger FVC compared with sitting, sitting is considered safer in case of lightheadedness. It is recommended that the position be consistent for repeat testing of the same patient. FVC should be converted to body temperature conditions and reported as liters under BTPS conditions.

Forced Vital Capacity

Forced vital capacity (FVC) is the most commonly performed test of pulmonary mechanics, and many measurements are made while the patient is performing the FVC maneuver (Fig. 20.2). Measuring FVC often occurs under baseline or untreated conditions. For baseline testing, patients should temporarily abstain from bronchodilator medications. Short-acting bronchodilators (e.g., β-agonist: albuterol; anticholinergic agent: ipratropium bromide) should not be used for 4 hours before baseline spirometry, whereas long-acting β-agonist bronchodilators and oral therapy with aminophylline should be stopped for 12 hours. When a patient's baseline results show airway obstruction, performing FVC after treatment (e.g., albuterol bronchodilator aerosol or metered dose inhaler) can help to determine if the treatment is effective. The FVC maneuver is also performed repeatedly during bronchial provocation testing.

Several properties of the spirometer must be present to accurately measure FVC: (1) the spirometer must display volumes or flows, (2) the spirometer must present a graph of volume and time or flow and volume, (3) the spirometer is either mechanical or electronic, and (4) the spirometer has a calculator or computer. The forced expiratory VC sometimes is followed by a forced inspiratory VC to produce a complete image of forced breathing called a *flow-volume loop* (see Fig. 20.2B).

RULE OF THUMB If you do not inhale it, you cannot exhale it. So, coach the inspiratory capacity enthusiastically to achieve the optimal total lung capacity. Then, coach for a forceful and complete exhalation to measure the FVC.

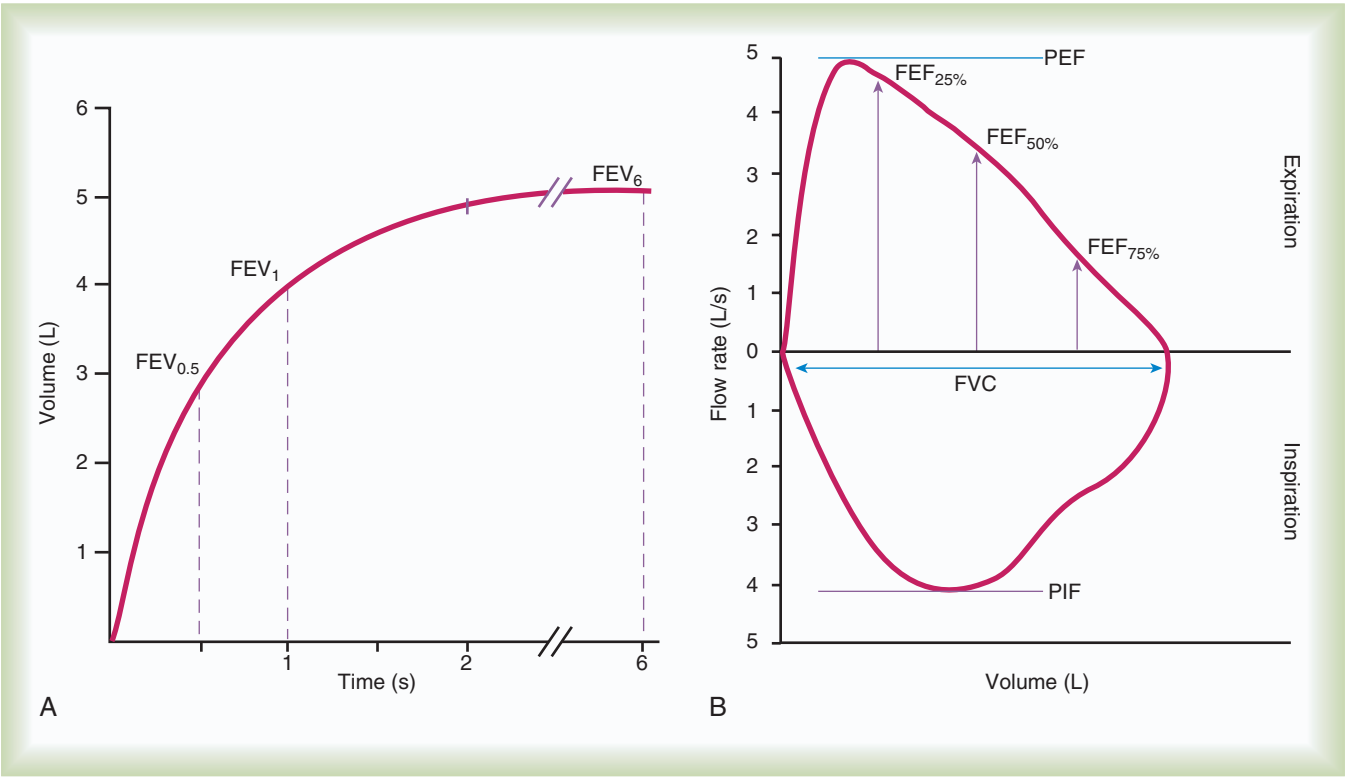

Fig. 20.2 Forced Vital Capacity *(FVC)*, Forced Expiratory Volumes, and Flow Rates. (A) Forced vital capacity on a volume-time graph. (B) Forced vital capacity on a flow-volume graph. *FEF*, Forced expiratory flow; *PEF*, peak expiratory flow; *PIF*, peak inspiratory flow.

To ensure validity, each patient must perform a minimum of three acceptable FVC maneuvers. To ensure reliability, the largest FVC and second largest FVC from the acceptable trials should not vary by more than 0.15 L. To perform an FVC trial, the patient should inhale rapidly and completely to TLC from the resting FRC level. The forced exhalation of an acceptable FVC trial should begin abruptly and without hesitation. The volume exhaled before the zero time point is called the ***extrapolated volume.*** To be valid, no more than 5% of the VC or 0.15 L is allowed to be exhaled before the zero time point (Fig. 20.3). An acceptable FVC trial also is smooth, continuous, and complete. A cough, an inspiration, a Valsalva maneuver, a leak, or an obstructed mouthpiece while an FVC maneuver is being performed disqualifies the trial. FVC must be completely exhaled or an exhalation time of at least 6 seconds with an expiratory plateau (i.e., no more gas exhaled) for 2 seconds thereafter must occur for adults and children older than 10 years; longer times are commonly needed for patients with airway obstruction and the end-of-test criterion for such patients may be a 15-second exhalation. A 3-second exhalation is acceptable for children younger than 10 years old. An end-expiratory plateau must be obvious in the volume-time curve (see Fig. 20.3); the objective standard is less than 0.025 L exhaled during the final second of exhalation. Consistent with its definition, the largest acceptable FVC (BTPS) measured from the set of three acceptable trials should be recorded as the patient's FVC.

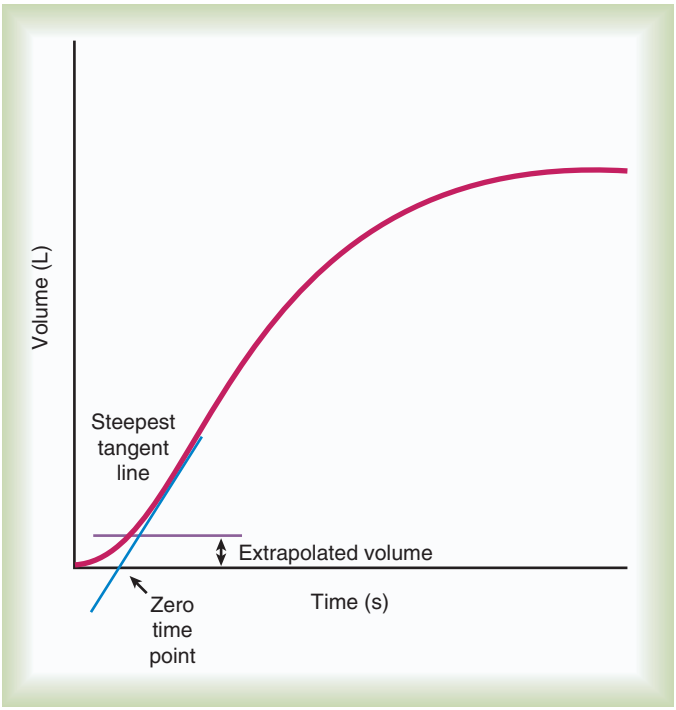

Fig. 20.3 Extrapolated volume and zero time point determination.

MINI CLINI

Reporting Reliable and Valid Results

Problem

A patient undergoes spirometry testing. A total of three trials are done, all of them deemed to be of good quality and validity. The following results are obtained:

	FEV_1 (L)	FVC (L)	FEV_1/FVC	Predicted
FVC (L)	3.4	3.3	3.5	4
FEV_1 (L)	2.7	2.8	2.75	3.6
FEV_1/FVC	0.79	0.85	0.76	0.9

Is the test reliable? Which values should be included in the final report?

Solution

Individual values for FEV_1 and FVC are within 0.15 L of each other, so the test is considered reliable. The best FEV_1 and the best FVC should be reported, even if they came from different trials. The report should also include percent predicted values for FEV_1 and FVC, which is calculated by dividing the "best" value by the "predicted" value. Note that ULN, LLN, and z scores were omitted for simplicity. In addition, FEV_1/FVC should be reported as decimals and should not have percent predicted calculated, or reported, to avoid confusion. The results should read:

	Best	Predicted	% Predicted
FVC (L)	3.5	4	86
FEV_1 (L)	2.8	3.6	78
FEV_1/FVC	0.8	0.9	XXXXXXXXXXXXXXX

Forced Expiratory Volume in 1 Second

During FVC testing, several other measurements are also made. FEV_1 is a measurement of the volume exhaled in the first second of FVC (see Fig. 20.2A). To ensure validity of FEV_1, the measurement must originate from a set of three acceptable FVC trials. The first second of forced exhalation begins at the zero time point (see Fig. 20.3). To ensure reliability of FEV_1, the largest FEV_1 and second largest FEV_1 from the acceptable trials should not vary by more than 0.15 L. Consistent with its definition, the largest FEV_1 (BTPS) measured is the patient's FEV_1. The largest FEV_1 may come from a different trial than the largest FVC.

The **forced expiratory volume in 1 second-to-vital capacity ratio (FEV_1/FVC)** is calculated by dividing the patient's largest FEV_1 by the patient's largest VC. The two values do not have to come from the same trial; the VC should be the largest one measured, even if measured as a slow VC or during inspiration. Note that during reporting, the value should be expressed in decimals, not percentages (e.g., 0.78, rather than 78%) and only the absolute value, LLN, and z score should be reported, but not percent predicted, to decrease the possibility of miscommunication.[2]

Peak Expiratory Flow

Peak expiratory flow (PEF) is difficult to identify on a volume-time graph of FVC. The peak flow is the steepest portion of the exhalation slope on an FVC curve. PEF is easy to identify on a flow-volume graph as the highest point on the graph (see Fig. 20.2B). PEF is sometimes measured independently of FVC with a peak flow meter. These devices are designed to indicate only the greatest expiratory flow rate. The validity of PEF rate is based on a preceding inspiration to TLC, and the results tend to vary greatly with effort. As a result, to help ensure reliability of PEF rate measurements, the two largest repeated measurements which fall within 5% of each other should be reported.

MINI CLINI

Decreased Forced Vital Capacity and Forced Expiratory Volume in 1 Second: Is It Obstruction or Restriction?

Problem

Both obstructive and restrictive diseases may exhibit decreased FVC and FEV_1. How can the two kinds of patterns be differentiated?

Solution

FVC and FEV_1 are reduced in both obstructive and restrictive diseases for different reasons. With restrictive disease, lung expansion is reduced. If a person can inhale only a small volume, he or she can exhale only a small volume. All lung volumes are smaller than normal, including TLC, FVC, and FEV_1.

Maximal Voluntary Ventilation

Another measurement of pulmonary mechanics is maximal voluntary ventilation (MVV). It is another effort-dependent test for which the patient is asked to breathe as deeply and as rapidly as possible for at least 12 seconds. MVV is a test that requires patient cooperation and effort, the ability of the diaphragm and thoracic muscles to expand the thorax and lungs, and airway patency. Because of the potential for acute hyperventilation and fainting or coughing, the patient should be seated. Measuring systems that incorporate rebreathing may minimize the effects of hyperventilation. After a demonstration of the expected breathing pattern is performed, the patient should be instructed to breathe as rapidly and as deeply as possible for at least 12 seconds. The patient's breathing is measured on a spirogram (Fig. 20.4) or electronically for the specific number of seconds (t) and the volume (V) breathed when the MVV is converted to liters per minute. As with all volumes measured on a spirometer, the recorded values should be in BTPS conditions. The validity of MVV depends on the duration of the maneuver, which should be at least 12 seconds; the breathing frequency, which should be at least 90 breaths/minute; and the average volume, which should be at least 50% of FVC. In addition, measured MVV should be compared with two other values: subject's $FEV_1 \times 40$ and predicted value for MVV. If the measured MVV is less than 80% of either of those values, a repeat test should be performed to ensure accuracy. Reliability is shown when the largest two measurements are within 20% of one another. The largest MVV (BTPS) should be reported.

Other values obtained during spirometry. During spirometry, a few additional measurements can be obtained, such as V_T, expiratory reserve volume (ERV), and IC. These values are usually interpreted in the context of other lung volumes and are discussed later in this chapter.

With obstructive disease, there is airway obstruction, which slows expiratory flow. FEV_1 is reduced because of the increased airway resistance, which decreases expiratory flow rates. FVC is

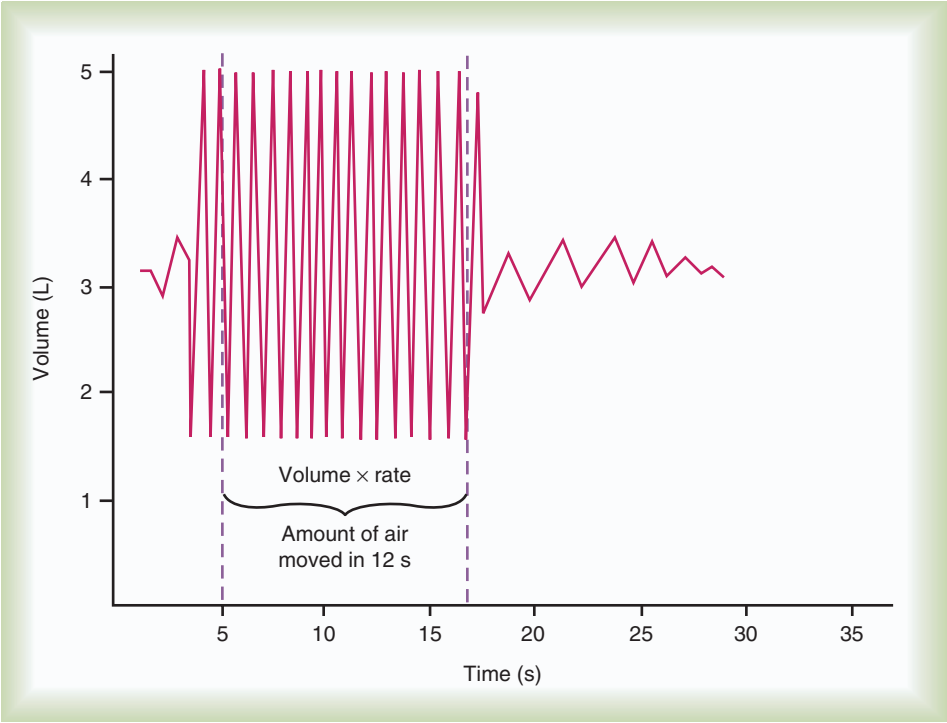

Fig. 20.4 Maximal Voluntary Ventilation Tracing. Actual ventilations recorded during a 12-s period.

reduced because airway obstruction in the bronchioles causes air trapping in the lung. This trapped air cannot be exhaled, which leads to FVC reduction.

To differentiate between obstructive and restrictive patterns of impairment, compare FEV_1 with FVC using the FEV_1/FVC ratio. Only individuals with airway obstruction will have the reduced FEV_1/FVC ratio. If it is less than the LLN, the diagnosis of obstruction can be made. Some older references use the absolute value of 0.7 (do not use percentages here, as discussed previously) as a cutoff to diagnose obstruction. This leads to underdiagnosis of obstruction in the elderly and is currently discouraged by the ATS guidelines.

As for the diagnosis of restriction, it cannot be reliably made on the basis of spirometry. Some clinicians may still use normal FEV_1/FVC ratio with reduced absolute values as "suggestive" of restriction; however, such practice is discouraged by the latest ATS guidelines.

An important caveat during interpretation of spirometry values is the concept of **"pseudorestriction."** Some patients with obstructive lung disease will not be able to exhale a significant portion of their VC during forced maneuvers, leading to smaller than actual FVC measurement. These patients will have reduced FVC, will have reduced FEV_1, and may actually have normal FEV_1/FVC ratio, suggestive of restrictive physiology, hence the name *pseudorestriction*. Other names include PRISm (preserved ratio with impaired spirometry) or "nonspecific" PFTs. In these patients, it is important to give them enough time to fully exhale by making sure that they reach a plateau at the end of FVC maneuver (see Fig. 20.3) to allow proper measurement of FVC. Comparing FVC to slow vital capacity (SVC, see later) is another method of looking for obstructive physiology. If the SVC is considerably larger than the FVC, this suggests an obstructive disorder which would need to be confirmed with additional testing.

Interpretation

The predicted normal FVC for a 20-year-old, 180-cm (71-in.) man approaches 5.60 L. A reduced FVC may occur with obstructive or restrictive impairments. Fig. 20.5 shows FVC from volume-time spirometer tracings for normal, obstructive, and restrictive conditions. The FVC values in both the obstructed and the restricted curves are shown as reduced volumes compared with the normal curve. The primary difference between the curve in the restricted patient compared with the curve in the obstructed patient is the slope of the tracing; obstructive diseases produce flattened slopes associated with lower flows and smaller FEV_1.

Fig. 20.6 displays the FVC from flow-volume tracings for obstructive and restrictive conditions. The shapes of these tracings are different; obstructive diseases produce lower peaks and lower flow rates at all lung volumes. This scooped appearance is sometimes referred to as "expiratory coving." Forced inspiratory flow rates sometimes are useful for identifying extrathoracic airway obstruction. In moderate and severe obstructive lung diseases, the FVC is reduced if weakened bronchiolar walls allow collapse and air trapping, causing an increased residual volume (RV). Some PFT laboratories compare the volumes of SVC and FVC to identify air trapping. VC is reduced in restrictive lung diseases because the patient's inhaled volume is reduced.

Although FEV_1 is measured as a volume, it is considered a flow rate. The predicted normal FEV_1 for a 20-year-old, 180-cm (71-in.) man is approximately 4.70 L. FEV_1 may be reduced

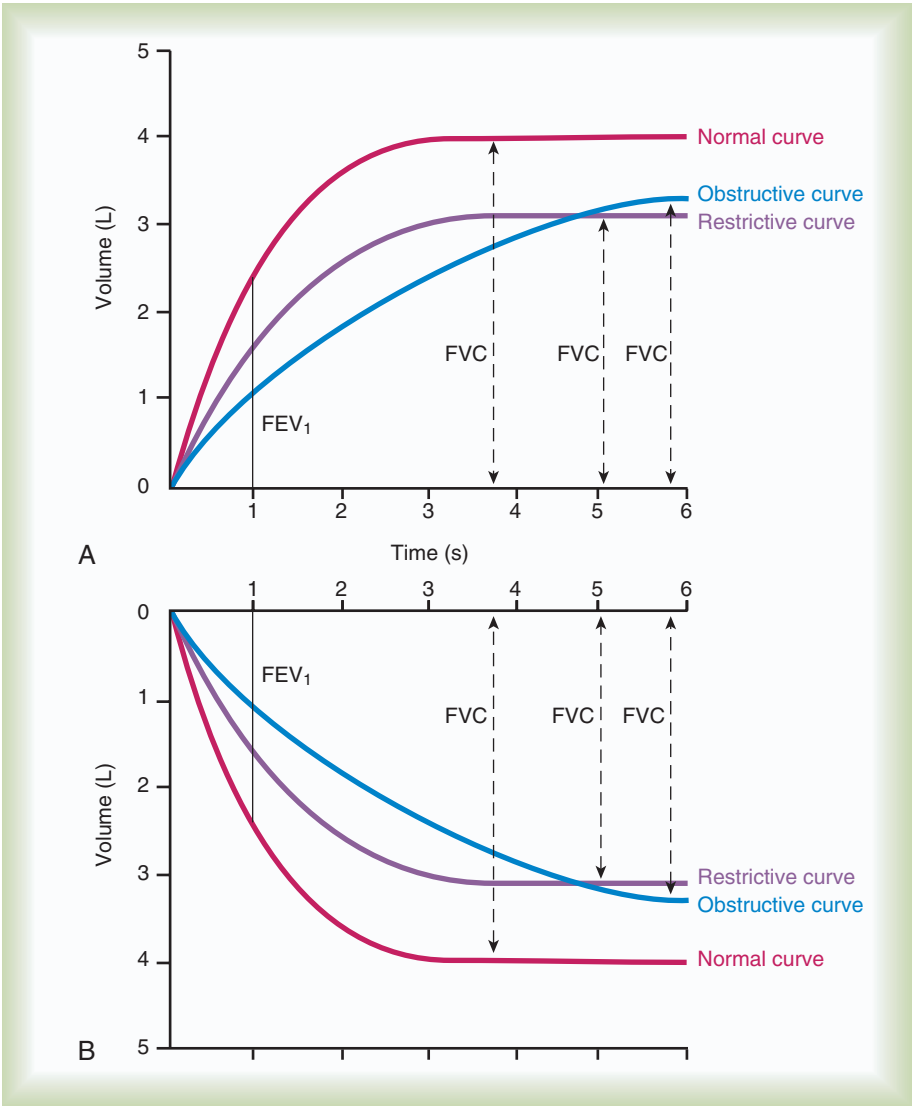

Fig. 20.5 Forced Vital Capacity *(FVC)* Curves Comparing Normal, Obstructive, and Restrictive Disorders. (A) Curves as they appear on commonly available spirometers with tracings beginning at the bottom left corner. (B) The same curves as they appear on some spirometers with tracings beginning at the upper left corner. *FEV_1*, Forced vital capacity in 1 second.

with obstructive or restrictive impairment. For patients with airway obstruction, FEV_1 measures the general severity of airway obstruction. For patients with restrictive impairment, FEV_1 may be reduced when the patient's VC is smaller than the predicted FEV_1.

The shape of the flow-volume loop ratio provides additional information about upper airway obstruction. Compared with the normal flow-volume loop, a fixed upper airway obstruction such as that may occur with tracheal stenosis often produces a curve that appears box-shaped (other descriptive terms used colloquially to describe this shape are "flattening" or "pancaking" of the curve). In Fig. 20.7a, both expiratory and inspiratory flows are decreased and limited by the solid obstruction; variable upper airway obstructions produce two different shapes depending on the site of the obstruction. Because the intra-airway pressure during a forced inspiration is less than atmospheric outside the thorax, a variable extrathoracic upper airway obstruction, such as that occurs with thyroid enlargement or weakening of the trachea above the thoracic inlet, limits inspiratory flow and "flattens" the inspiratory portion of the curve (see Fig. 20.7b). Variable intrathoracic obstruction, caused by tracheal tumor, would give the opposite effects and result in "flattening" of the expiratory portion of the curve (see Fig. 20.7c).

Similar to other PFT measurements, normal values of MVV are based on gender, age, and height. MVV is reduced in patients with moderate and severe airway obstruction. A measured value less than 75% of predicted is significant. The normal for men is approximately 160 to 180 L/min; it is slightly lower in women. In restrictive lung disease, MVV may be normal or only slightly reduced. Respiratory muscle strength is a primary determinant of MVV in patients with interstitial lung disease and an important determinant in patients with chronic obstructive pulmonary disease (COPD). Undernourished patients also may have a reduced MVV.

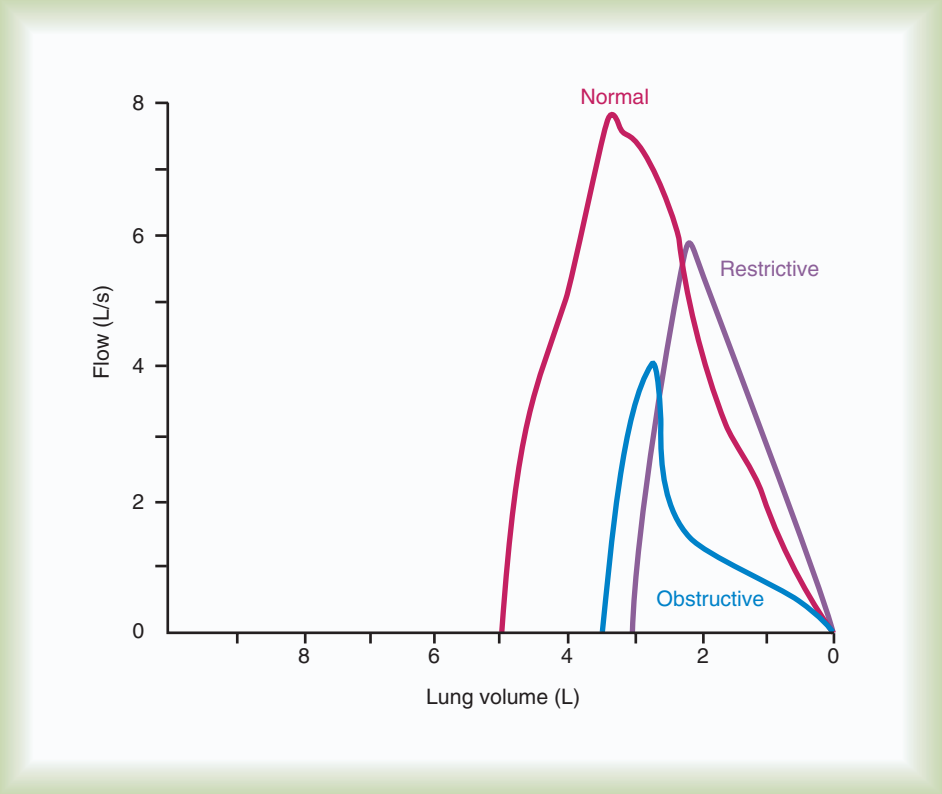

Fig. 20.6 Maximal expiratory flow volume curves of normal, obstructive, and restrictive patterns.

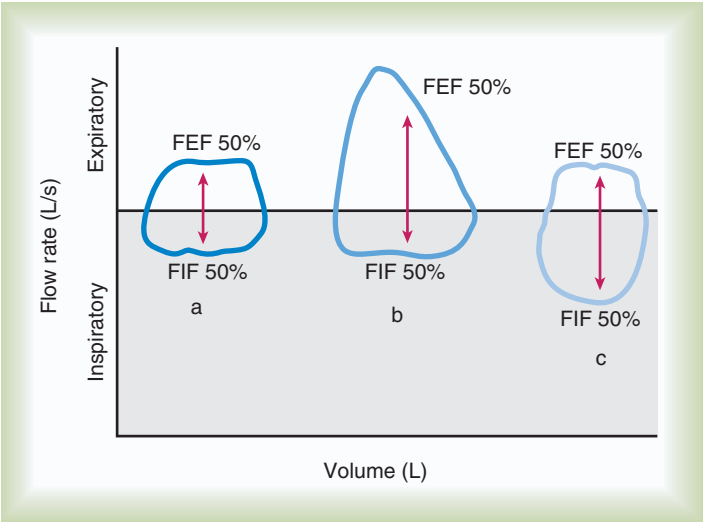

Fig. 20.7 Flow-volume loops of fixed upper airway obstruction *(a)*, variable extrathoracic upper airway obstruction *(b)*, and variable intrathoracic upper airway obstruction *(c)*. *FEF,* Forced expiratory force; *FIF,* forced inspiratory flow.

RULE OF THUMB Reduced FEV_1/FVC ratio is diagnostic of airway obstruction. Reduced total lung capacity is the sign of restriction.

Reversibility of Airway Obstruction

Based on the initial results of baseline spirometry, additional testing of pulmonary mechanics is often desirable. If the baseline test indicates airway obstruction, determining the reversibility of the obstruction is indicated. RTs also use the concept of reversibility when evaluating routine therapy by performing spirometry before and after therapy. In the laboratory, the FVC maneuver is often repeated at an appropriate waiting time of at least 15 minutes after the patient has received a bronchodilator administered by small volume nebulizer or metered dose inhaler. This laboratory protocol is commonly known as *spirometry before and after bronchodilator*. Reversibility of the airway obstruction indicates effective therapy. Although improvement in other measurements of pulmonary function is sometimes used, reversibility is defined by the ATS guidelines as an increase in either FEV_1 or FVC ≥12% of control *and* ≥200 mL.[6] Change is determined using the percent change formula (e.g., for FEV_1):

$$\%\,\text{Improvement} = \frac{\text{Post}FEV_1 - \text{Pre}FEV_1}{\text{Pre}FEV_1} \times 100$$

When interpreting test-to-test differences in the FVC, caution must be observed to compare FVC maneuvers with similar expiratory times. Longer expiratory times in patients who are obstructed can cause the FVC to be larger, creating the false impression that reversibility of airflow obstruction has occurred when the difference is due simply to a longer duration of exhalation.

RULE OF THUMB An increase in either FEV_1 or FVC ≥12% after bronchodilator administration generally indicates reversibility of airway obstruction.

Bronchoprovocation

When the patient's history suggests episodic symptoms of hyperreactive airways and airway obstruction, such as seasonal

or exercise-induced wheezing, and the results of baseline spirometry are normal, performing a bronchial provocation may be indicated.[9, 10] Bronchial provocation testing uses an agent to stimulate a hyperreactive airway response and to bring out airway obstruction. Although several types of provocations are possible, such as inhaling histamine or cold air or exercising, provoking a hyperreactive airway response by inhaling a cholinergic substance known as methacholine is the most popular technique with the most predictable results. The procedure usually begins with the patient inhaling a normal saline aerosol and then repeating the FVC maneuver. Some very sensitive patients exhibit hyperreactive airways with saline alone; a positive response to saline is defined as a decrease in FEV_1 of 10% or greater. The methacholine provocation protocol systematically exposes the patient to increasing doses (concentrations) of methacholine. Usually starting with a low dose of 0.03 mg/mL, patients inhale the methacholine aerosol and then repeat the FVC maneuver. A *positive response* to methacholine is defined as a decrease in FEV_1 of 20% or greater (another example of percent change). If a positive response does not occur with the initial concentration of methacholine, the methacholine dose is doubled to 0.06 mg/mL, and the FVC maneuver is repeated. The process of "double-dosing" and performing FVC maneuvers continues until there is a positive response or until the full dose, 16 mg/mL, is given. If a positive response occurs, treatment with a fast-acting bronchodilator is indicated, and sometimes administering O_2 is helpful. The final test report should include the lowest concentration of methacholine that caused the 20% decrease in FEV_1 in the form of $PD\%FEV_1$. For example, $PD_{22}FEV_1 = 4$ mg/mL indicates that the provocation dose of 4 mg/mL resulted in a 22% decrease in FEV_1.[10, 11]

It should be noted that given the nature and goal of this test to induce bronchospasm and that bronchospasm often occurs in patients with preexisting lung disease, certain precautions need to be taken when performing a methacholine challenge. Most notably, it is imperative that an evidence-based protocol be in place to address patients who respond to the test adversely by developing status asthmaticus or other life-threatening conditions. In general, the protocol should include the availability of fast-acting bronchodilators, a code/crash cart, and healthcare professionals who are trained in Advance Cardiac Life Support. Some laboratories require that the patient's baseline FEV_1 value exceed a certain threshold (e.g., 40% predicted) to perform a methacholine challenge test.

Lung Volumes and Capacities

The so-called lung compartments consist of four lung volumes and four lung capacities. A lung capacity consists of two or more lung volumes. The lung volumes are **tidal volume (VT)**, **inspiratory reserve volume** (IRV), **expiratory reserve volume (ERV)**, and **residual volume (RV)**. The four lung capacities are (1) TLC, (2) IC, (3) FRC, and (4) VC. These volumes and capacities are shown in Fig. 20.8. The lung volumes that can be measured directly with a spirometer or pneumotachometer include V_T, IC, IRV, ERV, and VC. Because the RV cannot be exhaled, the RV, FRC, and TLC must be measured using indirect methods.

MINI CLINI

Why Are Functional Residual Capacity and Residual Volume Increased in Emphysema?

Problem

In the advanced stages of pulmonary emphysema, FRC and RV are increased; in addition, VC is often decreased. Why do these changes occur?

Solution

When the ventilatory muscles relax, the opposing forces of lung recoil and chest wall expansion determine the size of FRC. Emphysema is characterized by a destruction of elastic tissue in the lung, which causes a lower lung recoil force. When lung recoil forces decrease, as in emphysema, chest wall expansion forces predominate and the chest wall expands outward, pulling the lung with it. As the lung stretches to a larger volume, its recoil force increases, and eventually equilibrium is reestablished between the lung and chest wall. This new equilibrium occurs at an increased lung volume, so FRC is increased. RV is increased in emphysema because VC is decreased owing to small airway obstruction. When a person with emphysema tries to exhale completely, the bronchioles collapse, trapping air in the lungs and increasing RV. Increased FRC is called *hyperinflation,* and increased RV is called *air trapping.*

Knowing TLC is necessary to identify patients with a restrictive pattern of pulmonary impairment. Measuring FRC is necessary to quantify hyperinflation, which may be associated with obstructive impairment such as with asthma and emphysema. Calculating RV is necessary to gauge any air trapping present in these and other obstructive conditions. Measurements of V_T, IC, ERV, IRV, and VC may be used in calculations of TLC or be useful to clinicians considering weaning parameters such as the rapid-shallow-breathing index (f/V_T) or inspiration goals of hyperinflation therapy. Standards for measuring lung volumes and capacities were initially published in 2005[5]; these standards focus primarily on the techniques to measure FRC. Following the measurement of FRC, measurements of ERV and VC enable calculation of TLC according to the formulas:

$$TLC = FRC + IC$$

or

$$TLC = (FRC - ERV) + VC$$

Values Measured During Spirometry

The V_T is measured directly from a spirogram (see Fig. 20.8). For the purposes of ensuring test validity and standardization, the patient should be in a sitting or reclining position and wearing a nose clip. It sometimes takes the patient 1 to 2 minutes to be at rest and become accustomed to the nose clip and mouthpiece. The patient breathes through a tight-fitting mouthpiece until a normal, rhythmic breathing pattern is established. Because V_T varies normally from breath to breath, an average V_T is a more reliable measurement. In the laboratory, an average V_T sometimes is measured during 3 minutes of quiet breathing while the spirometer records volumes and graphs volume and time. At the bedside, an average V_T usually is measured over 1 minute; the patient breathes normally into a spirometer that stores in memory each volume exhaled for 1 minute and computes an average. An alternative approach is to measure the total volume of air exhaled

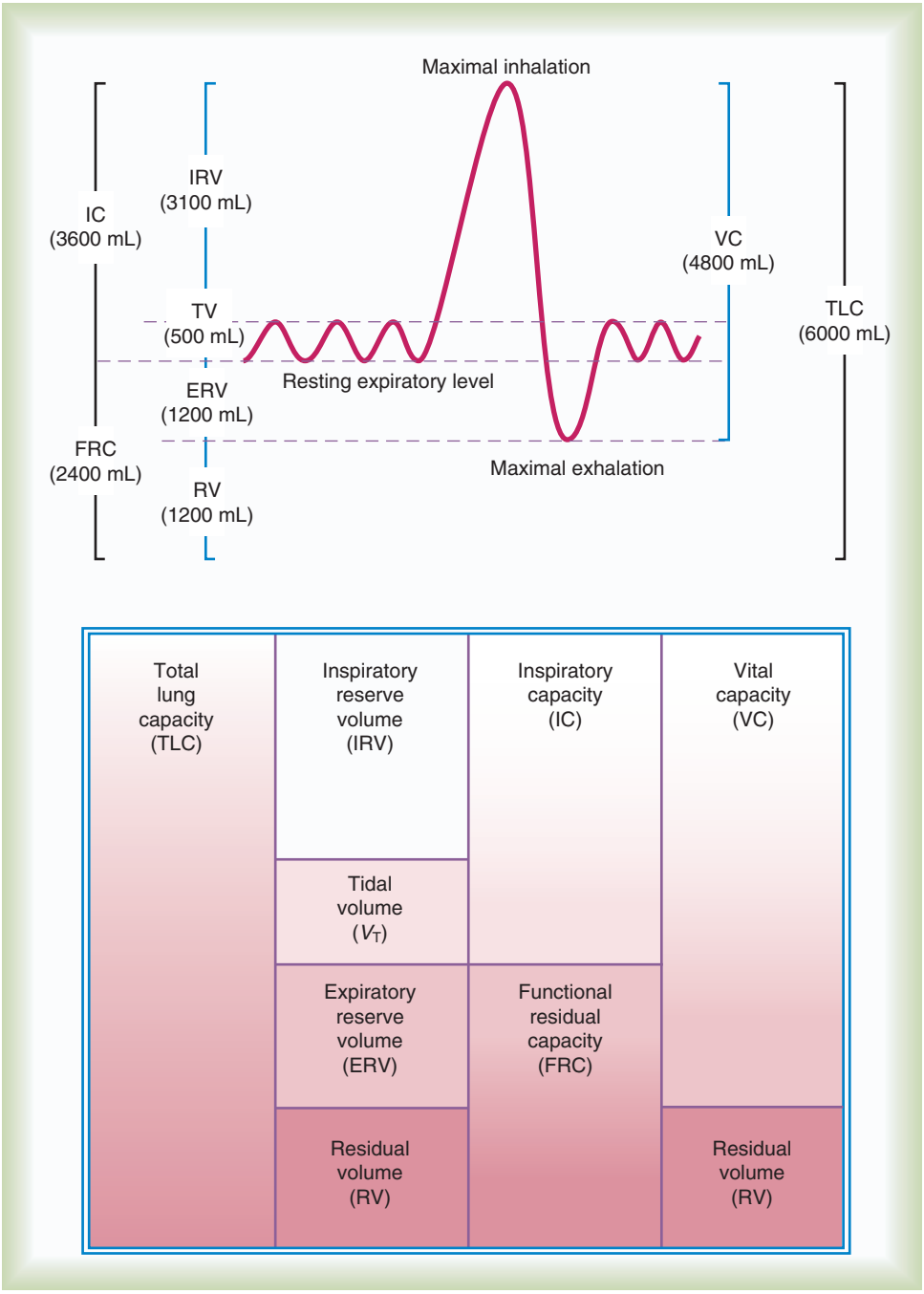

Fig. 20.8 Lung Volumes and Capacities. Volumes listed are average normal values for a young, healthy adult man.

for 1 minute known as $\dot{V}_E$ and divide by the breathing frequency (f) counted during the same period. The following formula can be used to calculate the V_T:

$$V_T = (\dot{V}_E \div f).$$

The IC is also measured directly from a spirogram. The patient is asked to inhale maximally from the resting FRC at the end of a normal effortless exhalation. To ensure validity, a consistent resting expiratory level should be obvious on the spirogram before inhaling. To ensure reliability, the IC should be measured at least twice, and the two largest measurements should agree within 5%. Because the definition of IC is the maximal volume inhaled, the largest measurement is the patient's IC.

The ERV is measured directly from the spirogram (see Fig. 20.8). The patient is asked to breathe normally for a few breaths and then exhale maximally. The ERV is the volume of air exhaled between the resting expiratory level (FRC) and the maximal exhalation level on the spirogram. To ensure validity, a consistent resting expiratory level should be obvious on the spirogram before exhaling maximally. To ensure reliability, like many other volumes and capacities, the ERV should be measured at least twice and the two largest measurements should agree within

5%. Because the definition of ERV is the maximal volume exhaled, the largest measurement is the patient's ERV.

The VC is the most commonly measured lung volume. There are several methods of measuring the VC. The VC can be measured during inspiration or during a slow prolonged expiration when air trapping is of concern. To measure the VC during inspiration, the patient exhales maximally and then inhales as deeply as possible. The volume of the maximal inspiration is called the inspiratory VC. To measure the VC during expiration, the patient inhales maximally and then exhales maximally, taking all the time necessary to exhale completely. When exhalation is slow, the exhaled volume is called the slow VC. An alternative method is to measure the IC and the ERV and add these volumes together for a "combined" VC, but this method should be reserved only for patients who cannot otherwise execute the VC. The VC also is measured when air is exhaled forcefully and as rapidly as possible. The VC measured using this technique is called the FVC, as previously mentioned in this chapter.

Values Not Measured During Spirometry

Because the RV cannot be exhaled (i.e., RV is by definition the air left in the lung after maximal exhalation), RV, FRC, and TLC cannot be measured directly with a spirometer or pneumotachometer. There are three indirect techniques to measure these lung volumes: (1) helium dilution, (2) nitrogen (N_2) washout, and (3) body plethysmography. The He dilution and N_2 washout techniques measure whatever gas is in the lungs at the beginning of the test, if the gas is in contact with unobstructed airways. The body plethysmographic technique measures all the gas in the thorax at the resting expiratory volume. Because the plethysmographic technique measures all gas in the thorax, including gas that is trapped distal to obstructed airways or gas in the pleural space, the lung volume measured by this technique is called the **thoracic gas volume** (TGV) (V_{TG}, or FRC_{Pleth}). In healthy individuals, TGV is identical to FRC measured by both the gas dilution and washout techniques. However, in patients with obstructive lung disease with gas trapping, TGV is often larger than FRC measured by other methods. TGV is also more complex and cumbersome to perform. Therefore, unless specifically requested by a physician, He dilution or N_2 washout methods are routinely used. The latter two allow measurements of either FRC or TLC. Once one of them is measured, the other can be calculated using the previous formulas. For simplicity, we will describe as follows only the maneuvers used to measure FRC.

Helium Dilution

The helium dilution technique for measuring lung volumes uses a closed, rebreathing circuit (Fig. 20.9).[5] This technique is based on the assumptions that the patient has no He in his or her lungs and that an equilibration of He can occur between the spirometer and the lungs. First, volume (V1) and concentration (C1) of He are measured at the beginning of the test. Next, the valve is turned to connect the patient to the breathing circuit, usually at the resting expiratory level of the FRC. The patient is connected to the He-air mixture, and the concentration of He is diluted slowly by the patient's lung volume. Wearing nose clips, the patient breathes normally in the closed circuit. Exhaled CO_2 is absorbed with soda lime, and O_2 is added at a rate equal to the patient's O_2 consumption. A constant volume is maintained to ensure accurate He concentration measurements. The patient rebreathes the gas in the system until equilibrium of He concentration is established. In healthy patients and patients with a small FRC, equilibration occurs in 2 to 5 minutes. Patients with obstructive lung disease may require 20 minutes to equilibrate because of slow gas mixing in the lungs. The He dilution time

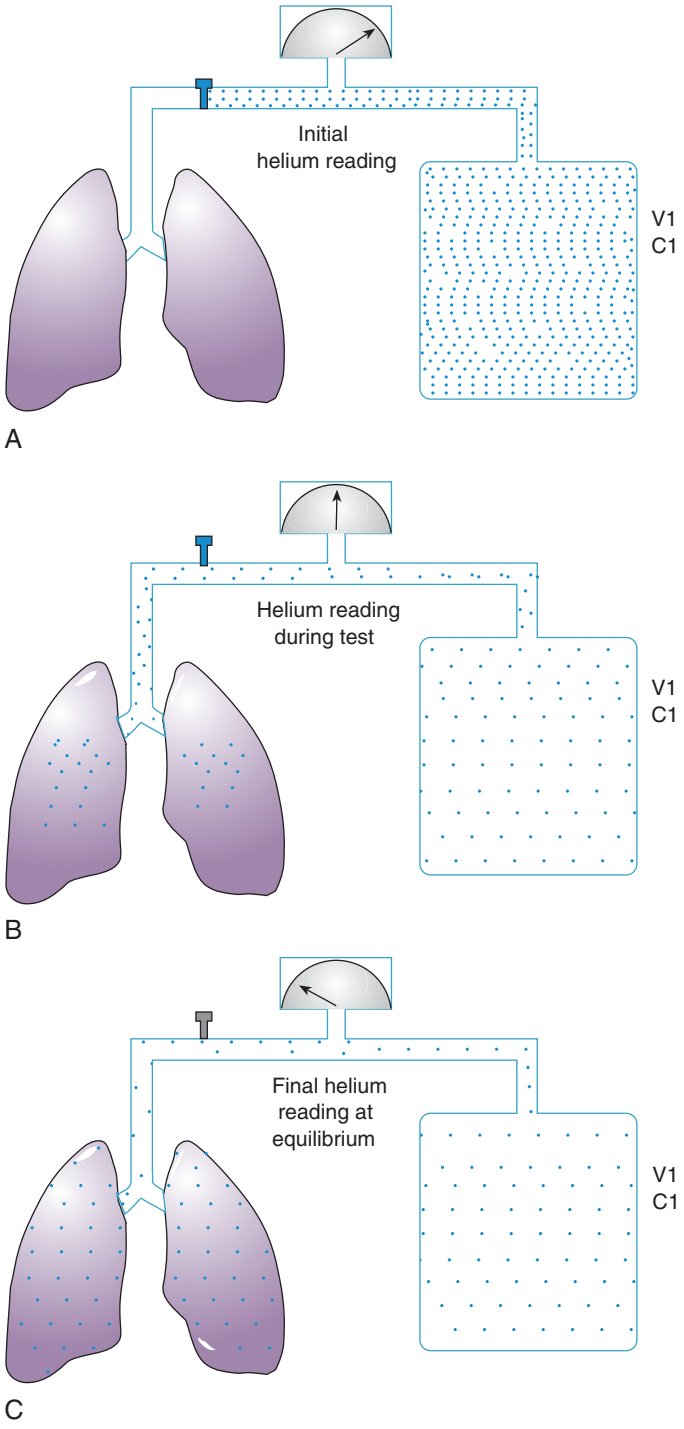

Fig. 20.9 Helium Dilution Method for Measuring Functional Residual Capacity. (A) Initial He readings, He volume *(V1)* and concentration *(C1)*, lung volume is at functional residual capacity. (B) He reading during test. (C) Final He concentration reading (C2) at equilibrium. See text for details.

or the duration of the test gives a reasonable indication of the distribution of ventilation.

For FRC to be calculated using the He dilution technique, several observations must be made: V1 and C1 (see earlier discussion), before the patient is connected to the breathing circuit; the final He concentration (C2) after He equilibrium between the spirometer and patient is established, the spirometer temperature, and the time necessary for He equilibration to occur. If there was no absorption of the He across the pulmonary capillaries,

$$V1 \times C1 = V2 \times C2$$

where V2 is the volume of the He at the end of the test. After measuring V1, C1, and C2, V2 is calculated:

$$FRC = V2 - V1$$

(see Fig. 20.9).

Corrections for temperature and He absorption are normally applied. All lung volumes and capacities must be reported under BTPS conditions. Volumes measured by spirometers are at ambient temperature, pressure, and saturated (ATPS) conditions and must be adjusted for the temperature difference between the spirometer and the patient's body temperature. This ATPS to BTPS adjustment can increase volumes 5% to 10%, and the difference is large enough to invalidate the test results, unless the correction is made. Although He is an inert gas with a negligible solubility in plasma, it is assumed that a small amount of He diffuses across the alveolar-capillary membrane. To account for the loss, 30 mL of BTPS-corrected volume is subtracted for each minute of He breathing, up to 200 mL for a 7-minute test. Once these corrections are made, TLC can be calculated using spirometry data.

Nitrogen Washout

The nitrogen washout technique uses a nonrebreathing or open circuit (Fig. 20.10).[5] The technique is based on the assumptions that the N_2 concentration in the lungs is 78% and in equilibrium with the atmosphere, that the patient inhales 100% O_2, and that the O_2 replaces all of the N_2 in the lungs. Similar to the He

MINI CLINI

Helium Dilution

Problem

During a helium dilution test, the following measurements are made:

	Start	End
He chamber volume	6 L	6 L
He concentration	12%	8%
O_2 concentration	30%	26%

Calculate functional residual capacity (FRC).

Solution

Since Helium is an inert gas that does not get absorbed in the lungs, it is assumed that we have the same amount of it at the beginning and the end of the test. The reason for the difference in its concentration is the fact that is now "diluted" in a larger volume (chamber + FRC).

$$V1 \times C1 = V2 \times C2$$

where V1 is 6 L, C1 is 12%, V2 is V1 + FRC, and C2 is 8% (see Fig. 20.9). Entering the values and solving for FRC gives the result: 3 L. Note that the similar calculation for O_2 would give a much different result, because O_2 is picked up by the lungs and its total content would be different at the beginning and the end of the test.

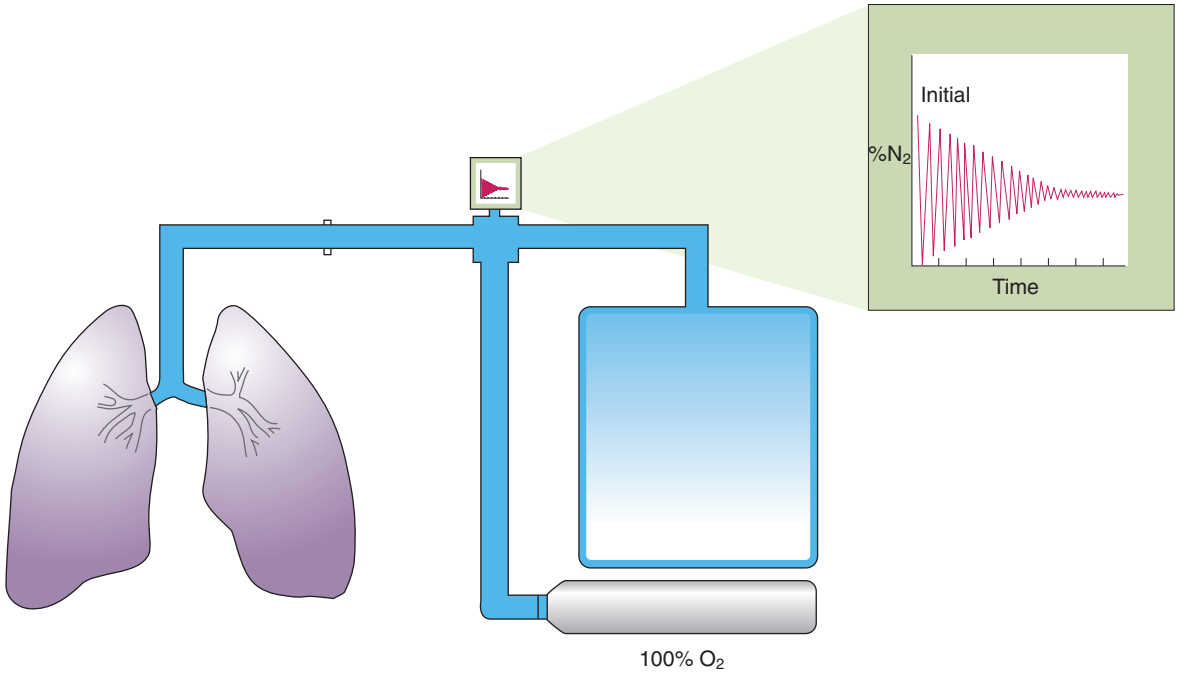

Fig. 20.10 Nitrogen washout method for measuring functional residual capacity, residual volume, and total lung capacity.

dilution technique, the patient is connected to the system at FRC. The patient's exhaled gas is monitored, and its volume and N_2 percentage are measured.

In general, two types of circuits are used to measure lung volumes with this technique. In one type of circuit, all of the exhaled gases are collected in a large container, where the volume and concentration of N_2 are measured. In the second type of circuit, the volume and concentration of each exhaled breath are measured separately and stored in a memory; the sum of the volumes and the weighted average of the N_2 concentration are calculated by a computer.

Wearing nose clips, the patient breathes 100% O_2 until nearly all of the N_2 has been washed out of the lungs, leaving less than 1.5% N_2 in the lungs. When the peak exhaled concentration of N_2 is less than 1.5%, the patient exhales completely, and the fractional concentration of alveolar N_2 (F_AN_2) is noted. Similar to the He technique, the time it takes to wash out the N_2 is approximately 2 to 5 minutes in healthy individuals and longer in patients with obstructive lung disease. The test must occur in a leak-proof circuit because the presence of any air increases the measured N_2 percentages and results in grossly elevated measurements of lung volume.

For FRC to be calculated by the N_2 washout technique, several measurements must be made: the total volume of gas exhaled during the test (V_E), the fractional concentration of exhaled N_2 in the total gas volume (F_EN_2), the fractional concentration of N_2 in the alveoli at the end of the test (F_AN_2), and the spirometer temperature. FRC can be calculated with the following equation:

$$FRC = \frac{V_E \times F_EN_2}{0.78 - F_AN_2}$$

The calculated FRC must be adjusted for the temperature difference between the spirometer and the patient's body temperature using the BTPS correction factor. During the test, some N_2 from the plasma and body tissues is usually excreted and exhaled with lung N_2. For this reason, another correction is needed, using duration of the test and the weight of the patient. Note that the computer interfaces used today in pulmonary function labs eliminate the need to manually calculate such corrections and essentially all other mathematical calculations used in PFTs.

Plethysmography

The plethysmography technique applies Boyle's law and uses measurements of volume and pressure changes to determine lung volume, assuming temperature is constant.[5] The plethysmography technique measures the volume of all compressible gas in the thorax, including gas trapped behind airway obstructions or in the pleural space. Gas in the abdomen also may be included in the measurement. The whole-body plethysmograph consists of a sealed chamber in which the patient sits (Fig. 20.11). Pressure transducers (electronic manometers) measure pressure at the mouth and in the chamber. An electronically controlled shutter near the mouthpiece allows the airway to be occluded periodically, measuring airway pressure changes under conditions of no airflow. Without airflow, pressure changes measured at the mouth are pressure changes in the alveoli. According to

MINI CLINI

Nitrogen Washout

Problem

The nitrogen washout method is used to measure FRC in a patient. At the end of a normal expiration, the patient is connected to the system and he begins to breathe a 100% oxygen from a bag. He exhales (via a one-way valve) into a test chamber. After 7 min the procedure is terminated and the volume and nitrogen concentration of the expired air bag are measured. The results are as follows:

Expired volume	100 L
N_2 concentration in test chamber	3.5%
N_2 concentration in final breath	1.5%

Calculate the patient's FRC.

Solution

FRC can be calculated using the following formula and entering known values into it.

$$FRC = \frac{V_E \times F_EN_2}{0.78 - F_AN_2}$$

Entering the given values:

$$V_E = 100\ L,\ F_EN_2 = 0.035,\ F_AN_2 = 0.015,$$

$$FRC = 4.57\ L$$

Note: FRC is elevated, suggestive of air hyperinflation. Increased test time of 7 min, instead of usual 2–5 min, also suggests obstructive pulmonary disease (see text for explanation).

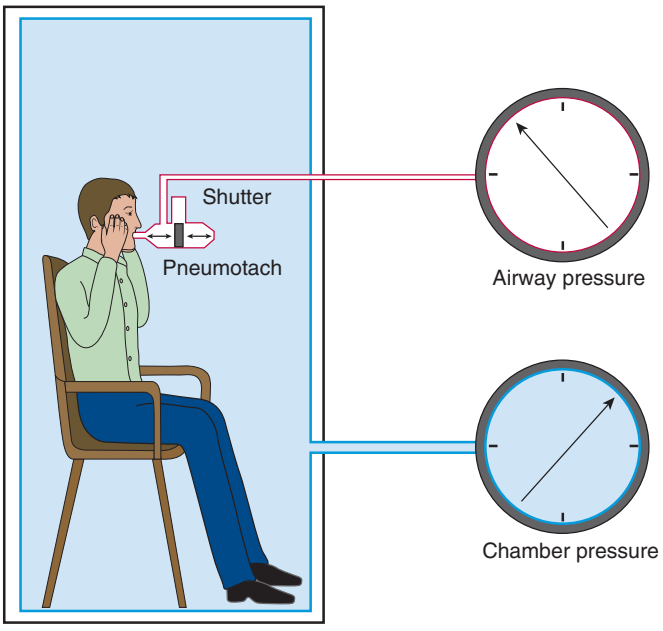

Fig. 20.11 Body Plethysmography Method for Measuring Lung Volumes. *V* is the change in gas volume in the lungs, as sensed by the chamber pressure manometer. *P* is the change in pressure produced by the respiratory efforts of breathing against the shutter, as sensed by the airway pressure manometer.

Boyle's law ($V \times P = k$), when temperature is constant, volume changes in the thorax create volume changes in the chamber, which are reflected by pressure changes in the chamber. When measurement of TGV is being done, the patient sits in the chamber and initially breathes normal tidal volumes through the mouthpiece. When the patient is near FRC, the shutter is closed at end expiration for 2 to 3 seconds. The patient holds his or her cheeks and performs gentle panting at 1 Hz (60 times per minute) or one pant per second. During panting, changes in airway pressure (ΔP) and changes in chamber volume (ΔV) are measured. Because the panting maneuver occurs with small pressure changes around barometric pressure, the simplified equation used to calculate TGV is:

$$TGV = P_B \times (\Delta V \div \Delta P)$$

where P_B is the barometric pressure in cm H_2O.

A series of three to five panting maneuvers should be performed. After panting, the patient should exhale completely to record ERV and then inhale maximally to record the inspiratory VC.

Because the body plethysmographic method of measuring FRC actually measures TGV, the value obtained for some patients may be larger than values resulting from either the He dilution or N_2 washout techniques. Such a difference occurs whenever there is gas in the thorax that is not in communication with patent airways, as might be the case in patients with pneumothorax, pneumomediastinum, or emphysema. Assuming that TGV actually represents FRC, calculations can be made for TLC and RV, similar to He dilution or N_2 washout methods.

RULE OF THUMB Plethysmography measures the entire chest volume, whereas helium dilution and nitrogen washout methods measure the volume of lung that is connected with outside air. For this reason, plethysmography may give more accurate FRC measurement in patients with bullous lung disease, such as emphysema.

Interpretation

Changes in lung volumes and capacities are generally consistent with the pattern of impairment. TLC, FRC, and RV increase with obstructive lung diseases and decrease with restrictive impairment. By definition, restrictive disease is present only when the TLC is decreased. Some lung volumes provide valuable diagnostic information. For example, TLC is always reduced in restrictive lung disease such as pulmonary fibrosis, unless obstruction and restriction occur together (because obstruction may be associated with increased TLC and fibrosis with a decreasing TLC, causing offsetting differences). Such a pattern may occur in an entity called "combined pulmonary fibrosis and emphysema." When obstruction and restriction occur together, the TLC may be a less sensitive measure of the restrictive impairment. Other volumes and capacities may remain normal with mild obstructive or restrictive disease. The pattern of lung volume changes and the proportion of FRC and RV to TLC are also important.

Normal values for lung volumes. The normal V_T is approximately 500 to 700 mL for an average healthy adult. In the normal population, great variation of tidal volumes and measurements beyond the normal range do not necessarily indicate a disease process. Conversely, normal V_T is often observed in both restrictive and obstructive lung diseases. V_T alone is not useful in characterizing whether there is restrictive or obstructive disease.

The normal IC is approximately 3.6 L, with a significant variation in the normal population. IC may be normal or reduced in restrictive and obstructive lung diseases. A reduction of IC occurs in restrictive lung diseases because the patient's inhaled volume is reduced and there is a reduction in TLC. In mild obstructive lung diseases, IC is usually normal. In moderate and severe obstructive diseases, IC can be reduced because the resting expiratory level of FRC has increased owing to hyperinflation of the lungs. An increase in IC may occur when the patient inhales from below the resting expiratory level when the measurement is performed; athletes and musicians who play wind instruments may have increased inspiratory capacities. RTs use the measurement of IC in clinical protocols to decide between methods of lung expansion therapy (see Chapter 43).

IRV is not commonly measured. Similar to V_T and IC, IRV can be normal in both restrictive and obstructive diseases and is not a useful diagnostic measurement. The normal value for IRV for an adult is approximately 3.1 L.

The normal adult ERV is approximately 1.2 L and represents approximately 20% to 25% of the VC. It can be either normal or reduced in obstructive and restrictive lung diseases. ERV is subtracted from FRC to calculate RV.

The normal value of the VC is 4.8 L and represents approximately 80% of TLC. Normal values for VC can vary significantly depending on age, gender, height, and ethnicity. A reduction of VC occurs in restrictive lung diseases because the patient's inhaled volume is reduced and there is a reduction in TLC. In mild obstructive lung diseases, the slow VC is usually normal if the patient exhales leisurely and has had enough time to exhale completely or if the VC is measured during inspiration. Measurements made from FVC provide valuable data for pulmonary mechanics and are often reduced in patients with obstructive disease.

RV, FRC, and TLC are the most important measurements of lung volumes. For adults, the normal TLC is approximately 6.0 L; RV is approximately 1.2 L and represents approximately 20% of TLC; and FRC is approximately 2.4 L, which represents approximately 40% of the TLC. RV and FRC are usually enlarged in acute and chronic obstructive lung diseases because of hyperinflation and air trapping (Fig. 20.12). TLC also may be increased in COPD. By definition, TLC is always reduced in restrictive lung diseases because of a loss of lung volume; RV and FRC are often reduced proportionately. Certain acute disorders, such as pulmonary edema, atelectasis, and consolidation, also cause a reduction of TLC and FRC.

Diffusing Capacity

The third major category of pulmonary function testing is measuring the ability of the lungs to transfer gases across the alveolar-capillary membrane. As discussed in Chapter 12, the diffusion of gases across a sheet of membrane depends on various factors; the partial pressure difference across the membrane, the

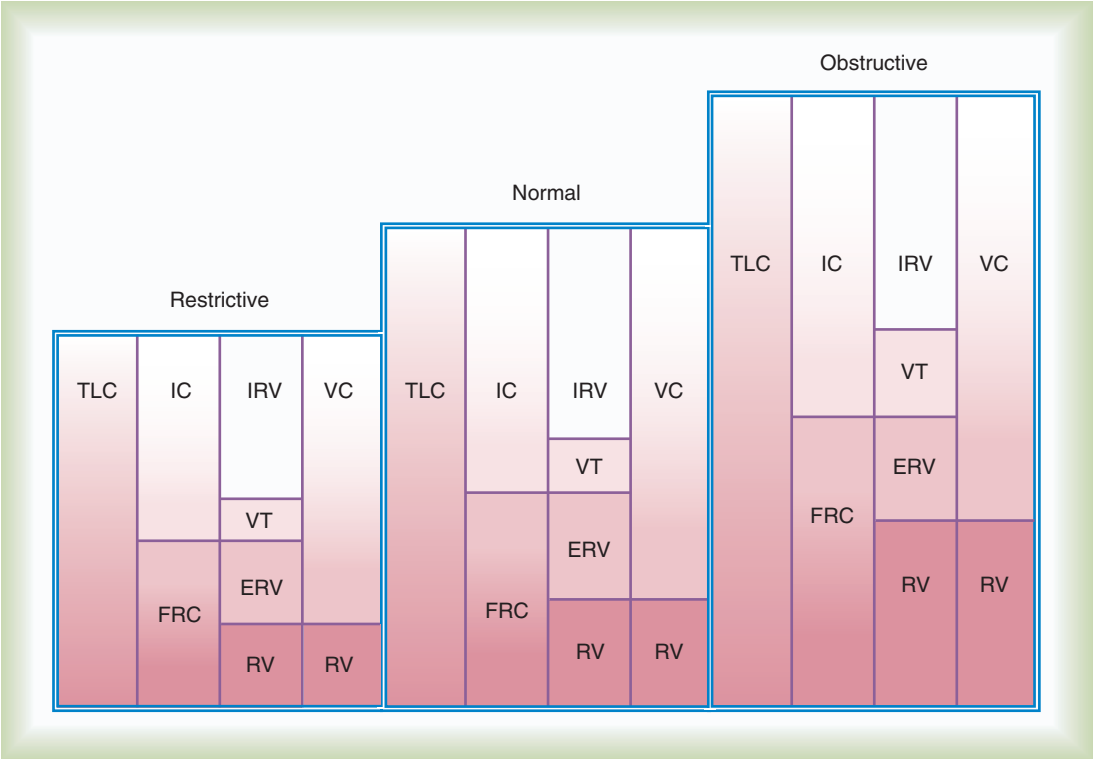

Fig. 20.12 Changes in lung volumes and capacities with pulmonary disease. *ERV,* Expiratory reserve volume; *FRC,* functional residual capacity; *IC,* inspiratory capacity; *IRV,* inspiratory reserve volume; *RV,* residual volume; *TLC,* total lung capacity; *VC,* vital capacity; *VT,* tidal volume.

characteristics of the gas in question, and the characteristics of the membrane itself:

$$V_{gas} = D_L \times (P_1 - P_2)$$

V_{gas} = Amount of the gas transferred into the lungs
P_1 = Partial pressure of the gas in the alveolus
P_2 = Partial pressure of the gas in the pulmonary capillary

Carbon monoxide (CO) is the gas normally used to measure the diffusing capacity (DL). The **diffusing capacity of the lung for carbon monoxide** (DLCO) is expressed in mL/min/mm Hg under standard temperature and pressure and dry conditions. CO is used as the transfer gas because CO is similar to O_2 in important ways. CO and O_2 have similar molecular weights and solubility coefficients. Similar to O_2, CO also chemically combines with hemoglobin (Hb). CO has a very high affinity for Hb and diffuses rapidly into the pulmonary blood, keeping the *pulmonary capillary partial pressure of CO* near zero. Consequently, the formula for the DLCO calculation can be rewritten as follows (replacing P_1 with P_ACO and P_2 with zero):

$$DL_{CO} = \frac{\dot{V}_{CO}}{P_ACO}$$

where $\dot{V}_{CO}$ is the amount of CO taken up by the lungs and P_ACO is the alveolar partial pressure of CO during the test.

Single-Breath Technique

There are several techniques for measuring the DL of the lung for CO, including steady-state, intrabreath, and rebreathing techniques, but the single-breath method (DLCO-SB) is the most common measurement technique because it is quick and reproducible. Standards for measuring DL of the lung and the reference values were updated in 2017.[2,8] During the single-breath method, the patient exhales completely to RV, rapidly inspires to TLC a volume of air containing small concentration of CO and He, maintains breath holding for 10 seconds, and then exhales at least 1 L rapidly. Helium is added to the inhaled gas mixture to help with the estimation of effective lung volume, as well as alveolar CO concentration (F_ACO). Note that F_ACO is different from the inhaled CO concentration because dilution by RV and this corrected value should be used in calculation of P_ACO. The dilution of CO is proportional to the dilution of He and can be calculated using inhaled (F_IHe) and exhaled (F_EHe) He concentrations. A sample of exhaled alveolar gas is collected and analyzed for expired CO (F_ECO). The **effective total lung capacity** (or alveolar volume, V_A) can be similarly calculated using measured VC and inhaled and exhaled He concentrations. The V_A is necessary to calculate $\dot{V}_{CO}$, and it is sometimes used in the determination of the DL of the lung-to-alveolar volume ratio ($DLCO/V_A$, discussed later). The total time of the test (t) is recorded and used in ultimate calculation of DLCO. To regulate the breath holding period, some measuring systems close the mouthpiece with a timed shutter. The suitable breathing pattern requires patient cooperation and coordination; some patients benefit from a timer as a visual aid.

It is important to note that the rate of CO transfer across the membrane is not uniform throughout the test. When a bolus of CO gas is inhaled, the rate of gas diffusion declines logarithmically with time, meaning that the rate of gas transfer at the

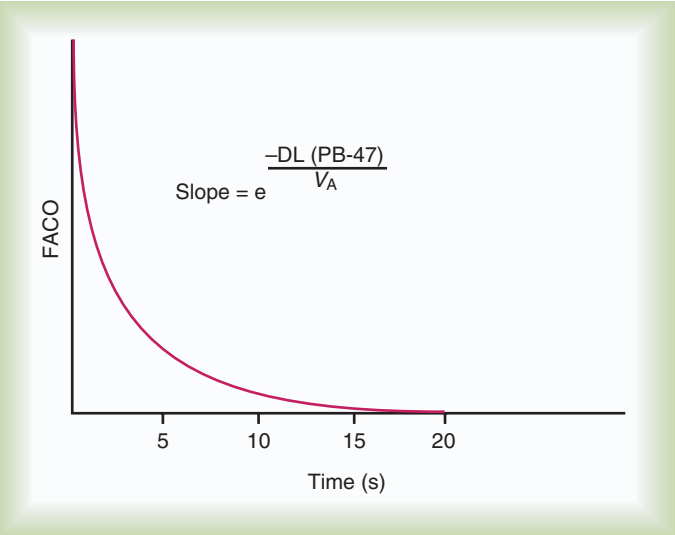

Fig. 20.13 Concentration of alveolar carbon monoxide after a single breath to total lung capacity.

beginning of the test (high CO concentration) is much greater than at the end of the test (low CO concentration). The single-breath method (DLCO-SB) is based on the diffusion decay curve described by Forster and colleagues (Fig. 20.13). The final formula for DLCO calculation incorporates all measurements used to calculate $\dot{V}_{CO}$ and P_ACO, as well as the correction for nonlinearity of CO transfer.[2]

The reliability of the DLCO is based on repeatability of the test. At least 4 minutes should be allowed between tests to allow an adequate elimination of CO from the lungs. In patients with obstructive airway disease, a longer period (e.g., 10 min) may be necessary. The actual DLCO reported should be the mean of two acceptable tests. A grading system (grades A to F), similar to other PFT (described earlier in this chapter) has been developed.[1,2]

Interpretation

Normal values for the DLCO using the single-breath technique are based primarily on a patient's age, height, and gender. A typical normal value for a 20-year-old healthy man is 40 mL/min/mm Hg.[2] Factors known to affect test results should be controlled or standardized; these include body position, activity, barometric pressure, P_AO_2, Hb and carboxyhemoglobin (COHb) levels, and pulmonary blood volume. To focus the test on diffusion through the alveolar-capillary membrane, the patient should be tested at rest in a seated position, should not breathe supplemental O_2 for 10 minutes before testing, and should not have an abnormal level of COHb before the test. Mathematical corrections can be applied for patients who cannot abstain from O_2. Performing the DL on patients who have recently smoked a cigarette or who have been exposed to environmental CO may hinder test validity. Patients should be told to refrain from smoking on the day of the test. All patients undergoing DL should have their Hb concentration measured, and a mathematical correction should be applied if it is abnormal. In addition, DLCO measurement may be altered in patients on supplemental O_2, or at high altitude. Provision of formulas that are used to obtain the raw DLCO measurement or to correct it for all of these variables is outside of the scope of this chapter and is given in the references.

BOX 20.3 Effect of Various Factors on Diffusing Capacity of the Lung for Carbon Monoxide

Factors That Decrease DLCO
- Anemia
- Carboxyhemoglobin
- Pulmonary embolism
- Diffuse pulmonary fibrosis
- Pulmonary emphysema

Factors That Increase DLCO
- Polycythemia
- Exercise
- Congestive heart failure
- Alveolar hemorrhage

DLCO, Diffusing capacity of the lung for carbon monoxide.

The **diffusing capacity ratio of the lung-to–effective total lung capacity ratio (DLCO/VA)** differentiates between diffusion abnormalities caused by having a small lung volume (e.g., chest wall restriction due to kyphoscoliosis) compared with diffusion abnormalities caused by abnormality of the alveolar-capillary membrane (e.g., interstitial fibrosis). Although commonly used in the past and still used by some clinicians and laboratories currently, reporting DLCO/V_A values should be avoided because it provides little meaningful information and can lead to confusion.[1]

Some clinicians argue that if the DLCO measurement has to be corrected for variables such as barometric pressure, Hb, COHb, V_A, etc. (see previous discussion) that have nothing to do with the gas transfer across the membrane, then it must *not* be the true diffusion that we are measuring with the DLCO. In fact, in European respiratory communities, K_{CO}, or transfer factor for CO is used, to differentiate it from the true diffusion properties of the lung. The most recent ATS guidelines encourage including both DLCO and K_{CO} on the report.[1]

The DLCO may be reduced from the predicted normal in patients with obstructive or restrictive lung diseases. With destruction of alveoli in pulmonary emphysema, with small lung volumes, and with interstitial fibrosis as in asbestosis, the DLCO may be decreased. Pulmonary embolism also may decrease the DLCO. The DLCO may be useful in identifying which patients with obstructive impairment are likely to experience desaturation during exercise and which may benefit from O_2 therapy. The DLCO may be increased in patients with polycythemia, congestive (left) heart failure (resulting from an increase in pulmonary capillary blood volume), and elevated cardiac output. Variables in health and disease that can alter the DLCO are summarized in Box 20.3.

INTERPRETATION OF THE PULMONARY FUNCTION REPORT

Interpretive strategies for pulmonary function testing abound. Most computer-based pulmonary function testing systems have

TABLE 20.4 Pulmonary Function Changes in Advanced Lung Diseases

Measurement	Normal[a]	Obstructive	Restrictive
V_T	500 mL	N or ↑	N or ↓
IRV	3.10 L	N or ↓	↓
ERV	1.20 L	N or ↓	↓
RV	1.20 L	↑	↓
IC	3.60 L	N or ↓	↓
FRC	2.40 L	↑	↓
TLC	6.00 L	N or ↑	↓
FVC	4.80 L	↓	↓
FEV_1	4.20 L	↓	N or ↓
FEV_1/FVC	> 0.70	↓	N or ↑
PEF	9.5 L/s	↓	N
MVV	160 L/min	↓	N or ↓
DLCO	40 mL/min/mm Hg	N or ↓	N or ↓
DLCO/V_A	6.6 mL/min/mm Hg/L	N or ↓	N or ↓

[a]Values for 20-year-old, 70-kg man.
DLCO, Diffusing capacity of the lung for carbon monoxide; *ERV,* expiratory reserve volume; *FEV_1,* forced vital capacity in 1 second; *FRC,* functional residual capacity; *FVC,* forced vital capacity; *IC,* inspiratory capacity; *IRV,* inspiratory reserve volume; *MVV,* maximal voluntary ventilation; *N,* no change; *PEF,* peak expiratory flow; *RV,* residual volume; *TLC,* total lung capacity.

MINI CLINI

Diffusing Capacity of the Lung for Carbon Monoxide in Chronic Obstructive Pulmonary Disease

Problem

A patient has spirometry and lung volumes typical of the obstructive pattern. FEV_1, FEV_1/FVC, and FVC are significantly reduced, and FRC and total lung capacity are increased. Two common obstructive diseases are chronic bronchitis and pulmonary emphysema. How can pulmonary function data differentiate between these two diseases? The answer is the DLCO.

Solution

Chronic bronchitis involves mostly airways and is characterized by chronic inflammation of the mucosa, hypertrophy of mucous glands, excessive mucus, and possibly bronchospasm, all of which narrow the airways. Pulmonary emphysema primarily involves alveolar structures and is characterized by destruction of alveolar architecture, elastic fibers, and alveolar-capillary membranes. Emphysema decreases gas-exchange surface area. Chronic bronchitis does not involve alveoli and does not change surface area for gas exchange. For these reasons, a decreased diffusion capacity is associated with emphysema rather than with chronic bronchitis. DLCO is a useful way to determine the extent to which emphysema may be present in a patient with chronic obstructive pulmonary disease. Of course, in reality, chronic bronchitis and emphysema often coexist in a single patient.

algorithms in their software programs for computer-assisted interpretations of the pulmonary function report. Table 20.4 summarizes pulmonary function changes that may occur in advanced obstructive and restrictive patterns of lung diseases, and Fig. 20.14 presents a simple algorithm to assess PFT results in clinical practice.[6]

When considering a pulmonary function report, the FEV_1/FVC ratio is a good place to start because it provides an initial focus as normal, restrictive, or obstructive impairment. When the FEV_1/FVC is less than the LLN, there is airway obstruction. FEV_1/FVC is normal in healthy individuals and patients with restriction. However, some clinicians still use a somewhat arbitrary value of 0.70. Although reliable in younger patients, using the fixed ratio of FEV1/FVC less than 0.70 versus the LLN value for FEV_1/FVC simplifies the issue and often overdiagnoses obstruction in elderly individuals.

The next to consider is TLC. If the TLC is less than the LLN, the patient has a restrictive impairment according to this algorithm. Patients with obstruction will often have normal or elevated TLC. Naturally, some patients may have a mixed obstructive/restrictive pattern. In those patients, TLC may be reduced, normal, or elevated.

Once an obstructive or restrictive pattern is ascertained, DLCO will help to differentiate between the conditions that do and do not affect the gas transfer across the alveolar-capillary membrane. If the percent predicted normal DLCO is less than the LLN, the patient has a diffusion impairment.

According to most recent ATS/ERS guidelines on PFT interpretation, the severity of obstructive *and* restrictive impairment is judged by the patient's FEV_1, and the severity of gas transfer is based on the DLCO.[6] Severity categories, based on percent predicted values, are outlined in Box 20.2. Use of other indices, such as FRC or TLC, to quantify the severity is controversial[6] and will not be discussed here. Although FEV_1 is used to quantify the severity of illness across the disease categories, it is important to note its limitations.[6] FEV_1 is a poor measurement of upper airway obstruction; it may not be suitable comparing different pulmonary conditions, it may not be reliable in the extremes of severity assessment, and FEV_1 does not correlate well with clinical symptoms or disease progression.

Sample Pulmonary Function Test Reports and Interpretation

Please note that the reports are made in line with the most recent ATS guidelines and they may appear different from the reports from various PFT labs that have not yet caught up with the most recent guidelines. Z scores were omitted for simplicity because they are not usually used during interpretation. Note that the interpretative strategies will also follow the most recent ATS guidelines; however, using "old" interpretive strategies would likely result in very similar, if not the same results.

Pulmonary Function Report 1

	Result	LLN	ULN	% Predicted
FVC (L)	3	4	6	60
FEV_1 (L)	2.8	3.2	4.8	70
FEV_1/FVC	0.94	0.78		
TLC (L)	3.96	5.76	8.64	55
FRC (L)	2	3.403	5.125	49
RV (L)	1.4	1.74	2.64	60
DLCO (mL/min/mm Hg)	15.9	28.9	41.5	47

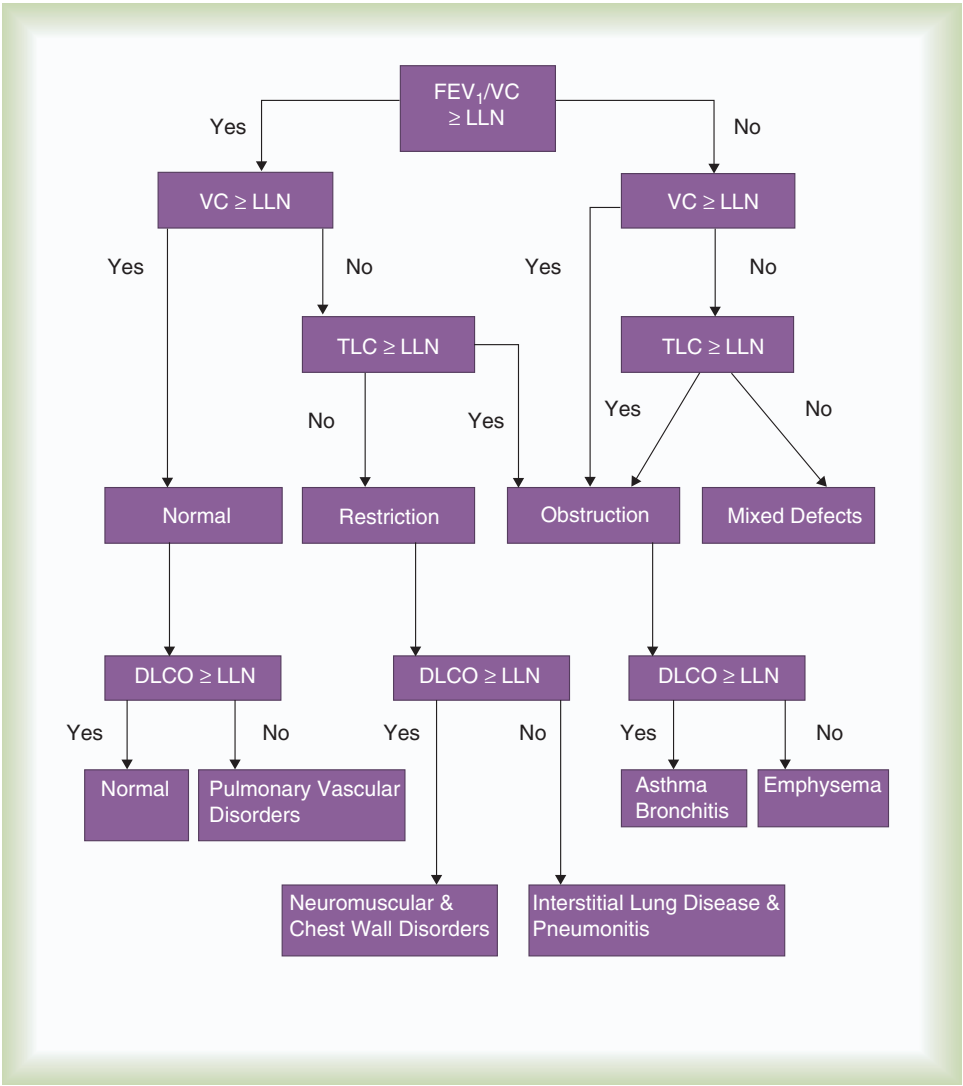

Fig. 20.14 A simple algorithm to assess pulmonary function test results in clinical practice. *LLN,* Lower limit of normal; *ULN,* upper limit of normal. (Adapted from Pelligrino R, Viegi G, Brusasco V, et al: Interpretive strategies for lung function testing. *Eur Respir J* 26:948, 2005.)

Although both FEV_1 and FVC are less than the LLN, the FEV_1/FVC is greater than the LLN, so there is no apparent airway obstruction. Because TLC is less than the LLN, the data suggest a restrictive impairment, and because DLCO is less than the LLN, there is also a diffusion impairment. RV and FRC are also proportionally reduced. Overall, this report shows a mild restrictive pattern with moderate decrease in gas exchange, consistent with pulmonary fibrosis.

Pulmonary Function Report 2

	PRE-BRONCHODILATOR				POST-BRONCHODILATOR			
	Result	**LLN**	**ULN**	**% Predicted**	**Result**	**% Predicted**	**Change (L)**	**% Change**
FVC (L)	3.3	4	6	66	4	80	0.7	21
FEV_1 (L)	2	3.2	4.8	52	2.5	62	0.5	25
FEV_1/FVC	0.57				0.62			
TLC (L)	5.51	4.32	6.58	105				
FRC (L)	4.55	2.52	3.76	146				
RV (L)	2.6	1.34	2.05	156				
DLCO (mL/min/mm Hg)	25.25	23.2	34.7	88				

Solution 2

The FEV_1/FVC less than the LLN; there is airway obstruction. FEV_1 is 52% of predicted; the obstruction is moderate. After bronchodilator inhalation, FEV_1 improved by 25% and 500 mL, showing effective treatment and partial reversibility of the airway obstruction. The large FRC and RV show hyperinflation and air

trapping, which also suggest obstructive disease. Diffusing capacity is in the normal range, indicating no diffusion impairment and no alveolar problems. Overall, this report shows a moderately severe obstructive pattern with hyperinflation and air trapping responsive to bronchodilators and consistent with acute hyperreactive airways disease, such as asthma.

Pulmonary Function Report 3

	PRE-BRONCHODILATOR				POST-BRONCHODILATOR			
	Result	LLN	ULN	% Predicted	Result	% Predicted	Change (L)	% Change
FVC (L)	3.5	4	6	66	3.8	76	0.3	9
FEV_1 (L)	2	3.2	4.8	50	2.2	55	0.2	10
FEV_1/FVC	0.57				0.62			
TLC (L)	5.51	4.32	6.58	105				
FRC (L)	4.55	2.52	3.76	146				
RV (L)	2.6	1.34	2.05	156				
DLCO (mL/min/mm Hg)	14.25	23.2	34.7	88				

Solution Report 3

This case is similar to case 2, but there are some important differences. The FEV_1/FVC is less than the LLN; there is airway obstruction. FEV_1 is 52% of predicted; the obstruction is moderately severe. After a single bronchodilator treatment, FEV_1 improved by 10% (remember to compute percent change)—not enough to show that bronchodilator therapy was immediately effective. The postbronchodilator change in the FVC was similarly too low to satisfy criteria for a significant response to a bronchodilator indicating partial reversal of airway obstruction. The large FRC and RV show hyperinflation and air trapping, which again suggest obstructive lung disease. DLCO is reduced, suggesting alveolar involvement. This report shows a moderately severe obstructive pattern with hyperinflation and air trapping not responsive to bronchodilators. There is diffusion impairment and alveolar disease. Overall, this report is consistent with COPD, especially emphysema.

Pulmonary Function Report 4

	PRE-BRONCHODILATOR				POST-BRONCHODILATOR			
	Result	LLN	ULN	% Predicted	Result	% Predicted	Change (L)	% Change
FVC (L)	4.92	4.52	6.45	92	5.16	109	0.24	5
FEV_1 (L)	2.95	3.46	5.24	68	3.24	75	.29	10
FEV_1/FVC	0.54				0.63			
TLC (L)	6.38	6	9.38	85				
FRC (L)	3.51	3.36	5	86				
RV (L)	1.58	1.7	2.52	75				
DLCO (mL/min/mm Hg)	31.2	29.8	46.5	84				

Solution Report 4

This case is similar to Case 3, but there are some important differences. The FEV_1/FVC is less than the LLN; there is airway obstruction. FEV_1 is 68% of predicted; the obstruction is mild. After a single bronchodilator treatment, FEV_1 improved by only 10%—not enough to show that the bronchodilator therapy was immediately effective. Lung volumes and diffusing capacity are within the normal range, so there is no hyperinflation, air trapping, or diffusion impairment. This report shows a moderate obstructive pattern not responsive to bronchodilators. Overall, this report is consistent with chronic bronchitis.

SUMMARY CHECKLIST

- Pulmonary function testing includes measurements of airway mechanics, lung volumes and capacities, and the diffusing capacity of the lung.
- The results of pulmonary function testing can aid in the diagnosis of disease and include patterns of obstructive and restrictive impairments, as well as presence or absence of gas exchange abnormalities.
- Pulmonary function testing provides objective data on which decisions may be made regarding the status of the patient, the selection of appropriate therapy, and the evaluation of therapeutic outcomes.
- Recently published ATS/ERS guidelines on measurement, reporting and interpretation of PFTs are considered the standards of practice across various respiratory professions and are fully endorsed by AARC.
- Important test characteristics, such as accuracy and error, sensitivity and specificity, validity, and reliability should be kept in mind when performing and interpreting PFTs.
- Absence or presence of disease is based on ULN/LLN values, whereas severity of disease is based on percent predicted values.
- Patients with obstructive lung disease exhibit reduced expiratory flows and possibly lung hyperinflation, whereas patients with restrictive lung disease exhibit reduced lung volumes and capacities.

- Abnormal FEV1/FVC ratio is a test of choice for diagnosing obstructive defects.
- A significant response to bronchodilator therapy is shown when either FEV1 or FVC increase by at least 12% and by at least 200 mL after a dose of inhaled bronchodilator.
- Brochoprovocation test may help to establish a diagnosis of obstructive lung disease if spirometry results were not diagnostic.
- TLC is the test of choice for diagnosing restrictive lung defects.
- There are three tests for measuring FRC: (1) helium dilution, (2) nitrogen washout, and (3) plethysmography. Choice of test depends on patient characteristics and abilities of individual PFT laboratories.
- DLCO-SB is the test of choice for evaluating diffusion properties of the lung.
- Raw DLCO results obtain from the testing will need to be adjusted to multiple variables, obtain during or in addition to DLCO-SB testing.
- Although pulmonary function testing cannot definitively diagnose any disease, when combined with the results of astute patient assessment, such testing can be useful in uncovering and determining the severity of obstructive disorders such as asthma (reversible) and COPD, or restrictive illnesses such as pulmonary fibrosis.

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21

Review of Thoracic Imaging

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CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- List the four tissue densities seen on a chest x-ray
- Describe how to evaluate the technical quality of a chest x-ray
- List the anatomic structures seen on the chest x-ray
- List the steps used to interpret chest x-ray exams
- Understand the value of a computed tomography scan and the use of intravenous contrast
- Understand the role of ultrasound, magnetic resonance imaging, and nuclear medicine in imaging the chest
- Describe the common pleural abnormalities
- Describe the common lung parenchyma abnormalities
- Know how to evaluate the location of an endotracheal tube
- Recognize the appearance of various catheters (central venous, peripherally inserted central catheter [PICC], port, Swan-Ganz) on chest x-ray exams

CHAPTER OUTLINE

KEY TERMS

air bronchogram
atelectasis
cephalization
chest x-ray
computed tomography (CT)
empyema
hydropneumothorax
infiltrates
interstitial lung disease
Kerley B lines
mediastinum
pleural effusion
pneumomediastinum
pneumothorax
radiograph
radiolucent
radiopaque
silhouette sign
situs inversus
solitary pulmonary nodule

Chest imaging is crucial in the practice of pulmonary and critical care medicine. It is essential that the respiratory therapist (RT) have a solid understanding of how to interpret chest radiographs to accurately assess patients. Various chest imaging techniques exist, including the conventional chest film (more accurately called a **radiograph**, **chest x-ray**, or roentgenogram after Conrad Wilhelm Roentgen, who first discovered the x-ray), computed tomography (CT), ultrasound, and magnetic resonance imaging (MRI). A separate branch of medicine that uses radioactive material to produce images is known as *nuclear medicine*.

This chapter summarizes important concepts in chest imaging for the RT. The basic elements of chest x-ray are addressed first, followed by more advanced techniques such as CT, MRI, ultrasound, and nuclear medicine. The role of various imaging techniques used to evaluate the different components of the chest (e.g., pleura, **mediastinum**, lung tissue [lung parenchyma]) are described and examples of abnormal findings are shown.

OVERVIEW OF THE CHEST X-RAY

A chest x-ray is produced by passing x-rays through the chest to photographic film or a detector. The resulting image is formed as x-rays strike the film or digital screen and darken/expose it. X-rays that pass directly through low-density tissue (e.g., air-filled

lung) strike the film in greater numbers and cause the resulting shadow to turn darker. X-rays that strike denser tissue (e.g., bone) are absorbed by the tissue to a greater extent and leave the exposed film lighter. The structures on the chest x-ray vary in shades of gray based upon the density of tissue through which the x-rays have passed.

Four different tissue densities are visible on a normal **chest x-ray.** The tissue types that produce these densities are *air, fat, soft tissue* (*water density* because soft tissues, similar to muscle, are mainly composed of water), and *bone.* Each tissue type absorbs different proportions of the x-ray beam, which results in a different appearance on the chest x-ray. Air in the lung, stomach, or intestines absorbs very few x-rays and appears virtually black (**radiolucent**). Fat absorbs a small amount of the x-ray beam and is usually seen as a light gray shadow. Soft tissue absorbs a slightly greater amount of the x-ray beam and is usually seen as a medium gray shadow. Bone or metal (such as from a pacemaker device or central venous catheter) absorbs a large fraction of the x-ray beam and is seen as a nearly white (**radiopaque**) shadow.

Historically, x-ray images were recorded on film and, once developed, were displayed by placing the film over a viewbox to illuminate the film for the observer. Currently, radiographs are recorded, displayed, and stored in digital format on a computerized picture archiving and communication system (PACS). To record a digital image, an x-ray detector (digital film) replaces the photographic film. A computer takes the data from the x-ray detector and creates the image. The resulting image is displayed on a computer monitor.

Compared with images recorded on traditional film, digital images have advantages for interpreting and retrieving the image. The display of digital images can be manipulated by adjusting contrast, brightness, and magnification. These adjustments allow findings that would be subtle and difficult to perceive on a traditional photographic film. Digital technology also facilitates simultaneous comparison of serial images taken over a period of days or weeks to help gauge changes in a patient's condition. For example, serial chest x-rays viewed side by side on a computer screen may reveal a shrinking opacity associated with a resolving pneumonia. Digital images also allow multiple people to view the image simultaneously and in different locations. For example, an RT in a critical care unit, a radiologist in the imaging department, and a critical care physician in another location may collaborate by simultaneously viewing a chest x-ray acquired from a patient who is deteriorating rapidly. Digital images can also be easily copied and recorded on compact discs so that patients can obtain digital copies of studies to take to their physicians. Increasingly, as hospitals share electronic medical record (EMR) systems, imaging studies can be accessed within these system by physicians and RTs at different hospitals. Thus technologic advancements have facilitated the transmission of information as patients move from one hospital to another.

The structures visible on a chest x-ray are seen only when tissue of one density is next to tissue of a different density. It is the contrast between densities of adjacent structures that allows the border between these structures to be seen. For example, the heart is visible as a soft tissue density in the middle of the chest because it is surrounded by the lungs, which are primarily air density. If the lungs on either side of the heart fill with water (due to pulmonary edema), the normal adjacent heart border would be invisible on the radiograph. This obscuring of the margin of adjacent structures because they have the same density is called the ***silhouette sign*** and can be useful to localize abnormalities within the chest. For example, the right middle lobe of the lung is located adjacent to the right heart border, so the disappearance of the right heart border on the chest x-ray (i.e., the presence of the silhouette sign) indicates an airspace opacity (such as pneumonia or atelectasis) in the right middle lobe. Stated simply, a right middle lobe pneumonia or atelectasis "silhouettes" the right heart border (Fig. 21.1).

When to obtain a chest x-ray is the decision of the attending physician. However, because the RT is at the bedside, the physician will often welcome the RT's suggestion to obtain a chest radiograph, as when a patient in the intensive care unit (ICU) suddenly deteriorates for no apparent reason. The RT must be familiar with the common clinical indications for obtaining a chest x-ray (Box 21.1).

Although a chest x-ray is important in evaluating patients with lung disease, it does have limitations. It may appear normal in a case of respiratory failure; this is common in patients with acute (e.g., pulmonary embolism) or chronic obstructive lung disease (e.g., emphysema that is not apparent on a chest x-ray). In addition, the chest x-ray may lag behind the patient's clinical condition. This situation is common in pneumonia, where a patient may present with the high fever and cough typical for pneumonia but an airspace opacity or infiltrate may not appear on a chest film until 12 to 24 hours later. Similarly, the airspace opacity on the chest x-ray may persist for days to weeks after the resolution of symptoms. Also, the chest x-ray represents a two-dimensional view and gives limited information as to the depth or thickness of anatomic or pathologic findings such as lung nodules/masses, consolidation, or heart size.

BOX 21.1 Clinical Indications for Obtaining a Chest X-Ray

Outpatient
Unexplained dyspnea
Severe persistent cough
Hemoptysis
Fever and sputum production
Acute severe chest pain
Positive tuberculosis skin or blood test

Inpatient
Placement of endotracheal tube
Placement of pulmonary artery catheter
Placement of central venous pressure catheter
Sudden onset of dyspnea or chest pain
Elevated or changing plateau pressure during mechanical ventilation
Sudden decline in oxygenation

Approach to Reading a Plain Chest X-Ray

A disciplined and systematic approach is required to obtain the maximal information from any diagnostic imaging study.

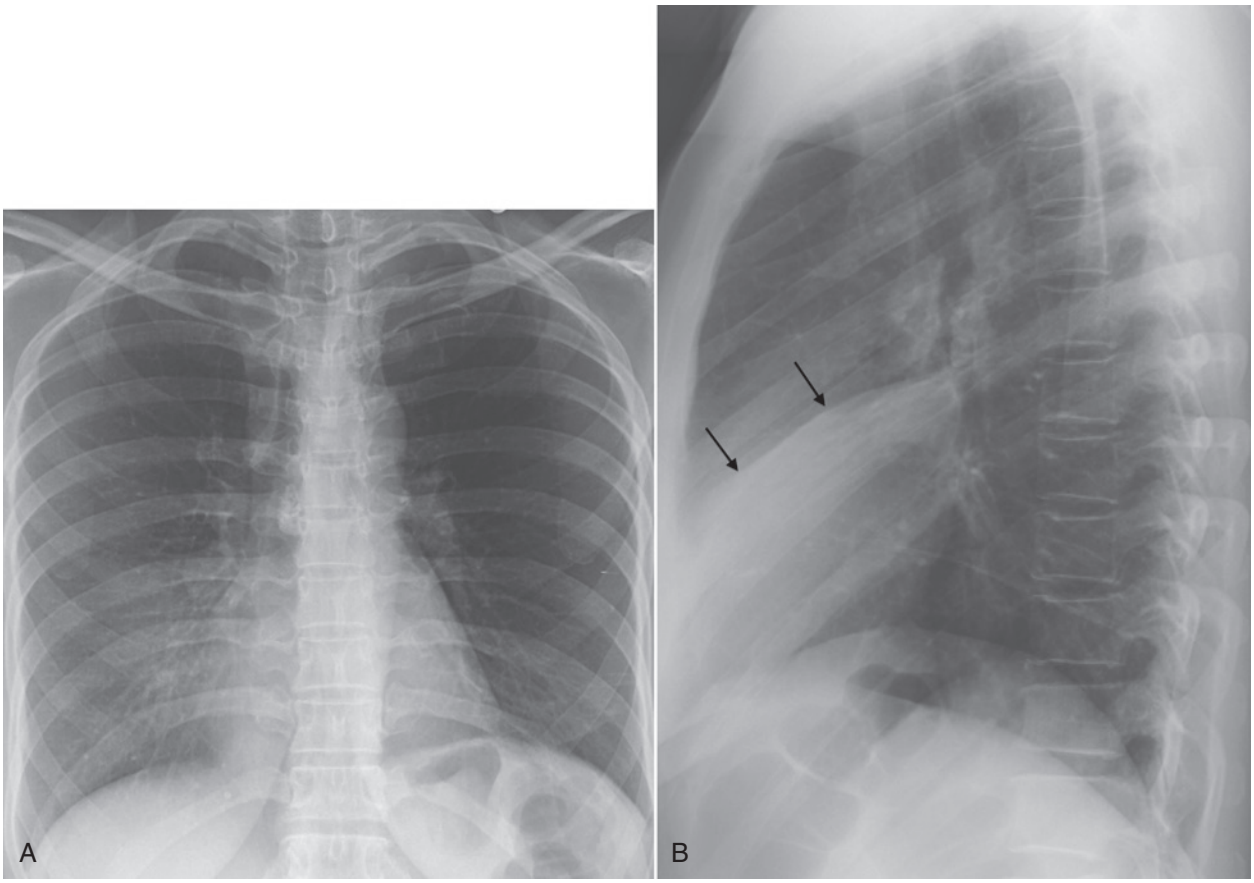


Fig. 21.1 (A) Posteroanterior view of the chest demonstrates obscuration or silhouetting of the right heart border because of airspace opacity in the right middle lobe. (B) On the lateral view, there is right middle lobe collapse *(arrows)* secondary to an obstructing primary lung neoplasm (adenocarcinoma).

Interpreting the chest x-ray provides an excellent example of this statement. An obvious abnormality such as a 6-cm mass is easily identified, even by the untrained observer. However, more subtle abnormalities (such as 1-cm pulmonary nodule representing a primary lung malignancy or free intraperitoneal gas due to ruptured bowel), with equal or even greater diagnostic importance, may go unnoticed if the observer is distracted by a more obvious abnormality. To avoid this pitfall, the observer must develop a step-by-step approach to the interpretation of chest x-rays, in a disciplined and consistent fashion, until it becomes routine. Whatever your individual approach, it is important to examine each chest x-ray in a thorough and systematic manner.

In broad terms, the steps in reviewing a chest x-ray are as follows:

- Confirm the correct patient's name on the radiograph to make sure you are reviewing the correct x-ray.
- Review the technique and quality of the examination: is the radiograph well centered (i.e., do the spinous processes project, overlying the trachea on a posteroanterior [PA] film), and is the degree of penetration of the beam adequate, too high (i.e., the lung parenchyma is too dark to see subtle changes), or too low (i.e., the lung parenchyma is too white, causing normal lung markings to appear abnormal)?
- Systematically review the anatomic structures on the chest film to assess their normality or abnormality. As a general rule, we encourage the RT to look at the lung parenchyma last, thereby encouraging looking carefully at other parts of the chest x-ray (e.g., the bones, soft tissues, areas below the diaphragm) that may provide important clues to what is going on with the patient.

In later sections of this chapter, the following areas are reviewed: (1) evaluation of the technical quality and adequacy of the film, (2) normal anatomic structures on a chest x-ray, (3) more sophisticated imaging techniques, and (4) major anatomic components seen on the radiograph.

Chest X-Ray Technique and Quality

Several technical factors should be routinely assessed when a chest x-ray is being interpreted:

1. Is the chest x-ray appropriately labeled?
2. Is the study performed with PA and lateral views, or is it an anteroposterior (AP) portable examination?
3. Is the entire chest imaged (i.e., are any structures not included)?
4. Was the patient properly positioned and were all sources of artifact addressed?
5. Were the optimal settings for the x-ray beam selected when the film was taken (the term used is *penetration,* which is similar to *exposure* on camera film)?

As the first step, the RT should check the patient's identity and all labels visible on the film. This step helps to avoid the

mistake of interpreting a chest x-ray for the wrong patient and establishes which side is which, because labels are often placed to indicate the patient's left or right side; such labeling of the side is important in cases where the patient's chest or abdominal contents are reversed—known as ***situs inversus***.

RULE OF THUMB In evaluating a plain chest x-ray, first assess the technical quality of the film—that is, is there rotation or is the patient positioned well? Is the penetration of the x-ray beam appropriate? Then use a step-by-step approach to view all the relevant structures.

Various abbreviations—named for the path of the x-ray beam—are used to describe the technique used to obtain a chest x-ray. The standard technique is a "PA and lateral." In the PA (posteroanterior) view, the patient puts his or her back to the x-ray source and the chest against the film. The x-ray beam leaves the source, passes through the posterior side of the patient, exits through the patient's anterior surface, and finally reaches the film. The term "*lateral*" indicates that the x-ray is taken from the side (Fig. 21.2B). PA and lateral views are usually performed in the radiology department with equipment that standardizes the distance (typically 6 ft) from the x-ray source to the film and where the x-ray technician can maximize the quality of each film. In addition, as noted, taking the film with the anterior chest closest to the film minimizes magnification of the heart.

MINI CLINI

Evaluating the Heart Size on a Portable Chest X-Ray

A standard PA chest x-ray is obtained with the patient standing and facing the film cassette. The x-ray beam first enters the patient's back and then passes through the chest to the film. The heart is located very close to the film with the standard PA view, and magnification of the heart shadow is minimal.

Problem

In the ICU, patients are generally too ill for a PA chest x-ray to be obtained. It is obtained with the patient lying in bed and the film cassette placed behind the patient. The x-ray beam passes from anterior to posterior, producing an AP portable chest film. In examining an AP portable chest x-ray, how is the appearance of the heart size affected?

Discussion

An AP portable chest x-ray is obtained with the patient's heart farther from the film, producing a heart shadow that is artificially magnified compared with the shadow produced with a PA chest film; this may give the appearance of an enlarged heart in some cases. The clinician interpreting an AP portable chest x-ray must keep this in mind to avoid misinterpreting the film as showing that the heart is enlarged (cardiomegaly). To illustrate this point, hold a flashlight 3 ft from a wall and turn it on. While holding the flashlight steady, place one hand in the beam. The shadow created by the hand becomes smaller as the hand is moved closer to the wall and farther from the light source (equivalent to a PA film) and bigger as the hand approaches the light source (equivalent to an AP film).

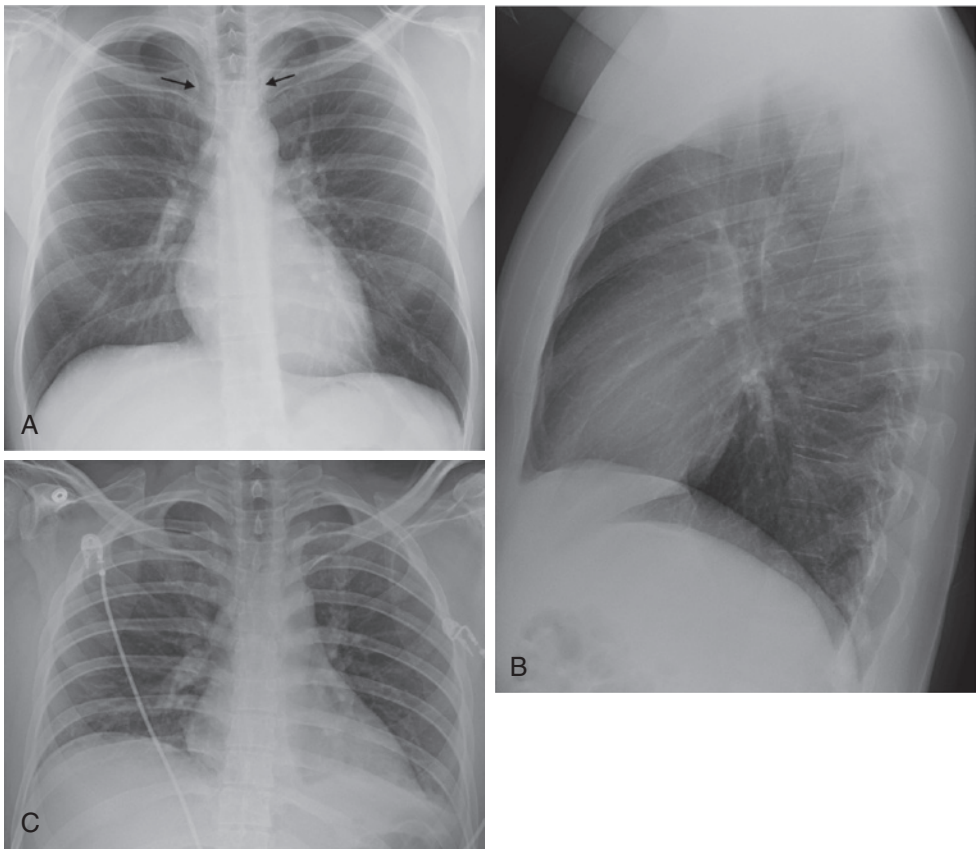


Fig. 21.2 Normal posteroanterior (PA) (A) and lateral (B) views of the chest x-ray. Note the medial ends of the clavicles *(arrows)* with the spinous process *(arrows)* framed between them (A). A subsequent follow-up anteroposterior (AP) (C) x-ray obtained shortly after the PA radiograph shows that the cardiac silhouette appears larger, due to magnification from the AP technique.

The AP (anteroposterior) chest x-ray is usually taken with a portable x-ray machine. The AP technique places the x-ray source in front of the patient with the film behind the patient's back. The source of the x-ray beam is usually much closer to the patient than with a PA film, although the distance varies from patient to patient. The closer x-ray source and the position of the patient both lead to a magnification of the heart's shadow (see Fig. 21.2C). The AP film is usually taken in the ICU because these patients are too ill to travel to the radiology department or to stand for a PA film. Overall, AP portable films are usually of lower quality than PA films. In interpreting the chest x-ray, evaluating the heart's size, and considering subtle findings that may be influenced by the film's quality and technique, the RT must take into account the view (AP or PA).

When a chest x-ray examination is performed, it is sometimes difficult to align the patient properly; therefore a portion of the chest may not be imaged. Although these problems are more common with portable (AP) examinations, they may also occur with PA and lateral x-rays. The RT should ask the following questions: (1) Is the entire chest included on the film? (2) Is the patient well positioned?

Patient rotation can make interpretation more difficult by projecting *midline* structures (e.g., the trachea) to the right or left. The observer can assess for rotation by comparing anterior structures such as the *medial* (toward the middle) ends of the clavicles with a posterior structure such as the spinous processes. In a perfectly positioned or aligned chest film, the spinous processes should appear midway between the medial ends of the clavicles and in the middle of the tracheal air column (see Fig. 21.2). Patient rotation makes the mediastinum appear unusually wide and obscures or distorts the appearance of the pulmonary arteries as they emerge from the mediastinum into the lung parenchyma.

The RT must also ensure that the film is adequately penetrated or exposed. An improperly penetrated x-ray film (see further on) may create a risk of misinterpreting the chest x-ray findings. A chest x-ray with proper exposure should show the intervertebral disc spaces through the shadow of the heart and allow the blood vessels in the peripheral regions of the lungs to be visualized. A chest x-ray that is underexposed or underpenetrated (i.e., due to too-low kilovoltage of the x-ray beam) does not allow one to see the intervertebral discs through the heart shadow and may make identification of abnormalities in soft tissue areas such as the mediastinum more difficult. Specifically, an underpenetrated film may cause the normal branching of the pulmonary arteries in the lung to appear abnormal and be misinterpreted as interstitial opacities, which may mimic pulmonary edema. Similarly, an overpenetrated x-ray overexposes the film, leaving the lung parenchyma black and making it difficult to visualize the peripheral blood vessels or abnormalities that may be present (e.g., airspace opacities secondary to pneumonia). This overpenetration makes evaluation of the lung parenchyma far more difficult. Adjustment of the contrast and brightness of the chest film on the computer display of a digital image improves the ability to see certain aspects of a chest x-ray with improper penetration. However, adjusting the display cannot completely overcome the loss of important details caused by an improperly exposed film.

MINI CLINI

Value of Proper Technique on a Chest X-Ray

Careful attention to the technical quality of a chest x-ray is important in both acquiring and interpreting the study. If the settings when the examination is taken are incorrect or if the patient is improperly positioned, this can lead to important changes in the appearance of the chest x-ray that can either hide important details or lead to misinterpretation.

Problem

A patient presents to the emergency department with chest pain. The initial radiograph obtained demonstrates decreased lung markings (Fig. 21.3), which the inexperienced observer may interpret as emphysema or a pneumothorax.

Discussion

The careful observer realizes that the findings on the chest x-ray may be due to overpenetration rather than an abnormality with the lung parenchyma. When radiographs were previously obtained on film, errors in either underpenetration or overpenetration were difficult to overcome. As this study was obtained using a digital detector, inadequate penetration can often be compensated for by changing the contrast or brightness on the digital screen. However, in some instances where the over- or underpenetration is severe, changing the contrast and brightness cannot correct the initial error and a repeat study may be necessary. A repeat chest x-ray (see Fig. 21.3) demonstrates normal lung markings without evidence of emphysema or a pneumothorax.

Anatomic Structures Seen on a Chest X-Ray

After the technical aspects of the chest x-ray have been reviewed, it is time to assess the anatomic findings. The main structures seen on a routine chest x-ray are listed next and illustrated in Fig. 21.4:

1. Bones (e.g., ribs, clavicles, scapulae, vertebrae)
2. Soft tissues (e.g., tissues of the chest wall, upper abdomen, lymph nodes)
3. Lungs (including the trachea, bronchi, and lung tissue or parenchyma)
4. Pleura (membranous covering of the lung, including the *visceral pleura* [the part attached to the lungs] and the *parietal pleura* [the part lining the inside of the chest wall]; although normally occupied by only a small amount of fluid, the space between the parietal and visceral pleura is called the *pleural space*)
5. Mediastinum (i.e., the tissues between the lungs in the center of the chest including the heart, large veins and arteries, trachea, esophagus, and lymph nodes). The mediastinum is bordered by the sternum anteriorly, the vertebral column posteriorly, the thoracic inlet superiorly (where the trachea enters the chest), and the diaphragm inferiorly.
6. Upper abdomen
7. Lower neck

The anatomy seen on the chest x-ray should be reviewed in a thorough and systematic manner. All of the previously listed anatomic structures must be individually assessed. When first interpreting radiographs, it is helpful for the RT to create a list of the anatomic structures that must be assessed and to check off the structures as they are reviewed. With experience, the checklist becomes routine.

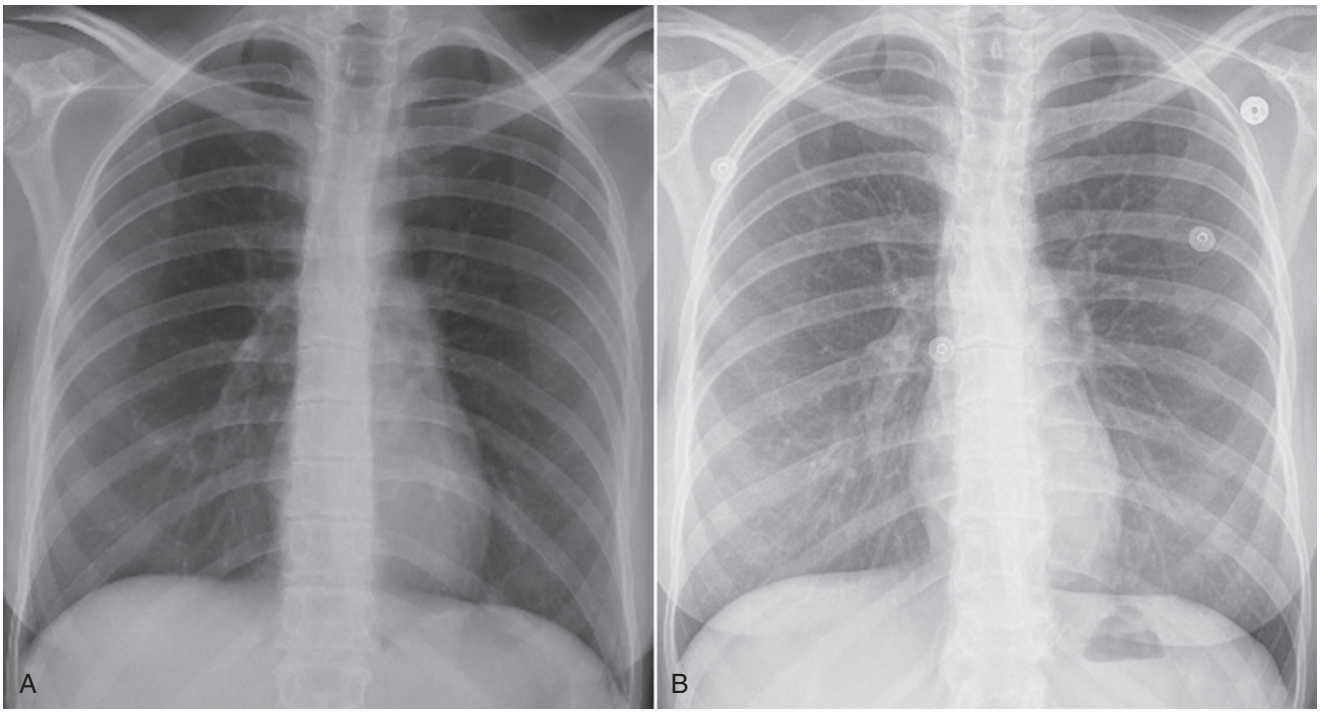
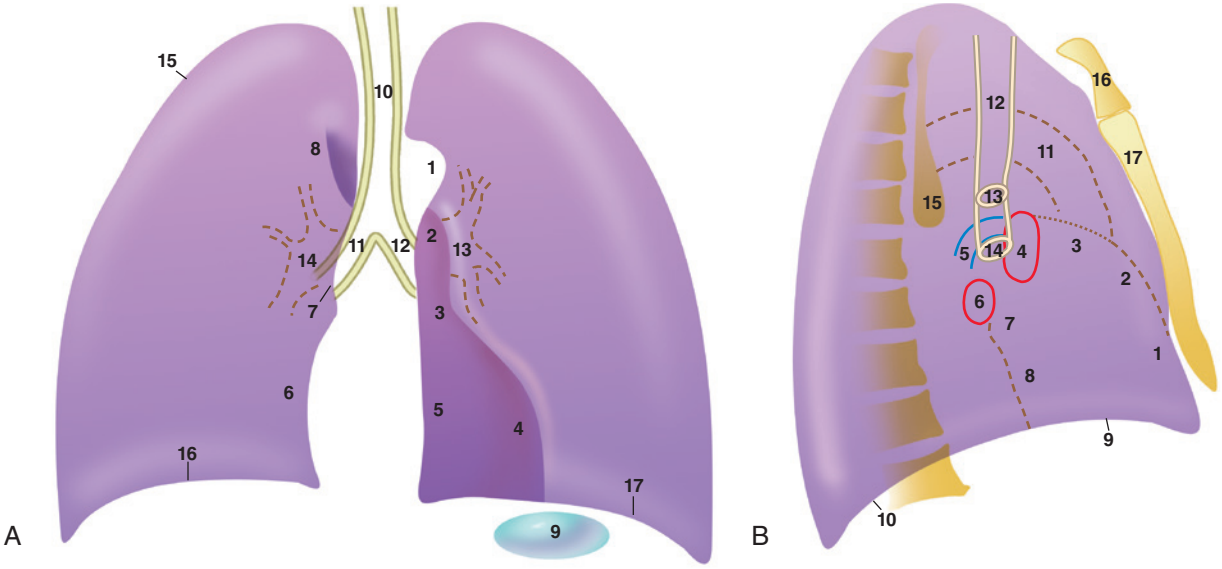


Fig. 21.3 X-Rays of the Chest Performed Several Hours Apart. (A) The chest x-ray is overpenetrated. The lung markings are difficult to visualize which can simulate emphysema or a pneumothorax. (B) A repeat chest x-ray performed with adequate penetration demonstrates normal lung markings bilaterally without evidence of emphysema or a pneumothorax.



1. Aortic arch
2. Main pulmonary artery
3. Left atrium
4. Left ventricle
5. Descending aorta
6. Right atrium
7. Ascending aorta
8. Superior vena cava
9. Gastric bubble
10. Trachea
11. Right main bronchus
12. Left main bronchus
13. Left pulmonary artery
14. Right pulmonary artery
15. Pleural line
16. Right hemidiaphragm
17. Left hemidiaphragm

1. Right ventricle
2. Pulmonary outflow tract
3. Main pulmonary artery
4. Right pulmonary artery
5. Left pulmonary artery
6. Pulmonary veins
7. Left atrium
8. Left ventricle
9. Right hemidiaphragm
10. Left hemidiaphragm
11. Aortic arch
12. Trachea
13. Right upper lobe bronchus
14. Left upper lobe bronchus
15. Scapulae
16. Manubrium
17. Sternum

Fig. 21.4 Schematic Diagrams of the Normal Structures Seen on a Chest X-Ray. (A) Posteroanterior view. (B) Lateral view.

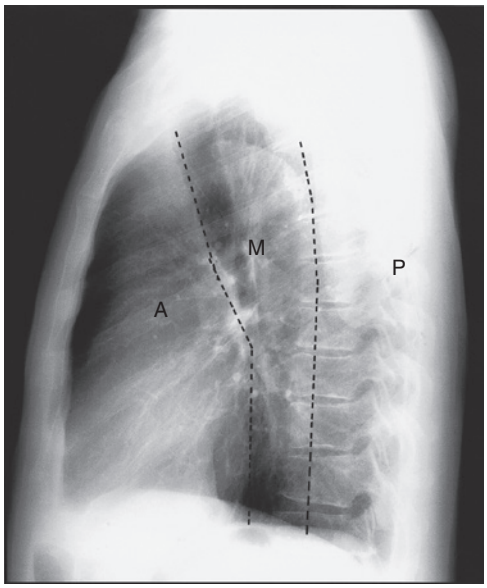


Fig. 21.5 Lateral view of the chest, indicating the divisions of the mediastinum: anterior *(A),* middle *(M),* and posterior *(P).*

Assessment of the chest wall should include evaluating for symmetry, rib fractures, or other bone abnormalities. Lung evaluation begins by assessing the lung volumes (size) and density. Any obvious differences in symmetry must be explained. Of the lung parenchyma, 80% to 90% is overlaid with bone in the form of ribs, clavicles, and the thoracic spine. The overlying bone may obscure important lung abnormalities. A lateral view is helpful in clarifying the presence or absence of suspicious lung abnormalities on frontal (PA or AP) projections. Pay specific attention to areas where subtle abnormalities may hide, including the lung apices (behind the clavicles), the area of lung that projects behind the heart, and the portion of lung that lies deep in the posterior sulcus (the extreme bottom of the lung projecting behind the dome of the diaphragm on the frontal view).

Review of the lung periphery on both frontal and lateral views discloses any pleural abnormalities, such as fluid in the pleural space (e.g., hydrothorax, hemothorax [blood in the pleural space]) or air in the pleural space (pneumothorax). Evaluation of the mediastinum should include an assessment of the heart's size. On the PA projection, the diameter of the heart's shadow (cardiac silhouette) should not exceed one-half the diameter of the chest. An enlarged cardiac silhouette may occur with congestive heart failure or with a pericardial effusion (fluid within the space that surrounds the heart encased within the pericardium). The lateral contours of the mediastinum should correspond to normal anatomic structures, as outlined in Fig. 21.5.

Advanced Chest Imaging Techniques

Computed Tomography of the Chest

Computed tomography (CT) scanning is an essential and commonly used imaging technique to assess the chest. CT exams are performed on specialized equipment that rotates an x-ray source and detectors in a circular path around the patient. The information thus obtained is displayed on a computer monitor as thin transverse sections or slices. Intravenous contrast is often used; it can give added information and can be particularly helpful in the evaluation of vascular structures (as in looking for pulmonary emboli or evaluating the aorta).

One advantage of CT exams over standard x-ray is that anatomy may be viewed from any angle and even shown three dimensionally. Additional advantages include its excellent anatomic detail, wide availability, and short examination time. Structures as small as 1 mm can be visualized, allowing for detailed anatomic depiction of the structures of the chest. Modern CT scanners are fast, with images of the entire chest obtained in less than 10 seconds, allowing for accurate and rapid assessment of critically ill ICU patients.

To perform a CT scan, a patient lies down on a specialized mobile table. As the scan begins, this table moves the patient through a circular opening in the CT scanner called a gantry. The gantry contains all the necessary equipment to generate the CT images (such as the x-ray tube and detectors, which are arranged in a circle around the patient). As the CT exam is performed, the x-ray source and detectors spin quickly around the patient in a circular motion as the patient moves the through the CT gantry on the table. The x-ray beams pass through the patient to detectors on the opposite side. The information from the detectors is next sent to a computer, which generates a two-dimensional image from the detector data. Each image created by the scan appears as a thin slice of the patient. Historically, after each CT image was obtained, the patient would be advanced in stepwise fashion until the entire chest was imaged. Modern CT scanners use numerous detectors (typically between 16 and 256) connected to a powerful computer, and patients pass rapidly through the scanner without stopping for each image. The term *spiral* or *helical* is applied to these more current CT scanners. Because CT scanners require the patient to lie down, remain motionless, and pass through a relatively small circular opening, special accommodations may be needed for some individuals. These accommodations may include providing supplemental oxygen for patients with orthopnea (dyspnea while lying down), sedation for pediatric patients or those with claustrophobia, and special scanners for morbidly obese patients (with a higher table weight limit and/or larger gantry opening).

Although CT scans depict the anatomy of the chest better than the standard chest x-ray, they expose the patient to more radiation, which varies depending on the specific CT technique used (Table 21.1). For example, a standard-dose chest CT examination exposes the patient to the equivalent of 70 chest x-rays. Ongoing research and technologic advancements have and will likely continue to lower the radiation dose of CT scans.

Chest CT provides an excellent view of the chest and allows imaging of portions of the chest that are poorly seen on chest x-rays. Areas such as the mediastinum, the lung apices, and the costophrenic sulci of the lungs (the normally sharp shadows where the diaphragm contacts the rib cage laterally), and the pleural surfaces all are well evaluated with CT. Chest CT is commonly performed to evaluate lung nodules and masses, the lung parenchyma, pleura, the great vessels of the chest, and the mediastinum. To evaluate blood vessels and soft tissue structures in close proximity, such as hilar lymph nodes, iodinated contrast can be helpful because contrast makes blood appear denser

TABLE 21.1 Radiation Dose of Common Thoracic Imaging Studies

Study	Radiation Dose (mSv)	Equivalent Normal Background Radiation
Chest x-ray (PA and lateral)	0.1	10 days
Chest CT (low-dose screen)	1.5	6 months
Chest CT (standard dose)	7.0	2 years
Coronary CT angiogram	12.0	4 years

CT, Computed tomography; *PA,* posteroanterior.

(radiopaque or white) and allows blood vessels to be distinguished from adjacent soft tissue.

Chest CT examinations are generally displayed with a slice thickness of 1 to 5 mm. Each image therefore will include everything within the 1- to 5-mm slice of tissue. Thin slices allow for maximal spatial resolution (i.e., the ability to separate objects that are close together). For example, to evaluate the lung parenchyma in a patient with suspected interstitial lung disease, thin slices, typically 1 mm thick, are used to evaluate the fine architecture of the lung; this is referred to as a high-resolution chest CT (HRCT). Thin slices are also helpful in the evaluation of small pulmonary nodules or to evaluate for pulmonary emboli on a pulmonary embolism study. A disadvantage of thin slices is that they have more image noise and there are more images to interpret. For example, pulmonary embolism studies performed with a 1-mm slice thickness generally have approximately 1000 images per study.

Chest CT serves as a valuable tool in screening high-risk individuals for lung cancer. Specifically, high-risk patients (those between the ages 55 of 77, who have smoked more than 30 pack-years, and who currently smoke or have stopped smoking within the past 15 years) may benefit from lung cancer screening. A large study of greater than 50,000 patients at high-risk for lung cancer demonstrated that the mortality rate or risk for death from lung cancer was reduced by 20% in patients who underwent screening chest CT versus a chest x-ray examination.[1] This technique uses lower radiation than standard chest CT studies—approximately one-fifth that of a standard chest CT.

Computed Tomography Angiography

The rapid scanning that can be performed on modern CT scanners has made CT angiography possible. To perform CT angiography, intravenous contrast dye is injected at a high rate to darken or opacify the vascular structures. A large-bore peripheral intravenous line in an antecubital vein or a peripherally inserted central catheter (PICC) or port catheter that can handle a high injection rate is required. CT angiography of the chest is most commonly utilized to evaluate the thoracic aorta (as for a dissection or tear in the aortic wall and the pulmonary arteries for a blood clot, also known as a pulmonary embolism). Advances in technology now allow for the visualization of pulmonary emboli in tiny peripheral arteries that were not visible on older CT scanners (Fig. 21.6).[2] More recent technologic advancements have made CT angiography of the coronary arteries possible, which can serve as an alternative to coronary artery catheterization.[3]

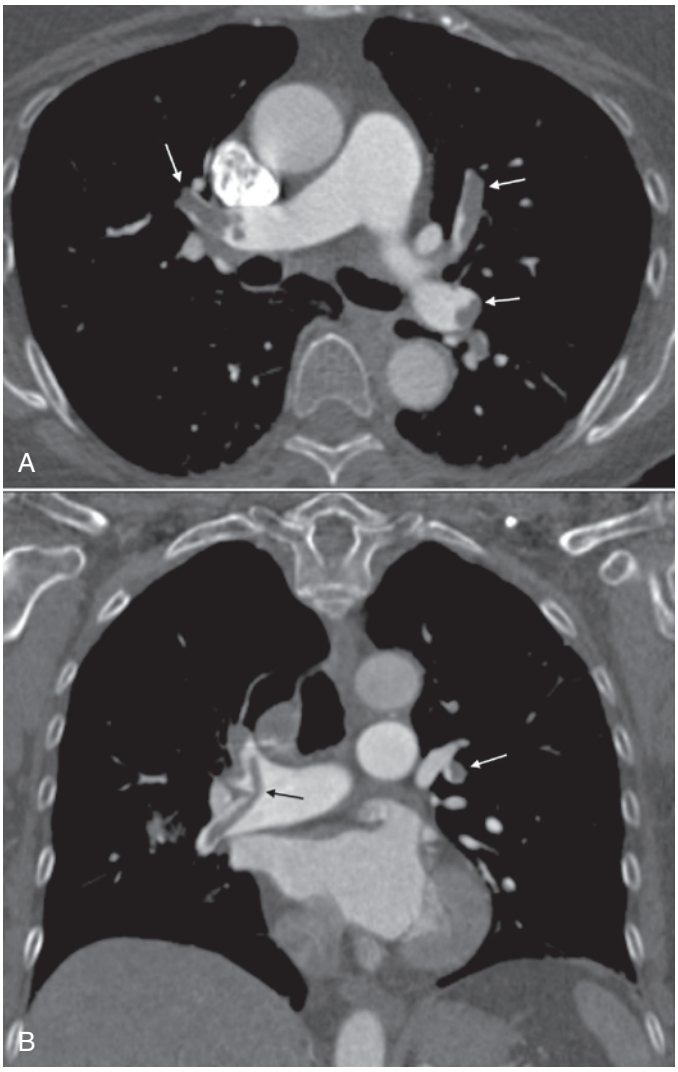


Fig. 21.6 Computed Tomography Angiogram of a Patient With Bilateral Acute Pulmonary Emboli. (A) The pulmonary emboli are seen as the dark filling defects *(arrows)* outlined by the white contrast-enhanced blood vessels *(arrows).* (B) Coronally reformatted image is helpful to visualize clot entering both the right upper and right lower lobar pulmonary arteries *(arrows).*

Three-Dimensional Reconstruction

The imaging processing capabilities of modern CT scanners allow for reconstruction of the chest in any direction and production of three-dimensional (3D) representations of some areas of the body (Fig. 21.7). These 3D images can be helpful for surgeons before surgery to visualize how anatomic structures may appear at the time of surgery. The images can also simulate what a physician would see during a bronchoscopy, referred to as *virtual bronchoscopy*.

Magnetic Resonance Imaging of the Chest

Magnetic resonance imaging (MRI) has many uses in the chest and is typically used as a problem-solving tool to answer specific clinical questions that cannot be answered by other imaging techniques such as a chest x-ray, chest CT, or ultrasound examination. MRI is generated by placing patients into a strong

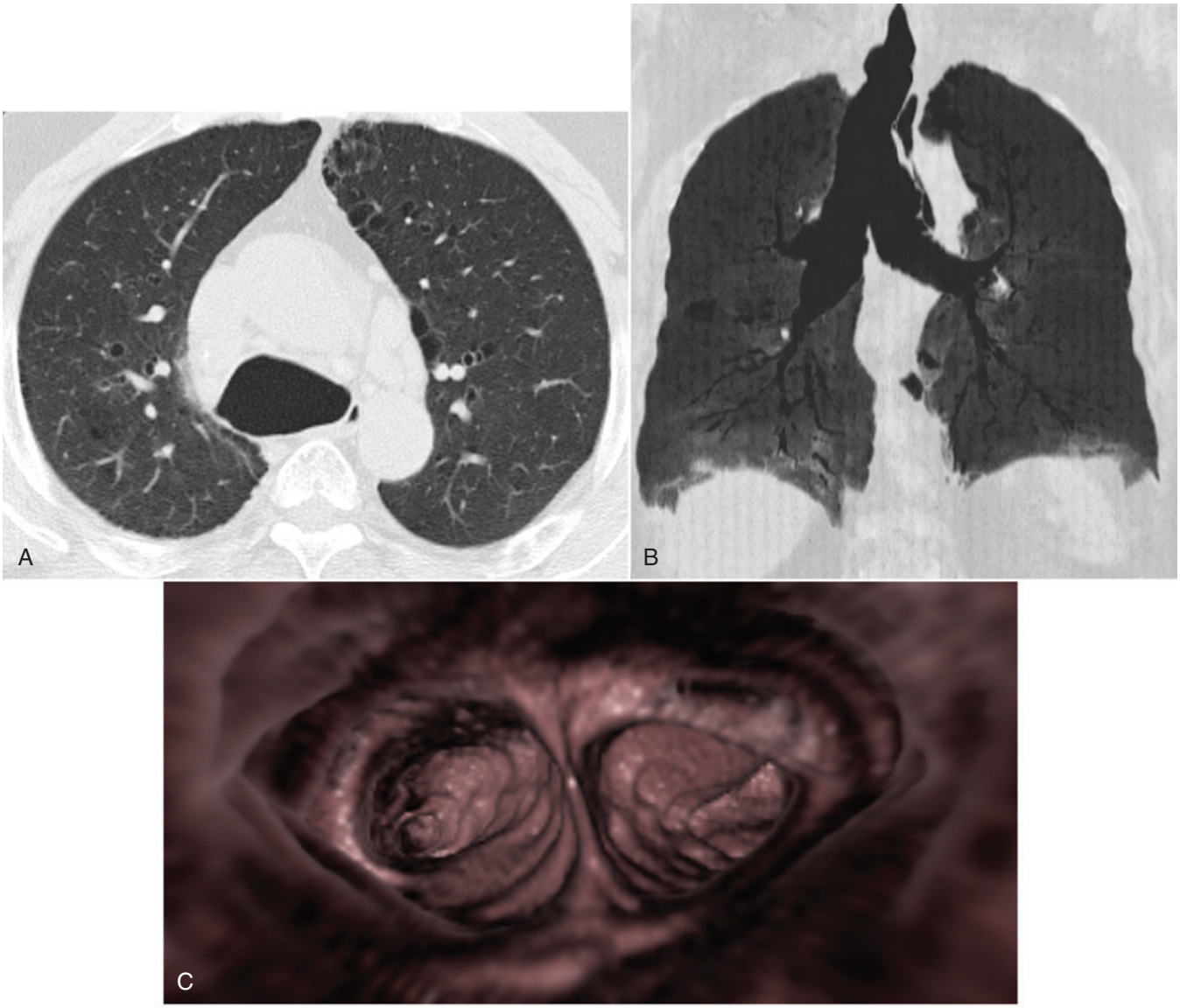


Fig. 21.7 Use of Two- and Three-Dimensional Images for Visualization of the Trachea. Axial computed tomography (A) image demonstrates a massively dilated trachea in a patient with tracheobronchomegaly (Mounier-Kuhn). A coronally reformatted minimum intensity projection (minIP) image (B) allows for visualization of the entire trachea and main stem bronchi. A three-dimensional image (C) endoluminal view of the inferior trachea looking downward at the carina with the left and right mainstem bronchi located on each side of the carina. The three-dimensional image, termed *virtual bronchoscopy,* can aid the bronchoscopist in planning a bronchoscopic procedure.

magnetic field. The physics of MR are complicated and beyond the scope of this chapter. Briefly, the strong magnetic field aligns nuclei with nonzero spins (nuclei that have an odd number of protons and neutrons), such as hydrogen atoms, with the magnetic field. Because hydrogen atoms are present in high concentration throughout the body (mainly water), they provide an excellent target for MRI evaluation. Pulses of radio waves are directed at the hydrogen nuclei, resulting in the alignment of hydrogen nuclei to change in orientation with the magnetic field. After the radio signal is stopped, the nuclei flip back to their original alignment and release their own radio waves. MRI uses the radio waves from the realigning nuclei to generate an image.

MRI has advantages over other imaging techniques in the chest that are useful in specific circumstances. MRI does not use x-rays and therefore does not expose patients to ionizing radiation, which is of particular importance in pediatric patients. MRI has superb soft tissue characterization, allowing for detailed analysis of soft tissue masses. The most common uses for MRI in the chest are for imaging the mediastinum, large vessels in the chest (e.g., for pulmonary emboli or vascular abnormalities), and the heart.[4] The superior soft tissue characterization of MRI allows for the confident diagnosis of a benign mediastinal mass (such as a thymic cyst or thymic hyperplasia) and can spare patients a percutaneous biopsy or surgery to establish a

diagnosis.[5] In patients in renal failure in whom there is clinical concern for a pulmonary embolism and who cannot receive intravenous contrast, an MR examination can be performed without contrast to establish a diagnosis. MR has only limited uses for imaging the lung parenchyma. For example, in a patient with lung cancer undergoing evaluation for possible resection, MRI can show whether a tumor has invaded the chest wall by determining if the lesion moves independently of the chest wall during both inspiration and expiration.

However, MRI does have significant limitations when applied to imaging the chest. MRI examinations take longer to acquire (at least 10 minutes and up to 1 hour) than other examinations (such as radiographs or CT); because of this, respiratory and cardiac motion are more significant obstacles. Imaging of critically ill ICU patients is therefore difficult because they may be unable to lie in the MR scanner for a long period of time. The lungs are primarily composed of gas; therefore there is little signal to generate images, as is required by MRI, making this modality less useful for evaluating the lungs.

In addition, the large magnet required for MR examinations generally contraindicates its use in patients with pacemakers or other significant iron-containing (also know as ferromagnetic) objects in their bodies to undergo MRI. A patient with a small metallic object in a crucial place, such as a surgical clip in the brain or eye, generally cannot undergo MRI. The powerful magnet will pull metallic objects into the magnet with great force, exposing both patients and health care providers to life-threatening risk. Medical equipment containing metal, such as ventilators and gas cylinders, also cannot be brought near the MR scanner. Deaths have been reported when metal objects (e.g., oxygen cylinders) have been brought into the magnetic field of the MRI, and RTs must be especially careful about this issue. In addition, special MRI-compatible ventilators that do not contain ferrous metals should be used when mechanically ventilated patients are being studied by this technique. As another precaution, MRI suites usually have well-marked warnings and areas beyond which conventional metal objects absolutely must not pass.

RULE OF THUMB Medical equipment containing metal (e.g., oxygen cylinders, conventional ventilators, infusion devices) must be kept away from the powerful magnet in an MRI machine. The hazard is that if such equipment enters the magnetic field of the MRI machine, the object will be pulled into the machine, endangering both the patient and medical personnel. Deaths have resulted from failure to observe this precaution. To prevent this, MRI suites usually have well-marked warnings and areas beyond which conventional metal objects absolutely must not pass. Also, special MRI-compatible medical equipment containing nonferrous metals is available.

Ultrasound

Ultrasound images are created by passing high-frequency sound waves into the body and detecting these waves as they bounce back (echo) from the tissues of the body. The pattern of the returning sound waves is used to generate an image of the tissue studied. Ultrasound of the chest is excellent for evaluating the heart (by echocardiography) and pleural fluid.[6]

Ultrasound imaging using small portable machines has become common practice in critical care units. Portable ultrasound units allow for the rapid assessment of heart function and volume status and are used to assist in many critical care procedures.[7] Ultrasound can accurately detect small pleural effusions and aid in performing a thoracentesis. Ultrasound is also commonly used to guide placement of central venous and arterial catheters. Blood vessels are easily identified using ultrasound. The compressibility of veins is used to differentiate veins from arteries (Fig. 21.8). Because the needle path can be clearly seen on the ultrasound screen, using ultrasound guidance for venous and arterial puncture allows the procedure to be more easily accomplished with less time, risk, and patient discomfort.

Nuclear Medicine

Nuclear medicine utilizes small amounts of radioactive material to diagnose and treat a wide variety of diseases. Radioactive material can be administered to patients by intravenous injection, inhalation, or oral ingestion. In the chest, the most commonly

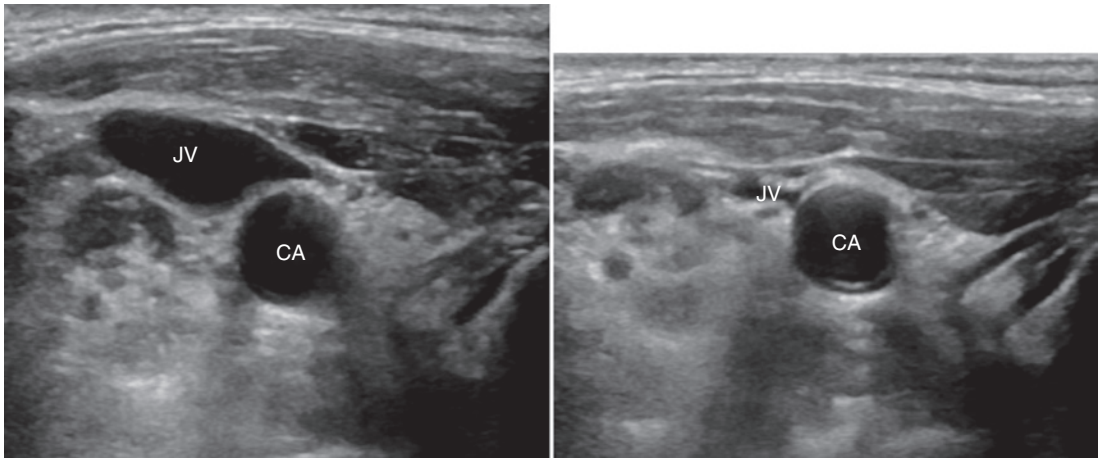


Fig. 21.8 Two ultrasound images of the right internal jugular vein *(JV)* and right carotid artery *(CA)*. In the first image, the jugular vein is distended; in the second image, the jugular vein is collapsed by gently applying pressure with the ultrasound transducer. The carotid artery did not compress.

performed nuclear medicine studies are *ventilation-perfusion (V/Q) scans* and *positron emission tomography-CT (PET-CT).* V/Q scans were initially the primary method to diagnose pulmonary emboli, although they have been largely replaced by chest CT angiography.[1] However, V/Q scans still have an important role in certain subsets of patients (such as those with renal insufficiency who may be harmed by intravenous contrast or in young patients where the V/Q scan may result in a lower radiation dose to the patient). PET-CT combines a nuclear medicine study (the injection of radioactive glucose) with chest CT and is used primarily to diagnose and stage disease in patients with suspected or known cancer. The radioactive glucose is selectively taken up by many cancer cells (and also by inflammatory cells), allowing areas of potential tumor involvement to be visualized. PET-CT is frequently used in the staging of cancers (including lung cancer [see Chapter 32]) in order to plan therapy.

The remainder of the chapter outlines commonly encountered abnormalities involving the pleura, lung parenchyma, and mediastinum. The findings of various imaging techniques are often a vital aspect of narrowing down the list of possible diseases (i.e., the differential diagnosis). You are encouraged to fine-tune your observational powers for assessing imaging studies because, as noted by Pasteur, "In the field of observation, chance favors the prepared mind."

RULE OF THUMB Three general steps to assessing a chest film are as follows:
1. Content assurance: Is the entire chest visible on the film?
2. Quality assurance: Is the chest x-ray properly exposed and centered?
3. Disciplined application of a personalized, consistent search pattern.

PLEURA

The thin membrane surrounding the lung parenchyma is referred to as the *pleura*. The lungs are surrounded by two thin pleural membranes. The outer pleural membrane, known as the *parietal pleura,* adheres to the inside of the chest wall, the upper surface of the diaphragm, and the lateral aspect of the mediastinum. The inner pleural membrane, or *visceral pleura,* closely adheres to the surface of each lung. The visceral pleura extends along the fissures that separate the lobes of the lung. The pleural membranes around the lung cannot be seen on a chest x-ray because they blend into the water density of the chest wall, diaphragm, and mediastinum. However, the visceral pleura separating the lobes can be seen if the pleural surface is parallel to the x-ray beam (as with the "minor" or "horizontal" fissure separating the right upper lobe from the right middle lobe on a PA chest x-ray). Although very thin, the visceral pleura separating the lobes is visible because it is contrasted with aerated lung on either side.

Pleural Effusion

A **pleural effusion** refers to the accumulation of excess fluid within the pleural space (see Chapter 27). In healthy individuals, it is estimated that 1 to 8 mL of pleural fluid is normally present.[8] Also normally, the diaphragm forms a dome that curves downward to attach to the chest wall on the lower ribs and thoracic and lumbar vertebra. On a chest x-ray, the arch of the diaphragm and the chest wall meet to form a point called the *costophrenic angle.* This angle is seen on both PA and lateral views (see Fig. 21.2). If the point of the costophrenic angle is rounded rather than sharp, it often indicates that a pleural effusion is present (Fig. 21.9).[9] This finding is sometimes referred to as "blunting of the CP angles." For a pleural effusion to cause blunting of the costophrenic angle on the frontal (PA/AP) view, at least 175 to 200 mL of pleural fluid must have accumulated. The lateral film detects smaller pleural effusions than are detected with the frontal view. The posterior costophrenic angle becomes blunted with 75 to 100 mL of fluid. The best view for detecting small amounts of pleural fluid is the lateral decubitus view, which is a frontal view taken as the patient is lying on his or her side with the side of the suspected pleural effusion down; 5 mL of pleural fluid can be detected on a decubitus radiograph.[10] As discussed later, ultrasound is also useful for detecting a pleural effusion.

Sometimes fluid can accumulate between the lung and the diaphragm and maintain a sharp costophrenic angle, hiding up to 500 mL of fluid.[11] Fluid that accumulates between the lung and the diaphragm is said to be in a *subpulmonic* location. The subpulmonic location is the first place pleural effusions accumulate in an upright patient.[12] The earliest sign of a left-sided pleural effusion on an upright chest x-ray is an increased distance between the inferior margin of the left lung and the stomach gas bubble. With a subpulmonic effusion, there may be an associated slight lateral shift of the point at which the diaphragm dips downward on the frontal chest x-ray (i.e., similar to a hockey stick with the blade toward the lateral chest wall).

If both air and fluid are contained within the same space, the interface between the air and the fluid forms a soft tissue density with a straight horizontal border that has air density above it. The interface may have a small meniscus on both sides. These straight, level interfaces between air and fluid are called *air-fluid levels*. An air-fluid level in the pleural space indicates the presence of a **hydropneumothorax** (Fig. 21.10), or both air and fluid in the pleural space.

Occasionally fluid accumulates in an unusual position, as within an interlobar fissure (which separates the lobes of the lung). Fluid is most commonly seen in the minor fissure, which is between the right middle and right upper lobes. Fluid within a fissure can be diagnosed on a chest x-ray by a characteristic biconvex lens-like, elliptical shape on either the PA or the lateral view (Fig. 21.11).

Pleural fluid is generally categorized as either a *transudate* or an *exudate* (see Chapter 27). However, an exudate cannot be distinguished from a transudate on a chest x-ray or chest CT. This distinction requires analyzing a sample of the pleural fluid. *Loculated* pleural fluid (fluid that does not move freely with changes in patient position) is more commonly seen in exudative effusions, hemothorax (blood in the pleural space), and empyema (infection of the pleural fluid).

Clues as to whether a pleural exudate results from inflammation or from cancer may be present on the chest x-ray. Clues that favor a malignant cause for a pleural effusion include the presence of pleural-based nodules, pulmonary nodules, or evidence of prior malignancy, such as surgical absence of the breast in a patient with breast cancer.

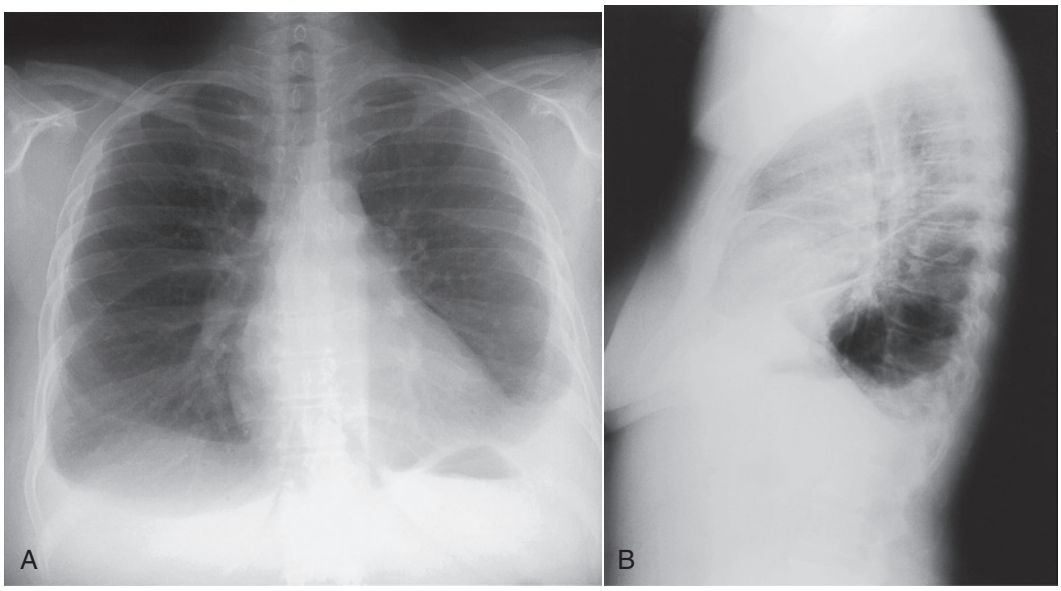


Fig. 21.9 Pleural Effusion. Posteroanterior (A) and lateral (B) chest x-rays in a 43-year-old patient with long-standing bilateral pleural effusions resulting from rheumatoid arthritis. Note that the bilateral meniscus sign is also visualized posteriorly on the lateral view.

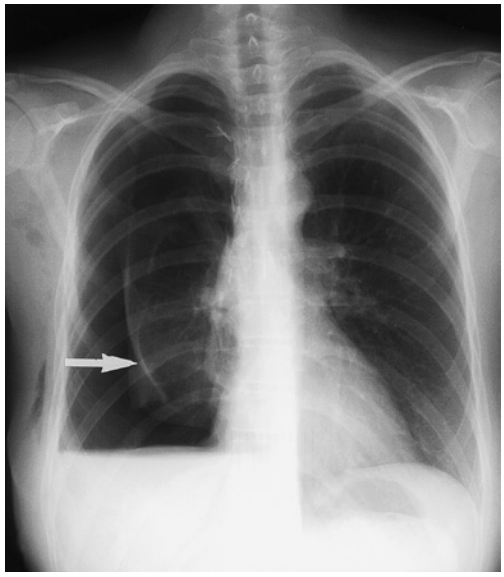


Fig. 21.10 Hydropneumothorax. Single posteroanterior view of the chest in a patient with a hydropneumothorax. Note the air-fluid level in the pleural space. The arrow points to the visceral pleura (lung border) being compressed by both air and fluid.

Ultrasound for Evaluating Pleural Fluid

Ultrasound reliably detects both small and large pleural effusions (Fig. 21.12). It is also useful in distinguishing pleural fluid from solid tissue[13] and readily identifies tissue bands associated with loculated effusions. Ultrasound is also helpful in guiding thoracentesis, in particular for small or loculated pleural effusions.

Computed Tomography

Pleural fluid can be easily identified on chest CT exams. In a supine patient, free fluid accumulates in the most dependent (posterior) portion of the chest. Pleural fluid that does not flow to the most dependent portion of the chest (i.e., the posterior portion of the chest when a patient lies down for a chest CT exam) is loculated.

With some forms of pleural disease, the pleural lining enhances (appears whiter) following intravenous contrast administration. Pleural thickening and nodularity are well seen on a contrast-enhanced CT scan. An elliptical pleural fluid collection with adjacent pleural thickening and enhancement suggests the presence of an **empyema** (see Chapter 27), which is infected pleural fluid.[14] The presence of gas within the pleural fluid without a recent history of surgery or needle insertion (which can introduce air) establishes the diagnosis of empyema (Fig. 21.13).

Pneumothorax

The term **pneumothorax** refers to the presence of air within the pleural space. The visceral pleura surrounding the lung becomes visible when air accumulates in the pleural space. A pneumothorax may occur spontaneously because of rupture of a *bleb* (a thin-walled subpleural gas-containing space deep to the pleura—a form of pulmonary air cyst) or from trauma or invasive procedures that puncture the pleura, such as transbronchial biopsy (see Chapter 22) or a percutaneous (CT-guided) lung biopsy. A pneumothorax may also occur as a complication of positive-pressure ventilation (which is called *barotrauma*). When the patient is upright, the air within the pleural space typically accumulates along the top (apex) of the lung and displaces the lung away from the chest wall. The clinician can detect a pneumothorax by observing a thin pleural line along the periphery of the lung with an absence of lung markings between the lung margin and the inner aspect of the chest wall (Fig. 21.14). If a diagnosis of pneumothorax is suspected, an upright chest x-ray should be obtained. Visualization of a small pneumothorax may be assisted by taking the chest x-ray when the patient exhales. When the patient is supine, the air within the pleural space moves to the highest point in the chest,

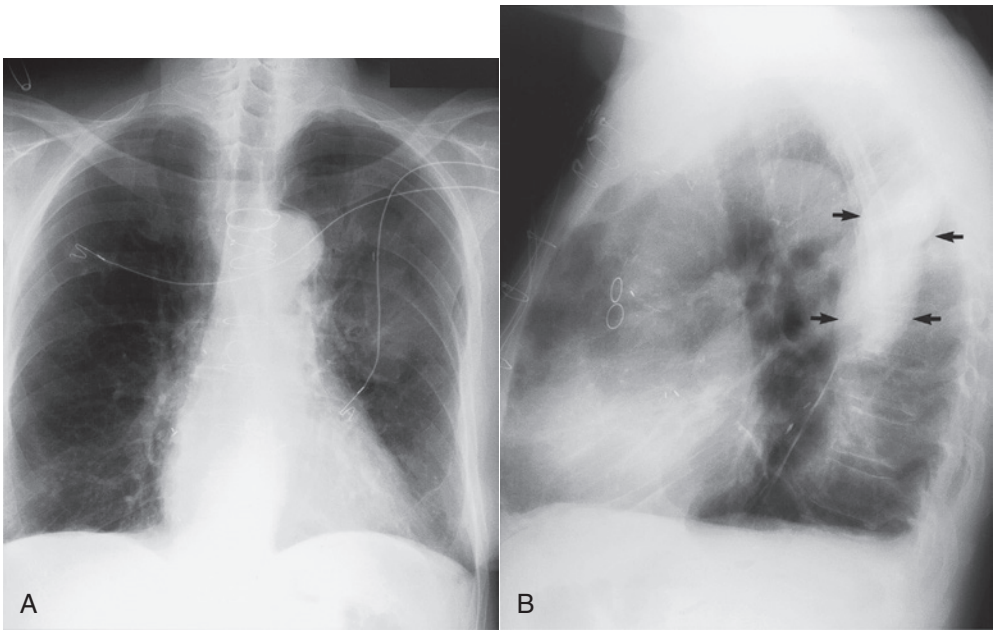


Fig. 21.11 Intrafissural Fluid. Two views of the chest showing fluid accumulating within the superior portion of the major fissure. In the posteroanterior view, (A) the fluid is seen as vague increased density in the left upper lobe. (B) Note the typical elliptic shape of the fluid on the lateral projection *(arrows)*.

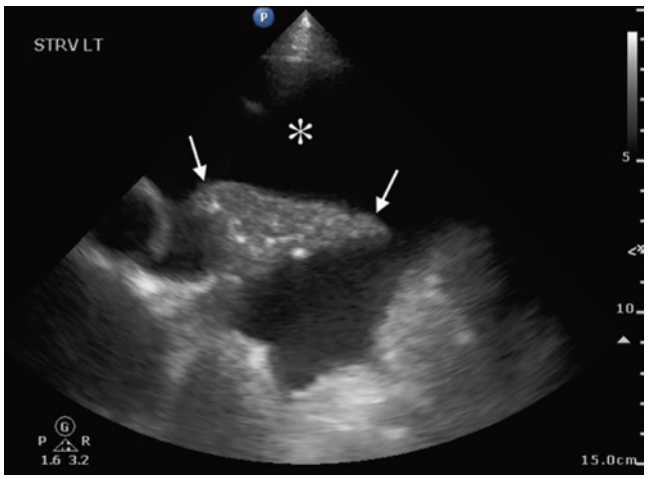


Fig. 21.12 Pleural Effusion. Ultrasound image demonstrates a large pleural effusion *(asterisk)*. Adjacent to the pleural effusion is a collapsed lung *(arrows)*.

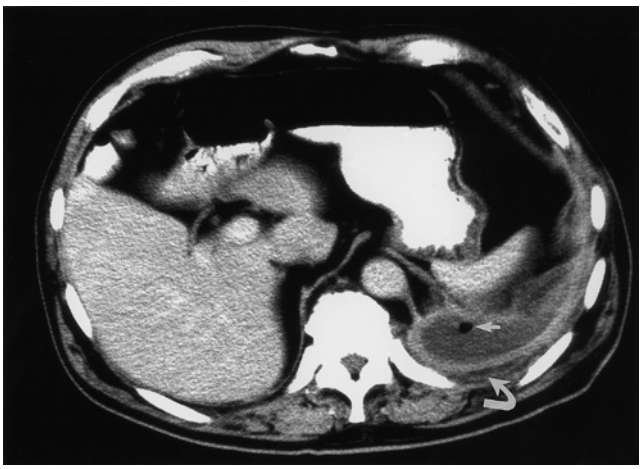


Fig. 21.13 Empyema. Cross-sectional computed tomography image shows an elliptic pleural fluid collection surrounded by thickened enhancing pleura (split pleural sign). The presence of the gas bubble *(short arrow)* within the fluid and the thickened extrapleural subcostal tissues *(curved arrow)* is strongly suggestive of empyema.

which is the anterior cardiophrenic sulcus.[15] Because air in this region may not create a visible edge between the pleura and the x-ray beam, radiographic clues to the presence of pneumothorax are more subtle in a supine patient.[15] A supine patient with a pneumothorax may have a *deep sulcus sign* (Fig. 21.15),[16] which refers to air accumulating anteriorly and outlining the heart's border below the dome of the diaphragm. In addition, the upper abdomen on the same side often shows increased lucency (i.e., the film is darker). If the diagnosis remains in doubt, a decubitus radiograph or cross-table lateral radiograph (in which the patient lies face up while the x-ray is directed across the body) can help make the diagnosis of pneumothorax. Ultrasound is an alternative to chest x-ray and is highly accurate in the diagnosis of a pneumothorax.[17]

A pneumothorax may be difficult to diagnose if a patient has bullous emphysema. If, after carefully examining the chest film, the RT is uncertain about the presence of a pneumothorax, a chest CT can resolve the question. Skin folds (i.e., when excess skin on the chest wall rolls over itself) can mimic a pneumothorax. To avoid mistaking a skin fold for a pneumothorax, the clinician should look carefully at what appears to be the lung margin. The absence of a pleural line along the lung margin and the presence of bronchovascular markings (i.e., markings of lung tissue and blood vessels) between the lung margin and the chest wall favors a skin fold rather than a pneumothorax.

Occasionally air within the pleural space may be under pressure or tension (Fig. 21.16); this is referred to as a *tension*

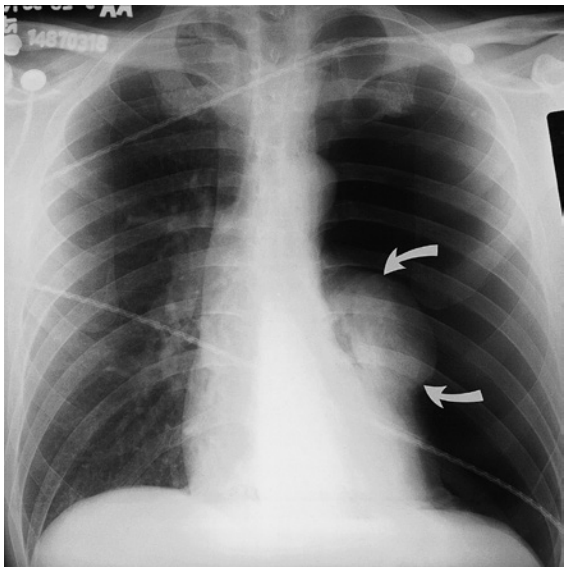


Fig. 21.14 Pneumothorax. Complete atelectasis of the left lung *(curved arrows)* resulting from a large left pneumothorax.

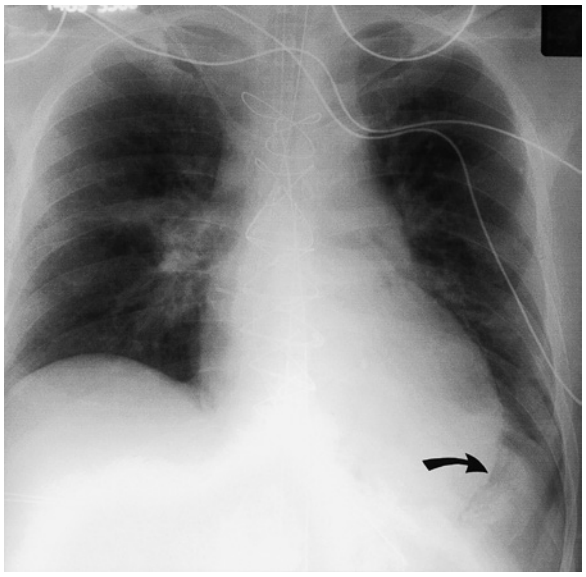


Fig. 21.15 Deep Sulcus Sign. Portable supine radiograph in a patient following median sternotomy. Note the increased lucency in the left upper quadrant. The highest portion of the thorax in a supine patient is the anterior cardiophrenic sulcus; this accounts for the well-defined low cardiac border *(arrows)* and the adjacent fat pad.

pneumothorax—an emergency that occurs when the tear in the pleura (which allows air to leave the lung and enter the pleural space) opens on inspiration but closes on expiration. Air continues to accumulate in the pleural space and can compress the heart and adjacent lung. Imaging features of a tension pneumothorax include inferior displacement of the hemidiaphragm on the side of the pneumothorax or mediastinal shift away from the pneumothorax. A tension pneumothorax requires immediate decompression with a chest tube, Heimlich valve, or needle aspiration of the air within the pleural space.

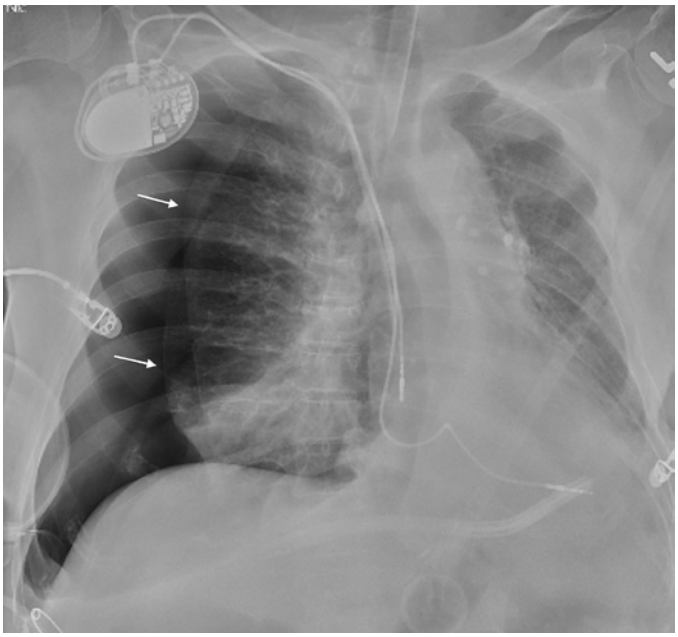


Fig. 21.16 Tension Pneumothorax. Portable chest x-ray after a recent liver transplant. Note the large right pneumothorax displacing the mediastinum to the left and the right hemidiaphragm inferiorly. These findings indicate the presence of a tension pneumothorax on the right, requiring immediate chest tube placement.

MINI CLINI

Use of the Silhouette Sign

Problem

A patient has an airspace opacity, secondary to pneumonia, in the lower half of the right lung. It is unclear if this abnormality is located in the right middle lobe or the upper portion of the lower lobe. Is there a way to identify the location of this infiltrate?

Discussion

If the right heart border is visible next to the airspace opacity or infiltrate, the pneumonia is located in the lower lobe behind the heart. If the right heart border is invisible, the airspace opacity must be located in the right middle lobe next to the right side of the heart. The disappearance of the right heart border in this circumstance is due to the silhouette sign. In this instance, pneumonia is considered a water density, and when two structures of similar density contact one another, the border between them (or the silhouette of the heart border) is not seen. Pneumonia in the upper segments of the lower lobe appears to be next to the heart on the PA chest film but does not obliterate the heart border in such cases because the water density of the pneumonia in the lower lobe is not adjacent to the water density of the heart. In this instance, the heart border is seen because the silhouette sign is not present.

LUNG PARENCHYMA

The lung parenchyma is made up of two main components: air sacs (alveoli) and interstitium (the supporting structures of the lung). Lung parenchymal disease often involves both components, although one component is usually affected more than the other.

Alveolar Disease

When alveoli are filled with material denser than air, they have a characteristic radiographic appearance regardless of the material

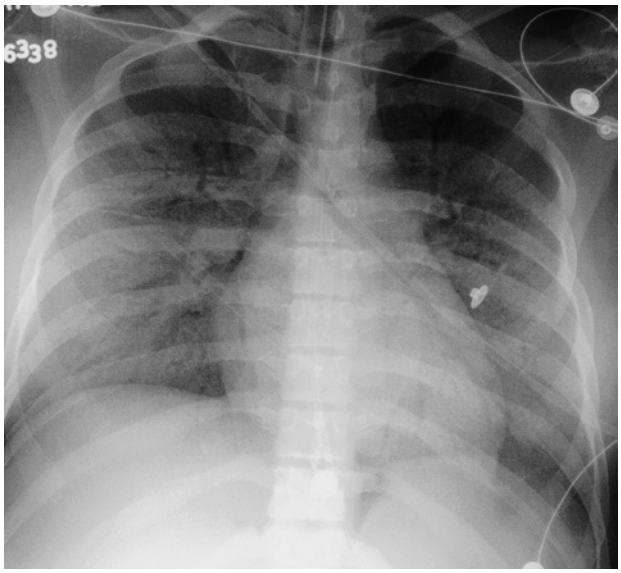


Fig. 21.17 Air Bronchograms. This portable radiograph shows increased density throughout both lungs highlighted by tubular lucencies. These are air bronchograms. They are visualized because of the alveolar filling that surrounds them. This typical alveolar filling pattern (airspace disease) suggests acute pneumonia, pulmonary hemorrhage, or pulmonary edema.

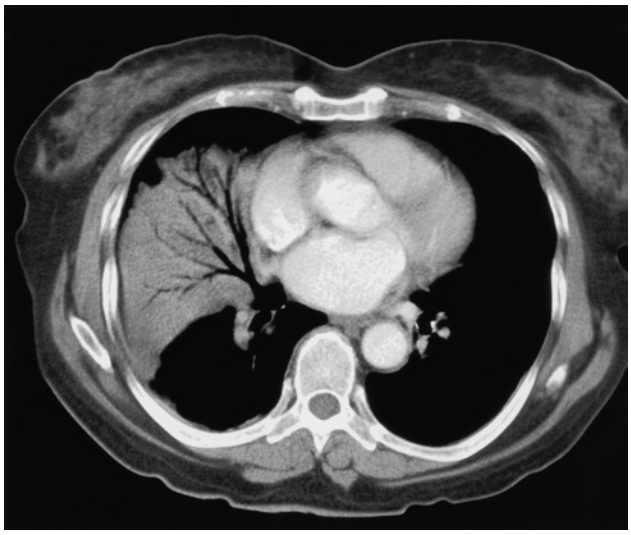


Fig. 21.18 Pneumonia, Right Middle Lobe. Computed tomography slice shows an alveolar filling process in the right middle lobe with tubular air bronchograms running through it. The patient is a 73-year-old woman.

that fills them. The type of fluid that fills the alveoli varies depending on the disease process. In the case of pulmonary edema, the alveoli are filled with a watery fluid that contains few cells. With bacterial pneumonia, the alveoli are filled with an exudative fluid containing numerous white blood cells (pus). In the case of pulmonary hemorrhage, the alveoli fill with blood. Both pneumonia and pulmonary hemorrhage can cause identical-appearing patchy, increased density shadows that tend to coalesce over time on the chest x-ray. These shadows are often referred to as *airspace opacities* or ***infiltrates.*** Although the term *infiltrate* is commonly used to describe an airspace opacity, caution should be used because some clinicians equate infiltrates with pneumonia whereas others take infiltrates to mean a much broader differential diagnosis, including pulmonary edema, pneumonia, or pulmonary hemorrhage.

The lucent tubular structures that course through dense airspace opacities or infiltrates on both chest x-rays and chest CT images are referred to as **air bronchograms** (Fig. 21.17). Normally patent airways are invisible in the outer two-thirds of the lung on a chest x-ray because of the lack of contrast between air in the airway and air in the lung parenchyma. However, the increased contrast produced by filling of the surrounding alveoli with fluid makes the airways more visible and causes the air bronchogram sign. Air bronchograms are the hallmark of infiltrates that fill alveoli (so-called *airspace disease*) (Fig. 21.18 and Box 21.2).

RULE OF THUMB Air bronchograms indicate that the imaging abnormality is located in the lung parenchyma and not in the pleural space, suggesting the presence of pneumonia.

Pulmonary Edema

Pulmonary edema is one of the most common chest x-ray findings in critically ill patients. It can be caused by vascular congestion, rupture of the pulmonary capillaries, or a combination of both. Edema from vascular congestion can be caused by failure of the left heart (cardiogenic pulmonary edema [see Chapter 31]), renal failure, or fluid overload. Breakdown in the integrity of the lung capillaries can also cause pulmonary edema, as in acute respiratory distress syndrome (ARDS; see Chapter 29).

The development of cardiogenic pulmonary edema can be described through a series of changes on the chest film. Before pulmonary edema develops, the pressure in the pulmonary veins increases. The increasing pressure in the pulmonary veins can be seen on the chest film as enlarging blood vessels that extend to the lung apexes. If the blood vessels in the upper lung zones are the same size or larger than the blood vessels in the lower lung zones, the vessels are said to be "cephalized" (Fig. 21.19). **Cephalization** of the pulmonary blood flow is often caused by left-sided heart failure.

As fluid builds up from the high venous pressures, thickening of bronchial walls *(peribronchial cuffing)* (see Fig. 21.19) and edema in the walls or septa that separate the lung lobules become

BOX 21.2 Radiographic Features of Alveolar Versus Interstitial Processes

Alveolar (Airspace) Disease
Air bronchograms
Fluffy opacities
Rapid coalescence
Acinar nodules
Segmental/lobar distribution

Interstitial Disease
Nodules
Linear/reticular opacities
Septal lines
Cysts
Honeycombing

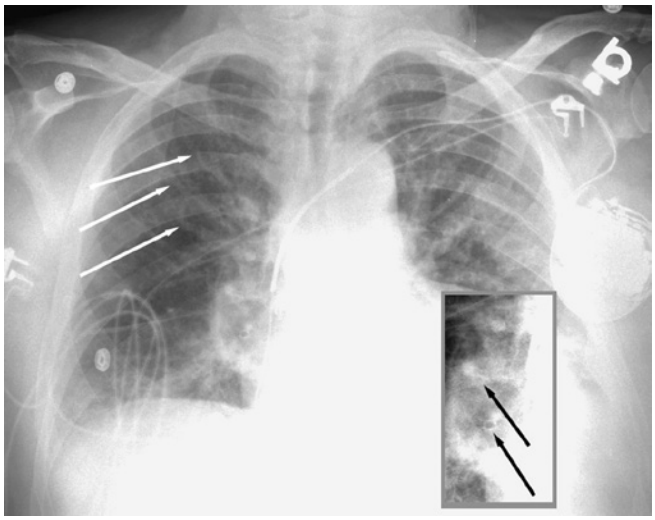


Fig. 21.19 Moderate Pulmonary Edema. Cephalization of blood flow is visible *(white arrows)*. The blood vessels to the apex of the lung are enlarged and similar in size to the blood vessels to the base of the lungs. The *inset* displays peribronchial cuffing *(black arrows);* the inset is from the right hilum of the same film but is enhanced to make the peribronchial cuffing easier to see.

evident. The thickened septa are most clearly seen as thin lines. Fluid may also accumulate in the lymphatics that drain the lung. Such accumulation within the lymphatics may appear on the plain radiograph as thin lines against the pleural edge that run perpendicularly away from the pleural edge. They are called **Kerley B lines** (Fig. 21.20).

RULE OF THUMB Radiographic signs of heart failure include the following:
- Cardiac enlargement
- Pleural effusions, usually bilateral
- Redistribution of blood flow to the upper lobes (cephalization of blood flow)
- Poor definition of the central blood vessels (perihilar haze)
- Kerley B lines
- Alveolar filling

These findings are shown in Fig. 21.20.

The development of pulmonary edema in the lung is seen first in the hila of the lungs by blurring of the normally distinct walls of the hilar blood vessels; this is followed by blurring and increased haziness caused by the edema progressing outward toward the pleura. The term *batwing appearance* is applied to the predominance of edema in the hilar regions of both lungs with progressively less edema in the more peripheral areas of the lungs (Fig. 21.21).

In addition to the previously mentioned classic signs of pulmonary edema, many patients with long-standing heart failure have an enlarged heart and pleural effusions. Such effusions from heart failure are usually bilateral, but if the effusion is visible only on one side, it is more common on the right than on the left.

The radiographic appearance of ARDS can be similar to other forms of pulmonary edema. Although they may appear similar, there are some key differences to help distinguish ARDS from pulmonary edema caused by high vascular pressures or congestive heart failure. The edema of ARDS (see Chapter 29) is patchy and bilateral and does not predominate in the central hilar regions. A chest film of a patient with ARDS also lacks cardiomegaly, cephalization, and Kerley B lines, which are often seen in cardiogenic pulmonary edema (see Chapter 31).

Interstitial Disease

Diseases that primarily involve the interstitium of the lung have a different radiographic appearance than alveolar disease (see Box 21.2). The interstitium of the lung represents the framework or scaffolding of the lung that supports the vessels and bronchi. The secondary pulmonary lobule is the smallest functional unit of the lung.[18] The *secondary pulmonary lobule* contains alveoli and alveolar ducts built around a central pulmonary arteriole and bronchiole, all surrounded by a thin sheet of fibrous connective tissue called the *intralobular septa*. Intralobular septa are invisible on a normal chest x-ray. Pulmonary edema due to poor left-sided heart function causes edema of the intralobular septa (see Chapter 31). As noted, short thin lines from the edematous intralobluar septa can be seen perpendicular to the pleura (see Fig. 21.19); these are Kerley B lines.

Interstitial lung disease (see Chapter 26) refers to a group of diseases that involve the lower respiratory tract. Chest x-rays of patients with interstitial lung disease may have several different appearances depending on the stage and type of interstitial lung disease (see Chapter 26). A chest x-ray of a patient with interstitial lung disease usually has diffuse, bilateral opacities. The opacities may resemble scattered, poorly defined nodules (nodular); a collection of scattered lines (reticular); a combination of both lines and nodules (reticulonodular); or *honeycombing,* which is the development of cystic spaces with well-defined walls seen in the periphery of the lung and resembling a honeycomb. Honeycombing represents irreversible scarring and indicates end-stage lung disease (Fig. 21.22). Lung volumes are generally decreased in patients with interstitial lung disease, a key finding that can aid in the diagnosis on a chest x-ray examination.

There are many types of interstitial lung disease. Causes include *occupational* exposures (e.g., to asbestos [asbestosis] or to silica [silicosis]) and *collagen vascular disease* (e.g., rheumatoid arthritis, scleroderma). The two most common interstitial lung diseases, *sarcoidosis* and *idiopathic pulmonary fibrosis,* have no known cause and are said to be idiopathic. Because many different types of interstitial lung diseases have similar appearances on the chest x-ray, the chest film rarely establishes the specific cause of interstitial disease. Clues to specific causes of interstitial lung disease on a plain chest film are reviewed in Table 21.2. HRCT has become an important tool in evaluating patients with suspected interstitial lung disease. HRCT is particularly helpful in diagnosing idiopathic pulmonary fibrosis because of a characteristic pattern with changes in the lower lobes exceeding those in the apices, a subpleural location, and the presence of honeycombing.[19-21]

Assessing Lung Volume

Incomplete expansion of a part of the lung, also called volume loss or *atelectasis,* is a common abnormality on chest x-rays, and the location and extent of volume loss produces characteristic

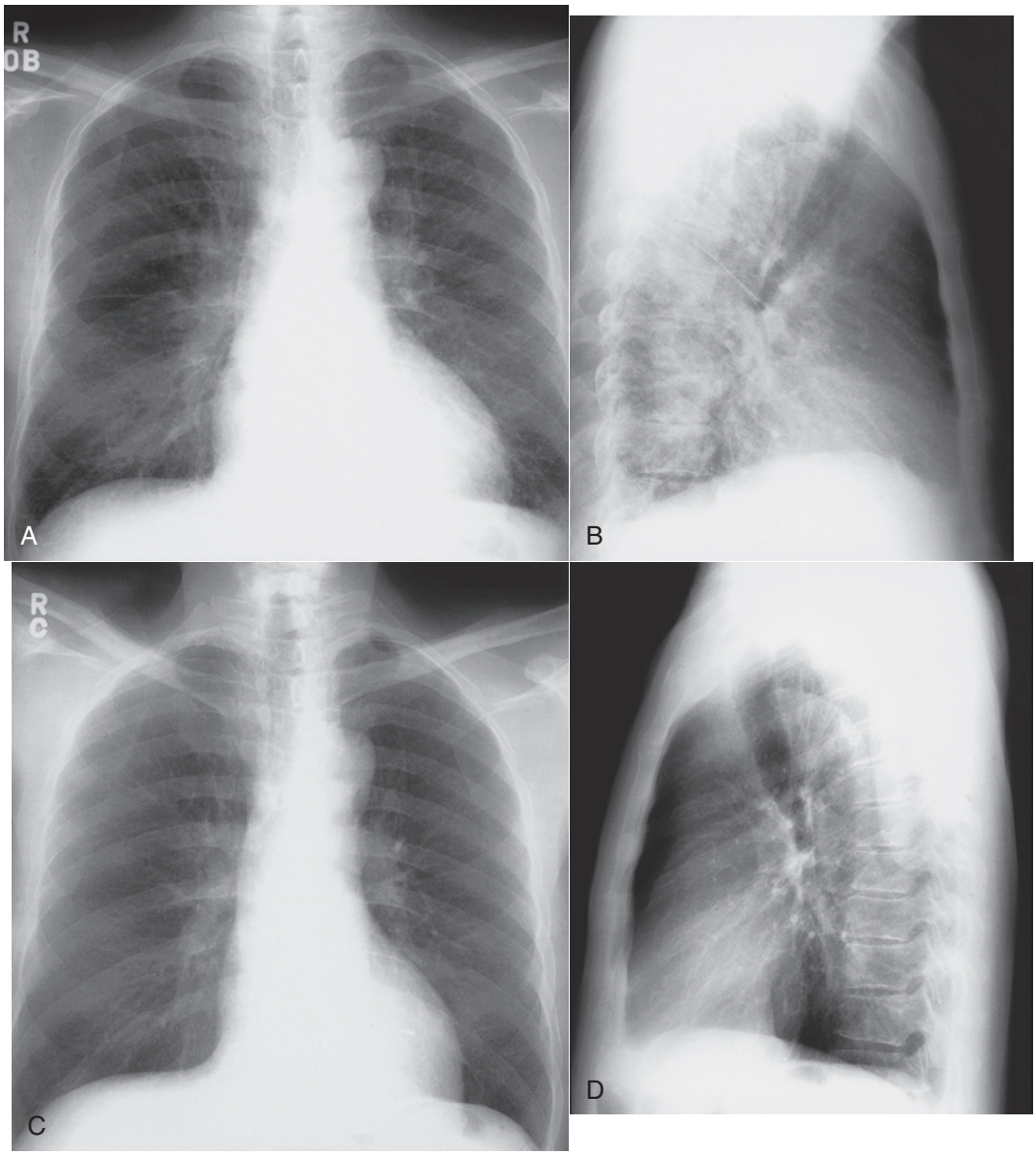


Fig. 21.20 Posterior (A) and lateral (B) chest films show an enlarged cardiac silhouette. The lateral lung margins are slightly displaced away from the inner chest wall in both costophrenic angles, which is consistent with bilateral effusions. There is thickening of the fissures on the lateral projection, indicating that the pleural fluid extends into the interlobar fissures. Numerous Kerley B lines are seen as linear densities extending to the pleural surface in the right lower chest. The definition of the central vessels is suboptimal, indicating interstitial edema. (C and D) The same patient after therapeutic diuresis. Note the decreased heart size, disappearance of Kerley B lines, and improved definition of the central pulmonary vasculature.

chest x-ray patterns. The degree of atelectasis can be described as subsegmental (involving less than a segment of lung), segmental (involving one or more segments of lung), or lobar (involving one or more lobes of the lung). A specific type of subsegmental atelectasis that has a classic radiographic appearance is called *plate-like* or *discoid* ***atelectasis*** (Fig. 21.23). Atelectasis commonly occurs after abdominal or thoracic surgery, adjacent to pleural effusions, or after pleural irritation from a rib fracture or pulmonary infarction.

Volume loss involving an entire lobe (lobar atelectasis) can sometimes be caused by central airway obstruction.[22] The collapsed lobe assumes the shape of a wedge, with the apex of the wedge at the hilum and its base on the pleural surface. This wedge is visible on a PA or lateral x-ray film, depending on which lobe is collapsed (Fig. 21.24). The central bronchial obstruction may be caused by cancer, a foreign body, or a mucous plug (Fig. 21.25). As shown in Fig. 21.26, a bulging convexity to the apex of the wedge may indicate a central tumor.

Atelectasis causes changes to the surrounding structures. As lung volume decreases, the surrounding tissues collapse to fill the space of the collapsed lung. The diaphragm becomes elevated on the side of the atelectasis, the mediastinum shifts toward the atelectasis, and poor expansion of the chest causes narrowing of the rib spaces. If the collapsed segment of the lung is in the upper lobe, the hilum and the minor fissure on the right are displaced upward.

RULE OF THUMB Radiographic signs of volume loss (atelectasis) include the following:

- Unilateral diaphragmatic elevation
- Mediastinal shift toward the atelectasis
- Narrowing of the space between the ribs
- Hilar displacement toward the atelectasis

See Figs. 21.23–21.26.

Assessment of lung volumes on a chest x-ray requires several observations. Rib counting is a popular method to assess lung volume. With a good inspiration, the sixth and sometimes the seventh anterior rib should project above the diaphragm. If more than seven anterior ribs are visible above the diaphragm, *hyperinflation* is present. Obstructive pulmonary disease is classically associated with increased lung volumes (hyperinflation). In patients with chronic obstructive pulmonary disease, there may also be an increase in the AP diameter of the chest, with associated enlargement of the retrosternal and retrocardiac (behind the sternum and the heart, respectively) airspaces and flattening of the hemidiaphragms. These findings are secondary signs of *pulmonary emphysema*. The only primary signs of emphysema are loss or shifting of pulmonary vessel markings and the appearance of the walls of bullous airspaces (Fig. 21.27).

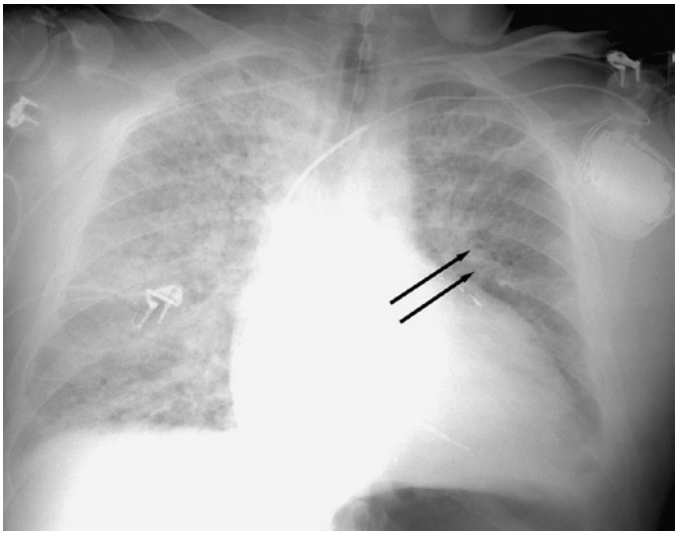


Fig. 21.21 Severe Pulmonary Edema. Both lungs are opacified in a batwing distribution. The hilar vessels are invisible because of the edema in the lung tissue surrounding these vessels. Peribronchial cuffing is indicated by the *black arrows*.

TABLE 21.2 Clues on Plain Chest X-Ray Indicating the Specific Cause of Interstitial Lung Disease

Clues on Radiograph	Cause of Disease
Pneumothorax	Lymphangioleiomyomatosis, Langerhans cell histiocytosis
Pleural effusion	Rheumatoid arthritis, systemic lupus erythematosus
Dilated esophagus	Scleroderma, CREST syndrome
Erosive arthropathy (shoulder joints, clavicles)	Rheumatoid arthritis
Mediastinal adenopathy	Sarcoidosis, progressive systemic sclerosis (scleroderma), metastatic cancer
Soft tissue calcification	Dermatomyositis, progressive systemic sclerosis (scleroderma)
Pleural plaque	Asbestosis

*CREST, C*alcinosis, *R*aynaud phenomenon, *E*sophageal dysmotility, *S*clerodactyly, and *T*elangiectasia.

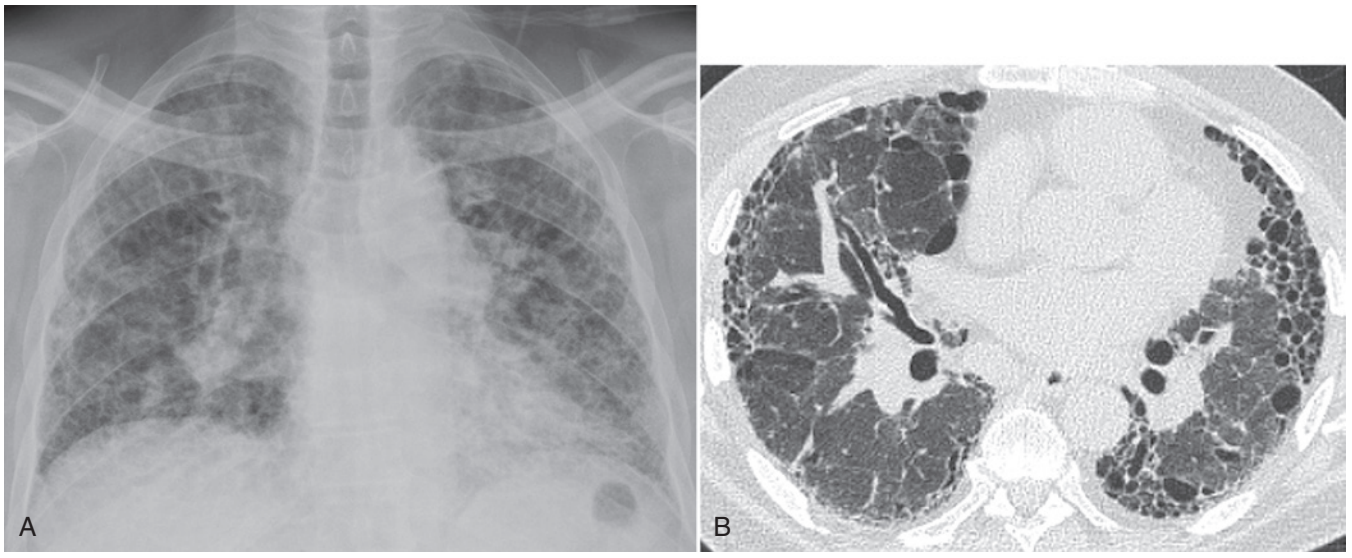


Fig. 21.22 Posteroanterior view (A) of the chest in a patient with shortness of breath. The chest x-ray shows interstitial lung disease. The lung volumes are small. Coarse linear and cystic lucencies represent pulmonary fibrosis. These findings are better visualized on the chest computed tomography image (B), where there is bronchiectasis, architectural distortion, and honeycombing. The patient has interstitial pulmonary fibrosis, the most common type of pulmonary fibrosis.

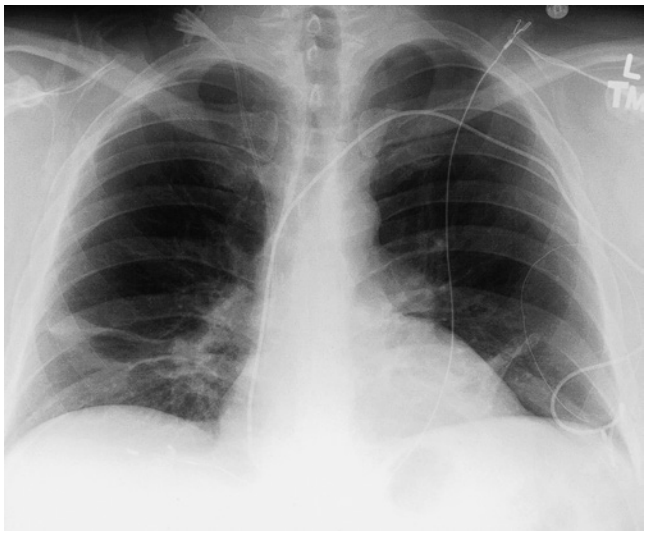


Fig. 21.23 Plate Atelectasis. Posteroanterior chest x-ray shows linear areas of plate atelectasis in both lower lobes.

RULE OF THUMB A good inspiratory effort by the patient is needed to obtain a good-quality chest x-ray examination. Visualization of 6 anterior or 10 posterior ribs above the level of the diaphragm on the PA view indicates a good inspiratory effort by the patient.

Because radiographic signs of emphysema (see Chapter 25) are apparent only with more advanced disease, the chest x-ray is generally considered insensitive for detecting obstructive lung disease. However, CT is far more sensitive and may show evidence of emphysema even when pulmonary function test results are normal.[23] Emphysema is often anatomically described in three patterns depending on which part of the secondary pulmonary lobule is affected. When only the central part of the lobule is affected, the pattern is called *centrilobular* or *centriacinar emphysema*. When the entire lobule is affected, the pattern of emphysema is called *panlobular* or *panacinar*. Finally, when the emphysema is confined to areas near the pleura, the pattern is called *paraseptal emphysema*. Fig. 21.28 shows a case of upper

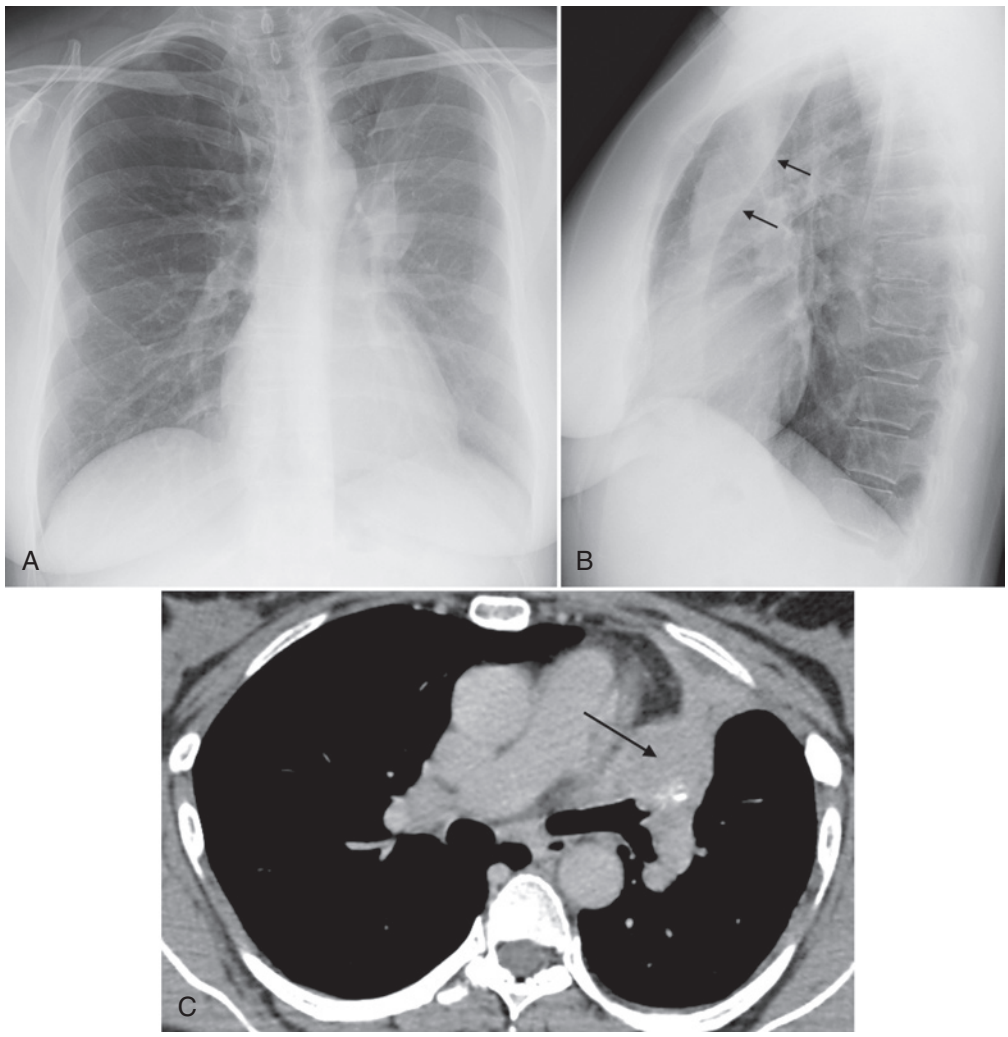


Fig. 21.24 (A) Posteroanterior view of the chest shows leftward mediastinal shift, a left hilar mass, and increased density overlying the left chest. (B) Lateral view shows a wedge of increased density *(arrows)* anteriorly with its apex at the hilum and its base on the pleural surface representing the collapsed left upper lobe. (C) Computed tomography image shows a partially calcified left hilar mass *(arrow)* with the collapsed left upper lobe distally. Biopsy of the mass revealed carcinoid tumor.

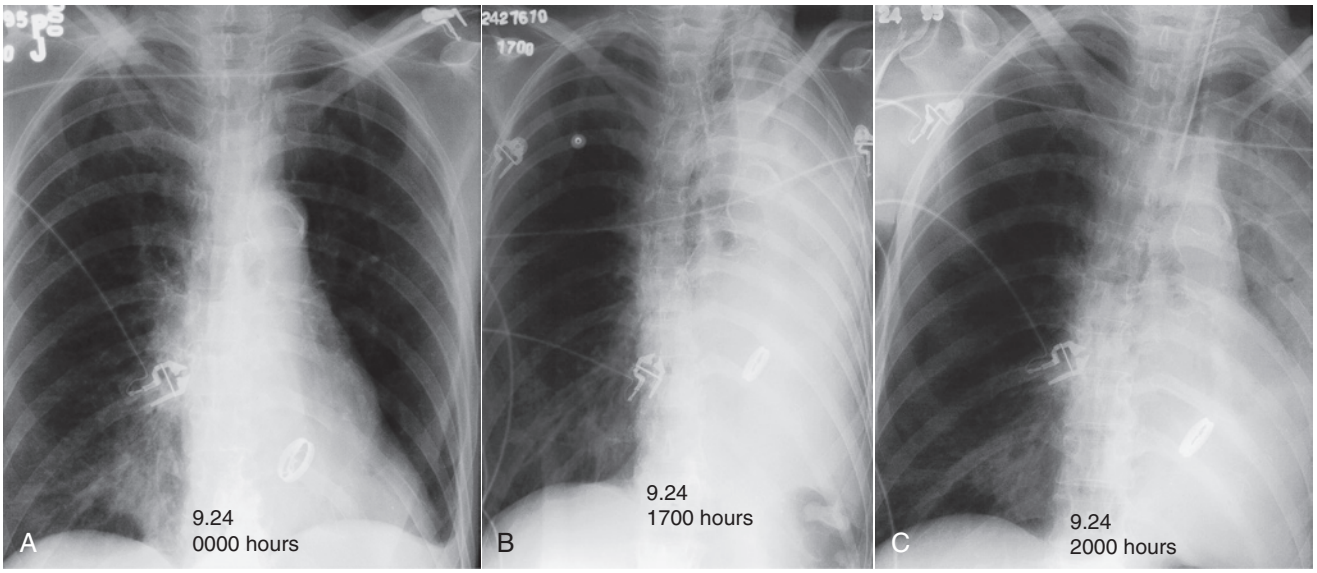


Fig. 21.25 Three Portable Chest Films Obtained Within a 20-Hour Time Span. (A) Good aeration of both lungs. (B) Film obtained 17 hours later shows complete opacification of the left hemithorax. Bronchoscopy performed after this film revealed a mucous plug in the left main bronchus. It was removed at bronchoscopy. (C) Partial reexpansion.

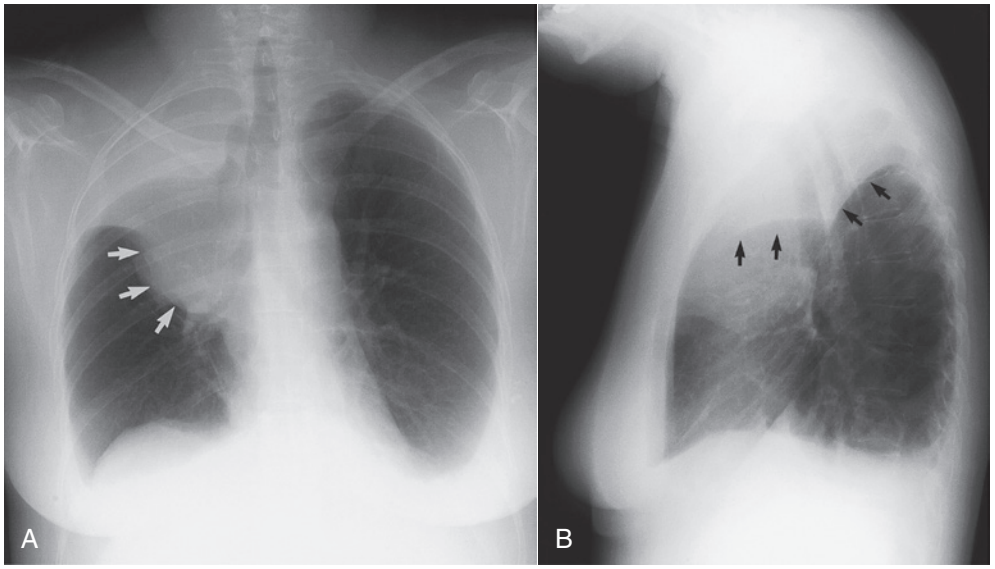


Fig. 21.26 Posteroanterior (A) and lateral (B) views of the chest in a patient with right upper lobe collapse. (A) Note the wedge opacity of the right upper lobe and the inferior bulge *(arrows)* of the minor fissure on the posteroanterior film. This bulge indicates the presence of a central mass. (B) The wedge shape of right upper lobe atelectasis *(arrows)* is well seen on the lateral film.

lobe paraseptal emphysema, characterized by cystic areas along the pleural surface. A chest CT scan may prove useful to help define which patients may benefit from treatments such as lung volume reduction surgery. Results of the National Emphysema Treatment Trial showed that patients with heterogeneous upper lobe–predominant emphysema (i.e., emphysema that is greater in the apices of the lung than in the bases) are good candidates for lung volume reduction surgery.[24]

Solitary Pulmonary Nodule

A **solitary pulmonary nodule** (SPN) is a parenchymal opacity smaller than 3 cm in diameter that is surrounded by aerated lung. Parenchymal opacities 3 cm or greater are referred to as lung masses. One or two SPNs are encountered in every 1000 chest x-rays. SPNs are important to identify because they may be caused by lung cancer or another malignancy that has spread or metastasized to the lung. The reported prevalence of malignancy in SPNs ranges from 3% to 6% in large surveys of the general population. In patients with SPNs who have surgical resection, 30% to 60% of the nodules are malignant.[25]

When first encountered, an SPN should be assessed for features listed in Table 21.3 that may help to establish a nonmalignant cause. The goal of imaging SPNs is to avoid resecting benign nodules while encouraging surgical removal of all potentially curable cancers. The axial anatomic display of CT, along with better density-discriminating powers, makes CT a preferred tool

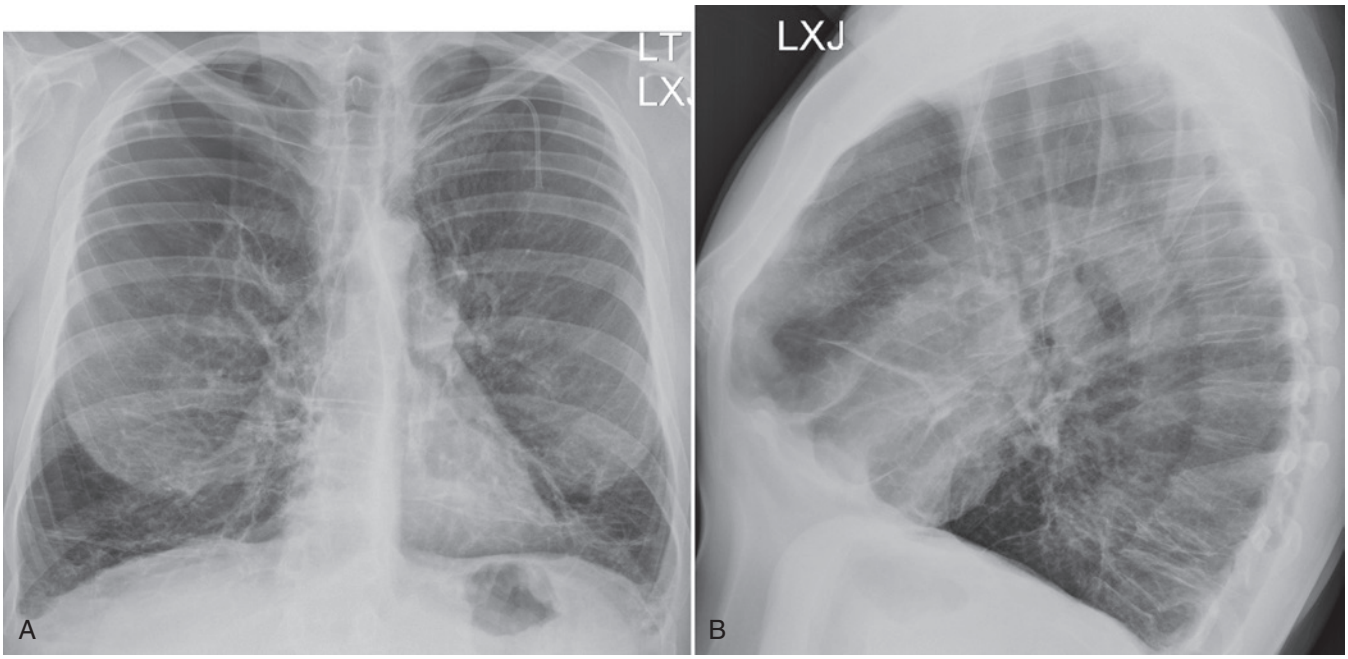


Fig. 21.27 Posteroanterior (A) and lateral (B) views of the chest of a patient with bullous emphysema, worse on the right. The lungs are hyperinflated with flattening of the diaphragms, increased retrosternal clear space, and areas in the upper lung zones that are devoid of any vascular markings.

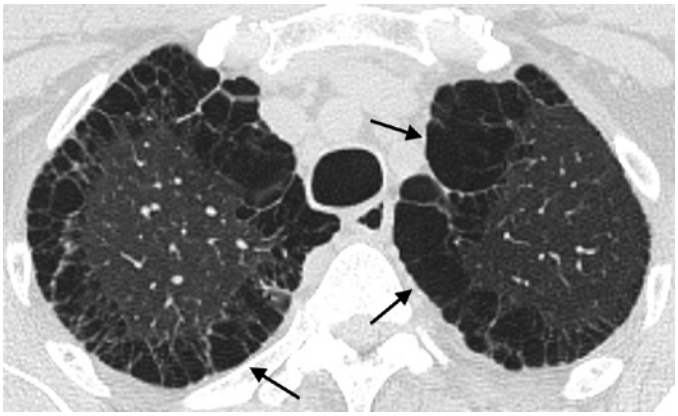


Fig. 21.28 Computed Tomography Image Through the Upper Lobes in a Patient With Pulmonary Emphysema. Numerous cystic lucencies are present in both lungs. Note the absence of bronchovascular markings within the lucencies. Most of the emphysematous areas are located in a peripheral distribution *(arrows)* along the pleural surface, representing paraseptal emphysema.

TABLE 21.3 Features Useful in Distinguishing Benign From Malignant Solitary Pulmonary Nodules

Feature	Favoring Malignant Nodule	Favoring Benign Nodule
Patient's age	>40 years old	<40 years old
Smoking status	Current or former smoker	Lifetime nonsmoker
Size of nodule	>3 cm	<3 cm
Shape of nodule	Lobulated	Spherical
Margins of nodule	Spiculated	Well defined
If cavity	Thick-walled	Thin-walled
Doubling time[a]	7–465 days	<7 or >465 days
Calcification	Rare, usually eccentric	Central, lamellar, popcorn

[a]Time necessary for the nodule to double in volume.

for evaluating SPNs. CT provides a detailed evaluation of the size, shape, border, and density of a nodule. For example, the presence of fat or the pattern of calcification can help to establish that a pulmonary nodule is benign (Fig. 21.29).

Central or lamellar swirls of concentric rings often result from calcification and strongly suggests a benign cause of an SPN or a granuloma. Eccentric (off-center), speckled, or amorphous calcification may be seen in lung cancer. A smoothly marginated round pulmonary nodule more often is benign, whereas a nodule with a lobulated, irregular, or spiculated border is more likely to be malignant (see Fig. 21.29). PET-CT is often very helpful in evaluating SPNs (Fig. 21.30). Nodules greater than 1 cm in diameter that take up the isotope used in PET-CT studies, fluorodeoxyglucose (FDG), are metabolically active and are more likely to be malignant than nodules without uptake. Unfortunately FDG uptake by a pulmonary nodule on a PET-CT is not specific for malignancy because infectious or inflammatory nodules (such as nodules caused by fungal infection with *Histoplasma,* areas of pneumonia) may also be FDG-avid and "light up." Similarly, slow-growing cancers (such as adenocarcinoma in situ) or small (<1 cm) malignant nodules may not take up FDG on PET-CT exams.

RULE OF THUMB Although a PET-CT scan can be useful in helping to evaluate whether a pulmonary nodule is benign or malignant, the test has limitations. Small nodules (<1 cm in diameter) can be PET-negative (i.e., they do not take up the FDG agent) despite being cancerous, and inflammatory nodules (e.g., due to infections) can be PET-positive despite not being cancerous.

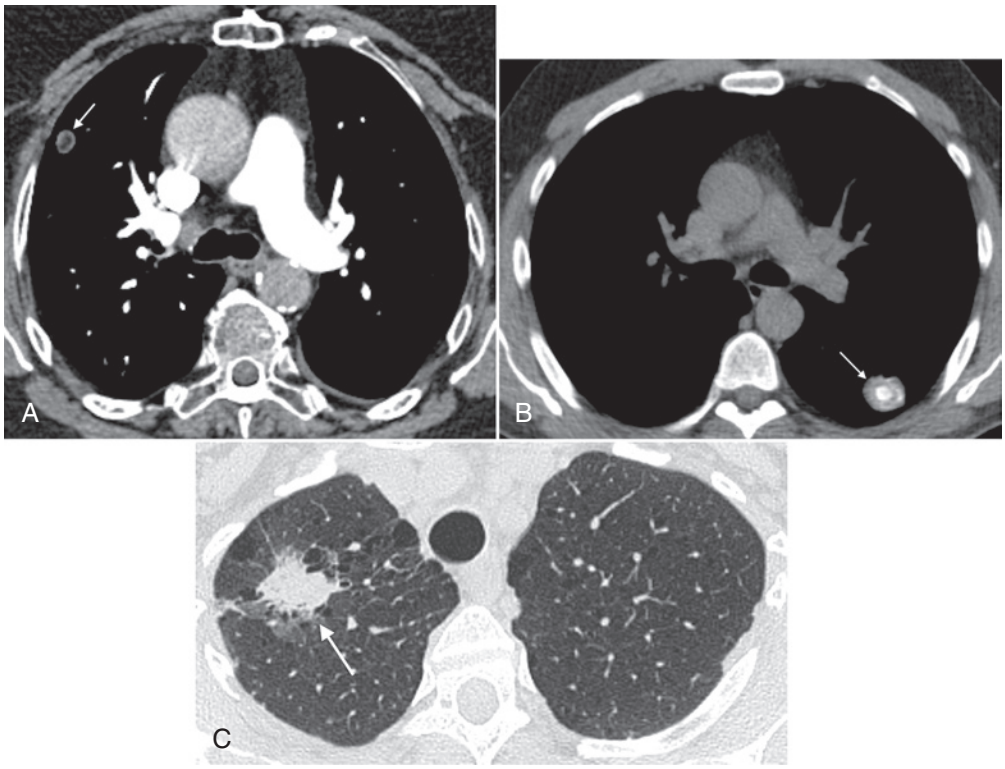


Fig. 21.29 Computed Tomography Examples of Solitary Pulmonary Nodules. (A) Nodular density in the right lung, containing fat. Note the same density within the nodule as the subcutaneous fat. This finding is diagnostic of a pulmonary hamartoma, a benign diagnosis requiring no further follow-up. (B) There is central calcification with this pulmonary nodule *(arrow)*, a benign form of calcification consistent with a granuloma. (C) The spiculated edge of this nodule *(arrow)* is suggestive of malignancy in this biopsy-proved primary lung adenocarcinoma.

MEDIASTINUM

The mediastinum consists of the structures that lie between the lungs—including the heart, great vessels, trachea, esophagus, and lymph. The mediastinum is divided into three compartments: (1) anterior, (2) middle, and (3) posterior. When a mediastinal abnormality is discovered, determining the precise location of the mediastinum is important to narrow the list of possible causes; this is called the *differential diagnosis*. The three mediastinal compartments are best defined on a lateral view (see Fig. 21.5). A line extending from the diaphragm along the posterior margin of the heart and the anterior margin of the trachea to the neck divides the anterior mediastinum from the middle compartment. A second line traversing the vertebral bodies 1 cm posterior to their anterior margins and extending from the neck to the diaphragm divides the middle from the posterior compartment. Some mediastinal masses are visible on both front and lateral projections, and the specific location within the mediastinum offers the first clue to diagnosis.

Table 21.4 lists the common causes of masses in the three mediastinal compartments. CT is the preferred imaging examination for evaluating most mediastinal masses. Fig. 21.31 shows the normal axial anatomic display on contrast-enhanced CT scan at the levels of the great vessels, aortic arch, carina, and cardiac chambers. The CT appearance of an anterior mediastinal mass (thymoma) is shown in Fig. 21.32. Fig. 21.33 shows a middle mediastinal mass (bronchogenic cyst) on an MRI examination. A large hiatal hernia located in the mediastinum can be easily confused with a mass on the frontal chest film but is easily seen on CT in Fig. 21.34.

TABLE 21.4 Mediastinal Abnormalities by Compartment

Anterior Mediastinum	Middle Mediastinum	Posterior Mediastinum
Thyroid or parathyroid mass	Aortic aneurysm (ascending/arch)	Aortic aneurysm (descending)
Thymic lesions	Lymphadenopathy	Neurogenic tumors
Lymphoma	Bronchogenic cyst	Lymphoma
Pericardial cyst/fat pad	Tracheoesophageal masses	Neurenteric cyst
Teratoma	Hiatal hernia	Bochdalek hernia[a]
Morgagni hernia[a]		
Ventricular aneurysm		

[a]Hernia in which the abdominal contents press through a gap in the diaphragm.

Pneumomediastinum

Pneumomediastinum, which is the accumulation of air in the mediastinum, is a form of barotrauma and may also be seen in cases of esophageal rupture (Fig. 21.35). This condition usually occurs in the distal portion of the esophagus in patients who

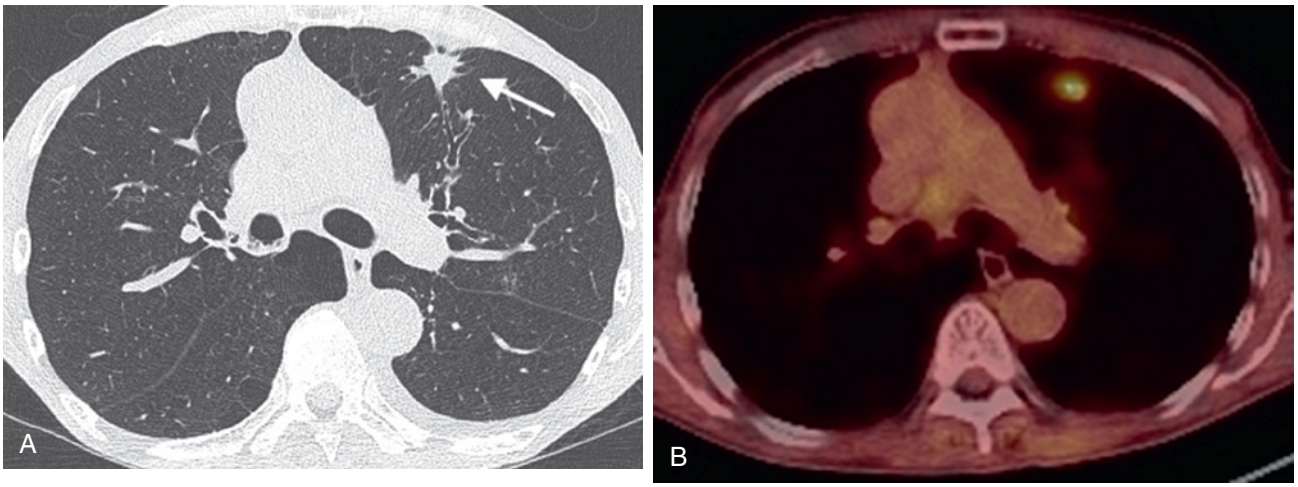


Fig. 21.30 (A) Chest computed tomography (CT) image of a speculated left upper lobe pulmonary nodule, indicated by the arrow. (B) A fused image (containing information from both a chest CT and information from the nuclear medicine exam) from a subsequent positron emission tomography-CT exam shows that the left-upper-lobe nodule is hypermetabolic, meaning that it takes up glucose. It appears yellow on the fused image. This nodule was biopsied and represents a primary lung adenocarcinoma.

undergo procedures to stretch or dilate the esophagus. Chest trauma may cause injury to the trachea or central bronchi (such as the trachea or mainstem bronchi), also allowing movement of air into the mediastinum. Rarely, air dissects down from the soft tissues of the neck after thyroid, parathyroid, or tonsillar surgery. Gas associated with a retrotonsillar abscess may extend inferiorly into the mediastinum through the fascial planes of the neck. Air that accumulates in the retroperitoneum may enter the mediastinum via openings in the diaphragm for the aorta or esophagus.

Catheters, Lines, and Tubes

Chest x-rays are commonly used to evaluate the position of catheters, lines, and tubes and to evaluate for potential complications that may arise from the placement of these devices. RTs must be skilled at examining the chest x-ray to determine the position of the endotracheal tube, chest tubes, central and peripheral catheters, and hemodynamic monitoring lines.

Endotracheal Tube

Endotracheal tubes are radiopaque, meaning that they block the transmission of x-rays and appear white on a chest x-ray. Radiographs are routinely obtained at the bedside after intubation to assess for correct endotracheal tube position. The chest x-ray shows the distal tip of the endotracheal tube and the carina. The position of the patient's neck is important. The neck position is usually neutral, but the position of the tip of the endotracheal tube can vary with neck position. Specifically, the endotracheal tube's position can move appropriately 4 cm toward the carina as the neck moves from full extension (high position) to full neck flexion (low position), which is one-third the length of the average adult trachea. In other words, when the neck is flexed, the endotracheal tube moves down deeper into the trachea. Although there is some variability in the literature, several studies suggest that when the head and neck are in the neutral position, the endotracheal tube should be positioned in the mid-trachea approximately 3 to 7 cm above the carina. Although it may be difficult to see on some chest x-ray images, the carina is generally located at the space between the T4 and T5 vertebral bodies in most adults.[26] Placement below the thoracic inlet (usually at C5 to C6 for adults) ensures that the tube is beyond the vocal cords (usually at C5 to C6). Fig. 21.36 shows an endotracheal tube that has been advanced too far into the airway and is positioned in the right mainstem bronchus. This creates a dangerous situation which can cause hyperinflation of the right lung and atelectasis of the left lung. Hypoxemia can result.

RULE OF THUMB The distal tip of the endotracheal tube should be positioned approximately 3–7 cm above the level of the carina in an adult patient.

RULE OF THUMB When the patient flexes his or her neck, the tip of the endotracheal tube moves down (into the lung). When the neck is extended, the endotracheal tube moves up (out of the lung toward the vocal cords). Thus proper positioning of an endotracheal tube is important to prevent its migration into a mainstem bronchus (usually the right mainstem bronchus) when neck flexion occurs or to prevent accidental extubation when neck extension occurs.

Tracheostomy Tube

Tracheostomy tubes should be two-thirds the diameter of the trachea and should project within the borders of the trachea on the radiograph. The tip should extend beyond half the distance from the stoma to the carina.

Central Line

A central venous catheter is typically placed via either the internal jugular or subclavian vein. A chest x-ray should be obtained after placement to assess the position and to exclude a procedural complication (e.g., pneumothorax, hemothorax). Ideally the tip of the central venous pressure catheter should be in the superior vena cava. This vessel usually forms at the level of the first

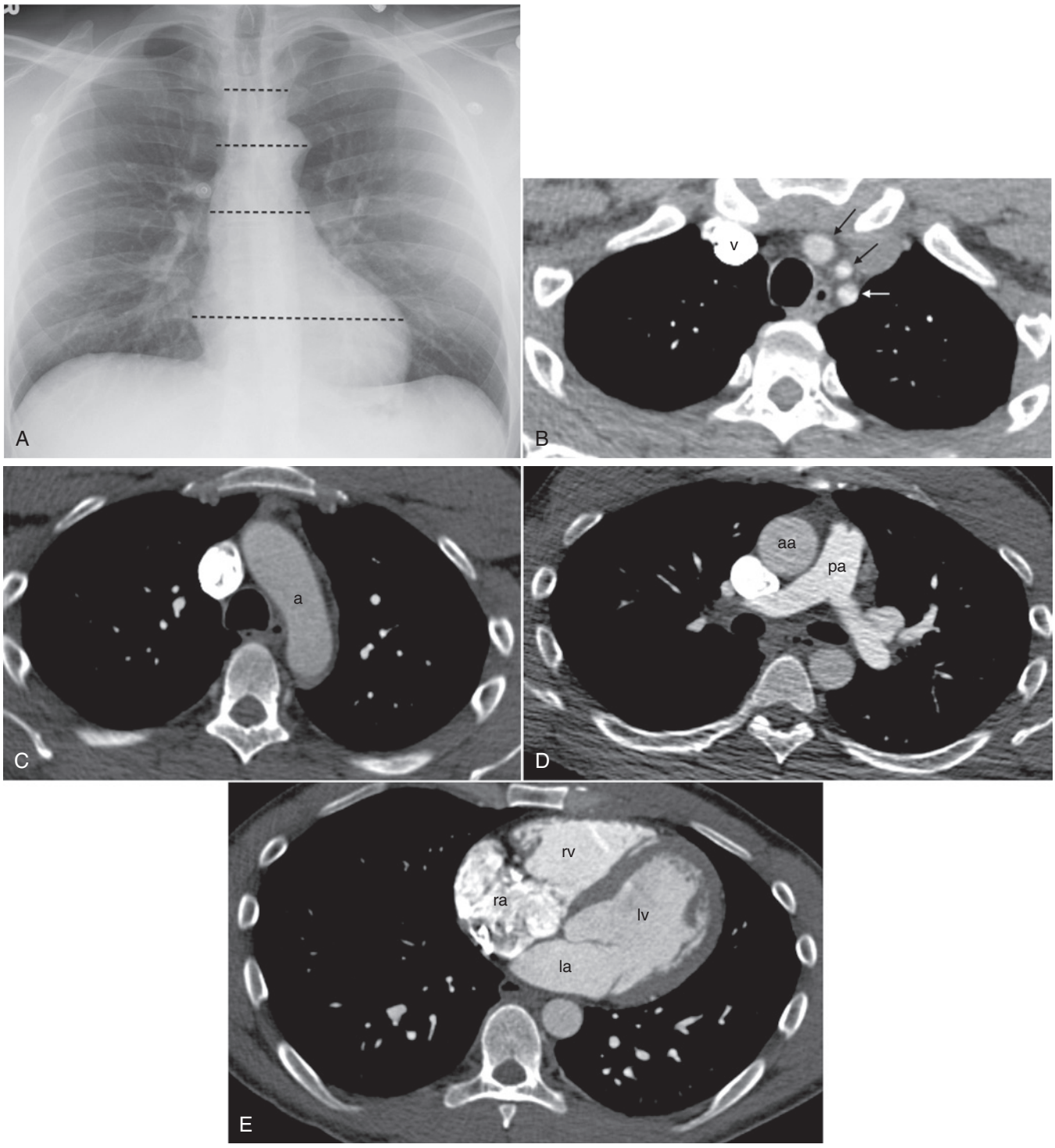


Fig. 21.31 (A) Posteroanterior chest x-ray indicating the four levels at which computed tomography scan slices (B) to (E) were obtained. (B) The most superior image is at the level of the great vessels. Contrast material fills the right brachiocephalic vein *(v)* and the three arch vessels, the right brachiocephalic, left common carotid, and left subclavian arteries. (C) At this level, the arch of the aorta *(a)* lies on the left side of the airway. The esophagus is seen in front of the vertebral body behind the airway. The opacified superior vena cava lies to the right of the arch anteriorly. (D) At the level of the pulmonary artery *(pa)* bifurcation, the right pulmonary artery crosses the mediastinum anterior to the right main bronchus. The vena cava lies to the right of the ascending aorta *(aa)*. The descending aorta is seen next to the vertebral body. (E) At the level of the heart, contrast material is seen filling the right atrium *(ra)* and crossing the atrioventricular (tricuspid) valve into the right ventricle *(rv)*. The thick, muscular left ventricular *(lv)* wall is visualized as it contracts. The left atrium *(la)* is seen anterior to the esophagus.

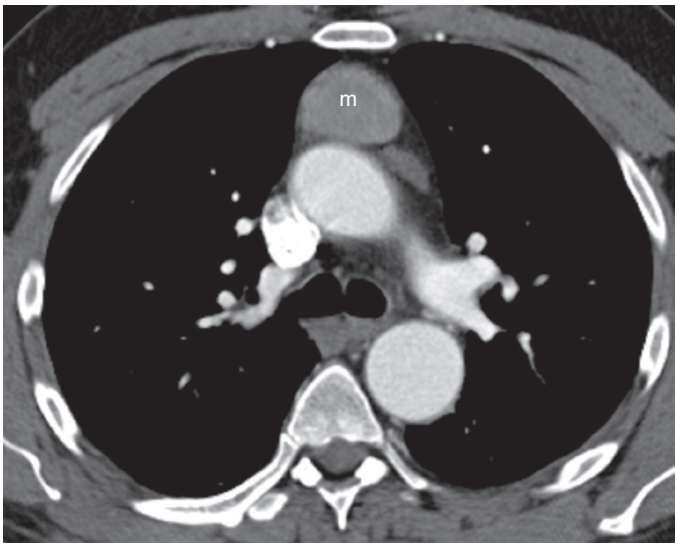


Fig. 21.32 **Anterior Mediastinal Mass.** Computed tomography slice at the level of the aortic arch shows a homogeneous encapsulated anterior mediastinal mass *(m)*. The diagnosis was thymoma.

anterior intercostal space where the brachiocephalic veins come together. The brachiocephalic veins contain valves, and these catheters ideally should be placed central to any valves.

Peripherally Inserted Central Venous Catheter

An alternative to placing a central venous catheter is a peripherally inserted central venous catheter (PICC), which is placed via a peripheral vein in either the left or right upper extremity. Advantages of a PICC are that it does not risk a pneumothorax, as would occur with central venous catheters; it can be used long term (often for several weeks); and it has a lower rate of infection than central venous catheters. The preferred location for a PICC is similar to that for a central venous catheter, with the tip of the catheter located in the superior vena cava.

Pulmonary Artery (Swan-Ganz) Catheter

Although not as commonly used as in the past, Swan-Ganz catheters are used to measure hemodynamic and central pressure variables such as pulmonary artery occlusion pressure (sometimes called the "wedge pressure"). Pulmonary artery catheters are

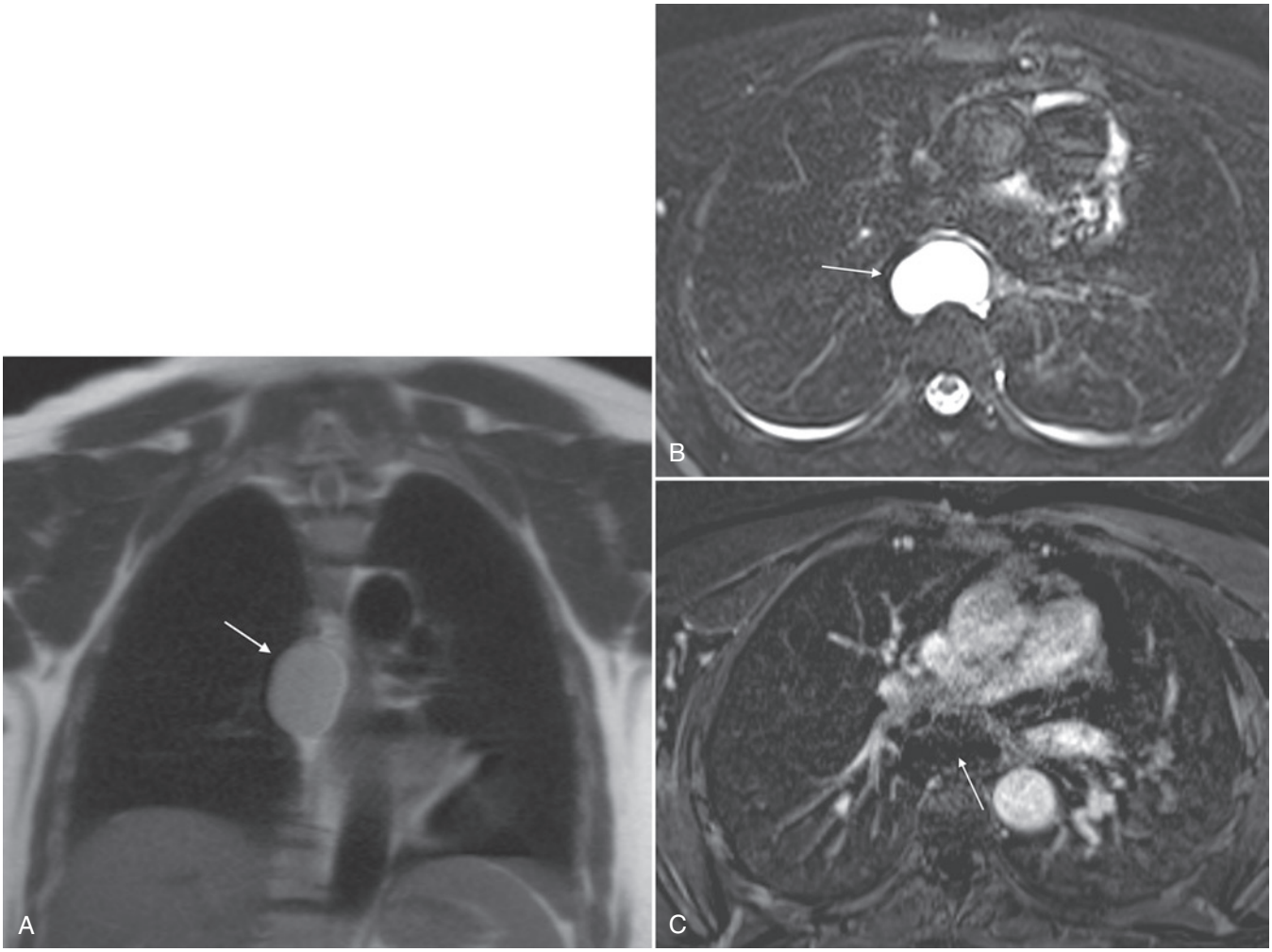


Fig. 21.33 **Middle Mediastinal Mass.** Magnetic resonance images demonstrate a subcarinal mass *(arrows)*. Coronal HASTE (A) and axial STIR (B) images demonstrate increased T2 signal (appearing gray or white) intensity in this mass, suggestive of a cystic lesion. Subtraction VIBE image (C) shows no enhancement (the mass is black), confirming no contrast enhancement. The diagnosis is a bronchogenic cyst, a benign lesion. HASTE, VIBE, and STIR refer to specific MRI imaging sequences and/or analyses used to optimize discrimination among tissue types. *HASTE*, Half-Fourier Single Shot Turbo Spin Echo; *VIBE*, Volumetric Interpolated Breath-Hold Sequence; *STIR*, TI Inversion Response.

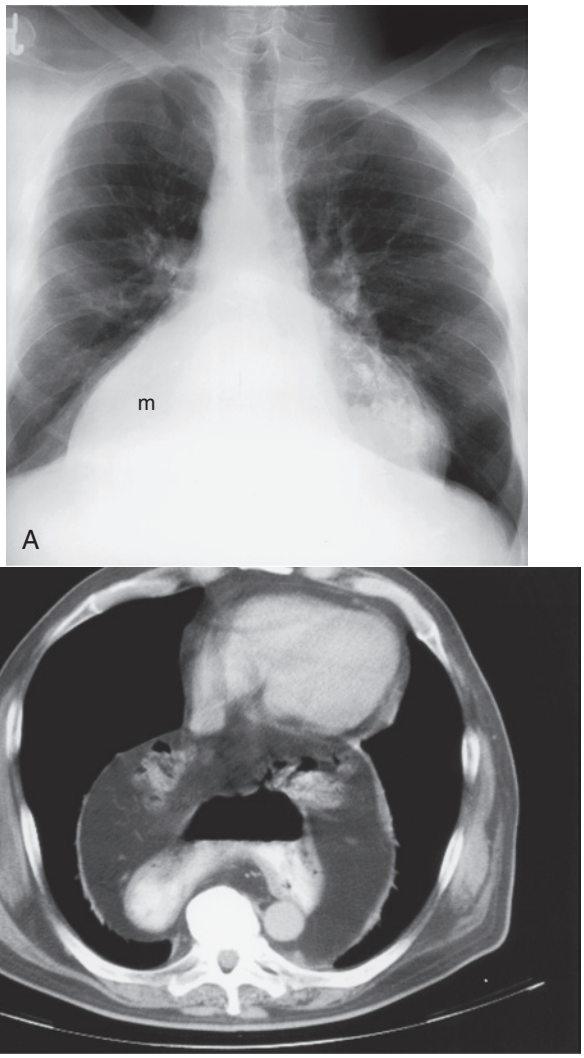


Fig. 21.34 Posterior Mediastinal Mass. (A) Posteroanterior chest x-ray shows a large soft tissue density *(m)* obscuring the right heart border and the right hemidiaphragm. (B) Computed tomography image at this level shows a large retrocardiac diaphragmatic hernia containing omentum and stomach.

placed at the bedside and ideally should reside in the proximal right or left main pulmonary arteries. They are floated into position using an inflatable balloon on the catheter tip. Because of this maneuver, they are placed in the right pulmonary artery more than 90% of the time. When the wedge or pulmonary artery occlusion pressure is measured, the balloon is inflated and the catheter moves out into a more peripheral vessel. As soon as the reading has been accomplished, the balloon should be deflated and the catheter pulled back to a central location. Persistent peripheral placement (i.e., when the catheter tip is far out in the lung parenchyma) can cause infarction of the lung beyond (distal to) the wedged catheter (Fig. 21.37) or result in injury to the pulmonary artery, such as formation of a pseudoaneurysm or even rupture.

Chest Tube

Chest tubes are small-bore to large-bore tubes placed into the pleural space from outside the chest wall (see Chapter 27). The most common indications for a chest tube are for a pneumothorax

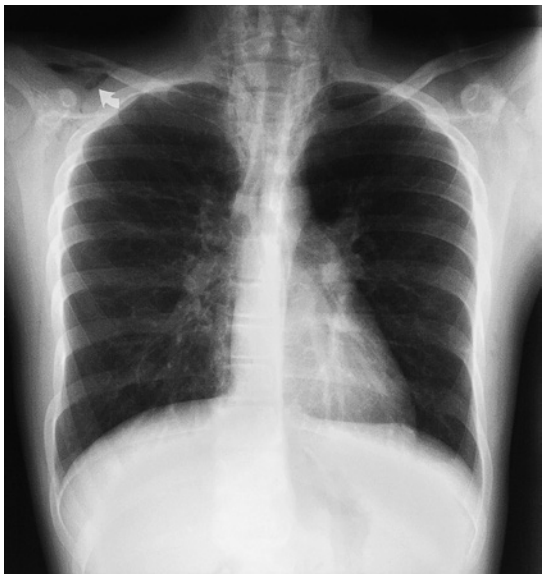


Fig. 21.35 Pneumomediastinum. Posteroanterior view of the chest of an 11-year-old child with asthma shows linear lucencies (free air) in the mediastinum and extending into the soft tissues of the neck bilaterally. Note the free air around the lateral aspect of the right clavicle *(arrow)*.

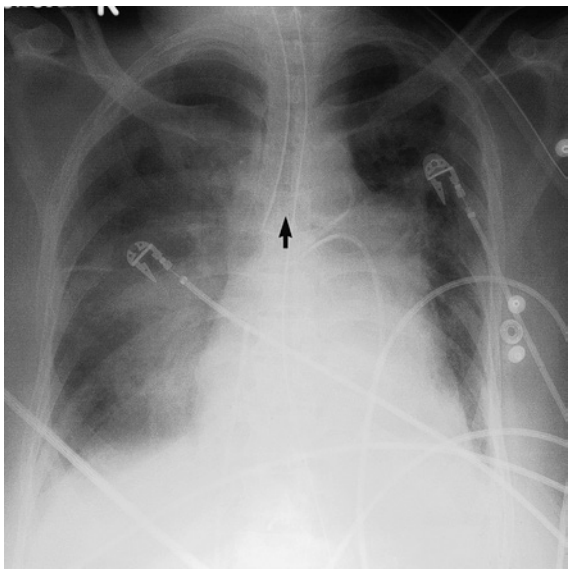


Fig. 21.36 Portable supine chest film shows malposition of an endotracheal tube in the right mainstem bronchus *(arrow)*.

(air in the pleural space) or an empyema (pus in the pleural space), although chest tubes may also be used to drain blood *(hemothorax)* or fluid *(hydrothorax)* or to install a sealant (e.g., the antibiotic doxycycline) to achieve closure of the pleural space, preventing a recurrent pneumothorax or hydrothorax. Radiographically, most chest tubes have radiopaque stripes along their axes so they can be seen on the chest x-ray. The chest tube should be within the pleural space; it usually follows the contour of the chest wall or diaphragm on the chest x-ray.

Intra-Aortic Balloon Pump

The intra-aortic balloon pump (IABP) is a counterpulsation device used to improve cardiac output and blood pressure in patients in cardiogenic shock. It is inserted through the femoral

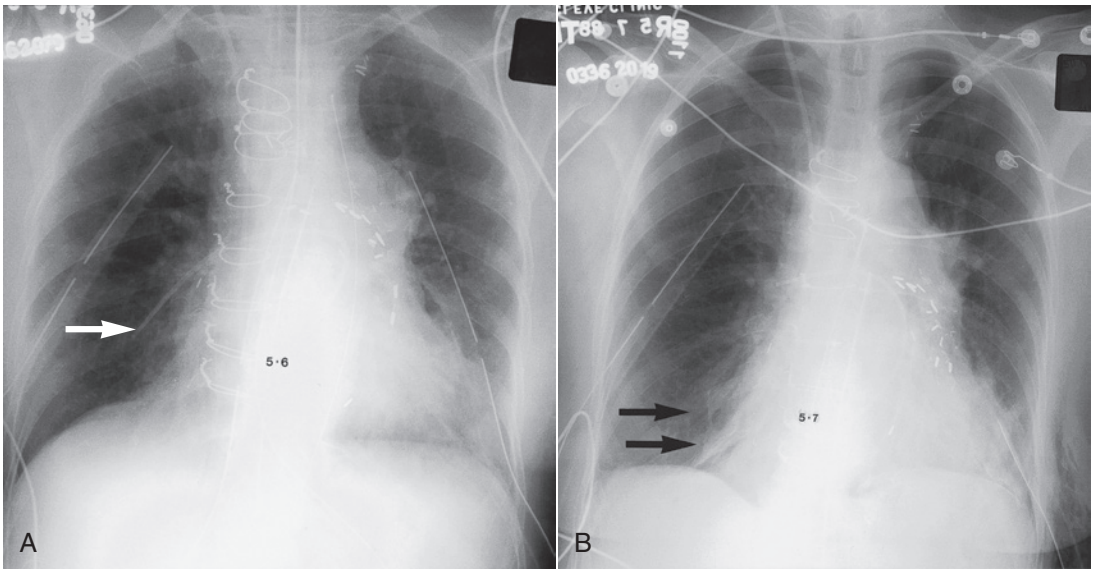


Fig. 21.37 Two Portable Supine Chest Films Obtained 30 Hours Apart. (A) Wedged Swan-Ganz (pulmonary artery) catheter in the right lower lobe *(arrow)*. (B) Film obtained after retraction of the catheter shows increased density at the site, reflecting an area of infarction caused by prolonged inadvertent wedging of the catheter *(arrows)*.

artery and advanced into the thoracic aorta. The device is approximately 26 cm long, and a radiopaque tip allows for radiographic verification of its position. The balloon inflates during diastole and deflates during systole to enhance perfusion of the coronary arteries and cardiac output. The radiopaque tip should reside just beyond the origin of the left subclavian artery within the proximal descending thoracic aorta. The carina can be used as a landmark with the tip of the IABP approximately 2 cm above the carina.[27] Correct positioning is important, as placement too proximally (superiorly) can occlude the branch aortic vessels to the neck and upper extremities, whereas placement too distally (inferiorly) can occlude vessels to the abdominal organs and intestines.

SUMMARY CHECKLIST

- Thoracic imaging is an important tool for evaluating the cause and degree of various pulmonary diseases. Various thoracic imaging techniques are available to diagnose and monitor patients with lung disease.
- The tissue densities seen on the plain chest x-ray are air, fat, soft tissue (water), and bone.
- The steps in interpreting the chest film include (1) reviewing the technique and quality of the chest film (rotation and penetration) and (2) taking a step-by-step, disciplined approach to reviewing all the anatomic structures seen on the chest film (i.e., bones, soft tissue, heart, lower neck, airways and lungs, pleura, mediastinum, upper abdominal contents).
- The lungs are considered radiolucent and the bones are radiopaque.
- The chest film is useful for detecting pleural diseases such as pleural effusion or pneumothorax.
- Airspace opacities in the lung represent alveolar filling usually caused by either water (pulmonary edema), blood (pulmonary hemorrhage), or pus (pneumonia).
- Air bronchograms are seen when air-filled airways are surrounded by consolidated lung.
- Radiographic signs of pulmonary edema secondary to heart failure include (1) redistribution of blood flow to the upper lobes, (2) Kerley B lines, and (3) alveolar filling.
- Signs of long-standing heart failure include cardiac enlargement and pleural effusions, which are usually bilateral.
- Signs of volume loss (atelectasis) in the lungs include (1) unilateral diaphragmatic elevation, (2) mediastinal shift, (3) narrowing of the rib spaces, (4) hilar displacement, and (5) fissure displacement.
- The chest film is useful in identifying the position of catheters and tubes. The tip of the endotracheal tube should be 3 to 7 cm above the carina when the neck is in a neutral position (i.e., neither flexed nor extended).
- CT provides much more anatomic detail than chest x-rays but exposes patients to more radiation.
- MRI is used less commonly for imaging the chest but has a role in evaluating vascular structures, mediastinal masses, and cardiac structures.
- Ultrasound can be useful in placing central lines, visualizing the presence of pleural fluid (e.g., to help guide thoracentesis), and detecting a pneumothorax.
- PET-CT can help differentiate between malignant (cancerous) and benign (noncancerous) lung nodules, but it has limitations.

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22

Flexible Bronchoscopy and the Respiratory Therapist

Danai Khemasuwan and Atul C. Mehta

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Understand the difference between rigid bronchoscopy and flexible bronchoscopy.
- Understand the preprocedure assessment, type of sedation, and patient monitoring during bronchoscopy.
- Identify the use of several class of medications to sedate the patients during flexible bronchoscopy.
- Describe the difference between conscious sedation and deep sedation.
- Understand the indications, contraindications, and complications of flexible bronchoscopy and various diagnostic techniques.
- Recognize the roles of advanced diagnostic techniques, including endobronchial ultrasound and electromagnetic navigation bronchoscopy.
- Understand the indications, contraindications, and complications of various therapeutic bronchoscopic techniques.
- Recognize the difference between each thermal ablation technique.
- Recognize the difference between silicone and metallic stents.
- Identify bronchial thermoplasty as an emerging nonpharmacologic option for patients with steroid-dependent asthma.
- Describe the role of bronchoscopic-assisted intubation in patients with a difficult airway.
- Describe the role of the respiratory therapist in assisting with bronchoscopy.
- Identify special considerations for bronchoscopy during mechanical ventilation.
- Understand physiologic and mechanical alteration associated with flexible bronchoscopy in intubated patients.
- Describe the method of calculation minute ventilation requirements during flexible bronchoscopy in patients with mechanical ventilation.

CHAPTER OUTLINE

KEY TERMS

airway stents
argon plasma coagulation
brachytherapy
bronchial washings
bronchial brushings
bronchial thermoplasty
bronchoalveolar lavage
capnography
cryotherapy
electromagnetic navigational bronchoscopy
endobronchial biopsy
fiberoptic bundles
laser photocoagulation
Mallampati classification
methemoglobinemia
moderate sedation
narrow band imaging
transbronchial biopsy
transbronchial needle aspiration
ultrathin bronchoscopy

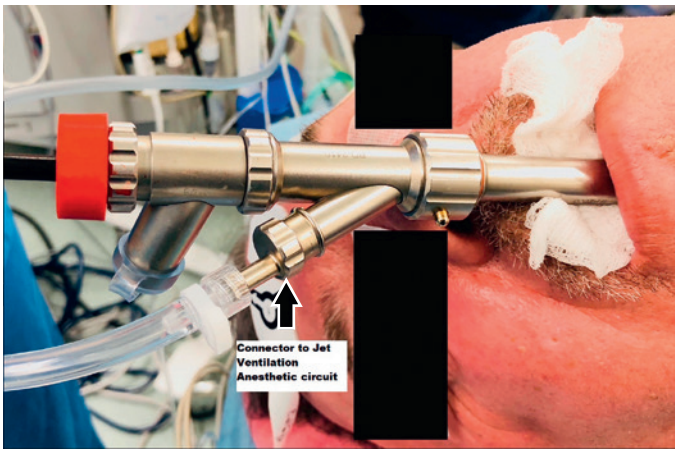

Fig. 22.1 Rigid Bronchoscope Inserted Into the Patient. *Arrow,* Connector to jet ventilator anesthetic circuit.

BOX 22.1 Indications for Rigid Bronchoscopy

- Large foreign body extraction
- Large volume tissue biopsies
- Management of massive hemoptysis
- Silicone or self-expandable stent placement
- Mechanical coring of lesion using beveled tip and sequential mechanical dilation
- Using of adjunct therapies in management of endobronchial obstruction
  - Laser: (e.g., YAG)
  - APC
  - Electrocautery
  - Cryotherapy
  - Balloon dilation
  - Microdebrider

APC, Argon plasma coagulation; *YAG,* yttrium-aluminum-garnet.

Bronchoscopy is one of the most commonly performed procedures in pulmonary medicine. Bronchoscopy allows physicians to access the inside of the airways for both diagnostic and therapeutic purposes. The procedure can be performed using either a rigid (Fig. 22.1) or a flexible bronchoscope (FB). A rigid bronchoscope is a hollow, straight tube of stainless steel with proximal side ports which are used to connect to anesthesia circuits and light source. A rigid bronchoscope is used most often by otorhinolaryngologists, thoracic surgeons, and interventional pulmonologists. The rigid tube is placed through the mouth, past the vocal cords and down into the trachea. It can be placed as far as proximal mainstem airway. The larger diameter of rigid bronchoscopy (RB) allows for large foreign body extraction, silicone stent deployment, and performing any ablative therapy on endobronchial tumors. Indications for RB are shown in Box 22.1. The tip of the RB can be used to lessen bleeding by applying pressure to a bleeding tumor. One of the main disadvantages of RB is that the patient needs to be deeply sedated and paralyzed for almost the entire length of the procedure.

In contrast, flexible bronchoscopy is more widely used by pulmonologists and is more available in various practice setting ranging from community settings to tertiary care hospitals. The focus of this chapter is on flexible bronchoscopy due to its widespread availability and popularity.

The first bronchoscopy was performed by a German laryngologist, Gustav Killian, in the early nineteenth century. He removed a foreign body via the translaryngeal route with direct bronchoscopy[1] using a rigid esophagoscope. In the United States, Chevalier Jackson is considered to be the pioneer of RB. He reported the first bronchoscopic resection of an endobronchial tumor in 1917.[2] Over time, the technology has progressed remarkably. In 1966, the FB was introduced by Shigeto Ikeda, a Japanese thoracic surgeon. In 1970, the Olympus Company introduced the first FB for commercial purposes. Since then, advancements have led to a wide array of minimally invasive endoscopic diagnostic and therapeutic techniques that will be discussed in this chapter.

This chapter deals with the essential elements of the procedure, including the equipment, indications, contraindications, variations in the procedures, and emerging technologies. In addition, the role of the respiratory therapist (RT) and special considerations when performing bronchoscopy on patients under specific conditions (e.g., during mechanical ventilation) are also described.

FLEXIBLE BRONCHOSCOPY

The FB uses **fiberoptic bundles** to light up the endobronchial tree. Based on the imaging system, FBs are divided into fiberoptic, video, or hybrid types. The fiberoptic bronchoscope carries a second fiberoptic bundle that gathers the images from the distal tip of the instrument, which is visualized through an eye piece. The video bronchoscope uses somewhat different technology which employs a miniaturized charge-coupled devices (CCDs) chip at its distal tip to gather the images from the endobronchial tree and transmit them to the image-processing unit. The hybrid instrument uses a fiberoptic imaging system but also has a CCDs chip to convert the information into a digital format. Most modern FBs use video technology, whereas thinner bronchoscopes are hybrid in nature.

The proximal end of the FB is the controlling unit of the instrument, which helps the operator perform desired maneuvers to control the distal tip of the FB (Fig. 22.2). The distal tip of FB can be flexed in two directions—up to 180 degree in anteflexion and up to 130 degree in retroflexion positions (see Fig. 22.2). In addition to these controls, the operator rotates the instrument on its axis using the wrist. More recently, Olympus also added a feature that allows axial rotation of the instrument without totally relying on wrist movement (see Fig. 22.2).

Today, flexible bronchoscopy has become a standard procedure because of its diagnostic value, safety, and ease of performance. The procedure can be performed in an outpatient setting, under local anesthesia and moderate (conscious) sedation. The indications for FB have grown over the past years (Box 22.2) and are extensive. Box 22.3 presents the contraindications to performing FB. There are a few absolute contraindications for FB, which include refractory hypoxemia, hemodynamic instability, acute bronchospasm, increased intracranial pressure, uncorrectable coagulopathy, and inability to obtain informed consent for the procedure.

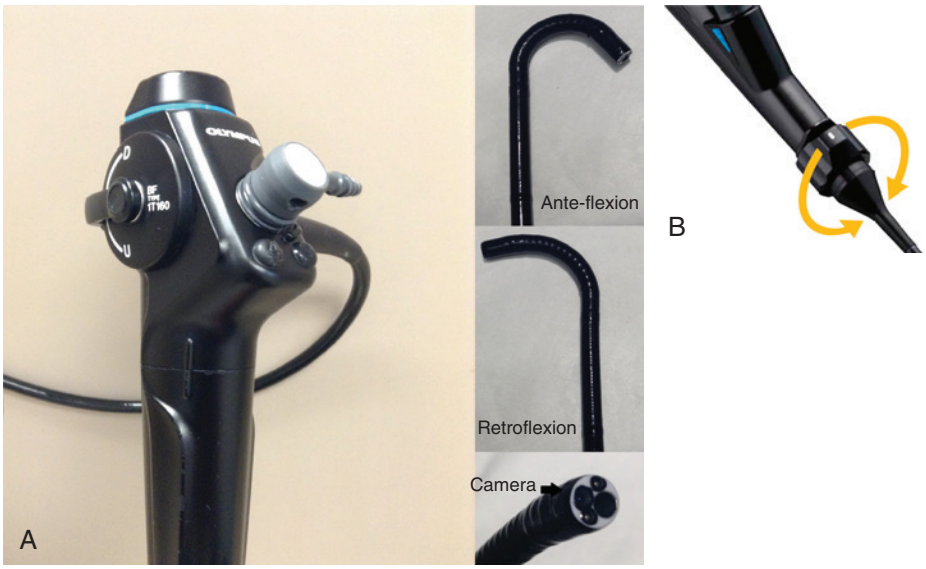

Fig. 22.2 (A) Flexible bronchoscope. *Left, inset:* Anteflexion *(top),* retroflexion *(middle),* and distal tip *(bottom).* (B) New Olympus scope with rotating function. (From Olympus Corporation, Tokyo, Japan.)

BOX 22.2 Indications for Flexible Bronchoscopy

- Hemoptysis
- Wheeze and stridor; suspected upper airway obstruction
- Pulmonary infiltrate of unknown cause
  - Infiltrates not responding to conventional treatment
  - Infiltrates in an immunocompromised host
  - Recurrent or unresolved pneumonia
  - Cavitary lesions
  - Interstitial infiltrates
  - New pulmonary nodule
- Unexplained lung collapse
- Suspected or known bronchogenic carcinoma
  - Staging
  - Follow-up after endobronchial treatments
- Mediastinal and hilar lymphadenopathy
- Lung transplantation
  - Evaluate airway anastomosis
  - Rejection surveillance
  - Cultures
- Endotracheal intubation
  - Bronchoscopy-assisted ET intubation
  - Confirm endotracheal tube position
  - Evaluate tube-related injury
- Evaluation of foreign body aspiration, chemical-related, or burn-related injury to the airway
- Unexplained superior vena cava syndrome
- Unexplained vocal cord paralysis or hoarseness
- Suspected fistulas (e.g., bronchopleural, tracheoesophageal and bronchoesophageal, trachea or bronchoaortic)
- Treatment of refractory asthma (bronchial thermoplasty)

BOX 22.3 Contraindications to Flexible Bronchoscopy

Absolute

- Refractory hypoxemia
- Lack of patient cooperation
- Lack of skilled personnel
- Lack of appropriate equipment and facilities
- Unstable angina
- Uncontrolled arrhythmias
- Increased intracranial pressure
- Uncorrectable bleeding diathesis

Relative

- Unexplained or severe hypercarbia
- Uncontrolled asthma attack
- Lack of patient cooperation
- Uncorrected coagulopathy
- Recent myocardial infarction
- Unstable cervical spine and impaired neck mobility
- Need for large tissue specimen

The discussion as to whether bronchoscopy is indicated or not involves the physician and often other members of the bronchoscopy team, including the RT. However, in the end, the final decision to perform the procedure must be individualized in conversation between the physician and the patient, based on the risks and benefits of the procedure.

Procedure, Sedation, and Monitoring

FB can be performed on spontaneously breathing patients via the oral or the nasal route and occasionally through a tracheostoma stoma. FB can also be performed on a patient with artificial airways such as endotracheal or tracheostomy tubes. Most

procedures are performed under moderate or deep sedation. When deep sedation is used, the procedure is performed via either a laryngeal mask airway or an endotracheal tube (ETT) of an appropriate size. As noted, RB is performed under deep sedation with muscle relaxation.

The goal of sedation is to improve the patient's comfort during the procedure and facilitate the procedure by minimizing patient movement and other potential interruptions. In addition to the risks for arrhythmias and fluctuations in blood pressure related to the procedure, airway manipulation during bronchoscopy may lead to coughing, hypoxemia, vomiting, bleeding, laryngospasm, and bronchospasm. All of these responses can affect the outcome of the procedure. Therefore, adequate sedation is a critical part of the procedure.

There is a wide range in the level of sedation that can be provided, including light sedation (anxiolysis), **moderate (conscious) sedation**, and deep sedation with general anesthesia. Moderate sedation is most commonly used during FB. At this level of sedation, patients can respond to verbal stimuli and demonstrate preserved protective airway reflexes. Several intravenous forms of benzodiazepines and opioids are commonly used during FB. Diazepam, midazolam, lorazepam, morphine sulfate, and fentanyl have been used either as a single agent or in combination based on the availability and physician preference.[3] The combination of a benzodiazepine (midazolam) and an opioid (morphine sulfate or fentanyl) has been shown to be safe and effective for sedation during FB. In addition, both benzodiazepines and opioids can chemically be reversed if necessary.[4] Propofol has also been proposed to be used in a combination with fentanyl in FB.[5,6]

Several techniques are used to apply local anesthetic agents to the upper and the lower airways. Using approximately 10 mL of 2% viscous lidocaine, "swish and swallow" is a simple and effective method to numb the upper airways. Another common method involves nebulizing 5 mL of 4% lidocaine.

The nasal passage is usually anesthetized using 5 mL of 2% lidocaine jelly. In addition, 1% to 2% of lidocaine is instilled directly into the lower airways through the working channel of the instrument in 2-mL aliquots during the procedure. The drug lidocaine has a very narrow therapeutic range. To help avoid unwanted hazards such as **methemoglobinemia**, the total dose of lidocaine should be limited to 5 to 7 mg/kg in adults (maximum of 400 to 500 mg in a 150-lb adult) during the procedure, with added caution in the elderly and in those with liver or cardiac disease.[7]

RULE OF THUMB For patient safety, to help avoid methemoglobinemia, the total dose of lidocaine should not exceed 7 mg/kg of body weight during a routine (<45 min) FB procedure. The use of benzocaine should be avoided as much as possible.

The assessment of the upper airway before the procedure helps identify those patients in whom it may be difficult to secure an airway in case of hypoventilation. The **Mallampati classification** is one of the most commonly used methods to identify individuals who may pose difficulty during intubation. The Mallampati score is assessed by having the patient open his or her mouth and protrude the tongue as much as possible without phonation (Fig. 22.3).

TABLE 22.1 American Society of Anesthesiologists Classification: Comorbid Conditions and Impact on Daily Living

ASA Class	Class Definition
I	A normally healthy patient
II	A patient with mild systemic disease
III	A patient with systemic disease that is not incapacitating
IV	A patient with an incapacitating systemic disease that is a constant threat to life
V	A moribund patient who is not expected to survive for 24 h with or without operation

MINI CLINI

Methemoglobinemia During Bronchoscopy

Problem

A respiratory therapist (RT) is assisting during a flexible bronchoscopy. The patient had local anesthesia with lidocaine nebulization and benzocaine spray. The patient developed central cyanosis and his oxygen saturation dropped to 85% via pulse oximetry. The procedure was aborted. An arterial blood gas check showed pH, 7.43; PCO_2, 43; and PO_2, 279; with an O_2 saturation of 85%. What condition should an RT consider in this situation?

Discussion

Methemoglobinemia should be suspected. Benzocaine, which is used as a local anesthetic, is a common cause of methemoglobinemia during such procedures. Benzocaine causes oxidization of the iron in hemoglobin (Hb) from the ferrous (Fe^{2+}) to the ferric state (Fe^{3+}). Fe^{3+} Hb is unable to carry O_2. The PO_2 is within normal range as shown by the machine measurement of dissolved O_2 in the blood, not in the Hb. Therefore, methemoglobinemia causes hypoxemia at the cellular level that is not detected by measuring PO_2 but can be uncovered by co-oximetry to measure methemoglobin directly. In terms of management, a methemoglobin level less than 30% usually resolves spontaneously over 15 to 20 hours after removal of the offending agent and with O_2 administration. Intravenous administration of methylene blue is the treatment of choice in patients when the methemoglobin levels exceed 30%.

RULE OF THUMB The Mallampati score should be assessed in every spontaneously breathing patient before flexible bronchoscopy.

Several maneuvers (e.g., chin-lift, jaw-thrust) may become necessary if the patient becomes oversedated during FB. In addition to an unfavorable Mallampati score, comorbidities can also affect the safety and outcome of the procedure. The recommendation from the American Society of Anesthesiologists (ASA) is to categorize patients based on their ASA score, which considers comorbid conditions and their impact on the patient's daily living (Table 22.1).[8]

During the FB procedure, continuous monitoring of oxygenation and hemodynamic stability are important. Pulse oximetry, heart rate, and blood pressure are monitored throughout the procedure. One of the most difficult parameters to monitor during FB is the depth of sedation. Intermittent boluses of sedation may be needed to ensure the adequate depth of sedation during the procedure. However, the depth of sedation must be balanced with the side effects of oversedation during and after

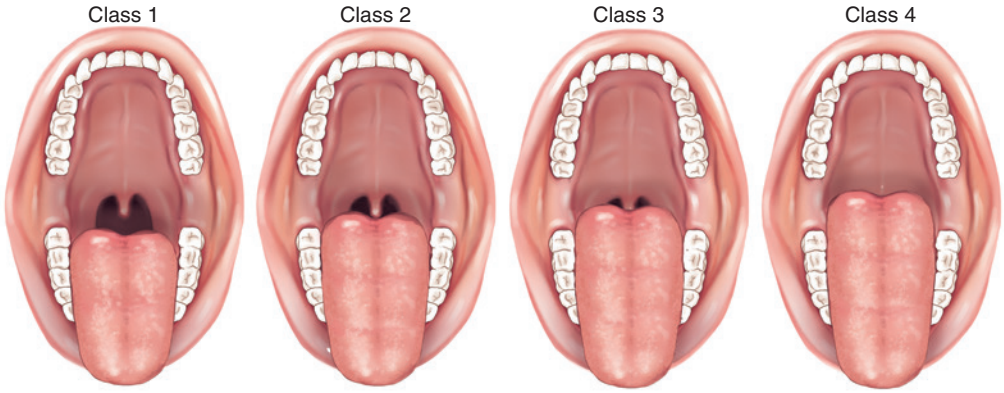

Fig. 22.3 Mallampati classification.

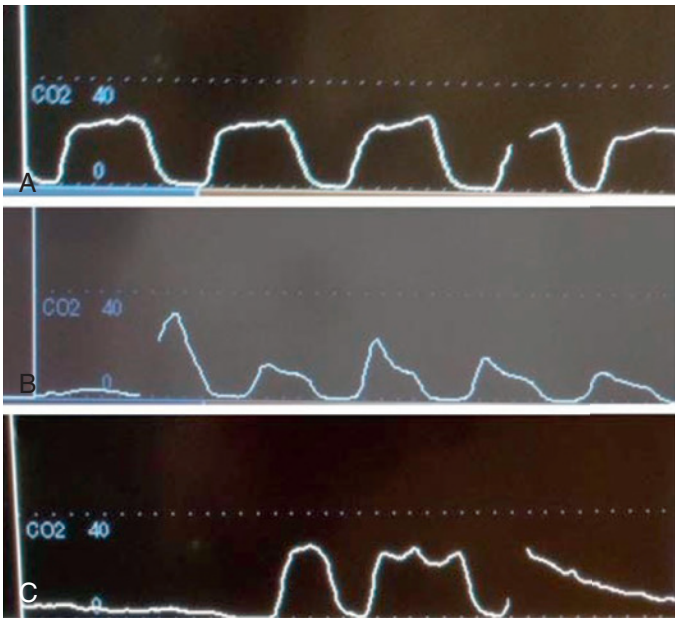

Fig. 22.4 (A) A normal capnography wave form of $EtCO_2$. (B) A capnography wave form demonstrating deteriorating ventilation as a result of airway obstruction during bronchoscopy. (C) A capnography wave form demonstrating the recovery of breathing pattern with patient stimulation and jaw thrust.

the procedure. To monitor the patient, the RT or other member of the bronchoscopy team should keep track of the patient's responses to verbal commands or spontaneous movements. Notably, chest movement may continue despite near total obstruction of the airway. To monitor the presence of a patient's slipping into deep sedation with associated hypoventilation, the ASA also recommends **capnography** monitoring while performing FB under moderate sedation.[9,10] Capnography is the real-time, noninvasive measurement and wave form display of the end-tidal carbon dioxide ($EtCO_2$). While a mainstream CO_2 sensor is frequently used in intubated patients, side-stream capnography is most useful in patients with spontaneous breathing. A fraction of gases from nasal cannula passed through the analyzer located in the monitor.[11] A simple, long, small bore tube may create a slight delay of CO_2 measurement by a few seconds. In spontaneous breathing patients, the actual $EtCO_2$ value may not be accurate. However, the trend and the shape of wave form can generally represent the degree of ventilation (Fig. 22.4).

RULE OF THUMB Continuous cardiac, blood pressure, and oximetry monitoring must be carried out during bronchoscopy. Capnography should be used if available.

DIAGNOSTIC BRONCHOSCOPY

A computed tomography (CT) scan of the chest should generally be performed (see Chapter 21) before all elective bronchoscopic procedures. The imaging information is very valuable in increasing the diagnostic yield of the procedure among patients suspected to have lung cancer. The scan also may eliminate the need for performing the procedure in 7% of patients.[12]

Diagnostic bronchoscopy begins with the examination of the upper airways. Proper upper airway examination is crucial to identify lesions involving nasal passages, pharyngeal, and laryngeal structures, including vocal cords. After examination of the upper airway structures, the lower airways are examined at least until the fifth- or sixth-generation bronchi. Examining bronchi deeper than this may be limited by the diameter of the bronchoscope. For diagnostic purposes, besides examining the airways, several different types of specimens can be collected through the working channel of the bronchoscope. Summaries of various diagnostic bronchoscopic techniques are presented in Table 22.2.

RULE OF THUMB A CT scan of the chest should generally be performed before all elective diagnostic bronchoscopic procedures in patients suspected of having lung cancer.

Bronchoalveolar Lavage

Bronchoalveolar lavage (BAL) is used to obtain specimens from the alveolar level of the lung. BAL is performed by instilling a small volume (up to 50 mL) of normal saline solution deep into the airways and then suctioning the instilled liquid back. BAL fluid contains both cellular and noncellular components of alveolar lining fluid (Fig. 22.5). As a form of "liquid lung" sample, the BAL fluid is thought to represent the contents of one million of alveoli as well as respiratory epithelial lining and colonizing organisms. BAL has become a standard diagnostic procedure in patients with pulmonary infiltrates of uncertain etiology (Box 22.4). A normal BAL sample includes 95% macrophages; 3% lymphocytes; 1% to 2% neutrophils, eosinophils, and basophils,

TABLE 22.2 Various Diagnostic Procedures With Flexible Bronchoscopy

Diagnostic Techniques	Methods	Diagnostic Roles	Complications
Bronchoalveolar lavage	Perform a good wedging, instilling a small volume of normal saline solution deep into the airways/alveoli and then suctioning the aliquot back	Infections, pulmonary hemorrhage, malignancy, Eosinophilic lung disease, pulmonary alveolar proteinosis, pulmonary, Langerhans cell histiocytosis, Lipoid pneumonia	Hypoxemia
Washing	Instilling a small volume of normal saline into tracheobronchial area, wedging is not necessary	Infections, malignancy	Hypoxemia
Brushing	Brushing the surface of the suspicious lesion	Malignancy	Focal bleeding
Endobronchial biopsy	Use of flexible forceps to obtain a tissue sample from a visible endobronchial lesion	Infections, malignancy	Focal bleeding, Hypoxemia
Transbronchial biopsy	Use of flexible forceps to obtain a tissue sample from lung parenchyma	Infections, allograft rejection, malignancy, sarcoidosis, Langerhans cell histiocytosis	Bleeding, pneumothorax
Transbronchial needle aspiration Endobronchial ultrasound guided	Use of flexible needle tip to obtain tissue sample from central airway or lung parenchyma. [a]Can be used with ultrasound guidance for needle aspiration for centrally located lesions	Malignancy, sarcoidosis,	Bleeding, mediastinitis, pneumomediastinum
Electromagnetic navigational bronchoscopy	Use low-frequency electromagnetic waves to locate peripheral nodules in real time with computer-generated guidance in three dimensions; in a combination with various diagnostic tools such as needle, brush, or forceps for biopsy	Malignancy, infections	Bleeding, pneumothorax

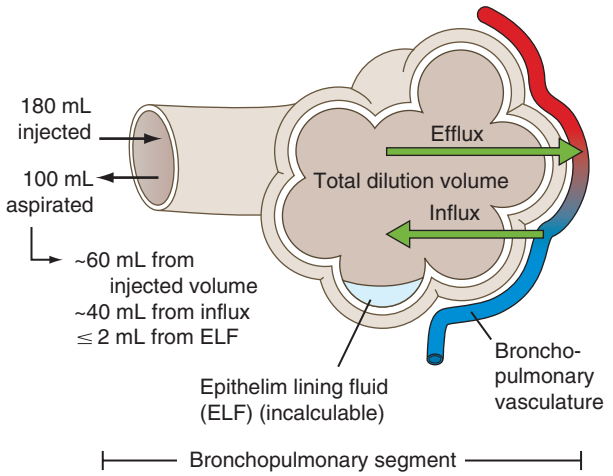

Fig. 22.5 Schematic presentation of the constituents of the bronchoalveolar lavage.

and few epithelial cells. In addition to routine culture and cell count, an estimation of the CD4/CD8 ratio of lymphocytes in the lavage fluid can be helpful in assessing the diagnosis of sarcoidosis and hypersensitivity pneumonitis.

Bronchoalveolar Lavage Technique

In order to minimize contamination of the working channel with the local organisms,[13-15] it is important to avoid using suction while inserting the FB through the nasopharynx and central airways. The amount of lidocaine used should be minimized to reduce its side effects, prevent its bacteriostatic properties from interfering with cultures, and avoid altering the cellular contents of the lavage fluid. The right middle lobe, lingual or the anterior segment of the right upper lobe is generally used to perform

BOX 22.4 Role of Bronchoalveolar Lavage in Diagnosis for Pulmonary Diseases

- Infection (e.g., bacteria, fungus, virus, and mycobacteria)
- Pulmonary hemorrhage
- Malignancy (e.g., solid tumor, lymphoma)
- Eosinophilic lung disease
- Pulmonary alveolar proteinosis
- Langerhans cell histiocytosis
- Lipoid pneumonia
- Diffuse alveolar hemorrhage

BAL in patients with diffuse diseases. With the patient in a supine position, gravity helps augment BAL return from these locations.[13,14] Meanwhile, in localized lung diseases, lavage is performed from the area of the focal abnormality.[14]

To obtain the lavage fluid, the bronchoscope is wedged at the level of fourth- or fifth-generation bronchus. A "good wedge" position means that the bronchoscope is advanced as far as possible while the distal lumen is still visible. In this position, BAL return is maximal. Twenty to 60 mL of normal saline are instilled into the appropriate bronchial segment and aspirated back manually for laboratory testing. In general, 15 to 20 mL of BAL volume is enough to conduct common laboratory tests such as microbiologic and cytologic tests; the total amount of fluid required may vary based on the differential diagnosis.[15]

Several complications may be associated with BAL. Hypoxemia is common, and its severity depends upon three factors: (1) the volume of fluid administered,[16] (2) the number of segments lavaged, and (3) the duration of the procedure. Introduction of 100 mL of lavage fluid can cause O_2 desaturation up to 7%, whereas 200 mL of lavage fluid can drop O_2 saturation up to

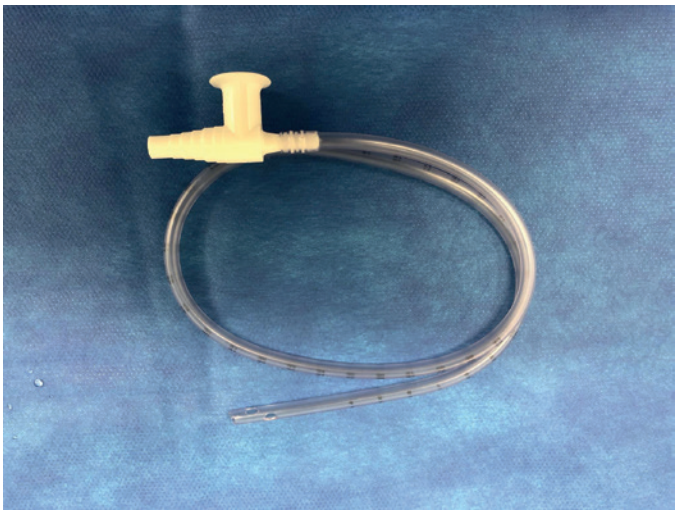

Fig. 22.6 Mini-bronchoalveolar lavage sampling catheter.

15% from the baseline value.[16] O_2 supplementation during BAL may lessen the degree of O_2 desaturation. Cases of pneumothorax from BAL have also been reported in patients with *Pneumocystis jiroveci* pneumonia and during therapeutic BAL for pulmonary alveolar proteinosis (PAP).[17,18]

RULE OF THUMB BAL should be obtained from the nondependent part of the lung to optimize the fluid return.

RULE OF THUMB Supplemental O_2 should be administered in all patients undergoing bronchoscopy to help avoid or minimize hypoxemia.

Mini-BAL is defined as non-bronchoscopic BAL (Fig. 22.6). Mini-BAL is most frequently performed in intubated patients when a catheter is passed through an ETT into the bronchi until the catheter lodges, after which saline is instilled for the lavage and then withdrawn. The volume of saline instillation is usually 25 mL or less. The return of fluid by aspiration is highly variable. Mini-BAL is a simple procedure for acquiring quantitative lower airway cultures in mechanically ventilated patients.[19] Colorimetric capnography can be used to confirm the tracheobronchial position of the catheter.[20] In some settings, RTs perform this procedure. Approximately 46% of mini-BAL cultures are found to contain at least one organism that is potentially contributing to a suspected episode of ventilator-assisted pneumonia.[21]

Bronchial Washings

Bronchial washings are generally obtained for a cytological examination for cancer and/or microbiologic analysis to diagnose mycobacterial or fungal infections. Unlike BAL, bronchial washings are obtained from the large airways. Bronchial washing is easy to perform, but is not very effective in diagnosing malignancy, successfully diagnosing only 22% to 29% of peripheral lesions[22,23] with a yield slightly higher for central lesions.[24,25] Bronchial washings are an inexpensive by-product of the bronchoscopy and are routinely obtained in patients suspected to have airway malignancy.[26]

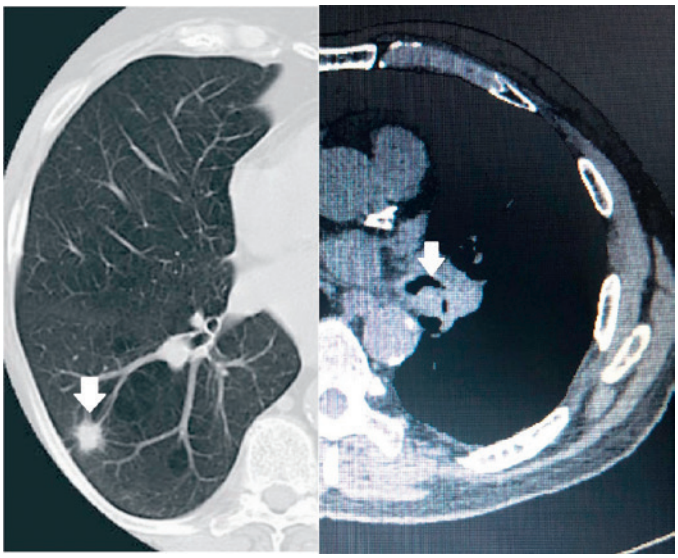

Fig. 22.7 *Left:* Peripheral lung nodule (located at ⅓ outer rim—arrow). *Right:* Central lung nodule (located in the proximal ⅔).

Bronchial Brushings

Bronchial brushings have been used as an adjunct diagnostic test in addition to endobronchial and transbronchial biopsies and transbronchial needle aspiration (TBNA). It involves brushing the surface of the suspicious lesion back and forth 5 to 10 times while rotating the handle. Brushes of various different diameters and bristle strengths are available in the market. Brushing is usually performed under direct visualization or with fluoroscopic guidance to avoid trauma to the bronchial mucosa and pneumothorax, respectively. Brushing can establish a diagnosis in 72% (range 44% to 94%) of patients with central lung cancers and in 45% of patients with peripheral lesions.[27,28] Centrally located cancers are found in the proximal ⅔ of visible bronchi (4th to 5th generation airway) and peripheral lesions are defined as occurring in the distal ⅓ (beyond 5th generation), which can be seen on the ⅓ outer rim on a chest X-ray or fluoroscopy (Fig. 22.7). Bronchial brushing is usually performed after obtaining all the other specimens to avoid bleeding or cellular degradation that may affect the overall interpretation of FB specimens. Once the specimen is collected, the cells are smeared onto a slide and the end of the brush is cut off and placed in a fixative solution for cytological examination.[29]

Endobronchial Biopsy

Endobronchial biopsy (EBBx) is a technique whereby flexible forceps are used to obtain a tissue sample from a visible endobronchial lesion. It provides specimens for histological examination. EBBx has been shown to successfully diagnose between 51% and 97% of central visible neoplasms.[30,31] The number of biopsy specimens that should be obtained depends on the suspected diagnosis. In patients suspected to have bronchogenic carcinoma, three biopsy specimens are often able to successfully diagnose almost all cases.[32] If the specimen is obtained from the surrounding necrotic tissue, the EBBx can fail to contain cancerous cells even though the patient has a malignancy. In such cases,

debridement of the necrotic tissue with the forceps or performing a TBNA may improve the overall diagnostic yield. EBBx of a highly vascularized lesion may lead to significant bleeding and must be undertaken with caution. The physician may take precautions such as instilling 5 mL to 10 mL of ice cold saline (−4°C) or 2 mL to 4 mL of either epinephrine or norepinephrine (1: 10,000) solution through the working channel of the bronchoscope to lessen the possible bleeding or using the TBNA approach.

Transbronchial Biopsy

Transbronchial biopsy (TBBx) is a technique of obtaining a specimen of the lung parenchyma by using flexible forceps positioned distally through the working channel of the bronchoscope. A large fenestrated alligator forceps is most commonly used to obtain the TBBx. Six to ten tissue specimens are obtained, depending on the suspected diagnosis. TBBx can be performed with or without fluoroscopic guidance (Fig. 22.8). The latter is a common practice while performing the TBBx in the intensive care unit setting.

The diagnostic value of TBBx varies depending on the underlying lung diseases and the patient population. For infectious diseases, 88% to 97% of cases of *P. jiroveci* pneumonia[33] and 57% to 79% of cases of *Mycobacterium tuberculosis* can be successfully diagnosed with TBBx.[34] In lung transplant surveillance, TBBx can detect the presence of allograft rejection in approximately 70% of cases.[35,36] In interstitial lung diseases, the diagnostic value is relatively low compared with the experience in infectious diseases. TBBx can successfully diagnose 40% to 90% of cases of sarcoidosis[37] and only 10% to 40% of those with Langerhans cell histiocytosis.[38] In a peripheral pulmonary nodule (PPN), the diagnostic value of TBBx depends upon the size and the location of the nodule. The presence of an airway leading to the nodule as seen on chest computed tomography scan is called a "positive bronchus sign" and, when combined with TBBx, increases the successful diagnostic yield from 31% to 79% for PPNs.[39]

The two major complications of TBBx are pneumothorax and bleeding. Adequate sedation and cough suppression are important to reduce the risk for pneumothorax arising from cough-induced barotrauma. Whenever available, fluoroscopy should be used to guide the TBBx, especially in patients with localized lesions. Fluoroscopy is also used to screen for pneumothorax after the TBBx.[40] The risk for developing pneumothorax is three times higher in mechanically ventilated patients compared to that among spontaneously breathing patients.[41,42] To reduce the risk for pneumothorax among the former group, the level of positive end-expiratory pressure (PEEP) level should be maintained below 5 cm H_2O. Also, in case of pneumothorax, prompt chest tube placement should be available.

Meanwhile, the prevalence of bleeding from TBBx is low (2% to 9%) in the absence of a bleeding tendency or coagulopathy; risk factors for bleeding after TBBx include renal insufficiency with creatinine greater than 3 mg/dL, pulmonary hypertension with a mean pulmonary artery pressure greater than 40 mm Hg, thrombocytopenia with platelets less than 50,000/mL, and international normalized ratio (INR) greater than 1.5.[43]

TBBx can be safely performed in patients who are receiving aspirin or nonsteroidal inflammatory drugs. However, several antithrombotic and antiplatelet therapies (e.g., clopidogrel) should be withheld for a specific period before TBBx (Table 22.3).[44] In the event of bleeding, wedging the bronchoscope in the involved subsegment helps tamponade, or compress, the bleeding site.

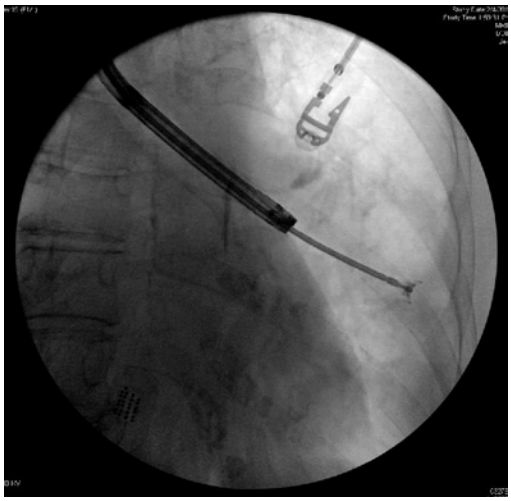

Fig. 22.8 Transbronchial biopsy under direct visualization with fluoroscopy.

MINI CLINI

Sudden Chest Pain and Clinical Deterioration During Bronchoscopy

Problem

An RT is assisting during an FB on a young female with suspected sarcoidosis. The patient is very anxious and, despite an adequate amount of narcotics and anxiolytic agents, continues to cough violently. The physician is performing TBBx under fluoroscopic guidance from the left lower lobe. In seven attempts, he manages to obtain three pieces of tissue before stopping the procedure. During the last attempt, the patient winced with mild pain. Soon after the last biopsy, the patient became tachypneic (respiration rate [RR] 30 breaths/min), with a heart rate of 110 beats/min, and the SpO_2 dropped to 82% on O_2 6 L/min via nasal cannula. Examination of the chest showed that it was tympanic on percussion with reduced breath sounds on auscultation on the left. What condition should the RT consider in this situation?

Discussion

The RT should consider pneumothorax in this situation and should also consider ruling out a tension pneumothorax. Pneumothorax is a potential complication following a TBBx.[45] The risk is further increased in the situation in which the patient cannot cooperate for the procedure and continues to cough during the biopsy. In this case, fluoroscopic examination can help confirm or rule out the condition. Meanwhile, the patient should receive an adequate amount of supplemental O_2 by a non-rebreather mask if needed. The RT should be prepared to assist the pulmonologist to place either a Heimlich valve or a chest tube, depending on the size of the pneumothorax and the patient's symptoms. If a tension pneumothorax is suspected, any size needle can be inserted into the pleural space and the air would be expected to rush out as the pressure is relieved.

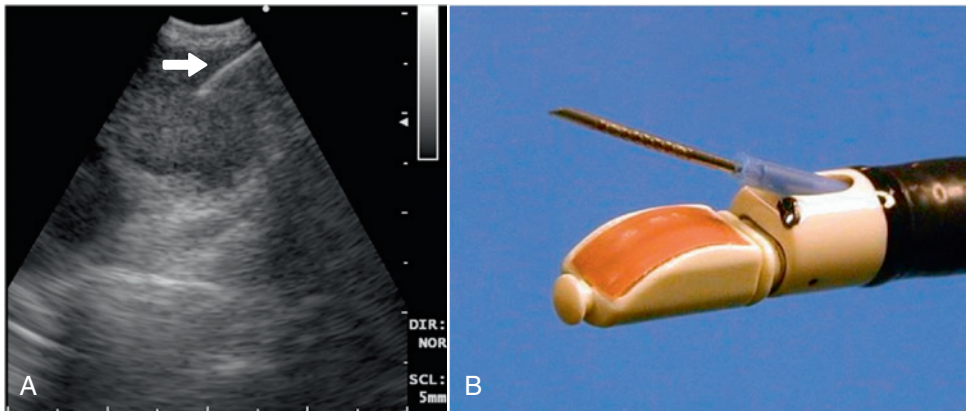

Fig. 22.9 (A) The distal tip of the endobronchial ultrasound endoscope with an aspiration needle. (B) Sonographic image of endobronchial ultrasound-transbronchial needle aspiration demonstrating needle inside lymph node.

TABLE 22.3 Antithrombotic Therapies and Recommended Interval Between Last Dose and Procedure[a]

Agents	Interval From Last Dose Before Procedure
Warfarin	3–5 days; or goal international normalized ratio <1.5
Unfractionated heparin	Intravenous 2–6 h
Low molecular weight heparin	24 h; depending on creatinine clearance
Dabigatran	1–2 days with creatinine clearance >50 mL/min 3–5 days with creatinine clearance <50 mL/min
Rivaroxaban	1 day with normal renal function 2–4 days with impaired renal function
Desirudin	2 h
Clopidogrel, ticlopidine, prasugrel, ticagrelor	5 days
Aspirin and dipyridamole	7–10 days

[a]Data from Baron TH, Kamath PS, McBane RD: Antithrombotic therapy and invasive procedures, *N Engl J Med* 369:1079–1080, 2013.

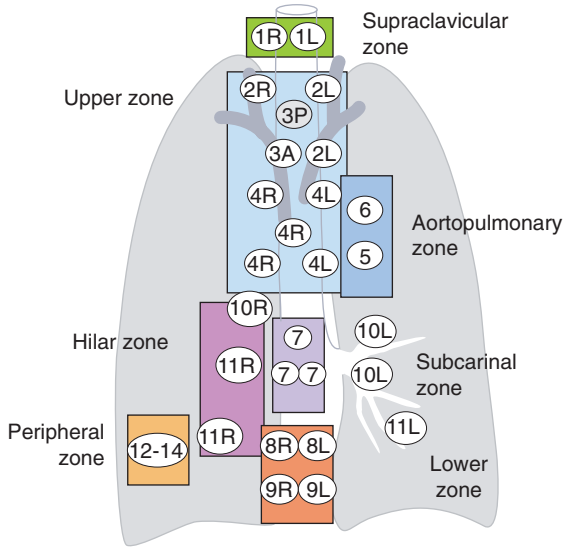

Fig. 22.10 The international association for the study of lung cancer (IASLC) lymph node map.

Transbronchial Needle Aspiration: Conventional and Ultrasound-Guided Procedures

Transbronchial needle aspiration (TBNA) is the technique that allows sampling tissue from the mediastinum or the peripheral lung by inserting needles through the bronchial wall. TBNA can be used to determine the cause of mediastinal lesions and PPNs in a minimally invasive fashion.[46,47]

With the availability of endobronchial ultrasound (EBUS), the accuracy of TBNA has improved dramatically. EBUS is essentially a bronchoscope with a linear ultrasound probe attached at its distal end. EBUS provides real-time ultrasonographic guidance for TBNA of target structures (Figs. 22.9 and 22.10). It has recently been found that in patients with potentially operable lung cancer, the diagnostic accuracy of EBUS-TBNA is far superior (98% diagnostic accuracy) to either positron-emission tomography or CT scans of the chest for mediastinal staging.[48,49]

Recently, the use of EBUS-TBNA has greatly expanded in the diagnosis and staging of non–small cell lung cancer because it is a minimally invasive procedure. Notably, mediastinal lymph nodes can be assessed more accurately with EBUS-TBNA than with conventional mediastinoscopy. Reported complications of EBUS-TBNA include pneumomediastinum, pneumothorax, mediastinitis, bacteremia, and, rarely, death.[50-53]

Today, genetic profiling of lung cancer is essential to identify biomarkers that significantly influence treatment decisions and responses. EBUS-TBNA can provide adequate tissue for genetic analysis.[54] The utility of EBUS-TBNA also has been investigated for restaging of lung cancer after chemotherapy, and evidence supports its use for this purpose.[55]

Electromagnetic Navigational Bronchoscopy

An advanced CT imaging technology has been innovatively combined with an electromagnetic navigation system to guide the biopsy of PPNs that lie beyond the reach of standard flexible bronchoscopy. **Electromagnetic navigational bronchoscopy** (ENB), peripheral EBUS, virtual bronchoscopy, ultrathin bronchoscopy,

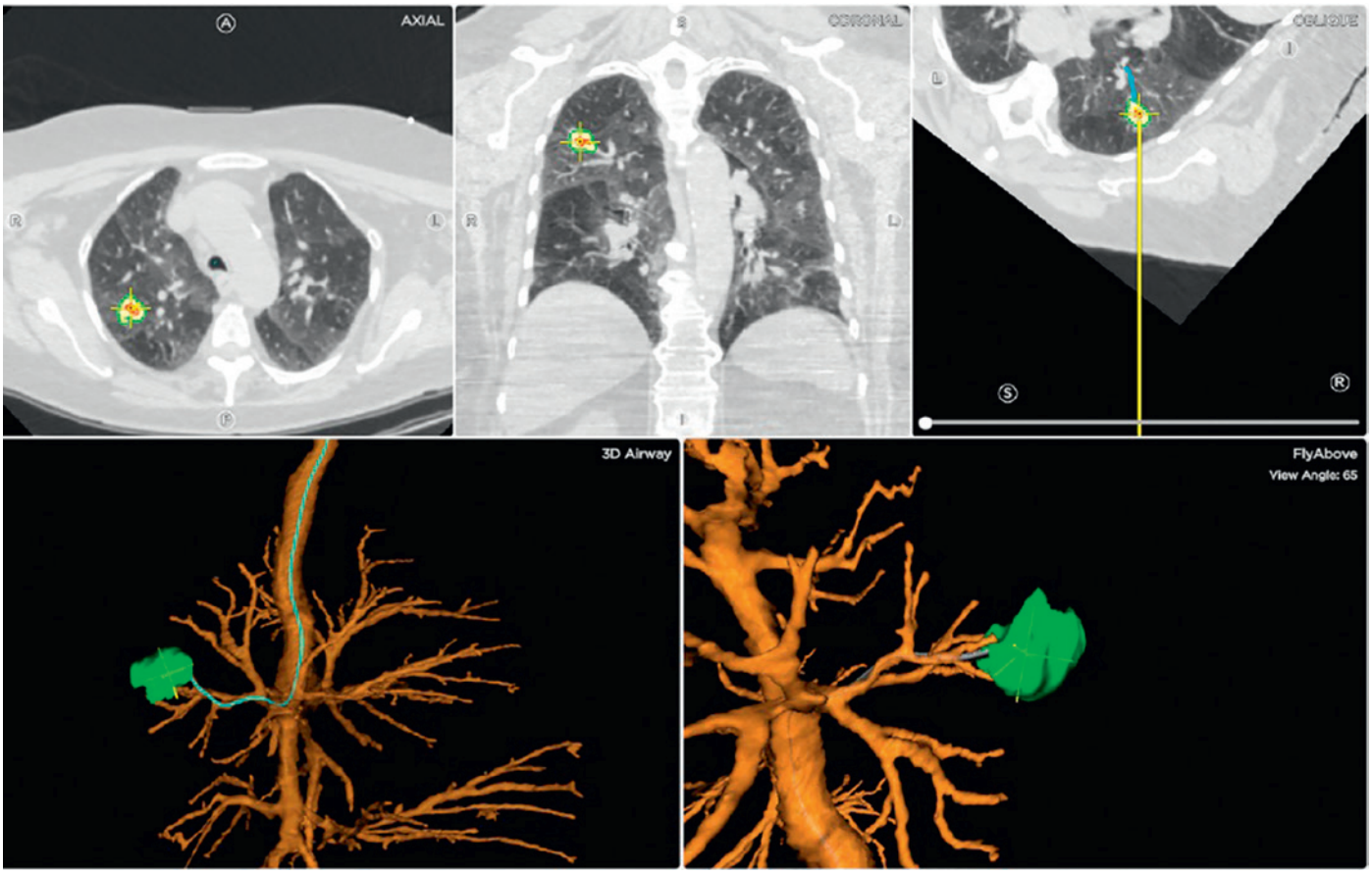

Fig. 22.11 Electromagnetic Navigation Monitor. Location of the pulmonary lesion is displayed in three different axes of computed tomography imaging.

and their combination have significantly increased the diagnostic value of FB for peripheral lesions, with an acceptably low complication rate of bleeding and pneumothorax.[56]

The ENB system uses low-frequency electromagnetic waves transmitted from a magnetic board placed below the patient's chest. As a result, the lesion can be visualized in real time with computer-generated guidance in three dimensions.

ENB is performed in several steps. The first step is planning the procedure by uploading high-quality CT images into the planning software. The software will generate the plan markers from the main carina to the lesion via multiple bronchial subsegments. The next step is aligning the virtual images to the patient's endobronchial anatomy, which is called the *registration* phase. Then the navigation is conducted by driving the locatable guide probe with its extended working channel (EWC) to the lesion, by following the three-dimensional CT images and the "tip view" (Fig. 22.11). Once the lesion is reached, the guide probe is removed, leaving the EWC in place. The position of the tip of the EWC may be confirmed by using the radial EBUS probe to determine the location of the lesion (Fig. 22.12). Various diagnostic tools such as needle, brush, or forceps for biopsy can be used through the EWC to obtain a tissue specimen. In terms of diagnostic value, ENB can successfully diagnose almost 75% of peripheral lesions, with accompanying pneumothorax in approximately 3.5% of such cases. The combination of radial probe EBUS with ENB can further increase the diagnostic value.[57,58]

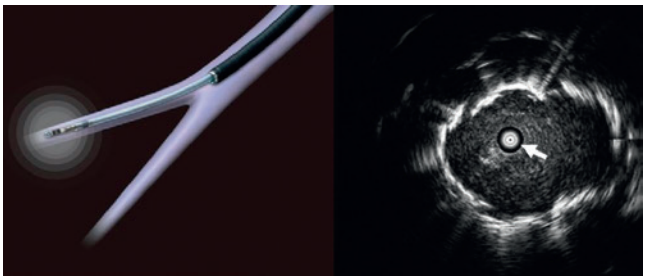

Fig. 22.12 Radial probe endobronchial ultrasound *(left)*. A radial probe is surrounded by lesion *(right, arrow)*. (*Left* from http://www.goldcoastrespiratoryandsleep.com.au/gcrsc-services.html.)

Ultrathin Bronchoscopy

The normal tracheobronchial tree divides approximately 24 times before it reaches the respiratory bronchioles. The external diameter of the adult FB is approximately 5.7 to 6 mm, which allows the physician to reach the fourth- or fifth-order bronchi. The ultrathin bronchoscope is approximately 2.8 mm in external diameter and can reach up to at least the eighth-order bronchi (Fig. 22.13). **Ultrathin bronchoscopy** can be helpful in diagnosing PPNs and can be used to inspect peripheral airways or to examine the airway beyond a pathologic airway narrowing.

The major technical challenge of performing ultrathin bronchoscopy is maintaining proper anatomic orientation in the peripheral airways. The instrument is seldom used without

Fig. 22.13 Comparison of the diameter of the tip of the ultrathin bronchoscope (2.8 mm) *(right)* with that of a standard-size bronchoscope *(left)*.

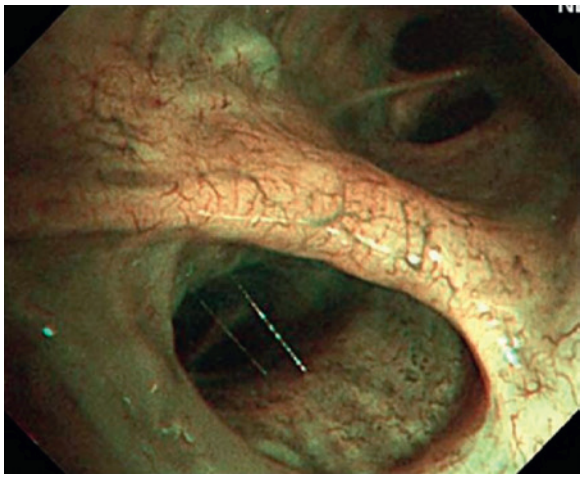

Fig. 22.14 Narrow band imaging.

real-time CT guidance, virtual bronchoscopy,[59] or a specially designed peripheral EBUS system. Another drawback of the ultrathin bronchoscope is its narrow working channel (1.7 mm) and miniaturized accessories (1 to 1.2 mm). These limit the diagnostic value of ultrathin bronchoscopy because the specimens that can be obtained are very small.

Narrow Band Imaging

Narrow band imaging (NBI) is a technique that uses specialized filters to separate wavelengths of white light and selectively emits red, green, and blue bands. The intensification of the blue band detects vessel growth and complex vessel networks in the bronchial mucosa and therefore may be useful to detect early malignant lesions (Fig. 22.14). The system involves two narrow band filters, one to detect 415-nm light that is absorbed by the surface level capillaries and a second to detect 540-nm light that is absorbed below the surface layer. NBI permits visualizing abnormal distribution and dilatation of blood vessels in the mucosa, which can be an early sign of malignancy.[60]

THERAPEUTIC BRONCHOSCOPY

FB has also been widely used for therapeutic purposes. Although the role of RB has declined, RB remains an invaluable tool for controlling a compromised airway, massive hemoptysis, silicone stent placement, and for removing asphyxiating foreign bodies. The major indication for RB is to manage central airway obstruction. Approximately 30% of patients with lung cancer may present with airway obstruction and its complications, such as hemoptysis, postobstructive pneumonia, and asphyxia.[61] Reducing the size of a tumor or establishing airway patency with or without stent placement can produce rapid relief of symptoms, improve quality of life, and increase survival.[62] The few contraindications to RB include the inability to hyperextend the neck and an unstable facial fracture.

Some of the common bronchoscopic therapeutic procedures that are performed through the FB are discussed in the following section. A summary of the various therapeutic bronchoscopic techniques is shown in Table 22.4.

Thermal Ablation of an Endobronchial Lesion

Newer modalities such as endobronchial electrocautery, **argon plasma coagulation** (APC), or **laser photocoagulation** can be used to coagulate, carbonize, or vaporize lesions that protrude into the airway lumen and obstruct the central airways. These modalities increase the temperature of the tissue by molecular agitation and can be applied either through a flexible or an RB. By applying the appropriate power density, the desired tissue reaction can be achieved.

Application of electrocautery requires use of accessories such as knives, snares, or probes. APC is a noncontact technique to apply electric current to an endobronchial lesion. The modalities involve application of an electrically charged argon gas through a special disposable catheter.[63] The presence of a pacemaker or a defibrillator is a relative contraindication to using these electrical modalities.[64]

Lasers can produce tissue reaction by thermal, photochemical, or electromagnetic effects. As stated earlier, it is the thermal effect of the laser that is mainly used to remove the endobronchial lesion. The most commonly used lasers for this purpose are neodymium: yttrium-aluminum-garnet (Nd-YAG) and neodymium: yttrium-aluminum-perovskite (Ng-YAP) lasers. Lasers produce more precise tissue reaction than the electrosurgery units.[65,66]

The thermal ablation of an endobronchial lesion in properly selected patients produces some relief in close to 90% of patients. Improper use of the thermal modalities can lead to perforation of the airway, vascular structures, or esophagus. In addition, hypoxemia, pneumothorax, bronchopleural, and bronchoesophageal fistulas are other reported complications.[65] In the presence of high FiO_2, endobronchial ignition has been reported as a rare complication of such therapies. As a result, the lowest FiO_2 needed to maintain adequate oxygenation (often at 40% or less) offers the highest possible safety margin. Refractory hypoxemia (i.e., an O_2 requirement of FiO_2 >40%) and extrinsic compression of the airway without an endobronchial lesion are contraindications to thermal ablation.

RULE OF THUMB During the application of "hot therapies" (thermal ablation) such as laser, electrosurgery, or argon plasma coagulation, the FiO_2 always should be maintained at or below 40% to prevent endobronchial fire.

TABLE 22.4 Various Therapeutic Procedures With Flexible Bronchoscopy

Therapeutic Techniques	Methods	Clinical Uses	Complications
Thermal ablation • Argon plasma coagulation • Laser photocoagulation • Electrocautery	• Ionized argon gas conducts electrons to spray on tissue surfaces, resulting in superficial coagulative necrosis • Thermal effect causes tissue coagulation and evaporation; photodynamic and electromagnetic effects • Coagulative necrosis at low temperature or tissue vaporization at high temperature. Energy can be delivered through several types of probes	Rapid palliation of central airway obstruction from either benign or malignant; Hemostasis for management of endobronchial hemorrhage	Hypoxemia, pneumothorax, bronchopleural and bronchoesophageal fistulas
Cryotherapy	Cause extracellular ice crystal formation and extraction of intracellular water; induces vasoconstriction, and endothelial injury leading to microthrombus formation and tissue necrosis	Slow palliation of central airway obstruction from malignancy, granulation tissue; organic foreign body extraction; may have roles in biopsy of lung parenchyma	Hypoxemia, pneumothorax, bleeding
Brachytherapy	Deliver short distance/local radiation therapy	Local treatment for endobronchial tumors	
Endobronchial stenting	Provide internal splinting of the airway lumen; immediate relief of airway obstruction from malignant or benign processes	External compression from malignancy; stabilizing airway patency after mechanical debulking of tumor; sealing esophagogastric-tracheobronchial fistula	Mucous impaction, bacterial colonization, migration, and granuloma formation
Bronchial thermoplasty	Thermal energy to reduce the airway smooth muscle (ASM) mass which can minimize bronchoconstriction and improve asthma symptoms	Severe asthma	In short-term (i.e., following the procedure), increases acute exacerbation risk

Cryotherapy

Cryotherapy is a method of destroying tissue by freezing and thawing. Cryotherapy leads to extracellular ice crystal formation and extraction of intracellular water. In addition, extreme cold induces vasoconstriction, and endothelial injury leading to microthrombus formation and eventually tissue necrosis. The cryoprobe can be used through either an FB or an RB. The cryogen (the agent that causes the freezing) is released from very-high-pressure storage to the atmospheric pressure. The sudden drop in the pressure leads to expansion of the cryogen and a drop in its temperature. This effect is also referred as Joule-Thompson effect. The cryoprobe is placed in contact with the target and the cryogen is released, producing a tissue temperature of −80°C. The temperature increases approximately 10°C per millimeter from the tip. Thus the effective zone for cryotherapy is approximately 5 to 8 mm. Multiple cycles of rapid freezing and gradual thawing are applied to cover the entire treatment area. The effect of cryotherapy depends on the sensitivity of the tissue. Cryoresistant structures (those which do not respond to cryotherapy) are fat, cartilage, nerve sheath, and connective tissue, whereas neoplasms, granulation tissue, skin, mucous membranes, nerves, and endothelium are cryosensitive. The cryosensitivity of the tissue mainly depends on its water content. Therefore, application of this technique to a cryosensitive tissue is essential for success.[67,68]

Cryotherapy has been used to treat patients with central airway obstruction. Cryotherapy is ideal for treating stent-related granulation tissue when the stent is made of an inflammable material. Cryotherapy can be also be used to remove organic foreign bodies, blood clots, and mucus plugs by cryoadhesion; ice crystal formation between the probe and the object that holds them together.[69] In addition, unlike the thermal ablation techniques, cryotherapy can be used safely when the patient requires a high FiO_2.

Recently, the cryoadhesion principle has been used for obtaining larger pieces of lung tissue compared to conventional TBBx and EBBx approaches (called cryobiopsy).[69] Several studies have shown that cryobiopsies yielded larger, more alveolated samples in various pulmonary conditions including lung transplant rejection and interstitial lung diseases.[70,71]

Brachytherapy

The term **brachytherapy** describes a method to deliver short distance radiation therapy. Brachytherapy involves temporary placement of encapsulated radioactive sources within or near a tumor through the bronchoscope. Brachytherapy is used as both in addition to external-beam radiation and as a palliative radiation option for lung cancer located near the airways. It also can be used in managing superficial endobronchial squamous cell carcinoma with a curative intent. In brachytherapy, a catheter is placed adjacent to the lesion and the location is confirmed by fluoroscopy. The catheter is then loaded with a radioactive source, usually radium or iridium, reaching a total dose of 500 to 4000 Gray over a precise duration.[72,73]

The main advantage of brachytherapy is that a higher dose of radiation can be delivered to the tumor cells while minimizing radiation to the normal tissue, thereby reducing complications. Brachytherapy is indicated in patients with inoperable lung cancer or cancer metastatic to the airways.

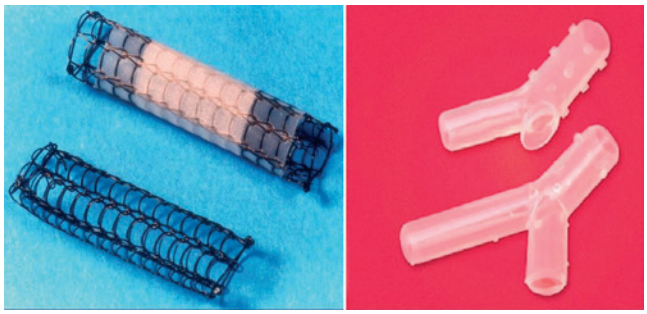

Fig. 22.15 Self-expanding metallic stents *(left)* and silicone stents *(right)*.

Endobronchial Stents

Stents are tubular devices designed for internal splinting of the airway lumen. **Airway stents** have been used to help reduce airway obstruction from malignant or benign processes that compress the airway from the outside. Airway stenting can offer immediate relief of acute respiratory distress, can allow successful extubation, and may prolong survival.[73,74] There are two major types of airway stents: metallic and silicone. Self-expanding metallic stents (SEMS) are commercially available in covered and uncovered forms (Fig. 22.15). Covered stents are designed primarily to prevent the growth of granulation tissue into the lumen of the stent. Current SEMS are made from nitinol, a nickel-titanium alloy that is well adapted for endobronchial applications. At room temperature, nitinol is extremely elastic. It can tolerate the extreme folding that is required when using a small deployment system but still return to its original shape without compromising its resistance to compression. The advantages of SEMS are ease of deployment, small internal-to-external diameter ratio, better conformity to the complex airway shapes, and ventilation across a lobar bronchial orifice (Table 22.5). The indications for SEMS placement include (1) extrinsic compression of central airways, (2) stabilizing airway patency after endoscopic removal of an intrinsic tumor, (3) sealing fistula between the airways and the gastrointestinal tract, and (4) managing of post–lung transplant anastomotic complications. SEMS is rarely used in benign central airway obstruction because there is a high-risk for stent-related granulation tissue formation. In 2005, the U.S. Food and Drug Administration issued a medical device safety warning against using SEMS for benign airway obstruction unless all other therapeutic options have been explored.[75]

Silicone stents have two major designs, straight and Y-shaped (for disease involving the carina). The stents are either made of transparent silicone (radiolucent) or silicone blended with barium sulfate (to make the stent radiopaque). The silicone stent is usually placed through a rigid bronchoscope. The advantages of silicone stents include easy customization, ease of repositioning/removal, minimal granulation tissue overgrowth, and lower cost than metallic stents. The indications for placing a silicone stent are similar to SEMS and include internal splinting for external compression/intraluminal growing cancer, benign strictures, collapsing airways, and tracheoesophageal fistulas. In terms of complications, mucous impaction (3.6%), bacterial colonization, migration (9.5%), and granuloma formation (7.9%) are most common. After stent placement, the patient should be given a stent alert card with details regarding the type, length/diameter, and location of the stent.

TABLE 22.5 Comparison of Silicone and Metallic Stent Properties

Comparison Factors	Metallic Stents	Silicone Stents
General Considerations		
Deployment	Flexible or rigid bronchoscopy	Rigid bronchoscopy only
Customization	No	Yes
Repositioning	Difficult	Easier
Conforms to complex airway	Yes	No
Internal-to-external diameter	Low	High
Elasticity	Excellent for nitinol	Poor
Mucociliary clearance	Yes for uncovered stents	No
Cost	More	Less
Complications		
Granulation tissue	More	Less
Migration	Less common	Significant
Fracture	Significant	Rare
Infection	More common	Less common
Tracheobronchial fistula formation	Possible	Very rare
Mucus impaction	Uncommon	Common

RULE OF THUMB SEMS should not be used in benign conditions unless all other therapeutic options have been exhausted.

Bronchial Thermoplasty

Bronchial thermoplasty (BT) is a nonpharmacologic treatment modality for asthma (Chapter 25). It uses thermal energy to reduce the airway smooth muscle (ASM) mass, thus minimizing bronchoconstriction. ASM has been found to play important roles in response to various stimuli with the production of growth factors, proinflammatory mediators, and adhesion receptors.[76] The thermal energy is delivered via the Alair system (Boston Scientific Co.), which is a radiofrequency catheter (Fig. 22.16). The catheter can pass through the working channel of an FB. The system delivers temperature-controlled thermal energy at 65°C for 10 seconds per each activation. BT is performed in a series of three separate bronchoscopy sessions, targeting different lobes of the lung except for the right middle lobe. This lobe is not treated due to concerns over stenosis of its small-diameter bronchus. [77]

In terms of clinical outcomes, BT can improve the patient's Asthma Quality of Life Questionnaire (AQLQ) score, decrease severe exacerbation, decrease days lost from school/work, and decrease emergency room visits, which led to FDA approval of BT for the treatment of severe asthma in 2010.[78] Long-term follow-up studies have demonstrated persistent benefits of BT, which have decreased severe exacerbations, ED visits, and hospitalizations significantly, by 45%, 55%, and 40%, respectively.[79]

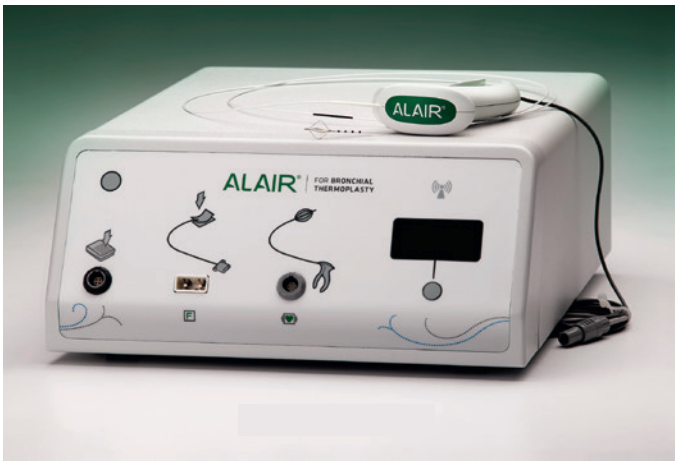

Fig. 22.16 Bronchial thermoplasty device *(top)*, and catheter *(bottom)*. (Courtesy Boston Scientific, ©2017 Boston Scientific or its affiliates.)

Bronchoscopy in Difficult Intubation

It may be difficult to establish an artificial airway by conventional means in patients with cervical and oropharyngeal trauma or redundant supraglottic soft tissue. The ASA Task Force on difficult airway recommends alternative techniques to overcome such airway challenges, including flexible bronchoscopy.[80]

A FB can help place an ETT through the mouth or the nose. The ETT is placed over the FB, the vocal cords are visualized, and the ETT is then advanced into the trachea. Using the FB to aid ETT placement also allows for awake intubations with topical anesthesia and is particularly useful in patients with cervical injury, when immobilization of the neck is crucial.[81] The bronchoscope also may help identify causes of acute hypoxemia and help remove secretions or blood in the airway. The limitations of this approach include operator inexperience and the need for patient cooperation.

THE ROLE OF THE RESPIRATORY THERAPIST IN BRONCHOSCOPY

The RT has a major supportive role during bronchoscopic procedures. The RT may collaborate with other members of the patient care team to determine if the procedure is indicated. The RT is often responsible for ensuring that all documentation is in place before the procedure and that a preprocedure "time-out" takes place to ensure that the right procedure is being performed on the right patient. During the preprocedure evaluation, the RT helps recognize the patient's O_2 requirement and arranges for adequate O_2 supplementation during the procedure. The RT also administers inhaled bronchodilators before or during the procedure if the patient exhibits bronchospasm.

FB is usually performed on spontaneously breathing patients through the mouth (transoral) or nose (transnasal). The RT assists preparing the upper as well as lower airways for the procedure using local anesthetic agents. In mechanically ventilated patients, the RT may help optimize the length and the size of the ETT, place a bite-block in place to protect the equipment, and adjust ventilator settings before and during the procedure. In addition to monitoring vital signs and O_2 saturation during the procedure, the RT may assist the physician in operating the bronchoscopic accessories, including brush, forceps, needles, laser fibers, cryoprobe, and APC probes. In patients with suspected ventilator-associated pneumonia, the RT may perform mini-BAL, which may guide the escalation and deescalation of antibiotic therapy. Furthermore, the RT often identifies and can assist in responding to an adverse event associated with FB, such as hypoxemia. These and other aspects of the role of the RT are summarized in Box 22.5.

MINI CLINI

Awake Intubation Using Flexible Bronchoscope in a Morbidly Obese Patient

Problem

An RT was called to assist with intubation of an obese patient (weighing 320 pounds with a body mass index of 63 kg/m^2). The patient presented with acute respiratory distress from lobar pneumonia. Initial assessment of the patient's airway indicated that intubation was likely to be difficult, with a Malampatti score of 3, along with a history of severe obstructive sleep apnea. Despite the history, there were no adverse features related to mouth opening, thyromental distance, and neck movement. The procedure team determined that awake, tracheal intubation using an FB was the most appropriate approach. The patient agreed. How should the procedure be done?

Discussion

The patient should be placed in an upright position. In addition to preoxygenating the patient, topical anesthesia plays important role in the awake intubation. Two percent viscous lidocaine can be used to anesthetize the oral cavity; either in a swished and swallow form or as a spray. The FB can then be inserted through an ETT. An oral guard should be placed to protect the FB in case the patient inadvertently bites down during the procedure. The FB is inserted through the mouth. Upon reaching the glottic chink, 2% lidocaine should be instilled via the working channel to anesthetize the vocal cords. Once, the tip of FB passes the vocal cords and is positioned at the distal trachea, the ET tube should be slid over the FB into the trachea. The ET tube is then positioned and secured, and the FB is withdrawn.

SPECIAL CONSIDERATIONS FOR BRONCHOSCOPY DURING MECHANICAL VENTILATION

In addition to the role of the RT described earlier, the RT plays an even more important role when bronchoscopy is performed on mechanically ventilated patients. It is most important to note that FB carries a higher risk when performed on patients with reduced cardiopulmonary reserve, particularly those requiring mechanical ventilation. In such patients, the RT must ensure that the airway is properly secured, verify adequate ventilation and gas exchange, monitor the patient, and quickly communicate the development of any complications to the physician and any other members of the bronchoscopy team.

In mechanically ventilated patients, it is important to consider that the bronchoscope will occupy a greater proportion of the airway than for spontaneously breathing patients. The external diameter of a standard FB is 5.7 mm, but in some situations a smaller (5 mm or less) or larger (6.4 mm) diameter scope may

BOX 22.5 Role of the Respiratory Therapist in Bronchoscopy

- Preprocedure
  - Help identify potential need for a bronchoscopy such as retained secretions or foreign body removal.
  - Verify physician's order or protocol; review medical record for contraindications (e.g., excessive clotting times), hazards, and informed consent.
  - Prepare/ensure proper function of equipment, including bronchoscope, light source, TV monitor, video recorder, medications, specimen traps.
  - Outline plan for adequate oxygenation during the procedure.
  - Evaluate patient for bronchospasm and administer aerosolized bronchodilators if required.
  - Assist nursing staff in applying topical anesthesia to the upper airways (nasal passages, oropharynx, hypopharynx).
  - Identify patient and perform pre-procedure "time-out."
  - Mechanically ventilated patients/bedside bronchoscopy
    - Establish adequacy of the length and the diameter of the endotracheal or the tracheostomy tube based on the indication.
    - Ensure a bite-block is in place to avoid equipment damage.
    - Adjust ventilator settings for the safety of the procedure while maintaining proper oxygenation.
- During the procedure
  - Monitor vital parameters during the procedure, including capnography (if available).
  - Help identify and respond to adverse reactions (e.g., hypoxemia or pneumothorax).
  - Administer adequate amount of supplemental oxygen all throughout the procedure by choosing proper appliances (nasal cannula, mask, bilevel positive airway pressure).
  - Provide proper positioning of the patient to maintain patency of the upper airways (jaw-lift, etc.).
  - Assist use of endobronchial accessories (bite block, oral airways, nasopharyngeal tube, biopsy forceps, brushes, etc.).
  - Set up instruments for rigid bronchoscopy and silicon stent placement.
  - Help attend to emergent situations (pneumothorax, bleeding).
  - Help in placement of chest or endotracheal tubes.
- Postprocedure
  - Determine adequate oxygenation and ventilation and respond to adverse reactions.
  - Disinfect and properly store equipment.
  - Document procedure and relevant details.

be used. The narrowest point in the upper airway (and point of maximal resistance) is the cricoid space, the diameter of which averages 14 mm in women and 18 mm in men.[82] Thus in nonintubated, spontaneously breathing patients, inspiratory and expiratory effort (measured by tracheal pressure) appear minimally affected in most patients (−5 and +3.5 cm H_2O, respectively). However, in intubated, spontaneously breathing patients, the resistance imposed by the bronchoscope may cause tracheal pressures to increase noticeably (−10 and +9 cm H_2O) and may reach clinically unacceptable levels (−20 and +20 cm H_2O) in some patients.[83] Therefore the minimum size ETT that should be in place in order to use a standard adult-sized 5.7-mm bronchoscope is a 7.5 to 8.0 mm internal diameter ETT.[84]

RULE OF THUMB The minimal sized ETT that can be used with a standard 5.7-mm bronchoscope has a 7.5 to 8.0 mm internal diameter.

MINI CLINI

Bronchoscopy-Induced Hypoxemia

Problem

An RT is assisting during a flexible bronchoscopy on a spontaneously breathing patient that is taking longer than expected because of other adjunctive procedures, including BAL. Shortly after instilling the lavage solution into the airway through the bronchoscope, the patient's O_2 saturation drops from 97% to 88% via pulse oximetry, her heart rate increases from 90 to 118, and the patient's skin color changes from pink to pale. What is the condition that an RT should consider in this situation?

Discussion

Hypoxemia should be suspected in this case. Given that the bronchoscope occupies a significant amount of the anatomic airway during this procedure, additional airway resistance can partially impede ventilation during the procedure. In addition, the BAL solution introduced into the airway can temporarily interfere with ventilation, and gas exchange and hypoxemia can occur. In addition, frequent and prolonged suctioning can lead to severe, prolonged hypoxemia. Pausing the procedure and administering a higher FiO_2 or even 100% O_2 will generally alleviate this problem and boost the pulse oximetry to more acceptable levels (mid-90%). Once monitored blood O_2 levels return to normal, the procedure can be resumed. The patient's oxygenation and overall clinical status should be continually monitored for the balance of the procedure and for a period following it.

PHYSIOLOGIC AND MECHANICAL ALTERATIONS ASSOCIATED WITH FLEXIBLE BRONCHOSCOPY IN INTUBATED PATIENTS

Complications associated with a flexible bronchoscopy in intubated patients are infrequent (<10%) and usually mild.[85] However, serious complications may occur (Table 22.6). These include the following (along with their reported prevalence): transient hypoxemia with SpO_2 less than 90% (8%), tension pneumothorax (14%), bronchial hemorrhage greater than 30 mL (6%), hypotension with mean arterial pressure less than 60 mm Hg (7%), and tachycardia greater than 140 beats per minute (4%).[85] Pneumothorax is primarily associated with lung biopsy procedures,[86,87] whereas the risk for significant bleeding after biopsy increases when the platelet count is below 50,000/mm^3.[85]

As noted elsewhere in this chapter, some degree of hypoxemia may occur during FB. In those with normal lungs, the PaO_2 can decrease by 10 to 30 mm Hg, whereas in critically ill patients, the PaO_2 may be reduced by 60 mm Hg.[85,86] Hypoxemia during FB is partly caused by suctioning through the bronchoscope. This decreases PEEP and functional residual capacity and promotes atelectasis. For example, setting the vacuum at 100 mm Hg through a standard 2-mm suction port can evacuate approximately 7 L/min of gas.[85] The problem is accentuated if tidal volume delivery also is significantly compromised during FB. In fact, frequent suctioning during FB also causes pronounced tidal volume loss.[83] Because FB commonly is used to remove mucus plugs, this problem may be unavoidable. Both the RT and the physician performing the bronchoscopy must be mindful of the frequency and duration of suctioning, along with the

total procedure time to limit the potential for severe, prolonged hypoxemia. The risk for significant hypoxemia is elevated in those with acute respiratory distress syndrome (ARDS) and in patients who are insufficiently sedated.[83] Patients undergoing FB should be pre-oxygenated using an FiO_2 of 1.0 for 15 minutes. Resolution of hypoxemia depends on the presence and severity of the underlying pulmonary disease. For example, hypoxemia tends to resolve within 15 minutes after FB in those with normal lungs, whereas hypoxemia may persist for several hours in those with severe lung disease.

TABLE 22.6 Physiologic and Mechanical Alterations Associated With Flexible Bronchoscopy in Intubated Patients

System	Effects	Comments/Interventions
Respiratory mechanics	High peak inspiratory pressures and pressure cycling	Obstruction by the bronchoscope causes back-pressure that is not transmitted to the lungs. Use of high inspiratory flow rates/brief inspiratory time will accentuate the problem and may greatly reduce minute ventilation. Intervention: *Volume control ventilation:* Use a lower peak flow rate or decreasing ramp pattern and increased inspiratory time. *Pressure control ventilation:* Increase the pressure control level and extend the inspiratory time. *Before bronchoscopy:* Assess minute ventilation demand and blood gases with the physician to determine if the patient might tolerate mild to moderate respiratory acidosis during the anticipated procedure duration. Monitor peak inspiratory pressure.
	Intrinsic PEEP	Increased expiratory resistance can cause a 30% increase in functional residual capacity and may cause high levels of intrinsic PEEP to develop. With an 8-mm endotracheal tube, intrinsic PEEP levels are generally <20 cm H_2O, but have been reported to rise to 35 cm H_2O when bronchoscopy has been attempted with a 7-mm tube. *Consider* removing or reducing PEEP by 50% during the procedure. Monitor blood pressure as a signifier for possible intrinsic PEEP buildup. Either a sustained downward trend or abrupt drop in systolic blood pressure may indicate decreased cardiac output.
	Circuit leak, suctioning, and tidal volume loss	Circuit leaks with substantial loss of tidal volume were a common problem until the creation of specialized bronchoscopy port endotracheal tube adapters. These are commercially available and have largely eliminated the problem. When encountered, the rule of thumb has been to increase the preset tidal volume by 30%–40% to compensate for the leak.[86] Use lower peak inspiratory flow rate and longer inspiratory time. Frequent, prolonged suctioning during FB can greatly reduce tidal volume regardless of ETT size. Monitor: • Expired tidal volume • End-tidal PCO_2 and VCO_2 (CO_2 excretion) if volumetric capnography is available, particularly in those with baseline hypercarbia, acidosis, or hemodynamically unstable.
Gas exchange	Hypoxemia	Pre-oxygenate for 15 min on FiO_2 of 1.[86] Ensure adequate sedation before and during FB. Ensure continuous pulse oximetry. Consider using recruitment maneuvers to improve functional residual capacity before and (if necessary) after FB in patients with marginal oxygenation. To the extent possible: • Minimize tidal volume loss. • Avoid using a brief inspiratory time. • Limit the frequency and duration of suctioning.
	Acute hypercapnia and acidosis	On average, $PaCO_2$ tends to increase by 8 mm Hg during FB.[86] This would decrease arterial pH by only 0.06; and even less in patients with chronic hypercapnia. This mild change in $PaCO_2$ should be interpreted in the context of clinicians adjusting mechanical ventilator settings to attempt to maintain adequate ventilation. Given the relatively brief procedure time for FB, concern over the impact of hypercapnia should be focused on clinically unstable patients. In at-risk patients: • The procedure time should curtailed. Periodic withdrawal of the bronchoscope to ensure adequate ventilation. • Clinicians should determine the limits of what an acute rise in $PaCO_2$ and decrease in pH would be acceptable during the procedure and use clinical equations to estimate the minimum acceptable minute ventilation that must be maintained (see Mini Clini for details). • When FB must be attempted in patients with significant acidosis, consideration should be given to pre-procedure buffer therapy with a non–CO_2 generating agent (i.e., THAM) often used for procedures requiring apneic oxygenation.

TABLE 22.6 Physiologic and Mechanical Alterations Associated With Flexible Bronchoscopy in Intubated Patients—*cont'd*

System	Effects	Comments/Interventions
Hemodynamics	Heart rate and cardiac arrhythmias	Hypoxemia and hypercapnia increase sympathetic tone, which can lead to tachycardia, myocardial ischemia, and arrhythmias, and may result in hypotension and/or cardiac arrest. Heart rate tends to increase by ~40% during FB.[88] The occurrence of major arrhythmias is 3%–11%. Reduce the risk for arrhythmias by: • Preoxygenation with an FiO_2 of 1 • Minimizing procedure time • Periodic withdrawal of the bronchoscope to ensure adequate ventilation Ensure continuous cardiac monitoring.
	Alterations in blood pressure and cardiac output	Mean blood pressure and cardiac output tend to increase during FB by ~30%.[88] Hemodynamic variables tend to return to normal ~15 min after completion of FB.[86]

ETT, Endotracheal tube; *FB,* flexible bronchoscopy; *PEEP,* positive end-expiratory pressure; *THAM,* tris-hydroxymethyl aminomethane.

TABLE 22.7 High-Risk Patients for Flexible Bronchoscopy

Conditions	Considerations
Asthma	Greater tendency for laryngospasm and bronchospasm[87,88] Tendency for greater reduction in lung function after FB when lavage or biopsies are done Hypoxemia not uncommon Pretreatment with bronchodilators immediately before FB In patients with unstable lung function, consider pretreatment with steroids several days before FB
Acute brain injury	Intracranial hypertension is a predominant concern. Procedural goal: intracranial pressure <20 mm Hg with cerebral perfusion pressure ≥70 mm Hg Causes of increased intracranial pressure include sympathetic stimulation from discomfort and hypercapnia, hypoxemia. Build-up of intrinsic PEEP decreases venous return, causing cranial venous pooling. Procedural sedation and strategies to maintain minute ventilation assume even greater importance. Employing continuous drainage when subdural catheters are present should be considered. Either curtailing procedure time or frequent periods bronchoscope withdrawal to resume baseline minute ventilation also should be considered.
Acute respiratory distress syndrome (ARDS)	Tendency is for severe hypoxemia and respiratory acidosis, particularly in those with severe ARDS (PaO_2/FiO_2 <100) due to low lung volumes and high dead-space ventilation. Risk is increased if hemodynamic instability is present (e.g., mean arterial pressure <65 mm Hg and/or high vasopressor requirements). Loss of PEEP is particularly problematic. Consideration should be given to preprocedure use of recruitment maneuvers to optimize lung volumes and oxygenation and THAM to control acidosis.
Coronary artery disease	Adrenergic discharge during FB in response to under-sedation, hypoxemia, and/or acute respiratory acidosis may cause myocardial ischemia, arrhythmias, hypotension are cardiac arrest. In nonintubated patients, the need for high doses of topical anesthesia with lidocaine may cause sinus arrest and atrioventricular block.

FB, Flexible bronchoscopy; *THAM,* tris-hydroxymethyl aminomethane.

RULE OF THUMB Hypoxemia during FB on mechanically ventilated patients is related to several factors, including loss of lung volume during suctioning, particularly if tidal volume delivery also is compromised. Hypoxemia occurs more frequently in those with ARDS and in those who are insufficiently sedated.

It is the RT's responsibility to effectively manage the most common of these complications (see Table 22.6). In addition, the RT must anticipate which patients are most likely to suffer significant adverse events during bronchoscopy (Table 22.7). Before the procedure, the members of the bronchoscopy team, including the RT, should assess the patient's condition, discuss which adverse effects are most likely to occur, and discuss how these potential complications should be managed. This discussion should include the anticipated procedure time, whether the original plan for the procedure should be modified, the sedation strategy, hemodynamic management, and ventilator management. The RT should especially focus on the minimum clinically acceptable level of minute ventilation needed to complete the procedure. Depending on the procedure goal (e.g., diagnostic, removal of secretions), bronchoscopy tends to last between 7 and 17 minutes.[88,89]

EMERGING BRONCHOSCOPIC INTERVENTIONS

In addition to the interventions described earlier, others are emerging and hold promise for the future. Endobronchial valves

MINI CLINI

Estimating the Minimum Minute Ventilation Requirements During Flexible Bronchoscopy in a Patient With Severe Respiratory Failure

Problem

A patient with ARDS has deteriorating oxygenation associated with a new infiltrate on chest x-ray. Gram-negative bacterial ventilator-associated pneumonia is strongly suspected, and FB is deemed necessary before adjusting antibiotic therapy because the suspected pathogen is likely to be multidrug resistant. The patient has a high minute ventilation demand of 13 L/min to maintain a pH of 7.40 and $PaCO_2$ of 40 mm Hg. The patient has sepsis and currently requires norepinephrine at 12 mcg/min to maintain a mean arterial pressure of 65 mm Hg. The physician decides that during FB, a pH of 7.24 would be tolerable for the estimated procedure time of 10 minutes. The RT is asked if there is a clinical formula to estimate what rise in $PaCO_2$ would likely produce the target minimum pH. In addition, the RT is asked to estimate the minimum minute ventilation needed during FB that would likely maintain pH at 7.24.

Discussion

In patients without chronic hypercapnia, an acute rise in $PaCO_2$ of 10 mm Hg produces a decrease in pH of 0.008.[89] Because tidal volume can be greatly reduced during FB, the RT can reasonably begin with an estimated $PaCO_2$ increase of 20 mm Hg. This would yield an estimated drop in pH of 0.16 units (20×0.008) and a pH of 7.24 ($7.40 - 0.16$). The clinical formula for corrected minute ventilation then can be used to estimate the minimum acceptable minute ventilation.[88]

$$VE_{min} = VE_{measured} \times (PaCO_2 \text{ measured} \div PaCO_2 \text{ upperlimit})$$

$$VE_{min} = 13\,L/min \times (40 \div 60)$$

$$VE_{min} = 13\,L/min \times 0.67$$

$$VE_{min} = 8.7\,L/min$$

Patients with high minute ventilation demands who require vasopressor support to maintain adequate perfusion may be particularly sensitive to sudden respiratory acidosis. The fact that this patient already requires the highest recommended dose of norepinephrine to maintain an adequate blood pressure is cause for concern about the safety of performing FB. The steps described previously are only estimates for guiding management during FB and assessing the risk-to-benefit ratio.

and coil placement are being studied in the management of patients with severe emphysema. If shown to be effective, they could represent an alternative to lung volume reduction surgery for severe emphysema. Recently, an endobronchial valve (called the Zephyr valve) has received FDA approval as a treatment option for patients with severe emphysema. Studies have shown that the patients with Zephyr valve experienced improved FEV1, exercise tolerance, dyspnea, and quality of life compared with standard of care for COPD.[90]

CONCLUSION

Bronchoscopy is a common diagnostic and therapeutic procedure that has reduced the need for procedures such has percutaneous needle aspiration, mediastinoscopy, thoracoscopy, and open lung biopsy. In many settings, RTs play a major role in identifying patients who may benefit from bronchoscopy, setting up the equipment, and assisting with the procedure itself, as well as monitoring patients undergoing bronchoscopy.

SUMMARY CHECKLIST

- BAL, biopsy, and TBNA are the most commonly used diagnostic procedures during FB. BAL obtains samples from the alveoli. Needle aspiration has a role in sampling mediastinal lymph nodes to diagnose lung cancer, sarcoidosis, and some infectious processes. Biopsy has value in diagnosing some infiltrative pulmonary diseases.
- Emerging advanced diagnostic procedures, including EBUS and ENB, play important roles in managing lung cancer. The specimens are adequate for molecular studies, which play an important role in planning treatment.
- Various thermal ablation techniques (e.g., laser) can be applied through either a rigid or FB to treat endobronchial lesions. The most important point is to ensure a low FiO_2 environment before using any thermal ablative therapy to minimize the risk of an endobronchial fire.
- Airway stenting has been used to maintain airway patency after dilation of any obstructed major airways. It is important to recognize the difference between silicone and metallic stents.
- Bronchial thermoplasty (BT) is a novel bronchoscopic technique for patients with severe asthma. BT has been shown to improve quality of life and to decrease severe exacerbation frequency, days lost from school/work, and emergency room visits.
- Endobronchial valves and coil placement are being studied in the management of patients with severe emphysema as a minimally invasive lung volume reduction therapy.
- Awake intubation using an FB can be safely performed in patients with a suspected difficult upper airway (e.g., large neck mass, morbid obesity, tracheal stenosis).
- The RT plays a vital role in assisting before, during, and after the bronchoscopy procedure. There are many aspects to this role, but they include ensuring appropriate documentation, preparing the patient and the equipment, patient monitoring, and responding to possible adverse events.
- When bronchoscopy is performed in mechanically ventilated patients, the RT must especially ensure adequate ventilation and gas exchange before, during, and after the procedure.

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23

Nutrition Assessment

Janet Reid-Hector

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Describe how a comprehensive nutrition assessment is conducted.
- Calculate and interpret body mass index.
- Distinguish between two forms of protein-energy malnutrition.
- List the biochemical indicators of nutrition status.
- Describe the clinical manifestations of malnourishment.
- Describe how to obtain and evaluate a nutrition history.
- Estimate daily resting energy expenditure.
- List the indications, contraindications, hazards, and limitations of indirect calorimetry.
- Describe how to prepare a patient for indirect calorimetry.
- Interpret the results of indirect calorimetry.
- Adjust resting energy expenditure values to reflect the actual patient energy needs.
- Describe the effects of malnutrition on the respiratory system.
- Describe how to identify patients at high risk for malnutrition.
- State when enteral nutrition and parenteral nutrition are needed.
- Identify and minimize common respiratory complications of enteral feedings.
- List specific nutrition guidelines for specific pulmonary diseases.
- Explain how common pulmonary medications affect nutrition.

CHAPTER OUTLINE

KEY TERMS

albumin
adenosine triphosphate (ATP)
anemia
anergy
anthropometrics
azotemia
basal metabolic rate (BMR)
body mass index (BMI)
cachexic/cachectic
cellular respiration
creatinine-height index (CHI)
catabolism
creatinine
essential nutrients
gluconeogenesis
ideal body weight
indirect calorimetry
kilocalories
Krebs cycle (tricarboxylic acid [TCA] cycle)
kwashiorkor
marasmus
macronutrients
micronutrients

metabolic cart
metabolism
nitrogen balance
normometabolic
parenteral
parenteral nutrition (PN)
protein-energy malnutrition (PEM)
retinol-binding protein
respiratory quotient (RQ)
resting energy expenditure (REE)
skinfold measurement
transthyretin

Essential nutrients are required for life, health, and well-being. Second to the provision of oxygen is the provision of specific nutrients—carbohydrates (CHO), protein, lipids, vitamins, minerals, and water (H_2O), to sustain the function, growth, structure, maintenance, and repair of the body. A human deprived of O_2 for minutes can no longer function. Similarly, a human deprived of essential nutrients for days to weeks will experience cell death and life will cease to exist.

Inside each cell is a special organelle, known as the mitochondria, or the cells' "powerhouse," in which specific biochemical processes of the **Krebs cycle (tricarboxylic acid [TCA] cycle)** generate energy from nutrients. **Cellular respiration** is the process through which cells convert the chemical energy in the three energy yielding nutrients (CHO, protein, lipids) to high energy phosphorylated nucleotides comprised of the currency of life. The most common "energy currency" of cells is **adenosine triphosphate (ATP)**, a molecule which stores a lot of energy in its phosphate bonds. These bonds are broken to release that energy needed to drive all the physiological mechanisms that maintain life.[1,2]

Because ATP is not stable over extended periods of time, it is not used for long-term energy storage. Instead, CHO in its monomer form (glucose) and lipids are used as long-term form of storage, and cells must constantly process those molecules to produce new ATP. This is the process of respiration. The process of aerobic respiration produces a large amount of ATP from each molecule of glucose broken down from complex carbohydrates. In fact, each molecule of glucose digested by a plant or animal cell yields 36 to 38 molecules of ATP.

The overall reaction for cellular respiration is: $C_6H_{12}O_6$(glucose) + $6O_2$(oxygen) → $6CO_2$ (carbon dioxide) + $6H_2O$(water) + ~38 ATP (adenosine triphosphate), and is summarized in Fig. 23.1.[1-3]

Adequate nutrition is essential for good health. The relationship between nutrition and respiratory status is reciprocal throughout the human life cycle. A fully functioning pulmonary system supports the body by providing oxygen needed for cellular **metabolism** of the three **macronutrients**: carbohydrates (CHO), proteins, and lipids. Adequate nutrient intake maintains optimal nutritional status thereby ensuring growth, development and maintenance of the pulmonary system, including its structural mechanisms. The strength and functioning of skeletal and respiratory muscles, as well as, the nervous system and immune system, are dependent on optimal nutrition. A person's nutritional status and ability to metabolize CHO, proteins, and fats is directly related to a healthy pulmonary system. Pulmonary disorders that have direct significant, nutritional implications include asthma, cystic fibrosis, bronchopulmonary dysplasia, chronic obstructive pulmonary disease (COPD), emphysema, and acute respiratory distress syndrome. The nutritional requirements and status of patients with pulmonary disease are established major factors that influence acute and long-term patient outcomes.[4] The systemic presentation of muscle dysfunction observed in patients with COPD, which involves the loss of strength (ability to develop maximal effort); and/or endurance (ability to maintain submaximal effort over time) is exacerbated by nutritional abnormalities and nutrient deficiencies. A balanced supply of nutrients is needed for proper respiratory function; O_2 is required for ATP synthesis and muscle function, including the respiratory muscles. Poor or inadequate nutrient intake disrupts energy use and impairs normal organ function. Conversely, disease can impair nutrient intake or alter metabolism, causing malnutrition (Fig. 23.2).[5-7]

Patients with respiratory disease are particularly challenged because it is difficult to breathe and swallow at the same time. Breathing provides the oxygen necessary for metabolism of nutrients to meet the energy needs of individuals. Nutrition affects the efficiency of the metabolic processes and influences the amount of oxygen needed and the amount of carbon dioxide exhaled. Nutrition is key to proper functioning of the immune defense system, thereby affecting the patient's susceptibility to infection and ability to deal with physiologic stress. The tissues organs that maintain defense against antigens or invading microbes, require sufficient nutrients to function at an optimal level. The skin affords the largest physical barrier, and the lungs,

Fig. 23.1 Cellular respiration.

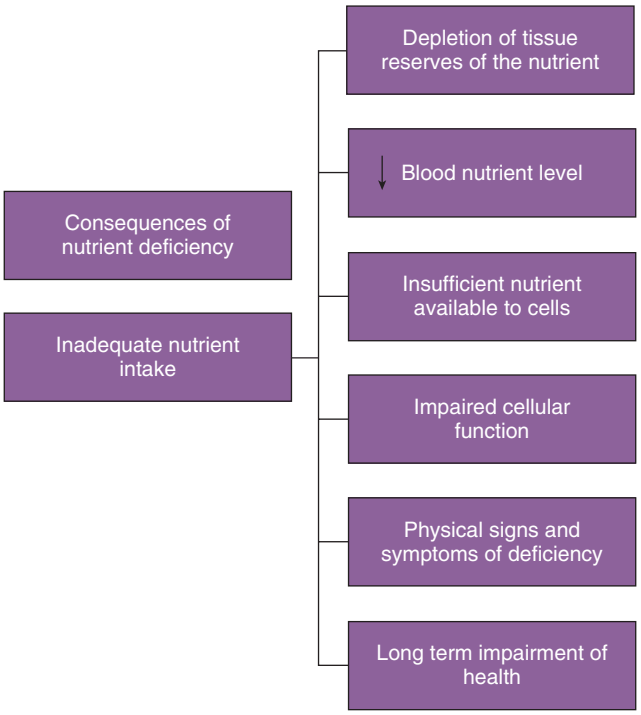

Fig. 23.2 Consequences of nutrient deficiencies.

mouth, and digestive tract are lined with membranes that block invading microorganisms. The linings of these organs are hyper sensitive to vitamin, protein, and other nutrient deficiencies, and examining of the skin and mouth often reveals signs of malnutrition.[2,4]

Understanding the role of and need for nutrition in maintaining normal respiratory function, and in treating pulmonary disease is important for respiratory therapists (RT). This chapter focuses on nutrition assessment—determining the nutrient needs of individuals.

NUTRITION ASSESSMENT

Nutrition assessment is the process of collecting and evaluating data to determine the nutrition status of an individual. Typically a registered dietitian (RD) gathers data to compare various social, pharmaceutical, environmental, physical, and medical factors to evaluate the nutrient needs of an individual. The purpose of nutrition assessment is to develop a *nutrition care plan* that ensures continual adequate nutrition for health. This is a critical process for the RT to understand as diseases of the pulmonary system varyingly increase energy requirements. In addition, complications and treatment of pulmonary disease affect the ability to ingest and digest adequate food and affect the circulation, cellular use, storage, and excretion of most nutrients. The increased work of breathing, chronic infection, and medical treatments used to treat pulmonary diseases, such as chest physical therapy and some medications, increase energy requirements. Medications such as bronchodilators, steroids, and antibiotics used to treat disease may have other nutritional implications and need to be considered in the nutritional evaluation and intervention. Patients with pulmonary disease usually present with a reduced nutritional intake attributed to fluid restrictions, gastrointestinal discomfort, vomiting, anorexia, shortness of breath, and decreased oxygen saturation when eating. A reduced ability to prepare foods because of fatigue and shortness of breath, impaired feeding skills, altered metabolism, and financial limitations all result in additional difficulties in achieving adequate nutritional intake. Also, some diseases, such as cystic fibrosis, affect not only the lungs but also the pancreas, resulting in inadequate production of certain enzymes necessary in the digestion of proteins, carbohydrates, and particularly fats. This puts patients with cystic fibrosis at risk for malnutrition, unless certain dietary supplements and pancreatic enzymes are taken to compensate.[4]

Data are obtained from numerous sources for nutrition assessment. Interviewing the individual or the caregiver to determine past and current eating practices is most helpful. Reviewing the patient's medical record provides additional information regarding pertinent social, pharmaceutical, environmental, and medical issues. Information gathered for a nutrition assessment is grouped into five domains: (1) food/nutrition-related history, (2) anthropometric measurements, (3) biochemical data and tests/procedures, (4) nutrition-focused physical findings, and (5) client history (Box 23.1).[8]

RULE OF THUMB The work of breathing is attributable to about 2% to 3% of the resting energy expenditure (REE) in the normal adult; however, in the pulmonary-compromised patient, approximately 25% of the REE can be attributed to the work of breathing.

Food-Related and Nutrition-Related History

Past dietary practices are identified to determine the pattern of food intake. Numerous means are available to determine food consumed by an individual. A registered dietitian may use a 24-hour recall or a usual daily intake recall, a food diary or food record, or a food frequency questionnaire. The 24-hour recall and the usual daily intake recall depends on past information in which the patient states the foods and amount consumed in an average day. This technique is easily incorporated into a clinical setting. Food frequency questionnaires incorporate information on the frequency and amount of the specific foods consumed and can help identify eating patterns. Patients are asked to write down daily everything they have eaten. The patient may record food intake over an extended time—most frequently, a 3-day or 7-day period.

Evaluation of Nutrition History

The information from a diet history may be evaluated for nutrient intake using a variety of tools, including the government-sponsored MyPlate platform, a nutrient analysis handbook, or a nutrient analysis software package.

MyPlate. The US Department of Agriculture and the US Department of Health and Human Services recommends balanced nutrition for US citizens.[9] The clinician or patient can go to http://www.choosemyplate.gov and compare diet history information to estimate the adequacy of the patient's diet.[10]

Nutrient Analysis Handbook. A handbook listing the nutrient content of specific foods may be used to calculate manually

BOX 23.1 Components of a Comprehensive Nutrition Assessment

Medical Chart
- History and physical examination
- Present diseases
- Current medications
- Activity level
- Physical assessment
- Social history

Anthropometrics
- Usual weight and height
- History of weight loss
- Actual versus ideal body weight
- Body mass index
- Body composition (triceps skin fold, arm muscle area)

Physical Assessment
- Signs of weight loss (cachexia)
- Edema that may mask weight loss
- Hair, skin, mouth, and tongue

Clinical Laboratory Tests
- Visceral proteins
- C-reactive protein
- Creatinine-height index
- Immune-related tests
- Nitrogen balance

Dietary History
- Usual food intake
- Food likes and dislikes
- Appetite

Total Caloric Requirements
- Resting energy expenditure predictive equations
- Indirect calorimetry

Access to Food
- Income
- Education
- Mobility
- Mechanical impediments

the adequacy of a 24-hour recall. This is a tedious and time-consuming task.

Nutrient Analysis Software. Computer programs can determine total calories, percent of calories of macronutrients (protein, carbohydrate, and fat), and units of **micronutrients** and fiber. The patient's individual foods and serving size are entered into a computer file to determine quickly the nutrient content of a diet history.

Anthropometrics

Anthropometrics refers to body measurements; the most frequently used are height and weight. Skin fold thicknesses, arm muscle measurements, waist and hip measurements, head circumference, and wrist diameter are useful body composition measurements when assessing nutrition status.

Height and Weight

A measured height and weight is preferred, but the clinician may ask the patient or caregiver for the height and weight. When recording these data, note the date and whether the height and weight were stated or measured.

Body mass index. **Body mass index (BMI)** expresses the relationship between weight and height and is used to classify patients as underweight, healthy weight, overweight, obese, or morbidly obese. The formula for calculating BMI in kilograms and meters is:

$$\text{BMI} = \frac{\text{Actual body weight (kg)}}{\text{height}^2\,(\text{m}^2)}$$

And when using pounds and inches is:

$$\text{BMI} = \frac{\text{Actual body weight (lb)} \times 703}{\text{height}^2\,(\text{in}^2)}$$

An Internet calculator for BMI is available at: http://www.cdc.gov/bmi.

RULE OF THUMB BMI categories for adults and children (male and female, age 2 to 20 years) are as follows.[11,12]

	Adult (BMI)	Children (BMI for Age)
Underweight	<18.5	<10th percentile
Healthy weight	18.5–24.9	10th–85th percentiles
Excessive weight	25.0–29.9	85th–95th percentiles
Obesity	>30	>95th percentile
Morbid obesity	>35	>99th percentile

Overweight and obesity. Simply defined, overweight and obesity occur over time with the consumption of too many calories or too little expenditure of calories through activity or exercise or both overconsumption and under expenditure. Other contributory factors include rare diseases, genetic predisposition, and loss of mobility through trauma or disease. Regardless, obesity occurs when too many calories are ingested for the amount of energy (calories) expended.

Kwashiorkor and marasmus. Undernutrition classifications include kwashiorkor and marasmus. Typically seen in children 6 to 18 months of age residing in impoverished areas of the world, **marasmus** results from a prolonged, extreme lack of calories and protein associated with food shortage, early weaning, or infrequent feeding of infants,[13] and obvious lack of muscle and fat characterize a child or adult with marasmus. Table 23.1 compares the two forms of protein energy malnutrition (PEM). **Kwashiorkor** results from a more sudden lack of protein and calories, as in a first-born infant weaned suddenly on the arrival of a new sibling, when a diet of nutrient-rich breast milk is traded for a nutrient-poor, cereal-based diet.[1,2] A protruding belly and edematous face and limbs are characteristic of kwashiorkor and result from decreased plasma proteins needed to maintain fluid balance and transport fat out of the liver.

Body Composition

Other anthropometric measurements useful in nutrition assessment evaluate body weight variations in individuals. Someone

TABLE 23.1 Comparison of Two Primary Forms of Protein-Energy Malnutrition

Parameter	Starvation (Marasmus)	Hypercatabolism (Kwashiorkor)
Cause	Inadequate energy intake	Response to injury or infection
Examples	Cancer, pulmonary emphysema	Sepsis, burns
Body habitus	Thin, wasted, cachexic	May be normal, edematous
Rate of malnutrition	Slow	Rapid
Metabolic rate	↓	↑
Fuel	Glucose/fat	Mixed
Catabolism	↓	↑
Gluconeogenesis	↓	Markedly ↑
Glucagon	↓	Markedly ↑
Insulin	↓	↑
Ketogenesis	↑	Slightly ↑
Catecholamines	Unchanged	↑
Cortisol	Unchanged	↑
Growth hormone	Increased	↑
Visceral proteins	Normal	Decreased ↓
Cytokines	Variable	Increased
Immune function	Normal	Impaired
Clinical course	Adequate responsiveness to short-term stress	Infections, poor wound healing, decubitus ulcers, skin breakdown
Mortality	Low unless related to underlying disease	High

with similar height may differ in the proportion of lean body mass, fat mass, and skeletal size. Common measurements are *arm muscle area* (index for muscle), *skin folds* (measures of fat), and waist-to-hip ratios. More sophisticated imaging technologies such as bioelectric impedance analysis or dual-energy x-ray absorptiometry scans determine body fat, body mass, ratio of intracellular water to extracellular water, and bone density, and are the most accurate arthrometric measurements for patients with nutritional disorders. These methods are expensive and are used more in research than clinical settings.[14,15]

Skin fold. **Skin-fold measures** subcutaneous fat with the assumption that it compromises 50% of total body fat. Usually the triceps and subscapular skin folds are the most useful for evaluation.[14] Skin-fold thickness measurements have limited clinical application in the acute care setting because of variation in proper equipment and examiner technique.

Arm muscle area. The triceps skin-fold measurement with the midarm circumference is used to calculate arm muscle area (AMA). The AMA indicates muscle stores available for protein synthesis or energy needs. AMA changes over time may signify protein or caloric deprivation and is useful as a predictor of mortality.[14,16]

Waist circumference. An alternative to BMI, waist circumference, can be a more accurate predictor of excess body fat and risks associated with obesity.[14,15,17] According to the US Department of Health and Human Services, the following individuals are at increased risk for developing chronic diseases[11]:

- Women with a waist circumference of more than 35 inches
- Men with a waist circumference of more than 40 inches.

The World Health Organization has recommended lower thresholds for waist circumference for Asian populations.[11] Therefore those at increased risk for developing chronic disease include:

- Asian women with a waist circumference of more than 31 inches.
- Asian men with a waist circumference of more than 35 inches.

Biochemical Indicators

Particularly significant laboratory values used in assessing nutrition status include serum proteins. Protein energy malnutrition may be reflected in low values for ***albumin***, ***transthyretin*** *(prealbumin), and* ***retinol-binding protein***. Blood levels of these markers indicate the level of protein synthesis and yield information about overall nutrition status. However, inadequate intake may not be the cause of low values; certain disease states, level of hydration, liver and kidney function, pregnancy, infection, and medical therapies may alter laboratory values for each of the circulating proteins.[14,15] The diagnosis of a nutritional disorder cannot be established based on a single laboratory value but requires other data to determine the nutritional status of the patient. Most laboratory values used in nutritional assessments lack sensitivity and specificity for malnutrition.[14,15]

Albumin

Albumin is the largest constituent protein in plasma. Because its half-life is only 14 to 21 days, its usefulness for monitoring the effectiveness of nutrition in the critical care setting is limited.[18] Albumin often reflects the metabolic response to and severity of disease, injury, or infection and can be a useful prognostic indicator. Albumin synthesis is affected by both nutrition and inflammation. Proinflammatory states diminish albumin production, and the combination of inflammation and hypoalbuminemia is linked with increased morbidity, mortality, and longer hospitalization.[4,18]

Transthyretin and Retinol-Binding Protein

Transthyretin, or *prealbumin,* has a half-life of 2 to 3 days, and retinol-binding protein has a half-life of 12 hours. Each of these proteins responds to nutrition changes more quickly than albumin. However, numerous metabolic states, diseases, therapies, and infections influence these laboratory values.[4,18]

Levels of each protein are influenced by many factors present in critically ill patients, and as visceral proteins, are more useful as markers of severity of illness, with limited reflection of nutrient deficiency. *Nonetheless, plasma proteins are useful in assessing the risk for future malnutrition.*[4,18] Inflammatory metabolism causes a 25% decrease in the synthesis of these visceral proteins; causing lean body mass depletion and anorexia. Therefore, it is important to evaluate their values with biomarkers of inflammation where there is a reverse relationship.

RULE OF THUMB Nutritional disorders cannot be made from a single laboratory value because, by themselves, they cannot adequately diagnose malnutrition. Instead, laboratory test results are used with other data as part of a comprehensive assessment of a patient's nutritional status.

RULE OF THUMB Increased metabolism associated with inflammation causes a 25% decrease in protein synthesis resulting in loss of lean body mass.

In proinflammatory states, the combination of inflammation and hypoalbuminemia is linked with increased morbidity, mortality, and longer hospitalization.

Biomarkers of Inflammation

Inflammation adversely affects a patient's nutritional status by both increasing **catabolism** and causing albumin leakage out of the vascular compartment. Inflammation triggers a chemical cascade that causes loss of appetite or anorexia, thereby decreasing dietary protein intake and further catabolism.[14,15]

The most commonly used clinical biomarker of inflammation is C-reactive protein (CRP), which increases with infection and inflammation while the production of albumin and prealbumin decreases.[19,20] Increased levels of C-reactive protein during stress, illness, and trauma have been linked to increased nutrition risk.[20] Other common biomarkers of inflammation include the white cell count and the erythrocyte sedimentation rate (ESR).[21]

Other Tests and Procedures

Creatinine-Height Index

Because the rate of **creatinine** formation in skeletal muscle is constant, the amount of creatinine excreted in the urine every 24 hours reflects skeletal muscle mass. Predicted values are based on gender and height, with reference values of approximately 18 mg/kg body weight per day for women and approximately 23 mg/kg body weight per day for men.[4,14] Factors that influence creatinine excretion and complicate its interpretation include age, diet, exercise, stress, trauma, fever, and sepsis.[4,21-23]

Nitrogen Balance (Protein Catabolism)

Approximately 16% of protein is nitrogen, and nitrogen is a major by-product of protein catabolism. Therefore, measuring **nitrogen balance** is an important aspect of nutritional assessment. The urinary excretion rate of nitrogen is used to assess protein adequacy. Nitrogen balance is calculated as follows:

$$\text{Nitrogen balance} = \text{Nitrogen intake} - \text{Nitrogen losses}$$

$$\text{Nitrogen intake} = \frac{\text{Protein intake}}{6.25}$$

$$\text{Nitrogen losses} = \text{Urine urea nitrogen (UUN) excretion in grams} + 3 - 5 \text{ g (for insensible losses)}$$

The dietary protein conversion factor is 6.25 g of nitrogen per 1 g of protein. The amount of nitrogen excretion in the urine is typically measured as the 24-hour urinary urea nitrogen. Between 3 g/day and 5 g/day is added to the 24-hour urinary urea nitrogen to estimate the average daily unmeasured nitrogen lost through other sources (skin and gastrointestinal [GI] sloughing, hair loss, sweat, feces). Theoretically, increasing exogenous protein reduces endogenous protein loss. However, the accuracy of 24-hour urine collection is limited by alterations in renal or liver function, large insensible losses (burns, high-output fistulas, wounds, or ostomies), and inflammatory conditions.[22]

Immune Status

Impaired immunity (**anergy**) is common in malnutrition, especially the kwashiorkor type. Two laboratory values, white blood cell count and percentage of lymphocytes, are indices of compromised immunity. The result is often a reduction in the total lymphocyte count. Many nonnutrition variables, including disease states and drugs, influence these laboratory values, so their usefulness in assessing nutrition status is questioned.[23]

Pulmonary Function

Pulmonary function test results may change with malnutrition. Respiratory muscle weakness reduces both maximal inspiratory and expiratory pressures and reduced vital capacity. These limitations in turn reduce the ability to maintain sufficient lung volumes to prevent atelectasis and produce an effective cough to clear secretions. Diminished strength and endurance of respiratory muscles increases the susceptibility to respiratory muscle fatigue and the inability to maintain effective spontaneous breathing. The negative effects of malnutrition on both respiratory muscle function and immunologic function increase the risk for respiratory infections and pneumonia.[24]

Skeletal muscle tissues, including the diaphragm and other respiratory muscles, lose muscle mass, leading to decrease in endurance and strength. In malnourished patients, respiratory muscle strength declines, resulting in decreases in forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV1), as the muscles of respiration as well as other skeletal musculature are catabolized for energy. In addition, the carbon monoxide diffusing capacity (DLCO) also decreases and is reflected in diminished gas exchange capacity of the lungs. The decline in FEV1 also correlates with a decreased **creatinine-height index (CHI)**, indicative of loss of muscle mass. Consequently, because immune antibodies are composed of proteins, persistent inadequate calorie and protein intake will compromise the immune system and restrict the body's ability to fight pneumonia or other infections.[4,13]

RULE OF THUMB Malnutrition promotes decline in respiratory muscle strength with resulting decreases in forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV1). The decline in FEV1 occurs with a corresponding decreased creatinine-height index (CHI), indicative of inadequate protein intake, and loss of muscle mass, that results in a cycle of diminished immune function, and limited capability to fight infections, including those that attack the respiratory system.

Nutrition-Focused Physical Findings

The physical signs of malnutrition often appear first in specific tissues where high cell turnover occurs[25] (e.g., hair, eyes, lips, mouth and gums, skin and nails), so incorporating the appearance of these features into the physical examination can alert the clinician to signs of nutrient deficiencies (Table 23.2 for physical signs and symptoms of potential nutrition disorders). In addition to malnutrition, other causes of these abnormalities

TABLE 23.2 Signs of Malnutrition on Respiratory Therapists Physical Exam

	Signs or Symptoms of Potential Nutritional Problems
Hair	• Look at the health of the patient's hair; check for sparseness, dyspigmentation, or easy pluck ability.
Nails	• Nails are fissured or ridged.
Skin	• Assess the skin for areas of drying, flaking, cracking, or pigment change, peeling skin with raw exposed areas, hyperpigmented plaques over areas of trauma. • Observe for decreased subcutaneous tissue: areas that are most affected are the legs, arms, buttocks, and face. • Observe for edema: areas that are most affected are the distal extremities and anasarca (generalized edema).
Mouth and upper extremities	• Observe for swollen parotid glands, changes in saliva production, or cheilosis, angular stomatitis, papillary atrophy. • Observe the amount of effort that can be generated during coughing. • Check for muscle weakness.
Abdomen	• Check for abdominal findings and observe for abdominal distension secondary to poor abdominal musculature. • Check for hepatomegaly secondary to fatty infiltration.
Weight	• Observe for cachexia, readily outlined bony structures with depression of the intercostal spaces; accessory muscles of respiration visible. • Observe for obesity.
Demeanor/ Affect	Observe for mental apathy and confusion.

The RT will often see nutritional deficiencies complicating an existing lung problem. Being alert to the effect of nutrition on respiratory function may help stabilize the condition of a patient with lung disease that was previously deteriorating because of nutritional neglect. When these signs are present in a patient, more sensitive and objective methods of assessment should be used to confirm or rule out compromised nutritional status.
From Ziegler J, Reid-Hector J: Nutritional assessment of patients with respiratory disease. In Heuer A, Scanlan CL, editors: *Wilkins clinical assessment in respiratory care*, ed 8, St Louis, 2017, Mosby.

include medical therapies, **anemia**, allergies, sunburn, medications, poor hygiene practices, aging, or various pathologic processes.[4,18,21] Patients with persistent malnutrition often appear very thin. When the bony structures of the chest are conspicuously visible, a patient is said to be **cachexic**. Special attention should be given to fluid retention because this can mask weight loss.[4,25-27] Other physical findings, such as skeletal muscle depletion, can be clinical indicators of inflammation or signs of systemic inflammatory response.

OUTCOMES OF NUTRITION ASSESSMENT

With nutritional intervention, patients improve their nutrient intake and reduce mortality and morbidity. Improved nutritional status increases the patient's tolerance of therapeutic regimens in the treatment of disease and decreases recovery time. The resulting economic benefits are multifaceted and include shorter and less frequent hospital stays, reduced need for medication or medical care or extended care, and increased years of productivity.[28]

BOX 23.2 Factors Influencing Energy and Macronutrient Needs

Energy Needs
- Height and weight
- Activity level
- Growth state: Infants through teens, pregnancy, and lactation
- Presence of infection or fever
- Surgery
- Trauma and fractures
- Presence of infection or inflammation

Protein Needs
- State of growth
- Surgery, trauma, fractures, and infection
- Renal (kidney) function
- Liver function
- Corticosteroid administration

Fat Needs
- Total energy needs
- Hyperlipidemia, and diabetes mellitus
- Liver, gallbladder, and pancreatic disorders
- Cardiovascular disease

MACRONUTRIENTS AND ENERGY REQUIREMENTS

The nutritional assessment is used to determine a nutrition care plan for the patient. Calorie or energy needs are fundamental to these recommendations. Several means are available to determine calorie needs. These include calculating total calories using a mathematical formula or predictive equation.

Macronutrients supply the energy requirements of the body. The three macronutrients are *protein, carbohydrate,* and *fat*. Each contributes to calorie intake with 4, 4, and 9 calories (kcal) per gram, respectively. Alcohol is the only other calorie source, with approximately 7 kcal/g. Box 23.2 outlines the factors influencing energy and macronutrient needs.

Estimating Energy Requirements

An individual's energy requirement represents the ratio of energy intake to energy expenditure relative to body weight, activity level, and stressors. The classic measure of energy expenditure is the **basal metabolic rate (BMR)**. Obtained after 10 hours of fasting, the BMR measures the number of calories (kcal) expended at rest per square meter of body surface per hour (kcal/m^2/h). BMR varies by body size, age, and gender. Caloric needs for energy expenditure increase beyond the BMR based on activity level, stage of growth (pregnancy, lactation), and extent of injury.

In clinical practice, interest is focused on a patient's *daily* energy requirements (**kilocalories** per day). Multiple methods are available for estimating daily energy needs. Predictive equations

BOX 23.3 Predictive Equations

Harris-Benedict Equations

Men: Resting metabolic rate (RMR) = 66.47 + 13.75(W) + 5(H) – 6.76 (A)

Women: RMR = 655.1 + 9.56 (W) + 1.7 (H) – 4.7 (A)

Equation uses weight (W) in kilograms (kg), height (H) in centimeters (cm), and age (A) in years.

Ireton-Jones Energy Equations (IJEE) 1992

Spontaneously breathing IJEE

(s) = 629 – 11 (A) + 25 (W) – 609 (O)

Ventilator dependent IJEE

(v) = 1925 – 10 (A) + 5 (W) + 281 (S) + 292 (T) + 851 (B)

Equations uses age (A) in years, body weight (W) in kilograms, sex (S, male = 1, female = 0), diagnosis of trauma (T, present = 1, absent = 0), diagnosis of burn (B, present = 1, absent = 0), obesity more than 30% above initial body weight from 1959 Metropolitan Life Insurance tables or body mass index (BMI) more than 27 kg/m^2 (present = 1, absent = 0).

Mifflin-St. Jeor Equations

Men: RMR = (9.99 × weight) + (6.25 × height) – (4.92 × age) + 5

Women: RMR = (9.99 × weight) + (6.25 × height) – (4.92 × age) – 161

Equations use weight in kilograms and height in centimeters.

Penn State Equations (PSU)

Also known as PSU 2010 (Modified Penn State Equation)

$$RMR = Miffin(0.71) + \dot{V}_E(64) + T_{max}(85) - 3085$$

Used for patients with BMI over 30 and older than 60 years old. Validated in 2010 by the ADA Evidence Analysis Library (EAL).

PSU 2003b (Penn State Equation)

$$RMR = Miffin(0.96) + \dot{V}_E(31) + T_{max}(167) - 6212$$

Used for patient of any age with BMI below 30 or patients who are younger than 60 years with BMI over 30. This equation was validated in 2009 by the EAL and is also referred to as the Penn State equation.

PSU 2003a (Penn State 2003a)

Invalidated in 2007 and 2009 by EAL

$$RMR = Miffin(0.85) + \dot{V}_E(33) + T_{max}(175) - 6433$$

(Use actual weight in all patients.)

From Academy of Nutrition and Dietetics. Evidence analysis library, 2014. Available http://www.andeal.org. Accessed May 15th 2018.

(Box 23.3) such as the classic *Harris-Benedict equation* are frequently used to estimate daily **resting energy expenditure (REE)**.

Several other predictive equations focus on specific patient populations and medical conditions. Additional data such as injury-stress, activity, medications received, and obesity have been added to improve accuracy. The *Mifflin-St. Jeor equation* is the most reliable in both nonobese and obese ill patients.[4,28,29] Other equations, such as the *Ireton-Jones* and *Penn State equations*, are used specifically in intubated patients to account for temperature and ventilation parameters. Although the predicted REE averages approximately 10% higher than the BMR, predictive equations may still tend to overestimate or underestimate actual energy need.[4,29]

To overcome the limitations of estimating formulas, energy needs can be measured using O_2 consumption and carbon dioxide production. From these data, an actual REE can be quickly computed. Indirect calorimetry is described in more detail later.

Energy needs vary according to activity level and state of health. Energy needs of sick patients can be significantly greater than predicted normal values. Energy needs for obese individuals are less because adipose tissue uses less energy than muscle. Energy needs should be reevaluated and adjusted whenever weight changes by more than 10 lb.

BOX 23.4 Clinical Situations in Which Indirect Calorimetry May Be Indicated

- Patients with morbid obesity
- Patients who are difficult to wean from ventilatory support
- Patients for whom weight estimates are unclear
- Patients with severe malnutrition
- Patients with high level of stress
- Patients at the extremes of weight or age
- Patients failing to respond to nutrition support

RULE OF THUMB To estimate the energy needs of an average adult in kilocalories per day, identify the goal and multiply the individual's actual body weight in kilograms times the factor listed as follows[27]:

Goal	Energy Needs (kcal/kg)
Weight maintenance	25–30
Weight gain	30–35
Weight loss	20–25

Indirect Calorimetry

Indirect calorimetry is the estimation of energy expenditure by measurement of O_2 consumption and CO_2 production. Data obtained can be used to assess a patient's metabolic state, to determine nutrition needs, or to assess response to nutritional therapy.[4,27,30] To guide practitioners in using indirect calorimetry, the American Association for Respiratory Care (AARC) has published the Clinical Practice Guideline: Metabolic Measurement Using Indirect Calorimetry During Mechanical Ventilation.[30]

Regarding the indications for indirect calorimetry, the determination of energy and protein needs by an empiric formula is sufficient for most patients. However, the use of indirect calorimetry improves nutritional care and reduces complications associated with underfeeding and overfeeding.[4,31] Specific clinical conditions supporting the need for indirect calorimetry as a tool in nutrition assessment are listed in Box 23.4.[27,30]

Equipment and Technique

Good calorimetry results require extensive preparation. Box 23.5 outlines the key preparatory steps to be taken before testing.[4,27,30,32] Indirect calorimetry can be performed with a Douglas bag, a Tissot spirometer, and CO_2 and O_2 gas analyzers. The patient's expired gas is collected in the Douglas bag, where it is sampled for O_2 and CO_2 concentrations; the Tissot spirometer measures expired volume. Commercially available **metabolic carts** are

BOX 23.5 Preparation for Indirect Calorimetry

30 Hours Before Test
- 24-Hour urine urea nitrogen collection (with sufficient time to receive result) if determination of carbohydrate, fat, and protein use desired

10 Hours Before Test
- Patient fasting if measuring energy requirements; if feeding is continued, results will reflect the patient's energy expenditure in response to feeding (may be spuriously high if patient is being overfed)

4 Hours Before Test
- Patient resting and avoiding physical activity, physical therapy, dressing changes

2 Hours Before Test
- Endotracheal tube suctioned for the last time before test; further ventilator changes or suctioning avoided

1 Hour Before Test
- Supine position, complete rest; analgesic or sedative administered if needed

BOX 23.6 Equations Used to Calculate $\dot{V}O_2$ and $\dot{V}CO_2$ Using the Gas-Exchange Method

$$\dot{V}O_2 = \dot{V}_E \times (3FiO_2 4) - (\dot{V}_E \times FeO_2)$$
$$\dot{V}CO_2 = \dot{V}_E \times FeCO_2$$
$$RQ = \dot{V}CO_2 / \dot{V}O_2$$

much easier to use. These automated systems either use a mixing chamber or perform breath-by-breath analysis. The breath-by-breath method provides real-time data, which may aid in ensuring optimal measurement conditions, particularly in mechanically ventilated patients.[32-34]

Open-circuit indirect calorimetry with a metabolic cart and mixing chamber is used during mechanical ventilation. Gas sampled from the inspiratory limb of the ventilator circuit is assessed for fractional inspired oxygen (FiO_2) using a paramagnetic or zirconium oxide O_2 analyzer. Volume exhaled by the patient is measured using a flow transducer. The patient's exhaled gas enters a mixing chamber, from which a sample is drawn to measure fractional expired carbon dioxide ($FeCO_2$) by infrared analysis and fractional expired oxygen (FeO_2). Exhaled gas is returned to the ventilator after volume and gas concentration measurements. After all measurements are obtained, O_2 consumption, CO_2 production, and ***respiratory quotient (RQ)*** are computed using the equations shown in Box 23.6. *All measurements must be corrected to standard temperature and pressure and dry conditions (STPD) before computation.*[34-36] The values are used in the abbreviated Weir equation to determine REE:

$$REE = [(O_2 \times 3.9) + (CO_2 \times 1.1)] \times 1.44$$

Indirect calorimetry is more difficult to perform on spontaneously breathing patients, especially patients breathing supplemental O_2. Although a mouthpiece with nose clips or a mask can be used to collect expired gas, these items tend to alter the patient's steady state and invalidate results.[4,33] Instead, most clinicians recommend using a plastic canopy that covers the patient's head. Expired gases are cleared from the canopy by a preset flow of air; expired gas concentrations are sampled and corrected for the air dilution.

Because standard modes of O_2 therapy do not deliver a consistent FiO_2 to spontaneously breathing patients, special delivery systems must be used. To overcome this problem, the clinician can substitute a precise O_2 mixture for the gas used to clear the canopy. Alternatively, a large gas reservoir (e.g., a Douglas bag) can be placed between an O_2 flow source and the subject to ensure a stable FiO_2 throughout the test procedure.[33-35]

Problems and Limitations

Indirect calorimetry is a technically complex procedure requiring rigorous attention to both instrument and procedure quality control. Regarding instrumentation, small errors in measurements can result in large errors in calculated O_2, CO_2, and therefore energy expenditure. For this reason, the calorimeters gas analyzers and volume measurement device must be properly calibrated before each patient use. Gas analyzers should be accurate to the hundredth percent and linear over the clinical range of O_2 concentrations.[32,35]

RULE OF THUMB The key to indirect calorimetry is that all inspired and expired air must be collected; improper calibrations of the gas analyzers and volume measuring devices will result in errors and results that cannot be clinically interpreted.

Regarding procedure quality control, it is essential that measurements be made during steady-state conditions. Although proper patient preparation (see Box 23.5) is helpful in this regard, steady-state conditions can be confirmed only during the test procedure itself. A common standard for ensuring steady-state conditions is five consecutive 1-minute averages with a variability of 10% of less.[36-39]

Perhaps the most significant problem in performing indirect calorimetry on mechanically ventilated patients is the presence of leaks (circuit, tracheal tube cuff, chest tubes).[4,39] Because any leak invalidates test results, no procedure should begin until a leak-free patient-ventilator-calorimeter system is confirmed. Other sources of error during open-circuit indirect calorimetry of mechanically ventilated patients are listed in Box 23.7.[4,39]

RULE OF THUMB The clinical efficacy of indirect calorimetry cannot be validated without accurate collection of all inspired and expired air, and any potential leaks in the closed ventilatory system leads to errors in the readings and uninterpretable results.

RULE OF THUMB The key to indirect calorimetry is that all inspired and expired air must be collected; improper calibrations of the measuring devices, and any potential leaks in the closed ventilatory system lead to errors in the readings and render the results invalid.

BOX 23.7 Sources of Error During Open-Circuit Indirect Calorimetry Of Mechanically Ventilated Patients

- Instability of FiO_2 because of changes in source gas pressure or ventilator or blender variability
- Delivery of high FiO_2 levels (>0.60)
- Inability to separate inspired and expired gases because of bias flow from flow-triggering systems, intermittent mandatory ventilation systems, or specific ventilator characteristics
- Presence of anesthetic gases or gases other than O_2, CO_2, and nitrogen in the ventilation system
- Presence of water vapor resulting in sensor malfunction
- Inappropriate calibration
- Adverse effect on functions of some ventilators (triggering, expiratory resistance, pressure measurement)
- Total circuit flow exceeding internal calorimeter flow (if using dilutional principle)
- Concurrent peritoneal dialysis or hemodialysis

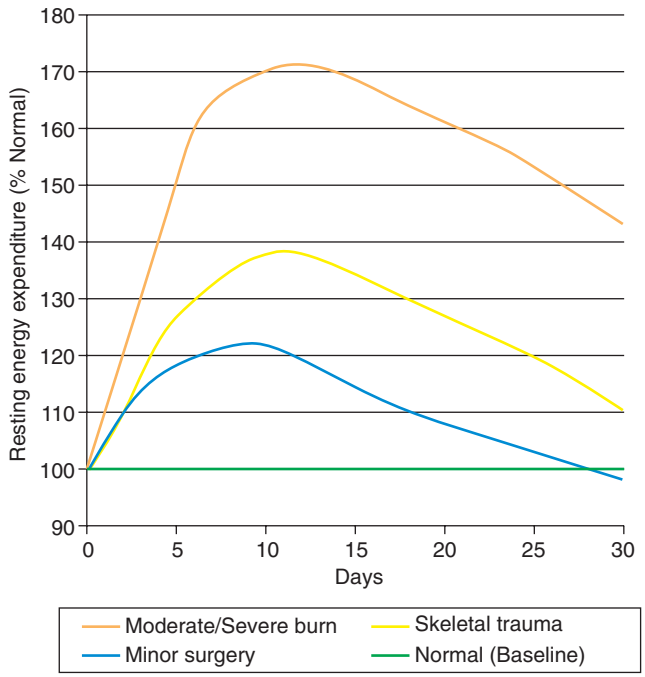

Fig. 23.3 Resting energy expenditure variation during illness and injury.

Interpretation and Use of Results

Results obtained from indirect calorimetry are used to assess metabolic status and plan nutrition support. Energy expenditure varies during illness and injury (Fig. 23.3),[4,34] which occurs in three phases: the stress response, the catabolic phase, and the anabolic phase. Because of the changing metabolic rate, it is important to reassess metabolic needs when there is a change in clinical status. Indirect calorimetry is an important tool because it can demonstrate these changes in energy expenditure. Energy expenditure can vary on a daily basis by 15% to 30%.[31]

In regard to assessing metabolic status, the first step is to compare the REE obtained by calorimetry with the REE predicted by predictive equations. If the calorimetry REE is within 10% of the predicted value, the patient is considered **normometabolic.** Measured REEs greater than 10% above predicted values indicate a hypermetabolic state, whereas values less than 90% of predicted indicate hypometabolism.

The second step in metabolic assessment is to interpret the RQ. The RQ is the ratio of moles of CO_2 expired to moles of O_2 consumed. Traditionally, the RQ has been used to determine substrate use, where carbohydrates have an RQ of 1.0, protein has an RQ of 0.82, and fat has an RQ of 0.7. Table 23.3 outlines the basic significance of the RQ relative to substrate use and traditional nutrition strategies.[4,33] RQ may have low sensitivity and reduced specificity in critically ill patients.[35-37] This finding limits the RQ as an indicator for substrate use and should be used only as a measure of test validity. If the RQ is outside its physiologic range of 0.67 to 1.3, this should alert the clinician to assess the validity of the study.

TABLE 23.3 Traditional Interpretation and Use of the Respiratory Quotient

Value	Interpretation	General Nutrition Strategy
>1.00	Overfeeding	Decrease total kilocalories
0.9–1.00	Carbohydrate oxidation	Decrease carbohydrates or increase lipids
0.8–0.9	Fat, protein, and carbohydrate oxidation	Target range for mixed substrate
0.7–0.8	Fat and protein oxidation	Increase total kilocalories

Note: Acute hyperventilation or acute metabolic acidosis increases the respiratory quotient (RQ) and can lead to misinterpretation. Metabolism of ketones or ethyl alcohol decreases RQ to less than 0.7.

RULE OF THUMB

RQ	0.67 to 1.3	Ideal range for test validity

Alternative Resting Energy Expenditure Measures

In patients with pulmonary artery catheters, REE can be measured using a modification of the Fick equation[4,37]:

$$\text{REE(kcal/day)} = \text{Cardiac output} \times \text{hemoglobin} \times (SaO_2 - S\bar{v}O_2) \times 95.18$$

In a patient with cardiac output of 4.2 L, hemoglobin of 11 g/dL, SaO_2 of 89%, and SVO_2 of 69%, the REE would be computed as follows:

$$\text{REE} = 4.2 \times 11 \times (0.89 - 0.69) \times 95.18$$
$$\text{REE} = 4.2 \times 11 \times (022) \times 95.18$$
$$\text{REE} = 879 \text{ kcal/day}$$

Another alternative method to assess REE in mechanically ventilated critically ill patients could be the use of VCO_2 measurements only, given that most mechanical ventilators provide the option to measure VCO_2 continuously. When VCO_2 is known, the Weir formula can be used to calculate VO_2, assuming the respiratory quotient RQ, is in the physiologic range of 0.67–1.2.

MINI CLINI

Nutrition Assessment in the Intensive Care Unit

Nutrition and Respiratory Problem

A 50-year-old woman presents with hemodynamic instability, hypoxemia, with a PaO_2 of 57 mm Hg (normal, 80 to 100 mm Hg). She is intubated and placed on the ventilator for septic shock. There is no clinical improvement on full ventilator support, and she is subsequently diagnosed with community acquired pneumonia and acute respiratory distress syndrome.

Medical history includes iron deficiency anemia, type 2 diabetes mellitus, morbid obesity, left lung lobectomy, episodic shortness of breath, fever, fatigue, and obstructive sleep apnea. She is admitted to the intensive care unit (ICU) for extracorporeal membrane oxygenation (ECMO) evaluation chest radiography, and bronchoscopy. The patient is started on broad-spectrum antibiotic therapy and oseltamivir; and continued on full ventilatory support. She is also treated with furosemide and metolazone, with a goal of net negative 1 Liter every 8 hours, with electrolytes supplemented. The patient becomes more hemodynamically stable and the RD and respiratory therapist (RT) collaborate to evaluate her nutritional requirements and to assess parameters for indirect calorimetry measurements.

Nutrition Assessment

Height: 162.6 cm, Admission Weight: 186.4 kg Dry Weight: 170 kg **Ideal Body Weight (IBW)**: 54.5 kg, Body Mass Index: 64.3 (per 170 kg)

Estimated Nutrition Goals: (per A.S.P.E.N./AND Guidelines [48, 16])

Energy: 1850 to 2400 kcal (11 to 14 kcal/kg, per 170 kg): Using the Penn State University equation recommended for mechanically ventilated patients, the RD sets a target goal of 2665 kcals/ day; Protein: 110 to 135 g (2 to 2.5 g/ kg, per IBW).

Nutrition Care Plan Diagnosis: Inadequate protein-energy intake related to increased nutrient needs, patient's clinical status as evidenced by patient nil per os status × 3 days.

Enteral Access: Nasogastric tube

Diet order: Nil per os

Skin: 2+ bilateral lower extremity chronic lymphedema.

Enteral nutrition (EN) support regimen recommendations: For the initial administration of feeding, the RD selects a 1.5-kcal/mL formula and starts administration at 20 mL/h, advancing by 10 mL every 8 hours until reaching the goal rate of 55 mL/h. on hospital day 3. This regimen provides 1320 mL formula, 1980 kcal, 82 g protein, and 1005 mL free water/per 24 hours.

Evaluation for Indirect Calorimetry (IC) Measurements by the RT

The RT evaluates and identifies desired patient parameters for valid IC measurements to include:

- Mechanical ventilation with fraction of inspired oxygen (FiO_2 ≤60)
- Positive end-expiratory pressure (PEEP) <10 cm H_2O
- Supine position capability for 30 minutes, in a quiet, thermoneutral environment, with patient displaying her usual patterns of voluntary muscle activity

The RT reviews the medical record and checks with nursing staff to ensure that administration of analgesics or sedatives were not given within 30 minutes of study initiation, with no painful procedures conducted within 1 hour of testing. The RT also establishes that general anesthesia was not administered within past 6 to 8 hours, ventilator settings remain unchanged within past 90 minutes before testing; and confirms with the RD and nurse that patient received stable nutrient delivery for 12 hours before initiation of study, on continuous feeding regimen if thermogenesis is to be included in the resting energy expenditure measurement. The RT checks for any problems that may result in contraindications for conducting IC, such as:

- Leaks around endotracheal or tracheostomy tube, including cuffless tubes
- Chest tube to suction and leaks around the chest tube
- Subcutaneous emphysema and communicating tracheal esophageal fistula
- Ventilatory modes that use bias flow or leak compensation

The RT completes a 20-minute IC study in which a 5-minute steady state is reached, and results are validated with measurement procedures, including:

1. Collect expired gas in a bag or Tissot spirometer for several minutes.
2. Analyze for carbon dioxide and oxygen (or oxygen and nitrogen).
3. Measure the volume of the gas collected in the bag.
4. Complete calculations:

   Evaluation of patient's steady state results:
   Oxygen consumption—450 (mL/min) coefficient of variation (3.4%)
   Carbon dioxide elimination 370 (mL/min) coefficient of variation (6%)
   Respiratory quotient—0.82 coefficient of variation (4%)
   Resting energy expenditure—2145 (kcal/day coefficient of variation [3.8%])
   ***Coefficient of variation goal is <10%

Discussion

A. Discuss the purpose of indirect calorimetry and why it is useful.

B. Interpret the results and compare to the predictive equation to the RT's indirect calorimetry measurements of the patient. Based on the results, suggest what changes would be made.

C. Discuss why it is critical that the RT ensures that there are no leaks in collection of exhaled gas.

(A) Critical illness can significantly affect metabolism, so an accurate measurement of the resting energy expenditure (REE) can help determine the energy requirements in ICU patients. REE (usually 70% of the total energy expenditure) can increase after burns, sepsis, trauma, and surgery. A precise calculation of energy expenditure may prevent overfeeding or underfeeding.

REE can be measured with indirect calorimetry using a metabolic cart, which is used to measure the oxygen consumption (VO_2) and carbon dioxide production (VCO_2). Every liter of oxygen consumed is equivalent to the energy cost of 5 kcal. Indirect calorimetry is a respiratory test that measures the patient's production of CO_2 and consumption of oxygen for approximately 30 minutes, until steady state is achieved. Results are worked into the modified Weir equation.

The test is useful in the patient on mechanical ventilation (MV) once a patient is relatively stable, with a fractional concentration of oxygen in inspired gas (FiO_2) <60% and peak end-expiratory pressure (PEEP) <10. Indirect calorimetry studies are helpful when overfeeding (diabetes mellitus, COPD, obesity) is undesirable and when underfeeding (renal failure, large wounds) is detrimental. It is highly recommended in patients whose physical or clinical factors promote alterations in energy expenditure (spinal cord injury), when drugs significantly alter energy expenditure (paralytic agents, β-blockers), and in patients who fail to respond as expected to calculated enteral/parenteral feeding administration.

A metabolic cart can also be used to assess the energy requirements and determine work capacity.

In general, metabolic cart is indicated for the following:

- To guide appropriate nutritional support
- To determine the oxygen cost of work of breathing and to help select appropriate ventilator mode and settings
- To determine the causes of increased ventilatory requirements (high glucose intake can increase carbon dioxide production, stimulating ventilation and complicating liberation from the ventilator)
- To measure cardiac output and aid with exercise physiology

(B) The patient's measured resting energy expenditure (REE) of 3145 kcal/day is higher than her original predicted energy needs and what her current enteral regimen is providing. A comparison of her measured REE to the daily average of 2135 kcal shows she is receiving only 67% of her nutrient needs. The patient is being underfed, therefore the RD will need to use nutrient dense liquid protein and fat modular added to the enteral formula to improve nutrient intake and aid with liberating from the ventilator.

MINI CLINI

Nutrition Assessment in the Intensive Care Unit—cont'd

Interpreting results of the patient's IC study requires the RT and RD to review whether the respiratory quotient (RQ) was within the human biological range of 0.67 to 1.3. RQ is the ratio of the volume of carbon dioxide produced (VCO_2) to the volume of oxygen consumed (VO_2). When values are outside of this range, the IC study should not be considered valid and the REE should not be used. Another parameter to review is patient's ability to achieve steady state. Steady state represents a period of metabolic equilibrium defined as a 5-minute interval in which the coefficient of variation for the REE (VO_2 and VCO_2) and the RQ are less than 10%. The patients' RQ of 0.82 serves to validate the IC. This patient reached a steady state, which also enhances the reliability of the IC, as the coefficients of variation were all less than 10%.

(C) IC measurements may be inaccurate in patients who require high levels of oxygen (FiO_2 ≥60%), high PEEP (>10 cm H_2O), air leaks, peritoneal or hemodialysis up to 4 hours after (the latter due to elimination of carbon dioxide across the artificial dialysis membrane). The key to indirect calorimetry is that all inspired and expired air must be collected; any potential leaks in the closed ventilatory system lead to errors in the readings or uninterpretable results.

Data from Mueller CM, Merritt RJ, McClave S, et al, editors: *The ASPEN adult nutrition support core curriculum*, ed 2, Silver Spring, MD, 2012, American Society for Parenteral and Enteral Nutrition; Ziegler J, Reid-Hector J: Nutritional assessment of patients with respiratory disease. In Heuer A, Scanlan CL, editors: *Wilkins clinical assessment in respiratory care*, ed 8, St Louis, 2017, Mosby.

In prolonged measurement periods, metabolic CO_2 production equals its excretion.

Nutritional RQ may be calculated considering 24-hours macronutrient delivery, using RQs of 1 for carbohydrates, 0.7 for fat, and 0.8 for protein. Nutritional RQ is calculated from the weighted average RQ for intake during the study period. For example, if the composition of the enteral formula is 16% protein, 49% carbohydrates, and 35% fat, the nutritional RQ is calculated as $0.16 \times 0.8 + 0.49 \times 1 + 0.35 \times 0.7 = 0.86$. After calculating nutritional RQ for the patient, EE:VCO_2 is calculated using the following rewritten Weir formula:

$$EE = 3.941 \times VCO_2\,(L/min) \div \text{Nutritional RQ} + 1.11 \times VCO_2\,(L/min) \times 1440.$$ [34,36,37]

RULE OF THUMB EE from ventilator-derived VCO_2 is accurate and more precise than predictive equations.

This method allows for continuous monitoring and is a viable alternative to indirect calorimetry.

EE (kcal/day) can be calculated at the bedside as $8.19 \times VCO_2$ (mL/min)

RULE OF THUMB Although predictive equations are highly useful tools in calculating a patient's energy expenditure needs, they do not always replace the need for performing indirect calorimetry, which is generally more accurate and provides additional information, including calculation of the RQ.

GENERAL ASPECTS OF NUTRITION SUPPORT

The primary goal of nutrition support is the maintenance or restoration of lean body (skeletal muscle) mass. This goal is accomplished by (1) meeting the patient's overall energy needs and (2) providing the appropriate combination of substrates to do so. The route of administration used to provide the support is also important.

Meeting Overall Energy Needs

When the patient's REE is derived, it needs to be adjusted to account for variations in activity and stress levels. If using a predictive equation, such as the Harris-Benedict or Mifflin-St. Joer equations, the predicted REE should be corrected for stress, activity levels, or both.[22] When the REE is derived from the Penn State equations or indirect calorimetry, a stress or activity factor should not be used.

BOX 23.8 Patients at High Risk for Malnutrition

- Underweight (BMI <18.5) or recent loss of 10% or greater of usual body weight
- Poor intake: Anorexia, food avoidance (e.g., psychiatric condition), nothing allowed by mouth (NPO) status for greater than 5 to 7 days
- Protracted nutrient losses: Malabsorption, enteric fistulas, draining abscesses or wounds, or renal dialysis
- Hypermetabolic states: Sepsis, protracted fever, extensive trauma, or burns
- Chronic use of alcohol or drugs with antinutrient or catabolic properties: Steroids, antimetabolites (e.g., methotrexate), immunosuppressants, antitumor agents
- Impoverishment, isolation, advanced age, limited mobility

Insufficient Energy Consumed

Malnutrition from undernutrition results from insufficient energy (calorie) intake over time. This insufficient intake leads to a state of impaired metabolism, in which the intake of essential nutrients falls short of the body's needs. Certain factors may place a patient at risk for malnutrition (Box 23.8).

Protein-Energy Malnutrition

Protein-energy malnutrition (PEM) has adverse effects on respiratory musculature and the immune response.[4,26] PEM may be either primary or secondary. Primary PEM results from inadequate intake of calories, protein, or both, and is typically seen only in developing countries.[22]

Secondary PEM is due to underlying illness. Illness may cause (1) decreased caloric or protein intake (e.g., anorexia, dysphagia), (2) increased nutrient losses (e.g., malabsorption or diarrhea), and (3) increased nutrient demands (e.g., injury or infection).[38,40]

RULE OF THUMB Fifty percent of hospitalized patients present with secondary PEM.

MINI–CLINI

Hospitalized Malnourished Patient

Mrs. Hernandez is a 70-year-old, underweight, African American patient with a HX of HTN, depression, and emphysema. She is 5'6" tall and weighs 100 pounds. She was recently seen by her primary doctor for signs of illness: fever, loss of appetite, fatigue, chills, dyspnea, and shortness of breath. She was diagnosed with bronchitis and started on a bronchodilator and corticosteroid nebulizer treatments as well as an oral antibiotic. However, she continued to feel ill without improvement, and became very confused with increased shortness of breath. She was taken to the hospital by ambulance and admitted with a diagnosis of pneumonia, and then started on 2 L of O_2 via a nasal canula and IV antibiotic. Mrs. Hernandez was placed on a regular diet. However, she ate sparingly and was not receiving the nutrients she needed.

Discussion

1. What are the main goals of medical nutrition therapy for this patient?
2. What factors are interfering with the patient's food intake?
3. What dietary recommendations might help Mrs. Hernandez get the nutrients that she needs during her hospitalization? And why should fluids be encouraged?

1. Patients with emphysema are more commonly underweight, appearing thin and often cachectic (nutritionally depleted). Emphysema produces a catabolic state that usually results in weight loss and mild hypoxemia. Nutritional depletion is evidenced by low body weight or body mass index (BMI) and a reduced triceps skinfold thickness measurement. Lean body mass may be decreased, although weight may be stable. BMI alone may not be indicative of a patient's nutritional status, and body composition measurement is preferred in this population to detect alterations in body compartments. Body composition can help differentiate lean body mass from adipose tissue and overhydration from dehydration because changes in hydration status can hide actual body wasting. In patients who retain fluids, it is important to carefully assess physical findings, anthropometric measurements, and biochemical measurements, and fluid status.

The main goals of medical nutrition therapy are to promote the achievement and maintenance of a healthy weight and to prevent muscle loss.

2. Several factors may impede food intake for patients with emphysema. Respiratory distress may interfere with chewing and swallowing. Appetite may also be affected by medications, depression or anxiety, or changes in taste perception. Physical changes in the diaphragm and lungs may reduce abdominal volume, creating early satiety. Some patients, because of their disability, may be unable to shop for food or prepare food without adequate support.

3. Because of her underweight status, Mrs. Hernandez may benefit from a high-calorie, high-protein diet with liquid supplements offered between meals. More frequent, small meals may be of benefit, since the lower energy content of small meals reduces the carbon dioxide load and abdominal discomfort, and dyspnea may be decreased when less food is consumed. Adequate fluids should be encouraged to help prevent the secretion of overly thick mucus. It may also be easier for some patients to drink fluid between meals in order not to interfere with their food intake.

When PEM is due to inadequate nutrient intake or excessive loss, the body responds by decreasing its metabolic rate, ventilatory drive, thyroid function, and adrenergic activity.[4,38,40] As calorie intake decreases, energy for metabolic processes is initially supplied by converting liver glycogen stores into glucose (***gluconeogenesis***). However, liver reserves of glycogen are adequate for less than 1 day at rest and only a few hours during exercise.[18] Thereafter, endogenous fat stores are mobilized in the form of free fatty acids (*ketogenesis*). When fat stores are depleted, nutrient needs must be met by catabolizing skeletal muscle protein. This type of PEM usually manifests as a gradual wasting process, as seen in patients with chronic diseases such as cancer and emphysema. The primary clinical sign is progressive weight loss.

When PEM results from increased nutrient demand, metabolism, thyroid function, and adrenergic activity all increase. Visceral protein levels tend to decrease early in the course of illness and are associated with impaired immunity.[37,38] This type of PEM typically occurs with acute catabolic disease, such as in sepsis, burns, or trauma. The two types of PEM are often referred to as *marasmus* and *kwashiorkor*,[13,18,22,40] as previously described (see Table 23.1).

Micronutrient Malnutrition

The same problems causing PEM can produce deficiencies in micronutrients. Deficiencies of nutrients that are stored only in small amounts (e.g., water-soluble vitamins) or lost through external secretions (e.g., zinc in diarrhea, fluid or burn exudate) are quite common.[18,22] Although the causes and results of micronutrient deficiencies are beyond the scope of this chapter, a few of the most common problems are described.

Signs of scurvy (vitamin C deficiency) may be observed in chronically ill patients and patients with alcoholism hospitalized for acute illnesses. Low folic acid blood levels are common whenever illness, alcoholism, or poverty is present. Alcoholism is also associated with thiamine deficiency. Zinc deficiencies impair immunity, clotting, and slow wound healing. Magnesium deficiencies can result in cardiovascular, neurologic, and electrolyte abnormalities (hypocalcemia, hypokalemia) and decreased respiratory muscle strength. Hypophosphatemia is seen frequently with cachexia or alcoholism, especially in patients receiving intravenous glucose or taking antacids. Severe hypophosphatemia can result in decreased muscle strength and contractility and acute cardiopulmonary failure.[4]

Respiratory Consequences of Malnutrition

Malnutrition affects all organ systems. In addition, malnutrition seems to interact with disease processes to increase the morbidity and mortality of respiratory, cardiac, and renal failure.[40,41] Specific effects of malnutrition on the respiratory system are listed in Box 23.9.[4,41]

Approximately one-third of all patients with acute respiratory failure have malnutrition. In these patients, the underlying diseases (e.g., sepsis, burns, trauma) increase energy expenditure and promote skeletal muscle catabolism. These patients are prone to hypercapnia and can be difficult to liberate from mechanical ventilation. Malnourished patients who require mechanical ventilation also have higher mortality rates than patients with normal nutrition status.[4,14,40]

Malnutrition also plays a role in COPD. The combined effect of increased energy expenditure (because of high work of breathing) and inadequate caloric intake contributes to a marasmus-type malnutrition. The resulting progressive muscle weakness

BOX 23.9 Respiratory Consequences of Malnutrition

Respiratory Muscle Dysfunction
- Loss of diaphragmatic mass and contractility
- Loss of accessory muscle mass and contractility

Effect on Control of Ventilation
- Decreased hypoxic and hypercapnic response

Increased Incidence of Respiratory Infections
- Decreased lung clearance mechanisms
- Decreased secretory immunoglobulin A
- Increased bacterial colonization

Changes in Lung Parenchymal Structure
- Unopposed enzymatic digestion
- Reduced production of surfactant

BOX 23.10 Underlying Causes of Malnutrition in Patients With Chronic Obstructive Pulmonary Disease

Increased Energy Expenditure
- Increased caloric cost of breathing
- Increased systemic inflammation
- Thermogenic effect of medications (e.g., bronchodilators)

Inadequate Caloric Intake
- Dyspnea while eating
- Chewing and swallowing difficulties
- Early satiety
- Taste alterations from medications, nasal cannulas, or a tracheostomy
- Suppressed appetite from medications (e.g., theophylline)

Psychosocial Factors
- Depression
- Poverty
- Difficulty shopping
- Tire easily when preparing food

BOX 23.11 Nutrition Status Changes Observable by Respiratory Therapists

- Mechanics of breathing can be affected by cachexia, obesity, pregnancy
- Increased coughing effort may indicate poor nutrition
- Viscosity of sputum, jugular venous pressure, ascites, and edema suggest fluid imbalance
- Lung crackles relate to fluid overload or oncotic pressure changes (loss of blood protein)
- Wheezing may be associated with food intolerances, alcohol, or aspirated food particles
- Late inspiratory crackles of atelectasis may result from decreased surfactant production from malnutrition
- S3 heart sounds of congestive heart failure may indicate fluid imbalance
- S4 heart sounds may be associated with severe anemia
- Pulmonary function measures may be related to:
  - FVC or FEV_1 decrease: Severe malnutrition
  - FVC: Excess fat weight
  - PEP and PIP decrease: Poor nutrition
  - Lung compliance: Fluid and serum albumin changes acutely or chronic malnutrition
- Arterial blood gas values may be related to:
  - $PaCO_2$ increases: Excess glucose, inadequate ventilation from lack of muscle energy
  - O_2 saturation, O_2 content, hemoglobin: Nutrition status
- Meal acceptance may be related to visible equipment—suction bottles, sputum specimens
- Lack of O_2 may increase difficulty of eating—ensure availability of O_2 via cannula if needed

FEV_1, Forced expiratory volume in 1 second; *FVC,* forced vital capacity; *PEP,* positive expiratory pressure; *PIP,* peak inspiratory pressure.

and dyspnea can limit caloric intake further, as can several profound psychosocial factors. Box 23.10 summarizes factors contributing to malnutrition in patients with COPD.[4,42] The RT may notice signs that could lead to malnutrition in patients for whom they provide care (Box 23.11).

Providing the Appropriate Combination of Substrates

After estimating energy requirements, the physician or registered dietitian determines the appropriate combination of macronutrients (protein, carbohydrate, fat) needed.

Protein

Amino acids or proteins are essential to maintaining or restoring lean body mass. Because illness usually increases protein catabolism and protein requirements, the Recommended Dietary Allowance (RDA) of 0.8 g/kg/day is generally insufficient for sick patients. Based on the assessment of the protein catabolism rate, protein intake may need to be doubled or tripled above the RDA (1.5 to 2.5 g/kg/day).[43] Ideally, approximately 20% of a patient's estimated caloric needs should be provided by protein. Higher percentages of protein may be needed in patients who are cachexic, have severe infections, or are otherwise critically ill. However, whenever high protein intake is administered, the patient should be monitored for progressive **azotemia** (blood urea nitrogen >100 mg/dL).[18,40]

Too much protein is harmful, especially for patients with limited pulmonary reserves. Excess protein can increase O_2 consumption, REE, minute ventilation, and central ventilatory drive.[43] In addition, overzealous protein feeding may lead to symptoms such as dyspnea.

Carbohydrate

Carbohydrates are the main source of fuel for the body. Adequate amounts of carbohydrates and fat help prevent protein catabolism. Glucose (dextrose) is the most commonly administered intravenous carbohydrate. Total calories per day from carbohydrates can range from 45% to 65%. In an average-sized patient, daily glucose provision is generally estimated at 200 g/day.[44]

For patients with pulmonary disease or patients requiring mechanical ventilation, high carbohydrate loads were initially blamed for increased CO_2 production and the RQ, resulting in increased ventilatory demand, O_2 consumption, and work of breathing.[45] More recent evidence indicates that this problem is

probably more closely related to total calorie load (overfeeding) than to the proportion of carbohydrate in the diet.[46,47] Therefore, overfeeding should be carefully avoided in patients with pulmonary disease and patients requiring mechanical ventilation.

Fat

The remaining calories (20% to 30%) should be provided from fat.[26,48,49] A minimum of 2% to 4% is needed to prevent essential fatty acid deficiency. Fat intakes greater than 50% of energy needs are associated with fever, impaired immune function, liver dysfunction, and hypotension.[16,18]

The initiation of nutrition support is determined by the patient's nutrition status, and the estimated length of time the patient will be unable to consume a diet by mouth to meet nutrition needs. To ensure satisfactory nutrition and metabolic response, early enteral nutrition begun within 24 to 48 hours provides significant benefits to critically ill patients, including reduced infectious complications and lengths of stay.[49]

RULE OF THUMB Begin enteral nutrition within 24 to 48 hours of intubation. Because nutrition is so important, nutritionally depleted or catabolic patients should never go without nutritional support for more than a day. To prevent alveolar collapse, surfactant is needed to lessen the surface-active forces that promote collapse of the lung. Malnutrition leads to decreased surfactant synthesis, as well as emphysematous changes in the lung. Humidity and mucociliary performance in the lung require adequate hydration. Smooth muscle function, macrophage activity, and secretion of immunoglobulins into mucus all depend on adequate administration of nutrients.[4,40,49]

ROUTES OF ADMINISTRATION

The two primary routes for supplying nutrients to patients are *enteral* (oral and tube feeding) and ***parenteral*** (peripheral or central venous alimentation). Box 23.12 provides guidelines for initiating nutrition support as recommended by the American Society for Parenteral and Enteral Nutrition.[48-50]

Enteral Feeding

Enteral feedings are the route of choice: "If the gut works, use it." The enteral route is safer and cheaper than the parenteral route. Enteral feeding stimulates gut hormones, exposes nutrients to the absorptive and metabolic controls of the intestinal tract and liver, and produces less hyperglycemia (providing for better immune function) than the parenteral route. In addition, the buffering capacity of enteral feeding can improve resistance against stress ulcers.[50] Finally, enteral feeding maintains a more normal intestinal mucosa than the parenteral route (the intestinal mucosa may undergo atrophy during parenteral nutrition [PN]).[15,49]

Enteral Tube Routes

There are six primary routes for enteral tube feeding: (1) nasogastric, (2) nasoduodenal, (3) nasojejunal, (4) gastrostomy, (5) jejunostomy, and (6) esophagostomy. Site selection depends on GI function, respiratory status, surgical state, and anticipated length of time the patient will be receiving tube feeding.

BOX 23.12 Guidelines for Initiation of Nutrition Support

Clinical Settings in Which Enteral Nutrition Should Be Part of Routine Care

- Protein-calorie malnutrition (>10% loss of usual weight) with inadequate oral intake of nutrients for previous 5 to 7 days
- Normal nutritional status with less than 50% of required nutrient intake orally for previous 7 to 10 days
- Severe dysphagia
- Moderate to severe pancreatitis (bowel rest anticipated beyond 5 to 7 days)
- Burns of greater than 15% total BSA in infants and children and greater than 25% total BSA in older children and adults
- Massive small bowel resection in combination with administration of total parenteral nutrition
- Low output (<500 mL/day) enterocutaneous fistulas

Clinical Settings in Which Parenteral Nutrition Should Be Part of Routine Care

- Patients with inability to absorb nutrients by the GI tract
- Severe malnutrition in the face of a nonfunctional GI tract (within 1 to 3 days)
- Severely catabolic patients with or without malnutrition when the GI tract is not usable within 7 to 10 days

BSA, Body surface area; *GI,* gastrointestinal.
From Mueller CM, Merritt RJ, McClave S, et al, editors: The ASPEN Adult Nutrition Support Core Curriculum, ed 2, Silver Spring, MD, 2012, American Society for Parenteral and Enteral Nutrition.

Gastric feedings are indicated if there are no physiologic factors affecting GI function (e.g., gastroparesis, delayed gastric emptying, or obstruction or upper GI tract surgery). Small bowel (duodenum and jejunum) feedings are indicated if the upper GI tract cannot be used. Intestinal feeding tube placement is recommended to minimize aspiration risk because it is believed to decrease the risk for gastric distention and gastroesophageal reflux; however, this remains controversial.[51]

Nasogastric and *nasoenteric* tubes are indicated for short-term enteral therapy (<30 days). The tubes are placed at the bedside and generally have a large internal diameter, which helps deliver viscous feedings and medications. *Nasoduodenal* and *nasojejunal* tubes are placed through the nose past the pylorus.

Long-term feeding tubes can be placed endoscopically and surgically. Percutaneous endoscopic placement of a feeding tube can be done to establish gastric (percutaneous endoscopic gastrostomy) or intestinal (percutaneous endoscopic jejunostomy) access. This method is preferred to surgical placement because of reduced costs associated with operating room time and the need for anesthesia.[52] Surgical laparotomy is indicated if endoscopy is contraindicated.

Tube Feeding Administration

There are three basic methods of tube feeding administration: bolus, intermittent, and continuous drip. *Bolus* feedings involve the rapid infusion of 250 to 500 mL of feeding several times daily. Feedings are provided by a syringe into the feeding tube port. There is an increased risk for aspiration associated with bolus feedings because of the rapid infusion of formula into the

TABLE 23.4 Enteral Product Reference Guide

Category	Indications	Examples
Oral supplements	Given with an oral diet to increase calorie and protein intake	Boost,[a] Ensure,[b] Carnation Breakfast Essentials
Standard/Polymeric	Made with intact nutrients. May vary in concentration (1.0–2.0 kcal/mL) and fiber content	Osmolite,[b] Jevity,[b] Promotel HN,[b] Nutren,[b] Isosource,[b] Fibersource,[a] Replete[a]
Blenderized	Made from natural foods and usually lower in sucrose and corn syrup than other formulas; beneficial if intolerance to synthetic formulas exists	Compleat,[a] Compleat Pediatric[a]
Elemental and semielemental	Impaired gastrointestinal function with impaired ability to digest or absorb intact nutrients	Peptamen,[b] Peptamen 1.5,[b] Tolerex,[b] Vivonex,[b] Vital,[a] Vital 1.5,[a] Vital HN[a]
Disease specific	Liver disease; renal disease; pulmonary disease; glucose intolerance; immune-enhancing; critically ill obese	Nutrihep[a]; Nepro,[a] NovaSource Renal,[b] Suplena,[a] Renalcal[b]; Pulmocare,[a] Oxepa,[a] Nutren Pulmonary[b]; Diabetisource AC,[b] Glucerna,[a] Glytrol[b]; Impact,[b] Pivot[a]; Peptamen Bariatric[b] Vital High Protein[a]
Modular	Need to modify a single nutrient (carbohydrate, protein, fat)	Beneprotein,[a] Benecalorie,[b] Promod,[a] Glutasolve,[b] Arginaid,[b] MCT oil[b]

[a]Nestle Health Sciences.
[b]Abbott Nutrition.

stomach. Nausea, vomiting, abdominal pain, and distension can develop in conjunction with this feeding route. This feeding method can be used only with gastric tubes and is primarily applied to patients who are stable and patients receiving enteral nutrition support at home.

Intermittent feedings are also administered several times per day and infused over at least 30 minutes. Feedings can be given only into the gastric cavity. Intermittent feedings are associated with the same problems as bolus feedings.

Continuous drip infusion provides a constant, steady flow of formula at a predetermined rate for a set period, generally 12 to 24 hours per day. Drip regulators roll clamps or pumps are used to control rates. Because the small bowel lacks storage capacity, feedings delivered beyond the pylorus must be provided by the continuous drip method. This method is preferred for critically ill patients because it is associated with reductions in gastric residual volume, abdominal distention, gastroesophageal reflux, and pulmonary aspiration.[53]

Trophic feeding is the practice of feeding minimal amounts (10 to 30 mL/h) of enteral nutrition with the primary goal to maintain GI function and integrity. Studies in mechanically ventilated patients with respiratory failure or ARDS show that trophic feedings resulted in fewer episodes of GI intolerance but resulted in similar clinical outcomes compared to early advancement to full enteral feedings.[54]

Enteral Formula Selection

Selection of an enteral formula depends on the patient's medical and surgical state, GI function, energy and nutrient needs, and route of administration. There are eight broad categories of enteral formulas: oral supplements, blenderized, whole-protein lactose-free, fiber containing, nutrient-dense, elemental, disease-specific, and modular. Table 23.4 describes the indications for the various enteral formulas and lists examples of commercial preparations.

Complications of Enteral Therapy

Complications associated with enteral nutrition are categorized as GI, mechanical, or metabolic. These may be avoided by careful selection of formulas, proper administration, and consistent patient monitoring.

Pulmonary aspiration is of significant concern in a critically ill patient with respiratory disease. Aspiration can occur because of one or more of the following factors: if the patient is lying flat, has a depressed gag reflux or vocal cord dysfunction, has delayed gastric emptying, or has improper tube placement. The incidence of pulmonary aspiration varies depending on the patient population and technique used to identify aspiration in the tube-fed patient. The three following practices have been proven to minimize aspiration risk[49]: (1) raise the head of the bed at least 30 degrees, (2) use of bowel motility agents such as metoclopramide, and (3) use post pyloric feeding with the continuous drip method in patients at risk for gastric atony or gastroesophageal reflux. Tube placement always should be verified by x-ray examination before feeding. Pulmonary aspiration has not been proved to be a result of high gastric residual volumes.[55]

Aggressive suctioning of oropharyngeal secretions can help prevent aspiration. The greatest risk is in patients with endotracheal tubes. Endotracheal tubes increase aspiration risk because they alter sensation, impair glottic closure, increase secretion volume, and act as "wicks" to allow secretions to enter the airway.[56] The use of special endotracheal tubes that provide continuous, low-level suctioning of subglottic secretions reduce the micro aspiration common in tube-fed patients.[41] The use of blue dye to detect aspiration is no longer a standard practice because of numerous problems, including a US Food and Drug Administration Public Health Advisory issued in 2003. Blue discoloration of body parts and fluids followed by refractory hypotension, metabolic acidosis, and death were reported in some patients receiving blue food dye.[42]

The routes of nutritional administration can be either enteral or parenteral. The preferred route is enteral. If a patient is intubated and cannot take food by mouth, enteral tube feeding is instituted. The last resort, when all other attempts at feeding are unsuccessful or not recommended, is **parenteral nutrition (PN)**. PN is the feeding of patients by direct infusion of nutrients into either a peripheral or a central vein. There is a reluctance to feed

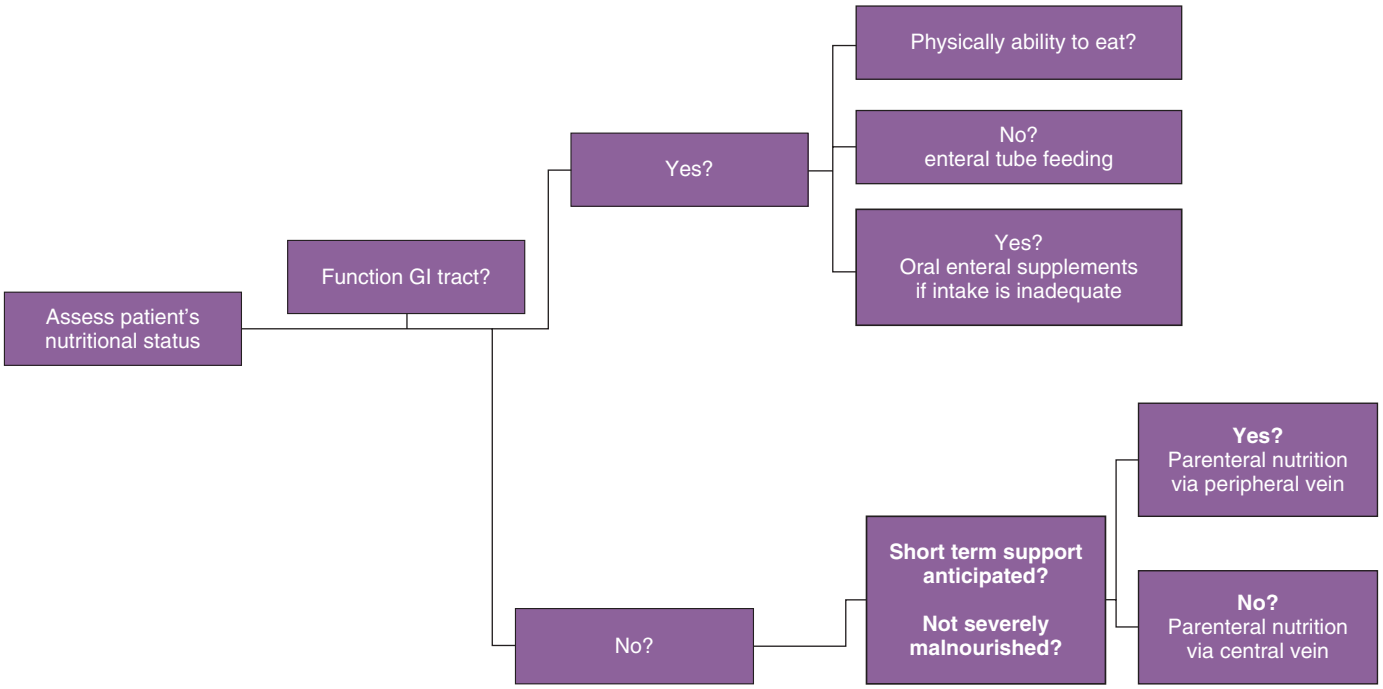

Fig. 23.4 Nutrition support decision tree.

patients by PN because it is not as efficient as the enteral route, it is expensive, and there are increased risks for complications such as infection. Fig. 23.4 outlines the nutrition support decision tree that the RT may use to assess and understand the most appropriate mode of nutrition intervention.

Parenteral Nutrition Support

When it is impossible to provide nutrition support through the GI tract, intravenous or PN support may be needed. PN support is administered through a peripheral or central vein. Ideally, the vascular access line should be restricted to nutrition use and maintained as a sterile route. Because the volume and concentration of nutrients given through a small vein are limited, peripheral PN is considered only for short-term support. Mechanical, infectious, and metabolic complications have been reported in patients fed parenterally.[57]

NUTRITION SUPPORT IN SPECIFIC CIRCUMSTANCES

Details on the appropriate nutrition support provided to the various types of patients seen by RTs are beyond the scope of this chapter. This section emphasizes key points related to nutrition support and management of the most common conditions encountered by practitioners.

General Guidelines for Critically Ill Patients

The general goal of nutrition support in critically ill patients is to provide the energy and protein necessary to meet metabolic demands and to preserve lean body mass. Nutritional support is also an important therapy in critical illness because it attenuates the metabolic response to stress, prevents oxidative cellular injury, and modulates the immune response. Nutritional modulation of the stress response includes early enteral nutrition, appropriate macronutrient and micronutrient delivery, and meticulous glycemic control.[54]

Table 23.5 outlines the general guidelines recommended to achieve these goals.[48,49]

Systemic Inflammatory Response Syndrome

The *systemic inflammatory response syndrome (SIRS)* underlies many critical illnesses, including *sepsis* and *acute respiratory distress syndrome (ARDS)*. Metabolism in systemic inflammatory response syndrome is characterized by increased total caloric requirements, hyperglycemia, triglyceride intolerance, increased net protein catabolism, and increased macronutrient and micronutrient requirements.[40]

Micronutrient requirements also are increased in SIRS. Because of the potential high losses of potassium, zinc, magnesium, calcium, and phosphorus, serum levels of these minerals need to be closely monitored and maintained within the normal range.[40]

Mechanical Ventilation

Adequate nutrition support is crucial for ventilator-dependent patients. During acute illness, proper nutrition helps prevent the loss of lean body mass. After the resolution of the acute phase of illness, good nutrition helps the muscles regain strength and improves the likelihood of successful liberation from mechanical ventilation.[22]

For most patients requiring ventilatory support, following the guidelines provided in Table 23.5 is generally sufficient. As always, care must be taken to avoid overfeeding and the increased ventilatory demands that follow. Patients with COPD present a special situation, in terms of both nutrition needs and ventilatory support. More details regarding these patients are provided in the next section.

TABLE 23.5 General Nutrition Guidelines for Chronically Critically Ill Patients

Category	Guideline
Route of delivery	Enteral nutrition is preferred when the gut is functional Start 24–48 h after resuscitation If gut is not functional, consider starting parenteral nutrition If enteral nutrition cannot provide goal within 7–10 days, consider starting parenteral nutrition
Energy need	Indirect calorimetry should be used when available for estimation of energy goal Target is 65% of goal within the first week Hypocaloric feeding recommended for obese (11–14 kcal/kg)
Protein	Provide supplemental protein to achieve 1.2–2.0 g/kg/day; 2.0–2.5 g/kg/day for obese
Glycemic control	An intensive insulin therapy protocol should be in place Goal: 110–150 mg/dL
Micronutrients	Adequate vitamins and minerals such as vitamins A, B_6, C, E; potassium; magnesium; zinc; iron; selenium; phosphate
Fluid	Approximately 1 mL/kcal
Specialized nutrients	Glutamine (may improve nitrogen stores), arginine (may improve immune system in surgical patients), and omega-3 fatty acids (may reduce inflammatory processes in ARDS/ALI)

ALI, Acute lung injury; *ARDS,* acute respiratory distress syndrome.
Data from Critical Illness Evidence-Based Nutrition Practice Guideline. Academy of Nutrition and Dietetics Evidence Analysis Library. Academy of Nutrition and Dietetics; 2012. Available at: www.andevidencelibrary.com. Accessed May 16, 2018 and Rousing ML, Hahn-Pedersen MH, Andreassen S, et al: Energy expenditure in critically ill patients estimated by population-based equations, indirect calorimetry and CO_2-based indirect calorimetry, *Annals of Intensive Care* 6:16, 2016.

MINI CLINI

Nutrition Support

Mrs. Reid is a 46-year-old woman who was diagnosed with Crohn disease 2 years ago. She was recently admitted to the hospital with an exacerbation of her Crohn disease—acute respiratory failure due to tracheobronchial involvement. She was severely malnourished and was found to have complete bowel obstruction with multiple adhesions. She is 5′4″ tall and weighs 108 pounds, with a usual weight of 122 lbs. She is scheduled for surgery and undergoes a small bowel resection to remove the diseased bowel and create a temporary ileostomy. Following surgery, she remains ventilator dependent, and a central line catheter placed to initiate total parenteral nutrition (TPN) with intralipids.

Discussion

1. Discuss Mrs. Reid's percent of weight loss and why was the patient started on TPN rather than enteral feedings or peripheral parenteral nutrition (PPN)?
2. Why is it important for the parenteral feedings to be initiated at a slowly administered infusion rate with close monitoring of the patient's electrolyte levels?

1. Using this simple calculation, you can assess that the patient has lost 11.4% of her usual body weight, which places her at significant risk for complications of malnutrition.

$$\text{Percent weight loss} = \frac{\text{usual weight} - \text{actual weight}}{\text{usual weight}} \times 100$$
$$= 122 - 108 \times 100 = 11.4\%$$

This patient cannot be given enteral feedings because her GI tract cannot be used at this time, due to exacerbation of Crohn disease, and her nutritional needs are too great for PPN. The healthcare team will need to work together to prevent complications related to TPN by using aseptic techniques when inserting the catheters or when changing tubing or a dressing that covers the catheter site; observe for unusual bleeding, wet dressings, and signs of infection (such as redness or swelling, around the catheter site), and unexplained fever. Routine inspections of equipment and monitoring of patient's symptoms will help to minimize the complications of catheter use.

Patients who are severely malnourished and who are fed too quickly may develop refeeding syndrome, which is characterized by fluid imbalances and hyperglycemia and in this case, worsening respiratory failure.

Nutrition support alone is insufficient to ensure liberation from mechanical ventilation of ventilator-dependent patients. For these patients, appropriate nutrition may need to be combined with a tailored exercise program designed to strengthen and retrain muscles.

Chronic Obstructive Pulmonary Disease

Malnutrition is common in patients with COPD and can occur in 30% to 60% of inpatients and 10% to 45% of outpatients.[58] Progressive weight loss from malnutrition is common in patients with COPD and appears to have two causes: (1) prolonged periods of insufficient caloric intake, coupled with (2) increased nutritional needs resulting from increased metabolism demand associated with chronic disease. Both malnutrition and low body weight seem to be factors associated with a poor prognosis.[59]

The degree of weight loss generally correlates with deterioration of pulmonary function values. COPD can create a cycle in which respiratory dysfunction promotes weight loss and weight loss further hinders respiratory function.[41] Fig. 23.5 illustrates the cycle.

Factors contributing to poor intake include fatigue, shortness of breath, frequent coughing, early fullness because of pressure on the abdominal cavity, increased dyspnea during eating, side effects from medications (nausea, vomiting, diarrhea, dry mouth, taste changes), and depression. The increased metabolic rate is due to the added effort to breathe and frequent respiratory infections, both of which increase calorie and fluid needs.

The goal is to increase nutrient intake carefully without overfeeding. Cachexic patients with COPD should be refed cautiously.[53] Functional capacity and the patient's overall health status may improve with an anabolic stimulus, such as exercise, along with nutrition supplementation.[60]

In patients with COPD, satisfactory conventional macronutrient allocations are 15% to 20% as protein, 50% to 60% as carbohydrates, and 20% to 30% as fat. Specialized nutrition formulation consisting of high fat and reduced carbohydrates have been marketed for patients with COPD; however, there is little evidence to support its use.[58,61] As previously stated, setting an appropriate total calorie load is more important than fine-tuning the ratio of carbohydrates to fat.

Given the positive link between dietary intake and knowledge of diet and health, effective patient education is crucial. Patients

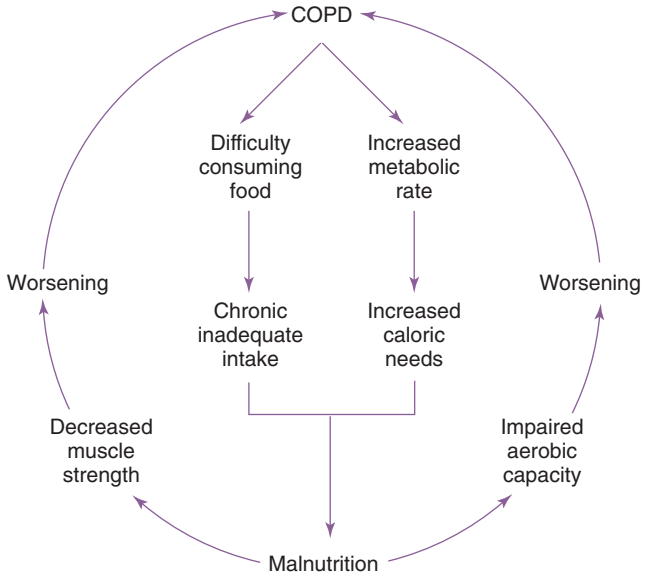

Fig. 23.5 The vicious cycle of respiratory impairment and malnutrition in chronic obstructive pulmonary disease *(COPD)*.

BOX 23.13 Nutrition Support for Patients With Pulmonary Disease

- Perform a complete nutrition assessment.
- Evaluate energy needs and provide an appropriate amount (do not overfeed or underfeed).
- Ensure protein balance.
- Monitor fluids and electrolytes, especially phosphorus.
- Evaluate vitamin and mineral status as indicated.

should be taught to select easy-to-consume, calorically dense foods. Emphasis should be placed on small, frequent feedings, and encourage use of high-calorie, high-protein nutrition supplements. Other considerations in providing nutrition support to patients with COPD are listed in Box 23.13.[60,62-64]

When patients with COPD are hospitalized for ventilatory failure, the clinical outcome is affected by nutrition support. Patients who receive adequate nutrition support are more readily weaned from mechanical ventilation than patients with diets deficient in protein and energy.

Asthma

Because breathing and eating are mutually exclusive, feeding should generally be avoided during severe asthma attacks. However, nutrient-dense, small meals high in quality protein, calories, vitamins, and minerals are recommended during prolonged, mild asthma attacks. Foods identified as allergens (most often milk, eggs, seafood, and fish) should be avoided. Fluid intake should be generous, unless contraindicated. Saturated fats may aggravate the airway, whereas omega-3 fatty acids may be beneficial; these are available in walnuts and flaxseed if the patient is allergic to fish.[62]

Cystic Fibrosis

Exocrine gland dysfunction associated with cystic fibrosis causes chronic lung disease with recurrent infections. The same disturbance causes pancreatic insufficiency. Metabolic problems in patients with cystic fibrosis are similar to metabolic problems in patients with COPD, with reduced intake and increased metabolic needs. However, the associated pancreatic insufficiency with cystic fibrosis also causes malabsorption of all nutrients, especially fat. The administration of pancreatic enzyme supplements with meals enhances absorption but requires trial and error and intense education on how to balance the amount of food and the intake of enzymes. In addition, the time spent in various treatment programs reduces the ability to consume small frequent feedings.

The three goals of nutrition management in cystic fibrosis are to (1) maximize nutrition intake through calorically dense foods, (2) balance intake with pancreatic enzymes to maximize absorption, and (3) provide a nutrition plan that meets the patient's changing clinical and psychosocial status.[63] Use of calorically dense foods and nutrition supplements consumed throughout the day has proved helpful in achieving weight gain.[63] Because of the malabsorption of micronutrients, vitamin and mineral supplementation is encouraged, especially of fat-soluble vitamins.[63] Helping patients with cystic fibrosis achieve optimal nutritional health may minimize the decline in pulmonary function and improve their quality of life.[4,14,65]

RULE OF THUMB Patients with cystic fibrosis tend to have a deficiency of enzymes produced in the pancreas and need for the digestion of fats. As a result, most patients with cystic fibrosis need to take digestive enzyme supplements to minimize the likelihood of a certain type of malnutrition.

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Methods to Increase Nutrient Intake in Chronic Obstructive Pulmonary Disease

Problem

An 82-year-old woman with known history of COPD has been hospitalized for several days and treated with multiple inhalers and nebulizers. She lost 12 pounds in the last month. She presents with muscle wasting, sparse hair, dry and cracked lips and skin. She reports decrease in oral intake because of shortness of breath and decreased appetite satiety. The dietitian receives a nutrition consult to evaluate the patient's nutrition status and provides nutrition counseling to prevent further weight loss.

Discussion

List sample foods and potential strategies the dietitian reviewed with the patient that the RT can reinforce with the patient.

- Dried fruits, nuts, popsicles, milkshakes
- Whole milk or skim milk powder added to milk, soup, gravies
- Nutrition supplements
- Puddings, custards, yogurt, ice cream
- Cream soups
- Add butter or oil or cheese to vegetables, soups, mashed potatoes, and rice
- Casseroles and egg dishes with sauces and gravies
- Peanut butter or other nut butters, spread on bananas, celery, crackers, apple slices, breads

SUMMARY CHECKLIST

- Nutrition assessment is the basis for developing a nutrition care plan.
- The components of a nutrition assessment include dietary history, anthropometry, biochemical indicators, nutrition-focused physical assessment, and client history.
- BMI is a comparison of weight to height used to determine underweight, healthy weight, overweight, obesity, or morbid obesity.
- Classifications of undernutrition, called *protein-energy malnutrition*, include kwashiorkor, marasmus, and a combination of the two (lack of circulating protein, starvation, and a mixture of the two).
- Laboratory values of albumin, transferrin, transthyretin, and retinal-binding protein may indicate malnutrition. C Reactive Protein may be elevated during acute illness, indicating an inflammatory response and causing low values of serum proteins.
- The Creatinine-Height Index reflects skeletal muscle mass.
- Nitrogen balance compares protein intake to nitrogen excretion in the urine.
- Observable signs in hair, eyes, lips, mouth and gums, skin, and nails may indicate malnutrition.
- REE may be determined by the predictive equations or indirect calorimetry.
- Estimation of total caloric need involves multiplying the REE by a factor that accounts for activity and stressors.
- Indirect calorimetry involves measurement of whole-body $\dot{V}O_2$, $\dot{V}CO_2$, and RQ; results are used to assess a patient's metabolic state, determine nutrition needs, or assess response to nutrition therapy.
- An RQ value greater than 1.00 indicates overfeeding and the need to decrease total calories; RQ between the ranges of 0.67 to 1.3 should be used as an indicator of test validity.
- Malnutrition is a state of impaired metabolism in which the intake of essential nutrients is less than the body's needs; marasmus is malnutrition associated with inadequate nutrient intake (starvation), and kwashiorkor is the hypercatabolic form.
- Malnutrition can affect the respiratory system by causing loss of respiratory muscle mass and contractility, decreased ventilatory drive, impaired immune response, and alterations in lung parenchymal structure.
- Approximately one-third of all patients with acute respiratory failure have malnutrition, mainly the hypercatabolic form; these patients are prone to hypercapnia, can be difficult to liberate from ventilatory support, and have higher mortality rates than patients with a normal nutrition status.
- In chronic lung disease, the combined effect of increased energy expenditure (due to increased work of breathing) and inadequate caloric intake contributes to a marasmus-type malnutrition.
- The primary goal of nutrition support is to maintain or restore lean body (skeletal muscle) mass by: (1) meeting the overall energy needs of the patient, and (2) providing the appropriate combination of macronutrients (protein, carbohydrate, and fat) and micronutrients (vitamins and minerals). Nutrition support also attenuates the metabolic response to stress, prevents oxidative cellular injury, and modulates the immune response.
- For most patients, a balance of 20% of daily calorie needs from protein, 50% to 60% from simple carbohydrate, and 20% to 30% from fat is adequate.
- Nutrients can be supplied enterally (oral and tube feeding) or parenterally (peripheral or central venous alimentation); the enteral route should be used whenever possible.
- The likelihood of aspiration during tube feedings can be minimized by raising the head of the bed at least 30 degrees, use of motility agents, and delivering the feeding beyond the pylorus using the continuous drip method.
- Nutrition support should be individualized according to patient needs and condition or disease process; accepted guidelines for the systemic inflammatory response syndrome (SIRS), COPD, mechanical ventilation, asthma, and cystic fibrosis should be followed.

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24

Pulmonary Infections

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CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- State the frequency and economic impact of pneumonia in the United States
- Discuss the current classification scheme for pneumonia and define hospital-acquired pneumonia, ventilator-associated pneumonia, and ventilator-associated events
- Recognize the pathophysiology and common causes of lower respiratory tract infections in specific clinical settings
- List the common microbiologic organisms responsible for community-acquired and nosocomial pneumonias
- Describe the clinical and radiographic findings seen in patients with pneumonia
- Describe risk factors associated with increased morbidity and mortality in patients with pneumonia
- Understand what a Gram stain is and what it can reveal about the potential cause of a patient's pneumonia
- State the criteria used to identify an adequate sputum sample for Gram stain and culture
- Describe the techniques used to identify the organism responsible for nosocomial pneumonia
- List the latest recommendations regarding empiric and pathogen-specific antibiotic regimens used to treat various types of pneumonia and the role of inhaled antibiotics in the treatment of these conditions
- Discuss strategies to prevent pneumonia
- Describe how the respiratory therapist aids in diagnosing and managing patients with suspected pneumonia

CHAPTER OUTLINE

KEY TERMS

antibiotic therapy
atypical pathogens
community-acquired pneumonia
fomites
hospital-acquired pneumonia
Hospital Readmission Reduction Program (HRRP)
lower respiratory tract infection
nosocomial pneumonia
pneumonia
tuberculosis
ventilator-associated events
ventilator-associated pneumonia

Infection involving the lungs is termed **pneumonia** or **lower respiratory tract infection** (LRTI) and is a common clinical problem in respiratory care practice. Today, pneumonia remains a major cause of morbidity and mortality in the United States and worldwide. Each year, 5 million people die from pneumonia worldwide. Five million cases of pneumonia occur annually in the United States, and 1.1 million require hospitalization.[1] Pneumonia is the eighth leading cause of death in the United States and the leading cause of infection-related mortality.[2]

In addition, pneumonia is one of six conditions for which hospitals may be penalized for excessive short-term (30-day) readmissions under the **Hospital Readmission Reduction Program (HRRP)** of the US Centers for Medicare and Medicaid Services (CMS). As a result, an understanding of the classification, pathogenesis, clinical manifestations, and treatment of pneumonia is important to clinicians and health care organizations to help design and implement an effective care plan for these patients.

CLASSIFICATION

Pneumonia can be classified based on the clinical setting in which it occurs (Table 24.1). This classification is useful because it predicts the likely organism and guides empiric antimicrobial therapy while a definitive microbiologic diagnosis is being awaited. The term *empiric therapy* refers to treatment that is started based on the most likely pathogen when the specific organism responsible is still unknown.

Community-acquired pneumonia (CAP) can be divided into two types—acute and chronic—based on its clinical presentation. *Acute* pneumonia presents suddenly over a few hours to several days. *Chronic* pneumonia develops more gradually, with worsening symptoms over days, weeks, or months.

Pneumonia acquired in health care settings is often caused by different microorganisms from those that cause CAP. Previously termed **nosocomial pneumonia**, this clinical entity has been further classified as **hospital-acquired pneumonia** (HAP) and **ventilator-associated pneumonia** (VAP). The 2016 Infectious Disease Society of America (IDSA)/American Thoracic Society (ATS) guidelines define HAP as a LRTI that develops more than 48 hours after admission and does not appear to be incubating at the time of admission. VAP is defined as a LRTI that develops more than 48 to 72 hours after endotracheal intubation.[3] Older guidelines included the category of health care–associated pneumonia (HCAP) to identify patients thought to be at risk for multidrug-resistant (MDR) pathogens coming from the community setting; HCAP was defined as pneumonia occurring in any patient hospitalized for 2 or more days in the previous 90 days in an acute care setting or who in the previous 30 days had resided in a long-term-care or nursing facility; attended a hospital or hemodialysis clinic; or received intravenous antibiotics, chemotherapy, or wound care.[4] This entity was not included in the updated guidelines because there is increasing evidence that many patients with HCAP are not truly at high risk for MDR pathogens and treating them for such does not improve outcomes.[5-7]

HAP and VAP are frequent complications of clinical care. Together, they are the most common hospital-acquired infections in the United States, accounting for 22% of all such infections.[8] Approximately 10% of patients requiring ventilation develop VAP,[9] which has an attributable mortality of 13%.[10] In two studies, VAP prolonged the length of mechanical ventilation by 7.6 to 11.5 days and prolonged hospitalization by 11.5 to 13.1 days,[11,12] with an average incremental per-patient cost of $40,000.[12] In selected populations, such as patients in the intensive care unit (ICU) and bone marrow transplant recipients, the crude mortality rate from HAP may approach 30% to 70%, with an attributable mortality of 33% to 50%. Certain microorganisms, such as *Pseudomonas aeruginosa* and *Acinetobacter* species, are associated with higher rates of mortality.[13]

TABLE 24.1 Classification and Possible Causes of Pneumonia

Classification	Likely Organisms
Community-Acquired: Acute	
Typical	*Streptococcus pneumoniae*
	Haemophilus influenzae
	Moraxella catarrhalis
	Staphylococcus aureus
Atypical	*Legionella pneumophila*
	Chlamydophila pneumoniae
	Mycoplasma pneumoniae
	Coxiella burnetii
	Respiratory viruses
Community-acquired: Chronic	*Mycobacterium tuberculosis*
	Histoplasma capsulatum
	Blastomycosis dermatitidis
	Coccidioides immitis
Immunocompromised host	*Pneumocystis jirovecii*
	Cytomegalovirus
	Aspergillus species
	Cryptococcus neoformans
	Reactivation tuberculosis or histoplasmosis
Nosocomial	
Aspiration	Mixed aerobes and anaerobes, gram-negative bacilli
Hospital-acquired	Mixed aerobic and anaerobic mouth flora
	S. aureus
	Enteric gram-negative bacilli
	Influenza and other respiratory viruses
	Mycobacterium tuberculosis
Ventilator-associated	*Pseudomonas aeruginosa*
	Acinetobacter species
	Enterobacter species
	Klebsiella species
	Stenotrophomonas maltophilia
	S. aureus

PATHOGENESIS

Six mechanisms may contribute to the development of pneumonia (Table 24.2). Knowledge of these mechanisms is important to both the understanding of the various disease processes and

TABLE 24.2 Pathogenesis of Pneumonia

Mechanism of Disease	Examples of Specific Infections
Inhalation of aerosolized infectious particles	Tuberculosis Histoplasmosis Cryptococcosis Blastomycosis Coccidioidomycosis Q fever Legionellosis
Aspiration of organisms colonizing the oropharynx	Community-acquired bacterial pneumonia Aspiration pneumonia Hospital-acquired pneumonia Ventilator-associated pneumonia
Direct inoculation of organisms into the lower airway	Hospital-acquired pneumonia Ventilator-associated pneumonia
Spread of infection to the lungs from adjacent structures	Mixed anaerobic and aerobic pneumonia from subdiaphragmatic abscess Amebic pneumonia from rupture of amebic liver abscess into the lung
Spread of infection to the lung through the blood	*Staphylococcus aureus* pneumonia arising from right-sided bacterial endocarditis Parasitic pneumonia: strongyloidiasis, ascariasis, hookworm
Reactivation of latent infection, usually in the setting of immunosuppression	*Pneumocystis jiroveci* pneumonia Reactivation tuberculosis Cytomegalovirus

MINI CLINI

The Gram Stain: What It Is and What It Reveals

Problem

A 32-year-old male, an unrestrained driver in motor vehicle accident, sustained head trauma leading to an intracerebral hemorrhage requiring surgical evacuation. He has been mechanically ventilated in the ICU for 7 days. He now develops fever, increasing respiratory secretions, and a new right-lower-lobe infiltrate on chest x-ray. A tracheal aspirate is sent for Gram stain, and culture. The stain yields moderate gram-negative rods (GNR) and many white blood cells (WBCs); culture is pending.

Discussion

Gram staining of clinical specimens helps to guide empiric clinical management of bacterial infections while definitive culture data are being awaited. The technique differentiates between various types of bacteria based on the biochemical properties of their cell walls. A clinical specimen is prepared by heat fixation, staining with crystal violet (purple) dye, decolorization, and counterstaining with safranin (pink) dye. Gram-positive bacteria (e.g., staphylococci and streptococci) retain crystal violet and appear purple with staining; gram-negative bacteria (e.g., *Pseudomonas aeruginosa, Acinetobacter baumanii*) do not retain crystal violet but take up safranin counterstain and thus appear pink. Visualization of the bacteria allows for characterization of their morphology ("cocci" [round] or "rods") and arrangement ("chains" or "clusters") as well as semiquantification of the number of organisms present. Based on gram-stain results, clinicians can make an educated guess regarding likely pathogens and select antibiotics accordingly.

RULE OF THUMB Prevent VAP using the following "VAP bundle"[14]:

- Use noninvasive positive-pressure ventilation when possible.
- Minimize sedation and interrupt it daily.
- Assess readiness to extubate daily.
- Perform spontaneous breathing trials with sedation turned off.
- Facilitate early mobility.
- Utilize endotracheal tubes with subglottic secretion drainage ports for patients expected to require more than 48 to 72 h of mechanical ventilation.
- Change the ventilator circuit only if it is visibly soiled or malfunctioning.
- Elevate the head of the bed to 30 or 45 degrees.

the formulation of effective strategies to minimize nosocomial spread.

Inhalation of infectious particles is a common route of inoculation; this is how pulmonary tuberculosis is acquired and it justifies the policy of respiratory isolation for patients with suspected or proved tuberculosis who are coughing.

Aspiration of oropharyngeal secretions is the second mechanism that may contribute to the development of LRTI. Healthy individuals may aspirate periodically, especially during sleep. Aspiration of even a small volume of oropharyngeal secretions, which can be colonized with potential pathogens such as *Streptococcus pneumoniae* and *Haemophilus influenzae,* may contribute to development of CAP. Certain patient populations are at risk for large-volume aspiration, such as those with impaired gag reflexes from narcotic use, alcohol intoxication, or prior stroke. Aspiration may also occur after a seizure, cardiac arrest, or syncope. Aspiration seems to be the major mechanism responsible for the development of some types of mixed aerobic and anaerobic, gram-negative, and staphylococcal HAPs. In intubated patients, chronic aspiration of colonized secretions through a tracheal cuff has been linked to the subsequent occurrence of pneumonia.

The Society for Healthcare Epidemiology of America (SHEA) and IDSA have created guideline recommendations to minimize risk of VAP,[14] which many institutions have incorporated into a "VAP bundle"; many of these recommendations aim to minimize ventilation duration and risk of aspiration.

Direct inoculation of microorganisms into the lower airway is a less common cause of pneumonia. In mechanically ventilated patients who undergo frequent suctioning of lower airway secretions, passage of a suction catheter through the endotracheal tube can dislodge biofilm and result in inoculation of colonizing organisms into the airways, leading to the development of VAP.

Direct spread of microorganisms to the lungs or pleural space from adjacent areas of infection, such as a liver abscess beneath the diaphragm, is an infrequent cause of pneumonia. This may occur in patients with amebic liver abscesses when rupture of the abscess through the diaphragm leads to the development of pulmonary infection or empyema.

Hematogenous dissemination is the spread of infection through the bloodstream from a remote site; it is an uncommon cause of pneumonia. It may occur in the setting of right-sided bacterial endocarditis, in which fragments of an infected heart valve break off and spread through the pulmonary arteries to the lungs, producing either pneumonia or septic pulmonary infarcts (areas

of dead lung tissue). Certain parasitic pneumonias—including strongyloidiasis, ascariasis, and hookworm—arise through hematogenous dissemination. In such cases, migrating parasitic larvae travel to the lungs through the bloodstream from remote sites of infection, such as the skin or the gastrointestinal (GI) tract.

Pneumonia may develop when a latent infection, acquired earlier in life, is reactivated. This may occur for no apparent reason, as is often the case for reactivation pulmonary tuberculosis. However, reactivation frequently occurs in the setting of a decrease in immune function, as is the case with *Pneumocystis jiroveci* (previously called *Pneumocystis carinii*) pneumonia. In developed countries, most healthy individuals have acquired *P. jiroveci* by age 3 years and show evidence of prior infection on blood tests. The organism remains dormant in the lung but may reactivate later in life and produce pneumonia in individuals with decreased cell-mediated immunity, such as those with HIV infection or patients receiving immunosuppressive therapy such as chemotherapy or high-dose steroids.

MICROBIOLOGY

The microbiology of CAP and HAP/VAP has been studied extensively. Knowledge of which organisms are most commonly associated with pneumonia in different settings is essential, as it guides the diagnostic evaluation and the selection of empiric antimicrobial therapy.

Historically, bacteria that cause CAP have been divided into two groups "typical" and "atypical" pathogens (see Table 24.1). Typical organisms include *Streptococcus pneumoniae, Haemophilus influenzae, Staphylococcus aureus*, *Streptococcus* species, *Moraxella catarrhalis,* and both anaerobic and aerobic gram-negative bacteria. **Atypical pathogens** include *Legionell*a species, *Mycoplasma pneumoniae, Chlamydophila pneumoniae*, and *Chlamydophila psittaci.* Historically, these pathogens were often not identified in clinical practice because—with exception of *Legionella* species—there were no widely available specific, rapid, or standardized tests to detect them. However, as molecular diagnostic techniques such as polymerase chain reaction (PCR) assays have become more widespread, these organisms are detected more frequently. Unfortunately, historical, physical examination, and laboratory findings have not proven helpful in distinguishing between infections due to typical versus atypical pathogens.

In most studies, *S. pneumoniae,* also called the pneumococcus, is the most commonly identified cause of CAP. In the preantibiotic era, this pathogen was responsible for more than 75% of cases[15,16]; however, more recent studies have isolated this organism in only 5% to 15% of cases in the United States.[17,18] This observed decline in likely related to a decrease in cigarette smoking as well as the pneumococcal vaccination of both children and adults, leading to "herd immunity."[19-22] Similarly, there has been a dramatic decrease in the incidence of *H. influenzae* pneumonia since the introduction of the type B *H. influenzae* (also known as *Hib*) vaccine in the 1980s.[23] In addition, there has been increasing recognition that respiratory viruses are common causes of CAP, either alone or as a coinfection with bacteria. With the introduction of molecular methods, respiratory viruses are detected in approximately one-third of cases of CAP in adults.[17,24-26] Atypical bacteria, primarily *Legionella* species and *M. pneumoniae*, account for 3% to 15% of patients with CAP requiring hospitalization.[17,24]

RULE OF THUMB *S. pneumoniae* is the most common cause of CAP.

Severity of illness and site of care also inform the microbiology of CAP. Among patients treated in the outpatient and non-ICU inpatient setting, *S. pneumoniae, M. pneumoniae,* and respiratory viruses are most common.[27,28] However, among patients ill enough to require ICU admission, *Legionella* species, gram-negative bacilli, *S. aureus*, and the pneumococcus are disproportionately more common.[17,24,29] Mixed aerobic and anaerobic aspiration pneumonia may account for 10% of cases. This cause of pneumonia should be considered for nursing home residents and for individuals with impaired gag reflexes or recent loss of consciousness.

Occasionally outbreaks of less common pathogens occur, both locally and globally; when this happens, these pathogens must be considered among patients presenting with CAP. For instance, atypical pneumonias due to endemic fungi such as *Histoplasma capsulatum* (central river valleys), *Blastomyces dermatiditis* (upper Midwest), and *Coccidioides immitis* (desert Southwest) are occasionally seen in the appropriate geographic settings. *Middle East respiratory syndrome* (MERS) has arisen as a global health concern. First described in Saudi Arabia in 2012, this coronavirus is found within the Arabian Peninsula and causes a severe respiratory illness with a 30% mortality rate. The first two cases imported to the United States were confirmed in 2014, both in travelers from Saudi Arabia.[30]

In most published series, no microbiologic diagnosis is established in 50% of patients. This is due to many factors, including the following:

- Inability of many patients to produce sputum
- Acquiring a sputum specimen after antibiotics have already been started
- Failure to perform diagnostic blood test routinely in all patients
- Failure to consider, or until recently—be able to identify—certain pathogens, including respiratory viruses, many of the atypical pathogens, and anaerobes

The common microbial agents producing HAP and VAP are summarized in Table 24.1; they include gram-negative bacilli, *S. aureus, Legionella* species, and occasionally respiratory viruses such as influenza or respiratory syncytial virus. These viruses are prevalent during the winter months, when they circulate in the community and are brought into the hospital by health care workers, visitors, or patients.

The relative frequencies and susceptibilities of the nosocomial pathogens that cause HAP may vary considerably from one institution to another. Knowledge of which organisms are most common within one's own institution and community, along with their drug-sensitivity profiles, has important implications with regard to selecting the best **antibiotic therapy,** the formulation of infection control policies, the investigation of potential outbreaks, and the selection of antimicrobial agents for the hospital formulary. For example, patients who develop severe VAP in ICUs with a high prevalence of carbapenem (a class of

MINI CLINI

Distinguishing Between Different Types of Nosocomial Pneumonia

Problem

A 52-year-old man with a history of severe low back pain is admitted to the hospital with a GI bleed due to the excessive use of nonsteroidal antiinflammatory drugs (NSAIDs, e.g., ibuprofen). He had not seen a doctor in 5 years. His presenting symptoms include epigastric abdominal pain, black stools, and dizziness with standing. Admission hemoglobin is 5.2 g/dL; WBCs are is 6.2 $\times$ 10^9/L. Red blood cells (RBCs) are transfused and he undergoes upper GI endoscopy, which reveals a large bleeding duodenal ulcer. Three days into his admission, the patient develops a fever to 40.2°C, shortness of breath, and cough. Laboratory testing reveals a WBC count of 16.8 $\times$ 10^9. Chest x-ray shows a patchy infiltrate in the right lower lobe. What type of pneumonia does this patient have? How might this infection have developed?

Discussion

The patient has HAP because he did not have any evidence of pneumonia at the time of admission and developed his infection more than 48 h into his hospital stay. He may have developed pneumonia due to the inhalation of infectious particles through exposure to patients or health care providers who have come to work despite having a respiratory illness. More likely, he aspirated oropharyngeal or gastric secretions during his upper endoscopy procedure or during a vomiting episode. Empiric antimicrobial coverage should target mixed aerobic and anaerobic mouth flora, *S. aureus,* enteric gram-negative bacilli, and potentially influenza, depending on the season.

antibiotics) resistance among gram-negative organisms such as *Klebsiella pneumoniae* and *Acinetobacter baumannii* may warrant empiric antimicrobial therapy for these organisms pending culture information.

Nosocomial pathogens capable of producing HAP can be transmitted directly from one patient to another, as in the case for tuberculosis. However, transmission from health care workers (including respiratory therapists [RTs]), contaminated equipment, or **fomites** (objects capable of transmitting infection through physical contact with them) is more common, especially for gram-negative bacilli, *S. aureus,* and viruses. The RT has an important role to play in preventing the transmission and development of nosocomial pneumonia. Handwashing and appropriate contact precautions, including disinfecting stethoscopes and nondisposable diagnostic and therapeutic equipment, are very important.

CLINICAL MANIFESTATIONS

Patients with CAP typically have fever and respiratory symptoms such as cough, sputum production, pleuritic chest pain, and dyspnea. Patients may also complain of hoarseness, sore throat, headache, and diarrhea. Fever, cough, and sputum production may occur in other illnesses as well, such as acute bronchitis or exacerbations of chronic bronchitis.

The clinical presentation of CAP in elderly patients warrants special mention because it may be subtle. Older individuals with pneumonia may not have a fever or cough and may simply present with shortness of breath, confusion, worsening congestive heart failure (CHF), or failure to thrive.

TABLE 24.3 Radiographic Patterns Produced by Pathogens in Community-Acquired Pneumonia

Pattern	Pathogens
Lobar consolidation	Bacterial
Bronchopneumonia	Bacterial
Pleural effusion	Bacterial
	Inhalation anthrax
Interstitial infiltrates	Viruses
	Pneumocytis jiroveci
Cavities	Mycobacteria
	Fungi
	Nocardia species
	Staphylococcus aureus
	Gram-negative bacilli
	Polymicrobial aerobic and anaerobic lung abscess
	P. jiroveci (rare)
Mediastinal widening without infiltrates	Inhalation anthrax
Rapidly progressive multilobar	*Legionella* species
	Streptococcus pneumoniae
	Endobronchial tuberculosis

HAP and VAP often present with a new onset of fever, elevated WBCs (leukocytosis), new sputum production (if not intubated), purulent endotracheal secretions (if intubated), and a new pulmonary infiltrate. Nonintubated patients may have a recent history of vomiting, seizure, or syncope during which aspiration of oropharyngeal or gastric secretions may have occurred. The diagnosis of HAP and VAP can be extremely difficult to make in patients with preexisting abnormalities on the chest x-ray, such as CHF or acute respiratory distress syndrome (ARDS). In mechanically ventilated patients, purulent tracheobronchitis (in which the airway but not the lung parenchyma is infected) may be accompanied by fever; in these as well as in patients with preexisting abnormalities on chest x-ray, the distinction between bronchitis and pneumonia can be especially difficult.

CHEST X-RAY

In patients with a compatible clinical syndrome, the diagnosis of CAP is established by the presence of a new pulmonary infiltrate on chest x-ray. Not all healthy outpatients with suspected pneumonia require a chest x-ray, and physicians may choose not to obtain one and instead to treat empirically for CAP in individuals with mild illnesses who are at low risk for complications.

Also, a normal chest x-ray does not exclude the diagnosis of pneumonia. The chest x-ray may be normal in patients with early infection, dehydration, or *P. jiroveci* infection. The pattern of chest x-ray abnormality is not diagnostic of the causative agent, although specific radiographic findings should suggest a specific microbial differential diagnosis (Table 24.3) (see Chapter 21).

Consolidation involving an entire lobe is called *lobar consolidation* (Fig. 24.1), whereas *bronchopneumonia* refers to the presence of a patchy infiltrate surrounding one or more bronchi without opacification of an entire lobe. Both radiographic patterns

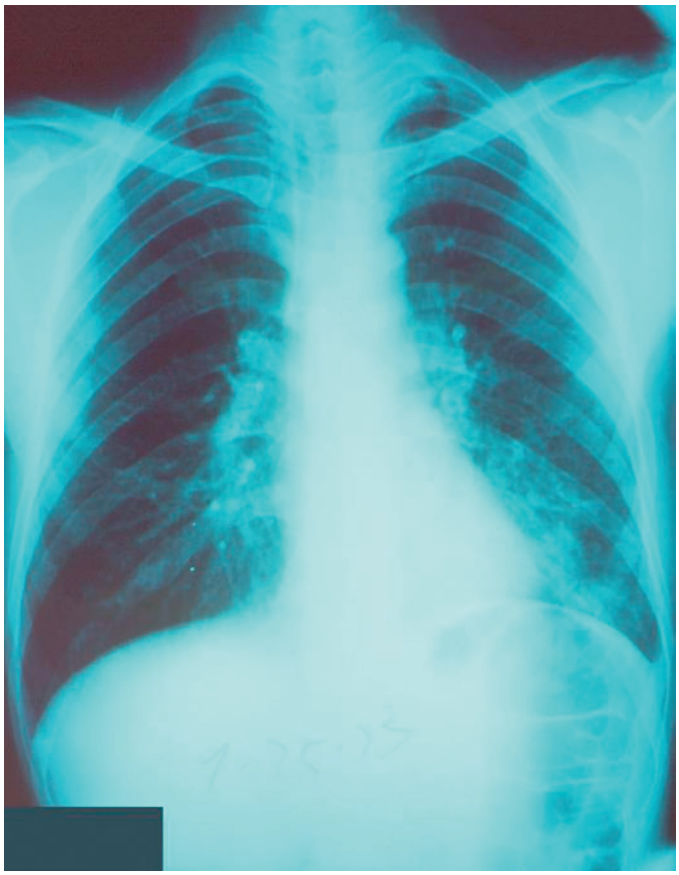

Fig. 24.1 Lobar pneumonia caused by *Streptococcus pneumoniae.* A 36-year-old previously healthy woman presents with an abrupt onset of fevers and shaking chills, cough productive of yellow sputum, and right-sided pleuritic chest pain. Chest x-ray reveals lobar consolidation. Sputum culture yields *S. pneumoniae.*

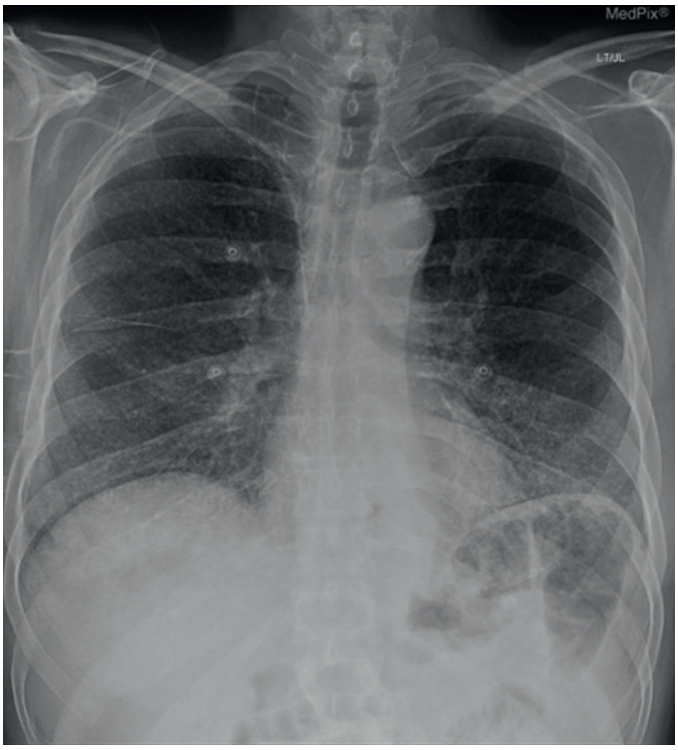

Fig. 24.2 *Pneumocystis jiroveci* pneumonia (PJP). A 23-year-old male intravenous drug user presents with a history of 2 weeks of dyspnea on exertion, nonproductive cough, and fevers to 40.4°C. The chest x-ray shows an interstitial infiltrate. HIV antibody test is positive, serum beta-D glucan level is elevated, and bronchoalveolar lavage *P. jiroveci* polymerase chain reaction is positive. The interstitial infiltrate in a "bat-wing" distribution is classic for PJP.

suggest the presence of a bacterial pathogen. Pleural effusions are common in patients with bacterial pneumonia and uncommon in patients with viral, *P. jiroveci, C. pneumoniae,* or fungal pneumonia. Pleural effusions are seen in approximately 10% of patients with *M. pneumoniae* and *Legionella* pneumonia and occur occasionally in patients with reactivation pulmonary tuberculosis. Interstitial infiltrates (Fig. 24.2), especially if diffuse, suggest viral disease, *P. jiroveci,* or miliary tuberculosis in patients with CAP. Cavitary infiltrates (Fig. 24.3) are seen in reactivation pulmonary tuberculosis; fungal pneumonias such as histoplasmosis, blastomycosis, and aspergillosis; nocardiosis; bacterial lung abscess; and, rarely, *P. jiroveci* pneumonia. Patients with severe staphylococcal or gram-negative pneumonias may develop small cavities called *pneumatoceles. Legionella* species should be considered in sicker patients with pneumonia of a single lobe, which quickly spreads to involve multiple lobes over 24 to 48 hours.

The chest x-ray may be helpful in diagnosing HAP in nonintubated patients with a suspected aspiration event and a previously normal chest x-ray. In such cases, development of a new infiltrate may confirm the clinical suspicion of aspiration pneumonia. The chest x-ray is often less helpful in the diagnosis of VAP because mechanically ventilated patients may have other reasons for radiographic abnormalities, such as ARDS, CHF, pulmonary thromboembolism, alveolar hemorrhage, or atelectasis. In these

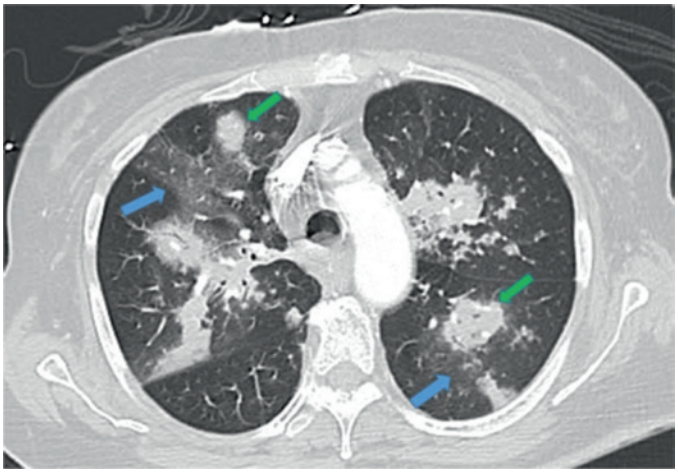

Fig. 24.3 Cavitary nodular pneumonia caused by *Aspergillus.* A 34-year-old woman undergoing induction chemotherapy for newly diagnosed acute myeloid leukemia presents with persistent neutropenic fevers and cough productive of scant he moptysis. Sputum cultures are negative, but serum galactomannan antigen is markedly elevated, highly suggestive of *Aspergillus* infection. Computed tomography reveals multicentric cavitary nodules, some of which have a halo of ground-glass opacity. These findings are classic for invasive pulmonary aspergillosis.

patients it can be difficult to confirm the diagnosis of a new nosocomial LRTI. A clinical diagnosis of pneumonia—defined as the presence of fever, purulent respiratory secretions, new leukocytosis, and a new pulmonary infiltrate—is sensitive but not specific for diagnosing VAP. Other strategies to diagnose VAP more accurately have been investigated.

RISK FACTORS FOR MORTALITY AND ASSESSING THE NEED FOR HOSPITALIZATION

An important first step in management is determining whether a patient with CAP requires admission to the hospital. Severity of illness and risk of death are the most important factors in making this decision, and much research has been devoted to identifying risk factors for poor outcomes among patients with CAP.[31-35] Risk factors predicting a high risk for death are summarized in Box 24.1. However, other factors must be also be considered, including the patient's ability to maintain oral intake, likelihood of medication adherence, history of mental illness, cognitive or functional impairment, active substance abuse, and living circumstances (e.g., homelessness or limited access to health care services should he or she worsen).

Because some variables are not known at the time a patient seeks treatment for pneumonia, such as the causative agent and whether bacteremia is present, more recent studies have evaluated the risk for death by using clinical and laboratory data that are readily available at the time of the initial evaluation. The Pneumonia Severity Index (PSI) is a clinical prediction tool that has been shown to effectively identify patients at low and high risk for death at 30 days following a CAP diagnosis.[31] The algorithm uses demographic, clinical, and laboratory data available at presentation to stratify the risk for death and the criteria for hospitalization in outpatient groups. Points are assigned for the presence of numerous variables, and cumulative point scores are used to stratify patients into one of five risk groups with predictable mortality rates (Tables 24.4 and 24.5). In this model, which has been validated in large prospective cohorts of patients, those at the lowest risk for death fall into groups I and II. In most instances, these patients may be treated successfully as outpatients unless they are hypoxemic, vomiting and unable to take oral antibiotics, noncompliant, or immunocompromised.

Due to the complexity of the PSI, many practitioners prefer a simpler stratification system, called CURB-65, whose name is derived from the following five variables:

- **C**onfusion
- **U**rea (blood urea nitrogen) greater than 20 mg/dL
- **R**espiratory rate ≥30 breaths/min
- **B**lood pressure ([BP] systolic <90 mm Hg or diastolic <60 mm Hg)
- Age **65** years or greater

Using this risk prediction model, patients with one or two risk criteria can be treated as outpatients, those with two criteria should be treated on general hospital wards, and those with three or more criteria should be admitted to the ICU.[36]

Many studies have also examined risk factors for developing HAP and VAP, which in broad terms can be divided into (1) factors that interfere with host defense and (2) factors that encourage exposure to large numbers of bacteria.[13] Examples of factors that interfere with host defense include the following:

- Underlying illnesses such as diabetes mellitus, malignancy, chronic heart and lung disease, and renal failure
- Critical illnesses such as sepsis and ARDS
- Therapeutic interventions such as endotracheal intubation, tracheostomy, and administration of medications such as sedatives and corticosteroids

Factors that promote exposure of the lung to pathogenic microorganisms include the following:

- Use of endotracheal or nasogastric tubes
- Contaminated ventilator equipment or water supplies
- Prior antibiotic therapy
- Neutralization of gastric pH

BOX 24.1 Risk Factors for Mortality in Community-Acquired Pneumonia

I. Patient variables
  A. Age above 50 years
  B. Male sex
  C. Comorbid illnesses
    1. Cerebrovascular disease
    2. Cancer
    3. Congestive heart failure
    4. Renal disease
    5. Liver disease
    6. Immunosuppression
    7. Alcoholism
    8. Diabetes mellitus
    9. Chronic lung disease
II. Clinical parameters at presentation
  A. Altered mentation
  B. Systolic hypotension <90 mm Hg
  C. Tachypnea >30 breaths/min
  D. Hypothermia (temperature <35°C)
  E. Fever (temperature >40°C)
  F. Pulse rate >125 beats/min
  G. Extrapulmonary site of infection
III. Laboratory and radiographic findings at presentation
  A. Arterial pH <7.35
  B. Blood urea nitrogen >30 mg/dL
  C. Serum sodium <130 mmol/L
  D. Glucose >250 mg/dL
  E. Hematocrit <30%
  F. Hypoxia (PaO_2 <60 mm Hg) or hypercarbia (PCO_2 >50 mm Hg) on room air
  G. White blood cell count $<4 \times 10^9$/L, $>30 \times 10^9$/L, or an absolute neutrophil count $<1 \times 10^9$
  H. Multilobar infiltrate
  I. Bacteremia
  J. Pleural effusion
  K. High-risk cause
    1. Gram-negative bacilli
    2. *Staphylococcus aureus*
    3. Postobstructive pneumonia
    4. Aspiration

From Fine MJ, Smith MA, Carson CA, et al: Prognosis and outcomes of patients with community-acquired pneumonia: a meta-analysis, *JAMA* 275:134–41, 1996.

TABLE 24.4 Pneumonia Severity Index Scoring System for Stratifying Risk of 30-Day Mortality in Adults With Community-Acquired Pneumonia

Variable	Points Assigned
Age	
Men	Age (years)
Women	Age (years) –10
Nursing home resident	+10
Comorbid illnesses	
Cancer	+30
Liver disease	+20
Kidney disease	+10
Cerebrovascular disease	+10
Congestive heart failure	+10
Physical findings	
Altered mentation	+20
Tachypnea >30 breaths/min	+20
Systolic hypotension <90 mm Hg	+20
Temperature <35°C or >40°C	+15
Heart rate >125 beats/min	+10
Laboratory and radiographic findings	
Acidemia (arterial pH <7.35)	+30
Azotemia (blood urea nitrogen >30 mg/dL)	+20
Hyponatremia (sodium <130 mmol/L)	+20
Hypoxia (PaO_2 <60 mm Hg)	+10
Hyperglycemia (glucose >250 mg/dL)	+10
Anemia (hematocrit <30%)	+10
Pleural effusion	+10

NOTE: Plus sign (+) denotes adding points; minus sign (–) denotes subtracting points (e.g., for women, points assigned equal age in years –10).
Modified from Fine MJ, Auble TE, Yealy DM, et al: A prediction rule to identify low-risk patients with community-acquired pneumonia, *N Engl J Med* 336:243–50, 1997.

TABLE 24.5 Risk Class Mortality Rates Using Pneumonia Severity Index Scoring System in Patients With Community-Acquired Pneumonia

Risk Class (Cumulative Point Score)	Mortality Rate (%)
I	0.1
II (≤70)	0.6
III (71–90)	2.8
IV (91–130)	8.2
V (>130)	29.2

NOTE: Patients in risk class I are below 50 years old and lack existing illness or physical findings listed in Table 24.4. Points are assigned to patients in risk classes II and higher.
Modified from Fine MJ, Auble TE, Yealy DM, et al: A prediction rule to identify low-risk patients with community-acquired pneumonia, *N Engl J Med* 336:243–50, 1997.

Although many studies have emphasized the substantial mortality rate (20% to 50%) for patients who develop HAP or VAP, few studies have examined the specific risk factors associated with mortality in hospital-acquired LRTI. For nonventilated patients, risk factors for mortality include bilateral infiltrates, respiratory failure, and infection with high-risk organisms.[37,38] In mechanically ventilated patients, factors associated with fatal outcome include the following[3,38,39]:

- Infection with high-risk organisms such as *P. aeruginosa*, *Acinetobacter* species, and *Stenotrophomonas maltophilia*
- Multisystem organ failure
- Nonsurgical diagnosis
- Therapy with antacids or histamine-2 (H_2)–receptor antagonists
- Transfer from another hospital or ward
- Renal failure
- Prolonged mechanical ventilation
- Coma or shock
- Inappropriate antibiotic therapy
- Hospitalization in a noncardiac ICU

MINI CLINI

Estimating Risk of Death From Pneumonia and Triaging Care

Problem

The RT is called to the emergency department to perform an arterial blood gas analysis on a 70-year-old woman with confusion and shortness of breath who is brought in by her husband. Her history is notable for diabetes mellitus, hypertension, and a recent stroke, which has resulted in left-sided weakness. The emergency physician ordered a chest x-ray, which showed a right lower lobe infiltrate and a right pleural effusion.

On physical examination, the patient is very sleepy. Her vital signs are temperature 35°C, blood pressure 85/50 mm Hg, heart rate 130 beats/min, and respiratory rate 24 breaths/min. Laboratory testing reveals the following:

- Peripheral WBCs, 3000/mm^3
- Blood urea nitrogen, 18 mg/dL
- Creatinine, 1.4 mg/dL
- Hematocrit, 31%
- Blood glucose, 262 mg/dL

The RT collects the arterial blood gas on room air, which shows a pH of 7.30; PaO_2, 58 mm Hg; and PCO_2, 25 mm Hg. Should the patient be admitted to the hospital or can she be discharged home? What risk factors does she have for death from pneumonia in the next 30 days?

Discussion

Using CURB-65 as a tool,[36] she meets 3 of the 5 criteria: confusion, low blood pressure (systolic BP <90 mm Hg, diastolic BP <60 mm Hg), and age ≥65 years. She should be admitted to the hospital and consideration should be given to placing her in the ICU. She also has many risk factors that place her at considerable risk of death (see Box 24.1), including: age greater than 50 years, cerebrovascular disease, diabetes mellitus, altered mentation, hypotension, tachycardia, acidemia, hyperglycemia, PaO_2, below 60 mm Hg, leukopenia, and a pleural effusion.

DIAGNOSTIC STUDIES

Community-Acquired Pneumonia

Many patients with CAP who are treated as outpatients never have a microbiologic diagnosis established. Many are treated based on the history and examination findings, with or without a chest x-ray to confirm the presence of an infiltrate. Patients who are sick enough to warrant hospitalization or consideration of hospitalization should undergo appropriate studies to stratify

BOX 24.2 Recommended Tests for Adults With Community-Acquired Pneumonia Warranting Consideration of Hospitalization

- Chest x-ray
- Complete blood count
- Blood chemistries
  - Glucose
  - Serum sodium
  - Blood urea nitrogen
- Arterial blood gas
- Sputum Gram stain and culture
- Additional sputum studies as clinically indicated
  - Acid-fast stain and culture for mycobacteria
  - Fungal stain and culture
  - Direct fluorescent antibody stain or polymerase chain reaction (PCR) for *Legionella* species
  - Stain, direct fluorescent antibody (DFA), or PCR for *Pneumocystis jiroveci*
- Blood cultures
- Pleural fluid analysis if sizable effusion is present
  - Cell count with differential
  - Glucose, protein, and lactate dehydrogenase
  - pH
  - Gram stain and routine aerobic and anaerobic culture
  - Fungal stain and culture
  - Acid-fast stain and culture for mycobacteria
- Additional other studies as clinically indicated
  - *Legionella* urinary antigen
  - Pneumococcal urinary antigen
  - Acute and convalescent sera for *Mycoplasma pneumoniae, Legionella* species, and *Chlamydophila pneumoniae*
  - Fungal serologies and/or antigen testing
  - HIV test for individuals 15 to 65 years old or for those engaging in high-risk behavior

risk for mortality and establish a microbiologic diagnosis (Box 24.2). Complete blood count (CBC), blood glucose, serum sodium, and blood urea nitrogen are all necessary to calculate a point score for estimating mortality risk. An arterial blood gas analysis is used to detect the presence of hypoxemia and acidemia, which indicate more serious illness.

The value of Gram stain and culture of expectorated sputum has been debated for years.[40] Many patients lack a productive cough, making collection of an adequate specimen difficult. Prior antibiotic therapy reduces the yield from both tests. However, sputum culture is positive in more than 80% of cases of pneumococcal pneumonia if a good-quality specimen can be obtained before or within 6 to 12 hours of antibiotic initiation.[41] In addition, finding of a predominant organism on Gram stain in an properly collected specimen can be very helpful in selecting appropriate antibiotic therapy.[42]

RULE OF THUMB A routine sputum culture can be interpreted only within the context of the sputum Gram stain. When many skin cells from the cheek (epithelial cells) are present or when no inflammatory cells are present in the Gram stain in patients who have adequate numbers of WBCs (i.e., are non-neutropenic), the culture result may be misleading.

TABLE 24.6 Sputum Culture Testing for Diagnosing Community-Acquired Pneumonia

Test	Suspected Pathogen
Gram stain, aerobic (routine) culture	Bacteria
Anaerobic culture	Anaerobes, *Actinomyces*
Fungal (Potassium hydroxide, Grocott) stain and culture	*Aspergillus, Histoplasma, Blastomyces, Coccidiomycosis, Cryptococcus*, etc.
Acid-fast bacilli (AFB) stain and culture	Tuberculosis and Nontuberculous Mycobacteria (NTM) species
Respiratory virus polymerase chain reaction (PCR) panel	Influenza, parainfluenza, respiratory syncytial virus, rhinovirus, adenovirus, human metapneumovirus, coronavirus
Legionella PCR	Legionella (L1 serotype and others)
Pneumocystis jiroveci PCR and direct fluorescent antibody (DFA), silver or toluidine blue stains	*P. jiroveci*

The RT has an important role in collecting an appropriate specimen of expectorated sputum. Ideally, the specimen should be obtained prior to starting antibiotics. Patients should be advised to rid their mouths of contaminating saliva by rinsing with water or spitting and then to expectorate a specimen from deep within the tracheobronchial tree into a sterile collection container. Prompt transportation of the specimen to the laboratory is essential and improves the diagnostic yield from culture.[43] Most microbiology laboratories screen the adequacy of the specimen; a satisfactory specimen contains more than 25 leukocytes and fewer than 10 squamous epithelial cells per high-power field on Gram stain.[44] In routine sputum culture, finding bacteria such as *S. pneumoniae* and *H. influenzae* must be interpreted within the context of the Gram stain because these organisms can colonize the oral cavity and their presence in culture may not signify true LRTI.

RULE OF THUMB The presence of *Candida* species on sputum smear or culture is almost never clinically significant.

Other stains and cultures of expectorated sputum should be obtained as dictated by the clinical circumstance, when management would be changed, or for purposes of tracking unusual or resistant organisms in an institution or population. Table 24.6 describes additional testing that can be sent depending on what pathogens are suspected.

Sputum induction can be a useful procedure for patients who have difficulty producing sputum spontaneously. The RT plays an equally important role in making sure that this procedure is done correctly. Patients with underlying lung disease (such as asthma or emphysema) should receive pretreatment with a fast-acting bronchodilator, such as albuterol, to prevent bronchospasm. The patient then inhales nebulized hypertonic saline, which irritates the airways and promotes the production of thin, watery mucus. The patient should then be instructed to perform huff coughs followed by a vigorous cough, which will enable the collection of any secretions that are in the airways. The

secretions may seem thin; it is important to label the sample as "induced sputum" so that it will not be discarded by the laboratory as an inadequate specimen.

RULE OF THUMB Occasionally it is very important to make a microbiologic diagnosis (e.g., of tuberculosis, *P. jiroveci*), for both treatment and infection control purposes. For patients who cannot produce sputum, induced sputum can be a valuable tool that allows patients to avoid the risks associated with bronchoscopy.

Blood cultures should be obtained in hospitalized patients with CAP and may be helpful in establishing the diagnosis in patients with typical bacterial pathogens. Blood cultures are positive in approximately 20% to 25% of inpatients with pneumococcal pneumonia but in fewer cases of pneumonia due to *H. influenzae* or *P. aeruginosa*.[45] Blood cultures are usually positive in cases of *S. aureus* pneumonia that develop by hematogenous spread; however, they are positive in only about 25% of cases where inhalation or aspiration is the suspected mechanism of acquisition.[46] Blood cultures are not helpful in patients with legionellosis, *M. pneumoniae, C. pneumoniae, P. jiroveci,* or viral infections.

Approximately 30% to 50% of cases of CAP are accompanied by a pleural effusion (so-called parapneumonic effusion). In this situation, the fluid itself is not infected but instead forms as a result of inflammation in the adjacent lung. However, empyema, or infection of the pleural space, can also complicate CAP. Thoracentesis is indicated for patients with large pleural effusions and those with smaller effusions who fail to respond to therapy or for whom the microbiologic diagnosis is not established. Pleural fluid should be tested for cell count, glucose, protein, pH, lactate dehydrogenase, gram staining and stains for acid-fast bacilli, and routine (aerobic), anaerobic, and mycobacterial cultures. Pleural effusions with a fluid pH less than 7.20, a positive Gram stain or culture, or fluid that appear grossly purulent on inspection require tube thoracostomy for drainage (see Chapter 27).[47]

Other studies may be helpful in establishing a microbiologic diagnosis in the appropriate clinical setting. *L. pneumophila* serogroup 1 accounts for 70% to 80% of cases of Legionnaire's disease.[48] The urinary antigen test for *L. pneumophila* serogroup 1 is a sensitive and rapid test and usually becomes positive within 3 days of illness onset. *Legionella* PCR testing is also available and highly sensitive; it has the advantage of detecting non–serogroup 1 *Legionella* species.

Serologic tests for immunoglobulin M (IgM) and IgG antibodies to *M. pneumoniae, Legionella* species, or *C. pneumoniae* are rarely helpful during the initial stages of pneumonia, but convalescent titers (i.e., drawn after recovery) 3 to 4 weeks later may permit a retrospective microbiologic diagnosis by showing a fourfold increase in IgG titer or the development of IgM antibody against a specific pathogen. Acute sera should be analyzed in patients who are critically ill with pneumonia and for whom the microbiologic diagnosis is unavailable. Fungal serologic findings are occasionally helpful in supporting the diagnosis of blastomycosis, histoplasmosis, or coccidioidomycosis pending culture isolation of the organism.

Fungal antigen assays are increasingly being used in settings where there is a high clinical suspicion for invasive fungal infection. Invasive aspergillosis is an important cause of pneumonia in immunocompromised hosts, particularly in those with prolonged neutropenia. Galactomannan is a polysaccharide that is a major constituent of *Aspergillus* cell walls. Galactomannan antigen testing is 71% sensitive and 89% specific for *Aspergillus* infection.[49] Similarly, 1,3-β-D-glucan is a cell wall component of many fungi, and levels of this molecule are elevated in many types of invasive fungal infection, including those with *Aspergillus, P. jirovecii*, *H. capsulatum*, and *C. immitis*. β-D glucan assays have a sensitivity of 77% and specificity of 85% for invasive fungal infection.[50] Both of these assays, however, have limitations.[50]

HIV testing should be performed in patients presenting with CAP, since infection with certain pathogens—such as *S. pneumoniae, H. influenzae,* and *P. jiroveci*—occur more often in patients with HIV infection, particularly in those with advanced disease, than in the average population.[51-53] In addition, nearly 15% of patients with HIV are unaware of their diagnosis, so every encounter with health care should be considered an opportunity to identify this population.[54]

Molecular techniques, such as DNA probes and PCR, are increasingly being used in clinical practice. These tests are highly sensitive and can be performed quickly, with a turnaround time of 2 to 3 hours in large hospital laboratories. Such testing allows for a rapid diagnosis, which has important implications for management decisions. Assays for specific organisms such as *M. pneumoniae* or *M. tuberculosis* have been developed. In addition, the generation of respiratory viral PCR panels has allowed for simultaneous testing for multiple viral pathogens, such as influenza, parainfluenza, and respiratory syncytial virus. These assays can be performed on both nasopharyngeal swabs and bronchoalveolar lavage (BAL) fluid, depending on the clinical circumstance.

Flexible bronchoscopy is usually reserved for severe cases of CAP, for immunocompromised individuals in whom opportunistic pathogens must be excluded, or for cases in which *P. jirovecii* infection is suspected. The yield from flexible bronchoscopy in patients with bacterial pneumonia is higher if it is performed before starting antibiotic therapy. Open lung biopsy is rarely indicated for patients with CAP.

Hospital-Acquired Pneumonia, Ventilator-Associated Pneumonia, and Ventilator-Associated Events

In an effort to better monitor and hopefully reduce ventilator-associated complications including VAPs, the Centers for Disease Control (CDC) Healthcare Safety Network implemented a **ventilator-associated events** (VAE) surveillance program in 2013. Its three-tier surveillance definition uses objective, readily available data to identify complications.[56] See Box 24.3 for definitions. These criteria were formulated for purposes of surveillance and quality improvement at the population level and not to aid clinically in diagnosis and treatment decisions. In the future, they may be utilized to inform reimbursement decisions. Interestingly, one study found that less than one-third of VAPs are identified

MINI CLINI

Importance of Clinical Setting for Determining the Cause of Pneumonia

Problem

You are caring for a 32-year-old man admitted to the hospital 24 h earlier with fever, shaking chills, and a new left-lower-lobe infiltrate. His WBCs on admission were 3500/mm^3, with 96% neutrophils and 4% lymphocytes. A sputum Gram stain showed many polymorphonuclear leukocytes and lancet-shaped gram-positive diplococci. Blood cultures have grown *S. pneumoniae* at 24 h. He remained febrile 24 h into therapy with penicillin G. While checking pulse oximetry, the RT notes that the patient is emaciated and that there are multiple needle tracks on each forearm. The patient admits that he uses intravenous heroin. What other tests are indicated?

Discussion

This patient, who is an intravenous drug user, has bacteremic pneumococcal pneumonia. These findings, along with the presence of cachexia and leukopenia with lymphopenia, should suggest the possibility of underlying HIV infection. An HIV test is indicated and should be performed after the patient's consent is obtained.

Both pneumococcal and *H. influenzae* pneumonia occur with higher frequency in HIV-infected individuals than in the general population. Occasionally an HIV-infected patient has his or her first contact with the health care system as a result of one of these infections. New guidelines recommend that all average-risk individuals ages 15 to 65 undergo testing for HIV once in their lives and persons at higher risk for HIV infection undergo more frequent testing.[55]

by the VAE criteria and that most VAPs are nonpreventable events,[57] suggesting that these definitions may not be useful tools in the clinical arena.

RULE OF THUMB The CDC's VAE definitions were designed to aid in surveillance and quality improvement and should not be used to guide patient management.

The accurate diagnosis of nosocomial pneumonia is challenging and has been the subject of intense investigation. Many techniques have been extensively evaluated (Box 24.4); however, none is perfect. The 2016 IDSA/ATS guidelines for the management of HAP and VAP recommend a *clinical diagnosis*, which is defined as the following: development of a new infiltrate on chest x-ray and decline in oxygenation in the setting of fever, purulent sputum, and leukocytosis in a hospitalized patient.[3] A clinical diagnosis lacks specificity because many other causes of pulmonary infiltrates exist in hospitalized patients, especially in patients on mechanical ventilation. In addition, hospitalized patients' airways can become colonized with gram-negative bacilli and staphylococci even in the absence of pneumonia. For this reason, the isolation of these organisms from sputum culture correlates poorly with the presence or absence of pneumonia.

Direct visualization of the lower airway by bronchoscopy in ventilated patients is sometimes helpful to support the diagnosis of VAP. In one study, the presence of distal purulent secretions, persistence of secretions surging from distal bronchi during exhalation, and a decrease in the PaO_2/FiO_2 ratio to less than 50 were independently associated with the presence of pneumonia.

BOX 24.3 Centers for Disease Control Definitions of Ventilator-Associated Events

Ventilator-associated condition (VAC)—Period of sustained respiratory deterioration, defined as a change in positive end-expiratory pressure (PEEP) ≥3 cm H_2O *or* FiO_2 ≥0.2 for 2 days following a sustained period of stability or improvement on the ventilator for 2 days or more.

Infection-related ventilator-associated complication (IVAC)—VAC accompanied by abnormal temperature (<36°C or >38°C) or white blood cell count (≤4000 or ≥12,000/mm^3) requiring initiation of new antibiotics that are continued for at least 4 days.

Possible and probable ventilator-associated pneumonia (VAP)—IVAC with laboratory and/or microbiologic evidence of respiratory infection.

- Possible VAP—Gram stain evidence of purulent pulmonary secretions or a sputum culture positive for pulmonary pathogen in a patient with IVAC
- Probable VAP
  - Purulent respiratory secretions *and* one of the following:
    - Positive culture of endotracheal aspirate ≥ 10^5 CFU/mL or equivalent semiquantitative result
    - Positive culture of bronchoalveolar lavage ≥ 10^4 CFU/mL or equivalent semiquantitative result
    - Positive culture of lung tissue ≥ 10^4 CFU/mL or equivalent semiquantitative result
    - Positive culture of protected specimen brush ≥ 10^3CFU/mL or equivalent semiquantitative result
  - OR one of the following (without requirement for purulent respiratory secretions):
    - Positive pleural fluid culture (specimen obtained during thoracentesis or initial placement of chest tube, not from indwelling chest tube)
    - Positive lung histopathology
    - Positive diagnostic test for *Legionella* species
    - Positive diagnostic test on respiratory secretions for influenza, respiratory syncytial virus, adenovirus, parainfluenza, rhinovirus, human metapneumovirus, or coronavirus

Modified from Centers for Disease Control and Prevention: Surveillance for Ventilator-associated Events, <http://www.cdc.gov/nhsn/acute-care-hospital/vae/>, Accessed June 2018.

BOX 24.4 Techniques for Diagnosing Nosocomial Pneumonia

- Clinical diagnosis
- Direct visualization of the airway by bronchoscopy
- Quantitative or semiquantitative cultures of
  - Endotracheal aspirates
  - Protected specimen brush (PSB) bronchoscopy specimens
  - Bronchoalveolar lavage (BAL) specimens
  - PSB or BAL specimens plus microscopic examination of recovered cells (cytology)
- Respiratory therapist (RT)–directed mini-BAL
- Transthoracic fine-needle aspiration

The presence of two of three of these factors had a sensitivity of 78% in diagnosing nosocomial pneumonia; these factors were absent 89% of the time when there was no pneumonia (89% specific).[58]

Quantitative and semiquantitative cultures of sputum cultures are often utilized to try to increase the specificity of culture results. Different studies have used various breakpoints for

quantitative cultures, ranging from 10^3 to 10^7 colony-forming units (CFU) per milliliter of respiratory secretions; a breakpoint of 10^6 CFU/mL appears to perform best, with a sensitivity of 68% to 82% and specificity of 84% to 96%.[59,60] When a semiquantitative approach is being used, the number of microorganism isolated is reported as rare, few, moderate, or many.

Respiratory secretions can be obtained in a number of different ways, each of which has its advantages and disadvantages. When a patient is able to expectorate sputum, a sample should be obtained noninvasively. In an intubated patient, a tracheal aspirate can also easily be obtained. Several invasive techniques are also available, though they require that the patient be intubated. BAL, in which a lung segment is lavaged with sterile saline through the bronchoscope and recovered fluid is cultured (see Chapter 22), has been studied extensively as a tool for diagnosing nosocomial pneumonia and has sensitivity of 47% to 66% and specificity of 71% to 88%.[61-64] One advantage of this approach is that the specific affected area of the lung can be visualized and sampled. However, a limitation is the potential for upper airway contamination of the specimen. A way to minimize this risk is to use a protected specimen brush (PSB), which makes use of a special double-catheter brush system; however, the sample obtained is smaller than that derived with other methods, leading to a lower sensitivity with this approach. RTs can also perform a mini-BAL (see Chapter 22), also known as a blind BAL or nonbronchoscopic BAL, in which a telescoping catheter is inserted into the lungs without visual guidance; a sample is then lavaged and sent for culture. The sensitivity and specificity of this approach is similar that of a traditional BAL.[65,66]

The 2016 IDSA/ATS VAP and HAP guidelines recommend noninvasive sampling (i.e., expectorated sputum and tracheal aspirate) with semiquantitative cultures over other methods when possible. This recommendation is based on evidence suggesting that outcomes are similar regardless of how specimens are obtained and how microbial growth is quantified. Noninvasive sampling can be completed more quickly, with fewer complications and resources. Similarly, semiquantitative cultures can be done more rapidly than quantitative cultures, with fewer laboratory resources and less expertise. Therefore these approaches are preferred.[3]

ANTIMICROBIAL THERAPY

Community-Acquired Pneumonia

The selection of antibiotic therapy for patients with CAP should be guided by several considerations, including the age of the patient, severity of the illness, presence of risk factors for specific organisms, and results of initial diagnostic studies. Pathogen-specific therapy should be used when clinical circumstances and initial evaluation strongly suggest the microbiologic diagnosis or when cultures or other studies confirm the cause. In many instances, initial studies fail to establish a diagnosis and empiric therapy must be started. Major classes of antibiotics used to treat pneumonia are listed in Table 24.7. Consensus guidelines for therapy have been published by ATS and IDSA (Table 24.8).[67] Therapy initiated within 4 hours of hospital admission has been associated with improved survival.[68]

For hospitalized patients, empiric treatment varies with the severity of illness. Patients from the regular ward who are stable

TABLE 24.7 Major Classes of Antibiotics Used in the Treatment of Pneumonia

Antibiotic Class	Representative Drugs
Penicillins	Penicillin G, ampicillin
Semisynthetic penicillins	Oxacillin, nafcillin
First-generation cephalosporins	Cefazolin
Second-generation cephalosporins	Cefuroxime
Third-generation cephalosporins	Cefotaxime, ceftriaxone, cefpodoxime
Antipseudomonal cephalosporins	Ceftazidime, cefepime
Carbapenems	Imipenem, meropenem, ertapenem
Monobactams (for penicillin and cephalosporin-allergic patients)	Aztreonam
β-lactam/β-lactamase inhibitor combinations	Ticarcillin/clavulanate, piperacillin/tazobactam, ampicillin/sulbactam
Fluoroquinolones	Levofloxacin, moxifloxacin, gemifloxacin
Macrolides	Clarithromycin, azithromycin
Tetracyclines	Doxycycline, minocycline
Aminoglycosides	Amikacin, tobramycin, gentamicin
Glycopeptides	Vancomycin
Oxazolidinones	Linezolid

TABLE 24.8 Empiric Regimens for Treatment of Hospitalized Adults With Community-Acquired Pneumonia

Patient Group	Likely Pathogens	Empiric Regimens
Hospitalized on ward	*Streptococcus pneumoniae, Haemophilus influenzae, Chlamydophila pneumoniae, Staphylococcus aureus, Mycoplasma pneumoniae,* anaerobes, viruses	Fluoroquinolone alone or β-lactam (cefotaxime, ceftriaxone, ampicillin, ertapenem) and macrolide
Critically ill, in intensive care unit (ICU)	*S. pneumoniae, Legionella* species, *S. aureus,* gram-negative bacilli, *M. pneumoniae, C. pneumoniae*	If *Pseudomonas aeruginosa* and methicillin-resistant *S. aureus* (MRSA) unlikely: beta-lactam (cefotaxime, ceftriaxone, ampicillin-sulbactam) plus either azithromycin or a fluoroquinolone If *P. aeruginosa* possible: intravenous antipseudomonal β-lactam (piperacillin-tazobactam, cefepime, imipenem, meropenem) plus fluoroquinolone or macrolide +/– aminoglycoside If MRSA possible, regimen already mentioned plus vancomycin

Modified from Mandell MA, Wunderink RG, Anzueto A, et al: Infectious Disease Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults, *Clin Infect Dis* 44:S27–S72, 2007.

TABLE 24.9 Pathogen-Specific Treatment Recommendations for Adults With Community-Acquired Pneumonia: Infectious Disease Society of America Guidelines

Pathogen	Recommended Regimen
Streptococcus pneumoniae	
Penicillin susceptible	Penicillin G or amoxicillin
Penicillin resistant	Ceftriaxone, cefotaxime, fluoroquinolone, or vancomycin
Haemophilus influenzae	Second- or third-generation cephalosporin, azithromycin, or TMP-SMX
Legionella species	Macrolide ± rifampin or fluoroquinolone alone
Mycoplasma pneumoniae	Macrolide or doxycycline
Chlamydophila pneumoniae	Macrolide or doxycycline
Staphylococcus aureus	
Methicillin susceptible	Semisynthetic penicillin ± rifampin or gentamicin
Methicillin resistant	Vancomycin or linezolid
Enterobacteriaceae	Third-generation cephalosporin ± aminoglycoside or carbapenem
Pseudomonas aeruginosa	Antipseudomonal beta lactam or carbapenem ± aminoglycoside
Influenza with suspected secondary pneumococcal or staphylococcal infection	Neuraminidase inhibitor (oseltamivir or zanamivir) and vancomycin or linezolid
Pneumocystis jiroveci	TMP-SMX (first line) Alternatives: Mild-moderate: atovaquone, clindamycin, and primaquine, or trimethoprim and dapsone Severe: intravenous pentamidine

TMP-SMX, trimethoprim-sulfamethoxazole.
Modified from Mandell MA, Wunderink RG, Anzueto A, et al: Infectious Disease Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults, *Clin Infect Dis* 44:S27–S72, 2007.

are treated differently from those ill enough to require ICU admission. See Table 24.8 for ATS/IDSA recommendations regarding empiric therapy regimens. For patients requiring ICU admission, consideration must be given to upfront empiric coverage of *Pseudomonas* and methicillin-resistant *S. aureus* (MRSA), as these pathogens often cause more serious infection.

Once a microbiologic diagnosis has been established, the antimicrobial regimen should be tailored to the isolated pathogen. Pathogen-specific treatment recommendations from the IDSA and ATS are summarized in Table 24.9. The narrowest-spectrum agent should be used whenever possible.

The duration of therapy for CAP is guided by the specific pathogen and the patient's clinical course. Recommendations have evolved from the traditional 14 days to a minimum of 5 days of therapy with clinical stability. Exceptions include Legionnaire's disease, *Pseudomonas* or *S. aureus* pneumonia, for which a minimum of 2 weeks of therapy is recommended. Older individuals and patients with comorbidities may also require longer courses of treatment. When fever has resolved and patients begin to improve clinically, oral therapy may be used to complete the

MINI CLINI

Evaluating Persistent Fever in Pneumonia

Problem

You are caring for a 68-year-old man admitted 1 week ago with bacteremic *S. pneumoniae* pneumonia. His admitting chest x-ray showed right-lower-lobe consolidation and a large right pleural effusion. He has a history of chronic obstructive pulmonary disease (COPD) and reports a 100 pack-year smoking history. He was treated initially with ceftriaxone and azithromycin until his blood cultures became positive. The organism was susceptible to penicillin, to which he was switched. Despite treatment, the patient has remained persistently febrile (39°C) and his chest x-ray has not shown improvement. Why is he not responding to therapy?

Discussion

Patients with CAP who have comorbid illnesses such as alcoholism or COPD may recover more slowly than healthy individuals despite appropriate therapy. Nevertheless, persistent fever 7 days into optimal treatment should prompt several considerations.

The two most likely concerns for this patient are (1) an undrained empyema and (2) an obstructing endobronchial malignancy, given his substantial smoking history. Other less likely considerations are drug fever; a new nosocomial infection; a missed pathogen that is not responsive to penicillin, contributing to his pneumonia; or a deep venous thrombosis resulting from bed rest.

The next step should be to repeat the history and physical examination. If these do not reveal a cause of the persistent fever, a thoracentesis should be performed to exclude empyema. If thoracentesis findings are negative, further investigation looking for an endobronchial-obstructing lesion with bronchoscopy should be considered.

treatment course. Failure of the patient's temperature to normalize within 4 or 5 days suggests a missed pathogen, a metastatic or closed-space infection (e.g., empyema), drug fever, or the presence of an obstructing endobronchial lesion. Empyema should be treated with tube thoracostomy (see Chapter 27). Abnormal findings on physical examination may persist beyond 1 week in 20% to 40% of patients despite clinical improvement. By 1 month, radiographic resolution occurs in 90% of individuals under 50 years of age.[69] After 1 month, radiographic abnormalities may persist in 70% of cases involving older individuals or in patients with significant underlying illnesses.[69]

RULE OF THUMB Empyema should be ruled out in patients with CAP and a large pleural effusion who fail to respond to therapy. Patients with CAP often get better before the chest x-ray shows any improvement.

Hospital-Acquired Pneumonia and Ventilator-Associated Pneumonia

Empiric and definitive therapy of nosocomial pneumonia is determined by institution-specific data regarding the most common organisms and their antibiotic susceptibility profiles and by patient-specific risk factors. Although general guidelines have been published,[3] the importance of local data cannot be overemphasized because there is great variation across regions and health care facilities regarding the prevalence and susceptibility profiles of specific pathogens.

Generally, in-hospital aspiration should be treated with a regimen that provides coverage against anaerobes and gram-negative bacilli, such as a beta-lactam/beta-lactamase inhibitor combination or clindamycin with a third-generation cephalosporin. If aspiration is not suspected, empiric coverage of *P. aeruginosa* and MRSA is usually recommended while additional culture data are being awaited. In critically ill patients, two agents with antipseudomonal coverage—usually an antipseudomonal beta lactam and an aminoglycoside—are used upfront due to concerns for possible drug resistance. If nosocomial legionellosis is present within an institution, a macrolide may be added to the empiric regimen. Although vancomycin has been the traditional drug of choice for MRSA pneumonia, evolving data suggest that linezolid may be better than vancomycin for this purpose. In a randomized controlled trial of vancomycin versus linezolid for treatment of MRSA pneumonia, clinical resolution of pneumonia occurred more frequently in patients treated with linezolid, but there was no difference in 60-day mortality between the two groups.[70] For VAP, empiric coverage may be targeted at organisms known to colonize the patient's oropharynx or pathogens that are present in the ICU.

As in the case of CAP, the duration of therapy for cases of nosocomial pneumonia is dictated by the clinical course. A study comparing 8 days versus 15 days of therapy in patients with VAP found comparable outcomes with both durations of therapy, although the rate of relapse was slightly higher in patients with *Pseudomonas* or *Acinetobacter* infections.[71] More prolonged courses of therapy may be required in patients who are slow to respond but are associated with a greater risk of new colonization with other organisms and the emergence of drug resistance. Failure of the patient to improve should prompt the following considerations: the presence of an occult empyema; an unrecognized pathogen; a new, unrelated nosocomial infection; or other noninfectious causes of fever common in the ICU, such as deep venous thrombosis, drug fever, occult pancreatitis, or acalculous cholecystitis (gallbladder inflammation without gallstones).

Inhaled Antibiotics

Inhaled antibiotics are sometimes used as an adjunctive therapy for patients with *P. aeruginosa* and other MDR gram-negative infections of the lower respiratory tract. The rationale for their use is maximal drug delivery to the site of infection while simultaneously limiting potential for systemic side effects. Inhaled forms of tobramycin, aztreonam, and colistin are currently approved by the US Food and Drug Administration (FDA) for use in patients with cystic fibrosis (CF), although they are often used in other settings of lower respiratory tract infections, such as non-CF bronchiectasis, VAP, COPD, mycobacterial disease, and following lung transplantation. In addition, injectable forms of gentamicin, amikacin, and ceftazidime can be nebulized "off-label" for similar indications. The 2016 ATS/IDSA HAP guidelines recommend use of both inhaled and systemic antibiotics for patients with VAP due to gram-negative bacilli that are susceptible only to aminoglycosides or colistin.[3] It must be acknowledged, however, that data to strongly support their use are lacking. Two randomized controlled trials evaluating nebulized antibiotics as an alternative or adjunctive agent to intravenous antibiotics in VAP demonstrated improved microbiologic outcomes but no impact on clinical or radiographic responses.[72,73] There are several risks associated with their use that must be considered. Bronchospasm is common and bronchodilators are often routinely administered before dosing in order to offset this side effect. Altered taste and throat irritation can also occur. Though rare, systemic absorption of inhaled agents can occur and lead to toxicity, particularly ototoxicity (hearing loss, vertigo, and ringing in the ears) and nephrotoxicity with inhaled aminoglycosides and colistin. Use of these agents also poses the risk of developing drug resistance, potentially limiting future treatment options.[74]

The RT has an important role in diagnosing and managing patients with CAP and nosocomial pneumonia. It is essential to help patients clear infected secretions and maintain adequate oxygenation. The usefulness of chest physiotherapy in the treatment of pneumonia is still unproved but some patients seem to benefit from it.

PREVENTION

Community-Acquired Pneumonia

Preventive strategies for CAP have focused on immunizing high-risk individuals against influenza and *S. pneumoniae.* Influenza is a risk factor for the subsequent development of CAP during the fall and winter months. In 2010, the Advisory Committee on Immunization Practices (ACIP) expanded its recommendation for influenza vaccination to include all individuals above 6 months of age.[75] Immunization is particularly important for individuals above 60 years (because it reduces the incidence of illness for this age group by half[76]) and for those with chronic lung or heart disease in whom the morbidity of influenza may be substantial. Studies suggest that widespread immunization of healthy working adults is cost-effective because the number of sick days taken and the number of visits to a physician are reduced.[77] Health care workers, including RTs, should be immunized annually to prevent transmission of influenza to patients.

Two pneumococcal vaccines are currently available: Pneumovax23 (which contains polysaccharides, or sugars present on the surface of the bacteria, of 23 different serotypes) and Prevnar13 (a conjugate vaccine in which the surface sugars from 13 different serotypes are linked to proteins to stimulate a stronger immune response). Vaccination is indicated for all individuals above 65 years of age and for individuals above 2 years who have functional or anatomic asplenia (i.e., lack of a spleen). Vaccination is also indicated in patients with chronic illnesses that have been associated with a higher risk of pneumococcal infection: CHF, chronic lung disease, chronic liver disease, current tobacco use, alcoholism, diabetes mellitus, cerebrospinal fluid leaks, cochlear implants, or conditions characterized by impaired immunity.[78] Routine pneumococcal vaccination of all health care workers is not currently recommended; health care workers who possess one of the specific indications for vaccination outlined previously should be immunized.

Immunity against *Bordetella pertussis* fades over time, leading to transmission from older adults to other adults and infants. In order to boost immunity among those at risk, the ACIP has recommended that the tetanus-diphtheria-acellular pertussis

TABLE 24.10 Strategies for the Prevention of Nosocomial Pneumonia

Strategy	Efficacy
Handwashing	Probably effective
Isolation of patients with resistant organisms	Probably effective
Infection control and surveillance	Probably effective
Enteral feeding rather than total parenteral nutrition	Possibly effective
Semierect position	Possibly effective
Sucralfate for bleeding prophylaxis	Possibly effective
Careful handling of respiratory therapy equipment	Possibly effective
Subglottic secretion aspiration	Possibly effective
Selective digestive decontamination	Unproved efficacy
Topical tracheobronchial antibiotics	Unproved efficacy

(Tdap) vaccine replace a tetanus-diphtheria (Td) vaccine booster in adults; these vaccinations are typically given every 10 years.[79]

Hospital-Acquired Pneumonia and Ventilator-Associated Pneumonia

The prevention of nosocomial pneumonia has been intensely studied over the past 30 years. Table 24.10 summarizes currently available strategies and their relative efficacy. No preventive strategy is uniformly effective. Many institutions now employ a "ventilator bundle" including several of these measures (see "Ventilator-Associated Pneumonia Bundle Rule of Thumb," earlier).

Handwashing is an important but frequently overlooked measure that can reduce nosocomial spread of infection. Handwashing is important even if gloves are worn; gloves should be changed between patients because they easily become contaminated with bacteria. In addition, other potential fomites such as stethoscopes, pens, and hard copy or mobile devices used for ventilator patient checks and charting medical record entry should be properly disinfected.

Infection control surveillance to detect outbreaks of nosocomial pneumonia with specific pathogens and to monitor antibiotic resistance patterns is important. Isolation and caring for infected patients in the same place can limit the scope and duration of outbreaks, especially in ICUs.

In patients requiring nutritional support, the use of enteral feeding via jejunostomy has been associated with a lower risk for nosocomial pneumonia than the use of total parenteral nutrition.[80] In addition, patients who are fed enterally (i.e., using the gut to feed) have a lower incidence of pneumonia if kept semierect rather than recumbent.[81] Interestingly, GI bleeding prophylaxis with sucralfate is associated with a lower risk for pneumonia compared with H_2-blockers or proton pump inhibitors (PPIs); the mechanism is unclear, but the drug itself may have antibacterial activity.[82,83] Careful handling of respiratory therapy equipment may reduce the risk for LRTI in ventilated patients. Condensate within the tubing may be colonized with bacteria and should be drained away from the patient because passage of this material into the airway may encourage colonization with nosocomial pathogens. Drainage of subglottic secretions may decrease the incidence of VAP but does not appear to affect mortality, length of ICU stay or mechanical ventilation, or antibiotic use.[84] Decontamination of the digestive tract with nonabsorbable antibiotics reduces the risk of HAP and VAP, but this practice is not routinely used due to the risk of prompting antimicrobial resistance.[85,86]

TUBERCULOSIS

Tuberculosis, caused by *Mycobacterium tuberculosis,* can sometimes mimic CAP and poses special management challenges for the RT. Knowledge of the epidemiology, clinical manifestations, diagnosis, infection control management, and treatment of patients with suspected or proved tuberculosis is essential.

Epidemiology

The epidemiology of tuberculosis in the United States has changed over the past 25 years. After the introduction of effective drugs to treat tuberculosis in the 1950s, the incidence of tuberculosis steadily declined. Tuberculosis increasingly became a disease affecting elderly patients, and most cases represented reactivation of old latent disease. With the emergence of the AIDS epidemic in the early 1980s, there was an increase in the incidence of tuberculosis in the United States and worldwide between 1985 and 1992. Thankfully the incidence has decreased since then. This resurgence was accompanied by dramatic shifts in the patients at risk and the clinical manifestations of the disease. MDR tuberculosis, defined as resistance to both isoniazid and rifampin, emerged as a major public health problem in some populations. Compared with the pre-AIDS era, tuberculosis now more often occurs in younger individuals with HIV infection, especially inner-city minority populations with a history of injecting drugs. Foreign-born nationals residing in the United States have accounted for half of the cases of TB reported annually in recent years.

Tuberculosis has increasingly become a disease affecting individuals of lower socioeconomic status—those in whom homelessness or crowded living conditions, poor access to health care, and unemployment have contributed to the persistence of the disease. Other risk factors include the presence of hematologic malignancies, head and neck cancer, and the receipt of medications such as corticosteroids and tumor necrosis factor α (TNF-α) antagonists.[87-89]

Pathophysiology and Clinical Manifestations

Tuberculosis is acquired by inhaling airborne droplets containing *M. tuberculosis,* and the lungs are the major site of infection. Microorganism-laden droplets are deposited in the terminal airways and cause a host immune response. Most exposed individuals successfully contain the infection and remain asymptomatic, although they remain at risk for reactivation of infection later in life, especially if they become immunosuppressed.

Patients with tuberculosis can present with pulmonary or extrapulmonary manifestations. The major syndromes of pulmonary tuberculosis include primary infection, reactivation, and endobronchial tuberculosis and tuberculoma.

Primary Tuberculosis

Symptomatic primary tuberculosis occurs in a few individuals shortly after exposure. Primary tuberculous pneumonia occurs

more often in children and HIV-infected individuals than in other populations. Fever is the most common symptom and occurs in 70% of patients; it persists for 14 to 21 days on average.[90] Chest pain and cough occur in a minority of patients. Chest x-ray shows hilar lymphadenopathy in 65%, pleural effusion in 33%, and an infiltrate in approximately 25%. Diagnosis may be difficult given the infrequency of cough and a pulmonary infiltrate.

Reactivation Tuberculosis

Reactivation tuberculosis develops months to years after initial infection and may occur spontaneously or in the setting of immunosuppression. In individuals without HIV infection, reactivation disease accounts for 90% of cases of tuberculosis. The most common symptoms include fever, cough, night sweats, and weight loss. Sputum production increases as the infection progresses and is occasionally accompanied by hemoptysis, which is seldom massive. Older patients may present with a more indolent illness in which fever and night sweats are absent. Physical examination is often unrevealing. Chest x-ray shows upper lobe disease in 80% to 90% of patients, and cavities are present in 20% to 40%.

Endobronchial Tuberculosis and Tuberculomas

Endobronchial tuberculosis involves the airways and may occur in both primary and reactivation tuberculosis. In primary tuberculosis, hilar nodal enlargement may impinge on the bronchi, resulting in compression and ultimately ulceration. In patients with reactivation disease, endobronchial involvement may occur as a result of direct extension from the parenchyma or pooling of secretions from upper lobe cavities in the dependent distal airways. Symptoms of endobronchial tuberculosis include a barking cough in two-thirds of patients, sputum production, wheezing, and hemoptysis. Exam often reveals wheezing. Chest x-ray frequently shows an upper lobe cavitary infiltrate with a lower lobe infiltrate on the same side. Extensive endobronchial disease may produce bronchiectasis.

Tuberculomas are rounded solitary mass lesions and may occur in primary or reactivation tuberculosis. They are often asymptomatic and may mimic malignancy. Tuberculoma is in the differential diagnosis of solitary pulmonary nodule and may be difficult to diagnose without biopsy or excision because expectorated sputum in patients with tuberculoma rarely shows *M. tuberculosis* on smear or culture.

Complications

Complications of pulmonary tuberculosis include tuberculous empyema, bronchiectasis, extensive pulmonary parenchymal destruction, spontaneous pneumothorax, and massive hemoptysis from rupture of a Rasmussen aneurysm in the wall of a cavity.

Extrapulmonary Tuberculosis

Extrapulmonary tuberculosis is defined as spread of *M. tuberculosis* infection beyond the lung and may involve virtually any organ. The central nervous system, musculoskeletal system, genitourinary tract, and lymph nodes (scrofula) are the most common sites of extrapulmonary tuberculosis. HIV-infected patients may develop rapidly progressive primary infection and present with both pulmonary and extrapulmonary disease. In patients with advanced AIDS, tuberculosis may manifest as disseminated disease with involvement of multiple organs, including lymph nodes, bone marrow, liver, and spleen. Symptoms in this setting include high fevers, sweats, and progressive weight loss. Findings on examination may include fever, wasting, and enlargement of the spleen and liver. Laboratory testing may show pancytopenia (decreased cell counts) and advanced immunodeficiency. Imaging studies often show mediastinal and abdominal lymphadenopathy and hepatosplenomegaly.

Diagnosis

The history is important in diagnosing and managing patients with suspected tuberculosis. In addition to asking about the patient's symptoms, the clinician should inquire about any history of tuberculosis, the presence of risk factors for acquiring tuberculosis and/or HIV infection, any history of travel, as well as potential contacts with individuals with known or suspected tuberculosis. The patient should be asked whether he or she has been previously treated, the drugs chosen, duration of treatment, and adherence to therapy. Risk factors for drug-resistant tuberculosis should be sought, which include prior treatment for tuberculosis, exposure to individuals with known drug-resistant disease or those with active tuberculosis who have been previously treated, travel to parts of the world with a high prevalence of drug resistance, or exposure to individuals with active tuberculosis from those areas.

The gold standard for diagnosing tuberculosis is culture isolation of the organism. The major disadvantage of culture is that *M. tuberculosis* may take 4 to 6 weeks to grow, thereby delaying diagnosis. Acid-fast staining of expectorated sputum, bronchoscopic specimens, and other body fluids or tissues is usually performed. In patients with pulmonary tuberculosis, it is estimated that 10^4 organisms per milliliter are required for the smear to be positive. Acid-fast smears are less sensitive than culture for detecting disease, and the presence of acid-fast bacilli on a smear does not prove the diagnosis of *M. tuberculosis* because nontuberculous mycobacteria (NTM) can produce disease in selected populations. More rapid diagnostic techniques for identifying *M. tuberculosis* in clinical specimens and for confirming the identity of the organism in culture are available in some centers. These techniques include nucleic acid amplification, nucleic acid probes, PCR genomic analysis, and molecular tests for chromosomal mutations associated with drug resistance.

A five-tuberculin-unit purified protein derivative (5 TU PPD) skin test or interferon-gamma release assay (IGRA) may be performed in individuals with suspected tuberculosis. Both tests evaluate for cell-mediated immunity to tuberculosis in individuals with prior exposure to the organism. A PPD consists of intradermal injection of tuberculin material, which stimulates a delayed-type hypersensitivity response mediated by T cells and causes skin induration within 48 to 72 hours. False-positive results can occur in patients with prior bacille Calmette-Guérin (BCG) vaccination or infection with NTM species. IGRAs are blood tests that measure T-cell release of the cytokine interferon-gamma after stimulation by antigens unique to *M. tuberculosis*. IGRAs

are unaffected by BCG vaccination status and most NTM infections (except *Mycobacterium marinum* and *Mycobacterium kansasii*) and require only a single patient encounter, all of which are advantages over the PPD.[91] Both tests become positive 3 to 8 weeks after infection. A positive skin test or IGRA supports the diagnosis in the appropriate clinical setting, but a negative result does not exclude the diagnosis. Patients with HIV infection, other causes of immunodeficiency, advanced age, or other comorbidities may be anergic and unable to mount either a positive skin test or IGRA result.[91,92]

Precautions

Patients hospitalized with suspected or proved active pulmonary tuberculosis should be placed in respiratory isolation in private negative pressure airflow rooms because they pose a risk for transmitting infection to others by coughing up aerosolized droplets containing *M. tuberculosis*. Individuals entering the patient's room should wear fit-tested National Institute for Occupational Safety and Health–approved N-95 or higher masks or respirators. A surgical mask should be placed on a patient with suspected or proven active pulmonary tuberculosis during transport outside the negative-pressure room.

RULE OF THUMB In order to minimize the risk of spread to others, patients with suspected or proven pulmonary tuberculosis should be placed on airborne isolation in negative-pressure-airflow rooms, and N-95 masks should be worn by all individuals entering the room. Patients must remain in isolation until sputum acid fast bacilli (AFB, especially *Mycobacterium* tuberculosis) smears return negative.

Treatment

Treatment recommendations for tuberculosis have been published by the ATS, the CDC, and the IDSA.[93] The goals of therapy are to cure the patient and prevent transmission of *M. tuberculosis* to others. Treatment must address clinical and social issues and should be customized to the patient's circumstance. At the outset, daily observed therapy (DOT) should be part of the treatment program; this consists of observing the patient taking the antituberculous medications. Treatment programs that use comprehensive case management and DOT have a higher rate of successful completion of therapy than other treatment strategies. Social service support, housing assistance, and treatment for substance abuse may be required for selected individuals with tuberculosis and should be part of the treatment plan. Patients with tuberculosis must be promptly reported to the local department of public health so that contact tracing can be performed. This includes identifying, if possible, the index case from whom the patient has contracted the infection and identifying close personal contacts to whom the patient may have transmitted *M. tuberculosis*.

Isoniazid, rifampin, pyrazinamide, and ethambutol are first-line antituberculous medications. Pending antimicrobial susceptibility results, treatment with four drugs is recommended. In patients with drug-susceptible pulmonary tuberculosis, many 6- to 9-month treatment regimens have been shown to be effective, as outlined in guidelines by the ATS, CDC, and IDSA.[93] Patients with MDR tuberculosis require more prolonged courses of therapy with multidrug regimens.

ROLE OF THE RESPIRATORY THERAPIST IN PULMONARY INFECTIONS

The RT plays a key role in managing patients with pulmonary infections, including helping to diagnose and treat the illnesses. Diagnostically, RTs participate in collecting sputum specimens or assisting physicians during bronchoscopy. In some settings, RTs may perform mini-BAL.

RTs often administer chest physiotherapy when indicated, as in patients with bronchiectasis and CF. They may also be involved in counseling patients in other clearance techniques, such as autogenic drainage and positive expiratory pressure (PEP) therapy. RTs also play key roles in modeling optimal infection control and prevention practices (e.g., handwashing, implementing and complying with respiratory precautions, vaccination) and in advising patients about preventive interventions, such as influenza, pneumococcal, and Tdap vaccines.

SUMMARY CHECKLIST

- CAP and nosocomial pneumonia are common and important clinical problems with significant morbidity and mortality.
- *S. pneumoniae* remains the most common cause of CAP. Gram-negative bacilli and *S. aureus* are the most common causes of nosocomial pneumonia, but their relative incidence and antimicrobial susceptibility profiles may vary across institutions.
- The mortality risk can be estimated at presentation for most patients with CAP, which helps in determining the need for hospitalization.
- Routine sputum cultures for patients with CAP must be interpreted within the context of the sputum Gram stain, which provides valuable information regarding the adequacy of the specimen and the predominance of potential pathogens.
- The accurate diagnosis of nosocomial pneumonia remains a challenge; none of the diagnostic methods currently available is completely reliable.
- The VAE surveillance program was instituted to monitor and reduce ventilator-associated complications, including VAP, but is not being used clinically at this time.
- Guidelines exist for the treatment of CAP and nosocomial pneumonia. When possible, pathogen-specific antibiotic therapy should be used.
- Inhaled antibiotics may play an adjunctive role in the treatment of pneumonia due to multidrug-resistant organisms
- Immunizing high-risk individuals against influenza and *S. pneumoniae* is the major strategy in preventing CAP.
- Strategies for preventing nosocomial pneumonia are not uniformly effective.
- Pulmonary tuberculosis may mimic CAP; the recognition and appropriate isolation, diagnostic evaluation, and management of individuals with possible pulmonary tuberculosis are essential.
- The RT can help to prevent nosocomial pneumonia by paying careful attention to basic infection control procedures such as handwashing.

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25

Obstructive Lung Disease: Chronic Obstructive Pulmonary Disease (COPD), Asthma, and Related Diseases

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CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- State definitions of chronic obstructive pulmonary disease (COPD), asthma, and bronchiectasis.
- Understand the major risk factors associated with COPD.
- Identify the common signs and symptoms associated with COPD.
- Describe a treatment plan for a patient with stable COPD and for a patient with an acute exacerbation of COPD.
- State the typical clinical presentation of a patient with asthma.
- Be able to differentiate between asthma and COPD.
- Describe a treatment plan for a patient with stable asthma and for a patient with an acute exacerbation of asthma.
- Understand the causes of bronchiectasis.
- Describe the treatment currently available for patients with bronchiectasis.

CHAPTER OUTLINE

KEY TERMS

acute exacerbation of COPD
airway hyperresponsiveness
airway inflammation
airway obstruction
alpha-1 antitrypsin deficiency
asthma
asthma-COPD overlap syndrome
bronchiectasis
bronchodilator
bronchospasm
chronic bronchitis
cystic fibrosis
emphysema
noninvasive ventilation
supplemental oxygen

The category of obstructive lung diseases is broad and includes chronic obstructive pulmonary disease (COPD) and **asthma** as the most common diseases and **bronchiectasis** and **cystic fibrosis** as less common forms. Airflow obstruction may also be a feature of other diseases such as sarcoidosis and congestive heart failure. This chapter reviews the major obstructive lung diseases, emphasizing their defining features, epidemiology, pathophysiology, clinical signs and symptoms, prognosis, and management. Cystic fibrosis is discussed in Chapter 35.

CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Overview and Definitions

The term *COPD* refers to a disease state characterized by the presence of airflow obstruction that does not reverse completely after **bronchodilator** treatment. Current guidelines by the American Thoracic Society (ATS) and the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines recommend the use of the term *COPD* to encompass both chronic

bronchitis and emphysema. The GOLD guidelines define COPD as follows:

COPD is a common, preventable, and treatable disease characterized by persistent respiratory symptoms and airflow limitation caused by airway and/or alveolar abnormalities, usually caused by significant exposure to noxious particles or gases. The chronic airflow limitation that is characteristic of COPD is caused by a mixture of small airways disease (e.g., obstructive bronchiolitis) and parenchymal destruction (emphysema), the relative contributions of which vary from person to person.[1] The spectrum of COPD is shown in Fig. 25.1, which presents a Venn diagram representing the major components of COPD—chronic bronchitis and emphysema. Although asthma is no longer conventionally considered to be part of the spectrum of COPD, the diagram shows that there is overlap between asthma and COPD. In actual practice, it may not be possible to distinguish between individuals with a history of asthma but with incompletely reversible airflow obstruction and individuals with COPD. Recently, this overlap has been recognized with the term "asthma-COPD overlap" syndrome (ACOS).

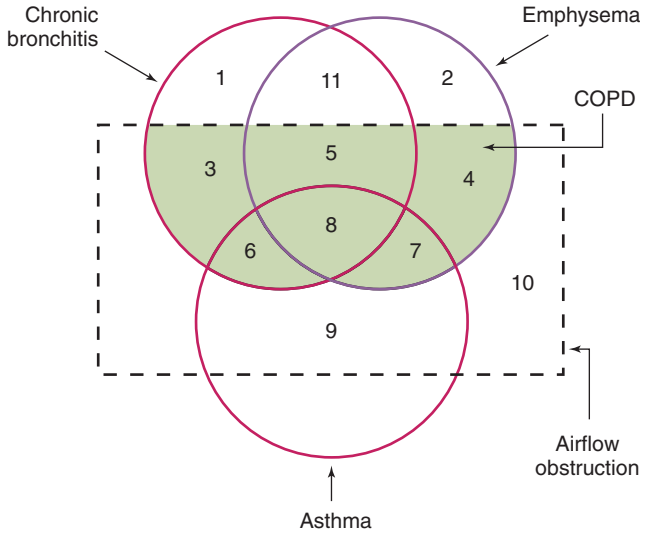


Fig. 25.1 Schema of Chronic Obstructive Pulmonary Disease *(COPD).* This nonproportional Venn diagram shows subsets of patients with chronic bronchitis, emphysema, and asthma. The subsets constituting COPD are *shaded.* Subset areas are not proportional to actual relative subset sizes. Asthma is by definition associated with reversible airflow obstruction, although in variant asthma special maneuvers may be necessary to make the obstruction evident. Patients with asthma whose airflow obstruction is completely reversible *(subset 9)* are not considered to have COPD. Owing to the fact that in many cases it is virtually impossible to differentiate patients with asthma whose airflow obstruction does not remit completely from patients with chronic bronchitis and emphysema who have partially reversible airflow obstruction with airway hyperreactivity, patients with unremitting asthma are classified as having COPD *(subsets 6, 7, and 8).* Chronic bronchitis and emphysema with airflow obstruction usually occur together *(subset 5),* and some patients may have asthma associated with these two disorders *(subset 8).* Individuals with asthma who are exposed to chronic irritation, as from cigarette smoke, may develop a chronic, productive cough, a feature of chronic bronchitis *(subset 6).* Such patients are often referred to as having *asthmatic bronchitis* or the *asthmatic form of COPD.* Individuals with chronic bronchitis or emphysema without airflow obstruction *(subsets 1, 2, and 11)* are not classified as having COPD. Patients with airway obstruction caused by diseases with a known cause or specific pathologic process, such as cystic fibrosis or obliterative bronchiolitis *(subset 10),* are not included in this definition.

The two major diseases that make up COPD—emphysema and chronic bronchitis—are defined in different ways. **Emphysema** is defined in anatomic terms as a condition characterized by abnormal, permanent enlargement of the airspaces beyond the terminal bronchiole, accompanied by destruction of the walls of the airspaces and loss of elastance. **Chronic bronchitis** is defined in clinical terms as a condition in which chronic productive cough is present for at least 3 months per year for at least 2 consecutive years. The definition specifies further that other causes of chronic cough (e.g., gastroesophageal reflux, asthma, and postnasal drip) have been excluded. Fig. 25.1 shows considerable overlap between chronic bronchitis and emphysema and some overlap with asthma—that is, when airflow obstruction is not completely reversible after bronchodilator therapy. Fig. 25.1 also shows that chronic bronchitis and emphysema can occur without airflow obstruction, although the clinical significance of these diseases usually comes from obstruction to airflow.

Epidemiology

COPD is one of the most frequent causes of morbidity and mortality worldwide.[2] The World Health Organization predicts that COPD will become the fifth most prevalent disease in the world and the third leading cause of worldwide mortality by 2030. In the United States, COPD is currently the third leading cause of death[3]; it is responsible for 143,560 deaths in 2015.[4] Estimates suggest that 30 million Americans are affected, although only 15 million U.S. adults have been diagnosed.[4-7] Prevalence by state in the United States ranges from 3.9% to 9.3%.[5] Data from the National Health and Nutrition Examination Survey (NHANES) suggest that among adults 25 to 75 years old in the United States, mild COPD (defined as forced expiratory volume in 1 second [FEV_1]/forced vital capacity [FVC] <70%, and FEV_1 >80% predicted) occurs in 6.9% and moderate COPD (defined as FEV_1/FVC <70% and FEV_1 ≤80% predicted) occurs in 6.6%.[2] COPD prevalence increases with aging, with a fivefold increased risk for adults older than 65 years compared with adults younger than 40 years, and some studies estimate a prevalence of 20% to 30% in adults older than 70 years.[8]

COPD has recently become more prevalent in women. Starting in the year 2000, COPD was responsible for the deaths of more women than men, and by 2009 women accounted for 53% of all COPD deaths in the United States.[9]

The growing health burden from COPD is caused in part by the aging of the population but mainly by the continued use of tobacco. Also, COPD is one of the conditions for which hospitals may be financially penalized for excessive short-term readmission rates under the federal government's Hospital Readmission Reduction Program (HRRP).[10]

Risk Factors and Pathophysiology

Although many risk factors exist for COPD (Box 25.1), in the United States the two most common are *cigarette smoking* (which has been estimated to account for 80% to 90% of all COPD-related deaths) and *alpha-1 antitrypsin (AAT) deficiency.*[11] Worldwide, exposure to biomass fuels (like cooking with wood or

BOX 25.1 Causes of Chronic Obstructive Pulmonary Disease[a]

Common Causes

- Cigarette smoking
- AAT deficiency
- Outdoor air pollution
- Long-standing asthma
- Biomass and occupational exposure (e.g., chronic exposure to wood smoke with poorly ventilated indoor cooking)

Less Common Causes

- Hypocomplementemic urticarial vasculitis
- Intravenous methylphenidate (Ritalin) abuse
- Ehlers-Danlos syndrome
- Marfan syndrome
- Cutix laxa
- Menke syndrome
- Salla disease[b]
- Alpha-1 antichymotrypsin deficiency[b]
- Human immunodeficiency virus infection (emphysema-like illness)

[a]Multiple causes (e.g., cigarette smoking and alpha-1 antitrypsin deficiency) may coexist in a single patient.
[b]Putative cause; firm evidence is unavailable.
AAT, Alpha-1 antitrypsin.

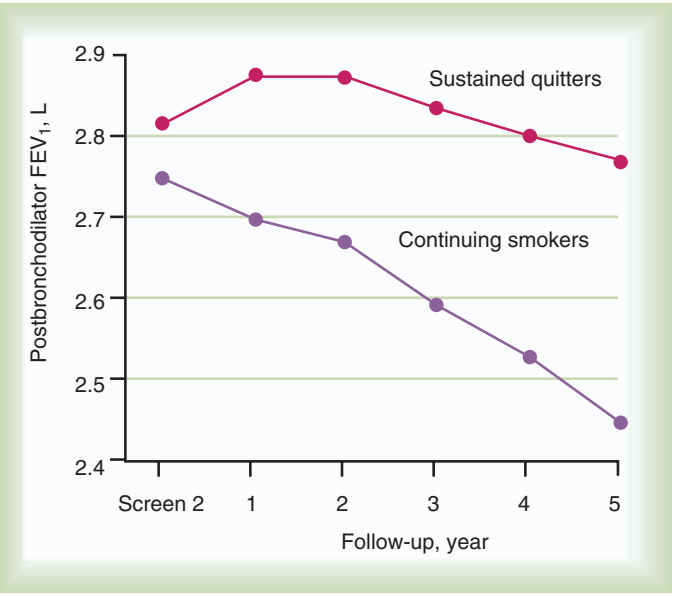


Fig. 25.2 Mean post-bronchodilator forced expiratory volume in 1 *(FEV_1)* for participants in the smoking intervention and placebo groups who were sustained quitters *(red circles)* and continuing smokers *(purple circles).* The two curves diverge sharply after baseline. (From Anthonisen SR, Connett JE, Kiley JP, et al: Effects of smoking intervention and the use of an anticholinergic bronchodilator on the rate of decline of FEV_1: the Lung Health Study. *JAMA* 272:1497–1504, 1994.)

natural product-burning stoves in enclosed spaces) also accounts for a major disease burden.[12]

Evidence linking cigarette smoking to the development of COPD is strong and includes the following:

- Symptoms of COPD (e.g., chronic cough and phlegm production) are more common in smokers than in nonsmokers.
- Impaired lung function with evidence of an obstructive pattern of lung dysfunction is more common in smokers than in nonsmokers.
- Pathologic changes of airflow obstruction and chronic bronchitis are evident in the lungs of smokers.
- So-called *susceptible smokers,* who represent approximately 15% of all cigarette smokers, experience more rapid rates of decline of lung function than nonsmokers.

Information from the Lung Health Study (Fig. 25.2) highlighted the accelerated rate of decrease of FEV_1 in smokers compared with former smokers who have achieved sustained quitting.[13,14] Overall, the strength of evidence implicating cigarette smoking as a cause of COPD has allowed the U.S. Surgeon General to conclude, "Cigarette smoking is the major cause of chronic obstructive lung disease in the United States for both men and women. The contribution of cigarette smoking to chronic obstructive lung disease morbidity and mortality far outweighs all other factors."[15]

As the second well-recognized cause of emphysema, AAT deficiency, sometimes called *genetic emphysema* or *α-1 antiprotease deficiency,* is a condition that features a reduced amount of the protein AAT, which may result in the early onset of emphysema and which is inherited as a so-called *autosomal codominant condition*. AAT deficiency accounts for 2% to 3% of all cases of COPD and affects 100,000 Americans but is under-recognized by health care providers.[16,17] Respiratory therapists (RTs) should be aware of AAT deficiency and suspect it in all patients with signs and symptoms of emphysema and especially in those without risk factors such as smoking.

Identifying individuals with AAT deficiency is simple, often requiring only a blood test of the serum AAT level. Importantly, RTs can contribute to detecting individuals with AAT deficiency (e.g., by suggesting or offering testing when airflow obstruction is diagnosed in the pulmonary function laboratory by an RT performing the test and by making patients aware of available free, home-based testing kits) (see http://www.alpha-1foundation.org). Several observations suggest the importance of detection: (1) first-degree relatives (e.g., siblings, parents, and children) may also be affected but unaware of their risk; (2) early detection allows appropriate monitoring and therapy, including the very important step of smoking cessation; and (3) for individuals with established emphysema, consideration can be given to available specific therapy, called *intravenous augmentation therapy* (which is the administration of purified AAT intravenously to individuals with severe deficiency of AAT). The risk for developing emphysema for individuals with AAT deficiency increases as the serum AAT level decreases to less than 11 µmol/L or less than approximately 57 mg/dL (with normal serum levels generally 100 to 220 mg/dL); these levels in serum define the so-called *protective threshold value,* which is the serum level below which the risk for emphysema is felt to increase. Cigarette smoking markedly accelerates the rate of emphysema progression in individuals with AAT deficiency.[18]

Study of AAT deficiency has helped formulate the protease-antiprotease hypothesis of emphysema.[18,19] In this explanatory model (Fig. 25.3), lung elastin, a major structural protein that supports the alveolar walls of the lung, is normally protected by

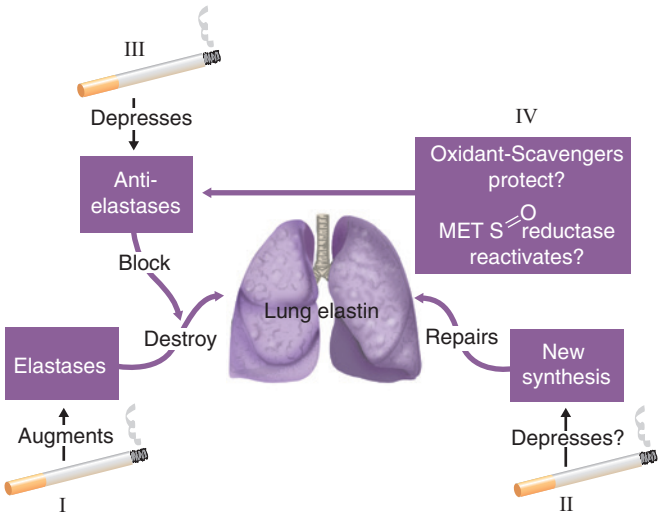


Fig. 25.3 Proposed Biochemical Links Between Cigarette Smoking and the Pathogenesis of Emphysema. *(I)* Smoking recruits monocytes, macrophages, and (through macrophage chemotactic factors) polymorphonuclear neutrophils to the lung, elevating the connective tissue "burden" of elastolytic serine and metalloproteases. *(III)* At the same time, oxidants in smoke plus oxidants produced by smoke-stimulated lung phagocytes (and oxidizing products of chemical interactions between these two) inactivate bronchial mucus proteinase inhibitor and alpha-1 antitrypsin, the latter representing the major antielastase "shield" of the respiratory units. *(III)* Other, unidentified water-soluble, gas-phase components of cigarette smoke (cyanide, copper chelators) inhibit lysyl oxidase–catalyzed oxidative deamination of epsilon-amino groups in tropoelastin and block formation of desmosine and presumably other cross-links during elastin synthesis, decreasing connective tissue repair. *(IV)* Antioxidants (ceruloplasmin, methionine-sulfoxide-reductase) may protect or reactivate elastase inhibitors, and other unidentified factors may modulate the chemical lesions induced in the lung by smoking to influence the risk for developing COPD. (Modified from Janoff A, Carp H, Laurent P, et al: The role of oxidative processes in emphysema. *Am Rev Respir Dis* 127[Suppl]:S31, 1983.)

AAT, a protein that defends the lung against tissue destruction by neutrophil elastase. Neutrophil elastase is a protein contained within a category of white blood cells called *neutrophils* that is released when neutrophils are attracted to the lung during inflammation (like smoking) or infection. Under normal circumstances of an adequate amount of AAT, neutrophil elastase is counteracted so as not to digest lung elastin; however, with severe deficiency of AAT (i.e., when serum levels decrease below the "protective threshold" serum value of 11 µmol/L, or 57 mg/dL), neutrophil elastase may go unchecked, causing breakdown of elastin and of alveolar walls.

COPD may also occur without active cigarette smoking or AAT deficiency (see Box 25.1).[20,21] Factors such as passive smoking, air pollution, occupational exposure, and airway hyperresponsiveness (AHR) may contribute to airflow obstruction that is not reversible.

The pathophysiologic mechanisms of airflow obstruction in COPD include inflammation and obstruction of small airways (<2 mm in diameter); loss of elasticity, which keeps small airways open when elastin is destroyed in emphysema; and active **bronchospasm**. Although traditionally considered to be characteristic of asthma, some reversibility of airflow obstruction has been

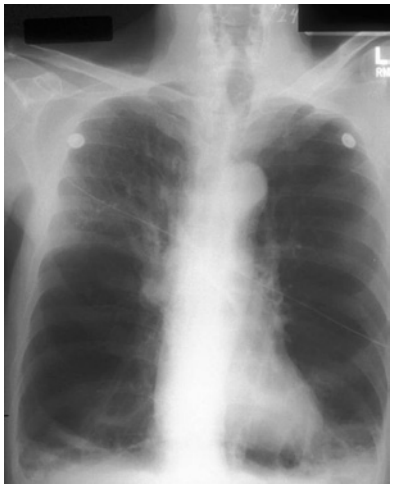


Fig. 25.4 Posteroanterior Plain Chest X-ray in a Patient With Severe Deficiency of Alpha-1 Antitrypsin and Emphysema. Note that the emphysematous changes (hyperlucency) are more pronounced at the lung bases than at the apexes.

observed in up to two-thirds of patients with COPD when tested multiple times with inhaled bronchodilators.[22]

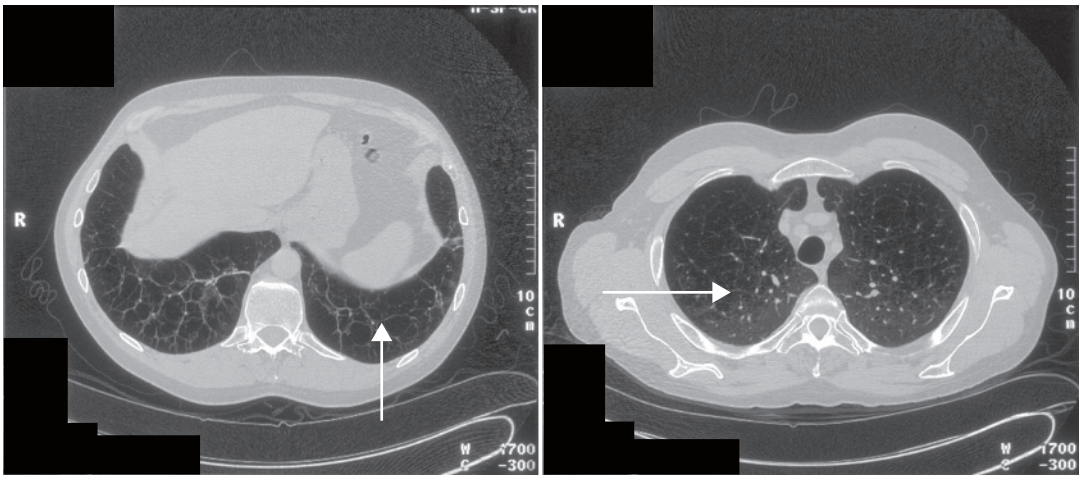
RULE OF THUMB When COPD occurs in a non-smoker, a young person, an individual with a family history of liver or lung disease, or an individual with emphysematous changes more pronounced at the lung bases than apexes on a chest radiograph (Fig. 25.4) or chest computed tomography (CT) (Fig. 25.5), AAT deficiency should be especially suspected. Still, guidelines suggest that *all* adult, symptomatic patients with COPD should be tested for AAT deficiency. RTs can play a key role in diagnosing AAT deficiency.

Clinical Signs and Symptoms

Common symptoms of COPD include cough, phlegm production, wheezing, and shortness of breath, typically on exertion. Dyspnea is often slow but progressive in onset and occurs later in the course of the disease, characteristically in the late sixth or seventh decade of life. A notable exception is AAT deficiency, in which dyspnea characteristically begins sooner (mean age is approximately 45 years).[11]

Table 25.1 reviews the characteristic features of emphysema and chronic bronchitis and emphasizes traits that should especially suggest the possibility of AAT deficiency, including early onset of emphysema, emphysema in a nonsmoker, a family history of emphysema, or emphysema with a chest x-ray (see Fig. 25.4) or CT (see Fig. 25.5), in which emphysematous changes are more pronounced at the lung bases than at the apexes (so-called *basilar hyperlucency*).[11,18]

Physical examination of the chest early on in a patient with COPD may reveal wheezing or diminished breath sounds. Later, signs of hyperinflation may be evident—that is, increased anteroposterior diameter of the chest (sometimes called a *barrel chest*), diaphragm flattening, and dimpling inward of the chest wall at the level of the diaphragm on inspiration (called the *Hoover sign*). Other late signs of COPD include use of accessory muscles of respiration (e.g., sternocleidomastoid), leg edema from cor pulmonale (also known as the right-sided heart failure that can develop



A B

Fig. 25.5 Computed Tomography Chest Image From an Individual With Severe Deficiency of Alpha-1 Antitrypsin. Note the changes of emphysema *(arrows)* are more pronounced in the lung bases (B) than in the lung apexes (A).

TABLE 25.1 Clinical Features of Chronic Obstructive Pulmonary Disease: Distinctions Between Chronic Bronchitis and Emphysema, With Emphasis on Distinguishing Features of Alpha-1 Antitrypsin Deficiency

Features	Chronic Bronchitis	Emphysema	Severe Alpha-1 Antitrypsin Deficiency
Symptoms and Signs			
Chronic cough, phlegm	Common	Less common	Less common, but may be present
Dyspnea on exertion	Less common	Common	Common
Cor pulmonale	Present (often with multiple exacerbations)	Present (but often in end-stage emphysema)	Present (but often in end-stage emphysema)
Age of patient at symptom onset	6th–7th decade	6th–7th decade	4th–5th decade (although late onset is possible)
Family history of COPD	Possible but not characteristic	Possible but not characteristic	Common in parents, children, and siblings
History of cigarette smoking	Present, often heavy	Present, often heavy	May be present, but COPD can occur in the absence of smoking
Physiologic Function			
Airflow (FEV_1, FEV_1/FVC)	Decreased	Decreased	Decreased
Lung volumes, residual volume	Normal	Increased, suggesting air trapping	Increased
Gas exchange, diffusion PaO_2	Often decreased	Often preserved until advanced stage	Often preserved until advanced stage
$PaCO_2$	May be increased	Often preserved until advanced disease, then elevated	Often preserved until advanced disease, then elevated
Diffusion capacity	Often normal	Decreased	Decreased
Static lung compliance	Normal	Increased	Increased
Chest radiograph	"Dirty lungs" with peribronchial cuffing, suggesting thickened bronchial walls	Hyperinflation, with evidence of emphysema; greater at lung apex than at lung base	Hyperinflation, with evidence of emphysema; frequently greater at lung base than at lung apex (basilar hyperlucency)

FEV_1, Forced expiratory volume in 1; *FVC*, forced vital capacity; *COPD*, chronic obstructive pulmonary disease.

from lung disease), mental status changes caused by hypoxemia or hypercapnia (especially in acute exacerbations of chronic, severe disease), or asterixis (i.e., involuntary flapping of the hands when held in an extended position, as in "stopping traffic").

RULE OF THUMB In patients with COPD, $PaCO_2$ is usually preserved until airflow obstruction is severe (i.e., FEV_1 <1 L), which is when $PaCO_2$ may characteristically increase.

RULE OF THUMB Digital clubbing is **not** caused by COPD alone, even if hypoxemia is present. Clubbing in a patient with COPD warrants consideration of another cause (e.g., bronchogenic cancer, bronchiectasis, interstitial lung disease, liver disease, inflammatory bowel disease, cystic fibrosis).

Management

In managing patients with chronic, stable COPD, the following goals must guide the clinician[1,23]:

- Establish the diagnosis of COPD.
- Optimize lung function.
- Maximize the patient's ability to perform daily activities.
- Simplify the medical treatment program as much as possible.
- Prevent infection, including vaccinations.
- Avoid exacerbations of COPD.
- Prolong survival.

In managing an **acute exacerbation of COPD**, additional considerations are to reestablish the patient to baseline status as quickly and with as little morbidity and mortality as possible.[24,25] Each of the treatments discussed in this section is considered in regard to these goals, recognizing differences in management between patients with chronic, stable COPD versus an acute exacerbation of COPD.

Establishing the Diagnosis

Although many diseases can give rise to obstructive lung disease, including some unusual entities such as chronic eosinophilic pneumonia, bronchiectasis, and allergic bronchopulmonary aspergillosis, the major challenge facing the clinician who encounters a patient with airflow obstruction is to distinguish COPD (i.e., emphysema or chronic bronchitis or both) from asthma. Distinguishing asthma from COPD may be very difficult in practice. This difficulty has been recognized by naming an overlap syndrome called the "ACOS". While definitive criteria for this syndrome are not yet agreed upon, patients are generally ≥35 years and have evidence for chronic persistent airflow limitation, that is, COPD with a smoking history of at least 10 pack years. For those patients who already have a diagnosis of asthma, a positive bronchodilator response (FEV_1 ≥12% and ≥200 mL increase after bronchodilator use), diurnal variability of peak expiratory flow or elevated exhaled nitric oxide levels (i.e., ≥50 ppb) are considered diagnostic of ACOS. For those who do not have a current diagnosis of asthma, prominent fluctuation in symptom burden, a vigorous bronchodilator response (usually an increase of 15% and ≥ 400 mL in FEV_1 after bronchodilator) and the presence of eosinophilia in blood (≥300 cells/mcl) suggest the presence of ACOS. Clinicians may consider allergy evaluation and treatment, use of inhaled corticosteroids, and even biological drugs typically used for asthma for patients with ACOS.[26]

After the diagnosis of COPD is established, another issue is whether the patient has an underlying predisposition to COPD, such as AAT deficiency or other cause listed in Box 25.1.[20,21] Underlying causes are present in fewer than 5% of patients with COPD, with AAT deficiency being the most common (2% to 3% of all patients with COPD in the United States).

Optimizing Lung Function

Stable Chronic Obstructive Pulmonary Disease

Although airflow obstruction from emphysema itself is irreversible, most (up to two-thirds) patients with stable COPD exhibit a reversible component of airflow obstruction, defined as a 12% and 200 mL increase in post-bronchodilator FEV_1 or FVC or both. For this reason, as shown in an algorithm developed by GOLD (Fig. 25.6),[1,22,25,26,34,35] bronchodilator therapy is recommended for patients with COPD.

MINI CLINI

Distinguishing Asthma From Chronic Obstructive Pulmonary Disease

Problem

You are asked to see a new patient in clinic with a history of asthma. The patient is a 60-year-old female who is a current smoker of 50 pack years. She notes a chronic productive cough and persistent shortness of breath, but denies nighttime wakening. She states her symptoms began later in life and denies a childhood history of asthma. Her pulmonary function test (PFT) reveals an FEV_1/FVC ratio <70% and FEV_1 noted to be 55% with no significant bronchodilator response. Review of records show an FEV_1 of 60% when she had spirometry performed 4 years prior. How would you characterize the patient's airflow obstruction based on her spirometry, history, and clinical symptoms?

Discussion

Distinguishing asthma versus COPD has been the topic of several clinical practice guidelines. A questionnaire that incorporated age of onset, smoking history, atopy status (i.e., the tendency to develop allergic diseases), and cough quality was able to correctly identify asthma versus COPD in 87.4% of cases.[27] Another questionnaire to help distinguish COPD included age, pack-years, worsening cough, breathing-related disability or hospitalization, phlegm quantity, and worsening dyspnea, demonstrating COPD with a sensitivity of 72% and a specificity of 82.7%.[28]

In some instances asthma and COPD cannot be distinguished owing to significant overlap of symptoms, which is a term known as ACOS. In one of the questionnaires mentioned above, a score designated as overlap between asthma and COPD represented 20% of the population studied. Another recent study showed ACOS criteria to be present in 15% of a COPD cohort.[27,29,30]

Asthma	COPD
Onset early in life (often childhood)	Onset in mid-life
Symptoms vary from day to day	Symptoms slowly progressive
Symptoms at night/early morning	Long history of tobacco smoking
Allergy, rhinitis, and/or eczema sometimes present	Dyspnea largely owing to exertion
Family history of asthma usually present	Presence of comorbidities
Largely reversible airflow limitation	Largely irreversible airflow limitation

Adapted from the Global Initiative for Chronic Obstructive Lung Disease.[1]

While the patient described in the example above gives a medical history of asthma, her history, symptoms, and the results of her breathing tests suggest she is more likely to have COPD.

Bronchodilators produce smooth muscle relaxation, resulting in improved airflow obstruction, improved symptoms and exercise tolerance, and decrease in the frequency and severity of exacerbations, but they do not enhance survival. The results of the Lung Health Study,[22] which compared the effects of inhaled ipratropium bromide (two puffs four times daily) with placebo in patients with mild, stable COPD, showed that regular, long-term use of ipratropium did not change the rate of decline of lung function but offered a one-time, small increase in FEV_1. More recently, a study of tiotropium for mild to moderate COPD showed a higher FEV_1 than placebo at 24 months and decreased the rate of decline in FEV_1, suggesting that earlier use of bronchodilators may lead to some improvement of obstruction over time.[36]

MINI CLINI

Determining the Severity of Chronic Obstructive Pulmonary Disease

Problem

You are asked to see a new patient in clinic who was recently discharged from the hospital with a COPD exacerbation. The patient describes being hospitalized at least twice per year because of lung problems and complains of severe dyspnea when walking up a hill. Spirometry showed an FEV_1 of 40% predicted after bronchodilator. How do you characterize the severity of COPD in this patient?

Discussion

The GOLD has created a classification system based on the severity of airflow obstruction measured by post-bronchodilator FEV_1.[1] According to this staging system, severity of COPD is graded based on the degree of airflow obstruction into one of the following four stages:

Stage	Description
I	Patients with FEV_1/FVC <70% and FEV_1 >80% predicted
II	Patients with FEV_1/FVC <70% and FEV_1 50%–79% predicted
III	Patients with FEV_1/FVC <70% and FEV_1 30%–49% predicted
IV	Patients with FEV_1/FVC <70% and FEV_1 <30% or FEV_1 <50% predicted plus chronic respiratory failure

The original GOLD guidelines from 2001 were revised in 2011 to include symptoms and exacerbation history and, in the 2017 version of the GOLD guidelines, COPD severity is graded first by post-bronchodilator FEV_1 strata (previously mentioned) and then by a letter combination (A to D) that characterizes the patient's symptoms (based on the Modified Medical Research Council [mMRC] and the COPD Assessment Test [CAT, see later) and frequency of COPD exacerbations, as follows[31]:

A = Low risk, low symptom burden
- Low symptom burden (mMRC score of 0 to 1 OR CAT score <10) AND
- Low exacerbation rate (0 to 1/year, not leading to hospitalization)

B = Low risk, higher symptom burden
- Higher symptom burden (mMRC score of ≥2 OR CAT of ≥10) AND
- Low exacerbation rate (0 to 1/year, not leading to hospitalization)

C = High risk, low symptom burden
- Low symptom burden (mMRC score of 0 to 1 OR CAT score <10) AND
- High exacerbation rate (≥2/year or at least 1 exacerbation leading to hospitalization)

D = High risk, higher symptom burden
- Higher symptom burden (mMRC score of ≥2 OR CAT of ≥10) AND
- High exacerbation rate (≥2/year or at least 1 exacerbation leading to hospitalization)

The new classification categorizes patients first by spirometric features and then adds severity of symptoms and exacerbation history to refine risk. As mentioned above, this system uses two different scales to define symptom burden–the modified Medical Research Council questionnaire (mMRC)[32] and the CAT.[33]

mMRC

0: Dyspnea with strenuous exercise
1: Dyspnea when hurrying on the level or walking up a slight hill
2: Walks slower than most people on the level, stops after a mile or so, or stops after 15 min of walking at own pace
3: Stops for breath after walking 100 yards or after a few minutes of level ground
4: Too breathless to leave the house or breathless when undressing

CAT

- Cough (none to all the time): Total 0–5
- Phlegm (mucus) in my chest: Total 0–5 (none to severe)
- Chest tightness: Total 0–5 (none to severe)
- Dyspnea walking flight of stairs: Total 0–5 (none to severe)
- Limitation for home activities: Total 0–5 (none to severe)
- Confident leaving home despite lung condition: Total 0–5 (very confident to nonconfident)
- Sleep quality: Total 0–5 (sound sleep to no sleep because of lung condition)
- Energy: Total 0–5 (full energy to none)

Both anticholinergic and adrenergic (β agonist) bronchodilators can improve airflow in patients with COPD, although some clinicians favor an inhaled anticholinergic medication (e.g., ipratropium bromide or tiotropium[34,35]) as first-line therapy (see Fig. 25.6).

The GOLD guidelines[1] recommend the use of short-acting β-adrenergic agents (≤6 hours) for symptomatic management of all patients with COPD. Also, the use of a long-acting β agonist (e.g., salmeterol) or a long-acting anticholinergic drug (e.g., tiotropium) can lessen the frequency of acute exacerbations of COPD.[35]

Other treatment options to optimize lung function include administering corticosteroids. Chronic oral steroids are rarely recommended for patients with stable COPD, but are used commonly to treat acute exacerbations of COPD (see later).[37,38] Results of several major clinical trials (e.g., Lung Health Study II, Euroscop, Inhaled Steroids in Obstructive Lung Disease [ISOLDE] study, and Copenhagen City Study, but not another trial, Towards a Revolution in COPD Health [TORCH] study) agree that inhaled corticosteroids do not significantly change the rate of decline of FEV_1 in patients with COPD, although their use is associated with a decreased frequency of acute exacerbations.[39-42]

Studies of combined salmeterol and fluticasone versus placebo in patients with COPD suggest that adding an inhaled corticosteroid (fluticasone) to the long-acting β agonist (salmeterol) can reduce the frequency of acute exacerbations of COPD but does not improve survival.[39,40] The finding of a higher rate of pneumonia in inhaled corticosteroid users is concerning. Overall, the GOLD guidelines[1] recommend use of inhaled corticosteroids in patients with significant symptoms and history of recurrent exacerbations (three episodes in the last 3 years).

Treatment with a methylxanthine (like theophylline) offers little additional bronchodilation in patients using inhaled bronchodilators and is generally reserved for the few patients with debilitating symptoms from stable COPD despite maximal conventional therapy. Research has shown lessened dyspnea in methylxanthine recipients despite a lack of measurable increases in airflow.[43] Side effects of methylxanthines include anxiety, jitteriness (tremulousness), nausea, cardiac arrhythmias, and seizures. To minimize the chance of toxicity, current recommendations suggest maintaining serum theophylline levels at 8 to 10 mcg/mL.

In patients with frequent exacerbations of COPD, drugs to minimize the risk of exacerbation should be considered (see later).

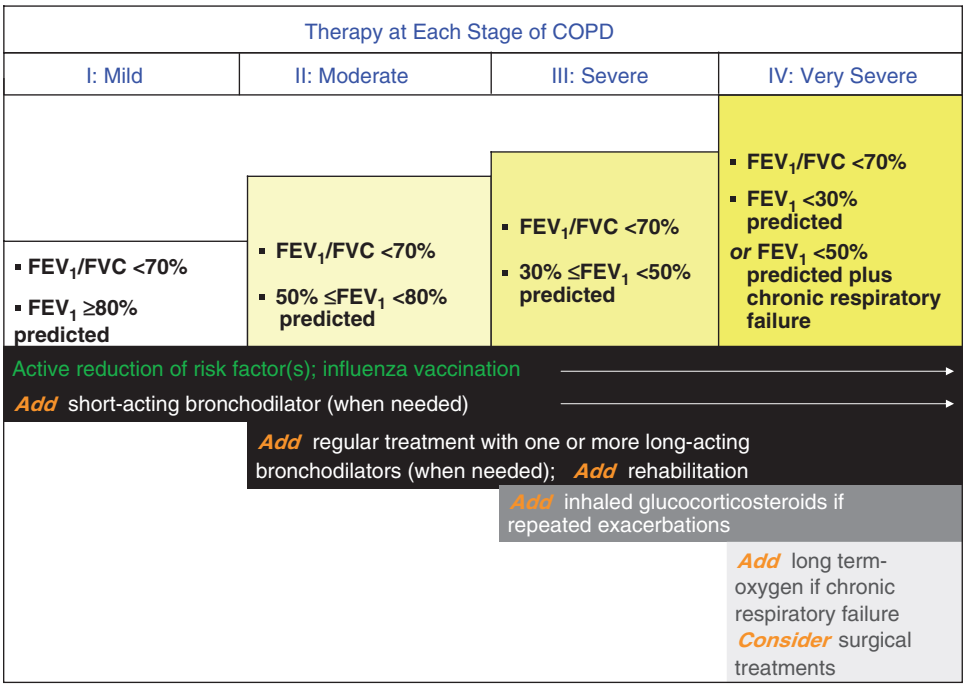


Fig. 25.6 Initial pharmacologic management of chronic obstructive pulmonary disease (COPD). *FEV_1*, Forced expiratory volume in 1; *FVC,* forced vital capacity. (From The Global Strategy for the Diagnosis, Management and Prevention of COPD: *Global Initiative for Chronic Obstructive Lung Disease [GOLD]*, 2018. http://www.goldcopd.com. Accessed May 22, 2018.)

In addition to drug therapy for COPD, non-invasive ventilation is being increasingly offered to patients with chronic hypercapnia accompanying stable COPD, with mixed data regarding effectiveness (see later and Chapter 50).

Acute Exacerbation of Chronic Obstructive Pulmonary Disease

Strategies for improving lung function during acute exacerbations of COPD generally include inhaled bronchodilators (especially β-2 agonists), antibiotics, and systemic corticosteroids. Owing to their rapid onset of action and efficacy, short-acting β-2 agonists are first-line therapy for patients with COPD exacerbation. Inhaled β-2 agonists are frequently administered through a nebulizer, although metered dose inhaler devices may have equal efficacy if administered appropriately.[1] A common practice is to administer 2.5 mg of albuterol by nebulizer every 1 to 4 hours as needed. Higher doses of albuterol (i.e., 5 mg) do not produce further improvement in pulmonary function and may cause cardiac side effects (like tachycardia).[44] Similarly, continuous nebulization of short-acting β-2 agonists in patients with COPD exacerbation is not recommended.

In addition to inhaled bronchodilator therapy, short-term systemic corticosteroids are recommended to reduce inflammation and improve lung function. An early randomized, controlled trial of intravenous methylprednisolone for patients with acute exacerbations showed accelerated improvement in FEV_1 within 72 hours.[45] Larger, more recent trials have confirmed the benefits of systemic corticosteroids in acute exacerbations and have shown that short-term oral courses (i.e., approximately 2 weeks) are as effective as longer courses (i.e., 8 weeks) with fewer adverse steroid effects.[46] More recent data show that for COPD patients with exacerbations presenting to the emergency room, 5 days of oral prednisone (40 mg/day) is as effective as 14 days of oral prednisone.[47]

For patients with acute exacerbations characterized by purulent phlegm, oral antibiotics (e.g., trimethoprim-sulfamethoxazole, amoxicillin, or doxycycline) administered for 7 to 10 days have produced accelerated improvement of peak flow rates compared with placebo recipients.[24,48,49] Owing to the risk of being infected with more virulent bacteria (e.g., *Pseudomonas aeruginosa*), patients who have severe COPD and an exacerbation may benefit from broader spectrum antibiotics, such as fluoroquinolones or aminoglycosides. Chapter 24 describes antibiotic therapy for these patients in more detail.

Finally, important elements of managing an acute exacerbation of COPD caused by purulent bronchitis include supplemental oxygen (O_2) to maintain arterial saturation 88% to 94%, inhaled bronchodilators, oral antibiotics, and a brief course of systemic corticosteroids.[24]

For patients with hypercapnia and acute respiratory acidemia accompanying an acute exacerbation of COPD, the clinician must also decide whether to provide ventilatory assistance. Although intubation and mechanical ventilation had historically been the preferred approach, more recent studies suggest that noninvasive positive pressure ventilation (see Chapters 46 and 50) can be an effective and the preferred alternative for patients with acute exacerbations of COPD.[50] Specifically, based on studies that show that noninvasive positive pressure ventilation can shorten intensive care unit (ICU) stay and avoid the need for intubation, the American Association for Respiratory Care

(AARC) consensus conference and guidelines on **noninvasive ventilation** from other official societies have endorsed use of noninvasive ventilation for such patients (unless a contraindication to noninvasive ventilation is present, see Chapter 50).[51,52]

Maximizing Functional Status

In symptomatic patients with stable COPD, maximizing their ability to perform activities of daily living is a priority. Pharmacologic treatments to maximize functional status include administration of bronchodilators to enhance lung function as much as possible, based on data that such drugs can lessen dyspnea and improve functional status ratings even though airflow is not increased.[2]

Comprehensive pulmonary rehabilitation is another important treatment for patients with COPD that has the goal of improving patients' ability to function.[53] As discussed in Chapter 56, pulmonary rehabilitation is a multidisciplinary intervention that consists of lower and upper extremity exercise conditioning, breathing retraining, education, and psychosocial support. Research suggests that although pulmonary rehabilitation does not improve lung function or survival, pulmonary rehabilitation results in decreased dyspnea perception, improved health-related quality of life, fewer days of hospitalization, and decreased health care usage. Pulmonary rehabilitation can be helpful in the early identification of COPD patients whose clinical status is deteriorating, so they can be quickly treated and the likelihood of hospital readmission reduced.[54,55]

Preventing Progression of Chronic Obstructive Pulmonary Disease and Acute Exacerbations, and Enhancing Survival

Cigarette smoking is widely recognized as the major risk factor for accelerating airflow obstruction in smokers. Although some individuals can continue to experience accelerated loss of lung function even after stopping smoking, smoking cessation can often slow the rate of decline of FEV_1 and restore the rate of lung decline to that seen in non-smokers.

Follow-up data from the Lung Health Study[13] confirm that a comprehensive smoking cessation program (including instruction, group counseling, and nicotine replacement therapy) can achieve sustained smoking cessation in 22% of participants and that the rate of annual FEV_1 decline in these sustained nonsmokers was significantly less than it was for continuing smokers, even over 11 years of follow-up.[14] Participation in aggressive smoking cessation can enhance survival rates in patients with COPD.[14]

Critical elements in achieving successful smoking cessation include identifying "teachable moments" (i.e., during episodes of illness in which smoking can be identified as a contributing factor[56]), identifying the role of smoking in adverse health outcomes, negotiating a "quit date," and providing frequent follow-up reminders from health care providers.[57] A helpful strategy during counseling is to use the five *A*s of smoking cessation[1]:

*A*sk if they are smoking
*A*dvise to quit
*A*ssess willingness to quit
*A*ssist by providing a plan
*A*rrange a follow-up

In this regard, the RT, who sees the patient frequently, has a special responsibility to provide frequent, constructive reminders about how very important it is to stop smoking.[58]

Among available treatments for COPD, **supplemental oxygen** is important because, similar to smoking cessation and lung volume reduction surgery (LVRS) in selected individuals, it can prolong survival in appropriate candidates.[59-62] Box 25.2 reviews the indications for supplemental O_2, and Fig. 25.7 shows the results of the American Nocturnal Oxygen Therapy Trial[59] and the British Medical Research Council trial of domiciliary O_2 (1980 to 1981).[60,61] Survival was improved when eligible patients used supplemental O_2 for as close to 24 hours as possible; survival improved less for patients using O_2 only 15 hours per day. No survival benefit was observed when O_2 was used during sleeping hours only. Patients should be assessed for supplemental O_2 use only after receiving optimal bronchodilator therapy because one-third of potential O_2 candidates can experience sufficient improvement with aggressive bronchodilation to avoid the need for

MINI CLINI

Recognizing and Managing an Acute Exacerbation of Chronic Obstructive Pulmonary Disease

Problem

A 70-year-old man with long-standing COPD is admitted to the hospital with an acute exacerbation. On physical examination, he is not dehydrated and examination shows diminished breath sounds bilaterally without wheezing. Pertinent laboratory values show a hematocrit of 54% (normal is 40% to 47%). An arterial blood gas (ABG) analysis performed with the patient on room air showed the following:

PaO_2 = 47 mm Hg
PCO_2 = 67 mm Hg
pH = 7.30
HCO_3^- = 34 mEq/L

How do you describe his current status, what do his current laboratory values suggest about his long-term gas exchange status, and what treatment should be considered?

Solution

The patient has an acute exacerbation of COPD. The acidemia (pH 7.30) on his ABG analysis suggests an acute increase in PCO_2 superimposed on chronic hypercapnia, which is suggested by the elevated serum bicarbonate (HCO_3^-), indicating renal compensation for chronic respiratory acidosis. Although his current hypoxemia may be caused by worsened gas exchange accompanying the current flare-up of COPD, his elevated hematocrit, in the absence of dehydration and consequent hemoconcentration, suggests chronic hypoxemia and secondary erythrocytosis. The goal of therapy is to restore his gas exchange to baseline and to avoid invasive or high-risk interventions, while optimizing survival.

To achieve these goals, treatment consists of aggressive use of bronchodilators, intravenous corticosteroids, supplemental O_2, and antibiotics (if there is evidence of acute lung infection, either bronchitis or pneumonia). In view of the patient's acute chronic respiratory acidemia, ventilatory support is indicated. As shown by several randomized, controlled trials, noninvasive positive pressure ventilation is an effective alternative to intubation.

BOX 25.2 Indications for Long-Term Oxygen Therapy

I. Continuous O_2
   A. Resting PaO_2 ≤55 mm Hg
   B. Resting PaO_2 56–59 mm Hg or SaO_2 89% in the presence of any of the following:
      1. Dependent edema, suggesting congestive heart failure
      2. P pulmonale on the electrocardiogram (P wave >3 mm in standard lead II, III, or aV_F)
      3. Erythrocytosis (hematocrit >56%)
         a. Reimbursable only with additional documentation justifying O_2 prescription and a summary of more conservative therapy that has failed

Modified from Tarpy SP, Celli BR: Long-term oxygen therapy. *N Engl J Med* 333:710–714, 1995.

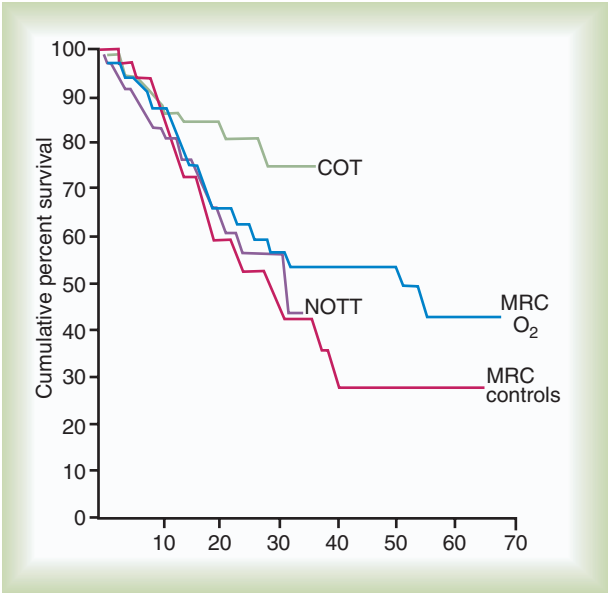


Fig. 25.7 Cumulative Percent Survival of Patients in the Nocturnal Oxygen Therapy Trial *(NOTT)* and Medical Research Council *(MRC)* Controlled Trials of Long-Term Domiciliary O_2 Therapy for Men Older Than 70 Years. MRC control subjects *(red line)* received no O_2. NOTT subjects *(purple line)* received O_2 for 12 hours in the 24-hour day, including the sleeping hours. MRC O_2 subjects *(blue line)* received O_2 for 15 hours in the 24-hour day, including the sleeping hours, and continuous O_2 therapy *(COT)* subjects *(green line)* received O_2 for 24 hours in the 24-hour day (on average, 19 hours). (Modified from Flenley DC: Long-term oxygen therapy. *Chest* 87:99–193, 1985.)

long-term supplemental O_2. Also, patients prescribed to receive supplemental O_2 during acute exacerbations should be reassessed several months later to determine whether they continue to need supplemental O_2.[63] RTs can play a key role in ensuring compliance with this recommendation and optimizing O_2 therapy.[64,65] Newer data from the Long-Term Oxygen Treatment Trial (LOTT)[66] address the role of supplemental O_2 in COPD patients with moderate resting hypoxemia (defined as SpO_2 at rest on room air of 89% to 93%) or with resting normoxemia but desaturation (to below SpO_2 of 90% for ≥ 10 seconds). In these patients randomized to supplemental O_2 (either 24 hours a day for those with moderate resting hypoxemia or with activity and sleep in those with exercise desaturation only), O_2 use neither showed benefit in decreasing time to death or first hospitalization nor in the rate of hospitalization, COPD exacerbation, COPD-related hospitalization, or various quality of life measures. In the light of the results of the LOTT trial, supplemental O_2 as close to 24 hours a day as possible remains indicated for COPD patients with severe resting hypoxemia (i.e., room air resting SpO_2 < 88%, PaO_2 < 55 mm Hg, or PaO_2 ≤59 mm Hg with cor pulmonale or polycythemia), but the indication for prescribing supplemental O_2 for those COPD patients with moderate resting hypoxemia or resting desaturation is weaker. Such treatment, if offered, should be individualized and continued only if there is clear subjective benefit to the patient.

BOX 25.3 Indications for 23-Valent Pneumococcal Vaccine Administration

Vaccination is recommended for the following adults:
- Adults age 65 years and older and adults of all ages with long-term illnesses that are associated with a high risk for contracting pneumococcal disease, including heart or lung diseases, diabetes, alcoholism, cirrhosis, or cerebrospinal fluid leaks
- Adults with diseases or conditions that lower the body's resistance to infections, including abnormal function of the spleen or removed spleen, Hodgkin disease, lymphoma, multiple myeloma, kidney failure, nephrotic syndrome, or organ transplantation, and adults who are taking drugs that lower the body's resistance to infections
- Adults with human immunodeficiency virus infection and acquired immunodeficiency syndrome (HIV/AIDS), with or without symptoms

Revaccination should be considered for the following groups:
- Individuals at the highest risk for fatal pneumococcal infection, such as individuals with abnormal function or removal of the spleen, who received the original pneumococcal vaccination (from 1979 to 1983) or who received the current vaccine (1983 to present) 6 years ago or longer
- Individuals shown to lose protection rapidly (e.g., individuals with nephrotic syndrome, kidney failure, or transplants), who received the current vaccine 6 years ago or longer
- Children 10 years old or younger with nephrotic syndrome, abnormal function or removal of the spleen, or sickle cell anemia, who received the vaccine 3–5 years ago
- Adults age ≥65 should also receive the 13-valent pneumococcal vaccine (Prevnar) followed 6–12 months later by the 23-valent vaccine (e.g., Pneumovax)

Finally, preventive strategies such as pneumococcal and annual influenza vaccinations, and other strict infection control practices such as avoiding contact with others who are sick, are recommended for all patients with chronic debilitating conditions such as COPD.[65] Specific indications for pneumococcal vaccination are presented in Box 25.3. Recommendations for those age 65 or older also include a 13-valent pneumococcal vaccine in addition to the existing 23-valent pneumococcal vaccine.

Other measures to prevent exacerbations of COPD include use of long-acting anticholinergic agents (e.g., tiotropium, aclidinium, umeclidinium), inhaled corticosteroids, especially in combination with long-acting β agonists, macrolide antibiotics (e.g., erythromycin and azithromycin),[67] phosphodiesterase-4 inhibition with roflumilast,[68] and antioxidants such as oral N-acetylcysteine.[69]

Noninvasive ventilation may offer a benefit to patients with chronic ventilatory failure accompanying COPD. When intensive noninvasive ventilation (titrated to lower $PaCO_2$, IPAP 22 to 24 cm H_2O, applied for at least 6 hours of the day) was instituted for patients with chronic hypercapnic respiratory failure owing to COPD, improved quality of life, reduced exacerbations and reduced mortality and readmissions were noted in two randomized control trials.[70,71] In another study, similar noninvasive ventilation regimen did not produce similar benefits when COPD patients were recruited at the time of an inpatient admission for hypercapnic respiratory failure.[72] Of note, 25% of those patients attained normal carbon dioxide levels after 3 months, suggesting the recruitment of a less severe group of patients for that trial.

Additional Therapies

Additional therapies for individuals with end-stage COPD include lung transplantation[73] and LVRS,[74-76] in which small portions of emphysematous lung are removed to reduce hyperinflation and improve lung mechanics of the remaining tissue. COPD is the most common current indication for lung transplantation. Lung transplantation is a consideration for patients with severe airflow obstruction (i.e., FEV_1 <20% predicted and a Body-mass index, Obstruction, Dyspnea, and Exercise [BODE] index >7 who are younger than 70 years old, and who are psychologically suitable and motivated). Double lung transplantation is preferred; nevertheless, because the supply of donor lungs to transplant is less than the number of patients needing lung transplantation, single-lung transplantation is also frequently performed. Although lung transplantation may be associated with significantly improved quality of life and functional status, major risks include rejection (manifested as bronchiolitis obliterans and progressive, debilitating airflow obstruction), infection with unusual opportunistic organisms, and death from these and other complications. The 5-year actuarial survival rate after lung transplantation in patients with COPD is approximately 54%[73] (Fig. 25.8).

LVRS has regained popularity after initial experiences were reported in 1957.[74] Study results of LVRS, including the large National Emphysema Treatment Trial, indicate that in selected subsets of patients with COPD (i.e., patients with heterogeneous emphysema that is upper lobe–predominant and who have low exercise capacity after pulmonary rehabilitation), LVRS can prolong survival, improve quality of life, and increase exercise capacity.[75,76] LVRS should not be considered in individuals with very severe COPD (i.e., characterized by FEV_1 <20% predicted with either a homogeneous pattern of emphysema or a diffusing capacity <20% predicted), because the mortality rate associated with LVRS in these patients is higher than in medically treated patients.[77]

Nonsurgical bronchoscopic techniques to achieve lung volume reduction have been developed in an attempt to reduce morbidity, mortality and cost. With the use of the bronchoscope,

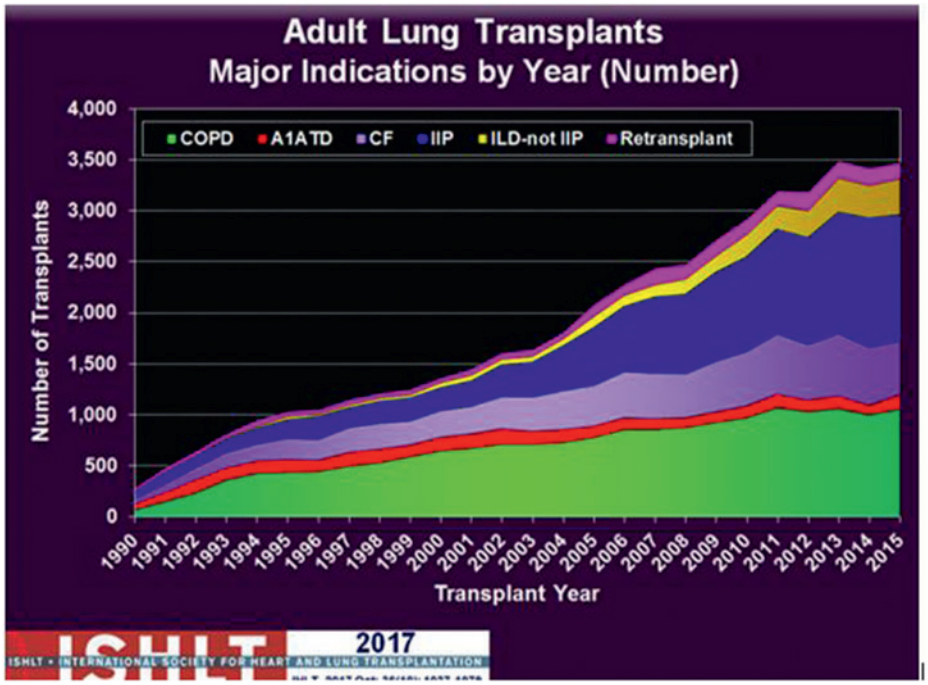


Fig. 25.8 Adult Recipient Kaplan-Meier Survival by Diagnosis (Transplants: January 1990 to June 2015). The overall survival rate of patients with alpha-1 antitrypsin deficiency is significantly higher than the survival rate of patients with chronic obstructive pulmonary disease *(COPD)* and interstitial lung disease *(ILD)*, which includes idiopathic pulmonary fibrosis (IPF). Similarly, the overall survival rate of patients with COPD is higher than the survival rate of patients with idiopathic pulmonary fibrosis. *AATD,* alpha-1 antitrypsin deficiency associated COPD; *COPD,* non-AATD associated COPD; *CF,* cystic fibrosis; IPAH, idiopathic pulmonary arterial hypertension. (From Yusen RD, Christie JD, Edwards LB, et al: *30th official adult lung and heart-lung transplant report, 2015 in the Registry of the International Society for Heart and Lung Transplantation*. http://www.ishlt.org. Accessed May 22nd 2018.)

deployment of unidirectional endobronchial valves or coils into the airways results in collapse of the targeted lung parenchyma.[78-82] Neither of these interventions are currently approved by the U.S. Food and Drug Administration (FDA) for the treatment of emphysema in the United States. Updated GOLD guidelines recommend their consideration (where approved outside the United States) for the purpose of improving exercise tolerance, health status, and lung function at 6 to 12 months after treatment, although no mortality benefit has been shown in any studies.[1]

Finally, for patients with AAT deficiency and established COPD, so-called *intravenous augmentation* with a purified preparation of AAT from human blood donors is recommended.[18] The best available evidence[83-86] suggests that for individuals with severe AAT deficiency and moderate degrees of airflow obstruction (i.e., FEV_1 35% to 60% predicted), weekly augmentation therapy may be associated with a slower rate of decline of lung function, a slower rate of loss of lung density on chest CT, and improved survival. Difficulties with intravenous augmentation therapy include the substantial expense (approximately $100,000 per year); the inconvenience of frequent intravenous infusions for life; and the infusion itself, which poses a theoretical risk for transmitting a blood-borne infection. Despite these drawbacks, the facts that augmentation therapy may slow the rate of FEV_1 decline, slows the rate of CT lung density loss, and is currently the only specific therapy for AAT deficiency have led to its endorsement in official guidelines from the ATS, the European Respiratory Society (ERS), and the Canadian Thoracic Society.[18,87]

ASTHMA

Definition

Asthma is a clinical syndrome characterized by **airway obstruction,** which is partially or completely reversible either spontaneously or with treatment; **airway inflammation;** and **airway hyperresponsiveness** (AHR) to various stimuli.[88-90] Past definitions of asthma emphasized AHR and reversible obstruction; however, newer and more accurate definitions of asthma focus on asthma as a primary inflammatory disease of the airways, with clinical manifestations of increased airway hyperreactivity and airflow obstruction caused by the inflammation.

Incidence

Asthma is a chronic illness that has been increasing in prevalence in the United States since 1980. The number of people with asthma in the United States grew from 20 million in 2001 to 25 million in 2010 (8% of the U.S. population). According to data from the National Health Interview Survey performed by the Centers for Disease Control and Prevention in 2016, 20.4 million adults and 6.1 million children (8.3% of American children) reported having asthma. Asthma accounted for 1.7 million emergency room visits in 2015.[91] Asthma also accounted for 11 million outpatient visits in 2014, and approximately 3500 deaths in 2016.[92,93] An analysis from 1999 to 2016 showed that asthma mortality significantly decreased, which was felt to be the result of an improvement in asthma management and prevention measures.[94,95]

A study from 2011 to 2016 showed that among the 6.8% of working adults with asthma, 44.7% had experienced an asthma attack and 9.9% had an asthma-related emergency room visit. The highest prevalence was in the healthcare and social assistance industry (8.8%).[96]

Etiology and Pathogenesis

In the genetically susceptible host, allergens, respiratory infections, certain occupational and environmental exposures, and many unknown hosts or environmental stimuli can produce the full spectrum of asthma, with persistent airway inflammation, bronchial hyperreactivity, and consequent airflow obstruction. When inflammation and bronchial hyperreactivity are present, asthma can be triggered by additional factors, including exercise; inhalation of cold, dry air; hyperventilation; cigarette smoke; physical or emotional stress; inhalation of irritants; and pharmacologic agents, such as methacholine and histamine.[97-99]

When a patient with asthma inhales an allergen to which he or she is sensitized, the antigen cross-links to specific immunoglobulin E (IgE) molecules attached to the surface of mast cells in the bronchial mucosa and submucosa. The mast cells degranulate rapidly (within 30 minutes), releasing multiple mediators including leukotrienes (previously known as *slow-reacting substance of anaphylaxis* [SRS-A]), histamine, prostaglandins, platelet-activating factor, and other mediators. These mediators lead to smooth muscle contraction, vascular congestion, and leakage, resulting in airflow obstruction, which can be assessed clinically as a decline in FEV_1 or *peak expiratory flow rate* (PEFR) (Figs. 25.9 and 25.10). This is the *early (acute) asthmatic response*, which is an immediate hypersensitivity reaction that usually subsides in approximately 30 to 60 minutes. In approximately 50% of asthmatic patients, however, airflow obstruction recurs in 3 to 8 hours.[99] This *late asthmatic response* is usually more severe and lasts longer than the early asthmatic response (see Fig. 25.10).[100] The late asthmatic response is characterized by increasing influx and activation of inflammatory cells such as mast cells, eosinophils, and lymphocytes.[100,101]

Clinical Presentation and Diagnosis

The diagnosis of asthma requires a two-pronged approach of clinical assessment supported by laboratory evaluation. Because no single measurement can absolutely establish the diagnosis, and physical examination can be entirely normal between episodes, the history plays a key role in suggesting, and later establishing, the diagnosis of asthma. The classic symptoms of asthma are episodic wheezing, shortness of breath, chest tightness, and cough. The absence of wheezing does not exclude asthma, and sometimes a cough can be the only manifestation. Not all wheezing is due to asthma, however. Partial obstruction of the upper airway by tumors, laryngospasm, aspirated foreign objects, tracheal stenosis, fluid from left (congestive) heart failure or functional laryngospasm (vocal cord dysfunction) can mimic the wheezing of asthma.

Confirmation of the diagnosis of asthma requires demonstration of a component of reversible airflow obstruction. PFTs may be normal in asymptomatic patients with asthma, but more commonly they reveal some degree of airway obstruction

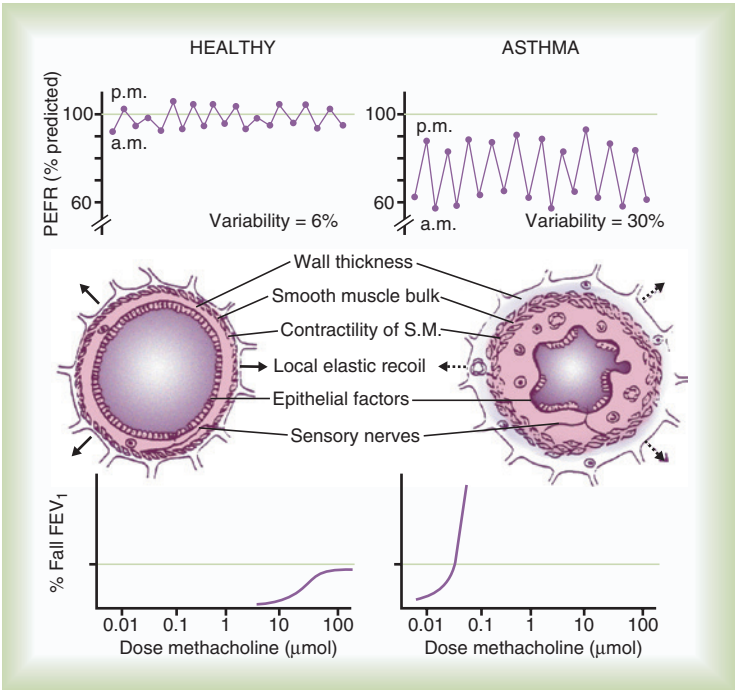


Fig. 25.9 Inflammation in Asthma. Cross sections of an airway from a healthy individual and a patient with asthma are shown. Multiple cells and multiple mediators are involved in asthma. Inflammatory cells, such as mast cells, eosinophils, lymphocytes, and macrophages, release a variety of chemical mediators, such as histamine, prostaglandins, and leukotrienes. These mediators result in increased wall thickness, airway smooth muscle hypertrophy and constriction, epithelial sloughing, mucus hypersecretion, mucosal edema, and stimulation of nerve endings. *Top,* Daily variability in peak airflow measurements. The normal increase in smooth muscle tone in the early morning, which causes airway narrowing in healthy individuals, is more exaggerated in asthmatics. *Bottom,* Dose-response curves to methacholine. *FEV_1*, forced expiratory volume in 1; *PEFR*, peak expiratory flow rate. (Modified from Woolcock AJ: Asthma. In: Murray JF, Nadel JA, editors: *Textbook of Respiratory Medicine*, Philadelphia, 1994, Saunders.)

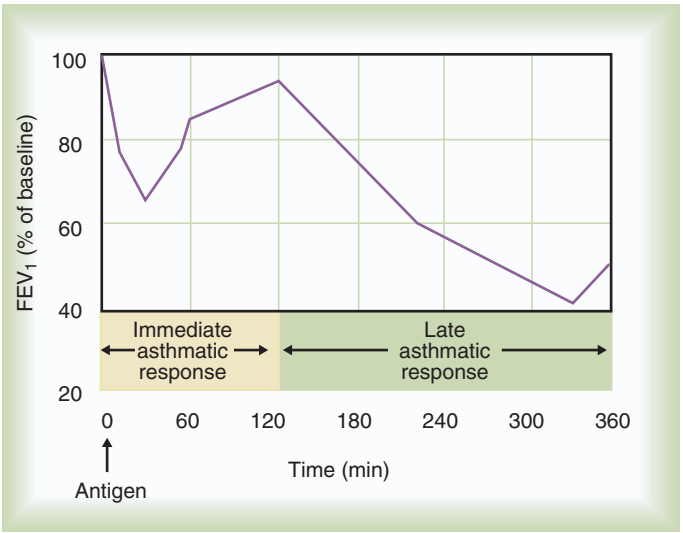


Fig. 25.10 Early and Late Asthmatic Responses. When a person with asthma is exposed to an allergen to which he or she is sensitized, the challenge results in a biphasic decline in respiratory function. An early asthmatic response occurs within minutes and usually subsides within 2 hours. In approximately half of asthmatic patients, a late asthmatic response occurs within 3 to 8 hours and may last for 24 hours or longer. *FEV_1*, Forced expiratory volume in 1. (Modified from Wiedemann HP, Kavuru MS: *Diagnosis and management of asthma*, Caddo, OK, 1994, Professional Communications.)

manifested by a decreased FEV_1 and FEV_1/FVC ratio. By convention, improvement in the FEV_1 by at least 12% and 200 mL after administration of a short-acting bronchodilator is considered evidence of reversibility. Spontaneous variation in self-recorded PEFR by 15% or more can also provide evidence of reversibility of airway obstruction. Elevated values of exhaled nitric oxide can also be used to support the diagnosis of asthma when eosinophilic inflammation is present.[102]

Patients with asthma evaluated in a symptom-free period may have a normal chest x-ray and normal PFTs. Under these circumstances, provocative testing can be used to induce airway obstruction. Bronchoprovocation is a well-established method to detect and quantify AHR. Pharmacologic agents, including acetylcholine, methacholine, histamine, cysteinyl leukotrienes, and prostaglandins, and physical stimuli such as exercise and isocapnic hyperventilation with cold, dry air have been used to detect, quantify, and characterize nonspecific AHR in asthma.

The most commonly used stimulus for bronchoprovocation is methacholine. The generally accepted criterion for hyperresponsiveness is a decrease in FEV_1 by 20% or more below the baseline value after inhalation of methacholine.

Elevated IgE levels and eosinophilia may be present in patients with asthma, but their presence is not specific and their absence does not exclude asthma, making them less useful for the diagnosis.[94-96] Although ABG analysis is not helpful or necessary

MINI CLINI

Recognizing Severity of Asthma

Problem

A 20-year-old woman with a diagnosis of asthma is seen in the outpatient clinic for increased dyspnea with exertion requiring daily use of short-acting bronchodilators. The patient complains of difficulty attending classes in college and wakes up a couple of times a week feeling short of breath. She describes two visits to the emergency department in the last 12 months because of asthma, requiring use of corticosteroids for a short period. Physical examination shows normal breath sounds bilaterally without wheezing. Spirometry shows FEV_1 of 78% predicted with FEV_1/FVC of 75%. How do you describe the severity of her asthma?

Solution

Classification of asthma severity is based on a combination of symptoms, medication requirements, and lung function. Although this patient has a spirometry consistent with mild airflow obstruction, her asthma is classified as moderately persistent because of the presence of daily symptoms, daily use of short-acting bronchodilators, frequent nighttime awakenings, limitation with normal activities, and history of exacerbations (see the following table).

Classification of Asthma Severity (Youths ≤12 Years of Age and Adults)

			PERSISTENT		
Components of Severity		**Intermittent**	**Mild**	**Moderate**	**Severe**
Impairment	Symptoms	≤2 days/wk	>2 days/wk but not daily	Daily	Throughout the day
FEV_1/FVC:	Nighttime awakenings	≤2 times/mo	3–4 times/mo	>1 time/wk but not nightly	Often 7 times/wk
18–19 years, 85%	Short-acting β-2 agonist use for	≤2 days/wk	>2 days/wk but not >1	Daily	Several times per day
20–39 years, 80%	symptom control (not prevention of		time/day		
40–59 years, 75%	exercise-induced bronchospasm)				
60–80 years, 60%	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
	Lung function	Normal FEV_1 between exacerbations	FEV_1 ≥80% predicted	FEV_1 ≥60% but <80% predicted	FEV_1 ≥60% predicted
			FEV_1/FVC normal	FEV_1/FVC reduced >5%	FEV_1/FVC reduced >5%
		FEV_1 >80% predicted			
		FEV_1/FVC normal			
		0–1/year	≥2/year		
		Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time for patients in any severity category.			
Risk	Exacerbations requiring oral systemic corticosteroids	Relative annual risk for exacerbations may be related to FEV_1.			

in diagnosing asthma, it can be helpful in assessing the severity of an acute asthma attack.

A patient experiencing an acute asthma attack usually has a low $PaCO_2$ as a result of hyperventilation. A normal $PaCO_2$ in such a situation is concerning because it indicates a severe attack and potential impending respiratory failure.

Management

The goal of asthma management is to maintain a high quality of life for the patient, uninterrupted by asthma symptoms, side effects from medications, or limitations on the job or during exercise. This goal can be accomplished by preventing acute exacerbations, with their potential mortality and morbidity, or by returning the patient to a stable baseline when exacerbations occur. Asthma management relies on the following four important components recommended by the National Asthma Education Program (NAEP) expert panel[94]:

1. Objective measurements and monitoring of lung function
2. Pharmacologic therapy
3. Environmental control
4. Patient education

Table 25.2 outlines the stepwise approach currently recommended for long-term management of asthma. This approach provides a framework for adjusting the dose of medication based on the severity of asthma in any patient at a particular time. This approach also takes into consideration the fact that asthma is a chronic and dynamic disease, which needs optimum control. Control of asthma is defined as minimal to no chronic diurnal or nocturnal symptoms, infrequent exacerbations, minimal to no need for β-2 agonists, no limitation to exercise activity, PEFR or FEV_1 greater than 80% predicted with less than 20% diurnal variation, and minimal to no adverse effects of medication.[94-96]

Objective Measurement and Monitoring

Objective measurement of lung function is particularly important in asthma because subjective measures, such as patient reports of the degree of dyspnea and physical examination findings, often do not correlate with the variability and severity of airflow obstruction. Spirometry is recommended as part of the initial assessment of all patients being evaluated for asthma and periodically thereafter as needed.

Either spirometry or PEFR measurement can be used to assess response to therapy in the outpatient setting, emergency department, or hospital. NAEP guidelines also recommend that home PEFR measurement be used for patients with moderate to severe asthma.

When patients learn how to take PEFR measurements at home, the clinician is better able to recommend effective treatment.

TABLE 25.2 Stepwise Approach to Long-Term Management of Asthma Based on Severity

Severity[a]	Clinical Features Before Treatment[b]	PEFR or FEV_1	Long-Term Preventive Medications	Quick Relief Medications
Step 4				
Severe persistent	Continuous symptoms	≤60% predicted	Inhaled corticosteroids ≥800–2000 mcg/day	Inhaled β-2 agonist as needed for symptoms
Red zone	Frequent exacerbations Nocturnal symptoms Symptoms limit activity	>30% variability	Long-acting bronchodilator[c] Oral corticosteroids	
Step 3				
Moderate persistent	Daily symptoms	>60%–<80% predicted	Inhaled corticosteroids ≥800–2000 mcg/day	Inhaled β-2 agonist as needed for symptoms, not to exceed 3–4 times per day
Yellow zone	Exacerbations affect activity and sleep Nocturnal symptoms more than once per week Daily use of short-acting β-2 agonist	>30% variability	Long-acting bronchodilator,[c] especially for nocturnal symptoms	
Step 2				
Mild persistent	Symptoms at least once per week but less than once per day	≥80% predicted	Inhaled corticosteroid, 200–500 mcg/day	Inhaled β-2 agonist as needed for symptoms, not to exceed 3–4 times per day
Yellow zone	Exacerbations may affect activity or sleep Nocturnal symptoms more than twice per month	20%–30% variability	Long-acting bronchodilator[c] for nocturnal symptoms	
Step 1				
Intermittent	Intermittent symptoms less than once per week	≥80% predicted	None needed	Inhaled β-2 agonist needed for symptoms but less than once per week
Green zone	Nocturnal symptoms not more than twice per month Asymptomatic with normal lung function between exacerbations	<20% variability		Inhaled β-2 agonist before exercise or exposure to allergen

[a]*Step-down:* Review treatment every 3–6 months. If control is sustained for at least 3 months, consider a gradual stepwise reduction in treatment. *Step-up:* If control is not achieved, consider step-up, but first review patient medication technique, compliance, and environmental control.
[b]The presence of one of the features of severity is sufficient to place a patient in that category.
[c]Long-acting β-2 agonist.
FEV_1, Forced expiratory volume in 1; *PEFR*, peak expiratory flow rate.
Modified from National Asthma Education and Prevention Program: Expert panel report 3 (EPR-3): guidelines for the diagnosis and management of asthma—summary report 2007. *J Allergy Clin Immunol* 120(Suppl):S94–S138, 2007.

Though somewhat effort-dependent, daily monitoring of PEFR helps detect early stages of airway obstruction. All PEFR measurements are compared with the patient's personal best value, which can be established during a 2- to 3-week asymptomatic period when the patient is being treated optimally.[94-96]

To help patients understand home PEFR monitoring, a zonal system corresponding to the traffic light system may be helpful (see Table 25.2). A PEFR measurement of 80% to 100% of the personal best is considered to be in the *green zone*. No asthma symptoms are present, and maintenance medications can be continued or tapered. A PEFR in the 60% to 80% range of the personal best is in the *yellow zone* and may indicate an acute exacerbation and requires a temporary step-up in treatment. A PEFR less than 60% of the personal best is in the *red zone* and signals a medical alert, requiring immediate medical attention if the patient does not return to the yellow zone or green zone with bronchodilator use.[90]

Pharmacotherapy

Pharmacotherapy for asthma is detailed in Chapters 36 and 40; however, the foundation for such therapy includes antiinflammatory agents such as corticosteroids that suppress the primary disease process and its resultant airway hyperreactivity.[105] Bronchodilators such as β-2–adrenergic agonists and anticholinergics relieve asthma symptoms. Owing to the fact that asthma is a disease of the airways, inhalation therapy is preferred to oral or other systemic therapy. Inhaled therapy using metered dose inhalers or dry powder inhalers allows high concentration of the medication to be delivered directly to the airways, resulting in fewer systemic side effects. Spacer devices can be used to

MINI CLINI

Asthma Management

Problem

You are asked to see a new patient in clinic with a history of asthma. The patient is a 22-year old female who presents 4 weeks after a visit to the emergency room owing to an asthma exacerbation. She completed a course of oral corticosteroids and reports her symptoms have improved but she continues to have nighttime awakenings 2 times a week as well as having to use a short-acting β agonist daily. She is not currently on a maintenance inhaler. Further questioning reveals that she recently started working at a florist and she has 1 cat and 1 dog.

Discussion

Based on the patient's clinical symptoms she is classified as moderate persistent asthma (see Table 25.2), which warrants maintenance inhaler therapy. Initial pharmacologic therapy can include a low-dose inhaled corticosteroid plus a long acting β agonist, leukotriene receptor antagonist, or theophylline, or medium-dose inhaled corticosteroid (see Table 25.2).

The patient should also be assessed for inhaler technique, as well as undergo asthma education and peak flow monitoring. Adherence should be assessed because on average most asthma patients have an adherence of 22% to 63% for their maintenance inhalers.[103] Assessment for environmental control is important because the patient describes having pets as well as a possible occupational exposure. The patient should be assessed for allergies and comorbid atopic diseases such as allergic rhinitis. She should monitor peak flows in her home as well as at her job to assess for occupational asthma.

MINI CLINI

Diagnosis of Wheezing

Problem

You are asked to see a patient with a history of wheezing. The patient notes that the wheezing has been continuous, has been present for several months, and has not responded to bronchodilator medications, including systemic corticosteroids and various inhaled bronchodilators.

Solution

The patient has either refractory asthma or a condition mimicking asthma. The aphorism "all that wheezes is not asthma" applies here, and the clinician should suspect alternative diagnoses. Features that are atypical for asthma in this patient are the continuous nature of the wheezing and its complete refractoriness to medication. With this in mind, consideration of other "wheezy" disorders should include abnormalities of the upper airway. Specifically, tracheal stenosis or fixed upper airway obstruction (e.g., caused by tracheal tumors) could account for the patient's symptoms. Another condition that mimics asthma is vocal cord dysfunction. Characteristically, vocal cord dysfunction causes stridor with convergence of the vocal cords on inspiration (a paradoxical response); however, vocal cord dysfunction can also cause expiratory wheezing, with closure of the vocal cords on expiration. Further assessment of this patient might include a flow-volume loop or a flexible bronchoscopic examination of the upper airway, observing both the vocal cords and the trachea to the level of the main stem bronchi.

Another important disease that can mimic asthma is congestive heart failure (CHF), which has been known to cause "cardiac wheezing." Distinguishing heart failure from asthma can be challenging because patients with CHF may not only wheeze but also exhibit transient AHR. Patients with severe CHF have abnormalities on their PFT as well, such as restrictive defects, obstruction, or inspiratory muscle weakness.[104] To distinguish between asthma and CHF, a simple physical examination (e.g., looking for rales that would suggest CHF, edema) and a chest x-ray (which might show cardiomegaly or pleural effusions in CHF), or lack of improvement from bronchodilator therapy, are ways to help the clinician distinguish CHF from asthma.

improve delivery of inhaled medication, but training and coordination are still required for patients using metered dose inhalers. Table 25.3 lists commonly used medications in the treatment of asthma. See Chapter 36 for more details on pharmacotherapy and Table 25.4 for a summary of common medications in asthma.

Anti–Immunoglobulin E Therapy

IgE plays a key role in the pathogenesis of asthma, and many asthmatic patients have elevated levels of IgE.[113] Corticosteroids do not inhibit synthesis of IgE by activated lymphocytes. Omalizumab, an antibody that binds IgE and blocks its biologic effects, has been approved by the FDA for patients with a history of perennial allergy and with moderate to severe asthma that is poorly controlled with inhaled corticosteroids.[114] Studies have shown that treatment with omalizumab allows reduction of the dose of inhaled glucocorticoids required to control symptoms and also a decrease in the number of asthma exacerbation episodes.[115] For this reason, the NAEP asthma guidelines recommend that omalizumab should be considered as adjunctive therapy for patients with severe persistent asthma.[94]

Anti-Interleukin 5 Therapy

IL-5 is a cytokine that promotes eosinophilic inflammation of the airway. There are three approved agents that target IL-5 or its receptor to reduce the impact of IL-5: mepolizumab and reslizumab (anti-IL-5 monoclonal antibodies) and benralizumab (an anti-IL-5 receptor α antibody). Mepolizumab has been shown to decrease oral corticosteroid use and reduce exacerbations in patients with severe persistent asthma and an eosinophilic phenotype (i.e., asthma characterized by a high peripheral eosinophil count on blood testing). Currently, mepolizumab is FDA-approved for add-on maintenance treatment of severe persistent asthma, and the NICE (National Institute for Health and Care Excellence) guidelines recommend a threshold eosinophil count of >300/μL for its use. Reslizumab is also approved by the FDA as add-on maintenance treatment for severe eosinophilic asthma (eosinophil count >400/μL).[116-122]

Benralizumab is FDA-approved as add-on for severe eosinophilic asthma (>300/μL) as well. Benralizumab works in a slightly different way than the other two drugs, in that it blocks the IL-5 receptor on immune cells and is considered to be more effective in lowering the number of eosinophils. Benralizumab has also been shown to reduce asthma exacerbations.[123,124]

Emergency Department and Hospital Management of Asthma

Emergency management of acute asthma should include early and frequent administration of aerosolized β-2 agonists and therapy with systemic corticosteroids. Frequent assessment for response with PEFR should be performed. The NAEP guidelines recommend that only selective β-2 agonists (i.e., albuterol, levalbuterol, pirbuterol) should be used in high doses to avoid cardiotoxicity.[94]

TABLE 25.3 Medications Commonly Used in the Treatment of Asthma or Chronic Obstructive Pulmonary Disease

Medication	Trade Names	Available Preparations	Usual Dosage	Comment
Inhaled Corticosteroids (Single Medication)				
Beclomethasone	Qvar	MDI 40, 80 mcg/inh 120 inh/unit	40–320 mcg bid	
Budesonide	Pulmicort Flexhaler	DPI 90, 180 mcg/inh, 120 inh/unit	360–720 mcg bid	
	Pulmicort Nebulizer	0.25, 0.5, 1 mg/2 mL single-dose ampules	0.5–2 mg bid	
Ciclesonide	Alvesco	MDI 80, 160 mcg/inh, 60 inh/unit	80–320 mcg bid	
Flunisolide	Aerospan	MDI 80 mcg/inh, 120 inh/unit	160–320 mcg bid	
Fluticasone furoate	Arnuity	DPI 100, 200 mcg/inh, 30 inh/unit	100–200 mcg daily	
Fluticasone propionate	Flovent diskus	DPI 50, 100, 250 mcg/blister, 60 inh/unit	100–1000 mcg bid	
	Flovent MDI	MDI 44, 110, 220 mcg/inh, 120 inh/unit	88–880 mcg bid	
	ArmonAir Respiclick	DPI 55, 113, 232 mcg/inh, 60 inh/unit	55–232 mcg bid	
Mometasone furoate	Asmanex MDI	MDI 100, 200 mcg/inh, 120 inh/unit	200–400 mcg bid	
	Asmanex Twisthaler	DPI 110, 220 mcg/inh, 30, 60, 120 inh/unit	220–880 mcg once/day in evening or 220 mcg bid	
Inhaled Corticosteroids (Combined Medication)				
Budesonide and formoterol	Symbicort	MDI 80,160 mcg/4.5 mcg/inh 60, 120 inh/unit	2 inh bid	
Fluticasone furoate and vilanterol	Breo Ellipta	DPI 100, 200 mcg/25 mcg/inh 30 inh/unit	1 inh daily	
Fluticasone propionate and salmeterol	Advair diskus	DPI 100, 250, 500 mcg/50 mcg/blister, 60 inh/unit	1 inh bid	
	Advair HFA		2 inh bid	
	AirDuo Respiclick	MDI 45, 115, 230 mcg/21 mcg/inh 60, 120 inh/unit	1 inh bid	
		DPI 55, 113, 232 mcg/14 mcg/inh, 60 inh/unit		
Mometasone and formoterol	Dulera	MDI 100, 200 mcg/ 5 mcg/inh 60, 120 inh/unit	2 inh bid	
Systemic Corticosteroids				
Prednisone	Many	Tablets 1, 5, 20, 50 mg	5–50 mg/day	
Methylprednisolone	Medrol	Tablets 2, 4, 8, 16, 24, 32 mg	4–48 mg/day	
	Solu-Medrol	IV 40, 125, 500, 1000 mg	1–2 mg/kg q4–6h	
Hydrocortisone	Solu-Cortef	IV 100, 250, 500, 1000 mg	4 mg/kg q4–6h	
Short Acting β-2 Agonists (SABAs)				
Albuterol				
	ProAir HFA	MDI 90 mcg/inh, 200 inh/unit	1–2 inh q4–6h prn	
	Proventil HFA	MDI 90 mcg/inh, 200 inh/unit	1–2 inh q4–6h prn	
	Ventolin HFA	MDI 90 mcg/inh, 200 inh/unit	1–2 inh q4–6h prn	
	ProAir Respiclick	DPI 90 mcg/inh, 200 inh/unit	1–2 inh q4–6h prn	
	Nebulizer	0.63, 1.25, 2.5 mg/3 mL solution	1.25–5 mg q4–8h prn	
		Tablets 2, 4 mg	2–4 mg q6–8h	
	Volmax	Sustained-release tablets 4, 8 mg	4–8 mg q12h	
Levalbuterol	Xopenex HFA	MDI 45 mcg/inh	2 inh q4–6h prn	
	Xopenex Nebulizer	80, 200 inh/unit	0.63–1.25 mg q6–8h prn	
		0.31, 0.63, 1.25 mg/3 mL solution		
Metaproterenol	Alupent	MDI 650 mcg/puff, 200 puffs/canister	2–3 puffs q3–4h, maximum 12 puffs/day	
	Metaprel	Solution 0.5%	2.5–10 mg q4–6h	
		Tablets 10, 20 mg	10 mg q6–8h	
Pirbuterol	Maxair	MDI 200 mcg/puff, 300 puffs/canister	1–2 puffs q4–6h, maximum 12 puffs/day	
Terbutaline	Breathaire	MDI 200 mcg/puff, 300 puffs/canister	1–2 puffs q4–6h	
	Bricanyl	Tablets 2.5, 5 mg	2.5–5 mg tid, maximum 15 mg/day	
		Solution 1 mg/mL	0.25 mg subcutaneously q15–30 min	

TABLE 25.3 MedicationsCommonly Used in the Treatment of Asthma or Chronic Obstructive Pulmonary Disease—*cont'd*

Medication	Trade Names	Available Preparations	Usual Dosage	Comment
Short-Acting β-2 Agonists/Short-Acting Antimuscarinic Combination (SABA/SAMA)				
Albuterol and ipratropium	Combivent Respimat Nebulizer	Respimat 100 mcg/20 mcg/inh, 120 inh/unit 2.5 mg/0.5 mg/3 mL solution	1 inh q6h prn 2.5/0.5 mg q6h as needed	
Long-Acting β-2 Agonists (LABAs)				
Arformoterol	Brovana	Solution 15 mcg/mL	15 mcg inhaled bid	
Formoterol	Perforomist Nebulizer	20 mcg/2 mL solution	20 mcg bid	
Indacaterol	Arcapta Neohaler	DPI 75 mcg/capsule, 30 inh/unit	1 inh daily	Not indicated in patients with asthma.
Olodaterol	Striverdi Respimat	Respimat 2.5 mcg/inh, 60 inh/unit	2 inh daily	
Salmeterol	Serevent Diskus	DPI 50 mcg/blister 28, 60 inh/unit	1 inh bid	
Short-Acting Antimuscarinic agents (SAMAs)				
Ipratropium bromide	Atrovent HFA Nebulizer	MDI 17 mcg/inh, 200 inh/unit 200 mcg/mL, 0.5 mg/2.5 mL vial	2 inh q6h prn 0.5 mg q6h prn	
Long-Acting Antimuscarinic Agents (LABAs)				
Aclidinium	Tudorza pressair	DPI 400 mcg/inh 30,60 inh/unit	1 inh/bid	M_2/M_3 muscarinic antagonist. Only approved for COPD.
Tiotropium	Spiriva Handihaler Spiriva Respimat	DPI 18 mcg/capsule 30, 90 inh/unit Respimat 2.5 mcg/inh 60 inh/unit	18 mcg daily (two inh of the contents of one capsule) 2 inh daily	
Umeclidinium	Incruse Ellipta	DPI 62.5 mcg/inh 30 inh/unit	1 inh daily	
Long-Acting Antimuscarinic Agent / Long-Acting β 2 Agonist Combination (LAMA/LABA)				
Glycopyrrolate and formoterol fumarate	Bevespi aerosphere	MDI 9 mcg/4.8 mcg/inh	2 inh bid	Not approved for patients with asthma.
Glycopyrrolate and indacaterol	Utibron Neohaler	DPI 15.6 mcg/27.5 mcg/capsule 60 inh/unit	1 inh bid	Not approved for patients with asthma.
Tiotropium and olodaterol	Stiolto Respimat	Respimat 2.5 mcg/2.5 mcg/inh, 60 inh/unit	2 inh daily	Not approved for patients with asthma.
Umeclidinium and vilanterol	Anoro Ellipta	DPI 62.5 mcg/25 mcg/inh, 30 inh/unit	1 inh daily	Not approved for patients with asthma.
Combined Medication (Anticholinergic + Long Acting β Agonist + Inhaled Corticosteroid)				
Fluticasone furoate and umeclidium and vilanterol	Trelegy Ellipta	DPI 100 mcg/62.5 mcg/25 mcg/inh	1 inh once/day	Not approved for asthma.
Methylxanthines				
Aminophylline		IV Tablets or capsules	Load 5–6 mg/kg, maintenance 0.5–0.9 mg/kg/h	
Theophylline	Theo-Dur Slo-bid Theovent Uniphyl (immediate or sustained release)		300–1200 mg/day divided q6–8h For immediate and q12–24h For sustained	

Continued

TABLE 25.3 MedicationsCommonly Used in the Treatment of Asthma or Chronic Obstructive Pulmonary Disease—*cont'd*

Medication	Trade Names	Available Preparations	Usual Dosage	Comment
Leukotriene Inhibitors				
Zafirlukast	Accolate	Tablets 20 mg	20 mg bid	
Zileuton	Zyflo	Tablets 600 mg	600 mg qid	
Montelukast	Singulair	Tablets 10 mg	10 mg daily	
Other				
Roflumilast	Daliresp	Tablets 500 mcg	500 mcg/day 250 mcg/day for the first 4 weeks is FDA approved because it is shown to decrease rates of discontinuing the medication owing to side effects.	PDE-4 inhibitor. Primary use prevention of COPD exacerbations, not indicated for acute bronchospasm or asthma.
Azithromycin	Zithromax	Tablets 250 mg, 500 mg	250 mg/day	Macrolide antibiotic associated with reduction in number of COPD exacerbations.[a]
N-Acetylcysteine (NAC)	Mucomyst	Tablets 300 mg, 600 mg	1200 mg/day	High-dose NAC is associated with decrease in exacerbation frequency in patients COPD.[b]
Omalizumab	Xolair	150 mg/5 mL	150–375 mg subcutaneously every month	Anti-IgE therapy only approved for patients with moderate to severe asthma
Mepolizumab	Nucala	100 mg SC	100 mcg subcutaneously (SC) every 4 weeks	Anti-IL-5 therapy for severe asthma with eosinophilic phenotype
Reslizumab	Cinqair	3 mg/kg IV	3 mg/kg IV every 4 weeks	Anti-IL-5 therapy for severe asthma with eosinophilic phenotype
Benralizumab	Fasenra	30 mg SC	30 mg SC start every 4 weeks × 3 doses then every 8 weeks	Anti-IL-5 receptor α antibody for severe asthma with eosinophilic phenotype

[a]Albert RK, Connett J, Bailey WC, et al: Azithromycin for prevention of exacerbations of COPD. *N Engl J Med* 365:689–698, 2011.
[b]Zheng JP, Wen FQ, Bai CX, et al: Twice daily N-acetylcysteine 600 mg for exacerbations of chronic obstructive pulmonary disease (PANTHEON): a randomised, double-blind placebo-controlled trial. *Lancet Respir Med* 2:187–194, 2014.
COPD, Chronic obstructive pulmonary; *DPI,* dry powder inhaler; *HFA,* hydrofluoroalkane; *IgE,* immunoglobulin E; *inh,* inhalations; *MDI,* metered dose inhaler.

Hospital and ICU care for patients with asthma should be aggressive. The goal is to decrease mortality and morbidity and to return the patient to preadmission stability and function as quickly as possible. Management includes supplemental O_2, as needed for hypoxemia periodic or short-term continuous administration of high doses of aerosolized β-2 agonists (limited only by tachycardia or tremor), high-dose parenteral corticosteroids (>0.5 to 1 mg/kg per day), and antibiotics if there is evidence of infection. Sedatives and hypnotics should be avoided. Symptoms, PEFR, and ABGs should be monitored.

For status asthmaticus, heliox (mixture of helium and O_2) can be combined with bronchodilator therapy. A pediatric study showed improved clinical asthma scores with this mixture, although the rates of emergency department discharge versus pediatric ICU admission were not significantly different.[125] As detailed in Chapters 6 and 42, the driving pressure is lowered in the large airways when a low density gas mixture is used, such as helium. Heliox-powered nebulization improves aerosol deposition owing to a reduction in turbulence, and the low density of helium allows the gas flow to be increased from 6 L/min to 10 to 12 L/min.

Patients with severe asthma and respiratory failure (hypoxemia, hypercapnia, increased work of breathing) need ventilatory support and present special challenges. Mortality rates for these patients can reach 22%, and complications are common, especially barotrauma. These complications can be minimized by reducing plateau pressure to <28 cm H_2O and driving pressure to <15 cm H_2O and by using small tidal volumes, allowing "permissive hypercapnia" if necessary.

Intravenous magnesium sulfate has bronchodilating properties and has been shown to improve pulmonary function in patients with severe asthma.[126] Other adjunctive therapies for status asthmaticus include inhalational anesthetic agents like isoflurane or halothane, which are known to bronchodilate, although these have never been evaluated in randomized clinical trials.[127]

TABLE 25.4 Summary of Common Medications Used in Asthma

Medication	Mechanism	Adverse Reactions/Side Effects
Inhaled corticosteroids (ICS)	First line for moderate persistent asthma. Act on various components of the inflammatory response in asthma. Decrease bronchial hyperreactivity and airflow obstruction. Reduce symptoms and mortality from asthma.[105]	Long-term high-dose ICS have fewer side effects than oral corticosteroids. Side effects like oropharyngeal candidiasis and dysphonia and controllable with spacer and rinsing the mouth after each treatment. Other side effects include skin bruising, increased risk for glaucoma and cataracts.
Oral corticosteroids	Effective to reduce the severity and duration of an asthma exacerbation, decrease emergency room visits and hospitalization, and reduce mortality.[105] Should be avoided as a long-term therapy owing to risk of side effects. If giving long-term, can consider antibiotic prophylaxis.	Skin bruising, risk for glaucoma and cataracts, osteoporosis, adrenal suppression, immunosuppression.
Leukotriene inhibitors (montelukast, zafirlukast, zileuton)	Mediators of inflammation and bronchoconstriction that play a role in the pathogenesis of asthma. Are all modestly effective for maintenance of mild to moderate asthma, but do not cause bronchodilation. Helps to reduce ICS dose especially in the treatment of children.[106,107]	Headaches, hypersensitivity reaction, influenza-like syndrome. May cause or "unmask" the diagnosis of eosinophilic granulomatosis with polyangiitis.[108]
β-2 adrenergic agonists	The most rapid and effective bronchodilators for treating acute bronchospasm, and can be given prophylactically for bronchoconstrictor challenges like exercise. They act by attaching to β receptors and cause smooth muscle relaxation and block mediator release from mast cells.	Do not prevent the late asthmatic response. Long-acting should not be used alone for maintenance therapy and must be combined with an ICS owing to concern for increased risk of death,[94-96,109-111] although short-acting β agonists remain safe.[101,103,105]
Methylxanthines (theophylline)	Added to long-term asthma management therapy and may be helpful in controlling nocturnal symptoms.	Efficacy limited by side effects of nausea, vomiting, headache, insomnia, seizures, and cardiac arrhythmias. Toxicity increases with blood levels greater than 15 mcg/mL. Levels of 8–10 mcg/mL are adequate for long-term therapy and associated with fewer side effects. Conditions that increase levels include acute viral infections, cardiac failure, hepatic disease, and use of medications like erythromycin or cimetidine. In these cases, the maintenance dose should be halved and blood levels monitored. Conditions that decrease levels include cigarette smoking and medications that increase hepatic clearance, like phenobarbital.[94-96]
Short-acting antimuscarinic agents (ipratropium)	Bronchodilates by reduction of intrinsic vagal tone and blocking vagal reflex. Adds bronchodilator affect to β 2 agonists and useful for treating cough-variant asthma.	Does not stabilize mast cells or prevent mediator release. Less potent of a bronchodilator than β 2 agonist.
Long-acting antimuscarinic agents (tiotropium)	Been shown to enhance asthma control (e.g., improved peak expiratory flow, increased FEV_1, and improved symptoms) when added to an inhaled corticosteroid compared with doubling the inhaled steroid dose.[112]	

FEV_1, Forced expiratory volume in 1.

When asthma control is achieved, hospital discharge criteria include not needing supplemental O_2; having a PaO_2 greater than 60 mm Hg and a stable PEFR or FEV_1, with values close to the patient's best or >70% of predicted; feeling that asthma symptoms are returning to preadmission levels and are not occurring at night; and 12- to 24-hour stability on discharge medications.[94-96]

RULE OF THUMB In a patient presenting with an acute asthma attack, $PaCO_2$ is usually low because of hyperventilation. A normal $PaCO_2$ in this situation indicates a severe attack and potential impending respiratory failure.

Bronchial Thermoplasty

Bronchial thermoplasty is an approved addition to treatment options for adults whose asthma remains uncontrolled despite use of inhaled steroids and long-acting β agonists.[128] Bronchial thermoplasty is a procedure in which a probe is introduced into the central airways through a bronchoscope and heat is applied (through radiofrequency waves) to airways of 3 to 10 mm diameter with the goal to reduce the airway smooth muscle mass, reducing the ability of the airways to constrict. Studies have shown that bronchial thermoplasty, in selected patients with documented airway hyperreactivity and FEV_1 >60%, improves asthma-specific quality of life and reduces the number of severe asthma exacerbation episodes and emergency department visits.[129,130] Moreover, data suggest that these effects are long-lasting (approximately 5 years) with regard to both asthma control (based on maintained reduction in severe exacerbations and emergency department visits for respiratory symptoms) and safety.[131] Bronchial thermoplasty was approved for use by the FDA in 2010. Bronchial thermoplasty is performed in specialized centers and a registry is maintained to understand the outcomes of patients who underwent this novel procedure.[132]

MINI CLINI

Assessing the Severity of an Acute Asthma Attack

Problem

You have just obtained an ABG analysis on a patient who sought treatment at the emergency department for an acute attack of asthma. How would the ABG analysis help you assess the severity of the attack?

Solution

In the early stages of an asthma attack, the ABG analysis shows a low $PaCO_2$ caused by hyperventilation. As the asthma attack progresses and the FEV_1 decreases to <25% of predicted, the $PaCO_2$ returns to normal. When the FEV_1 decreases to <15% of predicted, carbon dioxide retention begins to occur. Changes in the pH reflect changes in the $PaCO_2$ level. The following table summarizes the ABG abnormalities based on the severity of an asthma attack:

Asthma Attack Severity	Stage	PaO_2	$PaCO_2$	pH
Mild	I	Normal	Decreased	Increased
Moderate	II	Decreased	Decreased	Increased
Severe	III	Decreased	Normal	Normal
Very severe (respiratory failure)	IV	Decreased	Increased	Decreased

Immunotherapy

Immunotherapy (called "allergy shots" by patients) is based on the theoretical rationale that part of the immunologic response to an administered allergen is the production of an IgG-specific antibody to the allergen injected. This newly generated IgG does not affix to most cells but can react with the allergen diffusing into the tissues and "neutralize" it. Although immunotherapy is acceptable in the treatment of allergic rhinitis, its use in the treatment of asthma is not standardized and remains controversial; however, a meta-analysis of 88 randomized controlled trials of injection allergen immunotherapy for asthma reported that immunotherapy is effective, with evidence of significant reductions in asthma medications and symptoms and a reduction in the degree of bronchial hyperreactivity.[133]

Environmental Control

The association between asthma and allergy has long been recognized. Among patients with asthma, 75% to 85% are reported to have positive immediate skin test reaction to common inhalant allergens. A thorough history is essential to diagnosing whether a patient's asthma has an allergic component and determining the relationship between exposure to an allergen and the occurrence of symptoms. Skin tests are more helpful for excluding an allergen as a cause of asthma symptoms because clinical sensitivity to an aeroallergen is rare in the absence of a positive skin test, whereas many positive skin tests do not have clinical relevance.

To prevent allergic reactions in patients with asthma, environmental control measures to reduce exposure to indoor and outdoor allergens and irritants are essential. Patients should be advised to avoid outdoor antigens, primarily ragweed, grass, pollens, and molds. Exposure to outdoor allergens is best reduced by staying indoors with the windows closed, in an air-conditioned environment, particularly during the midday and afternoon, when pollen and some mold counts are highest. Patients who are allergic to indoor allergens, primarily house-dust components and indoor molds, should take steps to eliminate these allergens from the home environment (e.g., single-room air purifier). All warm-blooded pets, including small rodents and birds, should be removed from the house because they produce dander, urine, and saliva that can cause allergic reactions. House-dust mites depend on atmospheric moisture and human dander for survival. Essential house-dust mite control measures include encasing mattresses and pillows in airtight covers, washing the bedding in water of 130°F weekly, avoiding sleeping on upholstered furniture, and removing carpets that are laid on concrete.

Additional helpful control measures include reducing the indoor humidity to less than 50%, removing carpets from the bedroom, and using chemical agents to kill mites. Indoor air-cleaning devices, especially high-efficiency particulate air/aerosol filters, may be useful, but they cannot substitute for controlling the allergen source. Humidifiers are potentially harmful because they can harbor and aerosolize mold spores, and the increased humidity they generate may encourage production of both mold and house-dust mites.[94-96]

Patient Education

With close back-up by the informed physician, RT, or nurse, much of the day-to-day responsibility for managing asthma falls on the patient and the patient's family. Patient education is a powerful motivational tool, helping patients attain the skills and gain the confidence to control their asthma. Patient education involves helping patients understand asthma and learning and practicing the skills necessary to manage it. Patient education includes providing information; developing a partnership with the patient; involving the patient in decision-making; and demonstrating and observing asthma management practices such as the proper use of inhalers, nebulizers, and peak flowmeters.[109]

Special Considerations in Asthma Management

Special considerations in treating asthma (e.g., during pregnancy, with gastroesophageal reflux) are summarized in Table 25.5. Other occupational causes of asthma are listed in Table 25.6.

BRONCHIECTASIS

Clinical Presentation

Bronchiectasis refers to the abnormal, irreversible dilation of the bronchi caused by destructive and inflammatory changes in the airway walls. Bronchiectasis has the following three major anatomic patterns[138]:

1. *Cylindrical bronchiectasis:* Airway wall is regularly and uniformly dilated
2. *Varicose bronchiectasis:* Irregular pattern, with alternating areas of constriction and dilation
3. *Cystic bronchiectasis:* Progressive, distal enlargement of the airways, resulting in saclike dilations

Bronchiectasis is thought to result from damage to the bronchial wall by chronic inflammation. Predisposing conditions are listed in Box 25.4.

TABLE 25.5 Special Types of Asthma and Comorbidities/Situations Associated With Asthma

Type	Definition	Management
Exercise-induced asthma	Common in asthmatics especially after participation in outdoor activities with cold weather. May be related to heat loss from the airways.[100]	Prophylactic use of a short-acting β agonist.[134,135] Can consider adding a leukotriene inhibitor.[94,95]
Occupational asthma	2%–5% of all asthma episodes may be caused by exposure to a specific sensitizing agent in the workplace. Defined as variable airflow limitation or AHR caused by causes and conditions attributable to the work environment and not to stimuli encountered outside the workplace. Toluene diisocyanate is the most common cause of occupational asthma and is the best studied. Other causes of occupational asthma are listed in Table 25.6.	The treatment of occupational asthma is identical to treatment of other types of asthma; however, early diagnosis is important and in environmental control with cessation of exposure is key. Complete elimination of exposure is usually necessary because once sensitization has occurred, bronchoconstriction can be triggered by minimal subsequent exposure.[95,100]
Cough-variant asthma	Coughing may be the only complaint of patients with asthma. In such patients, the cough may be relieved by a bronchodilator or by avoiding inhaled allergens. If bronchospasm is not present at the time of examination and spirometry is normal (which is often the case), the diagnosis can be confirmed by showing reversible airway obstruction by a methacholine challenge test or suggested by elevated levels of exhaled NO.[102]	Ipratropium bromide may be particularly helpful in the treatment of cough-variant asthma. Otherwise, treatment is the same as other types of asthma.
Nocturnal asthma	Also known as nighttime asthma, which is a characteristic problem in poorly controlled asthma and is reported by more than two-thirds of patients who receive treatment that is less than ideal. Likely is caused by the known physiologic decrease in the airway tone during sleep, which has been attributed to variation in catecholamine and cortisol secretion. Aspiration of gastric acid may also play a role in some patients with increased symptoms at night.	After ensuring adequate antiinflammatory therapy, medications should be focused toward the night and especially the early morning hours, when the airway tone is lowest. Sustained-release theophylline and long-acting β-2 agonists such as salmeterol are particularly helpful for controlling nocturnal asthma symptoms.[94] Addition of a proton pump inhibitor medication such as esomeprazole has not been shown to enhance asthma control.[136]
Aspirin sensitivity	At least 5% of adults with asthma experience severe and even fatal exacerbation of asthma after taking aspirin or other nonsteroidal antiinflammatory drugs (NSAIDs). Many of these patients have nasal polyps, although the relationship is not causal. The presumed mechanism is the inhibition of the cyclooxygenase pathway by aspirin and NSAIDs, with shunting of arachidonic acid into the 5-lipoxygenase pathway, causing overproduction of bronchoconstrictor leukotrienes.	Individuals with asthma should avoid aspirin and nonsteroidal antiinflammatory drugs (NSAIDs, e.g., ibuprofen) and instead use alternatives such as acetaminophen. Patients should be informed that many over-the-counter medications contain aspirin and should be avoided as well.[94,100]
Asthma during pregnancy	During pregnancy, one-third of patients have worse control of their asthma, one-third have better control, and one-third are unchanged. The potential threat of adverse effects from asthma medications is far outweighed by the danger of uncontrolled asthma to the fetus and mother. Poorly controlled asthma during pregnancy can cause increased pre-eclampsia, perinatal mortality, increased prematurity, and low birth weight.	Patients should be counseled about the importance of continuing their medication to maintain good asthma control during pregnancy because several studies have shown that pregnant mothers tend to reduce their asthma medications during pregnancy. β-2 agonists, inhaled or oral corticosteroids can be used during pregnancy without significant risk for fetal abnormalities.[137]
Gastro-esophageal Reflux	The relationship between asthma and gastroesophageal reflux is controversial, although reflux is nearly three times more prevalent in patients with asthma than in persons without asthma. Presumably, acid reflux into the esophagus causes vagal stimulation, resulting in a reflex increase in bronchial tone in patients with asthma.	Patients should be counseled on lifestyle modifications to improve their reflux as well as consider elevating the head of their bed at night. Routine addition of a proton pump inhibitor to an asthma regimen has not been shown to enhance asthma control significantly.[136]
Sinusitis	Acute sinusitis and chronic sinusitis have been related to exacerbations and poor control of asthma by causing postnasal drip and interfering with nasal patency.	A limited CT scan of the sinuses can be considered for patients with uncontrolled asthma. If sinusitis is present, therapy with antibiotics for 2–3 weeks, nasal decongestants, and nasal corticosteroid inhalers may help improve asthma control.[94,100]
Surgery	Patients with asthma are predisposed to respiratory complications after surgery, including respiratory arrest during induction of anesthesia, hypoxemia and possible hypercapnia, impaired effectiveness of cough, atelectasis, and respiratory infection. The likelihood of these complications depends on the severity of the patient's airway hyperreactivity, the degree of airflow obstruction, and the amount of excess airway secretions at the time of surgery.	Optimizing the patient's lung function before surgery, including the administration of perioperative corticosteroids, is an important strategy for minimizing perioperative complications.[94,100]

AHR, Airway hyperresponsiveness.

TABLE 25.6 Occupational Causes of Asthma

Occupation or Industry	Agent
Laboratory animal workers, veterinarians	Animals (dander, urine protein)
Food processing	Shellfish, egg proteins, pancreatic enzymes
Dairy farming	Storage mites
Poultry farming	Poultry mites, droppings, feathers
Detergent manufacturing	*Bacillus subtilis* enzymes
Baking	Flour
Sawmill workers, carpentry	Wood dust (western red cedar, oak, mahogany, zebrawood, redwood)
Nursing	Psyllium
Refining	Platinum salts
Plating	Nickel salts
Stainless steel welding	Chromium salts
Cosmetology	Persulfate
Refinery workers	Vanadium
Rubber processing	Formaldehyde, ethylenediamine
Plastics industry	Toluene diisocyanate, trimellitic anhydride

BOX 25.4 Causes of Bronchiectasis

Local Bronchiectasis
- Foreign body
- Benign airway tumor (e.g., adenoma)
- Bronchial compression by surrounding lymph nodes (e.g., middle lobe syndrome)

Diffuse Bronchiectasis
- Cystic fibrosis
- Ciliary dyskinesia disorders (e.g., Kartagener syndrome, Young syndrome)
- Hypogammaglobulinemia
- Alpha-1 antitrypsin deficiency
- Allergic bronchopulmonary aspergillosis
- Rheumatoid arthritis
- Sjogren syndrome
- Serious childhood lung infection (e.g., from whooping cough, measles, or influenza)

Evaluation

The hallmark of bronchiectasis is the chronic production of large quantities of purulent sputum, often following repeated respiratory infections such as those associated with cystic fibrosis. Dyspnea is variable and depends on the extent of involvement and the underlying disease. Hemoptysis occurs frequently and is usually mild, but severe hemoptysis can be seen. Radiographic studies confirm the diagnosis by showing airway dilation. A chest x-ray may show cystic spaces and tram tracks (thin parallel lines representing the airway walls). CT is the diagnostic standard for bronchiectasis; the diagnosis of bronchiectasis is established when the diameter of the bronchus exceeds the diameter of the adjacent pulmonary artery branch.[139] Owing to the fact that reversible airway changes consistent with bronchiectasis can follow pneumonia, CT should be deferred for 6 to 8 weeks after pneumonia resolves. Only then can a diagnosis of bronchiectasis be made with confidence.

Management

Antibiotics and bronchopulmonary hygiene are the mainstays of bronchiectasis management. Antibiotics can be given as needed or following a regularly scheduled regimen. Sputum cultures may be helpful in guiding antibiotic choice. Inhaled aminoglycosides may be a useful option for patients with chronic colonization by *P. aeruginosa*. Additionally, inhaled fluoroquinolones (e.g., ciprofloxacin) are currently being evaluated in patients with cystic fibrosis and non-cystic fibrosis bronchiectasis.[140] Infection by *P. aeruginosa* in patients with bronchiectasis is a marker of severity but is not linked to accelerated decline in pulmonary function.[141] Secretions can be cleared by chest physiotherapy with postural drainage, cough maneuvers, and humidification. While high-frequency chest wall oscillation vest therapy is standard of care for cystic fibrosis (CF), it has also shown some benefit in small studies of non-CF bronchiectasis for improving symptoms of breathlessness, cough and ease of sputum expectoration; some, but not all, studies have shown an improvement in FEV_1 as well. Typically, the vest treatment—which produces high-frequency, small-volume oscillations in the airways that help mobilize secretions—is given for 20 to 30 minutes twice a day.

Inhaled bronchodilators may be helpful in some patients because accompanying airflow obstruction is common, and β agonists like albuterol and salmeterol improve mucociliary clearance.[138,142] Inhaled hyperosmolar saline or mannitol may be helpful in clearing secretion in patients with bronchiectasis. A literature review concluded that dry powder mannitol improves tracheobronchial clearance in patients with bronchiectasis, patients with cystic fibrosis, those with asthma, and normal individuals.[143] Hypertonic saline has been studied to a limited extent in bronchiectasis and may be helpful. In cases that are complicated by massive hemoptysis, embolization of the bleeding bronchial artery may be helpful. Surgical resection should be reserved for the few patients with localized areas of bronchiectasis who develop massive hemoptysis or who are severely symptomatic despite appropriate medical therapy.[144-146]

ROLE OF THE RESPIRATORY THERAPIST IN OBSTRUCTIVE LUNG DISEASE

RTs play key roles in all aspects of managing patients with obstructive lung diseases; they are involved in diagnosis, acute treatment, and follow-up and monitoring. In diagnosing obstructive lung diseases, RTs often perform the lung function testing that indicates the presence of airflow obstruction that is essential for diagnosis. Because of their close involvement with patients, RTs also play important roles in recognizing clinical features such as the presence of copious secretions, hemoptysis, or other findings that may eventually lead to a confirmed diagnosis of bronchiectasis, asthma, or COPD.[147] RTs have been shown specifically to enhance the diagnosis of **alpha-1 antitrypsin deficiency** by informing patients in the Pulmonary Function Laboratory with fixed airflow obstruction or COPD patients in rehabilitation about the recommendation to be tested and the means to do so. In the current environment of value-based care in which all

healthcare providers must function at the "top of their license," RTs are increasingly at the front line of diagnosis and may be the first healthcare provider that patients see in evaluation for dyspnea.[148]

In acute management, hospital-based RTs often administer medications and therapies to patients with acute exacerbations of asthma or COPD. Examples include the delivery of bronchodilators in small-volume nebulizers, administration of chest physiotherapy in the management of bronchiectasis, and setup of supplemental O_2. For patients with severe exacerbations, ICU management of arterial lines, blood gases, and mechanical ventilation (with both noninvasive and conventional mechanical ventilation) usually involves RTs in key management roles. In managing patients with bronchiectasis, RTs are pivotal in administering chest physiotherapy and instructing in the use of flutter valves and percussive vests that may be critical parts of acute management.

Finally, in follow-up of patients with obstructive lung diseases, RTs are involved in counseling (e.g., smoking cessation, medication management), administering pulmonary rehabilitation programs, and certifying and recertifying long-term supplemental O_2 therapy. RTs working in home care may conduct home visits to patients and set up and adjust equipment in the home. This description of activities of the RT in care of the patient with obstructive lung disease demonstrate that RTs are indispensable caregivers for patients with asthma, COPD, and bronchiectasis and that the care of patients with obstructive lung diseases constitutes a major component of RTs' activities.

SUMMARY CHECKLIST

- The spectrum of obstructive lung diseases includes COPD (consisting of emphysema and chronic bronchitis), asthma, and bronchiectasis. Airflow obstruction may be a feature of other lung diseases as well, such as sarcoidosis, and congestive heart failure.
- COPD features persistent airflow obstruction despite therapy.
- Classically, asthma causes airway obstruction that is fully reversible with therapy and features symptoms such as episodic wheezing, shortness of breath, chest tightness, and cough.
- Bronchiectasis features permanent dilation of bronchi or bronchioles on chest imaging (often chest CT) and may result from various causes (e.g., childhood lung infection, cystic fibrosis, hypogammaglobulinemia).
- Major risk factors for COPD include cigarette smoking, chronic exposure to noxious fumes (e.g., cooking with biomass fuels in enclosed spaces), and genetic factors, the best characterized of which is AAT deficiency.
- The most common symptom of patients with COPD is dyspnea. Cough, chronic phlegm production, and wheezing may also be present.
- Goals in treating COPD are to improve airflow, maximize the patient's functional status, reduce symptoms, avoid exacerbations, and prolong the patient's survival as possible.
- Important treatments for COPD include inhaled bronchodilators, inhaled corticosteroids, supplemental O_2 when indicated, pulmonary rehabilitation, and preventive vaccinations (e.g., against influenza and pneumococcus). Lung transplantation and LVRS are also available for specific subsets of patients with advanced disease.
- The goal of stable asthma management is to maintain a high quality of life for the patient, uninterrupted by asthma symptoms, side effects from medications, or limitations on the job or during exercise. This goal can be accomplished by objective measurements and monitoring lung function, pharmacologic therapy, environmental control, and patient education.
- The goals of emergency management of acute asthma are to decrease mortality and morbidity and to return the patient to preadmission stability and function as quickly as possible. These goals are accomplished by supplemental O_2 and frequent administration of high doses of aerosolized β-2 agonists, high-dose parenteral corticosteroids, and antibiotics if there is evidence of infection.
- The hallmark of bronchiectasis is the chronic production of large quantities of purulent sputum. Dyspnea is variable and depends on the extent of involvement and the underlying disease. Antibiotics and bronchopulmonary hygiene are important treatments.

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26

Interstitial Lung Disease

Jeffrey T. Chapman and Jason Bordelon

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Organize and distinguish among the interstitial lung diseases (ILDs).
- Understand that some ILDs have specific causes while most patients will have ILD from an unknown cause leading to a specific pattern of injury.
- Interpret symptoms, examination signs, and pulmonary function test results in ILD.
- Describe radiographic patterns and how they can diagnose some ILDs.
- List causes, exposures, or pathologic characteristics associated with selected ILDs.
- Know in which patients and how to manage ILD with nonspecific therapies.
- Understand which patients should be treated with therapy specific to the type of ILD.
- Understand end-of-life issues with ILDs.

CHAPTER OUTLINE

KEY TERMS

asbestosis
connective tissue disease
corticosteroids
hypersensitivity pneumonitis
idiopathic pulmonary fibrosis
interstitial lung disease
lymphangioleiomyomatosis
occupational interstitial lung disease
organizing pneumonia
pulmonary Langerhans cell histiocytosis
sarcoidosis
silicosis

Interstitial lung disease (ILD) refers to a broad category of lung diseases rather than a specific disease process.[1,2] This category includes illnesses affecting the lung parenchyma with different causes, treatments, and prognoses. These disease processes are grouped together because of similarities in their clinical presentations, appearance on chest x-ray and computed tomography (CT), and physiology.

An organizational scheme is presented in Fig. 26.1. In evaluating patients with an ILD, diseases with known causes or associations, such as diseases related to specific exposures, diseases associated with systemic conditions, and diseases with a known genetic basis must be considered first. However, most patients are classified with an ILD of unknown cause, the so-called *idiopathic interstitial diseases*. Their disorder is classified by pathologic pattern. Using this organizational scheme to guide a careful and complete history, one is able to understand the disease processes and work efficiently toward an accurate diagnosis and treatment.

The histologic abnormalities of the ILDs involve the pulmonary interstitium to a greater extent than the alveolar spaces or airways. Fig. 26.2 illustrates the components of the normal

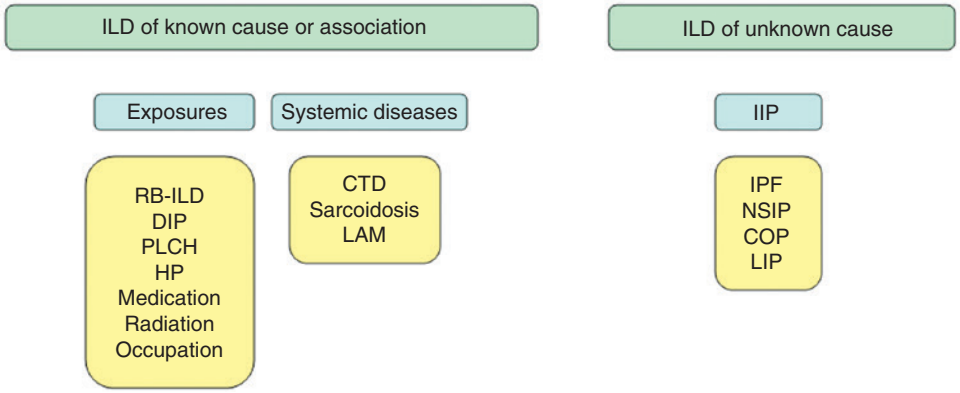

Fig. 26.1 Current Organization of Interstitial Lung Disease *(ILD). COP,* Cryptogenic organizing pneumonia; *CTD,* connective tissue disease; *DIP*, desquamative interstitial pneumonitis; *HP*, hypersensitivity pneumonitis; *IIP*, idiopathic interstitial pneumonia; *IPF,* idiopathic pulmonary fibrosis; *LAM,* lymphangioleiomyomatosis; *LIP,* lymphocytic interstitial pneumonia; *NSIP,* nonspecific interstitial pneumonitis; *PLCH,* pulmonary Langerhans cell histiocytosis; *RB-ILD*, respiratory bronchiolitis–associated interstitial lung disease.

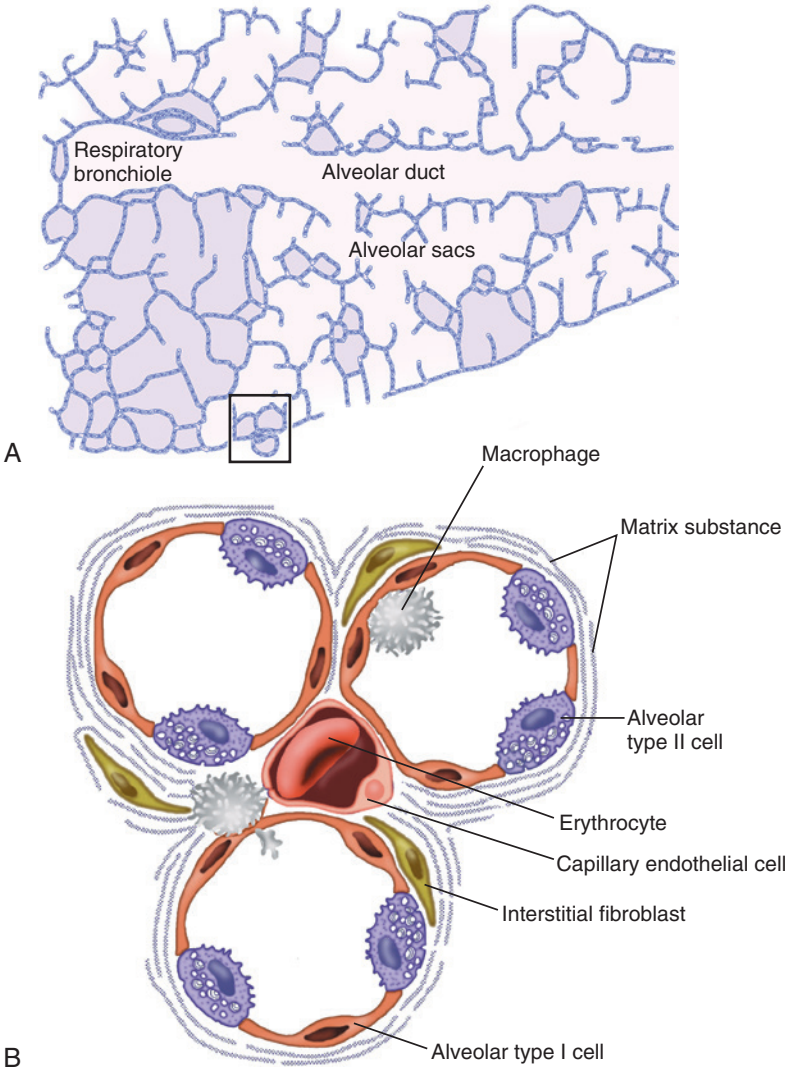

Fig. 26.2 (A) Diagram of the pulmonary parenchyma shows the respiratory bronchiole, alveolar duct, and alveolar sacs. (B) The constituents of the interstitial space, including type I and type II alveolar epithelial cells, a capillary with vascular endothelial cells and erythrocytes in transit, resident macrophages, interstitial fibroblasts, and matrix substance.

pulmonary parenchyma. The interstitium is the area between the capillaries and the alveolar space. In the normal state, this space allows close contact between gas and capillaries with minimal connective tissue matrix, fibroblasts, and inflammatory cells such as macrophages. The interstitium supports the delicate relationship between the alveoli and capillaries, allowing for efficient gas exchange. After an injury, the lung must respond to the damage and repair itself. If the exposure or injury persists or if the injury repair process is imperfect, the lung may be permanently damaged with abnormal interstitial tissue replacing the normal capillaries, alveoli, and healthy interstitium.

These pathologic abnormalities can lead to impairment in lung function. Gas exchange is impaired due to $\dot{V}/\dot{Q}$ mismatching, shunt, and decreased diffusion across the abnormal interstitium. The work of breathing in patients with ILD is increased because of decreased lung compliance. Together, these impairments cause exercise intolerance, seen in all ILDs. If the injury that causes the ILD or the abnormal repair from injury is not halted, progressive tissue damage occurs, leading to worsening disability and possibly death.

CHARACTERISTICS OF INTERSTITIAL LUNG DISEASE

Clinical Signs and Symptoms

Many ILDs have similar clinical features and are not easily distinguished based on history or examination. Symptoms are generally limited to the respiratory tract. However, extrapulmonary symptoms should not be ignored because they may point to an ILD associated with a systemic diagnosis. Exertional breathlessness (dyspnea) and a nonproductive cough are the most common reasons that patients with ILD seek medical attention. Other respiratory symptoms, such as sputum production, hemoptysis, pneumothorax, or wheezing, can occur and may suggest specific diseases (Table 26.1). If the patient also has prominent extrapulmonary symptoms, such as myalgia, arthralgia, sclerodactyly (tightening of the skin over the fingers), gastroesophageal reflux, or Raynaud phenomenon (discoloration of the digits, often initially with a white color because of spasm of the arteries that supply the digits), ILD resulting from underlying **connective tissue disease** may be present (Table 26.2).

TABLE 26.1 Unusual Pulmonary Findings and Likely Diagnosis

Pulmonary Findings	Disease	Frequency
Hemoptysis	LAM	Rare
Chyloptysis (coughing up chyle)	LAM	Rare
Pneumothorax	LAM, BHD	Common
Wheeze	Sarcoidosis, LAM	Common
Chylous pleural effusion	LAM	Common
Exudative pleural effusion	RA	Common

BHD, Birt-Hogg-Dubé syndrome; *LAM,* lymphangioleiomyomatosis; *RA,* rheumatoid arthritis.

Physical Examination

Many patients with ILD have bilateral fine inspiratory crackles, which usually are most prominent at the lung bases. However, some diseases, such as sarcoidosis and lymphangioleiomyomatosis (LAM), may manifest with only decreased breath sounds without abnormal breath sounds despite markedly abnormal chest imaging. Expiratory wheezing is uncommon in ILD and its presence suggests either airway involvement as part of the primary disease process (LAM, sarcoidosis, respiratory bronchiolitis–associated interstitial lung disease [RB-ILD], desquamative interstitial pneumonitis [DIP], pulmonary Langerhans cell histiocytosis [PLCH]) or concomitant airways disease, such as emphysema or asthma. Signs of pulmonary arterial hypertension with right ventricular dysfunction, such as lower extremity edema or jugular venous distension, may occur late in the course of any ILD. Examination also may show features of an underlying connective tissue disease, including synovitis, joint deformities, or skin rash.

Radiographic Features

ILDs manifest as abnormal lung parenchyma that casts abnormal radiographic shadows. For most ILDs, the chest x-ray shows reduced lung volumes with bilateral reticular or reticulonodular opacities. However, the chest x-ray has limited value because the three-dimensional abnormalities are shown in two dimensions from which depth cannot be determined. High-resolution cross-sectional imaging using CT provides detailed images representing pulmonary pathology.[3] High-resolution CT images allow

TABLE 26.2 Extrapulmonary Findings and Likely Diagnosis

Extrapulmonary Findings	Disease	Frequency
Raynaud phenomenon	All CTD	Common
Arthralgia	All CTD	Common
Myalgia	Polymyositis	Common
Large muscle weakness	Polymyositis	Common
Sclerodactyly	Scleroderma	Common
Rheumatoid skin nodules	RA	Rare
Fingertip fissures	Antisynthetase syndrome	Common
Dorsal hand rash	Dermatomyositis	Common
Facial rash	Dermatomyositis	Common
Exudative pleural effusion	RA	Common
Shawl distribution skin nodules	TSC	Common
"Pencil eraser" facial skin nodules	BHD	Common
Central nervous system benign cortical tuber	TSC	Common
Abdominal angiomyolipoma	LAM	Common
Renal cancer	BHD	Common
Cardiomyopathy	Sarcoidosis, polymyositis	Rare
Cardiac conduction block	Sarcoidosis	Rare
Violaceous facial skin nodules	Sarcoidosis	Common
Subcutaneous nodules	Sarcoidosis	Common
Cranial neuropathy	Sarcoidosis	Rare
Small fiber neuropathy	Sarcoidosis	Rare

BHD, Birt-Hogg-Dubé syndrome; *CTD,* connective tissue disease; *LAM,* lymphangioleiomyomatosis; *RA,* rheumatoid arthritis; *TSC,* tuberous sclerosis complex.

noninvasive evaluation of ILDs and are a key element in making a confident diagnosis and managing ILD.[4]

The most important pattern to recognize on chest x-rays and high-resolution CT images is usual interstitial pneumonitis (UIP), the pathologic pattern of injury seen in the disease idiopathic pulmonary fibrosis (IPF). The chest x-ray (Fig. 26.3A) and high-resolution CT images (see Fig. 26.3B) in UIP typically show increased attenuation, whiteness, which is bilateral, patchy (abnormal areas separated by normal lung), peripheral (abnormal pleural edges), and basilar (affecting the lower parts of the lung predominantly). Frequently, the abnormal fibrosis leads to so-called honeycomb cysts at the edges of the most abnormal lung and bronchiectasis where the airways are dilated to a larger size than the accompanying pulmonary artery. Honeycomb cysts are so named because they look like a honeycomb, with thick walls surrounding air. Faint ground-glass abnormalities, which are increased whiteness of the lung tissue without distortion of the underlying blood vessels or bronchi, are absent or minimal in UIP. Pleural disease, air trapping, micronodules, and significant lymphadenopathy are not seen, although two-thirds of patients with UIP can have mild mediastinal adenopathy.[5]

RULE OF THUMB In patients with spontaneous pneumothorax and interstitial infiltrates, LAM or PLCH should be considered.

In contrast to UIP, cellular nonspecific interstitial pneumonitis (NSIP) is a pattern of injury dominated by inflammation and has imaging findings distinct from those with UIP. Ground-glass attenuation (patchy fine whiteness in the CT images) predominates.

RULE OF THUMB Calcification along the pleura on a chest x-ray suggests previous exposure to asbestos. Although such calcified areas (called *plaques*) do not cause symptoms or physiologic abnormality, they can provide a clue that the cause of ILD is asbestos exposure.

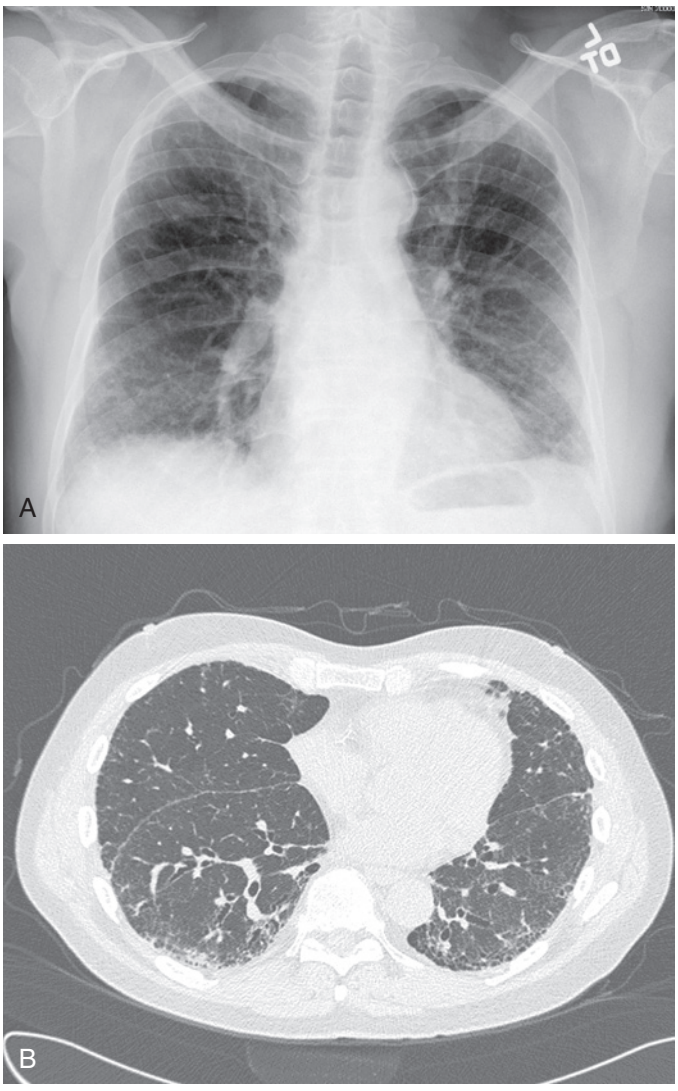

Fig. 26.3 (A) Posteroanterior chest x-ray showing the characteristic features of idiopathic pulmonary fibrosis, a common interstitial lung disease. Notice the bilateral lower zone reticulonodular infiltrates and the loss of lung volume in the lower lobes. (B) Chest computed tomography image shows the peripheral nature of the fibrosis.

Physiologic Features

Similar to the radiographic findings, specific ILDs can vary considerably regarding the degree of physiologic abnormalities. However, a restrictive physiologic impairment is the most common finding.[6] With this restrictive pattern, both forced expiratory volume in 1 second (FEV_1) and forced vital capacity (FVC) are diminished, and the FEV_1/FVC ratio is preserved or even above normal. Lung volumes are reduced, as is the diffusing capacity of the lung for carbon monoxide (DLCO). This reduction in diffusing capacity reflects a pathologic disturbance of the alveolar-capillary interface, reflecting the abnormality in the interstitium of the lung.

In almost all ILDs, the lungs have reduced compliance and require above normal transpleural pressures to ventilate (Fig. 26.4). This lack of compliance results in small lung volumes and

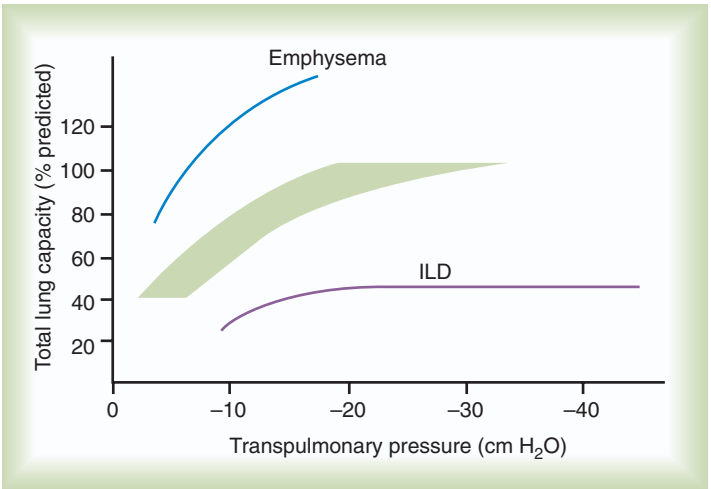

Fig. 26.4 **Static Pressure-Volume Curve.** The compliance characteristics of the lung are illustrated with a plot of lung volume against the corresponding transthoracic pressure measured during static (i.e., no flow) conditions. The *shaded area* represents the range of values expected with a normally compliant lung. The line labeled *ILD* represents an example of a patient with interstitial lung disease *(ILD)*. At any particular lung volume, the transthoracic pressure is greater than expected. For comparison, the line labeled *Emphysema* shows the compliance characteristics of patients with emphysema.

increased work of breathing, and increased driving pressures if mechanical ventilation is required.

Rarely, a pattern of physiologic obstruction may be seen. This obstruction can be the result of the primary disease process (e.g., LAM, PLCH, or sarcoidosis in some patients) or accompanying emphysema or asthma.[7] If ILD develops in a patient with significant emphysema (a condition called "combined pulmonary fibrosis with emphysema" [CPFE]), the opposing physiologic effects of the two disease processes (i.e., restriction for the ILD and obstruction from the emphysema) may result in deceptively normal spirometry and lung volume measurements and apparently normally compliant lungs. For example, emphysema might cause lung volumes to increase, whereas the restriction would be reflected by decreased lung volumes. The net effect of both processes in the same patient could be a normal lung volume. However, because both emphysema and ILD result in impaired gas exchange, the DLCO is significantly decreased.

RULE OF THUMB Among smokers with IPF, normal spirometry and lung volumes with reduced DLCO suggest the presence of coexisting emphysema. Consider CPFE in this situation.

SELECTED SPECIFIC TYPES OF INTERSTITIAL LUNG DISEASE AND THERAPIES

Exposure-Related Disease

Tobacco-Associated Lung Disease

Although the association of first-hand tobacco smoke and obstructive lung disease is common and well known, tobacco smoke is also an avoidable cause of ILD. Although the association is rarer than with obstructive lung disease, first-hand tobacco smoke inhalation can lead to three types of ILD in susceptible individuals: (1) RB-ILD, (2) DIP, and (3) PLCH. The first two disorders manifest as overly abundant macrophages in the lung in reaction to tobacco smoke. In RB-ILD, macrophages accumulate in the respiratory bronchioles leading to bronchiolar remodeling and fibrosis of adjacent alveoli. As expected for a disease with combined airway and alveolar injury, pulmonary function testing reveals mixed restriction and obstruction with air trapping. High-resolution CT images show this mixed pathologic location with indistinct centrilobular nodules (Fig. 26.5). In DIP, the increased macrophages fill the alveoli, manifesting as restrictive impairment on pulmonary function testing and diffuse ground-glass attenuation on high-resolution CT imaging (Fig. 26.6).

Pulmonary Langerhans cell histiocytosis (PLCH) is the third interstitial manifestation of tobacco smoke. Increased numbers of polyclonal macrophages are accompanied by fibroblasts and eosinophils in nodules concentrated around small airways. These nodules are star-shaped (or stellate) and destroy adjacent lung tissue, leading to the classic high-resolution CT image of stellate nodules associated with cysts, as seen in Fig. 26.7. Although adult smoking-associated PLCH is pathologically similar to childhood Langerhans cell histiocytosis, the adult form does not involve bone and has not proved to respond to chemotherapy as the childhood form does. The relationship of these two disorders has yet to be defined.

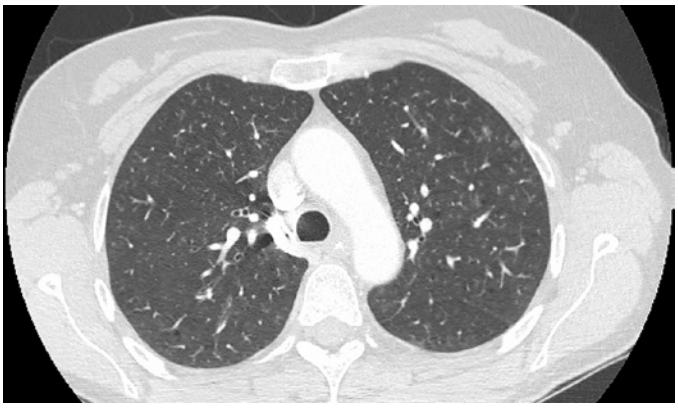

Fig. 26.5 Respiratory Bronchiolitis–Associated Interstitial Lung Disease (RB-ILD). There are numerous indistinct centrilobular nodules. Air trapping can be seen in RB-ILD but is not present in this case.

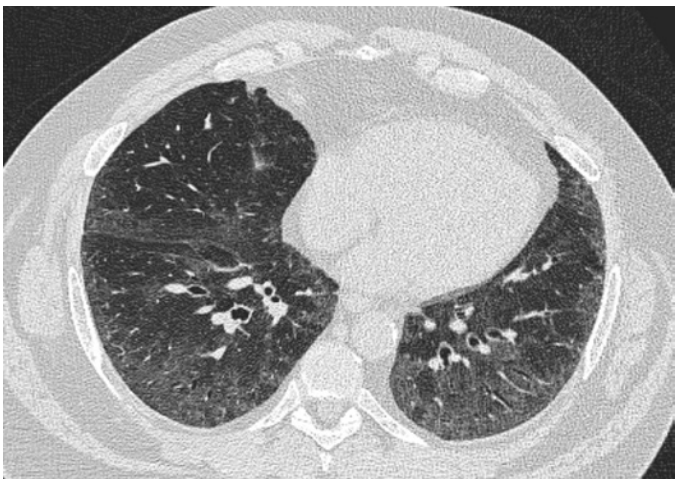

Fig. 26.6 Desquamative Interstitial Pneumonitis. Note the diffuse ground-glass attenuation.

In each of these three diseases, the primary treatment is stopping smoking completely. With abstinence from smoking, most patients either minimally improve or remain stable,[8] but a few progressively worsen, sometimes to the point of needing lung transplantation. The use of immunosuppressive medications is generally not effective.[9]

Drug-Related and Radiation-Related Disease

Many drugs have been associated with pulmonary complications of various types, including interstitial inflammation and fibrosis, bronchospasm, pulmonary edema, and pleural effusions. Drugs from many different therapeutic classes can cause ILD, most commonly chemotherapeutic agents, antibiotics, antiarrhythmic drugs, and immunosuppressive agents (Box 26.1). Treatment is avoidance of further exposure and systemic corticosteroids in markedly impaired or declining patients.

RULE OF THUMB Exposure to the chemotherapeutic agent bleomycin can lead to interstitial lung disease and is accentuated by exposure to increased fractional inspired oxygen (FiO_2), even months after last drug exposure. Thus supplemental oxygen (O_2) should be used only if absolutely necessary for patients with bleomycin-induced ILD.[10]

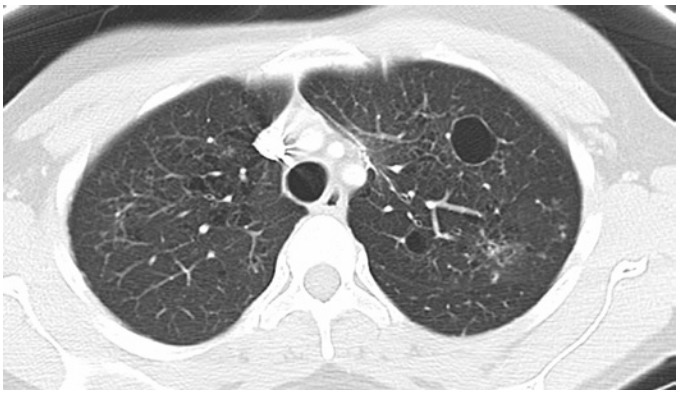

Fig. 26.7 Pulmonary Langerhans Cell Histiocytosis. Note the left upper lobe cysts and indistinct stellate-shaped nodule around an airway, which will become a cyst.

BOX 26.1 Drugs Associated With the Development of Interstitial Lung Disease

Antibiotics
- Nitrofurantoin
- Sulfasalazine

Antiinflammatory Agents
- Leflunomide
- Methotrexate
- Etanercept
- Infliximab

Cardiovascular Agents
- Amiodarone
- Tocainide

Chemotherapeutic Agents
- Bleomycin
- Mitomycin C
- Busulfan
- Cyclophosphamide
- Chlorambucil
- Melphalan
- Methotrexate
- Etoposide
- Vinblastine
- Imatinib

Drugs Used in an Illegal Way
- Heroin
- Methadone
- Talc as an intravenous drug contaminant

Exposure to therapeutic radiation used to treat cancer may result in ILD. Patients presenting within 6 months of radiation therapy generally have ground-glass abnormalities thought to represent acute inflammation. The ground-glass abnormalities can occur in both radiation-exposed tissue and unexposed tissue. Short-term systemic corticosteroid treatment can improve lung function. In contrast, radiographic abnormalities that develop more than 6 months after therapy typically appear as densely fibrotic tissue. On CT scan, a straight line indicating the margin

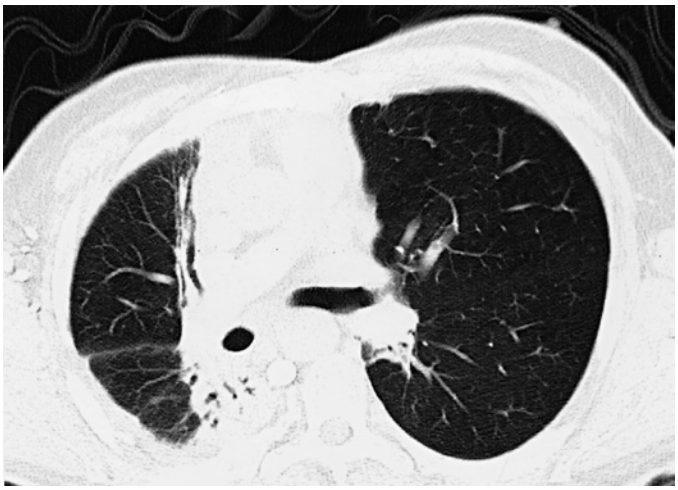

Fig. 26.8 High-resolution computed tomography slice shows dense fibrosis with a non-anatomic straight line boundary.

of radiation is frequently evident, as seen in Fig. 26.8. These patients do not improve with corticosteroid therapy and treatment is supportive.

Hypersensitivity Pneumonitis

Hypersensitivity pneumonitis (HP) is a cell-mediated immune reaction to inhaled antigens in susceptible persons.[11] Patients must be sensitized by an initial exposure, with re-exposure leading to either an acute or chronic HP. Patients with acute HP present to medical attention with a few days of shortness of breath, chest pain, fever, chills, malaise, and a cough that may be productive of purulent sputum. Patients who are chronically exposed to low levels of inhaled antigens may develop subtle interstitial inflammatory reactions in the lung that do not result in noticeable symptoms for months to years and can present with severe, impairing disease, which can be very difficult to distinguish from IPF.

Common organic antigens known to cause HP include bacteria and fungi, which may be found in moldy hay (farmer's lung) or in the home environment, in particular, in association with central humidification systems (humidifier lung), indoor hot tubs, and animal proteins (e.g., bird breeder's lung). Inorganic antigens from vaporized paints and plastics also can lead to HP. Many established antigens are listed in Table 26.3, along with the typical source of exposure and the associated syndrome.

Because the relationship between exposure and lung disease may not be obvious, a careful systematic occupational, environmental, and avocational history is crucial. Elements that strongly suggest a diagnosis of HP are exposure to an appropriate antigen and the correct timing of symptom onset to the exposure. Blood samples may be obtained to determine whether there has been an antibody response to certain antigens associated with HP (serum precipitins). However, the presence of such antibodies cannot establish the diagnosis of HP because many individuals develop antibodies in the absence of disease. Likewise, the absence of detectable antibodies does not rule out the diagnosis of HP because the culprit may be an antigen that is not included in the blood test panel that is analyzed.[12]

Specific therapies for HP are strict antigen avoidance and immunosuppression with corticosteroids in patients with

TABLE 26.3 Causes of Hypersensitivity Pneumonitis

Antigen	Exposure	Syndrome
Bacteria		
Thermophilic Bacteria		
Saccharopolyspora rectivirgula	Moldy hay	Farmer's lung
Thermoactinomyces vulgaris	Moldy sugarcane	Bagassosis
Thermoactinomyces sacchari	Mushroom compost	Mushroom worker's lung
Thermoactinomyces candidus	Heated water reservoirs	Humidifier lung Air conditioner lung
Nonthermophilic Bacteria		
Bacillus subtilis, Bacillus cereus	Water, detergent	Humidifier lung Washing powder lung
Fungi		
Aspergillus species	Moldy hay	Farmer's lung
Aspergillus clavatus	Barley	Malt worker's lung
Penicillium casei, Penicillium roqueforti	Cheese	Cheese washer's lung
Alternaria species	Wood pulp	Woodworker's lung
Merulius lacrymans	Rotten wood	Dry rot lung
Penicillium frequentans	Cork dust	Suberosis
Aureobasidium pullulans	Water	Humidifier lung
Cladosporium species	Hot tub mists	Hot tub HP*
Trichosporon cutaneum	Damp wood and mats	Japanese summer-type HP
Animal Proteins		
Avian proteins	Bird droppings, feathers	Bird-breeder's lung
Urine, serum, pelts	Rats, gerbils	Animal handler's lung
Chemicals		
Isocyanates, trimellitic anhydride	Paints, resins, plastics	Chemical worker's lung
Copper sulfate	Bordeaux mixture	Vineyard sprayer's lung
Phthalic anhydride	Heated epoxy resin	Epoxy resin lung

HP, Hypersensitivity pneumonitis.

symptomatic or physiologically impairing disease. In acute HP, corticosteroids seem to hasten recovery but do not improve ultimate lung function.[13] Patients with chronic HP, those with fibrosis on CT scan have a shorter survival and the benefit of long-term immunosuppression is unknown.[14]

Occupational Disease

The three most common types of **occupational interstitial lung disease** are **asbestosis**, chronic **silicosis**, and coal workers' pneumoconiosis. Awareness of the associated risk and reduction in exposure has greatly reduced the frequency of these diseases. However, they remain common in developing countries and among emigrants from these countries.

Predictable clinical and radiographic abnormalities occur in susceptible patients who have been exposed to asbestos.[15] These abnormalities include pleural changes (plaques, fibrosis, effusions, atelectasis, and mesothelioma) and parenchymal scarring and lung cancer.

RULE OF THUMB Asbestos exposure alone increases the risk for lung cancer minimally (1.5 to 3.0 times). However, asbestos exposure and cigarette smoking act synergistically to increase greatly the risk for cancer.

Asbestos exposure also may result in benign asbestos pleural effusions or an entity known as *rounded atelectasis*. Benign asbestos pleural effusions characteristically appear many years after initial exposure to asbestos (e.g., 10 to 20 years) and may be asymptomatic or may be associated with acute chest pain, fever, and dyspnea. Benign asbestos pleural effusions usually resolve on their own, but may recur. Treatment is drainage to reduce symptoms. Rounded atelectasis typically manifests as a pleural-based parenchymal mass that may be mistaken for cancer. The characteristic CT features, such as local volume loss, pleural thickening, and the "comet tail" appearance of bronchi and vessels curving into the lesion, help distinguish rounded atelectasis from carcinoma.

The term *asbestos-related pulmonary disease* encompasses all of these entities, whereas *asbestosis* is reserved for patients who have evidence of parenchymal fibrosis from asbestos exposure. Most patients with asbestosis have had considerable airborne asbestos exposure for many years (i.e., usually >20 years) before the lung disease becomes apparent. Exposure frequently is associated with occupations such as shipbuilding or insulation work. Patients report very slowly progressive dyspnea on exertion[16] and have crackles on lung examination. Physiologic testing shows restrictive impairment with a reduced DLCO. The chest x-ray shows bilateral lower zone reticulonodular infiltrates similar to infiltrates seen in IPF. With an appropriate exposure history, the presence of radiographic pleural plaques or rounded atelectasis indicates asbestos as the likely cause of ILD, although neither history nor radiographic findings are required for establishing the diagnosis. Surgical lung biopsy and finding so-called asbestos bodies can establish a definitive diagnosis, but surgical biopsy is infrequently performed due to the age and frailty of these patients. No medical therapy has been shown to improve or decrease progression of asbestosis. Severe impairment typically occurs 30 to 40 years after exposure, making almost all patients ineligible for lung transplantation because of advanced age. Management of asbestosis is supportive.

Chronic silicosis results from chronic exposure to inhaled silica particles. Occupations that commonly involve exposure to silica include mining, tunneling, sandblasting, and foundry work. The chest x-ray shows upper lung zone–predominant abnormalities characterized by multiple small nodular opacities in the central lung tissue. These nodules (simple silicosis) are asymptomatic and may never progress or cause symptoms. However, in susceptible individuals, the nodules coalesce into large midlung zone masses known as *progressive massive fibrosis*. Some patients with abnormal chest x-rays report few, if any, symptoms and may have normal lung examination and pulmonary function testing. Many patients are impaired and have mixed restrictive and obstructive impairment with reduced diffusion capacity. The physiologic impairment may remain stable or, if progressive,

massive fibrosis occurs, may progress even without continued exposure. Symptoms are typically exertional dyspnea and variable mucus production.

Patients with silicosis are at increased risk for lung cancer, and the risk is increased when combined with exposure to tobacco smoke, diesel exhaust, or radon gas. Patients with silicosis develop active tuberculosis 2 to 30 times more frequently than those without silicosis.[17] This association is especially important in populations with a high frequency of human immunodeficiency virus infection, which markedly increases the risk for silicosis-associated active tuberculosis.

Coal workers' pneumoconiosis develops as the result of chronic inhalation of coal dust. In the past, it was assumed that silica dust was responsible for the pulmonary disease seen among coal miners because the clinical and radiographic features are quite similar to those of chronic silicosis. However, it is now recognized that coal workers' pneumoconiosis and silicosis are the result of different exposures. Simple coal workers' pneumoconiosis, characterized by multiple small nodular opacities on the chest x-ray, is asymptomatic. Cough and shortness of breath do not develop unless the disease progresses to progressive massive fibrosis similar to that seen in silicosis.

There are no proven therapies for either silicosis or coal workers' pneumoconiosis other than eliminating future exposure. In patients with significant obstructive impairment or mucus production, inhaled bronchodilators and **corticosteroids** may relieve some symptoms. Exacerbations can be frequent and are treated with antibiotics and systemic corticosteroids.

Interstitial Lung Disease Associated With a Systemic Disease

Connective Tissue Disease

ILD is a well-known complication of connective tissue diseases.[18] The most commonly implicated disorders are scleroderma, rheumatoid arthritis, Sjögren syndrome, polymyositis/dermatomyositis, and systemic lupus erythematosus.

In any of these disorders, pulmonary involvement may remain undetected until significant impairment is present, because these patients may be inactive owing to the underlying connective tissue disease. In addition, severity of the pulmonary and nonpulmonary manifestations do not always correlate. In some instances, the lung disease may overshadow or may occur earlier than other symptoms of the systemic disease. Dyspnea and cough, as with all ILDs, are the most common symptoms. On chest examination, crackles or wheezing are typically found. Lung physiology is usually restrictive with decreased DLCO but may be obstructive especially with Sjögren syndrome owing to collections of lymphocytes in bronchioles.

High-resolution CT findings are variable and range from normal to ground-glass abnormalities, to reticular and fibrotic changes.[19] The pathologic pattern of injury with these diseases is equally diverse and correlates with the high-resolution CT findings. Inflammatory injury patterns are most commonly seen, such as NSIP and organizing pneumonia. The NSIP inflammatory injury pattern appears as ground-glass abnormalities on high-resolution CT scan, whereas organizing pneumonia is shown by patchy consolidated lung with air bronchograms. Both of these pathologic patterns can improve with aggressive immunosuppression. At the other end of the pathologic response spectrum is fibrotic injury, which manifests as UIP and shows reticular fibrotic opacities and honeycomb cystic changes on high-resolution CT scan. These abnormalities typically do not improve with immunosuppression, although long-term controlled studies are lacking.

Specific treatment of connective tissue disease–associated ILD must be individualized. Patients with evidence of extrapulmonary inflammation, an inflammatory pathologic pattern such as NSIP or organizing pneumonia on high-resolution CT or biopsy, or rapidly progressive symptoms, are usually treated with prolonged immunosuppressive agents such as cyclophosphamide, azathioprine, mycophenolate, or tacrolimus.[20,21]

The Scleroderma Lung Study showed that one year of oral cyclophosphamide modestly improved lung function compared with modest decline in the placebo group.[22] However, after 1 year off immunosuppressive therapy, the patients treated with cyclophosphamide worsened and were indistinguishable from the untreated patients.[23] Owing to significant side effects with cyclophosphamide, the Scleroderma Lung Study II was performed comparing 1 year of cyclophosphamide followed by 1 year of placebo to 2 years of mycophenolate. Both groups demonstrated significant and equal benefit.[24] Owing to less side effects, mycophenolate is now the treatment of choice for scleroderma-related ILD.

Polymyositis-associated ILD is being increasingly recognized as a common disease entity. Patients usually present with "mechanic's hands," consisting of thickened skin and painful fingertip fissures, and 50% have Jo-1 antibodies on antinuclear antibody testing. Lung pathologic results typically show fibrotic NSIP or organizing pneumonia. As would be expected with these inflammatory patterns of injury, patients usually benefit from immunosuppression.

Sarcoidosis

Sarcoidosis is an idiopathic (of unknown cause) multisystem inflammatory disorder that commonly involves the lung.[25] It is the most common ILD in the United States. The tissue inflammation that occurs in sarcoidosis has a characteristic pattern in which the inflammatory cells collect in microscopic nodules called *granulomas*. In contrast to IPF, sarcoidosis is more common among young adults than among older adults. Sarcoidosis often follows a benign course of inflammation without symptoms or long-term consequences that spontaneously improves.

The most common manifestation of sarcoidosis is asymptomatic hilar adenopathy. Less frequently, the chest x-ray shows parenchymal opacities in the midlung zone that may be nodular, reticulonodular, or alveolar. When symptoms occur, cough, chest pain, dyspnea, and wheezing are most common. Pulmonary physiology may be normal, restrictive, obstructive, or mixed, all with reduced DLCO. Obstructive impairment may be related to endobronchial granulomatous inflammation or scarring.[26]

Corticosteroids are commonly used to treat sarcoidosis, but treatment usually is reserved for patients with marked symptoms or physiologic impairment attributable to the disease.[27] Although corticosteroids almost always reduce active sarcoid inflammation, long-term side effects should limit the duration of steroid

treatment. For patients requiring long-term immunosuppression, alternative immunosuppressive agents should be used.[28] Involvement of other organs that may require corticosteroid therapy include cardiac involvement, uveitis, and peripheral or central nervous system involvement with cranial nerve abnormalities. Disease activity is difficult to detect in many patients. Serum angiotensin-converting enzyme levels and gallium scans are not well correlated with disease activity, and their routine use is discouraged.[29]

Lymphangioleiomyomatosis

Lymphangioleiomyomatosis (LAM) is a rare disorder of abnormal smooth muscle tissue proliferating around small airways and leading to severe obstruction and destruction of alveoli with resultant thin-walled cyst formation.[30] All patients are women, although both men and women with tuberous sclerosis complex can develop lung pathologic findings identical to those of LAM that is called *tuberous sclerosis complex LAM*. This peculiar pathologic process is caused by abnormalities in the *TSC-2* gene.[31]

Dyspnea on exertion and an obstructive ventilatory impairment with reduced DLCO is almost always present, except in very early disease. Disease progression is variable; some women have steadily worsening lung function during midlife, whereas some elderly women experience extremely slow decline over many years. Risk factors for worsening lung function include a significant bronchodilator response and possibly pregnancy. Other important disease manifestations include pneumothorax from a ruptured subpleural cyst. Unilateral or, less commonly, bilateral chylothorax is seen in about one-third of patients. This results from lymphatic obstruction by abnormal smooth muscle tissue. Treatment with a low-fat diet or blocking gut fat absorption is usually ineffective, and pleurodesis (i.e., sealing the pleural space by instilling an irritant solution to cause the visceral and parietal pleura to stick together [Chapter 27]) is required. Pleurodesis does not preclude subsequent lung transplantation.

Sirolimus, which blocks the abnormal *TSC-2* gene and inhibits LAM cell proliferation, has recently been shown to stabilize lung function in comparison with placebo and has become standard therapy in LAM patients with abnormal lung function.[32] Additional treatment is with inhaled bronchodilators and inhaled corticosteroids while selected patients may ultimately require lung transplantation.

Interstitial Lung Disease of Unknown Cause

Idiopathic Interstitial Pneumonias

Despite a careful history, physical examination, and high-resolution CT scan, most patients are not found to have an exposure or systemic illness as a cause of ILD. These patients have a disorder isolated to the lung termed *idiopathic interstitial pneumonia (IIP)*. Prognosis and potential therapies are completely dependent on the type of pathologic pattern of IIP.

Idiopathic pulmonary fibrosis. **Idiopathic pulmonary fibrosis** (IPF) is the most common IIP and is a progressive fibrotic disease isolated to the lung.[33] Although the precise cause of IPF is unknown, studies have demonstrated that susceptible individuals have lung injury from diverse causes, such as metal dust, farming dust, tobacco smoke, subclinical gastric aspiration, and mechanical stress from abnormal surfactant proteins that lead to abnormal lung healing and progressive fibrosis.[34] Most patients are older than 60 years, and IPF is extremely unusual in persons younger than 40 years. Patients present with chronic cough and exertional dyspnea, and high-resolution CT suggests a fibrotic process.

The diagnosis of IPF is made by noting a lack of exposure or systemic disease known to cause ILD and determining UIP as the pathologic pattern of injury. The diagnosis of UIP is made when high-resolution CT shows bilateral and basilar-predominant peripheral reticular fibrosis and honeycomb cystic change with absence of significant ground-glass abnormalities, micronodules, and air trapping. Without these classic findings, a surgical lung biopsy is needed for diagnosis.[35,36] Patients who do not have IPF can have UIP on surgical lung biopsy (e.g., connective tissue disease), so this pattern of injury and repair is not unique to IPF.

Most patients die as a result of progressive fibrotic lung disease within 4 years of diagnosis. Data show that approximately half of patients die with gradually progressive disease over several years.[37] The other half experience stable lung function or minimal decline for months to years and then have sudden worsening over a few weeks or months, leading to death.[38]

RULE OF THUMB In IPF severity of dyspnea, restrictive physiologic defect, DLCO impairment, degree of pulmonary arterial hypertension degree of fibrosis on high-resolution CT, and SaO_2 desaturation on exertion predict a higher risk of death.[39] Serial parameters that predict poor survival include worsening dyspnea, FVC, and DLCO.

Specific treatment for IPF is now available after decades of IPF trials showing no benefit with aggressive immunosuppression[40-42] and various other drugs (e.g., interferon γ,[43] etanercept,[44] bosentan, macitentan, ambrisentan, sildenafil,[45] imatinib,[46] warfarin, *N*-acetylcysteine,[47] and azathioprine in combination with both oral corticosteroids and *N*-acetylcysteine).[48] Pirfenidone and nintedanib, both molecules with multiple antifibrotic properties, have been shown to slow disease progression in patients with IPF.[49,50] Either of these two drugs should be offered to all patients who have an established diagnosis of IPF as long as side effects are tolerable, since the medications do not improve lung function or halt lung function decline.

Studies have demonstrated coexisting pulmonary arterial hypertension in IPF, leading to worse exercise intolerance and increased mortality.[51,52] Significant pulmonary arterial hypertension is suggested in patients with markedly reduced diffusion capacity but relatively preserved FVC. Medications that benefit pulmonary arterial hypertension such as bosentan and sildenafil have not proved beneficial for IPF either with or without pulmonary arterial hypertension.[53,54]

Nonspecific interstitial pneumonia. NSIP is an IIP with diffuse inflammation seen on surgical lung biopsy.[55] Patients are on average 7 to 10 years younger than patients with IPF, but considerable overlap exists. The degree of accompanying interstitial fibrosis varies. The most common presentation of NSIP is fibrotic NSIP. This type involves fibrosis and inflammation. Cellular NSIP is less common. Patients present with chronic or subacute cough and

dyspnea. High-resolution CT shows predominant ground-glass abnormalities in cellular NSIP and both ground-glass abnormalities and fibrotic changes in fibrotic NSIP. Given that there is significant clinical and radiographic overlap between fibrotic NSIP and IPF, surgical lung biopsy is frequently required to distinguish these two entities, such as when elements of classic UIP are not present on high-resolution CT images.

The prognosis is much better for NSIP than IPF, with most patients surviving 7 to 10 years. Immunosuppression with oral corticosteroids and cytotoxic immunosuppressive agents is the primary therapy. Type and duration of therapy are guided by disease activity and degree of inflammation on biopsy and ground-glass abnormalities on high-resolution CT. Pathologic NSIP is found frequently as an IIP and is the most common pattern of injury seen in connective tissue disease–associated ILD. Owing to this frequent association, many authors consider NSIP a connective tissue disease isolated to the lung.[56,57]

Organizing pneumonia. **Organizing pneumonia** (OP) is the newer, revised term for *bronchiolitis obliterans organizing pneumonia*. The term *cryptogenic organizing pneumonia* is used when this pattern of injury occurs as an IIP, and it is termed *organizing pneumonia* when found in the setting of connective tissue disease. Patients with organizing pneumonia are typically younger than patients with IPF and present with acute or subacute dyspnea and cough. Approximately one-third describe a preceding viral illness. However, no other risk factors are known. High-resolution CT shows alveolar filling with air bronchograms mimicking acute pneumonia, and the patient with classic organizing pneumonia presents after having failed to improve despite several courses of antibiotics. Diagnosis usually requires surgical lung biopsy, especially if the clinical and radiographic features are uncertain because small areas of organizing pneumonia can be seen in various inflammatory and fibrotic disorders on transbronchial lung biopsy. Surgical lung biopsy specimens show young fibroblasts within the alveoli that are presumably recovering from an injury. The alveolar basement membrane is intact, allowing for significant recovery if the inflammation or injury can be suppressed.

Most patients improve with oral corticosteroids (0.5 to 1 mg/kg for 6 to 12 weeks). However, many patients have recurrence after corticosteroid withdrawal and require long-term immunosuppressive agents.

Lymphocytic Interstitial Pneumonia

Lymphocytic interstitial pneumonia is a rare disorder of polyclonal lymphocyte aggregates that accumulate diffusely in the interstitium.[58] The diagnosis almost always requires surgical lung biopsy. Patients are typically younger than patients with IPF and present with subacute dyspnea and cough. Pulmonary function testing may show a mixed picture, and high-resolution CT typically shows diffuse ground-glass attenuation with variable amounts of fibrosis. Most patients respond well to oral corticosteroids, with a few requiring long-term immunosuppression. Lymphocytic interstitial pneumonia is frequently associated with connective tissue diseases, especially Sjögren syndrome, and with immunodeficiency, and these possibilities should be investigated in all patients with lymphocytic interstitial pneumonia.

MINI CLINI

Clinical Deterioration in a Patient With Interstitial Lung Disease

Problem

A 50-year-old man with fibrotic NSIP is being treated with oral corticosteroids and cyclophosphamide. After 6 months of therapy, he begins to report progressive breathlessness. Why is this occurring?

Solution

Many ILDs follow a gradually progressive course to end-stage disease and death. The available treatments may result in temporary improvement or slow progression of the disease. These treatments seldom are curative, however. Progressive symptoms (exertional dyspnea or cough) in a patient being treated for ILD often, although not always, indicates disease progression.

The following possibilities must be considered and separated from progression of the disease:

1. *Superimposed infection:* Immunosuppressive agents used in the management of some ILDs increase the risk for infection in the lung and elsewhere. Common bacteria or uncommon opportunistic infections may be responsible. Pneumonia may be difficult to detect radiographically because of preexisting radiographic abnormalities, and bronchoscopy with bronchoalveolar lavage and transbronchial lung biopsy may be needed.
2. *Drug reaction:* Almost all medications used to treat ILD have been reported to be capable of causing an adverse pulmonary reaction. Some medications, such as methotrexate, have been described to result in pulmonary reactions in 5% to 10% of users. An adverse drug reaction should be considered in all patients with ILD who are being actively treated, particularly if there is a clear temporal relationship between starting the medication and the new or progressive respiratory symptoms.
3. *Steroid-related muscle weakness.* This is a less common complication of corticosteroid therapy and can cause exercise intolerance that can be difficult to separate from progression of the underlying lung disease. Steroid-related muscle weakness (steroid myopathy) is difficult to diagnose because the weakness can result in worsening of the underlying restrictive physiologic defect. When proximal muscle weakness occurs in combination with progressive respiratory symptoms, the possibility of steroid myopathy should be considered. A greater than 20% drop in the FVC in the supine position compared with the sitting position suggests bilateral diaphragmatic dysfunction.
4. *Pulmonary embolism:* Inactivity as a result of disease-related physiologic impairment and right ventricular dysfunction may be a risk factor for thromboembolic disease. A sudden decline in respiratory status, sometimes associated with pleuritic chest pain, should raise the possibility of acute pulmonary embolism.
5. *Lung carcinoma:* Patients with pulmonary fibrosis have an increased risk for lung cancer, and the development of lung cancer can contribute to clinical decline.

TABLE 26.4 Nonspecific Therapies for Interstitial Lung Disease

Therapy	Details
Supplemental oxygen	Continuous rather than pulsed delivery of O_2 is preferred because the desaturation with activity seen in most patients is not corrected with pulse therapy, and pulse units vary greatly in the amount of O_2 delivered.[61] For other modes of supplemental oxygen delivery, see Chapter 42.
Pulmonary rehabilitation and exercise therapy	Pulmonary rehabilitation improves physical activity quality of life in patients with ILD. Pulmonary rehabilitation should be continued as monitored exercise therapy as when exercise is stopped the gains dissipate over a few months.[62]
Vaccinations and infection avoidance	All ILD should receive the pneumococcal vaccine per U.S. Centers for Disease Control and Prevention guidelines and a yearly influenza virus vaccine. Additionally, we recommend that patients practice good hand hygiene (frequent handwashing). We do not recommend use of masks or special antibacterial products. Patients treated with prednisone in doses greater than 15 mg daily or with a steroid-sparing immunosuppressant should receive Pneumocystis prophylaxis (e.g., with oral trimethoprim-sulfamethoxazole, inhaled pentamidine, etc.).
Gastroesophageal reflux prevention	GERD is found in many patients with ILD and symptoms of GERD should be actively sought. If present, GERD should be treated, and although only studied in IPF, treatment of GERD is associated with lower IPF-related mortality.[63]
Lung transplantation	The only therapy shown to prolong life in patients with end-stage, particularly fibrotic, ILD is lung transplantation.[64] Transplantation has been performed successfully in the management of most ILDs. A recommendation for lung transplantation must consider the significant risk of dying after lung transplantation at 1 year (10%–25%) and 5 years (50%–60%). Many patients with ILD are older than the upper age limit of "physiologic" age 65, though lung transplantation is being offered to older individuals at some centers.
End of life care	Palliative care should be provided, ideally in the patient's home when the patient with ILD deteriorates and reversible causes such as infection or PE are unlikely.[65]

GERD, Gastroesophageal reflux disease; *ILD,* interstitial lung disease; *IPF,* idiopathic pulmonary fibrosis; *PE,* pulmonary embolism.

MINI CLINI

Tobacco Use and Interstitial Lung Disease

Problem

A 30-year-old woman has ILD and is a current smoker. She is concerned that quitting on her own is too difficult and comments that tobacco use is associated with emphysema, not with scarring. Should she be encouraged to quit smoking? Why or why not?

Solution

Yes! Although the association between tobacco use and COPD is well known, the relationship with ILD is less well-appreciated. Smoking is a risk factor for the development of IPF but not the sole cause. However, the IIPs of DIP, RB-ILD, and PLCH have a strong association with cigarette smoking.

6. *Atherosclerotic vascular disease:* Many patients with ILD have independent risk factors for atherosclerotic vascular disease. They may have an unrelated cardiac disease, such as coronary artery disease, left ventricular dysfunction, or valvular disease, which can be mistaken for a worsening of the pulmonary process.

Each of the possible explanations for the patient's breathlessness should be considered before concluding that progression of the ILD is the cause of worsened dyspnea.

NONSPECIFIC THERAPIES

Several therapies should be considered in all types of ILD depending upon the patient's degree of impairment and physiology and these are listed in Table 26.4.

Almost all patients with DIP, RB-ILD, and PLCH are current or former tobacco smokers. As with other toxic exposures, complete avoidance of all smoke is important for these patients. In RB-ILD and PLCH, physiologic stabilization and occasionally even improvement can occur after stopping smoking. In DIP, the benefits of smoking cessation are unclear.

In addition to having concerns about these specific disease considerations, patients with ILD of any type cannot afford to risk developing additional, smoking-related cardiorespiratory impairment. The patient should be strongly encouraged to stop smoking.

SUMMARY

The entities grouped as ILDs are a diverse group of illnesses of varied cause, treatment, and prognosis. These diseases generally manifest as chronic, progressive dyspnea on exertion and cough. Findings on examination are often limited to the chest in the form of fine, inspiratory crackles. The most common finding on chest x-ray is diffuse reticular or reticulonodular infiltrates with reduced lung volumes. Pulmonary function testing usually reveals restrictive physiology and decreased diffusion capacity; however, other patterns can be seen. Therapy depends on the underlying disease and may consist of immunosuppressive drugs and the avoidance of disease-inducing exposures.

ROLE OF THE RESPIRATORY THERAPIST IN INTERSTITIAL LUNG DISEASE

- The respiratory therapist (RT) sees patients with ILD in one of two settings—as an outpatient or when the patient is hospitalized. RTs assess and treat outpatients in several manners. In the role of pulmonary function technician, the RT assesses disease burden and serial changes in lung function. At the initial evaluation, the RT needs to provide accurate spirometry, lung volume, and DLCO, along with 6-minute walk distance

and saturation, because these measures have important prognostic value. At subsequent visits, serial changes in these parameters are important to assess a patient's response to therapy or disease progression. Besides having important prognostic values, changes in lung function over time help determine whether to continue therapy or refer eligible patients for lung transplantation.

- RTs determine supplemental O_2 requirements at rest and with exertion and recommend the appropriate delivery amount, mode, and source of O_2. Also, RTs typically perform outpatient pulmonary rehabilitation, which can benefit many patients with ILD. RTs also may administer inhaled pentamidine, which is used to prevent *Pneumocystis jirovecii* infection in patients receiving immunosuppressive drugs for an ILD.
- The needs of patients with ILD change when admitted to the hospital. The RT plays a crucial role in assessing supplemental O_2 needs and delivering O_2 by the proper mode (nasal cannula, face mask, high-flow O_2 with non-rebreathing face mask, or intubation and mechanical ventilation). If obstructive impairment is suspected, the RT can recommend and deliver the appropriate bronchodilators or inhaled corticosteroids. Owing to the tenuous nature of these patients, careful monitoring by the RT of patients with ILD is required to prevent hypoxemia and its acute complications.
- Patients with ILD can progress to having severely impaired lung function and require mechanical ventilation for survival. In partnership with the other members of the patient care team, the RT must understand the treatment goals of the patient and must assess whether mechanical ventilation is indicated. Most patients with severe ILD will not meaningfully benefit from mechanical ventilation as it will only prolong the course of dying. However, in select cases, patients who are awaiting lung transplantation or who have a potentially reversible process, mechanical ventilation may bridge survival until lung transplantation or lung improvement.[59] The RT must be aware of the need for reduced tidal volumes, the potential lung injury that is associated with ventilation with large tidal volumes, and the potential need for elevated pressures to drive adequate ventilation because of decreased compliance.
- Patients who are awaiting lung transplantation or who develop severe primary graft dysfunction shortly after transplantation are candidates for extracorporeal membranous oxygenation (ECMO). Ideally, candidates for ECMO should be younger, have no significant comorbidities, and already be listed for lung transplantation or have no significant contraindications to quick listing.[60] While on ECMO, the lung should be rested as much as possible to prevent worsening ILD, and if possible the patient should be ambulated.

SUMMARY CHECKLIST

- ILDs are a diverse group of illnesses that can be organized into groups based on related causes.
- These diseases generally cause chronic, progressive dyspnea on exertion and cough.
- Findings on examination are often limited to the chest in the form of fine, inspiratory crackles.
- The most common chest x-ray finding is diffuse reticular or reticulonodular infiltrates with reduced lung volumes.
- Pulmonary function testing usually reveals restrictive physiology and decreased diffusion capacity; however, other patterns can be seen.
- Causes of the ILDs are diverse but are most frequently from exposure (tobacco, hypersensitivity pneumonitis antigens, silica, asbestos), autoimmune dysfunction (sarcoidosis, connective tissue disease associated), and abnormal injury healing (IPF).
- Treatment for IPF is now available with pirfenidone and nintedanib, both of which reduce the decline in lung function.
- Non-specific treatment may be considered in all ILD patients (e.g., supplemental O_2, pulmonary rehabilitation), but specific ILD treatment depends on the underlying disease and may consist of antifibrotic drugs for fibrotic disorders, immunosuppressive drugs for immune mediated disorders, and avoidance of disease-inducing exposures.

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27

Pleural Diseases[a]

Joseph Cicenia

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Describe the anatomy and function of the visceral and parietal pleura.
- Describe how pleural effusions occur and the difference between transudative and exudative effusions.
- Identify common causes of transudative and exudative pleural effusions.
- Write definitions of chylothorax, hemothorax, and pneumothorax.
- Describe the impact of moderate to large pleural effusions on lung function.
- State the role of the chest x-ray in recognizing pleural effusions.
- State the purpose of thoracentesis and the potential complications.
- Identify the definitions of spontaneous, secondary, and tension pneumothorax.
- Describe the diagnosis and treatment of pneumothorax, including the use and function of chest tubes and three bottle collection systems.

CHAPTER OUTLINE

KEY TERMS

alveolopleural fistula
bronchopleural fistula
chest tube
chyle
chylothorax
empyema
exudative pleural effusion
hemothorax
parietal pleura
pleural effusion
pleurisy
pleurodesis
pneumothorax
primary spontaneous pneumothorax
re-expansion pulmonary edema
secondary spontaneous pneumothorax
stomata
tension pneumothorax
thoracentesis
transudative pleural effusion
visceral pleura

A wide variety of pleural diseases affect respiratory function. An understanding of pleural anatomy, physiology, and pathology is essential for the respiratory therapist (RT) to deliver effective respiratory care. This chapter focuses on the two major diseases that occur in the pleural space: pleural effusion and **pneumothorax**.

[a]With acknowledgement and appreciation of Dr. Charlie Strange for his authoring of this chapter in earlier editions of this book.

THE PLEURAL SPACE

The pleura is a thin membrane that lines the lung itself, the inside of the chest wall, the diaphragm, and the mediastinum (Fig. 27.1). The pleural is divided into two regions: the **visceral pleura** covers the lung parenchyma (including within the interlobar fissures) and the **parietal pleura** covers the inside of the thoracic cavity. The two pleural surfaces meet at the lung root, located at the hilum (Fig. 27.2). Differentiation of the pleural surfaces is important, because each has its own unique physiologic

properties and anatomy. A small amount of fluid, known as the pleural fluid, typically floats freely within the space between the visceral and parietal pleura. It is thought that this thin layer of fluid serves as lubricant to allow the lung to slide freely along the chest wall during breathing. The space where the fluid circulates is called the pleural space, and it is considered a "potential space" such that it can accommodate large amounts of fluid, which can occur in disease states. Normally, the right and left pleural spaces do not communicate, as they are completely separated by the mediastinum.

The parietal pleura can be further subdivided into the regions it covers, including the rib surface (costal pleura), the diaphragm (diaphragmatic pleura), and the mediastinum (mediastinal pleura). Within the parietal pleura there are capillaries and lymphatic channels called *stomas*, and the parietal pleura is relatively thin compared with the visceral pleura. The parietal pleura is also richly innervated by sensory nerves, which originate in different areas depending on the area of pleura. Intercostal nerves supply the costal pleura, whereas the diaphragmatic pleural is supplied by the phrenic nerve. Thus stimulation of the diaphragmatic pleura will cause pain referred to the shoulder, whereas stimulation of costal pleural nerves will cause pain in the chest wall along the distribution of the corresponding costal nerve.

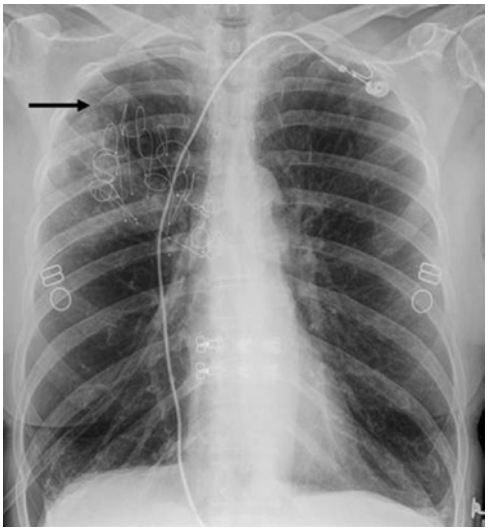

Fig. 27.1 The presence of a pneumothorax is diagnosed by identification of a pleural line *(arrow),* in this case after bronchoscopic placement of lung volume reduction coils. A hydropneumothorax requires identification of both a pleural line *(arrow)* and the air-fluid interface of pleural fluid that causes a straight line in the chest. A high-quality monitor is needed to optimally detect the pleura.

The visceral pleura is relatively thick, almost 2 to 3 times the thickness of the parietal pleura. The visceral pleura also has blood vessels running through it but no lymphatic stomas. Furthermore, the visceral pleura have a thick layer of connective tissue separating it from the lung. These differences in thickness impact fluid generation and drainage, with most of this occurring in the parietal pleura. The visceral pleura has no sensory innervation and thus can be manipulated without causing any pain.

The average person has approximately 8 mL of pleural fluid per hemithorax.[1] It is estimated that this pleural fluid has a total protein concentration similar to that of interstitial fluid elsewhere in the body: between 1.3 and 1.4 g/dL.[2]

The pleural space is under negative pressure except during forced expiration. This is an important concept, because if the pleural space pressure was positive, the lungs would collapse. The intact thoracic rib cage provides elastic recoil pressure outward, whereas the intrinsic recoil pressure of the lung is inward toward the lung hilum. The diaphragm further decreases the intrapleural pressure below atmospheric pressure to allow inspiration to occur. The overall contribution of each results in a normal pressure within the pleural space between 0 and −5 cm H_2O. In an upright person, the pressure is more negative at the top of the lung than at the bottom of the lung because of the weight of the lung and the effects of gravity. An important effect of the negatively pressurized pleural space is that fluid can move into the pleural space from adjacent sites when a communication is present.

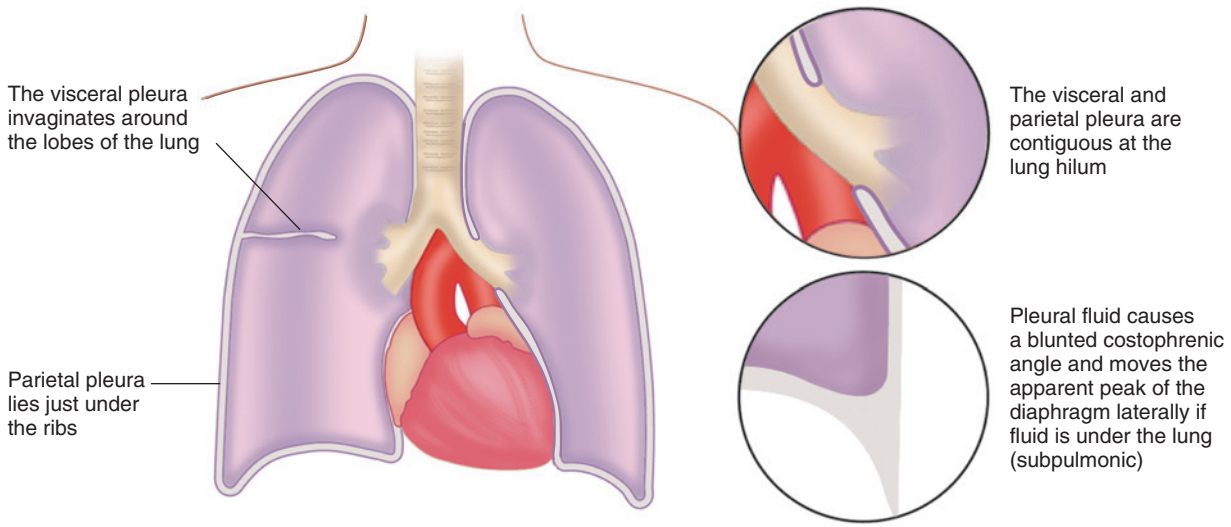

Fig. 27.2 Anatomy of the pleura.

PLEURAL EFFUSIONS

Any abnormal amount of pleural fluid in the pleural space is called a **pleural effusion**. The many causes of pleural effusion are categorized according to the factor that causes it and the content of the fluid.[3] Pleural fluid will accumulate in the pleural space when fluid formation overcomes the ability to drain the fluid.

Pleural fluid is normally produced from capillaries within the parietal pleura, and exits the pleural space through lymphatic **stomata**. The lymphatic stomata have a larger capacity to remove fluid compared to the normal rate of production, by almost 20 times. Normal production occurs at 0.01 mL/kg/h, and removal capacity is 0.20 mL/kg/h. Any process that results in alterations of production, removal, or both will result in a pleural effusion. Since parietal pleural stomata connect with intercostal lymphatic vessels under the ribs that drain posteriorly into the mediastinum, any process that impairs flow into the mediastinum will cause removal capacity to go down. Once in the mediastinum, these lymphatic vessels enter lymph nodes before draining into the thoracic duct, a large lymphatic channel within the chest, which empties into the left subclavian vein. Abnormalities along this path will also result in diminished fluid removal from the pleural space. Since pleural fluid arises from capillaries within the pleural membranes, any process that favors translocation across those capillaries into the pleural space will increase fluid formation, and if this is to a point that overwhelms the capacity for removal, a pleural effusion will also occur.

Transudative Effusions

Any pleural effusion that forms when the pleural space is intact is called a **transudative pleural effusion**. These generally occur due to systemic factors, and not due to factors impacting the pleura directly. Several pleural fluid testing schemes have sought to help identify a transudate by comparing values of the fluid to corresponding values in the serum. A pleural fluid total protein concentration less than 50% of the serum total protein level and lactate dehydrogenase (LDH) values in the pleural fluid less than 60% of the serum value indicate the presence of a so-called transudative pleural effusion. In the absence of serum values, an absolute pleural fluid LDH level less than two-thirds normal for serum suggests the presence of a transudate. These tests are best known as "Light criteria."[4] It should be remembered, however, that the designation of a transudate is contingent upon its cause not its corresponding lab values.

The classification system listed in Box 27.1 is not perfect, and refinements continue to be proposed. For practical purposes, the laboratory values used to assess the cause of a pleural effusion help narrow the possible causes of pleural fluid formation.

Transudative pleural effusions form when hydrostatic and oncotic pressures are abnormal (Fig. 27.3).[5] The list of diseases that cause transudative pleural effusions is short. Therefore, these diseases, listed as follows, remain relatively easy to diagnose.

Congestive Heart Failure

Elevation of pressure in the left atrium and pulmonary veins is the defining feature of *congestive heart failure* (CHF). Elevation

BOX 27.1 Causes of Pleural Effusion

Transudative pleural effusion
- Congestive heart failure
- Cirrhosis
- Nephrotic syndrome
- Hypoalbuminemia
- Lymphatic obstruction
- Peritoneal dialysis
- Atelectasis
- Central venous catheter in pleural space
- Urinothorax

Exudative pleural effusion—neoplastic disease
- Carcinoma
- Lymphoma
- Mesothelioma

Exudative pleural effusion—infectious disease
- Bacterial infection
- Tuberculosis
- Fungal infection
- Paragonimiasis
- Viral pleurisy

Exudative pleural effusion—pulmonary embolism and gastrointestinal disease
- Pancreatic disease
- Intraabdominal abscess
- Splenic infarction
- Esophageal perforation
- Abdominal surgery
- Endoscopic variceal sclerotherapy

Exudative pleural effusion—collagen vascular disease
- Rheumatoid pleurisy
- Systemic lupus erythematosus
- Drug-induced lupus
- Immunoblastic lymphadenopathy
- Sjögren syndrome
- Familial Mediterranean fever
- Churg-Strauss syndrome (eosinophilic granulomatosis with polyangiitis)
- Granulomatosis with polyangiitis (formerly called *Wegener granulomatosis*)

Exudative pleural effusion—drug-induced pleural disease
- Nitrofurantoin
- Minoxidil
- Dantrolene
- Methysergide
- Bromocriptine
- Amiodarone
- Procarbazine, bleomycin, mitomycin
- Methotrexate

Miscellaneous diseases and conditions
- Benign asbestos pleural effusion
- Post-cardiac injury syndrome (Dressler syndrome)
- Meigs syndrome
- Yellow nail syndrome
- Sarcoidosis
- Pericardial disease
- Fetal pleural effusion
- Uremic pleural effusion
- Trapped lung
- Radiation pleurisy
- Amyloidosis

Electrical burns

Hemothorax

Chylothorax

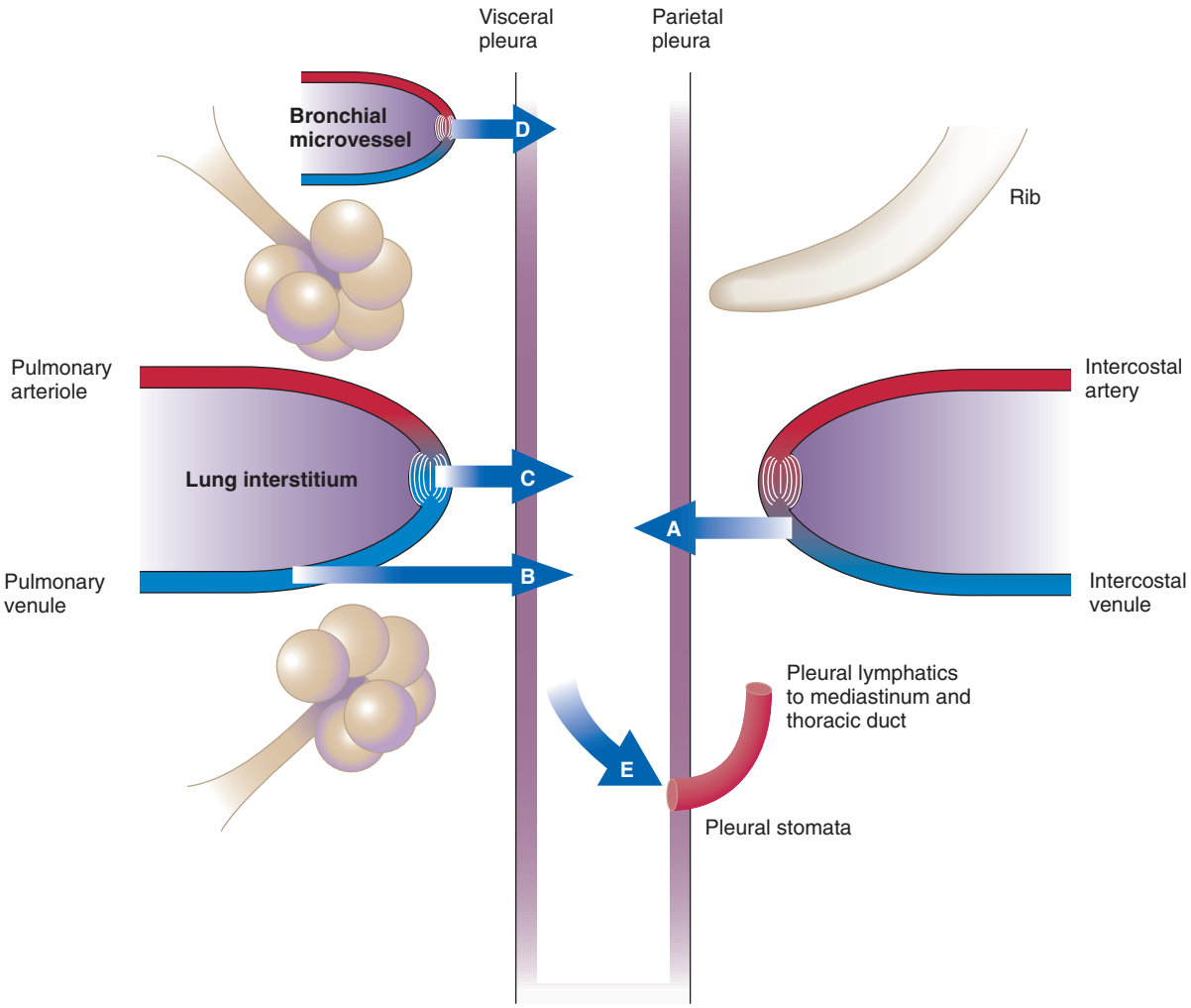

Fig. 27.3 Pleural fluid formation requires both excess fluid formation and decreased elimination. In diseases such as pulmonary arterial hypertension, in which right-sided heart pressure is increased and systemic veins, such as the intercostal veins *(A)*, are pressurized, pleural fluid does not form because pleural fluid formation is not increased and lymphatic drainage remains intact. However, when left ventricular failure causes pulmonary venule pressure *(B)* to increase, the addition of interstitial lung water overwhelms the drainage and produces a transudative pleural effusion. Injury to the capillaries *(C)*, as in pneumonia or acute respiratory distress syndrome, causes fluid to leak into the lung interstitium and pleural space at increased rates. Under these conditions, fibrin can occlude the pleural lymphatic vessels *(E)* and cause fluid to accumulate. The bronchial microvessels *(D)* supply the pleura with blood and likely participate to some extent in production of pleural fluid.

of pulmonary venous pressure increases the amount of interstitial fluid in the lung. In severe cases, flooding of the alveoli causes pulmonary edema, but in less severe cases, interstitial lung water increases and decompresses into the pleural space. Because systemic venous pressure also is elevated, there is limited capability to remove pleural fluid through the intercostal veins. Therefore, pleural fluid must be predominantly removed by the lymphatic vessels. Pleural effusions result when the capacity of pleural lymphatic drainage is overwhelmed.[6]

CHF is the most common cause of pleural effusions in clinical practice. The effusions can be massive, filling the entire hemithorax and compressing the lung. More commonly, they are small and bilateral. When pleural effusions from CHF are unilateral, they are twice as commonly on the right side as on the left; thus an isolated left pleural effusion resulting from CHF is unusual, and the occurrence of a unilateral left pleural effusion should cause suspicion of causes other than CHF. The effusions of CHF are rarely drained because outcome is heavily influenced by successful management of the underlying CHF, which also clears the effusions.[7]

RULE OF THUMB Pleural effusions associated with congestive heart failure are usually bilateral, but when unilateral, they are twice as commonly right-sided as unilaterally left-sided.

Nephrotic Syndrome

In *nephrotic syndrome* (also known as *nephrosis*), the kidneys leak more than 3 g of protein per day into the urine. Because

patients become protein depleted, there is insufficient oncotic pressure within the blood to hold appropriate amounts of fluid within the blood vessels. These patients become edematous, and fluid leaks into the lung interstitium and pleural space. Effusions are common in nephrotic syndrome. It is thought that nephrotic syndrome is a risk factor for venous thromboembolism, so pulmonary embolism should be considered in these patients as a cause of the pleural effusion if the clinical situation warrants.

Hypoalbuminemia

Hypoalbuminemia is caused by a variety of debilitating diseases, such as AIDS and chronic liver disease. Pleural effusions rarely form until the serum albumin level is less than 1.8 g/dL. The mechanism of formation of pleural fluid is identical to that of nephrotic syndrome. Low protein levels in the blood allow fluid to leak into interstitial tissues and the pleural space.

Liver Disease

End-stage liver disease causes transudative fluid to accumulate in the abdomen. This fluid is called *ascites*. Because the pleural space is under negative pressure during inspiration and because ascitic fluid often is under positive pressure, any small defect in the diaphragm can draw ascitic fluid into the pleural space to form what is called a *hepatic hydrothorax*.

All ascitic fluid can end up in the chest because of the pressure gradient, and true ascites can be absent. This condition often is quite difficult to manage except with methods that limit ascites formation, such as sodium restriction and diuretics. Excessive pleural fluid is present in approximately 6% of patients with ascites, and 70% of these fluid collections are on the right side.[8]

Atelectasis

When segments of the lung collapse, intrapleural pressure becomes more negative and can produce small effusions. With relief of bronchial obstruction and postoperative pain, these effusions may go away.

Lymphatic Obstruction

Lymphatic obstruction within the mediastinum causes poor pleural fluid removal from the pleural space, although the pleural space is otherwise normal. The most common condition that causes this abnormality is cancer that metastasizes to the mediastinal lymph nodes or that obstructs the pulmonary veins. This condition should be differentiated from a true malignant pleural effusion, defined as having actual cancer cells within the pleural space.

Rare Causes of Transudative Pleural Effusion

There are other rare causes of transudative pleural effusions. Urinothorax occurs after rupture of the ureter, causing a urine leak into the retroperitoneal space that refluxes into the chest. The pleural fluid in urinothorax has a low pH. A central venous line that is inappropriately placed into the pleural space can put large amounts of transudative fluid into the pleural space before this abnormality is recognized. The level of glucose in the pleural fluid can be very elevated if there is glucose in the intravenous solution that is being administered.

Exudative Effusions

In contrast to a transudate, an **exudative pleural effusion** is caused by inflammation in the lung or pleura that results in a direct effect upon the pleura itself. This type of pleural effusion contains more protein and inflammatory cells than does a transudative effusion. Because therapy for pleural effusion depends on the cause, **thoracentesis** often is performed to determine the specific biochemical and cellular characteristics of the pleural effusion. Box 27.1 lists the common causes of exudative pleural effusion. They account for approximately 70% of all pleural effusions.

Parapneumonic Effusion

Pleural effusions form in pneumonia because inflammation in the lung increases interstitial lung water and pleural fluid production. Most effusions are small and resolve with resolution of the bacterial pneumonia.[9] However, if the effusion is not small, it should be sampled via thoracentesis, with appropriate lab studies to determine if the fluid is at risk to become a complicated parapneumonic pleural effusion, in which a more definitive drainage procedure should be done.[10] Complicated parapneumonic pleural effusion develops when the pleural fluid has a high enough protein content to clot. The clotting causes fibrin strands to span the visceral and parietal pleura. The net result is collection of pleural fluid into different pockets called *loculi* within the pleural cavity. These often cannot be drained by a single **chest tube**.

Progression to **empyema** is marked by the presence of bacteria within the pleural space, seen as pus or bacteria on Gram stain. Empyemas require drainage, usually by chest tube placement or by surgery. Whether complicated parapneumonic effusions require drainage remains controversial, although most physicians perform drainage because some of these effusions can progress to empyema.[10]

Parapneumonic effusions are common causes of persistent fever among intensive care unit (ICU) patients with pneumonia. Sampling by thoracentesis is commonly performed to exclude empyema. Pleural fluid drainage can improve ventilation and dyspnea if the volume of fluid removed is large.[11]

Viral Pleurisy

Viral lung infections (**pleurisy**) can cause pleural inflammation, small pleural effusions, and pain. The effusions may be so small they may be overlooked on a routine chest radiograph, and even when they can be seen, the effusions often are too small to sample. Pleural pain, which is called *pleurodynia*, and which can be the result of many other pleural processes, often is difficult to manage. The typical patient with pleurodynia has shallow respirations; deeper breaths are limited by pain. The subsequent atelectasis can cause hypoxemia caused by shunting.

Tuberculous Pleurisy

In many parts of the world, any lymphocyte-predominant exudative effusion is considered tuberculosis until proved otherwise. Tuberculous pleural effusions occur when an area of prior tuberculosis infection reactivates and ruptures through the visceral pleural surface, causing an exudative inflammatory effusion. The

resultant pleural effusion is an immune reaction to the tuberculosis, rather than an infection of the pleural space per se. Though tuberculous effusions tend to be small to moderate, they may be excessively large and span the entire hemithorax. Tuberculous pleural effusions may resolve spontaneously, often with subsequent progression of the tuberculous infection in the lung.

Although these patients need respiratory isolation, only 25% of them have sputum that subsequently grows *Mycobacterium tuberculosis.* The purified protein derivative (PPD) skin test result is negative in 30% of patients when they come to medical attention but turns positive in 6 to 8 weeks in almost everyone.[12] Though recently serum interferon gamma assays have been used in the diagnosis of latent and active TB, they have no role in the diagnosis of tuberculous effusion.

Diagnosis of tuberculous effusions relies on high suspicion and a characteristic lymphocytic exudative profile of pleural fluid. Definitive diagnosis is usually made through finding a pathologic pattern of granulomas on biopsy of pleural tissue. Recent studies have shown that high levels of pleural fluid adenosine deaminase (ADA) or pleural fluid interferon gamma can also be diagnostic. Definitive diagnosis can also be made by isolation of Mycobacterium tuberculosis from sputum, pleural fluid, or pleural biopsy specimen.[13]

Malignant

Malignant disease is the most common cause of large unilateral pleural effusions among persons older than 60 years. Common cancers that form malignant pleural effusions include lung cancer and breast cancer, although any cancer can metastasize to the pleural surface. The effusions usually are lymphocyte predominant; malignant cells are found during cytologic examination of the pleural fluid.

Some malignant pleural effusions, such as those from lymphoma, respond to therapy for the malignant disease. However, most patients with symptomatic malignant pleural effusions need primary therapy with **pleurodesis** or placement of an indwelling tunneled pleural catheter. Pleurodesis describes the process of fusing the visceral and parietal pleural membranes and is described in more detail later in this chapter. If pleurodesis cannot be achieved, palliation through indwelling tunneled pleural catheters is an option.[14]

Postoperative Effusion

A variety of operations involving the chest or upper abdomen produce pleural fluid.[15] Effusions after cardiac surgery usually are predominant on the left side and tend to be bloody. These effusions are particularly prevalent after a cutdown of the internal mammary artery for coronary artery bypass.

Small transudative pleural effusions are common when there is any atelectasis in the lung. Upper abdominal operations cause inflammation of the diaphragm. The resulting effusion has been termed a *sympathetic* effusion. Lung surgery in which the lung is unable to fill the thoracic cavity leaves a space under negative pressure, which fills with inflammatory pleural fluid. When the lung is unable to fill the space because of small postoperative size or visceral pleural fibrosis, the resulting pleural effusion can never be completely drained because of the "trapped lung."

Chylothorax

The thoracic duct is a lymphatic channel that runs from the abdomen through the mediastinum to enter the left subclavian vein. The thoracic duct collects and transports **chyle** (a milky fluid consisting of fat droplets and lymph) into the central venous system. Disruption of the thoracic duct anywhere along its course can cause leakage of **chyle** into the mediastinum, which then may rupture into the pleural space and cause a **chylothorax**. The most common causes of rupture are malignancy (50%), surgery (20%), and trauma (5%).[16] The thoracic duct courses through the right side of the mediastinum in the lower thoracic cavity before crossing to the left side of the mediastinum at the level of the fourth to sixth thoracic vertebra (T4 to T6). Rupture below this level causes right-sided pleural effusion, whereas rupture above this level causes left-sided pleural effusion containing chyle.

In a patient who has eaten recently, the effusions are milky white as a result of the presence of chylomicrons (microscopic fat particles) absorbed by abdominal lymphatic vessels. In a fasting patient, these effusions usually are yellow, but they may be bloody. Regardless of the color, presence of emulsified fat droplets imparts a milky or glistening appearance to the fluid. When this is seen, specific studies should be done on the fluid to evaluate for chylous effusion. A pleural fluid triglyceride concentration greater than 110 mg/dL confirms the diagnosis of chylothorax.[17] Computed tomography (CT) should be performed to evaluate the cause of the chylothorax.

RULE OF THUMB A value of the triglyceride level in the pleural fluid above 110 mg/dL defines the fluid as a chylous pleural effusion. This should prompt consideration of the causes of chylothorax.

Hemothorax

Hemothorax is the presence of blood in the pleural space. Hemothorax is arbitrarily defined as a pleural fluid hematocrit more than 50% of the serum value. Small amounts of blood in otherwise clear fluid can turn the fluid red, so measurement of the pleural fluid hematocrit is necessary to make this diagnosis.

A hemothorax is seen most commonly after blunt or penetrating chest trauma. Any vein or artery in the thorax can bleed into the pleural space. A chest tube usually is inserted to monitor the rate of bleeding and determine whether the source is arterial or venous.[18]

Connective Tissue Diseases

Pleural effusions are found in a variety of connective tissue diseases, although the effusions usually are small. Effusions caused by inflammation of small blood vessels are the most common chest manifestation of systemic lupus erythematosus (SLE). Pleural effusions often accompany pericardial effusions in SLE and disappear with corticosteroid therapy.

Rheumatoid arthritis produces a characteristic effusion with a very low glucose content and low pH. These effusions can cause visceral pleural fibrosis and a trapped lung.

Uremic Effusion

Uremic pleurisy occurs under the same conditions as uremic pericarditis, which is inflammation of the pericardium (or sac enclosing the heart). The typical patient is undergoing dialysis that is inadequate in duration or frequency. Although the cause of pleural and pericardial inflammation in kidney failure remains unknown, the inflammatory process can take weeks to resolve.

Miscellaneous Causes

Discussion of the other causes of exudative effusions is beyond the scope of this chapter. Nevertheless, thoracentesis that yields findings compatible with any of those in the systemic diseases listed in Box 27.1 can narrow the differential diagnosis.

Physiologic Importance

Mechanics of Ventilation

Pleural effusions cause lung atelectasis because the capacity of the thorax to expand is limited and fluid collapses the lung. Spirometry can show restriction in individuals with pleural effusions. Studies correlating the volume of pleural fluid removed with improvement in forced vital capacity (FVC) show much variability from patient to patient.

RULE OF THUMB The patient's vital capacity improves by approximately one-third of the pleural fluid volume removed. The remainder of the pleural fluid volume causes diaphragmatic compression and chest wall expansion. Some patients have a delay of 24 to 48 hours before the improvement can be seen as atelectasis resolves. Lack of any improvement suggests that lung consolidation or endobronchial obstruction is present. Improvement is less when the underlying disease is acute respiratory distress syndrome (ARDS).

Dyspnea is common with pleural effusions, even when lung mechanics are relatively preserved. The mechanisms remain unknown but are likely associated with abnormalities in gas exchange and respiratory mechanics, impaired diaphragm function, and altered hemodynamics.[19] Dyspnea relief is variable after pleural fluid removal. Some patients have symptomatic relief after removal of small pleural fluid volumes. Others can actually have more dyspnea if the fluid is removed in situations such as trapped lung, in which neural activation may increase with fluid withdrawal.

In rare instances, the pleurae thicken with a disease process sufficient to cause fibrothorax. Technically, fibrothorax is any process that causes fibrosis of the thoracic cage that affects pulmonary function. Fibrothorax can be caused by diseases of the skin (e.g., fibrothorax that occurs, rarely, in scleroderma), soft tissue, bone (e.g., myositis ossificans, a disease in which muscles calcify), or pleura. The causes of pleural thickening significant enough to produce restriction include severe asbestos pleurisy, rheumatoid pleurisy, complicated trauma, cancer, and empyema. Treatment of fibrothorax from a pleural cause requires surgery, which is rarely performed because it is a very difficult operation.

Hypoxemia

Most patients with a pleural effusion have an increased alveolar-arterial (A-a) gradient (see Chapter 12) and a reduced P:F ratio resulting from the pathologic changes in the lung that are causing the effusion (see Chapter 12). Oxygenation can worsen after thoracentesis because changes in ventilation/perfusion ($\dot{V}/\dot{Q}$) matching are not instantaneous. Recovery to baseline PO_2 and subsequent improvement usually occurs a short time after thoracentesis.[19]

Diagnostic Tests

Chest Radiography

The chest x-ray is the most common method of detecting a pleural effusion (see Chapter 21). It is important that, if possible, the chest x-ray be obtained with the patient in an upright position to show a pleural fluid meniscus at the costophrenic angles. Many ICUs have rules that all chest x-rays are taken with patients sitting upright to optimize the value of the test. When the same patient undergoes radiography in the supine position, the effusion is distributed throughout the posterior part of the chest. The chest x-ray shows a generalized haze, which interferes with detecting pulmonary infiltrates and quantifies the amount of fluid in the pleural effusion.

Lateral decubitus chest x-rays (see Chapter 21) are performed by having patients lie on their side with the radiograph taken across the bed or table. This technique can show an effusion as small as 5 mL. This technique is used less often than other tests.

Ultrasonography and Computed Tomography

Pleural fluid can be detected easily with ultrasonography of the chest. Ultrasound can also detect the presence of fibrous strands, or loculations, that have developed in the pleural fluid. The sensitivity of ultrasonography for pleural effusions is high, although ultrasonography is an operator-dependent study. Small portable ultrasound machines with high diagnostic accuracy have become available to localize the presence and location of pleural effusions. Most physicians use them routinely to optimize thoracentesis success.

CT scanning of the chest is the most sensitive study for identifying a pleural effusion. A contrast-enhanced scan is needed to delineate the pleural membrane and differentiate peripheral lung consolidation from pleural fluid. In addition to showing the size and location of a pleural effusion, the chest CT scan often gives information about the underlying lung parenchyma and the primary process causing the effusion.

Thoracentesis

In thoracentesis, pleural fluid is sampled percutaneously by means of inserting a needle into the pleural space (Fig. 27.4). Administering an adequate local anesthetic ensures a painless procedure if care is taken to place lidocaine at the skin insertion site, along the periosteum of the involved rib, and at the parietal pleura, which is richly innervated with sensory nerve fibers. Diagnostic sampling of pleural fluid for cell counts, cultures, chemistries, and cytologic examination usually can be performed with a single syringe and a small needle. Samples for pleural pH should be kept from contact with room air. Pleural fluid drainage with lung re-expansion involves placing a larger catheter into the pleural space.

Thoracentesis involves the following three major risks: (1) intercostal artery laceration, (2) infection, and (3) pneumothorax.[20] Both an artery and a vein course under every rib, and the

vessels become increasingly serpiginous with aging. Ensuring needle passage just over the rib margin makes bleeding during thoracentesis rare.

Because infection can be introduced into the pleural space, maintaining sterility during the procedure is necessary. In some situations, the risk for infection is so high that thoracentesis rarely should be performed. When a lung is surgically removed, the space fills with sterile fluid. An infection introduced into this space usually requires open surgical drainage. Any trapped lung also carries a high risk for empyema because of the inability of the visceral and parietal pleura to meet and contain any infectious process. Needle puncture remains one of the most common causes of pneumothorax (see discussion of pneumothorax later in this chapter).

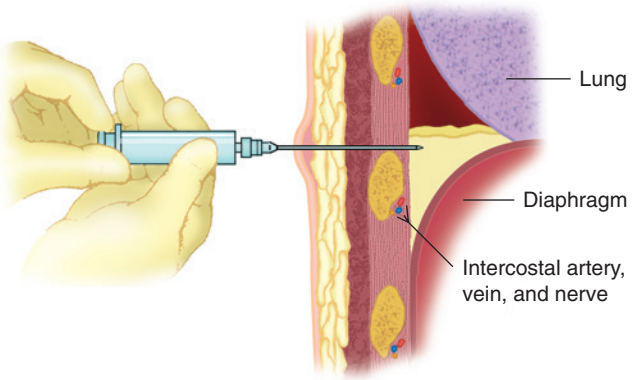

Fig. 27.4 The technique of thoracentesis involves passage of a needle just above the rib. If the needle is placed too low on the chest, the diaphragm or organs below the diaphragm can be punctured. Diagnostic thoracentesis can be performed with small amounts of pleural fluid.

Chest Thoracotomy Tubes

Chest tubes currently are manufactured in a variety of sizes and shapes, from 7 to 40 Fr catheters. Catheter choice is frequently a matter of physician preference. The letter "F" stands for "French," a unit of width of the tube with larger numbers indicating wider tubes. The French size is three times the external diameter for the catheter in millimeters, so that a 6 Fr catheter has a 2 mm external diameter. Larger tubes are less likely to become obstructed and are capable of high airflow rates. Smaller tubes are easier to place over guidewire systems and cause less pain.

RULE OF THUMB The French size indicates three times the diameter of a tube in millimeters. For example, a 6 Fr tube has a 2 mm external diameter.

Intercostal placement is designed for the skin and soft tissue to approximate the tube and prevent air from entering the pleural space from the outside. The chest tube is then connected to a water-sealed chamber, which usually is contained within a commercially marketed three-bottle system that also regulates pleural pressure and is used to measure pleural fluid volume (Fig. 27.5).

RULE OF THUMB Chest tubes are usually removed when the volume of pleural fluid that comes out is less than 50 mL/24 h. To optimize pleural space drainage, chest tubes should not be kinked. Higher volumes suggest that the primary process has not been treated adequately. Daily monitoring of pleural fluid volume requires that the pleural fluid drainage system not be tipped over. Volumes should be recorded in the medical chart and marks made on the pleural drainage system to help determine the best time for chest tube removal.

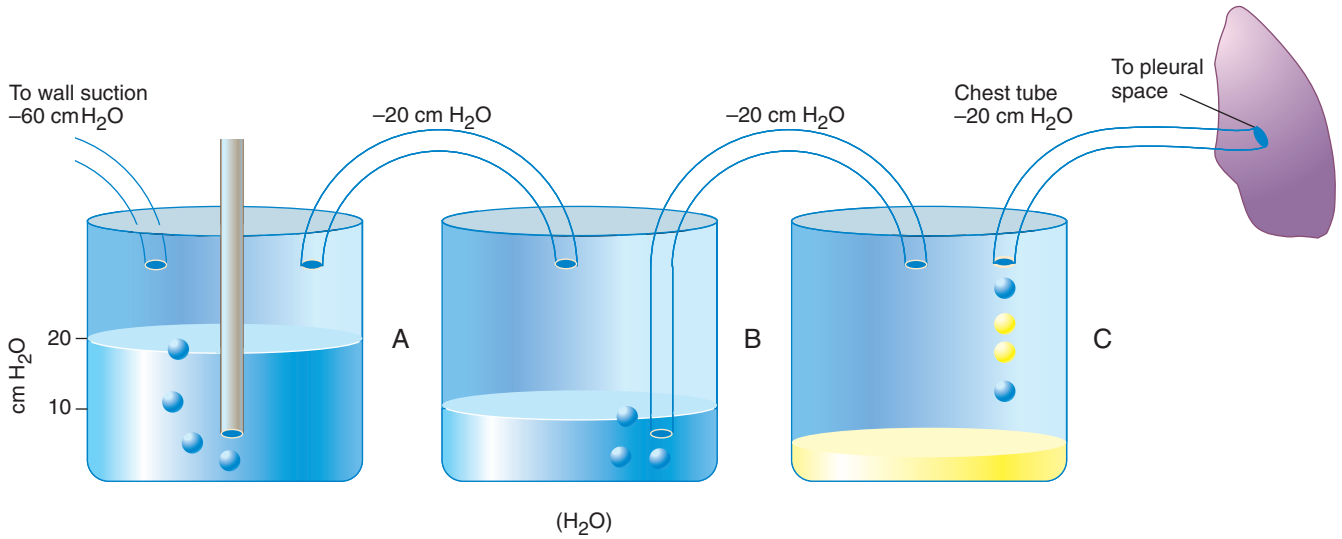

Fig. 27.5 The standard three-bottle system is the basis for all commercial chest tube drainage systems. Pleural fluid and pleural air enter compartment *C*, which serves as a fluid collection trap so that the water-seal fluid volume will not rise (compartment *B*) and create resistance to air escaping the chest. Air cannot be inspired into the chest because of the water in compartment *B*. Open entrainment of room air through a submerged tube in compartment *A* buffers the amount of wall suction applied (–60 cm H_2O) to the height of the water column to standardize the pressure (–20 cm H_2O) transmitted to the chest.

Chest Tube Drainage Systems

Three bottle systems are now integrated into commercially available chest drainage systems that house each of the bottle components into a compact system. These commercial systems will house a water-seal chamber, suction control chamber, and a collection chamber in one container, and all will have a one-way valve that prevents air or fluid from returning into the chest. Commercial systems vary slightly, and the therapist should be aware of each commercial unit's design, set up, and functionality, as determined by the manufacturer. In general, the water seal is usually set at the 2 cm mark, and the suction control component is set at the −20 cm H_2O level (which can be adjusted on many units, if ordered by the physician). The suction control component of the system is what determines the suction level (regardless of the degree of wall suction).

Systems are set up at the bedside using sterile water. The water seal chamber is first filled to the level recommended by the manufacturer. Next, the suction control chamber is filled to the desired level (usually −20 cm H_2O). The drain is then connected to a vacuum (usually wall suction), and suction is increased slowly until bubbling appears in the suction control chamber. Avoid excessive bubbling, as this can result in accelerated evaporation of the water in the chamber, which, in turn, will change the suction pressure. After the chest tube drainage system is set up, the chest tube should be secured to the collection system.

Water levels in the water seal and suction control chambers should be checked daily to ensure that evaporation has not changed volumes significantly. If there is an active air leak, bubbling will be seen in the water seal chamber. Bubbling should only occur during expiration (unless a large air leak is present). If bubbling occurs throughout the respiratory cycle, then the system should be checked for leaks or loose connections.

The chest tube and chest tube system should be checked frequently, looking for tube migration, subcutaneous emphysema, or kinking of the tube. Kinking of the tube can be especially serious because it can result in development of expanding or **tension pneumothorax**. Kinking should be suspected if there are no fluid fluctuations (the fluctuations are known as "tidaling") in the water seal chamber. Another cause of loss of tidaling includes tube occlusion by fluid or clot, or unintended clamping of the tube.

RULE OF THUMB Fluctuation of the water level, known as tidaling, should normally occur in the water seal chamber with respiratory effort. During spontaneous inspiration, the water level should increase, and during spontaneous expiration, it should decrease. However, this should reverse normally if the patient is on mechanical or positive-pressure ventilation. If tidaling does not occur, check for tube kinking, clamping, or occlusion.

As a rule of thumb, the chest tube should only be clamped temporarily (for instance, when changing the chest tube drainage unit). Stripping and milking of the chest tube should also be avoided, as this could create significant negative pressure within the tube; clots should be gently squeezed forward into the chest tube collection unit.

Thoracoscopy

The video-assisted thoracoscope is ideally designed for diagnostic and therapeutic work in the pleural space. Thoracoscopy is generally a procedure done by thoracic surgeons in the operating room, done by placing instruments through ports placed between the ribs such that direct visualization of the pleural space can occur. Typically this will be done utilizing three ports: one for instruments that contain a light source and video camera, one for instruments that could move tissue and lung aside, and one for instruments that can take biopsies. "Medical" thoracoscopy is sometimes performed by those trained in this procedure. This procedure can be performed in a medical procedure room using local anesthesia and conscious sedation. Medical thoracoscopy is reserved for more basic cases and should only be done by highly trained individuals.

Pleurodesis

Pleurodesis is the process of fusing the parietal and visceral pleura by causing a fibrotic reaction that prevents further pleural fluid formation and seals the pleural space. Methods to produce pleurodesis include surgical abrasion of the pleural surface and the application of intrapleural chemicals such as doxycycline, minocycline, and talc. Talc has been applied as a powder suspended in sterile saline solution and injected through the chest tube (talc slurry) or dusted through a thoracoscope (talc insufflation). The success rate of talc pleurodesis, approximately 90%, is higher than that of all alternatives except surgical abrasion.[21,22] Pleurodesis is used most commonly in managing symptomatic pleural effusions caused by cancer.

Although pleurodesis of benign effusions, such as those occurring with CHF, nephrotic syndrome, and idiopathic chylothorax, has been performed successfully, the procedure is discouraged for pleural effusions that are not malignant. Most pleural effusions are best managed by controlling the underlying condition.[23]

Pleuroperitoneal Shunt and Indwelling Catheter

In refractory pleural effusions that cannot be treated adequately with pleurodesis, a small pump (PleurX, CareFusion, San Diego, CA) can be placed subcutaneously and tubes placed in the pleural and peritoneal spaces. The pleuroperitoneal connection has a one-way valve and a pumping mechanism to allow the patient to expel pleural fluid from the negatively pressurized chest to the positively pressurized peritoneum. The pleuroperitoneal shunt is placed as a last resort for refractory pleural effusions for which there is no other treatment.

More commonly, an indwelling catheter is placed into the pleural space and tunneled under the skin to prevent infections. This catheter then exits the skin and has an adapter that hangs outside of the body. The patient or family member then connects this catheter to vacuum bottles that fill with pleural fluid. In this way, pleural fluid can be removed at home for recurrent effusions. If the pleural space is kept dry, a pleurodesis often results, and the catheter can then be removed.[24]

Teaching is facilitated by online resources from the catheter manufacturer that provide reading materials for home use. However, there is no substitute for hands-on training. If a PleurX

MINI CLINI

Indwelling Catheter Care

Problem

A patient with a malignant pleural effusion has an indwelling pleural catheter (PleurX) placed during his hospitalization and is now ready for hospital discharge. The nurse on the ward asks you to assist with discharge planning of the patient with this device.

Solution

The care of an indwelling catheter at home requires the involvement of a dedicated caregiver who needs to be taught about proper catheter care, timing and technique of drainage, and vacuum bottle inventory. There is often one individual in a hospital that is most knowledgeable to provide this teaching. Often, this person is an RT. Note that the brand name of PleurX (Becton Dickinson, Franklin Lakes, NJ) is unique to the first company that advanced this technology and that other catheter systems are also available.

catheter is available on the hospital ward, dedicated time for teaching home care is best done a few days before hospital discharge. This allows the home care provider to have a better comfort level and causes fewer questions after the patient returns home.

One major risk is infection. The risk for infection is sometimes worse than with other wounds, because many of these patients have cancer and may be immunosuppressed by chemotherapy or radiation. Infection can occur at the skin surface or by introducing an infection at the vacuum bottle adapter. The skin wound should be kept covered with a clean dressing, and signs of colored discharge or redness should prompt medical evaluation. A suture is left in place for some time after placement, and a suture abscess should prompt medical evaluation. To prevent introducing bacteria inside the catheter, the adapter should be cleaned before vacuum bottle attachment.

The number of vacuum bottles needed and the timing of drainage is determined by the volume of pleural fluid on previous drainage days. The goal of the catheter is to keep the pleural space dry enough to allow a natural pleurodesis by growth of cancer cells between the parietal and visceral pleura. The other goal is dyspnea relief. Vacuum bottle inventory and access is determined by local resources but should be preplanned.

Ultimately, the management of a PleurX catheter and whether it can be removed is a medical team decision best informed by a diary of pleural fluid volume removal and the patient's medical condition. RTs should know about this device and its care.

PNEUMOTHORAX

Pneumothorax is air in the pleural space. Although air can enter the pleural space from outside the body, as occurs in sucking chest wounds, most cases of pneumothorax occur when disruption of the visceral pleura allows air from the lung to enter the pleural space. Pneumothorax is discussed according to the causative (etiologic) factor because traumatic pneumothorax is managed differently from spontaneous pneumothorax.

Chest pain, which is typically sharp and abrupt, occurs in nearly every patient with pneumothorax. Palpation of the chest wall does not worsen the pain, although respiratory efforts may be difficult. Dyspnea occurs in approximately two-thirds of patients when decreases in vital capacity and PO_2, probably as a result of airway closure at low lung volumes, cause $\dot{V}/\dot{Q}$ defects and shunting. When a spontaneous pneumothorax is evacuated, hypoxemia may persist in some patients.

The following sections describe the diseases that cause pneumothorax and the important treatment differences among them.

Traumatic

Blunt and Penetrating Chest Trauma

Traumatic pneumothorax can be caused by either blunt or penetrating wounds of the thorax. The common causes of penetrating wounds include gunshots and knife punctures. In many cases, penetrating trauma to the chest can be managed conservatively with a chest tube. The clear indications for entering the chest surgically are associated injuries to the intercostal or pulmonary arteries, or injury to the heart or great vessels, with resultant uncontrolled bleeding into the pleural space. In these situations, the pneumothorax becomes secondary.

In blunt trauma to the chest, pneumothorax can be the result of a rib fracture that punctures the lung parenchyma and allows air to leak into the pleural space. For this type of injury, a chest tube is placed, and the rib fractures need no specific therapy. Another common injury is alveolar rupture at the pleural surface, which breaks through the pleural membrane and leaks air directly into the pleural space.

Two special injuries that produce pneumothorax are tracheal fracture and esophageal perforation or rupture. Tracheal fracture results from severe deceleration injury, such as that which may occur in a serious motor vehicle accident (usually a chest against a steering wheel or air bag), and often occurs along with fractures of the anterior aspect of the first through third ribs. In this case, urgent bronchoscopy is appropriate to identify the injury and its location, because tracheal fracture must be corrected surgically. Esophageal rupture is usually the result of trauma; esophageal perforation can be a complication of an upper GI endoscopy. Both injuries can produce an air fluid level in the pleural space. The level of amylase in the pleural fluid is typically elevated from a salivary (not pancreatic) source. Fluid pH may also be low (< 6.0). Patients with esophageal rupture are usually very ill and require urgent endoscopic and/or surgical management.[25]

Large-caliber chest tubes (generally >28 Fr) are placed for trauma-related pneumothoraces to allow exit of blood and blood clots, which can be difficult to remove through small-bore catheters. Chest tubes between 28 and 32 Fr seem to be comparable to larger chest tubes (>36 Fr) in the management of traumatic pneumothorax, with or without concurrent hemothorax.[26] Air leaks from an injured lung can be large. When bleeding is a major component of pleural injury, two chest tubes are used: a posterior chest tube to drain blood that is gravity-dependent and an anterior and apical chest tube to drain air that moves to the lung apex in the absence of pleural disease.

Iatrogenic

Iatrogenic (healthcare provider–caused) pneumothorax is the most common type of traumatic pneumothorax. Common causes are punctures of the lung from needle aspiration lung biopsy, thoracentesis, and central venous catheter placement. Unusual

causes, such as feeding tube placement into the pleural space, also have been recorded. Because the pleural rupture is typically small in the absence of parenchymal lung disease, these lung punctures usually resolve within 24 hours and can be observed without chest tubes as long as serial chest x-rays are obtained. If the pneumothorax enlarges or becomes symptomatic during this time, then a decision to place a chest tube is usually made. Typically, since these air leaks are small (since they are usually from needle sticks), pneumothorax can be treated with smaller percutaneous chest tubes (18 to 24 Fr).

Neonatal

In radiographic series, spontaneous pneumothorax occurs in 1% to 2% of all infants soon after birth.[27] The cause of pneumothorax is likely high transpulmonary pressure during birth coupled with transient bronchial blockade caused by meconium, mucus, or aspiration of blood that can produce transpulmonary pressure gradients as high as 100 cm H_2O.

Recognizing pneumothorax is difficult because breath sounds are transmitted widely through the chest of the neonate. A shift of the heart sounds away from the side of the pneumothorax may provide a clue. Transillumination of the chest with a high-intensity light is used in some centers. Almost all neonates with pneumothorax need a chest tube.

Spontaneous

Spontaneous pneumothorax is defined as any pneumothorax caused by the escape of air into the pleural space without an obvious cause. Spontaneous pneumothoraces are of two types: (1) **primary spontaneous pneumothorax**, in which there is no underlying lung disease, and (2) **secondary spontaneous pneumothorax**, in which underlying lung disease is present.

Primary

Primary spontaneous pneumothorax occurs without underlying lung disease. In a way, this term is a misnomer, because high-resolution CT scans have shown the presence of small subpleural blebs in more than 80% of patients.[28]

Primary spontaneous pneumothorax usually occurs in patients in their late teenage years or early 20s. Patients often are tall, slender, and frequently male, and the lungs and pleural membrane may not have grown at the same pace; the result is airspace enlargement and a thin pleural membrane.

Results of some studies suggest that cigarette smoking is a risk factor in more than 90% of cases of primary spontaneous pneumothorax.[29] The smoking history is typically short, and smoking cessation is recommended.

Secondary

Secondary spontaneous pneumothorax occurs in patients with underlying lung disease. In most cases, the underlying lung disease is chronic obstructive pulmonary disease with some component of emphysema. Pneumothorax also can occur with asthma and cystic fibrosis, usually during an exacerbation of disease.

Interstitial lung diseases in which lung volumes are spared, such as sarcoidosis, bronchiolitis obliterans with organizing pneumonia, Langerhans cell histiocytosis, and lymphangioleiomyomatosis, have a higher incidence than do diseases without any component of obstruction.

Depending on the extent of parenchymal lung disease, pneumothorax in this population can be devastating. A Veterans Affairs cooperative study included 185 patients with secondary spontaneous pneumothorax and monitored them for 5 years.[30] Although only three patients died of pneumothorax, the mortality rate in the series was 43%. Severe underlying lung disease caused most of these deaths. This finding suggested that most pneumothoraces occur in patients with severe lung dysfunction. The degree of dyspnea is out of proportion with the size of pneumothorax in this group of patients because pulmonary reserve is already diminished. Due to diminished pulmonary reserves in these patients, pneumothorax in this cohort of patients should almost always be initially treated with a chest tube. Because the recurrence rate of pneumothorax is high in these patients (up to 50% in 3 years), pleurodesis, either through video-assisted thoracoscopic surgery (VATS) or nonsurgical chemical pleurodesis, is recommended for prevention of recurrent pneumothorax.

Catamenial Pneumothorax

Catamenial pneumothorax occurs in association with menstruation and usually is recurrent and right-sided. The reason for the right-sided predominance is unclear. Many patients have endometriosis on the pleural surface, although it may be impossible to see because of hormonal involution during menses. Once the diagnosis is considered, catamenial pneumothorax is not difficult to manage in that most patients do not have a recurrence if ovulation is suppressed.

Barotrauma disrupts alveoli and allows air to enter the interstitium of the lung. Rupture of the visceral pleura allows air to produce a pneumothorax, or the air can travel along the low-resistance tissue planes of the bronchovascular bundles and through the hilum of the lung to enter the mediastinum. From the mediastinum, air has easy access to the retroperitoneal space, including the scrotum and the neck. The presence of subcutaneous air does not necessarily mean that pneumothorax has occurred, although the risk factors for its development are present.

Air under pressure in the pleural space can enter the subcutaneous tissues through the intercostal incision made for chest tube placement. Subcutaneous air often is seen on a chest x-ray after chest tube placement, but the air rarely spreads unless the chest tube is occluded.

MINI CLINI

Subcutaneous Emphysema

Problem

A patient with ARDS experiences subcutaneous emphysema. How does the clinician determine where the air leak is occurring? Is a pneumothorax always present?

Solution

Subcutaneous emphysema occurs when air enters the soft tissues. Although physical examination reveals subcutaneous bubbles, the patient's family needs to be reassured that the condition is rarely, if ever, physiologically significant. What is important to recognize, however, is that alveolar disruption has occurred, most commonly as the result of barotrauma.

In the absence of pneumothorax, there is no way to determine which lung is causing subcutaneous emphysema. For any deterioration in gas exchange, chest x-rays should be repeated. Because air in the mediastinum can displace the mediastinal parietal pleura, it can be difficult to tell without chest CT whether a small pneumothorax is present. Because patients often are too unstable to be moved, a chest tube sometimes is placed because the potential benefits are greater than the risks.

Complications of Pneumothorax

Tension Pneumothorax

Tension pneumothorax occurs when air in the pleural space exceeds atmospheric pressure. The radiographic appearance includes mediastinal shift to the contralateral side, diaphragmatic depression, and expansion of the ribs. The lung does not necessarily collapse completely if it is involved with a disease process such as ARDS.

Not all patients with radiographic tension have the physiologic changes commonly associated with tension pneumothorax. However, almost all pneumothoraces that occur during mechanical ventilation enlarge if not drained.[31]

As pressure in the thorax increases and mediastinal shift places torsion on the inferior vena cava, venous return to the right side of the heart decreases. Cardiac output decreases, and hypotension with tachycardia results. Hypoxemia occurs as the lung continues to compress because of intrapulmonary shunting through the collapsed lung.

The RT can help make the diagnosis of tension pneumothorax by recognizing these findings, especially in patients at risk. Treatment is emergency decompression of the chest. This procedure usually is done with an 18-gauge intravenous catheter (e.g., Jelco, Smiths Medical, Dublin, OH) inserted just over the second rib on the anterior aspect of the chest in the midclavicular line. Catheter placement should elicit a rush of air through the catheter, and this sign confirms the diagnosis. The blood pressure should recover rapidly, and many other adverse findings often rapidly improve. However, resolution of hypoxemia depends more on complete lung re-expansion and can be delayed. The soft intravenous catheter can be left in place while a more conventional chest tube is inserted. Newer small-gauge percutaneous pneumothorax kits are now available. These kits allow for rapid insertion of small-bore pigtail tubes for the management of pneumothorax, with similar placement over the second rib in the midclavicular line.

RULE OF THUMB Tension pneumothorax is a clinical diagnosis made at the bedside in more than 50% of cases. The clinical signs are diminished breath sounds, hyperresonance to percussion, tachycardia, and hypotension.

RTs are well-positioned to make a timely diagnosis because ventilator alarms, including high-pressure alarms (see Chapter 52) give early warnings.

Re-Expansion Pulmonary Edema

Re-expansion pulmonary edema occurs in a lung that has been rapidly reinflated from low lung volumes, particularly when the pneumothorax has been long-standing or when the pressure gradient across the lung has become high. This might occur when there is endobronchial obstruction from cancer, mucus, or blood.

For many years, it was believed that alveolar edema occurs because intraalveolar pressure becomes negative and pulls fluid from the vasculature. However, the lung fluid has high protein content, a finding that suggests blood vessels have been injured as well.

One of the proposed mechanisms of vascular injury is a phenomenon of reperfusion injury caused by reactive oxygen species. Support for this hypothesis has come from experimental studies that have shown that administering antioxidants before re-expansion decreases the amount of re-expansion pulmonary edema.

Regardless of the cause, lung re-expansion in nonemergency situations should proceed slowly, and transpulmonary pressure should not become excessive. Most physicians who insert a chest tube for a large pneumothorax first place it to the water seal without suction, to allow the air to drain passively and slowly. Making sure that the lung remains expanded when active suction on the chest tube chamber is turned off increases confidence that the initial reason for the pneumothorax has resolved. If the lung is not completely inflated on the subsequent chest x-ray, the chest tube is placed back on suction. Re-expansion pulmonary edema can also occur after drainage of large pleural effusions.

Diagnosis

The diagnosis of pneumothorax is established with chest x-ray or ultrasound. The diagnosis requires a high-quality film to visualize a visceral pleural line. In the ICU, as many as 30% of cases of pneumothorax may be missed on a chest x-ray in retrospect. Impediments to diagnosis include a low-quality chest x-ray or using a computer monitor, supine position of the patient, concomitant presence of mediastinal air, and subpulmonic or mediastinal position of the pneumothorax. Diagnosis is enhanced with additional upright chest x-rays or decubitus views.

The size of a pneumothorax is difficult to assess with a chest x-ray, because a two-dimensional picture is being taken of a three-dimensional thorax. Size can be estimated with volume equations and can be confirmed with CT if needed.

RULE OF THUMB The size of a pneumothorax on a chest x-ray can be estimated with the knowledge that the volume of the lung and thorax is proportional to the cube of their diameters.

For example, on a chest x-ray, the chest measures 8 cm from the spine to the lateral chest wall. A pneumothorax is measured 2 cm from the chest wall:

$$\text{Volume of the lung} = (6\text{ cm})^3 \approx 216\text{ cm}^3$$
$$\text{Volume of the hemithorax} = (8\text{ cm})^3 \approx 512\text{ cm}^3$$
$$\text{Lung size} = 216/512 = 42\%$$
$$\text{Pneumothorax size} \approx 58\%$$

The equation shows the large volume of lung that a pneumothorax can displace despite a "small" distance from the lung to the chest wall. Use of the equation is not as accurate as chest CT because many pneumothoraces collapse asymmetrically.

The diagnosis of pneumothorax by ultrasound occurs when the normal finding of lung sliding is lost. Ultrasound is not capable of judging the size of the pneumothorax because air in the pleural space does not transmit sound waves, and the lung is not seen.

Therapy

Oxygen

Supplemental oxygen should be administered to all patients who have a pneumothorax. Most of the air in a pneumothorax is nitrogen (N) because O_2 is readily absorbed. If an air leak is continuing, supplemental O_2 rather than N leaks into the pleural space. After an air leak has been stopped, administering O_2 decreases the blood and tissue partial pressure of N surrounding the pleural space. Pneumothorax resolution is normally 1.25% of the air per day. O_2 speeds recovery by increasing the gradient of N from the pleural space to the pleural tissues.

Observation

Although there is no high-quality evidence comparing conservative and interventional management of primary spontaneous pneumothorax, several society guidelines and consensus statements recommend observation in patients with small pneumothoraces that are asymptomatic.[32] A small iatrogenic pneumothorax also should be managed with observation. Primary spontaneous pneumothorax often is observed for 4 hours in the emergency department (ED) before discharge to home follow-up care, as long as the pneumothorax is not found to enlarge on serial chest x-rays. Discharged patients should have ready access to emergency care facilities and should be advised to return if they experience any worsened dyspnea or pain.

During observation, it is important to record the respiratory rate and any signs of deteriorating respiratory function, including perception of dyspnea. A decrease in the patient's oxygen saturation can be an early warning of pneumothorax enlargement. Any deterioration indicates that the pneumothorax must be drained.

Simple Aspiration

Simple aspiration can be used in the ED when pneumothorax is first detected. A small catheter is placed into the pleural space, and air is sequentially evacuated with a three-way stopcock until no more air can be removed. If more than 4 L of air is aspirated and no resistance to further aspiration is felt, a chest tube is needed for continuing pleural air leak.

The goal of aspiration is to re-expand the lung. Many patients have a pneumothorax from air leak that subsequently heals between the time of onset and the time that treatment is sought in the ED. Patients with primary spontaneous pneumothorax who undergo simple aspiration for lung re-expansion and who have a stable chest x-ray 4 hours after aspiration can go home without hospital admission.

Chest Tubes

Chest thoracostomy tubes (chest tubes) come in a variety of sizes, from 7 to 40 Fr, and can be connected to a variety of one-way devices (e.g., Heimlich valves) that prevent entry of air into the pleural space from the outside environment. Regardless of chest tube size and the presence of a Heimlich valve or water seal, the effectiveness of chest tube placement for pneumothorax resolution depends more on lung surface healing than on the device used.

Small-bore chest tube. One simple device is a small-bore 7 Fr catheter with a one-way valve apparatus (Heimlich valve) that prevents movement of air back into the chest. Small-bore catheters can be placed with a small skin incision followed by either a guidewire and dilator technique or a trocar to get through the parietal pleura.

All chest tubes used to drain pneumothorax should be directed to the apex of the lung. Small-bore catheters can be placed in the second intercostal space anteriorly in the midclavicular line or laterally in the chest from the fifth through the seventh intercostal space.

It can be difficult to determine whether a Heimlich valve has an ongoing leak unless it is placed to seal underwater. This procedure can be done in the ED by placing the Heimlich valve into a cup of water or by placing it in line with a water-seal chamber to see whether an air leak is continuing after lung expansion. Some newer versions of Heimlich valves have air bladders such that one can visually see one end of the bladder open as air escapes through the valve.

Large-bore chest tube. Large-bore chest tubes usually are connected to a commercial equivalent of a three-bottle system to collect any pleural fluid present, determine whether an air leak is ongoing, and measure intrapleural pressure (Fig. 27.6). Insertion of large-bore catheters can be done percutaneously, using a wire with serial dilators up to the size of the tube being placed; several commercial kits of various sizes are available on the market. Large-bore catheters can also be placed surgically with the use of local anesthetic and blunt dissection of soft tissue down to the parietal pleura.

Dissection should be wide enough to allow insertion of a finger into the pleural space to ensure that no adhesions are holding the lung close to the insertion site and to allow unobstructed entrance of the tube into the pleural space, where it can be directed to the position of choice.

Chest tubes are secured with sutures. The insertion distance should be recorded and be checked on subsequent days to ensure that the chest tube does not migrate outward. Should the most proximal hole in the tube emerge from the skin, air will enter the tube, and it will appear as if the lung is persistently leaking.

Another problem of apparent chest tube leak can occur when the insertion wound is large enough to allow air entry into the pleural space. This usually is accompanied by a sucking sound at the entrance, which can be occluded with petroleum gauze.

A chest x-ray is routinely obtained ideally, including a lateral view to best allow the precise placement of the tube to be visualized. In addition, many chest tubes end up in the major fissure, where their function may be suboptimal.

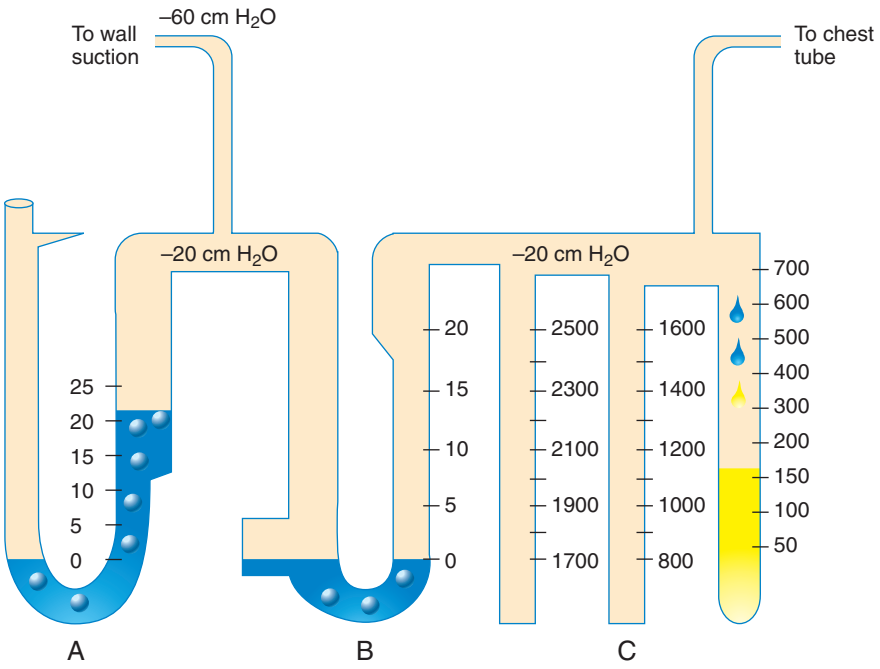

Fig. 27.6 The Pleur-evac chest tube collection system collects fluid in compartment *C* so that it will not spill into the water-seal compartment *B*. A patent chest tube should cause respiratory variation to be seen on the scale adjacent to compartment *B*, which measures intrapleural pressure. Compartment *B* also is the place to see bubbles if an air leak is present. The water level in compartment *A* controls intrapleural pressure and should be adjusted daily.

Chest tube removal remains a highly variable practice. Removal of a chest tube as soon as an air leak visually ceases is associated with a 25% rate of recurrence of pneumothorax. The recurrence rate is near zero when chest tubes are removed 48 hours after the air leak no longer is seen in the water-seal chamber.[32] A common practice of clamping the chest tube, with chest x-rays before and after a 4-hour observation period, can be accompanied by the return of pneumothorax. For this reason, many clinicians discourage clamping the chest tube. If symptoms develop during chest tube clamping, the clamp should be removed immediately and the presence of air leak assessed.

Bronchopleural Fistula

Two terms are used for continuing air leaks from the lung through a chest tube. A **bronchopleural fistula** (BPF) is a large air leak that classically was described after surgery in which the airway was cut. Because some surgeons insist that BPF be reserved for this situation, the term **alveolopleural fistula** has been recently used for large air leaks that come from the lung tissue and that do not heal rapidly. Many patients with persistent air leaks are receiving mechanical ventilation, and positive airway pressures contribute to perpetuating the pleural air.

Because persistent air leaks can leak large quantities of air, more than one chest tube may be used to assure that the visceral pleura is in contact with the chest wall. This maneuver results in tamponade of the site of the air leak and allows pleural healing to occur.

Therapy for BPF involves meticulous monitoring of tidal volume, airway pressures, and positive end-expiratory pressure (PEEP); avoidance of auto-PEEP; and consideration of bronchoscopic closure or thoracoscopic surgery.[33]

Pleurodesis

Patients who have had one pneumothorax are more likely than the general population to have a second. The recurrence rate is greater than 30% among patients with primary spontaneous pneumothorax and approximately 40% among patients with secondary spontaneous pneumothorax. These high recurrence rates indicate that preventing a recurrent pneumothorax should be a priority, particularly for patients in whom pneumothorax may be life-threatening. Preventing recurrence involves producing adhesions between the parietal and the visceral pleurae in the involved area and is termed *pleurodesis*.

The most noninvasive approaches to pleurodesis involve chemical sclerosis of the pleural space through the chest tube once the pleural air leak has stopped. The two most common preparations used for pleurodesis currently in the United States include 500 mg of doxycycline or 5 g of talc mixed into a 50-mL syringe of sterile saline solution. The agent is injected through the chest tube into the pleural space. Then the chest tube is clamped for 2 hours before drainage is allowed.

More invasive methods have included thoracoscopy with pleural poudrage (blowing talc onto the pleural surface under direct visualization), pleural abrasion through a thoracoscope, and thoracotomy with pleurectomy (removing the pleural surface to ensure lung adhesion). Recent guidelines have suggested that surgical pleurodesis is superior to talc slurry instillation through a chest tube for spontaneous pneumothorax management,

MINI CLINI

Alveolopleural Fistula

Problem

Pneumothorax develops in a patient undergoing mechanical ventilation for pneumonia. A 20 Fr chest tube is placed, and the lung fails to re-expand, although a large amount of air is passing through the water-seal chamber. The patient's minute ventilation is 20 L/min to keep gas exchange stable. What is the problem?

Solution

The problem is an alveolopleural fistula caused by a large hole in the pleura that is difficult to manage. The lung surface of patients with underlying emphysema can contain large bullae that do not heal readily once ruptured. Large pleural holes also can develop in patients with necrotizing pneumonia and those who have undergone surgery on the lung.

with slurry reserved only for those who are not surgical candidates.[34]

Because the diseases that produce pneumothorax often involve both lungs, patients may experience sequential events in opposite lungs. In this situation, median sternotomy with bilateral abrasion or pleurectomy can be performed, particularly for patients at considerable risk for developing a pneumothorax, such as divers and aviators.

The Fanning equation tells us that humidified airflow through a chest tube is proportional to the chest tube radius to the fifth power. Therefore, the chest tube radius is the most important determinant of maximal airflow. Airflow through large air leaks has been measured as high as 16 L/min, a volume impossible to remove through a chest tube smaller than 24 Fr, regardless of the amount of pressure applied.

This patient should receive a second, larger chest tube. The seal of the chest tube at the skin surface should be inspected to ensure that no air is entering the body from the outside. The position of both chest tubes should be confirmed either by x-ray examination or by hand to ensure the tubes are in the pleural space. Once the lung is expanded, the minute ventilation should decrease because effective alveolar ventilation will be improved.

Flow through stopcocks and chest tube collection devices is governed by the same considerations as chest tube size. The manufacturer of the chest tube collection device that is used in your hospital will have the resistance figures necessary to ensure that 16 L/min of airflow can be accommodated.

The following simple calculations suggest that the excess difference in returned V_T (450 to 300 mL or 150 mL) is due to air passing through the BPF:

30 breaths/min
(150 mL differential = 4.5 L of pleural ventilation)

One other problem is that large amounts of carbon dioxide (CO_2; up to 20%) may be removed through the chest tube.[35] Removal of CO_2 is beneficial because it allows lower V_T and respiratory rates for any given PCO_2. However, as the BPF closes, CO_2 will no longer be eliminated through the chest tube but only through the endotracheal tube, necessitating higher minute ventilation to maintain CO_2 clearance. This need for higher

MINI CLINI

Measuring a Pleural Air Leak

Problem

Pneumothorax develops in a patient with ARDS, and a chest tube is placed to re-expand the lung. Before the pneumothorax developed, the patient was ventilated easily at a rate of 16 breaths/min (see Chapter 46), which delivered a tidal volume (V_T) of 500 mL, and was exhaling 450 mL (a small difference caused by endotracheal cuff leak and tubing compliance). Since the pneumothorax developed, the patient needs a rate of 30 breaths at the same V_T to keep the $PaCO_2$ level the same. Exhaled V_T is 300 mL. What is the approximate size of this patient's air leak? What ventilation options are appropriate?

Solution

Although research laboratories can measure airflow through a chest tube precisely with a pneumotachometer, clinical care can be provided by estimating the pleural air leak.

MINI CLINI

Management of a Bronchopleural Fistula

Problem

A 40-year-old trauma patient with ARDS cannot be ventilated because of a large (16 L/min) BPF located entirely in the left lung. If surgery is not possible, what ventilatory options would be appropriate?

Solution

Two ventilatory interventions have been attempted for large BPFs. The first is placement of a double-lumen endotracheal tube, which can carry most ventilation and PEEP on the right lung while underventilating the lung with the fistula to aid in its closure.[37] Long-term double-lumen ventilation is difficult because of tenuous tube position, the need for continuous paralysis, difficulty with secretion clearance, and high airway resistance through the small endotracheal tube lumens.

minute ventilation might falsely suggest that ARDS is worsening, when in reality the BPF is closing.

Nevertheless, when the air leak is measured with every ventilatory change, the mode of ventilation that minimizes air leak is the one most likely to allow pleural healing. Breath-by-breath analysis shows the difference between delivered V_T and exhaled V_T and approximates the volume of the pleural leak.

PEEP can be a major cause of large air leaks and should be turned off unless necessary for maintaining PO_2. Because there is no such thing as a true plateau pressure when air is exiting a BPF, V_T should be adjusted to produce the lowest peak airway pressure that can sustain ventilation and oxygenation. Position the patient so that the lung with the air leak is down (i.e., in the bed).[36]

Auto-PEEP can be impossible to measure if the fistula is large and decompressing the airways. Therefore, long expiratory times are preferred. Trials of pressure-controlled and high-frequency jet ventilation are appropriate. In a practical sense, these adjustments are the same ones made to prevent barotrauma in the first place and are limited by the severity of lung injury, which requires more support than would optimally close the air leak.

The second intervention is applying positive pressure to the chest tube. This back pressure increases resistance across the

BPF and allows the remainder of the lung to better ventilate. One simple way to add chest tube resistance is to connect a PEEP valve to the expiratory port of the water-seal chamber.[38] PEEP usually is placed at the same level as the ventilator PEEP. Inspiratory pressures exceed PEEP, and air flows through the chest tube. However, as expiratory pressures equilibrate, PEEP can be held within the lung, allowing the beneficial effects on oxygenation.

Pressurizing the chest tube entails synchronous closure of the chest tube during inspiration and requires specialized equipment that must be set up under controlled conditions.[39] When used in combination with an in-line PEEP valve, BPF flow can be slowed during both inspiration and expiration.

These techniques usually increase the volume of intrapleural air. The net effect on oxygenation requires careful bedside observation, because hypoxemia can worsen with any degree of lung collapse. Tension pneumothorax can also occur, so the patient must be monitored closely.

ROLE OF THE RESPIRATORY THERAPIST IN PLEURAL DISEASES

The RT may play an important role in both the diagnosis and management of pleural disease. Diagnostically, the RT's careful palpation and auscultation of the chest may show the dullness and decreased breath sounds that may prompt suspicion of a pleural effusion and lead the physician to order the imaging studies to confirm the presence of a pleural effusion. The RT who is managing the ventilator is often in the earliest position to appreciate a pneumothorax because the patient's ventilatory function would change when a pneumothorax develops. Furthermore, the RT may be called on to assist in performing a thoracentesis or placing a chest tube. Therapeutically, the RT may be called on to assist in setting up the fluid collection chamber after the chest tube is placed or in performing a talc pleurodesis. This broad spectrum of potential roles for the RT makes knowledge of the diagnosis and management of pleural disease essential for the capable RT.

SUMMARY CHECKLIST

- Pleural effusions form when excess pleural fluid is produced by the lung or chest wall in sufficient quantities to overcome the resorptive capacity of the pleural lymphatic vessels.
- Pleural fluid analysis is the key to understanding the specific cause of any pleural effusion.
- Transudates have a pleural fluid total protein level less than 0.5 and an LDH level less than 0.6 of the respective serum values. Common causes of a transudative effusion include CHF, nephrosis, and cirrhosis.
- Pleural fluid drainage returns approximately one-third of the lung volume as measured by FVC. The other two-thirds of fluid drainage allow the diaphragm to rise and the chest wall to normalize.
- Pneumothorax size is underestimated with a one-dimensional view of the chest. Measurement accuracy requires a three-dimensional perspective.
- The risk factors for pneumothorax and pneumomediastinum are the same. Air ruptures a pleural membrane in pneumothorax, and air passes through the lung hilum in pneumomediastinum.
- Oxygen therapy speeds resolution of all pneumothoraces by improving N absorption.
- Chest tube flow depends on tube size, stopcock size, and collection system resistance.
- Breath-by-breath measurement of an air leak can be approximated by the difference between inspired and expired volumes (in the absence of endotracheal cuff leaks).
- The mode of ventilation that produces the least fistula airflow is the most likely to produce healing.
- Methods to decrease BPF airflow include lowering *tidal volume*, lowering respiratory rate, lowering PEEP, and avoiding auto-PEEP. In more severe cases, positioning the affected lung down, double-lumen tube ventilation, adding PEEP valves to the chest tube, inspiratory chest tube occlusion, or thoracic surgery should be considered.

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28

Pulmonary Vascular Disease

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CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- State how many patients develop venous thromboembolism each year.
- Describe how and where thromboemboli originate.
- Describe how pulmonary emboli alter lung and cardiac function.
- Identify the clinical features and electrocardiographic, chest x-ray, and arterial blood gas findings associated with pulmonary embolism (PE).
- Describe how PE is diagnosed and managed.
- Describe the hemodynamic findings associated with pulmonary hypertension (PH).
- Describe the mechanisms responsible for pulmonary arterial hypertension (PAH).
- State who is at risk for the development of PAH.
- Identify the clinical features associated with PAH.
- Identify factors associated with worse outcomes in PAH.
- Describe the treatment used to care for patients with PAH.
- Describe the pathogenesis and management of PH associated with chronic obstructive pulmonary disease.

CHAPTER OUTLINE

KEY TERMS

deep venous thrombosis (DVT)
pulmonary embolism (PE)
pulmonary arterial hypertension (PAH)
pulmonary hypertension (PH)
venous thromboembolism (VTE)
ventilation-perfusion ($\dot{V}/\dot{Q}$) scan

The vessels of the lung can be affected by many conditions, including clots and narrowing of the pulmonary arteries, conditions referred as **pulmonary embolism (PE)** and **pulmonary hypertension (PH)**. PE occurs when a fragment of the thrombus in the venous system travels to pulmonary circulation. The thrombus usually originates in the deep veins of the lower extremities and therefore is called **deep venous thrombosis (DVT)**. **DVT and PE** are grouped in the category named **venous thromboembolism (VTE)**. PH is a term that defines an increase in the pressure in the pulmonary arteries that results from conditions that affect the lung vessels, lung parenchyma, and/or the heart.

This chapter reviews disorders associated with the pulmonary vasculature and predominantly focuses on VTE and **pulmonary arterial hypertension (PAH)**. PAH describes a particular subgroup of patients with PH who have progressive narrowing of the pulmonary arteries that, if left untreated, leads to right heart failure (cor pulmonale) and death.[1]

VENOUS THROMBOEMBOLIC DISEASE

Venous thromboembolism (VTE) is a major national health problem with an annual incidence of 117 cases per 100,000 persons (i.e., DVT at 48 cases per 100,000 and PE at 69 cases per 100,000), a ratio that increases with aging and is higher in males compared to females.[2] VTE is treatable but requires prompt diagnosis and treatment to avoid serious consequences, since

TABLE 28.1 Frequency of Venous Thrombosis in Various Hospitalized Patient Groups

Group	Frequency (%)
Orthopedic (e.g., fractured hip)	54–67
Urologic (e.g., prostatectomy)	25
Surgical patients older than 40 years	28
Gynecologic surgery	18
Cardiovascular surgery (e.g., acute myocardial infarction)	39
Obstetrics	3

From Arroliga AC, Matthay MA, Matthay RA: Pulmonary thromboembolism and other pulmonary vascular diseases. In George RB et al., editors: *Chest medicine: essentials of pulmonary and critical care medicine*, ed 3, Baltimore, 1995, Williams & Wilkins.

one third of deaths from PE occur within 1 hour of the onset of symptoms. In more than 70% of patients who die of PE, the diagnosis is not suspected.[3-5] This underrecognition is supported by the frequent (1.5% to 30%) detection of VTE in routine autopsies of adult patients.[4,6,7]

Patients with undiagnosed PE have a higher mortality rate (approximately 30%)[8] when compared with those in whom the condition was promptly recognized and treated (mortality rate <8% with generally favorable long-term outcome).[9] Therefore, a high index of suspicion to detect the disease is essential, particularly in patients at risk for VTE such as those with multiple injuries, immobilization, or intravascular catheters (Table 28.1). Because clinical findings of VTE are frequently misleading,[10] objective tests are needed to confirm or exclude the diagnosis.

Pathogenesis

PE is a frequent complication of DVT[11]; however, the actual source of PE is found in only half of the patients.[5] PE usually arises from detached portions of venous thrombi that form in deep veins of the lower extremities or pelvis (86%). A small percentage of PE arise from the right-sided heart cavities (3.15%) or from the superior vena cava (3%).[5]

Venous thrombosis can be due to inherited and/or acquired conditions, and in more than 80% of cases, a risk factor can be identified. Conditions that favor thrombus formation include blood that is not moving (*stasis)*, blood that is more likely to clot (hypercoagulable state), and vessel wall abnormalities (factors known as Virchow triad). Causes of blood stasis include local pressure, venous obstruction, immobilization, congestive heart failure, shock and dehydration, varicose veins, and enlargement of the right heart chambers. Several conditions increase the blood coagulability and predispose to VTE (see Table 28.1).[12] The most frequent causes of an inherited hypercoagulable state are the factor V Leiden and prothrombin gene mutations, which together account for 50% to 60% of cases.[13] Meanwhile, the major acquired conditions associated with thrombus formation are recent major surgery, trauma, immobilization, atrial fibrillation, antiphospholipid antibodies, malignancy, myeloproliferative disorders, pregnancy, and use of oral contraceptives.[14] Vessel wall abnormalities are found most often in patients who have sustained trauma or have undergone major surgery. In general, more than one risk factor is responsible for VTE.[15]

Pathology

PE is more frequently observed in the lower lobes of the lung and more commonly in the right rather than in the left lung, a phenomenon related to how pulmonary blood flow is distributed.[6] Embolism to the pulmonary arteries produces pulmonary hemorrhage in the poorly perfused or infarcted lung (i.e., lung that is irreparably damaged because of sustained loss of blood flow) in less than 10% of cases. Infarction due to thromboembolism is less common in the lung than in other tissues because the lung has two blood supplies—namely the pulmonary arterial and the bronchial circulations (see Chapter 9).

At a capillary level, extensive connections exist between the pulmonary and bronchial circulations that prevent serious damage to lung tissue that is deprived of its pulmonary artery supply.[6] Cardiovascular diseases may affect the bronchial circulation, which may lead to lung tissue necrosis when emboli occur. Pulmonary infarction is associated with thromboembolic obstruction of a medium-sized pulmonary artery and generally occurs at the lung bases, where it usually presents as a wedge-shaped opacity on chest images.

RULE OF THUMB PE is a complication of venous thrombosis. Patients with clots in the proximal venous system of the lower and upper extremities are at high risk for developing PE.

Pathophysiology

The sudden obstruction of a pulmonary arterial branch causes a decrease or total cessation of blood flow to the distal area of the lung. This interruption of blood flow can cause respiratory and hemodynamic alterations.[16] The obstruction of the pulmonary artery by a clot increases the alveolar dead space (in which areas of the lung parenchyma are ventilated but not perfused), causes bronchoconstriction, and decreases the production of alveolar surfactant. As a compensatory mechanism, the body increases the total ventilation ($\dot{V}$), which in turn contributes to the sensation of dyspnea that accompanies PE and results in hypocapnia. Further **ventilation-perfusion** ($\dot{V}/\dot{Q}$) mismatching may be caused by bronchoconstriction from hypocapnia, regional hypoxia, and the production of serotonin and histamine.[17]

Not all patients with PE have significant arterial hypoxemia, but the presence of a widened alveolar-arterial oxygen tension gradient and reduced arterial O_2 tension (PaO_2) are common.[18] Hypoxemia develops because of the $\dot{V}/\dot{Q}$ mismatch, intrapulmonary shunt, and in some cases, shock. Shock is caused by marked obstruction of the pulmonary vasculature or by numerous small emboli in the presence of cardiopulmonary disease. In this case, cardiac output decreases, peripheral O_2 extraction increases and the oxygen saturation of the venous blood markedly falls. In patients with elevated right heart pressures, an intracardiac right-to-left shunt may develop through a patent foramen ovale (a cardiac condition present in one-third of the population; see Chapter 10).[16,17] Moreover, the depletion of pulmonary surfactant

as a result of embolic occlusion can lead to atelectasis and intrapulmonary shunt, which also cause hypoxemia.[16,19]

The main consequence of PE is the increased resistance to blood flow caused by obstruction of the pulmonary arterial bed. The hemodynamic impact is determined by the extent of the pulmonary circulation involved (cross-sectional area), the underlying cardiopulmonary reserve, and the neurohumoral response to the embolism. PH develops when 50% or more of the pulmonary vascular bed has been occluded.[16,17] When PH occurs, the right ventricle must work harder to maintain the same flow. This added strain results in dilation and dysfunction of the right ventricle. When the mean pulmonary arterial pressure increases to greater than 40 mm Hg during an acute first PE, the right ventricle fails, and hemodynamic collapse and death occur.[20] Therefore, a massive PE should be suspected any time there is unexplained hypotension accompanied by an elevated central venous pressure (jugular vein distension).[21]

Death from massive PE is the result of cardiovascular collapse rather than respiratory failure. Although the usual course of PE is to resolve rapidly (because the body dissolves the embolism with endogenous fibrinolytic agents), permanent residual disease does occur.[22-24] Overall, fewer than 10% of patients with acute PE have lung perfusion defects after 6 weeks, and approximately 3% to 4% develop long-standing PH (i.e., chronic thromboembolic pulmonary hypertension; CTPH).[25]

Clinical Features

A high index of suspicion is crucial to make the diagnosis of VTE. Unfortunately, no specific signs or symptoms indicate the presence of VTE, and a significant proportion of patients are asymptomatic (32%).[3,26] The physical findings of DVT in the lower extremities include redness and warmth in one-third of patients and swelling and tenderness in three-fourths of patients. In addition to the lack of sensitivity, the physical examination is not specific for diagnosing DVT. For instance, in patients who have swelling above and below the knee, fever, and a history of immobility and cancer, the likelihood of finding DVT is only 42%.[27]

The most frequent symptoms in patients with PE are dyspnea, followed by pleuritic chest pain (sharp pain predominantly during inhalation) and cough (Table 28.2).[28] The onset of dyspnea is usually rapid, within seconds (46%) or minutes (26%) of the PE.[28] Hemoptysis occurs in 13% to 20% of patients. The combination of dyspnea of sudden onset, fainting, and acute chest pain should raise suspicion of PE. In one study, this combination of symptoms was present in 96% of patients with confirmed PE, compared with 59% of patients in whom PE was suspected but not confirmed.[29] In some patients, dyspnea lasts only a few minutes, and this episode may be wrongly dismissed as being trivial.[16,18,29,30] There are no characteristic physical findings of PE. The most frequent physical findings include tachypnea, rales on chest examination, and tachycardia. Other common physical findings include an accentuated pulmonary component of the second heart sound (loud P_2) consistent with PH. Fever may be present in as many as 54% of patients.[18,29,30] Similar to what occurs in the diagnosis of DVT, fewer than 35% of patients in whom PE is clinically suspected actually have it.[3]

TABLE 28.2 Clinical Characteristics in Patients With PE and No Cardiopulmonary Disease

Symptoms	Frequency (%)
Dyspnea at rest or with exercise	73
Pleuritic pain	44
Calf or thigh pain	44
Cough	34
Orthopnea	28
Wheezing	21
Signs	**Frequency (%)**
Tachypnea	54
Tachycardia	24
Rales	18
Decrease breath sounds	17
Loud P2	15
Jugular venous distension	14

From Stein PD, Beemath A, Matta F, et al: Clinical characteristics of patients with acute PE: data from PIOPED II, *Am J Med* 120:871–879, 2007.

Because the clinical features lack specificity and treatment is anticoagulation (which carries risk of bleeding over time), confirming or excluding the diagnosis with appropriate testing is necessary.

Chest X-Ray

The chest x-ray cannot confirm or exclude the presence of PE but is helpful to rule out other life-threatening conditions, such as pneumothorax or pneumonia, which can present in a similar way. In patients with dyspnea, a normal chest x-ray may be a clue to the presence of PE; however, the plain chest x-ray is abnormal in more than 80% of the patients with PE.[31] Some of the abnormalities include enlargement of the right descending pulmonary artery (66%), elevation of the diaphragm (61%), cardiomegaly (55%), and pleural effusion (50%). Patchy radiographic opacities or round nodular lesions next to the pleural surface are present in patients who have pulmonary infarction or atelectasis. Other less common findings noted in 25% to 30% of patients with PE include the *Westermark sign*, in which there is pulmonary hyperlucency caused by a marked reduction in blood flow, and the *Hampton hump*, a pleural-based opacity in the costophrenic angle that represents alveolar hemorrhage from a pulmonary infarction.[29,31,32]

Electrocardiogram

The electrocardiogram (ECG) is helpful to rule out other diagnoses, such as acute myocardial infarction and pericarditis. The ECG is frequently abnormal in patients with PE (87% of the time), but the ECG abnormalities are usually nonspecific; tachycardia and ST-segment depression are the most common.[29] Abnormalities such as depression of the ST segment and T-wave inversion in V_1 and V_2 may be present. An $S_IQ_3T_3$ pattern (S wave in lead D_I and Q wave with negative T wave in D_{III}) is associated with massive PE and is present in 19% of such patients (see Chapter 18).[27]

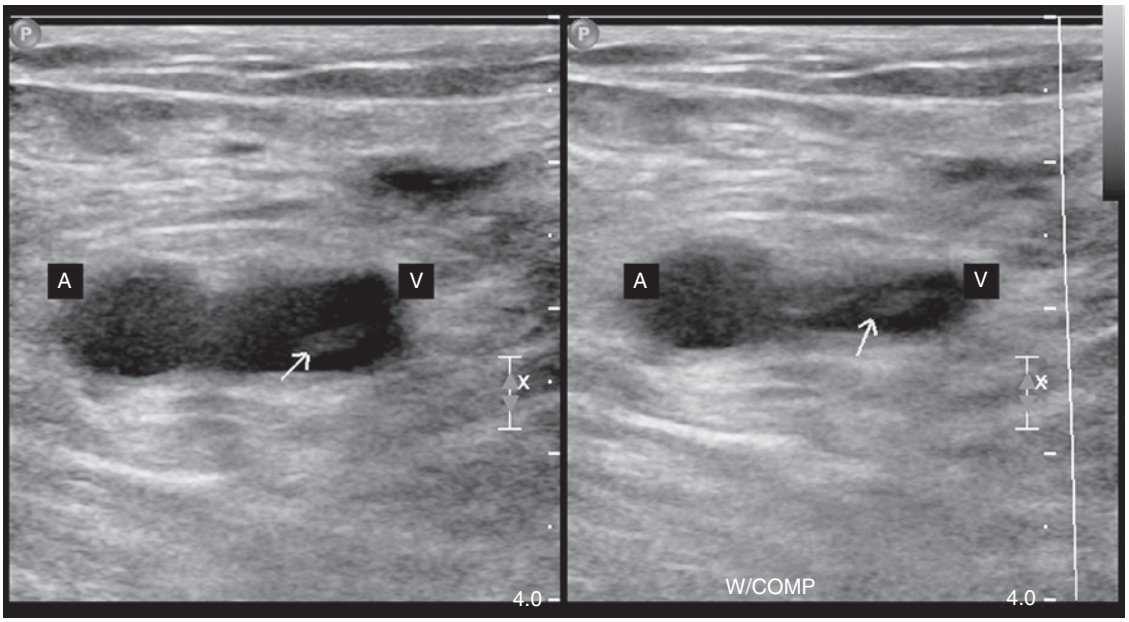

Fig. 28.1 Deep Venous Thrombosis Diagnosed by Ultrasonography. In the left panel, an intraluminal thrombus is visible in the right common femoral vein *(arrow)*. The right panel shows incomplete collapse of the femoral vein due to the presence of a clot. *A,* Femoral artery; *V,* femoral vein.

Arterial Blood Gases

Most patients with acute PE have hypoxemia and hypocapnia,[29] but 15% to 25% of subjects have a PaO_2 greater than 80 mm Hg.[18] Although a widened alveolar-arterial oxygen gradient and a lower PaO_2/FiO_2 ratio are frequently present, a normal alveolar-arterial oxygen gradient is noted in approximately 20% of patients with documented PE.[18,29,33] As such, the arterial blood gases cannot establish or exclude the diagnosis of PE. Massive PE with hypotension and respiratory collapse can result in hypercapnia and respiratory acidosis.

Diagnostic Modalities

The diagnosis of VTE relies on the diagnosis of DVT and/or PE. Importantly, the absence of one condition does not exclude the other.

By-Products of Plasmin Activation

The degradation of fibrin (an essential component of clots) by plasmin releases cross-linked split products called D-dimer, which is a global biomarker of coagulation activation. Low levels of D-dimer are commonly detected; however, higher levels are found in VTE disease. The D-dimer test is particularly useful in the outpatient and emergency department settings for the evaluation of patients with suspected DVT[34] and PE.[35] The D-dimer test has good sensitivity and negative predictive value but poor specificity and positive predictive value. In other words, this test is excellent for ruling out DVT or PE, particularly when the pretest probability for these conditions is low. In fact, a negative D-dimer result is as diagnostically useful as a normal lung scan or duplex ultrasonography for excluding PE or DVT. However, a positive D-dimer determination is insufficient for diagnosing VTE and further investigations are needed.[34-36] In hospitalized patients, D-dimer levels may be elevated as a result of comorbid conditions; therefore an imaging evaluation is preferred in this setting.[35]

Testing for Lower-Extremity Deep Venous Thrombosis

The Wells score is frequently used to evaluate the clinical pretest probability of DVT. This score is calculated using the following clinical parameters: presence of cancer, immobilization, localized tenderness, swelling, edema, previous DVT, superficial collateral veins, and absence of an alternative diagnosis.[37] In cases in which there is a moderate to high pretest probability, compression ultrasonography is commonly used to confirm the diagnosis of DVT.

Compression ultrasonography has proved to be sensitive and specific for diagnosing symptomatic proximal DVT. This noninvasive and portable test is the modality of choice for diagnosing DVT. DVT is diagnosed when deep veins are not compressible and/or have an echogenic filling defect, a free-floating thrombus, or no Doppler flow.[38] Of these, the most reliable DVT sign is the lack of vein compressibility (Fig. 28.1). The sensitivity and specificity of compression ultrasound for detecting a proximal lower-extremity thrombus in symptomatic patients vary between 95% and 100%.[38,39]

Testing for Pulmonary Embolism

Echocardiography can suggest the diagnosis (new or worsening dilation or dysfunction of the right ventricle or right heart thrombus); however, it lacks sensitivity (53%) because echocardiographic findings are usually normal in hemodynamically stable patients. Specificity is better (83%); nevertheless, right ventricular abnormalities could be due to conditions other than PE such as PH.[40] Despite these limitations, echocardiography provides valuable prognostic information to guide treatment decisions.[41,42]

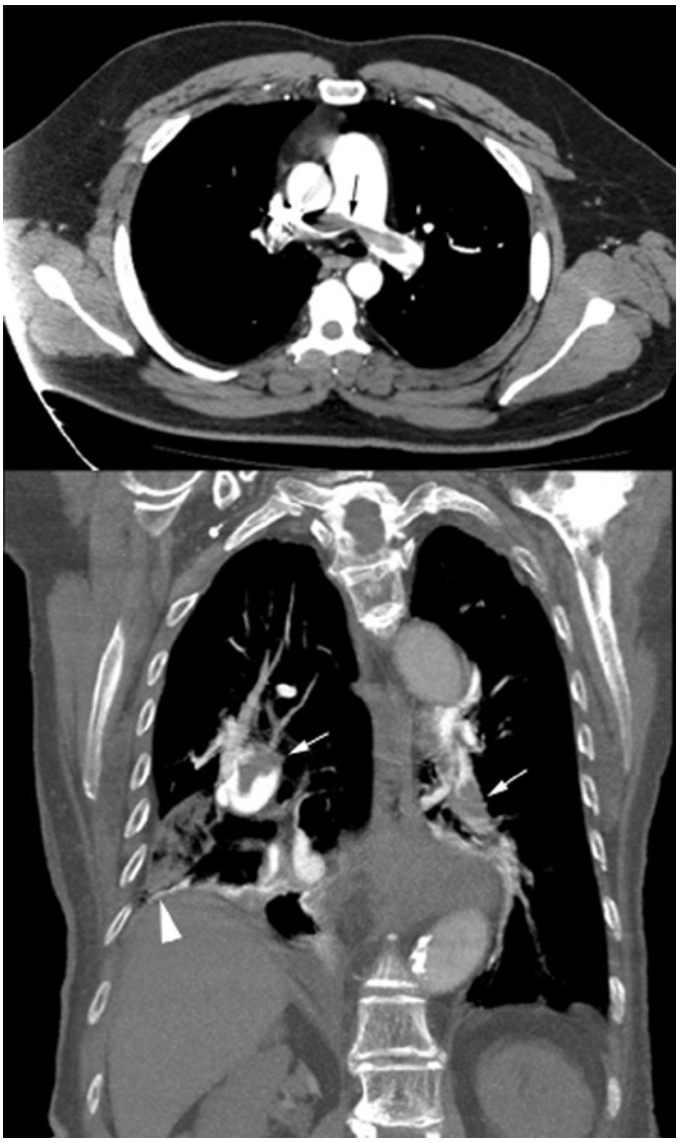

Fig. 28.2 Pulmonary Embolism (PE) Diagnosed by Computed Tomography Angiography. Axial (at the level of the pulmonary artery bifurcation, upper panel) and coronal cuts (just anterior to the thoracic spine, lower panel) showing the presence of PE involving the right and left pulmonary arteries, also known as saddle embolism *(arrows)*. On the coronal cut, there is a wedge-shaped area in the right lower lobe that represents lung infarction *(arrowhead)*.

Computed tomography angiography (CTA; Fig. 28.2) is currently the primary diagnostic modality for diagnosing PE,[43,44] given its high sensitivity and specificity, cost effectiveness, wide availability (particularly on urgent and emergent bases), and benefit of recognizing alternative diagnoses (e.g., pneumonia, pneumothorax).[45,46] The reported sensitivity of CTA ranges from 53% to 100%, and the specificity ranges from 81% to 100%.[44] This variability is due to radiologists' diverse expertise and variable image quality.[47] Studies indicate that CTA scanning detects PEs involving main and lobar emboli. However, this test is generally unable to detect smaller PEs in the distal branches of the pulmonary arteries. Multicenter trials suggest that helical CT scanning is safe to use for ruling out PE, at least in patients with a low or intermediate clinical probability of embolism. The Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) II trial evaluated the accuracy of multidetector CTA alone and combined with venous-phase imaging (CTA-CTV) for the diagnosis of acute PE. Excluding inconclusive studies (6%), the sensitivity of CTA was 83% and the specificity was 96%. The sensitivity increased to 90% when using CTA-CTV. The predictive value of either CTA or CTA-CTV was high with a concordant clinical assessment, but additional testing was necessary when the clinical probability was inconsistent with the imaging results.[44,48] Fig. 28.3 summarizes the diagnostic approach to PE using CTA.

TABLE 28.3 Likelihood of Identifying PE on Pulmonary Angiogram Based on Results of V/Q Lung Scan and Clinical Probability

Scan Interpretation	High Clinical Probability	Intermediate Clinical Probability	Low Clinical Probability
High probability	96%	88%	56%
Intermediate probability	66%	28%	16%
Low probability	40%	16%	4%
Near normal/normal	0%	6%	2%

From Arroliga AC, Matthay MA, Matthay RA: Pulmonary thromboembolism and other pulmonary vascular diseases. In George RB et al., editors: *Chest medicine: essentials of pulmonary and critical care medicine*, ed 3, Baltimore, 1995, Williams & Wilkins.

V̇/Q̇ scanning is in general reserved for patients in whom CTA is contraindicated (i.e., iodine allergy and renal failure) or inconclusive. V̇/Q̇ scanning involves the inhalation of a radiolabeled gas (usually xenon-133 or technetium-99 m) and the intravenous injection of macroaggregated albumin tagged with a gamma-emitting radioisotope (technetium-99m–labeled macroaggregated albumin). The distribution of lung ventilation (V̇) and perfusion (Q̇) is studied, and areas of mismatch where Q̇ is less than V̇ are sought. The presence of mismatches most often indicates PE. In the presence of parenchymal abnormalities, the V̇ defect coincides with the Q̇ defect, and matched abnormalities are found. Matched V̇/Q̇ defects are usually not due to PE. A normal or low probability V̇/Q̇ scan excludes the presence of a clinically significant PE in the context of a low clinical probability of PE.[49,50] An intermediate probability scan is inadequate to confirm or exclude the presence of PE. Better sensitivity and estimation of the PE size can be obtained by using V̇/Q̇ single-photon emission computed tomography (SPECT).[46]

Pulmonary angiography is necessary when a definitive diagnosis of PE cannot be obtained with noninvasive investigations. Pulmonary angiography uses x-ray imaging to expose the contrast dye injected directly into the pulmonary arteries by special catheters. Signs of acute PE include filling defects and cutoffs of the pulmonary arteries. Table 28.3 presents the probability of finding PE with angiography on the basis of results of V̇/Q̇ scan and clinical probability.[51] A definite diagnosis of PE can be established with noninvasive diagnostic tools in more than two-thirds of cases.[52]

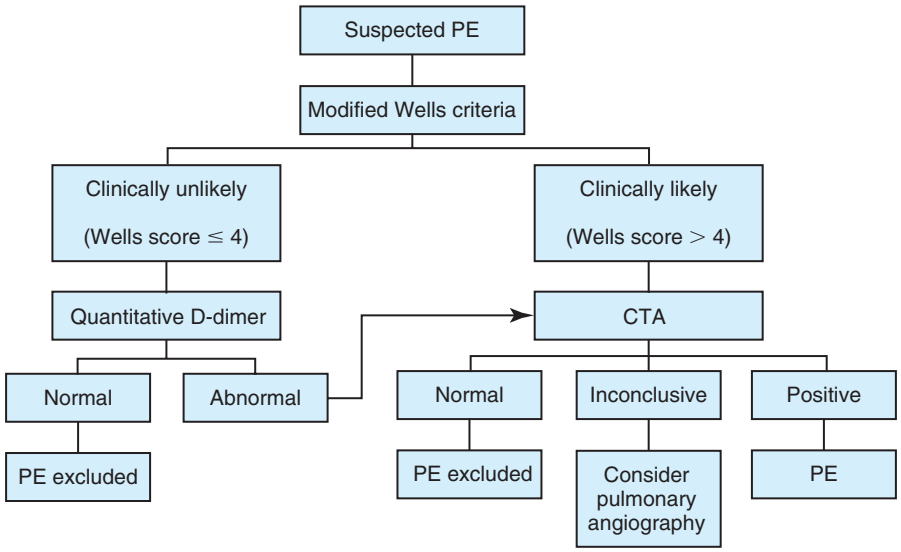

Fig. 28.3 Strategy for Diagnosis of Pulmonary Embolism *(PE)* Using D-Dimer and Computed Tomography Angiography *(CTA).* Diagnosis is based on clinical suspicion (using the Wells modified criteria) and the results of CTA scan. The modified Wells criteria include the following: clinical symptoms of deep venous thrombosis (DVT; 3 points), other diagnoses less likely than PE (3 points), heart rate >100 (1.5 points), immobilization ≥3 days or surgery in previous four weeks (1.5 points), previous DVT/PE (1.5 points), hemoptysis (1 point), and malignancy (1 point). (Modified from van Belle A, Buller HR, Huisman MV, et al: Effectiveness of managing suspected PE using an algorithm combining clinical probability, D-dimer testing, and computed tomography, *JAMA* 295:172–179, 2006.)

MINI CLINI

Respiratory Distress After Hip Replacement

Problem

You are asked to evaluate a 65-year-old man who has undergone right hip replacement. On the third day after surgery, the patient experienced dyspnea and pleuritic chest pain in the right hemithorax. On physical examination, his heart rate is 120 beats/min; respiratory rate is 25 breaths/min; and blood pressure is 120/85 mm Hg. The lungs are clear, and the heart examination does not show any gallops or murmurs. Arterial blood gas measurements on room air show a pH of 7.49; $PaCO_2$, 30 mm Hg; and PO_2, 85 mm Hg. The chest x-ray is unremarkable. What is your differential diagnosis, and how should you treat this patient?

Discussion

The differential diagnosis is extensive and should include an ischemic cardiac event such as an acute myocardial infarction as well as bacterial pneumonia. The type of chest pain is not typical of myocardial infarction. An electrocardiogram is of value because in patients with ST elevation myocardial infarction (STEMI), elevation of the ST segments is distinctive of the acute phase. Other laboratory data include elevation of the creatinine kinase and troponin levels, although these tests may become abnormal after several hours. The normal chest x-ray decreases the likelihood of the presence of pneumonia.

Because of the history of surgery on the right hip, DVT and PE are the most likely diagnoses. The next examinations are duplex ultrasonography of the lower extremities followed by a chest CTA or $\dot{V}/\dot{Q}$ scan. DVT should be sought in patients diagnosed with PE to investigate the origin of the thrombus and assess prognosis, because individuals with PE and coexisting DVT are at increased risk for death.[53] The presence of a "normal" PaO_2 of 85 mm Hg in this patient may be misleading. The wide alveolar-arterial gradient probably is caused by the presence of a pulmonary embolus. The patient should be anticoagulated.

TABLE 28.4 Simplified Pulmonary Embolism Severity Index

	Score[a]
Age > 80 years	1
History of cancer	1
History of chronic cardiopulmonary diseases (i.e., heart failure and/or chronic lung disease)	1
Heart rate of 110 beats/min or above	1
Systolic blood pressure less than 100 mm Hg	1
Arterial oxyhemoglobin saturation less than 90%	1

[a]A score of 0 represents low risk. A score of 1 or more indicates high risk.
The 30-day mortality was 1% in the low-risk group and 11% in the high-risk group.
Modified from Jimenez D, Aujesky D, Moores L, et al.: Simplification of the pulmonary embolism severity index for prognostication in patients with acute symptomatic pulmonary embolism, *Arch Intern Med* 170(15):1383–1389, 2010.

Risk Assessment

The mortality risk of a PE varies among patients, depending on a variety of factors. The mortality risk is higher in patients with PE and high-risk simplified Pulmonary Embolism Severity Index (sPESI) score (Table 28.4),[54] right ventricular dysfunction, elevated N-terminal probrain natriuretic peptide and/or troponin T, and concomitant DVT.[55-57] An online risk calculator that estimates the 30-day mortality after PE is available at www.peprognosis.org.

RULE OF THUMB The risk of death from PE is increased in the elderly and patients with history of cancer, presence of chronic cardiopulmonary disease, tachycardia, hypotension, and hypoxemia.

Treatment

Prophylaxis

Prophylactic therapy reduces the risk of VTE in patients at risk. The frequency of proximal DVT varies from 2% to 4% among general surgical patients undergoing minor surgery to 40% to 80% among patients at the highest risk, such as those who undergo hip or knee surgery.[58] Patients at moderate to high risk include patients admitted to the intensive care units[59,60] and those with acute spinal cord injury, myocardial infarction, ischemic stroke, or other medical conditions, such as obesity, heart failure, renal failure, hypercoagulable states, and history of recurrent VTE.[58] In part because the use of thromboprophylaxis is variable,[58] patients admitted to medical intensive care units develop DVT in 33% of cases.[61] VTE prophylaxis reduces the risk but does not eradicate its occurrence or related mortality in hospitalized patients.[62,63]

Most hospitalized patients who are immobile or have risk factors for VTE, particularly those without an increased risk for bleeding, need pharmacologic thromboprophylaxis. Pharmacologic choices for prophylaxis include low-dose subcutaneous unfractionated heparin, low-molecular-weight heparin (enoxaparin and dalteparin) and the factor Xa inhibitor (fondaparinux).[64-67] Mechanical measures to reduce venous stasis include early ambulation, graduated compression stockings, intermittent pneumatic calf compression devices, and venous foot pumps. Mechanical methods are reserved for patients without risk factors for VTE or who have contraindications to anticoagulant thromboprophylaxis.[68,69] Current prophylactic strategies for DVT and PE are summarized in Table 28.5. VTE prophylaxis is traditionally continued until the patient is ambulatory.[69]

RULE OF THUMB Most hospitalized patients who are immobile need prophylaxis for VTE.

Management of Venous Thromboembolism—Anticoagulation

Unless there is a contraindication (e.g., recent bleeding, head trauma, etc.), anticoagulation is begun when the diagnosis of VTE is first suspected and continued until it is ruled out by appropriate testing. The rationale for this approach is based on the high mortality observed soon after the VTE.

Unfractionated heparin is the time-honored drug treatment, but low-molecular-weight heparin (e.g., enoxaparin, etc.) is widely used.[70] Heparin is an indirect thrombin inhibitor with immediate action that is relatively safe. It forms a complex with antithrombin, inactivating thrombin, factor Xa, and to a lesser extent, factors XIIa, XIa, and IXa. Unfractionated heparin is administered as a bolus followed by a continuous infusion following a normogram to keep an activated partial thromboplastin time (aPTT) greater than 1.5 times the control value.[58,71-73] Low-molecular-weight heparin is administered subcutaneously, once or twice a day, and does not characteristically require blood test monitoring to ensure therapeutic benefit.[70] This agent has been shown to be cost-effective when compared with intravenous heparin therapy. The complications of heparin administration include major bleeding (3.8%) and thrombocytopenia caused by immunoglobulin G antiheparin antibodies (2.5% to 3%). If thrombocytopenia or bleeding occurs, heparin should be discontinued promptly.

There are several oral anticoagulants that are FDA-approved for the treatment of VTE disease. These include antagonists of vitamin K (warfarin) and of factor Xa (rivaroxaban,[74,75] apixaban,[76] edoxaban),[77] as well as direct thrombin inhibitors (dabigatran).[78] Parenteral anticoagulation (i.e., heparin) is given before dabigatran and edoxaban but not before rivaroxaban and apixaban.[67] Parenteral anticoagulation is overlapped with warfarin.[67]

In patients with VTE and no cancer, anticoagulation therapy with dabigatran, rivaroxaban, apixaban, or edoxaban is preferred over warfarin.[67] In patients with VTE and cancer, low-molecular-weight heparin is preferred over other alternatives.[67] Duration of therapy varies between 3 months for provoked VTE (e.g., immobilization post hip surgery) to long-term anticoagulation for recurrent unprovoked VTE or VTE in the setting of active

TABLE 28.5 Thromboembolism Risk and Recommended Thromboprophylaxis in Hospitalized Patients

Risk		DVT Risk Without Prophylaxis	Suggested Option
Low	a) Minor surgery in mobile patient	< 10%	a) No specific prophylaxis
	b) Medical patients fully mobile		b) Early and aggressive ambulation
Moderate	a) For general and abdominal-pelvic surgery	10%–40%	a) LMWH, UF heparin, or fondaparinux
	b) Medical patients, bed rest or sick		b) LMWH, UF heparin, or fondaparinux
	c) High bleeding risk		c) Mechanical prophylaxis
High	a) Hip or knee arthroplasty, major trauma, hip fracture, and spinal cord injury	40%–80%	a) LMWH, fondaparinux, apixaban, dabigatran, rivaroxaban, UF heparin, coumadin (INR 2–3) for a minimum of 10–14 days.
	b) High bleeding risk		b) Mechanical prophylaxis

LMWH, Low-molecular-weight heparin; *UF*, unfractionated. Mechanical prophylaxis includes graduated compression stockings or intermittent pneumatic compression. Recommendations suggest thromboprophylaxis in acutely ill hospitalized patients until they regain mobility.
Modified from Guyatt GH, Akl EA, Crowther M, et al.: Executive summary: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines, *Chest* 141(Suppl 2):7S–47S, 2012.

cancer.[67] Patients with low-risk VTE who have adequate support at home can be treated at home or discharged early from the hospital.[67]

Management of Deep Venous Thrombosis

The role of thrombolytic therapy with streptokinase, urokinase, or tissue plasminogen activator is not well-defined in managing acute DVT. The administration of early thrombolytic therapy decreases the pain and the incidence of postthrombotic syndrome (characterized by persistent pain, swelling, skin discoloration, and/or venous ulceration), but the risks (i.e., bleeding) and benefits of this particular therapy are not well established.[71,79] Thrombolytic therapy may be indicated in patients with massive proximal DVT and risk of limb gangrene.[80] Knowledge of the patient's values and preferences must be used to guide the best decision.[81]

For patients in whom anticoagulation is contraindicated (e.g., because of bleeding risk), placement of a filter in the inferior vena cava (IVC) to prevent embolism of clot to the pulmonary arteries is an option. Another reason for placing an IVC filter is recurrent PE despite adequate anticoagulation or cardiovascular instability (patient would not be able to tolerate another PE). IVC filter placement reduces the risk of PE in the period immediately after insertion but is associated with a higher incidence of recurrent DVT over time.[67]

Management of Pulmonary Embolism

The management of PE depends on the extent and status of the cardiopulmonary system. Therapy with heparin, whether unfractionated or low molecular weight, followed by warfarin or newer anticoagulants, is the treatment of choice. Adequate anticoagulation within the first 24 hours will decrease the risk of recurrent PE, which is associated with higher mortality.[82]

In patients with severe hypoxemia, acute right heart failure,[83] or shock, thrombolytic therapy may be considered for lysis of the emboli.[67] Hemodynamic instability due to massive PE is an accepted indication for thrombolytic therapy and is defined by a systolic blood pressure less than 90 mm Hg or drop of 40 mm Hg or more for more than 15 min or need for vasopressors/inotropic support. Thrombolytic treatment is indicated because these patients have an increased hospital and 90-day mortality.[84-86] Other options in the care of a patient with massive PE, in whom thrombolysis is either contraindicated or unsuccessful, include catheter tip embolectomy (physical removal of the embolism) or surgical pulmonary embolectomy.[67] Because of associated risks, these techniques should be used in centers with appropriate experience.[87]

Patients with an acute PE need supportive measures. Supplemental oxygen should be administered to patients who have hypoxemia. Adequate analgesia should be prescribed for patients who have pain and anxiety. Resuscitation with fluids and vasopressor agents is necessary for patients who develop hypotension and shock.

Prognosis

If left untreated, PE carries an overall mortality rate of 30%.[88] Early death is due to shock and/or a secondary embolic event. Long-term mortality is related to predisposing comorbidities and recurrent PE. Although the mortality from PE has decreased in recent years,[88] the death rate for the first episode of PE among hospitalized patients may be as high as 17.4% at 3 months.[89] Recurrent PE carries a much higher mortality rate, since only a quarter of patients will survive 3 months.[90]

Pulmonary Embolism Response Teams

Because the overall complexity of treating PE has increased over the recent years, several hospitals have created multidisciplinary pulmonary embolism response teams (PERT). Particularly in challenging cases, the PERT can help decide the best interventions for a particular patient—for example, type of anticoagulation, dose, type and route of administration of thrombolysis (intravenous vs. catheter directed), advanced intravascular interventions, surgical embolectomy, placement of inferior vena cava filter, and so on.[91]

PULMONARY HYPERTENSION

PH is defined by an elevation in mean pulmonary arterial pressure ≥25 mm Hg at rest.[92] PH is grouped into five categories, a classification that was last updated in 2013 by the Fifth World Symposium on Pulmonary Hypertension (Table 28.6).[93,94] The importance of the clinical system, besides allowing a better understanding of pathophysiology, is to give a framework for managing and treating different conditions known to cause PH. The first category, namely *PAH*, is characterized by narrowing of small and medium-sized pulmonary arteries,[95] manifested by an elevation in pulmonary arterial pressure associated with high pulmonary vascular resistance (≥3 Wood units) and normal left ventricular filling pressures (pulmonary artery occlusion pressure ≤15 mm Hg).[92,93,96] PAH is associated with several conditions, including collagen vascular disease, congenital heart disease, cirrhosis of the liver, human immunodeficiency virus, and drugs and toxins (diet pills or anorexigens).[93,94] In patients in whom no underlying etiology of PH can be identified, the disease is referred to as idiopathic pulmonary arterial hypertension (IPAH).[97-100]

The most common causes of PH are the ones associated with heart or lung diseases. Heart disease that can cause PH include left ventricular systolic or diastolic dysfunction (heart is not able to pump or relax effectively) and valvular disease. PH due to lung diseases is further divided into several groups: PH associated with chronic obstructive lung disease, interstitial lung disease, other

TABLE 28.6 Simplified Clinical Classification of Pulmonary Hypertension

1. Pulmonary arterial hypertension (PAH)
2. Pulmonary hypertension owing to left heart disease
3. Pulmonary hypertension owing to lung diseases and/or hypoxia
4. Chronic thromboembolic pulmonary hypertension (CTEPH)
5. Pulmonary hypertension with unclear multifactorial mechanisms

Modified from Simonneau G, Gatzoulis MA, Adatia I, et al.: Updated clinical classification of pulmonary hypertension, *J Am Coll Cardiol* 62(Suppl 25):D34–41, 2013.

diseases with mixed obstructive and restrictive patterns, sleep breathing disorders, alveolar hypoventilation, chronic exposure to high altitude, and developmental abnormalities.

PH can develop after one or more PE that is not fully reabsorbed. This entity is known as CTEPH.[101] In addition, PH can be associated to or may result from a variety of conditions grouped in PH with unclear or multifactorial mechanisms. A rare type of PH, namely pulmonary venoocclusive disease, is characterized by narrowing of the small pulmonary venules. Although challenging, recognizing pulmonary venoocclusive disease is important, given that the response to PAH-specific treatment is limited and lung transplantation is frequently needed. Patients with pulmonary venoocclusive disease commonly develop pulmonary edema when treated with PH-specific therapies.

Pathogenesis

The initial event of PAH likely involves an insult to the pulmonary endothelium (the cells that line the blood vessel) in patients with certain genetic predispositions.[102-104] This damage to the endothelium alters the balance between vasoconstrictive mediators (such as thromboxane and endothelin-1) and vasodilators such as nitric oxide and prostacyclin, resulting in vasoconstriction. Vasoconstriction might not be the primary event, but it is an important factor in the pathogenesis of PAH.[105-107] In addition to vasoconstriction, there is inflammation, thrombosis, cell proliferation, apoptosis (programmed cell death), and fibrosis, all of which can lead to pulmonary vascular remodeling and irreversible PAH.[108]

As it is for PAH, the mechanisms involved in the development of PH in patients with heart or lung diseases remains unknown. The same holds true for the development of CTEPH after an inadequate resolution of PE, a chronic condition that only occurs in 3% to 4% of patients after an acute PE.[25]

Epidemiology and Clinical Findings

The prevalence of idiopathic and heritable PAH is estimated to be 5 to 15 cases per million adults.[109,110] Overall, PH affects all age groups as well as both genders. Idiopathic and connective tissue disease-associated PAH are more common among women than among men, with a ratio of 3:1. Idiopathic PAH can occur at any age, although it is more common from ages 20 to 50 years. Approximately 7% of all cases of PAH are heritable.

On average, the diagnosis of PAH is delayed for 2 years after the onset of symptoms.[111] The condition frequently is misdiagnosed as asthma, anxiety, or depression because it presents with vague respiratory symptoms. The most common initial symptom is dyspnea (60% of patients). Other common symptoms include chest pain (50% of patients), probably due to a deficit in the oxygen supply to the subendocardial region of the right ventricle or compression of the left main coronary artery, and syncope (passing out; 8% of patients) due to an insufficient cardiac output, predominantly with activities. Less frequent symptoms include cough, hemoptysis, hoarseness (a condition called Ortner syndrome, caused by stretching or trapping of the left recurrent laryngeal nerve by enlarged pulmonary arteries), and Raynaud phenomenon (blanching of the fingers on exposure to cold).

Physical findings associated with PAH include a loud second heart sound and a right-sided third or fourth heart sound. Other common signs are a palpable right ventricular heave and pulmonary and tricuspid regurgitation murmurs. Signs of right ventricular failure such as swelling of the legs (edema), enlargement of the liver (hepatomegaly), and jugular vein distension are common. Cyanosis occurs as a result of low cardiac output or right-to-left shunt in patients with a patent foramen ovale or advanced stages of congenital heart diseases. The chest x-ray shows enlargement of the main and hilar pulmonary arteries, "pruning" (or narrowing) of the peripheral pulmonary arteries, enlargement of the right heart chambers, and pleural effusion,[112] although the chest x-ray may remain normal in 6% of patients.

Diagnosis

The diagnosis of PH is commonly suggested by an echocardiogram, which is the recommended method for screening. However, a definitive diagnosis of PH requires a right heart catheterization showing a mean pulmonary artery pressure of 25 mm Hg or greater. Before proceeding with right heart catheterization, PH guidelines suggest considering whether the patient has a significant heart or lung disease that could explain the degree of PH. Given the high prevalence of pulmonary hemodynamic abnormalities in advanced diseases of the heart and lung, mild degrees of PH are expected and may not need further exploration, particularly since there are no effective specific PAH treatments for PH associated with these conditions.

Results of the right heart catheterization may show pre-, post-, or mixed pre- and postcapillary PH. This division is essential to adequately characterize the pulmonary hemodynamic abnormalities, narrow the potential causes of PH, and guide treatment (Table 28.7).[113] Once the diagnosis of precapillary PH is made with right heart catheterization, PAH is a diagnostic possibility. The recognition of PAH is of great importance, as there are many FDA-approved therapies for this condition.

Other disorders associated with precapillary PH need to be ruled out, such as PH associated with lung disease, CTPH and PH associated with sarcoidosis, sickle cell disease, or other unclear and/or multifactorial mechanisms. This distinction is relevant because PAH-specific therapies are not FDA approved for precapillary PH other than PAH or inoperable or persistent CTPH after pulmonary thromboendarterectomy.[96]

Tests routinely ordered to establish the etiology of PH include blood testing, pulmonary function testing, echocardiogram, $\dot{V}/\dot{Q}$ scan, and pulmonary artery catheterization. Laboratory tests include a complete blood cell count, comprehensive metabolic panel, HIV serology, rheumatologic panel, and liver function tests. Laboratory tests help identify conditions associated with PAH such as systemic sclerosis, systemic lupus erythematosus, and mixed connective tissue. Pulmonary function tests are useful to identify significant restrictive or obstructive airway disease. The most common abnormality on pulmonary function testing in patients with PAH is a low carbon monoxide capacity (DLCO), associated with relatively normal pulmonary mechanics. Arterial blood gases are not routinely done in patients with PAH, but when performed, they frequently reveal mild degrees of hypoxemia and hypocapnia. Gasometric abnormalities are due to

TABLE 28.7 Hemodynamic Types of PH

Definition	Characteristics	Clinical Groups
PH	mPAP ≥25 mm Hg	All
Pre-capillary PH	mPAP ≥25 mm Hg PAOP ≤15 mm Hg	1. Pulmonary arterial hypertension 2. PH due to lung disease 4. Chronic thromboembolic PH 5. PH with unclear and/or multifactorial mechanisms
Post-capillary PH	mPAP ≥25 mm Hg PAOP>15 mm Hg	2. PH due to left heart disease
Combined pre- and postcapillary PH	mPAP ≥25 mm Hg PAOP>15 mm Hg PVR>3 Wood units	2. PH due to left heart disease 5. PH with unclear and/or multifactorial mechanisms

mPAP, Mean pulmonary artery pressure; *PAOP*, pulmonary artery occlusion pressure, *PVR*, pulmonary vascular resistance.
Data from "2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS)." Nazzareno Galie, Marc Humbert, Jean-Luc Vachiery, Simon Gibbs, Irene Lang, Adam Torbicki, Gerald Simonneau, Andrew Peacock, Anton Vonk Noordegraaf, Maurice Beghetti, Ardeschir Ghofrani, Miguel Angel Gomez Sanchez, Georg Hansmann, Walter Klepetko, Patrizio Lancellotti, Marco Matucci, Theresa McDonagh, Luc A. Pierard, Pedro T. Trindade, Maurizio Zompatori and Marius Hoeper. *Eur Respir J* 46:903–975, 2015. *Eur Respir J* 46(6):1855–1856, 2015.

right-to-left shunt through a patent foramen ovale, decreased mixed venous oxygenation (due to a low cardiac index), and imbalances in the $\dot{V}/\dot{Q}$ match.[114]

The transthoracic echocardiogram may show dilatation of the right ventricle and right atrium, diminished contractility of the right ventricle and tricuspid regurgitation (Fig. 28.4). On certain occasions, the echocardiogram may identify congenital heart diseases such as atrial or ventricular septal defects that can lead to PAH. One especially important noninvasive test is the $\dot{V}/\dot{Q}$ lung scan, which helps rule out CTPH, a mimic of PAH that has different treatment—that is, thromboendarterectomy in those with disease located in the main, lobar, or segmental arteries, or balloon pulmonary angioplasty in those with more distal disease.[115] In patients with PAH, the $\dot{V}/\dot{Q}$ scan may be normal or show only patchy subsegmental perfusion defects. In patients with CTPH, the $\dot{V}/\dot{Q}$ scan reveals segmental perfusion defects; however, confirmation of the suspected pulmonary vascular obstructions with pulmonary angiography is necessary.

Right heart catheterization is required to confirm the diagnosis and determine the presence of vasoreactivity, degree of hemodynamic impairment, and prognosis of patients with PAH (Fig. 28.5). The pulmonary vasoreactivity test is generally performed using inhaled nitric oxide, and a pronounced decrease in mean pulmonary artery pressure during this gas inhalation may support the long-term use of calcium channel blockers as PAH treatment.[116] Patients with severe degrees of PH have worse prognoses. Severe PH is defined hemodynamically as high right atrial pressure and pulmonary vascular resistance, as well as low cardiac index or mixed venous oxygenation (tested in blood obtained from the pulmonary artery).[12,97-100,117]

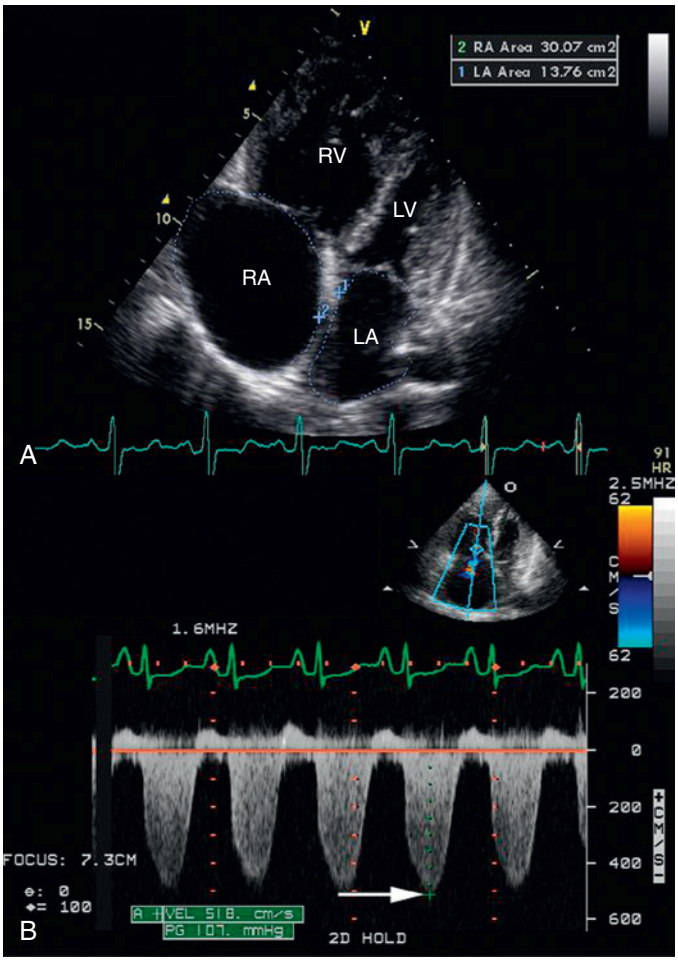

Fig. 28.4 Echocardiography in Pulmonary Hypertension. Apical four-chamber view of the heart, revealing enlarged right atrial and ventricle compressing the left cardiac chambers *(panel A)*. Doppler echocardiography showing tricuspid insufficiency jet *(arrow)* used to estimate the right ventricular systolic pressure (in this case 107 mm Hg). *LA,* Left atrium; *LV,* left ventricle; *RA,* right atrium; *RV,* right ventricle.

Management of Pulmonary Hypertension

Pulmonary arterial hypertension can be life threatening and carries a poor prognosis.[1] Without therapy, only 33% of patients are alive 5 years after PAH diagnosis. With treatment, the survival at 5 years is around 65%.[118] There are several markers that indicate a poor prognosis (mortality in the first year after diagnosis higher than 10%) in PAH. These markers include clinical signs of right heart failure, syncope, World Health Organization (WHO) functional class III or IV, 6-minute walk distance less than 165 m, plasma N-terminal prohormone of brain natriuretic peptide greater than 1400 ng/L, cardiopulmonary exercise testing with a peak VO_2 less than 11 mL/min/kg (less than 35% of predicted) and VE/VCO_2 slope of 45 or greater, echocardiography that reveals enlarged right atrium and/or pericardial effusion and right heart catheterization showing a high right atrial pressure (15 mm Hg or above), low cardiac index (less than 2.0 L/min/m^2), or decreased pulmonary artery blood oxygenation (SvO_2; less than 60%).[119]

A risk calculator based on the Registry to Evaluate Early and Long-Term PAH Disease Management (REVEAL) score has proven

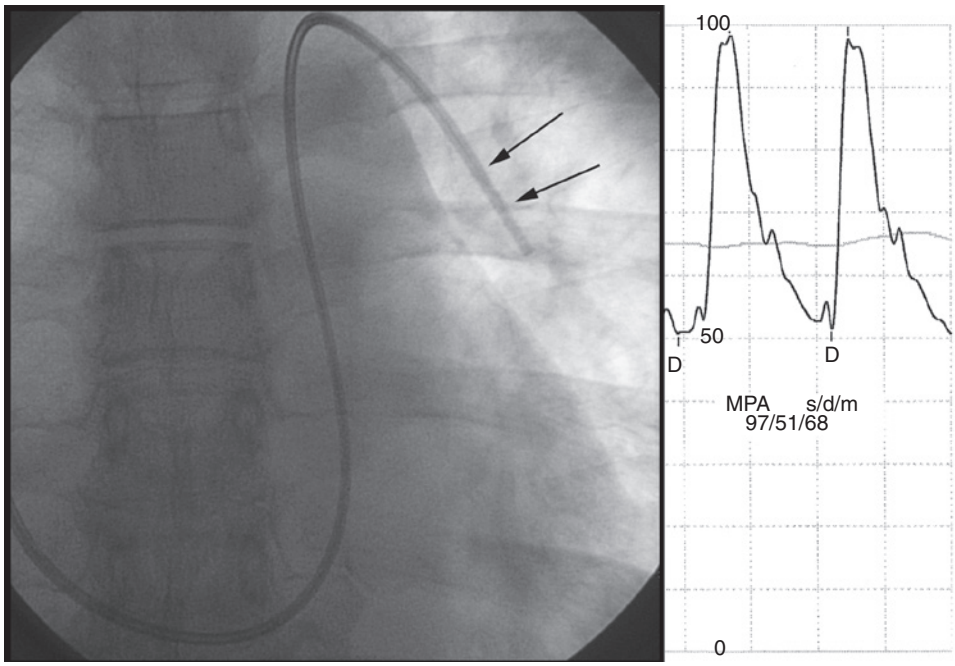

Fig. 28.5 Right Heart Catheterization in Pulmonary Hypertension. On the *left panel,* a pulmonary artery catheter is observed in the left pulmonary artery *(arrows).* On the *right panel,* the corresponding pulmonary artery pressure tracing is shown, confirming the diagnosis of pulmonary hypertension. In this case, the pulmonary artery systolic, diastolic, and mean pressures were 97, 51, and 68 mm Hg, respectively.

of value to predict the prognosis of PAH patients.[120,121] The REVEAL risk score calculator is a composite of 12 elements considered important for outcome including age, gender, WHO functional class, type of PAH, 6-minute walking distance, lung diffusion of carbon monoxide (DLCO), presence of pericardial effusion on echocardiogram, hemodynamic parameters, renal function, and plasma levels of N-terminal prohormone of brain natriuretic peptide.[120,121]

Recent analyses from three PH registries suggest that PAH patients who sustain or achieve a low-risk category[117] during follow-up have better prognosis.[122-124] The lower risk parameters include a WHO functional class I or II, 6-minute walk distance greater than 440 m, plasma N-terminal prohormone of brain natriuretic peptide less than 300 ng/mL, right atrial pressure less than 8 mm Hg, cardiac index of 2.5 L/min/m^2, or greater and SvO_2 above 65%.

RULE OF THUMB Treatment of patients with PAH is focused on achieving the largest number of low-risk parameters, since the more of these, the better the prognosis.

During the past 3 decades, treatment has improved considerably.[96,119,125-130] Current treatment options include using calcium channel blockers, prostanoids, endothelin receptor antagonists, phosphodiesterase-5 inhibitors, and soluble guanylate cyclase stimulators. Based on the results of recent trials, combination therapy either up front (both therapies at the same time) or sequentially (adding a second treatment after a few months of single therapy) is now favored.[96,131-134] A meta-analysis showed that combination therapy in PAH reduces clinical worsening by 38%, predominantly by decreasing nonfatal endpoints.[134] After initiation of PAH therapy, patients are followed every 3 to 6 months with WHO functional class, 6-minute walk distance, plasma N-terminal prohormone of brain natriuretic peptide, and right ventricular function on echocardiography.[96,135] In general, right heart catheterization is repeated when PAH therapies are changed or the patient shows no improvement or worsening.[96] Given that the treatment for PAH is complex and sometimes challenging, it is recommended that these patients are treated at a center with experience in managing this disease.[96]

General Measures

Oral anticoagulation is commonly used in patients with IPAH unless there is a contraindication to anticoagulation[136,137]; however, its benefits are less apparent when added to PAH-specific therapies.[138,139] The role of anticoagulation in other forms of PAH is less clear, and anticoagulation may not be beneficial.[136,139] Supplemental oxygen should be used to maintain oxygen saturation greater than 90%, given than hypoxemia is a major cause of pulmonary vasoconstriction. This is of particular importance in air travel or when staying at places with an altitude above 1000 m. Diuretics are indicated for volume overload, and digoxin might be indicated acutely for patients with refractory right ventricular failure.[129,130] Pregnancy is generally contraindicated in women with PH.

Calcium Channel Blockers

These agents should be considered only in PAH patients who have a definite hemodynamic response to a short-acting vasodilator test during right heart catheterization. Given its very short half-life (seconds) and minimum side effects, inhaled nitric

oxide is routinely used to test the pulmonary vasoreactivity.[116] Nitric oxide is usually administered by mask or nasal cannula at 10–40 parts per million for 2 to 5 minutes.[116] Protocols for using nitric oxide vary by institution. We use 40 ppm of nitric oxide delivered on room air (or the fraction of inspired oxygen needed to keep a pulse oximetry saturation greater than 90%) for 5 minutes. Others use 40 ppm of nitric oxide combined with 100% oxygen. Alternative agents include intravenous epoprostenol, intravenous adenosine, or inhaled iloprost. Unfortunately, only a small fraction of PAH patients qualify for and benefit from long-term therapy with oral calcium channel blockers.[129,130] Patients with PAH other than idiopathic, heritable or anorexigen-induced usually have a negative acute vasodilator testing or, even if the testing is positive, they do not respond to long-term calcium channel blockers.[116]

Prostanoids

Several prostanoids are currently available for treating patients with severe PAH, including epoprostenol, treprostinil, and iloprost. An oral selective IP prostacyclin-receptor agonist (i.e., selexipag) received FDA approval for the treatment of PAH.[133] Epoprostenol is delivered via continuous intravenous infusion, improving exercise capacity, hemodynamic variables, and survival in PAH patients.[140] Common side effects include headache, flushing, jaw pain, diarrhea, nausea, skin rash, and musculoskeletal pain. Catheter-related complications include infection and thrombosis.

Another prostanoid, treprostinil, has a longer half-life and is delivered subcutaneously,[141] intravenously,[142] by inhalation,[143] or by oral delivery. In addition to side effects seen with epoprostenol, patients receiving treprostinil subcutaneously may also experience pain at the infusion site (usually the abdomen). Inhaled treprostinil is administered by using the Tyvaso™ Inhalation System (ultrasonic, pulsed-delivery device). Inhaled treprostinil is started at 3 inhalations, 4 times a day, and if tolerated, the dose is increased by 3 inhalations every 1 to 2 weeks, up to 9 inhalations, 4 times a day. Side effects include cough and throat irritation. Oral treprostinil is associated with gastrointestinal side effects and requires a slow titration.

Oral selexipag reduces disease progression and the risk of hospitalizations for PAH, even when combined with other PAH therapies.[133] Oral selexipag is also associated with gastrointestinal side effects.[96] Iloprost is a prostacyclin analogue that is delivered by inhalation.[144] Due to the relatively short duration of action, iloprost needs to be taken as 1 to 2 inhalations, 6 to 9 times a day. Iloprost is administered using the I-neb AAD system. Common side effects of inhaled prostanoids include cough, flushing, and headache.[125,126,129,130] To avoid treatment interruptions in the event of an equipment malfunction, patients on intravenous or inhaled prostanoids should have easy access to a backup infusion pump or inhalation system, respectively.

Endothelin-Receptor Antagonists

Endothelin antagonists represent another class of medications available for treating PAH. They include bosentan, ambrisentan, and macitentan. Bosentan improves walking distance, hemodynamic variables, and functional class in patients with PAH.[145] The main side effect of bosentan is an asymptomatic increase in hepatic aminotransferase levels, which necessitates monitoring liver function at least monthly in all patients. Ambrisentan[146,147] and macitentan[132] are once-daily medications that do not need monthly hepatic aminotransferase testing. All endothelin receptor antagonists are potent teratogens, and very careful contraception must be observed by patients receiving these medications.

Phosphodiesterase-5 Inhibitors

Sildenafil, a phosphodiesterase type 5 (PDE5) inhibitor, reduces pulmonary arterial pressure and is effective in treating PAH.[127] By inhibiting PDE-5, sildenafil stabilizes cyclic GMP (cGMP, the second messenger of nitric oxide [NO]), allowing a more sustained effect of endogenous NO, which is a practical way of utilizing the NO-cGMP pathway. Tadalafil, a long-acting PDE5 inhibitor that is given once instead of thrice daily like sildenafil, also improves outcomes in PAH.[148,149] These medications are usually well tolerated; rarely, patients can have vision or hearing loss, priapism, and hypotension.

Soluble Guanylate Cyclase Stimulators

Riociguat directly stimulates soluble guanylate cyclase, increasing its sensitivity to nitric oxide. Riociguat is used for the treatment of patients with PAH and CTPH[150] who are not candidates for pulmonary thromboendarterectomy (i.e., surgery to remove clots from the pulmonary artery) or in whom the PH persists or recurs after thromboendarterectomy surgery.[151] This medication is associated with embryo-fetal toxicity; therefore, patients need to follow strict recommendations to avoid pregnancy.

Surgical Therapy

Atrial septostomy. The role of balloon atrial septostomy in treating patients with PAH is uncertain. Septostomy might be of benefit in the setting of severe disease with recurrent syncope and/or right heart failure despite maximal medical therapy. The shunt at the atrial level increases the systemic output and decompresses the right atrium and right ventricle, alleviating signs and symptoms of right heart failure. Balloon atrial septostomy is a high-risk procedure and should be performed only in experienced centers to reduce the procedural risks.[129]

Lung transplantation. Lung transplantation is indicated in individuals with severe PAH refractory to medical therapy.[152] Patients who undergo lung transplantation have an immediate decrease in pulmonary artery pressure and rapid improvement in right heart function.[129] The perioperative mortality of lung transplantation is higher in PAH, but after the immediate postoperative period, patients commonly have an excellent response with dramatic improvements in symptoms and quality of life.[153] Unfortunately, by the time PAH patients are considered for transplantation, they are usually poor candidates due to the comorbidities that accompany PAH.

RULE OF THUMB In patients with shortness of breath who have an unremarkable physical examination, the presence of a low DLCO and normal pulmonary mechanics suggests a pulmonary vascular cause (e.g., PH).

MINI CLINI

Dyspnea and Near-Syncope

Problem

A 35-year-old woman has shortness of breath. She had an episode of near-syncope approximately 6 months ago; a diagnostic evaluation was done, and the results were inconclusive. The physical examination shows a loud second heart sound. A chest x-ray shows cardiomegaly. The forced vital capacity and forced expiratory volume in 1 second are normal, but the DLCO is only 40% of the predicted value. What is the cause of the dyspnea and the low DLCO?

Discussion

This patient could have PH of unknown cause—that is, idiopathic pulmonary artery hypertension (IPAH). She has physical findings consistent with high pressure in the right side of the heart (a loud second heart sound), and she has symptoms that are common in this disorder, such as dyspnea and near-syncope or syncope. The differential diagnosis is broad, but a low DLCO in the presence of normal lung mechanics could indicate an abnormality of the pulmonary vasculature.

Pulmonary Hypertension in Chronic Lung Disease

PH is a frequent complication of chronic obstructive pulmonary disease (see Chapter 25). Approximately 50% of elderly patients with COPD have PH with significant reduction in survival and quality of life. The PH associated with COPD is multifactorial, but chronic hypoxemia is the most important factor. Acute alveolar hypoxia causes a potent pulmonary vasoconstrictive effect. Sustained alveolar hypoxia eventually leads to medial hypertrophy, fibrosis of the intima, and narrowing of the lumen of the pulmonary blood vessels.

Other factors responsible for PH in COPD patients include the loss of vascular surface caused by destruction of lung parenchyma, compression of the vascular bed as a result of hyperinflation, hyperviscosity of the blood due to polycythemia, and left ventricular diastolic dysfunction. The presence of PH in patients with COPD correlates with the severity of the disease. Patients with severe hypoxemia (PaO_2 55 mm Hg or lower) have higher pulmonary artery pressures, although the mean pulmonary artery pressure rarely exceeds 35 to 40 mm Hg.[154-157] Patients with COPD with a mean pulmonary artery pressure higher than 35 to 40 mm Hg have worse prognosis.[158-160]

Oxygen therapy is the main treatment for patients with PH due to COPD. PAH-specific therapies are sometimes used in very selected patients with COPD and severe PH; however, there is a lack of evidence to support their use and concern that pulmonary vasodilators may worsen the $\dot{V}/\dot{Q}$ match and hence worsen oxygenation.

An ECG is the test of choice to assess for the presence of PH. If the echocardiogram is consistent with the diagnosis, pulmonary artery (also known as right heart) catheterization is needed to confirm the diagnosis, determine the severity, and exclude left heart disease. For the diagnosis of IPAH, underlying diseases associated with PAH must be excluded. A normal $\dot{V}/\dot{Q}$ scan and/or pulmonary angiogram exclude chronic thromboembolic disease. A CT scan of the chest and pulmonary function tests is needed to exclude parenchymal lung diseases, and blood serologic tests are essential to screen for connective tissue diseases. A 6-minute walk test helps determine the functional capacity of the patient and assess her response to treatment. Several treatment options are currently available for patients with PH. The best therapeutic option depends on the severity of the disease and whether the patient has pulmonary vasoreactivity with nitric oxide.

ROLE OF THE RESPIRATORY THERAPIST IN PULMONARY VASCULAR DISEASE

Respiratory therapists (RTs) can play a key role in diagnosing and managing individuals with pulmonary vascular disease. The astute RT may help diagnose venous thromboembolism and PH by recognizing signs and symptoms of DVT/PE and PH (e.g., acute onset of dyspnea, pleuritic pain, pedal edema, worsening hypoxemia, hypotension, etc.). Communication with the managing physician to point out these findings and to suggest an adequate workup may prove lifesaving.

Therapists may also play an important role in both preventing and managing pulmonary vascular disease. Ensuring patients' compliance with vascular compression stockings can help prevent PE. Therapists take part in the care for patients with PH, as in administering nitric oxide during a pulmonary vasodilator challenge and managing inhaled therapies that are used to treat PAH (e.g., inhaled iloprost and treprostinil).

KEY POINTS

- Venous thromboembolism (DVT and PE) is an important cause of morbidity and mortality among hospitalized patients.
- Early recognition and treatment of VTE are essential and can be lifesaving. One-third of the deaths caused by PE occur within 1 hour of the symptom onset. The mortality rate in the group of patients with PE that goes undiagnosed is 30%; if the venous thrombosis is recognized and managed, the mortality rate is less than 8%.
- The point of origin of PE is DVT of the lower extremities or pelvis in 86% of cases.
- Most of the time, the clinical presentation of PE and DVT is nonspecific. A high index of suspicion is important to make the diagnosis in patients at risk.
- Prophylactic therapy reduces the risk of venous thromboembolism in patients at risk, but unfortunately, prophylactic therapy is underutilized.
- Pharmacologic choices for prophylaxis include low-dose subcutaneous heparin, warfarin, low-molecular-weight heparin, and novel anticoagulants. Mechanical measures include early ambulation and pneumatic calf compression devices.
- Management of venous thromboembolism includes anticoagulation therapy (heparin, warfarin, and novel anticoagulants).
- IPAH is a rare disease that mainly affects young adults.
- Management of IPAH includes the administration of vasodilators (calcium channel blockers, prostanoids, endothelin receptor antagonists, phosphodiesterase 5 inhibitors, and soluble guanylate cyclase stimulators). Lung transplantation is an option for refractory cases.

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29

Acute Respiratory Distress Syndrome

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CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Diagnose patients with acute respiratory distress syndrome (ARDS) using currently recommended criteria (Berlin criteria).
- Differentiate normal lung function that prevents pulmonary edema versus common disease mechanisms that lead to pulmonary edema, including nonhydrostatic edema (e.g., ARDS) and hydrostatic pulmonary edema (e.g., congestive heart failure).
- Describe the effect pulmonary edema has on lung function, including gas exchange and lung compliance.
- Identify the histopathologic findings associated with the exudative phase and the fibroproliferative phase of ARDS.
- Describe the common risk factors associated with triggering the onset of ARDS.
- Quantify the impact of ARDS on individual patients (e.g., mortality and morbidity), hospitals, and healthcare systems.
- Describe how mechanical ventilation can cause lung injury and how ventilator-induced lung injury can be avoided.
- Explain importance of tidal volume using lung protective ventilator strategies.
- Describe how ventilator settings (e.g., mode, tidal volume, positive end-expiratory pressure [PEEP], inspiratory time, and respiratory rate) can be adjusted for patients with ARDS.
- Explain the benefits of PEEP in ARDS.
- Describe changes in the pressure-volume curve (P-V curve) in ARDS and implications of lower inflection point (LIP) and upper inflection point (UIP).
- Understand the rationale for "permissive hypercapnia" during ARDS management.
- Explain the indications for conservative fluid management during ARDS.
- Discuss nonventilatory supportive care that can be offered to patients with ARDS, including use of checklists.
- Discuss management strategies for patients with ventilator dyssynchrony, including pharmacologic and nonpharmacologic therapies.
- Describe the use of innovative and alternative strategies for assisting ventilation in ARDS, including modes of mechanical ventilation, prone positioning, neuromuscular blockade (paralytics), extracorporeal support, and other interventions.
- Describe the current status of evidence to support the use of pharmacologic therapies (e.g., nitric oxide, surfactant, corticosteroids) in treating patients with ARDS.

CHAPTER OUTLINE

KEY TERMS

acute hypoxemic respiratory failure
acute lung injury
acute respiratory distress syndrome
airway pressure release ventilation
barotrauma
congestive heart failure
conservative fluid management
driving pressure
extracorporeal carbon dioxide removal
extracorporeal membrane oxygenation
high-frequency ventilation
hydrostatic pulmonary edema
inspiratory-to-expiratory ratio
nonhydrostatic pulmonary edema
lung protective ventilation
multiple organ dysfunction syndrome
permissive hypercapnia
positive end-expiratory pressure
prone positioning
pulmonary edema
ventilator-induced lung injury
volutrauma

Acute hypoxemic respiratory failure may develop in many clinical settings and is a common reason for admission to the intensive care unit (ICU). Acute hypoxemia has several causes. It occurs when oxygen is unable to reach the blood in enough quantity to allow function. This can happen because of abnormalities involving the airway (e.g., tumor, mucous plug), the alveoli (e.g., bacterial or viral pneumonia), the pulmonary vasculature (e.g., pulmonary embolus), and more, as discussed in other chapters. One of the most common causes of acute hypoxemic respiratory failure is abnormal leakage of fluid (pulmonary edema) from the vascular space (i.e., alveolar capillary) into the alveoli. Pulmonary edema was classically described as a manifestation of heart failure, when the hydrostatic pressure in the venous pulmonary capillaries was elevated (leading to leak to the alveoli) due to poor heart performance. Approximately 50 years ago, it was recognized that pulmonary edema can also happen without heart failure (noncardiogenic), a manifestation of alveolar injury.[1] This chapter will focus on understanding the diseases that cause pulmonary edema formation by highlighting one common source of pulmonary edema known as the **acute respiratory distress syndrome** (ARDS).[2,3] In addition, the chapter will explore the clinical syndrome of ARDS, including current management strategies, and the vital role of the respiratory therapist (RT) in helping manage ARDS.

PHYSIOLOGY OF PULMONARY EDEMA

Liquid and Solute Transport in the Lungs

A key component of normal lung function is to maintain a net flux of fluid through the lung parenchyma. For maximal gas exchange, the entire cardiac output passes through the extensive capillary network that surrounds the alveolar airspaces. The walls of the alveolus are separated from the capillary walls by the very thin lung interstitium (Fig. 29.1), which minimizes the distance for gases (i.e., O_2 and CO_2) to diffuse between the airspace and blood. However, this small barrier also needs to hold the fluid from the capillary and lung interstitium from entering the alveolar airspace. There is a normal physiologic amount of fluid that leaks into the alveoli, and a mechanism to clear it, thus keeping a balance. If the balance is broken, pulmonary edema results. In

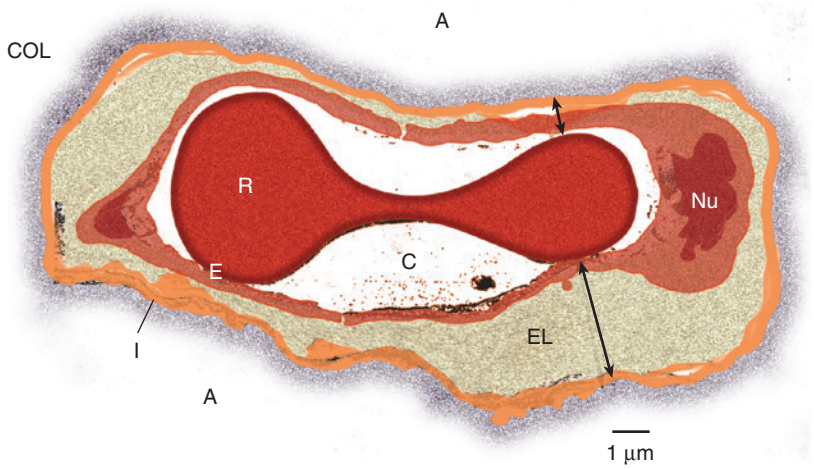

Fig. 29.1 Cross section of an alveolar wall shows the path for O_2 and CO_2 diffusion. The thin side of the alveolar wall barrier *(short double arrow)* consists of type I epithelium *(I)*, interstitium formed by the fused basal laminae of the epithelial and endothelial cells, capillary endothelium *(E)*, plasma in the alveolar capillary *(C)*, and the cytoplasm of the red blood cell (RBC) *(R)*. The thick side of the gas-exchange barrier *(long double arrow)* has an accumulation of elastin *(EL)*, collagen *(COL)*, and matrix that separates the alveolar epithelium from the alveolar capillary endothelium. As long as the RBCs are flowing, O_2 and CO_2 diffusion probably occur across both sides of the air-blood barrier. *A,* Alveolus; *Nu,* nucleus of the capillary endothelial cell. (Human lung surgical specimen, transmission electron photomicrograph.)

MINI CLINI

In a patient with suspected diastolic heart failure, where the left atria will have higher volume and pressures, the pulmonary venous pressure will be elevated, leading to increased hydrostatic pressure and increased alveolar interstitial fluid. When the amount of interstitial fluid is elevated, it can fill the interlobular septal spaces. This is the space separating the lung lobules. When this happens, the normally invisible septal spaces can be seen on a chest x-ray as linear interstitial opacities (known as *Kerley lines*) at the lung periphery (see Fig. 29.4A; see also Chapters 21 and 31 for more detailed discussions).

this chapter, we will summarize only the essential details needed to understand the key concepts of ARDS, whereas more complete details on these principles are provided in Chapters 9 and 10.

Unlike every other organ, the entire cardiac output for the body circulates through the lungs every minute, and the massive surface area of the capillary network provides a low–hydrostatic pressure (5 to 12 mm Hg) for the blood to come into close contact with alveolar gases. The interstitial space between the alveolus and capillary is very thin (<0.5 μm) and separated into two compartments: (1) the relatively stiff *alveolar side* between the capillaries and the alveolar epithelium and (2) the more compliant *nonalveolar side* around the capillary wall (see Fig. 29.1). The physical properties of the interstitium allow absorption of water and solutes. This *interstitial fluid* leads to a hydrostatic pressure, known as interstitial pressure, which is similar to but opposes the hydrostatic pressure in the vascular space. The interstitium, particularly the nonalveolar component, is highly compliant and able to accommodate relatively large increases in fluid volume in the interstitium without significant change in interstitial hydrostatic pressure or leakage of fluid into the alveolar airspace.

The net exchange of fluids between the capillaries and the interstitium of the lungs is determined by the combined influences of hydrostatic and osmotic forces within each compartment. Under normal conditions, a small fraction of fluid normally filters from the capillaries into the interstitial space of the lungs.[4] The lung lymphatic drainage system is the primary system for removing the filtered fluid and protein from the lungs. Drainage is assisted by the presence of a modest pressure gradient within the interstitium (higher pressure near the alveolus than the nonalveolar interstitium and terminal lymphatic vessels), and intrathoracic pressure changes during respiration. Backward flow is prevented by the presence of one-way lymphatic valves, and lymphatic fluid drains ultimately into the superior vena cava via the thoracic duct.[5] Once the capacity of the interstitium to capture fluid is surpassed and the rate of fluid accumulation exceeds the rate of lymphatic drainage, fluid must next begin to accumulate within the alveoli, an entity typically referred to by clinicians as **pulmonary edema**. Although accumulation of interstitial fluid leads to reduced efficiency of gas exchange, the accumulation of intra-alveolar fluid typically results in far more serious impairment of oxygenation and ventilation.

Hydrostatic Versus Nonhydrostatic Edema

The diseases that cause pulmonary edema are typically categorized as either hydrostatic or nonhydrostatic edema. To clarify the distinction between hydrostatic and nonhydrostatic edema, a simple analogy is to consider the intravascular hydrostatic force within the capillary as a body of water and the alveolar barrier as an impermeable dam with pumps that help regulate the water levels behind the dam (Fig. 29.2). Hydrostatic pulmonary edema occurs when the pressure or volume of water exceeds the capacity of the dam's pumps to maintain the water levels. Water then floods the land below the dam (the alveolus in this metaphor). Nonhydrostatic pulmonary edema occurs when the dam is cracked or damaged (the pump still works well) and the water leaks through it onto the land below the dam. It should also be noted that the type or color of water is different in nonhydrostatic edema because the cracks in the dam permit leakage of more sediment, which in patients is composed of serum proteins and inflammatory cells (e.g., neutrophils).

BOX 29.1 Causes of Hydrostatic Pulmonary Edema

Cardiac
- Left ventricular failure
  - Systolic (e.g., myocardial infarction, myocarditis)
  - Diastolic (e.g., left ventricular hypertrophy)
- Valvular heart disease (e.g., aortic, mitral)

Volume Overload
- Excessive fluid administration
- Renal failure
- Hepatic failure
- Hypoalbuminemia (e.g., malnutrition)

Hydrostatic Pulmonary Edema

Hydrostatic pulmonary edema is often also called *cardiogenic pulmonary edema* or **congestive heart failure** (CHF; see Chapter 31) because of its close association with cardiac abnormalities in intravascular hydrostatic pressures that cause edema. Increased hydrostatic pressures in the pulmonary veins lead to increased hydrostatic pressures in the alveolar capillaries that increase fluid leakage out of the capillary. In most patients, elevation of pulmonary venous pressures is caused by increased pressures in left-sided heart pressures (left atrial or left ventricular end-diastolic pressure), which are key characteristics of left-sided CHF, both diastolic and systolic (Box 29.1). In the setting of increased hydrostatic pressure, the endothelial and epithelial barriers remain intact and impermeable to large proteins and molecules. As a result, the fluid that accumulates within the alveoli, when measured from bronchoalveolar lavage (BAL) fluid samples, has characteristics identical to those of normal interstitial fluid, which typically contain minimal cells and low protein levels. In CHF, similar fluid can accumulate in other body spaces (e.g., pleural effusions, peritoneal ascites) for the same reasons and are typically referred to as transudative fluid collections or transudates.

Nonhydrostatic Pulmonary Edema

Nonhydrostatic pulmonary edema, also called *noncardiogenic pulmonary edema*, results from injury to the vascular endothelium

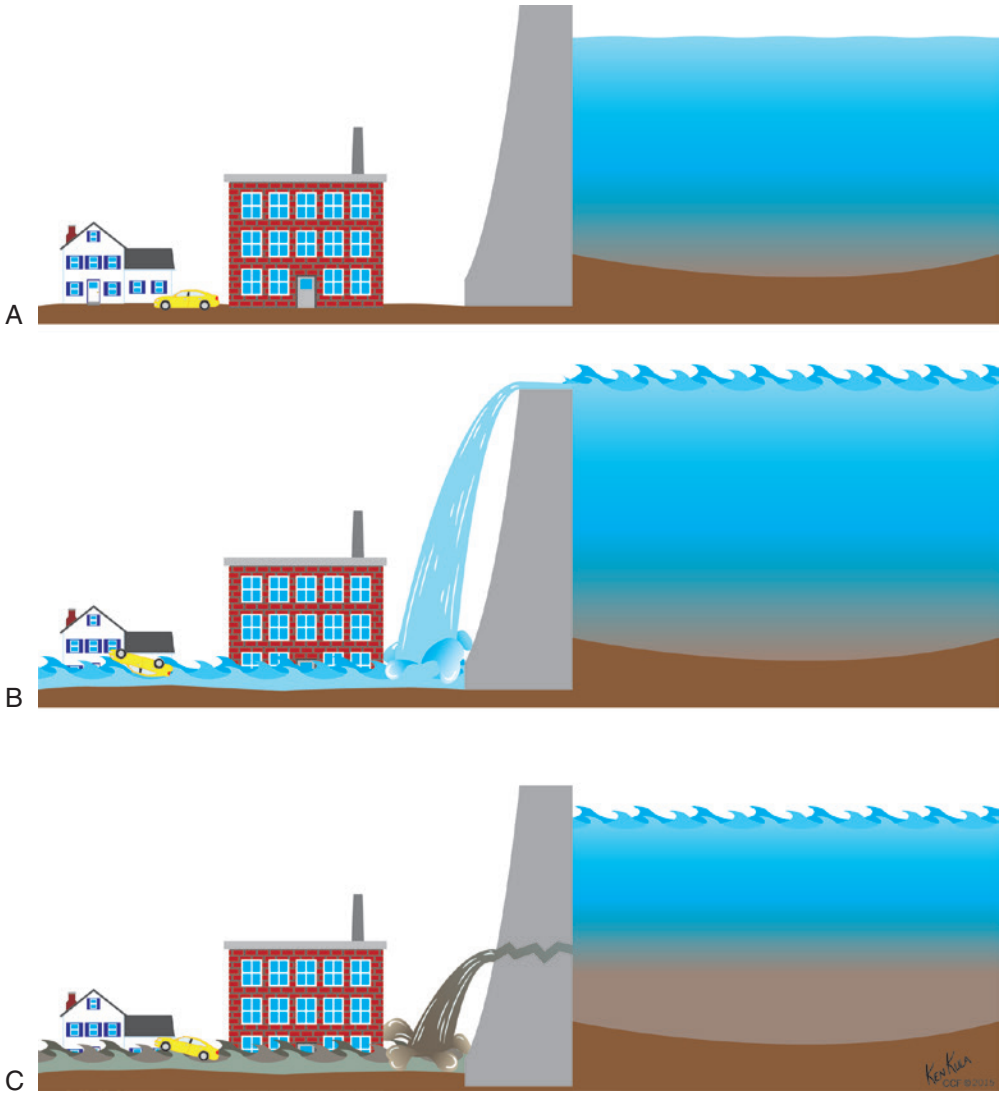

Fig. 29.2 The intact dam (A) represents the normal condition in which oncotic and hydrostatic forces (Starling forces) are balanced, keeping the town dry (where the town represents the alveolar space). (B) The dam remains intact but the water level has risen, overwhelming the dam (i.e., exceeding the forces that resist alveolar flooding) and flooding the town representing the alveoli. This condition resembles hydrostatic pulmonary edema. (C) A crack in the dam (simulating the alveolar-capillary interface) allows water through the dam, flooding the town. Note that the water flooding the town is darker because it contains more sediment and mud from the lake. The condition in (C) simulates the damage to the alveolar-capillary interface that accompanies inflammation in acute respiratory distress syndrome, causing nonhydrostatic pulmonary edema. The muddier water flooding the town (representing the alveolar space) in (C) than in (B) represents the more proteinaceous, inflammatory nature of the fluid that floods the alveoli in nonhydrostatic pulmonary edema.

and/or alveolar epithelium. This injury creates a loss of integrity in the barrier between the vascular and alveolar spaces (like cracks in a dam; see Fig. 29.2). In contrast to hydrostatic pulmonary edema, nonhydrostatic pulmonary edema is associated with increased total lung water despite normal microvascular hydrostatic pressure. All causes of ARDS feature disruption of endothelial and epithelial barriers and typically occur under conditions associated with widespread microvascular injury to the lungs. Vascular endothelial injury in the lungs causes increased permeability and allows fluid to pass from the capillaries into the interstitial space. As protein-rich fluid enters the alveolar interstitium from the vasculature, the osmotic gradient is drastically changed and no longer opposes fluid movement from the capillary into the lung. This process is likely aided both by damage to the normally impermeable alveolar epithelial barrier, which is a key feature of ARDS, and by impaired alveolar fluid clearance in ARDS.[6,7]

Many acute illnesses can lead to the development of ARDS (Box 29.2). Regardless of the cause, ARDS is typically associated with an influx of polymorphonuclear neutrophils, which release inflammatory by-products, such as proteases, phospholipases, and oxygen radicals into the lung.[8,9] These processes lead to

BOX 29.2 Clinical Features of Congestive Heart Failure and Acute Respiratory Distress Syndrome

Features Common to Both

- Symptoms of anxiety, dyspnea, tachypnea
- Decreased compliance and reduced lung volumes
- Hypoxemia (mild to severe), often requiring ventilator assistance
- Chest x-ray shows diffuse alveolar and interstitial infiltrates

Features Favoring CHF

- Suggestive clinical history (see Box 29.1)
- Symmetric pulmonary infiltrates, cardiomegaly, or pleural effusions on chest x-ray (see Fig. 29.2)
- Elevated pulmonary artery catheter wedge pressure (18–30 mm Hg)
- Bronchoalveolar lavage fluid: Low protein and minimally increased cellularity
- Prompt (<12 to 24 h) and lasting response to diuretics and CHF therapy

Features Favoring ARDS

- Clinical history of a risk factor for ARDS (see Box 29.3)
- Asymmetric, peripheral infiltrates on chest radiograph (see Fig. 29.3)
- Bronchoalveolar lavage fluid: Very high protein level and marked cellular influx
- Transient improvement with CHF therapy, but uncommon to significantly improve during initial 12–36 h

ARDS, Acute respiratory distress syndrome; *CHF,* congestive heart failure.

degradation of the endothelial and epithelial barriers and recruit additional neutrophils to continue the inflammatory cascade. In contrast to hydrostatic pulmonary edema, the alveolar fluid that accumulates in ARDS typically demonstrates very high levels of protein, neutrophils, and total cells (Fig. 29.3) and would be comparable to and consistent with exudative pleural fluid collections or exudates (see Chapter 27).

Although neutrophils play a central role in the development of ARDS, multiple pathways lead to the inflammatory cascade in the lung and subsequent loss of alveolar membrane integrity. Other chemical insults (e.g., gastric aspiration), inhalational injury (e.g., of noxious gas such as chlorine), or immunologic pathways (e.g., tumor necrosis factor [TNF] or interleukin-8 [IL-8]) all contribute to the hemodynamic and inflammatory events characteristic of ARDS.[10,11] Sepsis, one of the most common causes of ARDS, features activation of many of these inflammatory pathways. The relative contributions and exact roles of these inflammatory mediators in the pathogenesis of ARDS are not known. Attempts to control the inflammatory response in sepsis and ARDS by blocking specific mediators (e.g., steroids and antibodies to TNF and IL-1) unfortunately have not proved beneficial and are not currently used in the clinical management of patients with ARDS.

It is important to note that acute illnesses associated with the development of ARDS also can lead to widespread systemic organ injury (e.g., renal failure, encephalopathy), which is caused by the same inflammatory pathways leading to vascular injury, local tissue injury, and fluid leak in those organs, as seen in the lungs. This syndrome of diffuse organ impairment is frequently referred to as the **multiple organ dysfunction syndrome** (MODS).[12,13] ARDS is the pulmonary manifestation of MODS, and MODS is a common cause of death in ICUs. In contrast to ARDS, illnesses that lead to hydrostatic pulmonary edema typically do not cause MODS.

Gas Exchange and Lung Mechanics in Pulmonary Edema

Pulmonary edema is characterized by reduced lung and chest wall compliance (restrictive physiology) and refractory hypoxemia. The stiff lung and chest wall lead to increased work of breathing. Patients with pulmonary edema of any cause use a higher fraction (25% to 50%) of their total metabolic output to support their increased work of breathing. If the insult is not reversed, the combination of hypoxemia and increased work of breathing leads to respiratory failure and the need for ventilatory assistance. In most cases the severity of lung dysfunction and hypoxemia is more severe and more prolonged in the nonhydrostatic pulmonary edema of ARDS, when compared with the hydrostatic pulmonary edema caused by CHF (see Chapter 31).

In addition to the replacement of air with fluid in the alveolar spaces, the problems with gas exchange and increased work of breathing seen in ARDS are also caused by the inflammatory nature of the intra-alveolar fluid causing impaired surfactant synthesis, secretion, and function. The resulting surfactant abnormalities lead to increased alveolar collapse (i.e., atelectasis), due to the loss of surfactant's natural effects on lowering surface tension at the air–liquid interface in the alveolus.[14] The negative effects of alveolar consolidation and atelectasis on pulmonary gas exchange are worsened by a loss of the normal vascular response to alveolar hypoxemia. Normally, pulmonary arteries in areas of alveolar hypoxia will constrict as a physiologic response to preserve ventilation/perfusion $\dot{V}/\dot{Q}$ matching. However, in ARDS, this normal vasoconstrictive response is impaired in hypoxic areas; thus nonaerated alveoli receive higher blood flow than needed, which contributes to severe $\dot{V}/\dot{Q}$ mismatching and an intrapulmonary right-to-left shunting of blood flow (leading to hypoxemia).

In summary, pulmonary edema may arise from acute illnesses associated with increased pulmonary venous pressure (hydrostatic pulmonary edema or CHF) or may result from conditions associated with acute injury to the lung, in which the normal barriers to fluid movement within the lungs is disrupted, such as in ARDS. Although CHF and ARDS are distinct disease processes that require very different management strategies, differentiating these two forms of pulmonary edema in patients is frequently challenging because signs and symptoms of both are often very similar. The remainder of this chapter will focus on the distinct characteristics and management approaches for ARDS. In so doing, the reader should gain further ability to understand which characteristics and management approaches are both similar and distinct to CHF.

DEFINITION AND DIAGNOSIS

Early in the 20th century, the clinical problem of respiratory distress shortly after birth was identified in premature infants,

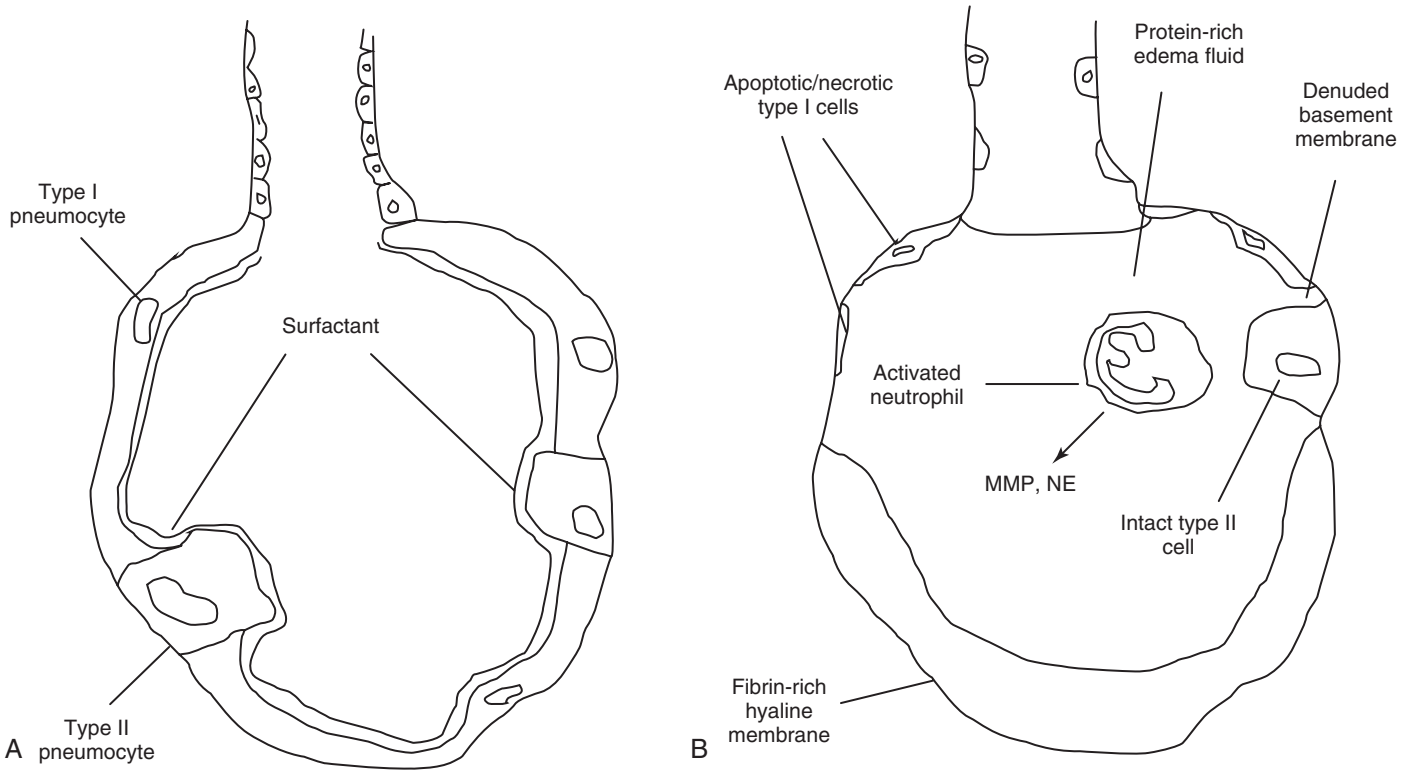

Fig. 29.3 The illustration compares a normal alveolus (A) and an alveolus with acute respiratory distress syndrome (ARDS) (B). The normal alveolus includes intact type I and II pneumocytes along with a layer of surfactant at the air-liquid interface over the epithelium. In ARDS, there is injury and loss of type I cells through apoptosis and necrosis, some preservation of typically dysfunctional type II cells and depletion and inactivation of surfactant. The alveolar lumen becomes filled with protein-rich fluid from leak of serum, activated neutrophils releasing mediators like matrix metalloproteinases *(MMP)* and neutrophil elastases *(NE)*, and leak of serum coagulation factors that form fibrin-rich hyaline membranes lining the alveolar wall. (Modified from Prudhomme JB, Ware LB: Acute lung injury and acute respiratory distress syndrome: mechanisms and potential new therapies, *Drug Discov Today: Dis Mech* 1:123–128, 2004.)

and by mid-century, the principal mechanism for the respiratory distress syndrome (RDS) in neonates was identified as a deficiency of surfactant.[14] Soon thereafter, a similar syndrome was recognized in adults, and the term "adult" respiratory distress syndrome (ARDS) was created.[1] Over the next 25 years, establishing a consistent definition for ARDS was challenging due to its close similarity during the initial clinical presentation of patients with other, more common diseases (e.g., CHF, pneumonia).

Criteria for Clinical Syndrome

In response to these challenges, a consensus definition for the "acute" respiratory distress syndrome (ARDS) was created in 1994 with the collective input of established experts from across Europe and the United States and is commonly referred to as the American-European Consensus Conference (AECC) definition.[15] Because the syndrome of ARDS in children (older than newborns) is not significantly different from that in adults, the AECC definition included all patients beyond newborns and discontinued use of the term *adult* in the title of ARDS. The AECC definition includes five central components: (1) reduced lung compliance, (2) hypoxemia (ratio of $PaO_2/FiO_2 < 300$), (3) bilateral infiltrates on chest radiograph, (4) an acute illness associated with the development of ARDS that can trigger the onset of ARDS, and (5) no evidence of CHF (typically based on direct measurements from an invasive pulmonary artery catheter of vascular filling pressures on the left side of the heart; see Chapter 31). The AECC definition also created the term known as **acute lung injury** (ALI), which shares all characteristics of ARDS except the severity of hypoxemia in ALI is less severe (PaO_2/FiO_2 of <300) as compared with ARDS (PaO_2/FiO_2 of <200). The AECC definition served as the "gold standard" for identifying and enrolling patients with ARDS into clinical trials for almost 20 years. The combination of this consistent definition and enhanced collaboration between investigators around the world led to dramatic discoveries and marked improvements in the outcomes of patients.

In 2012 the definition of ARDS was revised and updated by a new international consensus group that met in Berlin, Germany, in 2011.[16] These updates were made in response to limitations

of the AECC criteria that had been identified. The new criteria included in the revised definition are commonly referred to as the Berlin definition or Berlin Criteria. The key new features of the Berlin Criteria include the following:

1. Discontinuation of the use of the term "acute lung injury" (ALI), which had proven to be nothing more than redundant terminology without adding meaningful value.
2. Creation of three categories for ARDS disease severity (mild, moderate, and severe) based on ranges of PaO_2/FiO_2 ratio and levels of **positive end-expiratory pressure** (PEEP).
3. Inclusion and acceptance of noninvasive techniques to estimate left heart pressures, including echocardiography.
4. Enhanced specificity for interpretation of chest radiographs when determining the presence of bilateral infiltrates or opacities most characteristic of nonhydrostatic pulmonary edema.
5. Greater specificity regarding the time frame by which the development of the disease may still be considered "acute" (<1 week of the triggering condition).

Since its introduction, researchers and clinical trials have primarily used these updated definitions. Although they are not believed to differ dramatically, clinicians and readers should consider the importance and potential impact of these different criteria when comparing the results of research prior to and after creation of the new criteria.

RULE OF THUMB The PaO_2/FiO_2 is calculated using the PaO_2 obtained from an arterial blood gas (ABG) analysis and the FiO_2 at the time the ABG value was obtained. When calculating PaO_2/FiO_2, it is important to remember the difference between a fraction and a percent. In other words, a patient who is receiving 40% supplemental O_2 has a FiO_2 of 0.40 (not 40). As an example, the PaO_2/FiO_2 of a patient on 50% (FiO_2 0.5) whose PaO_2 is 90 mm Hg calculates to be 180. Assuming the patient met the other points of the Berlin Criteria to have acute respiratory distress syndrome (ARDS), the PaO_2/FiO_2 would indicate that the patient has moderate ARDS.

BOX 29.3 Etiologic Risk Factors That Trigger Acute Respiratory Distress Syndrome

Direct Injury
- Pneumonia (viral, bacterial, fungal)
- Gastric aspiration
- Toxic inhalation (phosgene, cocaine, smoke, high concentration of oxygen)
- Near drowning
- Lung contusion

Indirect Injury
- Sepsis and prolonged shock
- Burn injury (chemical or heat induced)
- Multiple trauma
- Transfusions (TRALI)
- Pancreatitis
- Gynecologic causes (abruptio placentae, amniotic embolism, eclampsia)
- Drug effect (e.g., *trans*-retinoic acid for acute leukemia)
- Sickle cell crisis

TRALI, Transfusion-related acute lung injury.

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After obtaining a careful history and physical exam, the most common and rapidly available test to help differentiate congestive heart failure (CHF) from acute respiratory distress syndrome (ARDS) is a chest radiograph. It is often difficult to distinguish between CHF and ARDS based on the radiographic findings alone. CHF is often associated with cardiomegaly, perihilar infiltrates, and pleural effusions, whereas ARDS is more often associated with the presence of peripheral alveolar infiltrates, air bronchograms, sparing of the costophrenic angles, and normal cardiac size (Fig. 29.4). It must be noted that interpretation of portable chest radiography with patients lying supine in the intensive care unit is more difficult and may reduce the ability to readily identify these unique characteristics. Alveolar infiltrates in both entities can be diffuse and tend to occur in dependent lung zones but tend to form more in a gradient (worsening from anterior to posterior) in ARDS, which can be best seen on computed tomography imaging of the chest in ARDS (Fig. 29.5).

Distinguishing Acute Respiratory Distress Syndrome from Nonhydrostatic Pulmonary Edema in Clinical Practice

Despite the specific details of published definitions for ARDS and nonhydrostatic pulmonary edema, the clinical differentiation of ARDS from hydrostatic pulmonary edema (e.g., caused by CHF or volume overload from either advanced renal or hepatic disease) at the bedside of critically ill patients based on the Berlin Criteria can be challenging, even for experienced clinicians. In Box 29.2, clinical features that are common to both hydrostatic pulmonary edema and ARDS and those that can distinguish each are outlined. Patients presenting with hydrostatic pulmonary edema are much more common than ARDS and should be considered whenever the history or physical examination findings suggest one of the causes of CHF listed in Box 29.3. A clinical history of infection, recent trauma, or risk factors for aspiration may be present in either patient group, but the presence of these risk factors (triggers) favors a diagnosis of ARDS. To emphasize the difficulty in distinguishing the cause of pulmonary edema, many patients with ARDS are older and have preexisting illnesses that also place them at risk for CHF.

Intuitively, invasive measurement of hemodynamic variables using a pulmonary artery catheter (also called right heart catheter or Swan-Ganz catheter) would seem to offer a definitive way to differentiate hydrostatic and nonhydrostatic edema. However, in practice, the measurement of the cardiac output or pulmonary arterial pressure either invasively or noninvasively has not been shown to be essential for diagnosis of ARDS or beneficial in the daily management of ARDS patients.[17] The increasing availability and accuracy of noninvasive assessment of cardiac function by

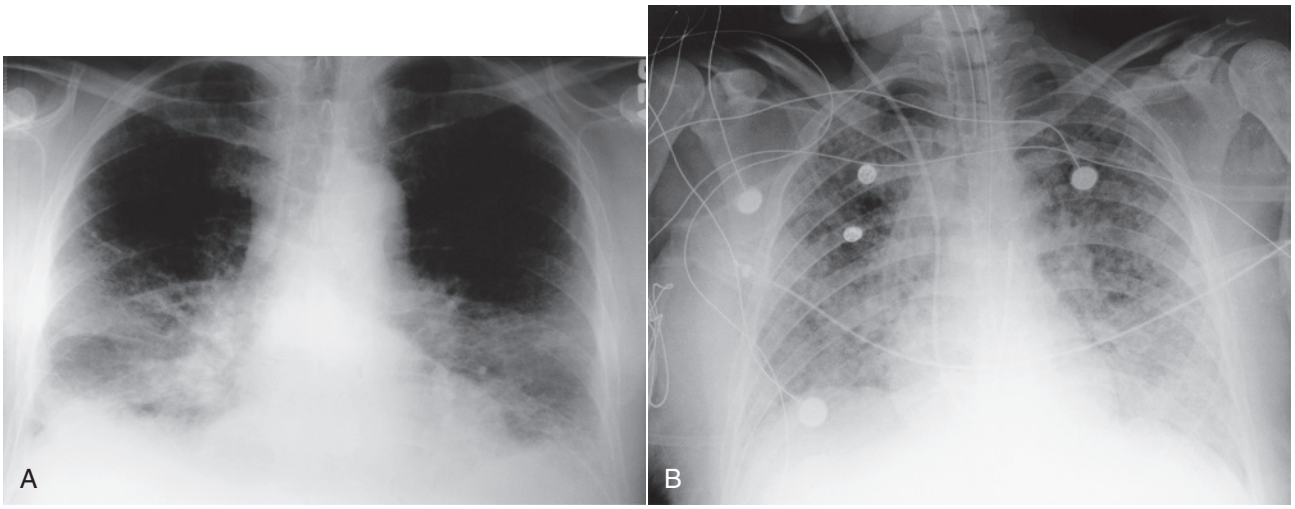

Fig. 29.4 Chest x-rays show the typical radiographic features of congestive heart failure (CHF) and acute respiratory distress syndrome (ARDS). (A) CHF is characterized by cardiomegaly, interstitial infiltrates, bilateral perihilar and basilar alveolar infiltrates, and bilateral pleural effusions, which cause blunting of the costophrenic angles. (B) ARDS is commonly associated with normal cardiac size, diffuse peripheral alveolar infiltrates, and minimal or absent pleural effusions.

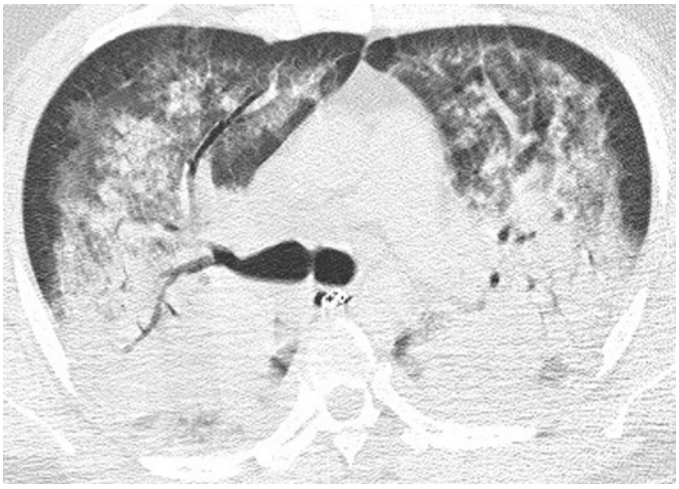

Fig. 29.5 Chest computed tomography image of a patient with bilateral acute respiratory distress syndrome (ARDS). As seen, there is a gradient of infiltrates that worsens progressively from anterior to posterior. The cause of ARDS in this case was indirect due to septic shock from an extrapulmonary (intra-abdominal) source. (From Elicker BM, Jones KT, Naeger DM, et al: Imaging of acute lung injury, *Radiol Clin N Am* 54:1119–1132, 2016.)

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A careful history and evaluation of the overall clinical presentation often are the most useful means by which congestive heart failure (CHF) and acute respiratory distress syndrome (ARDS) can be initially differentiated in a patient who has refractory hypoxemia and bilateral infiltrates on the chest x-ray. For example, a patient presents to the emergency department with complaints of increased cough and shortness of breath and a low-grade fever (38.2°C). His medical history includes a long history of systolic heart failure (ejection fraction of 20% to 25% on recent echocardiogram). On examination, he has rales noted in both lung bases, engorged neck veins, bilateral lower extremity edema, and bilateral infiltrates with cardiomegaly on chest x-ray. His PaO_2/FiO_2 on 50% FiO_2 is 175. His white blood cell count is within normal range, and he has no other signs of systemic inflammatory response syndrome (SIRS) or other organ failure (e.g., renal, hepatic, central nervous system).

means of echocardiography, when combined with other physical examination features (capillary refill and mottling), can provide reliable information that can effectively guide clinical decision making.

Another potential method of separating CHF from ARDS is based on differences in the composition of the alveolar edema fluid. As described earlier, the inflammatory nature of this exudative fluid with ARDS is reflected by the increased inflammatory cells and serum proteins (versus transudative fluid in CHF), which can both be quantified in fluid obtained from a bronchoscopy with BAL. Collecting BAL is not uncommon in ARDS to provide diagnostic insights regarding respiratory infections that may have served as the initial triggering source for ARDS, but BAL analysis is typically not performed to distinguish hydrostatic pulmonary edema from ARDS.

Based on this presentation, the patient most likely has CHF, despite his fever and a PaO_2/FiO_2 (P/F) ratio less than 200. A brisk response to routine management for CHF (e.g., diuretics, antihypertensives) would be expected and further confirm the diagnosis.

Histopathologic Findings

The changes in the lung tissue in ARDS are typically separated into two phases based on the overall duration of the disease process: (1) the acute exudative phase (1 to 7 days) and (2) the fibroproliferative or also called organizing phase (3 days to weeks).

The exudative phase is characterized by diffuse damage to alveoli and blood vessels and the influx of proteinaceous fluid and inflammatory cells into the interstitium and alveolar spaces. As characterized in Fig. 29.3, there is capillary congestion, intra-alveolar edema, and injury/death of pneumocytes that form the alveolar wall, which includes type I pneumocytes (the predominant structure cells lining the alveoli) and type II pneumocytes (which make and secrete surfactant).[18,19] There is also cellular

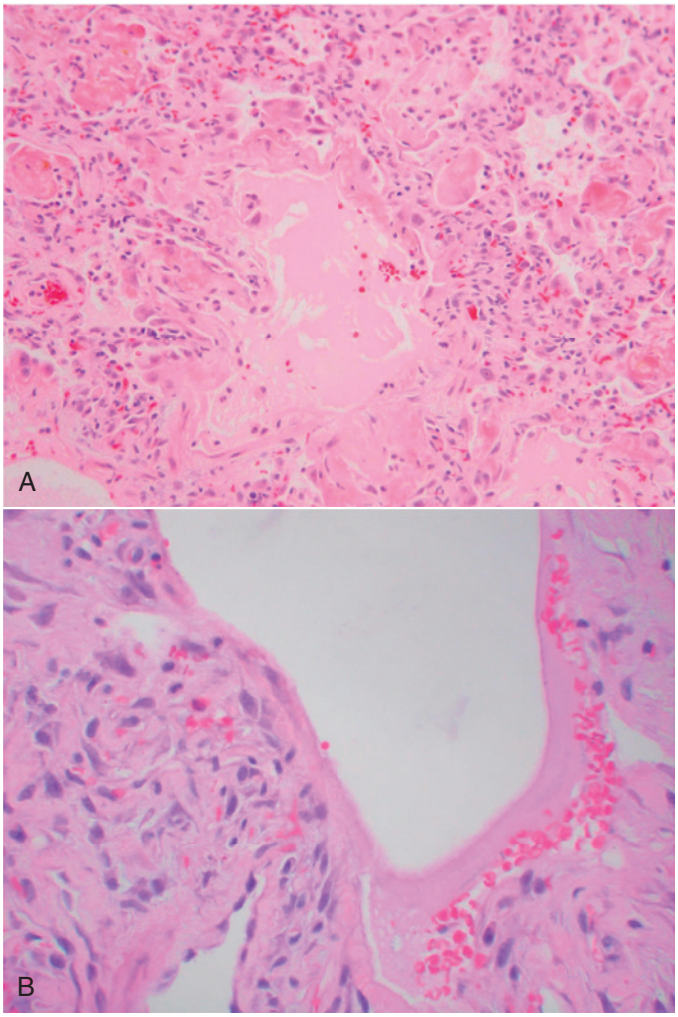

Fig. 29.6 Light microscopic image demonstrating characteristic changes of acute respiratory distress syndrome (ARDS), which are often called diffuse alveolar damage by pathologists. (A) Low magnification demonstrating extensive infiltration of inflammatory cells, thick and edematous alveolar interstitium and intra-alveolar hyaline membranes. (B) Higher magnification to better illustrate the hyaline membrane tightly adherent to the alveolar wall and extravasation of erythrocytes into the interstitium. (From Castro CY: ARDS and diffuse alveolar damage: a pathologist's perspective, *Semin Thorac Cardiovasc Surg* 18:13–19, 2006.)

injury to the lining (endothelium) of the pulmonary capillaries. The alveolar spaces are lined with *hyaline membranes*, which are composed of cellular debris and condensed plasma proteins (Fig. 29.6). As a result, an early name for ARDS was "hyaline membrane disease." When the primary condition that triggered the onset of ARDS is quickly identified and treated, the exudative phase is typically short, lasting only a few days, and is fully reversible, leaving no significant chronic signs of injury to the lung.

After the cause of lung injury is controlled, a process of lung repair begins. On pathologic examination, this appears as an overabundance of alveolar type II pneumocytes and infiltration or proliferation by fibroblasts within the alveolar basement membrane and intra-alveolar spaces. Fibroblasts drive intra-alveolar and interstitial fibrosis. The extent of fibrosis determines the degree of pulmonary disability in patients who survive ARDS. The exact mechanisms controlling lung remodeling in ARDS are not well established but very likely involve by-products of inflammatory cells (e.g., proteases, antiproteases, IL-6) and various growth factors (transforming growth factor [TGF]-α, TGF-β).[20] However, the remodeling process after ARDS is quite variable. Typically, patients have nearly complete normalization of lung compliance and oxygenation 6 to 12 months after the illness, with a persistent slight impairment of the diffusing capacity. However, in a small percentage (5% to 10%) of patients, the architecture of the lung does not fully return to normal and patients can experience chronic respiratory disability related to irreversible pulmonary fibrosis and obliteration of the pulmonary vasculature. The extent of recovery depends on the severity and duration of the initial trigger that led to ARDS and the influence of potential secondary forms of injury that may develop over the patient's complete hospital course. Secondary forms of lung injury include nosocomial infection, O_2 toxicity, and forms of **ventilator-induced lung injury** (VILI), which will be reviewed in detail later in this chapter.

KEY FEATURES

Risk Factors (Triggers) and Host Susceptibility

In the Berlin Criteria, an essential component of ARDS is that the patient must have an associated illness that stimulates an acute inflammatory response that leads to lung injury. These acute illnesses are typically referred to as risk factors or triggers for ARDS.[21,22] It has been proposed that the risk factors for ARDS should be categorized into problems that lead to either direct injury or indirect injury to the lung (see Box 29.3). In this concept, direct injury occurs as the result of triggers that begin in the lung (e.g., pneumonia and aspiration) and create an acute inflammatory reaction, within the lung, that initially leads to injury of the alveolar epithelium and subsequent damage to the interstitium and capillary endothelium injury. Conversely, indirect injury is caused by acute illnesses that begin outside of the lung (e.g., pyelonephritis, trauma or massive hemorrhage) and trigger an acute systemic inflammatory reaction that initially injures the capillary endothelium via circulating inflammatory mediators, which leads to subsequent injury of the interstitium and alveolar epithelium. Some studies suggest that the response of patients to treatment in ARDS may differ depending on whether the initial injury is direct versus indirect. However, thus far, this distinction has not proven to predict response to treatment or other important clinical outcomes.

It is important to recognize that only a minority of patients with risk factors for ARDS ultimately develop the full clinical syndrome. The key factors that determine which patients will develop ARDS are the severity and duration of the risk factor, and variables that lead some patients to be more susceptible. Sepsis is the most common cause, but even among all patients with sepsis, fewer than 20% will develop ARDS. As the severity of sepsis increases, the likelihood of ARDS developing increases dramatically and can exceed 50%. Among direct insults that lead to ARDS, pneumonia is the most common. Pneumonia caused by influenza infection is believed to carry an especially high risk for developing ARDS and a higher severity of ARDS once it develops.[23] As for the susceptibility of the host to develop ARDS,

important variables are increased age (i.e., age >50 years), liver disease, alcoholism, and genetic polymorphisms related to inflammatory mediators (e.g., IL-1, TNF, and surfactant).[24] Evidence suggests that cigarette smoking may also increase susceptibility to ARDS.[25]

One approach to improving outcomes in ARDS is to design studies that advocate starting therapy in advance of ARDS in population at risk. In 2014 the National Institutes of Health (NIH) launched the Prevention and Early Treatment of Acute Lung Injury Network (PETAL), which became the successor to the ARDS Network (1994–2014).[26,27] A priority for their trials and other ARDS clinical trial groups is the focus on patients with acute diseases who are at high risk to progress to ARDS. Methods to better predict patients at high risk have been developed and are continuously being refined as more data from trials become available. The Lung Injury Prediction Score is one such predictive tool and has been used to target preventive measures or therapies on at-risk populations and reduce the incidence of ARDS.[28,29]

Epidemiology and Outcomes

The exact prevalence of ARDS (including ALI) varies depending on the population. The ARDS estimates in the United States (reported in 2005) suggest that each year, there are 75 to 90 cases per population of 100,000 ($PaO_2/FiO_2 \leq 300$), which represents almost 200,000 cases for the entire country. In a recent multicenter, international study (LUNG SAFE),[30] 10% of patients admitted to the ICU had ARDS and 24% of all patients required mechanical ventilation. The prevalence of ARDS severity was 31% mild, 47% moderate, and 23% severe.

The survival of patients with ARDS seems to have changed over time and population.[31] The early mortality rates associated with ARDS between the late 1960s and the early 1990s were very high (i.e., 60% to 80%). Given our ability to maintain respiratory function in ARDS using mechanical ventilation, only a small minority (10% to 15%) of patients with ARDS die from respiratory failure. The most common cause of death in patients with ARDS relates to the original risk factor that triggered ARDS and from the MODS. Fortunately, the mortality rate over the past 20 to 25 years has declined dramatically, with most recent mortality rates typically reported between 20% and 40% and some experience as low as 20%.[32] The implementation of lung protective strategies, recognition, and adjunctive interventions have decreased the incidence. However, recognition of ARDS is poor (40% of cases are missed!) and the implementation of lung protective strategies is not universal. In the latest international study the overall mortality of ARDS while patients were still in the ICU of 35% and overall mortality prior to hospital discharge of 40%. Although the correlation is not as high as bedside clinicians often think, mortality in ARDS is also associated with ARDS severity (lower P/F ratio) with mortality in mild ARDS of approximately 30% to 35% and as high as 45% to 50% in severe ARDS.[30]

Beyond a risk for death, many important morbidities affect survivors of ARDS, including a long period on mechanical ventilation, time in the ICU and hospital, and slow recovery of lung function. Lessening these morbidities has increasingly become the primary target for recent, large ARDS clinical trials. As the duration of the time spent on mechanical ventilation has declined, so has the number of days in the ICU and hospital. However, the recent increasing use of long-term acute care facilities has made these comparisons with early experience more complicated. Recovery of lung function as assessed by pulmonary function tests such as spirometry, diffusion capacity (DLCO), and 6-minute walk test (6MWT) demonstrates that ARDS survivors typically recover more than 80% of lung function over 3 to 12 months.[33] The rate of recovery depends on several variables, including ARDS severity, the original risk factor, patient age, and more. Recovery of vital capacity, expiratory volume, and total lung capacity typically occur earliest, whereas recovery of DLCO and 6MWT is more prolonged.

In addition to outcomes primarily linked with lung function, morbidities are associated with the other aspects of ICU care that are needed in managing ARDS patients (e.g., sedation, delirium, and immobility) that have long-term impact on other organ function, such as muscle strength and cognition. Using a variety of techniques to assess muscular and cognitive function, survivors of ARDS consistently demonstrate prolonged impairments in both for at least 6 to 12 months; however, in some patients, the changes may never reverse. Consequently, increasing attention and urgency has been placed on identifying and using supportive care strategies (e.g., early mobility, minimizing delirium, optimal fluid balance, nutrition) to minimize these morbidities and accelerate recovery.

RULE OF THUMB Although acute respiratory distress syndrome (ARDS) was once considered a diagnosis that carried a high likelihood for death (≥70%), current rates of survival in patients with ARDS are much higher, with more than 50% to 70% surviving. As a result of our ability to provide protective approaches to mechanical ventilation that reduce harm, very few patients with ARDS die from respiratory failure. The severity of patients' hypoxia does correlate with mortality, but transient periods of hypoxemia do not significantly increase the likelihood for death. Most patients who die from mechanical ventilation die from the disease that triggered the ARDS. Accurate early diagnosis and treatment of the disease that triggered ARDS is a key to survival. For the respiratory therapist, this means that even patients with severe hypoxemia must undergo diagnostic tests that require transportation to radiology (e.g., computed tomography scans) or may transiently disrupt their ventilation (e.g., bronchoscopy).

THERAPEUTIC APPROACH

The hallmark of treatment of ARDS is supportive care with mechanical ventilation with disease-specific treatment of the underlying risk factors. Identifying and treating the cause of ARDS is an important step to stop progression of the lung injury. After diagnosis, the care focuses on preventing further injury (lung and other organs) and supporting the body while it recovers. This section presents an overview of the current approach to mechanical ventilation, adjunctive therapies that assist respiratory function, rescue strategies of ventilation, and key principles of nonventilatory support that should be prioritized in the care of patients with ARDS.

As previously mentioned, early efforts to improve outcomes in ARDS were largely unsuccessful due to large variations in definitions of ARDS and management approaches. In response

BOX 29.4 Goals and Priorities for Mechanical Ventilation in Acute Respiratory Distress Syndrome

1. Lung protective strategy
   a. Low tidal volume—using predicted body weight
   b. Low plateau or driving pressure
   c. PEEP titration—minimize derecruitment
2. Goals for gas exchange
   a. Permissive hypercapnia
   b. Avoidance of hyperoxia and hyperoxemia

PEEP, Positive end-expiratory pressure

to this challenge, the NIH launched a multicenter network of investigators and institutions to specifically collaborate on clinical treatment strategies for ARDS, a group that has since been known as the ARDS Network (ARDSNet).[26] It is important to note that the launch of ARDSNet in 1994 coincided with the creation of the original AECC ARDS definition. Several landmark clinical trials by ARDSNet, its successor PETAL Network (2014 to present), and other clinical trial groups have completed trials that demonstrated improvements in patient outcomes, including increased survival.[27] Over this same time, additional study networks focused on ARDS have successfully formed outside the United States, including in Canada, Europe, Australia, and New Zealand, and have provided equally important contributions.

Mechanical Ventilation and Other Respiratory Supportive Care

Mechanical ventilation is the cornerstone of supportive care for patients with ARDS. In general, the three goals of mechanical ventilation are safety, comfort, and liberation from mechanical ventilation. Safety encompasses two main clinical objectives: ensuring gas exchange and preventing further lung injury caused by mechanical ventilation or VILI. Comfort focuses on ensuring synchrony with the ventilator and balancing the work of breathing distribution. Keeping in mind these goals and clinical objectives of ventilation, one can see that some are more important at different stages of ARDS. In the early exudative phase of ARDS, the main goal is to ensure gas exchange and prevent further lung injury. As the disease process resolves and the patient–ventilator interaction and awareness are more important, comfort and liberation become the main goals. This does not mean that each goal is mutually exclusive, but it does help to explain choices about which mode of ventilation to apply to a given patient at a given time. For this chapter, we will review and summarize the key elements of goals for mechanical ventilation that most apply to the care of patients with ARDS (Box 29.4), while more detailed examination and review of the principles and applications of mechanical ventilation are provided later in the book (see Chapters 46 to 49).

Setting Tidal Volume

Although mechanical ventilation provides lifesaving support to patients with ARDS and other forms of acute respiratory failure, mechanical ventilation can be dangerous and can cause VILI. Although there are multiple forms of VILI, the most important

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Tidal Volume

Tidal volume (V_T) in mechanical ventilation should be kept within a safe range to prevent lung injury. The size of V_T most recommended is 6 (4 to 8) mL/kg of predicted body weight (PBW) (not actual body weight). PBW is determined by knowing a patient's gender and height, and tables with formulas for calculating PBW are readily available. It is important for the respiratory therapist (RT) to accurately calculate each patient's PBW (using their gender and measured or estimated height) when starting mechanical ventilation. For example, a man who is 6 feet tall and weighs 224 lbs. (100 kg) has a PBW of only 70 to 75 kg. Using his PBW and the V_T target of 6 mL/kg, the ventilator should be set for a V_T of 420 to 450 mL. If his actual body weight were incorrectly used, a V_T of 600 mL would have been selected and would be too large and could lead to VILI and increased mortality. Many RTs carry reference cards with safe V_T based on height and sex for rapid reference. The RT should also consider whether the patient has any history of surgical lung resection (e.g., pneumonectomy or lobectomy), which results in smaller predicted lung capacity. For a patient who has undergone pneumonectomy, the selected V_T should be reduced by approximately 50%.

and well-established forms of VILI are volutrauma and barotrauma.[34] ***Barotrauma*** is the rupture of alveolar structures, presumably due to excessive airway pressure, that results in gross leakage of air outside of the lung parenchyma into adjacent tissue spaces (e.g., pneumothorax and pneumomediastinum). ***Volutrauma*** is similarly a form of injury to the alveolar structure; however, rather than a clinically recognizable leak of air, there is microscopic cellular injury to the alveolar and capillary walls, causing them to become leaky. This cellular injury then becomes the trigger for an inflammatory cascade that may trigger or worsen ARDS. The strategy of using a tidal volume (V_T) that avoids volutrauma is commonly referred to as low tidal volume ventilation (LTVV) or ***lung protective ventilation*** (LPV).

In 2000 a landmark clinical trial (the ARMA trial) was completed and published by the ARDS Network using LPV and demonstrated a 22% relative reduction in mortality in patients with ARDS managed with a "low stretch" or low V_T approach. The study compared a strategy of low V_T (6 mL/kg predicted body weight [PBW]) versus a larger V_T of 12 mL/kg PBW, which had been the standard for practice in ICUs across the United States and world for more than 40 years.[35] The survival benefit of low V_T transformed the standards for care of patients with ARDS and is considered one of the most important reasons for the dramatic improvements in mortality and morbidity associated with ARDS over the past 10 to 15 years. More recent trials of mechanical ventilation in patients without ARDS indicate that VILI may happen in any mechanically ventilated patient and that LPV is the preferred approach for choosing a V_T in most clinical settings. These trials include even patients requiring only brief exposures to mechanical ventilation during elective abdominal surgical procedures.[36]

Positive End-Expiratory Pressure

The use and critical importance of PEEP in ARDS were highlighted in the original report of ARDS in adults older than 50 years ago,[1] and over the ensuing years, the effects of PEEP on

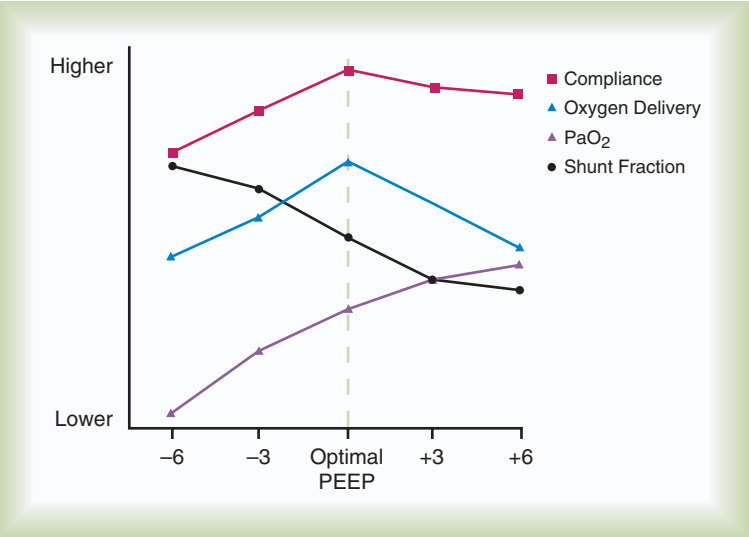

Fig. 29.7 Determination of optimal positive end-expiratory pressure *(PEEP)* from simultaneous measurements of hemodynamic (DO_2), gas exchange (shunt fraction and arterial oxygenation *[PaO_2]*), and physiologic values. Optimal PEEP does not correspond to PEEP associated with optimal pulmonary gas exchange. When adjusting PEEP, the clinician should consider its effects on systemic DO_2 and lung compliance such that systemic organ injury and lung injury are minimized.

lung compliance, oxygenation, and cardiac output have been well characterized. As Fig. 29.7 highlights, the effects of PEEP on lung compliance and oxygen delivery vary based on pressure used and patient-specific factors.

The rationale for using PEEP requires understanding the pressure-volume (P-V) curve of the lung. The P-V relationship can be established for a given patient by measuring lung volume during step increases in airway pressure. The classic P-V curve has an S, or sigmoid, shape (Fig. 29.8). The initial limb has large changes in pressure that are associated with only small increases in volume, the middle limb has the "best" change in pressure per volume, and the final limb again has large pressure changes with smaller increases in volume. Compliance is defined as the relationship between change in volume (ΔV) and change in pressure (ΔP) or ΔV/ΔP, and the middle limb represents the most compliant portion of the curve. The P/V curve also demonstrates a lower inflection point (LIP; point at which the lower limb shifts to the middle limb) and an upper inflection point (UIP; point at which the middle limb shifts to the upper limb). The LIP represents the point at which recruitment (i.e., opening) of alveolar units begins, and typically also the point below which alveolar units close (i.e., collapse or atelectasis) if airway pressure at end expiration drops below. The UIP represents the point beyond which further expansion of alveolar units becomes more difficult and more likely to cause injury from overdistension. From the physiologic standpoint, PEEP reduces lung collapse thereby increasing the amount of aerated lung, a phenomenon often referred to as *recruitment*.[37]

During mechanical ventilation, the goals for titration of PEEP are staying above the LIP to avoid repeated cycles of alveolar collapse. Although creating P-V curves and quantitation of the LIP and UIP can be performed on patients receiving mechanical ventilation, measuring P-V curves is both technically challenging and time consuming and requires patients to be heavily sedated.

MINI CLINI

The pressure-volume relationship is most easily understood by considering the effort required to blow up a party balloon. The start of balloon inflation is often difficult and requires high pressure to get air to enter the balloon. After reaching a certain pressure threshold, inflation becomes easier. At this threshold, the pressure in the balloon has risen above the equivalent of the lung's lower inflection point (LIP) and is now on the steep part of its P-V curve. Eventually, the balloon gets close to maximum inflation and it once again becomes hard to fill it any further, which is its upper inflection point (UIP). Many children have identified that having an adult start blowing up a balloon (getting it beyond the LIP) makes the job easier. This is essentially what positive end-expiratory pressure (PEEP) is doing, keeping the lung open above its LIP with each respiratory cycle, which achieves recruitment of previously deflated lung units and prevention from deflation of open lung units.

Because measurements of LIP and UIP are not done routinely, titration of PEEP is typically performed using estimates from more available daily data of pressure and volume recorded mechanical ventilation.

In ARDS, the challenge of estimating the P-V relationships to determine the "best" PEEP settings is even greater. The P-V curves are flatter and more deviated to the right (see Fig. 29.8), which creates a smaller window for the settings to maximize benefits while avoiding overdistension. It must also be noted that in ARDS, the P-V relationships are highly dynamic and depend on the patient's overall condition, can change rapidly due to fluctuations in the patient's lung compliance (e.g., pneumonia, pulmonary edema), synchrony with mechanical ventilation, and more. Finally, the use of PEEP is further complicated by the potential adverse hemodynamic effect of PEEP to decrease venous return to the right heart. Thus determining PEEP levels in patients with ARDS requires frequent reassessment and adjustments.[38]

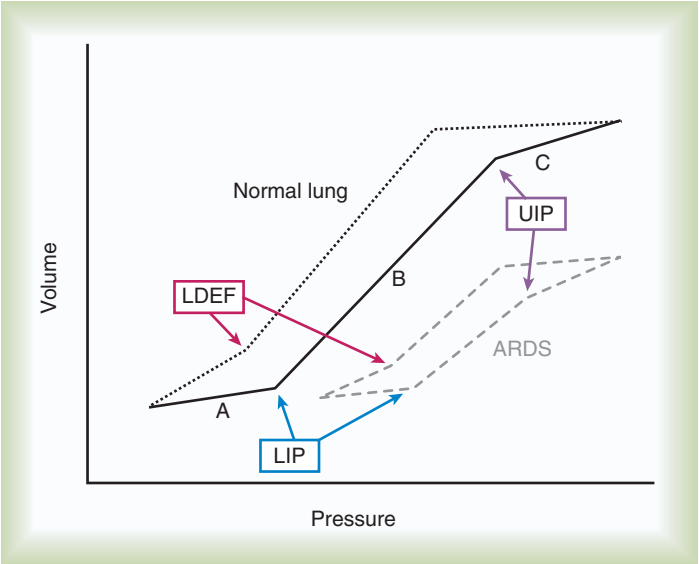

Fig. 29.8 Typical pressure–volume relationships during normal conditions and during acute respiratory distress syndrome *(ARDS)*. At low lung volume, inspiratory pressure increases faster than lung volume *(line A)* owing to high alveolar surface tension. As alveoli open, surface tension decreases, and the pressure required to increase lung volume further decreases *(line B)*. The lower inflection point *(LIP)* occurs between *lines A* and *B* and represents the volume above which most alveolar units are open. The upper inflection point *(UIP)* occurs at near-maximal lung volume and corresponds to the point at which further increases in pressure result in minimal increases in lung volume *(line C)*. Pressure applied above the *UIP* is associated with alveolar distension. During the expiratory phase of the respiratory cycle *(dotted line)*, the lower deflection point *(LDEF)* is the point below which lung volumes slowly decrease (alveolar units collapse). During ARDS *(gray dashed curve)*, pressure-volume relationships change such that higher pressure is needed to maintain alveolar patency, and alveolar distension occurs at lower V_T levels. Near-maximal lung volumes are typically achieved at an inspiratory pressure of approximately 35 cm H_2O in normal conditions and during *ARDS*. Attempts to increase inspiratory pressure to more than 35 cm H_2O provide little additional ventilation and substantially increase the risk for injury to the lungs. During *ARDS*, the *LIP* often occurs at a pressure of 5 to 15 cm H_2O. Positive end expiratory pressure at levels greater than *LIP* may prevent end-expiratory alveolar collapse and reduce lung injury due to alveolar shear stress.

The most reliable method to accurately set PEEP in ARDS remains unknown with some prioritizing oxygenation, lung compliance, or radiographic imaging (computed tomography).[39] A comparison of setting PEEP based on lung mechanics versus oxygenation using tables generated during ARDS Network trials (Fig. 29.9)[40] favored the table approach.[38,41] The majority of trials assessing different levels of PEEP in ARDS do not demonstrate an optimal PEEP strategy; but higher levels of PEEP in more severe disease (P/F ratio <150) may lead to decreased mortality and less use of rescue strategies.[42,43]

RULE OF THUMB Changes in physiologic markers (oxygenation, compliance) take time after changing the level of positive end-expiratory pressure (PEEP). When decreasing PEEP, the changes in physiology become evident early, usually within 5 min. On the other hand, when increasing PEEP, the changes in physiology make take at least 60 min to become fully evident and may continue to change with time.[44]

MINI CLINI

Avoiding Ventilator-Induced Lung Injury

Problem

How can ventilator-induced lung injury (VILI) be minimized in patients with acute respiratory distress syndrome (ARDS) through adjustments of positive end-expiratory pressure (PEEP) and tidal volume (V_T)?

Discussion

Alveolar injury can occur through either shear stress occurs when alveoli collapse during expiration and are reopened as the next V_T is delivered or overdistension, which leads to rupture or tearing of alveolar structures. Patients with ARDS are prone to developing each of these types of VILI due to impaired surfactant and decreased lung compliance. Alveolar collapse at end-expiration (the lower inflection point [LIP] of the P-V curve; see Fig. 29.8) leading to shear stress can be avoided by enough PEEP to keep up above the LIP. Using a smaller V_T (6 mL/kg of predicted body weight [PBW]) then assures that the changes in pressure during tidal ventilation do not exceed the upper inflection point (UIP) and create injury through overdistension. When combined, low tidal volumes and optimized levels of PEEP are the basic elements of lung-protective ventilation (LPV) that minimizes risk for VILI.

Because the recruitment of lung units is a key physiologic benefit of increasing PEEP levels, many investigators and clinicians use transient large increases in PEEP to generate greater recruitment that may be sustained even after return of PEEP levels to their prior levels, and this technique is typically referred to as a *recruitment maneuver*. Although short-term benefits in gas exchange are consistently reported in trials that include recruitment maneuvers, benefits on survival or other longer-term patient outcomes have not been shown. In the ARDS Network ALVEOLI trial, which compared the impact of two different (low versus high) PEEP titration tables, use of recruitment maneuvers was discontinued due to lack of benefit. A more recent multinational study comparing a standard PEEP titration table to patients treated with recruitment maneuvers concluded that use of recruitment maneuvers was harmful and increased mortality.[45]

RULE OF THUMB In most patients with acute respiratory distress syndrome (ARDS), positive end-expiratory pressure (PEEP) levels less than 20 cm H_2O are generally preferred. Levels of PEEP greater than 20 cm H_2O should *not* be routinely used unless the benefits of higher levels of PEEP are supported by objective end points, such as improved lung compliance (see Fig. 29.7) or optimal alveolar recruitment (see Fig. 29.8).

Managing Airway Pressures

Since publication of the ARDSNet ARMA trial (Low V_T), emphasis on RT training for mechanical ventilation in ARDS has focused on early initiation and maintenance of low V_T. However, the approach to mechanical ventilation in ARMA also included goals for maximal *plateau airway pressure* (Pplat; see Chapter 47) of 30 cm H_2O or less in the low V_T group versus 50 cm H_2O or less in the high V_T group. As expected, Pplat was significantly lower in the low V_T group (difference between groups of approximately 8 to 10 cm H_2O) over the first 7 days, whereas differences

Lower PEEP/higher FiO_2

FiO_2	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7
PEEP	5	5	8	8	10	10	10	12

FiO_2	0.7	0.8	0.9	0.9	0.9	1.0
PEEP	14	14	14	16	18	18–24

Higher PEEP/lower FiO_2

FiO_2	0.3	0.3	0.3	0.3	0.3	0.4	0.4	0.5
PEEP	5	8	10	12	14	14	16	16

FiO_2	0.5	0.5–0.8	0.8	0.9	1.0	1.0
PEEP	18	20	22	22	22	24

Fig. 29.9 Tables for positive end-expiratory pressure *(PEEP)* titration. The tables presented include the low- and high-PEEP titration tables created by the acute respiratory distress syndrome network for landmark clinical trials on mechanical ventilation and frequently used in hospital protocols across the United States. (From ARDS Network website. http://www.ardsnet.org/files/ventilator_protocol_2008-07.pdf.)

in PEEP levels between the groups during the same time were minimal (≤1 cm H_2O) during that same time.[35] As a result, most institutional ventilator protocols for management in ARDS include not only low V_T goals but also goals to maintain Pplat at 30 cm H_2O or less, including lowering V_T when needed.

When considering the most compliant portion of the P/V curve (see Fig. 29.8), it has long been debated whether ventilator goals to achieve inspiration should primarily target a change in volume (ΔV, same as V_T) or a change in pressure (ΔP, also referred to as ***driving pressure***).[46] To calculate driving pressure, it represents the increase in airway pressure during inspiration (level above PEEP) that is not influenced by airway resistance (which affects peak inspiratory pressure but not Pplat) and becomes the difference between Pplat minus PEEP. To address this question, a recent comprehensive analysis used compiled published data on pressure and volume relationships from multiple previously completed clinical trials (>3000 enrolled subjects) including the ARMA trial.[47] The authors concluded that maintaining lower driving pressures (ideally ≤15 cm H_2O) more closely correlated with mortality than maintaining V_T. Although highly provocative and intriguing, no prospective randomized trial has yet been completed to demonstrate that clinicians should adjust practice to prioritize driving pressure over V_T, but future trials are likely to be available soon. In the interim, bedside providers should consider both important and aim to maintain both targets whenever possible.

MINI CLINI

Drive Pressure

Problem

Increasing positive end-expiratory pressure (PEEP) may improve lung recruitment and oxygenation but may also increase the plateau pressure (Pplat), which may indicate the upper inflection point (UIP) of the pressure-volume (P/V) curve is being reached or exceeded and creating risk for VILI from overdistension. How do we know if a patient may need tidal volume (V_T) less than 6 mL/kg predicted body weight (PBW)?

Discussion

Some experts advocate looking at and prioritizing the pressure changes caused by a given V_T in addition to just the V_T. This change in pressure (ΔP) during inspiration is called the driving pressure and is the difference in pressure above PEEP at the end of inspiration (not including the influence of airway resistance). For example, what is the driving pressure in a patient on lung-protective ventilation (LPV) with a PEEP of 10 cm H_2O, receives a V_T = 450 mL that leads to a peak inspiratory pressure of 32 cm H_2O and Pplat of 28 cm H_2O? In this patient, driving pressure is 18 cm H_2O (Pplat – PEEP), which is a level that is higher than desired, and could lead to ventilator-induced lung injury (VILI) and increase mortality. Although not all, some clinicians might attempt to lower V_T and thereby lower ΔP as long as adequate gas exchange targets can be maintained.

Selecting the Mode of Mechanical Ventilation

For decades, experts debated which mode of mechanical ventilation is best for ARDS. Despite extensive efforts, no clear ventilator mode has proven superior, and in practice, clinicians may employ multiple modes to achieve the goals of LPV including V_T, PEEP, Pplat, and ΔP. To further simplify the issue, the mode of ventilation should principally serve the goals of safety (i.e., avoiding VILI) while also ensuring adequate ventilation and oxygenation to maintain the patient's frequently evolving cardiorespiratory and metabolic needs. More complete details outlining mechanical ventilation and the available associated modes are provided in Chapter 46.

Naturally, the mode that most directly achieves the goal of controlling V_T is volume control. In this mode, the clinician sets the V_T (6 mL/kg of PPBW) and the ventilator delivers the target V_T on every breath, whether patient-initiated or not. However, the potential shortcoming to this mode is patient–ventilator dyssynchrony, which may result in patient discomfort, increased work of breathing, increased oxygen consumption, and delivery of large (unsafe) tidal volumes. In response to this limitation,

many ventilator manufacturers have refined volume control modes to use other targeting schemes. For example, on the Maquet Servo-I (Rastatt, Germany), volume control has a dual targeting scheme, which turns into a pressure-controlled breath when the patient initiates a sufficient inspiration. On the Drager Evita XL (Lubeck, Germany), when the Autoflow feature is activated, volume control converts to a pressure control mode with an adaptive targeting scheme.[48,49]

As an alternative to volume control, patients may be placed on a pressure-control mode, the V_T depends on the set inspiratory pressure above PEEP and a set inspiratory time. However, the same limitations noted for volume control can lead to variations in V_T. To improve the safety and utility of pressure control ventilation for LPV, newer ventilators include technologic such as adaptive or intelligent targeting schemes in which the inspiratory pressure is automatically adjusted to achieve a target V_T. Whether these technologic advances lead to advantages that provide improved clinical care for patient–ventilator unknown.[50]

In any ventilator mode, variation in patient effort and dyssynchrony is a challenge. Often this can be resolved with sedation, analgesia, and/or neuromuscular blockade (NMB) to blunt patient respiratory effort. However, the adverse effects of these pharmacologic interventions must be considered and are increasingly recognized as affecting the long-term outcome of ARDS survivors. The therapist, in collaboration with nurses and physicians, should individualize ventilator mode to first maintain LPV principles, followed by balancing between reduction of patient-ventilator dyssynchrony and avoidance of excessive sedation.

Respiratory Rate and Inspiratory Time

ARDS is associated with alveolar consolidation, $\dot{V}/\dot{Q}$ mismatching, increased physiologic shunt, and dead space ventilation. In addition, critically ill patients typically have elevated rates of metabolism and CO_2 production, explaining why patients with ARDS require much higher minute ventilation to maintain $PaCO_2$ in the normal range. The challenge is that we use low V_T to prevent lung injury in ARDS, resulting in the need to increase the ventilator rate to achieve adequate $PaCO_2$ levels. In conventional practice, the respiratory frequency is kept below 35 breaths/min. The concern with faster ventilator rates is that these faster rates will not allow adequate time for exhalation, leading to air trapping (auto-PEEP) and overdistension of the lung, which can eventually worsen oxygenation and reduce cardiac output.[51] Thus, in managing patients with ARDS, the clinician must resist the urge to correct the $PaCO_2$ value to normal. Instead, in the absence of a contraindication to hypercapnia (e.g., elevated intracranial pressure), we allow hypercapnia ("**permissive hypercapnia**") with a goal to maintain the arterial pH at no less than 7.15 to 7.20.[52] Even when $PaCO_2$ rises to a point during which pH may become dangerously low (e.g., pH <7.15), the goal of trying to keep V_T at 6 mL/kg PBW remains. Correction of pH can also be achieved by either pharmacologic supplementation (intravenous [IV] or oral) of bicarbonate or physiologic retention of bicarbonate by the kidneys. In rare instances, extracorporeal removal of CO_2 is considered, and it is discussed later in this chapter.

MINI CLINI

Problem

My patient's carbon dioxide is climbing with lung protective ventilation (LPV). What should I do?

Discussion

The use of a lower tidal volume (V_T) in LPV often will result in worsened gas exchange, with patients demonstrating worsening oxygenation and ventilation, including lower P/F ratios, higher levels of $PaCO_2$, and lower pH. These seemingly adverse effects of LPV on arterial blood gases (ABGs) often create confusion and concern for families and care providers, including respiratory therapists (RTs). However, these changes are not associated with worse overall patient outcomes (e.g., as measured by mortality or time on mechanical ventilation). Quite the contrary, by continuing LPV, the patient's best opportunity for survival is achieved.

Closely related to the ventilator rate is the inspiratory time (Ti), which is the means by which clinicians and RTs adjust the **inspiratory-to-expiratory ratio** (I:E ratio). As discussed earlier, normal I:E is typically 1:≥2. In contrast to intubated patients with obstructive lung diseases (e.g., chronic obstructive pulmonary disease [COPD], asthma) who need I:E rates with even longer expiratory times, patients with acute respiratory distress syndrome (ARDS) have stiffer lungs and require less time for exhalation. As a result, I:E ratios of 1:1 are generally recommended in ARDS, and are achieved by using increasing Ti by decreasing inspiratory flow rates, which often results in desirable reductions of plateau airway pressure (Pplat) and driving pressures to maintain targets for LPV.

It must be remembered that as respiratory rates are increased and Ti is prolonged, risks for air trapping and auto–positive end-expiratory pressure (auto-PEEP) will naturally increase. Diligent monitoring for auto-PEEP during the management of mechanical ventilation in patients with ARDS is essential. Although auto-PEEP (like routine PEEP) may lead to improved oxygenation, when left undetected, auto-PEEP can lead to increased Pplat, alveolar overdistension, and VILI.

Oxygen Titration

Administering high levels of supplemental O_2 (FiO_2) can cause direct lung injury as a result of O_2 toxicity. O_2 toxicity is considered to be time and dose dependent; that is, the longer the exposure and the higher the FiO_2, the worse the injury will be. Although no formal recommendations currently exist, most hospitals have developed protocols and guidelines that instruct RTs to continuously titrate and minimize the FiO_2 and PEEP while targeting SpO_2 between the range of 88% and 96%. This range also happens to be consistent with the range used for delivery of LPV in all ARDS Network trials since ARMA, and most large clinical trials conducted by other clinical trial groups.

In recent years, increasing concern and attention has developed regarding greater focus and priority being placed on the careful titration of oxygen in critically ill patients to minimize potential risks of hypoxia, hyperoxia, and hyperoxemia.[53] Much of the attention for previously unrecognized toxicity from hyperoxemia using conventional approaches oxygen titration originated from

retrospective evidence in the acute and emergency room management of patients with both myocardial infarction and stroke. Recently completed randomized trials have further amplified the concern and strengthened the level of evidence in those settings.[54,55] Likewise, in the more general setting of patients receiving mechanical ventilation (ARDS and otherwise), multiple studies and trials have strengthened the case for targeting lower levels of FiO_2 and maintaining SpO_2 less than 95% to 96%.[56,57]

Adjunctive Strategies to Improve Lung Function

In many patients with ARDS, in particular those with severe hypoxemia (defined as P/F ratio <100 in Berlin Criteria or <120 to 150 in many clinical trials), clinicians often consider additional therapies beyond conventional mechanical ventilation using LPV. In this section, we review a spectrum of therapies that are available and can be added to the care of patients with ARDS as supplemental management while continuing a conventional LPV ventilation approach is presented.

Prone Positioning

The distribution of lung injury in patients with ARDS is heterogenous, and changing the position of the patient can result in improved $\dot{V}/\dot{Q}$ matching within the lungs. Alveolar consolidation in ARDS tends to be most pronounced in the dependent lung zones (posterior regions when patient is lying supine), where blood flow is greatest. For many years, experiments have been conducted with positioning the patient so that aerated lung fields (nondependent lung zones) become dependent by positioning the patient in the prone position (i.e., placing chest and face down, Fig. 29.10). So-called *proning* the patient recalls the old adage to "put the good lung down."[58] The mechanisms by which **prone positioning** improves oxygenation are not fully known. Some proposed mechanisms include improved matching of ventilation with perfusion, increased functional residual capacity, increased cardiac output, more effective drainage of upper and lower airway secretions, and improved diaphragmatic excursion. Ventilation in the supine position causes compressive forces on the dorsal airspaces, resulting in "derecruitment" of lung units, and the phenomenon is reversed by ventilation in the prone position.

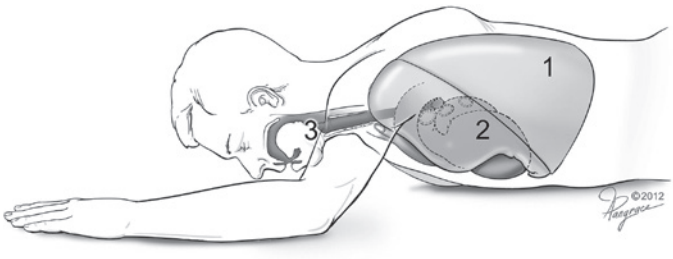

Fig. 29.10 Illustration outlining the three theoretical benefits of prone positioning: *1,* the posterior lung has a larger surface area for gas exchange which reduces V/Q mismatch; *2,* shifting the heart anterior offloads its weight from the surrounding lung tissue; and *3,* the large airways move to a gravitationally dependent position that better facilitates drainage of posterior and lower-lobe secretions. (From James MM, Beilman GJ: Mechanical ventilation, *Surg Clin North America* 92:1463–1474, 2012.)

Recent studies have demonstrated the advantages of prone ventilation (as compared with continued supine ventilation) beyond just improved oxygenation. The most successful and widely recognized of those trials, PROSEVA, was a multicenter European trial that used early introduction (<36 hours after intubation) of proning in patients with persistent, severe ARDS (P/F ratio < 150 for >12 hours).[59] Patients received a minimum of ventilation in the prone position for a minimum of 16 hours each day until oxygenation improved enough to discontinue. Most importantly, the outcome benefits to patients in the PROSEVA trial include improved survival. As a result, at many tertiary referral centers in the United States, prone positioning is currently considered to be the standard of care for patients with sustained severe ARDS after optimization of conventional strategies for mechanical ventilation with LPV and titration of PEEP.

Delivery of prone positioning to patients with ARDS requires experienced and committed bedside staff (nursing and RT) to facilitate turning and prevention of complications (e.g., inadvertent removal of indwelling catheters, skin breakdown), especially for obese patients. Some patients may not tolerate prone ventilation or may have a relative contraindication to proning, such as open surgical wounds or late-trimester pregnancy. However, as more centers gain experience and comfort with the logistics of rotating patients, acceptance and use of prone position has increased and become a first-line adjunctive therapy to assist in oxygenating the patient with severe ARDS.

Neuromuscular Blockade

Neuromuscular blocking paralytic agents have been used for decades to enhance compliance and synchrony with mechanical ventilation in patients with ARDS. With severe dyspnea and/or patient–ventilator dyssynchrony, a substantial portion of arterial O_2 content can be consumed by the increased work of the accessory respiratory muscles. Therefore, in patients who continue to remain hypoxemic despite optimizing ventilator settings and adequate sedation, a trial of NMB by bolus or continuous IV infusion is frequently performed.

Although the earliest studies of NMB consistently demonstrated improvements in oxygenation, they did not address whether NMB was associated with any survival advantage. A multicenter randomized trial, referred to as ACURASYS, considered 90-day in-hospital mortality as the outcome measure after treatment with a bolus followed by a 48-hour infusion of the paralytic drug cisatracurium.[60] The group receiving NMBs showed improved survival at 90 days after study onset, more days off the ventilator, and a lower incidence of barotrauma. Similar to prone positioning, the benefit of NMB was most evident in patients with severe ARDS (P/F ratio <120). In contrast to prone positioning, acceptance of NMB in severe ARDS among experts due to limitations in the ACURASYS trial. In particular, concerns for prolonged muscle weakness after use of NMB remain high particularly in the high percentage of critically ill patients who also receive corticosteroids for various indications during their ICU admission. Although no such effect was seen in ACURASYS, perhaps related to the short duration of paralysis, the study design did not include rigorous monitoring for

this important complication. As a follow-up to ACURASYS, a large multicenter trial of NMB is currently being completed by the PETAL Network (www.petalnet.org). It must be noted, that due to easier administration of NMB, as compared with prone positioning, many hospitals continue high use of NMB in severe ARDS. Use of NMB in patients with only mild to moderate ARDS who are stable on conventional ventilation should be avoided.

Inhaled Vasodilators

In ARDS, the potential benefits of pulmonary vasodilators delivered via the airway (as compared with intravenously) is based on delivery of the vasodilator will be distributed to well-ventilated portions of the lung, where the vasodilator leads to local vasodilation. In this way, well-ventilated areas of the lung receive a greater portion of the total pulmonary blood flow, which results in improved oxygenation by reducing shunt fraction and $\dot{V}/\dot{Q}$ mismatch (Fig. 29.11). For more comprehensive details regarding the administration of inhaled vasodilators, see Chapters 28, 36, and 42.

Nitric oxide (NO) and prostacyclin are naturally occurring potent vasodilators that play a critical role regulating blood flow within the normal lungs. NO is a highly soluble gas that diffuses readily through various tissues. Prostacylin is a naturally occurring prostaglandin, and several analogues have been pharmacologically developed (e.g., epoprostenol [Flolan]) and are standard of care in pulmonary arterial hypertension (see Chapter 28). Although not gaseous, epoprostenol and other prostacyclin analogues can be nebulized and provide effects similar to inhaled NO. The cost of NO and its patented delivery system (INOmax, Ikaria, Perryville, IL) is high, causing many institutions to limit its use. Nebulized epoprostenol serves as a less expensive alternative to NO at many centers.[61]

Despite initial enthusiasm for the potential benefits of inhaled NO in ARDS, an early large multicenter randomized trial demonstrated only short-term benefit in oxygenation but no change in survival or duration of ventilator support.[62] Subsequent systematic reviews and meta-analyses have also been completed and resulted in similar findings.[63] No large clinical trials of nebulized prostacyclin analogues have been completed in ARDS but are not expected to provide different results. The discrepancy in the effects of inhaled vasodilators—improvements on oxygenation without effect on longer-term patient outcomes—further emphasize that changes in oxygenation do not correspond closely to patient-centered outcomes in ARDS. We recommend that use of inhaled vasodilators be limited to patients with the most severe forms of ARDS (P/F < 80) and used only as a bridge to maintain oxygen while initiating more invasive adjunctive therapies (e.g., extracorporeal support).

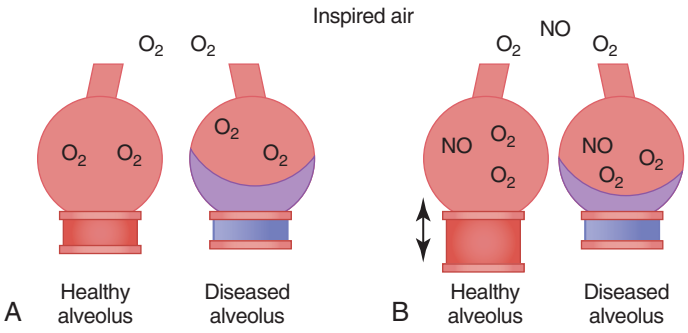

Fig. 29.11 The damage of acute lung injury and acute respiratory distress syndrome is heterogeneous. (A) Despite autoregulatory changes that favor vasodilation of well-oxygenated alveoli, perfusion goes to both the healthy, unaffected alveoli and the diseased alveoli that are unable to oxygenate blood. This results in $\dot{V}/\dot{Q}$ mismatch or a shunt-like state, resulting in deoxygenated blood returning from the lung and hypoxemia. (B) The addition of inhaled nitric oxide *(NO)* to the inspired gas results in vasodilating the capillaries adjacent to healthy alveoli, thereby promoting increased blood flow to the "good" alveoli and diminishing the percentage of blood going to diseased alveoli. This change results in improved $\dot{V}/\dot{Q}$ match and improved oxygenation.

Corticosteroids

As detailed earlier, a hallmark of ARDS is an intense, systemic inflammatory cascade that leads to a spectrum of injuries to the alveolus during the early acute phase in all cases and in the subacute fibroproliferative phase in the smaller subset of cases that require prolonged ventilatory support. The potential benefits of steroids in ARDS to reduce the burden of the inflammatory insult has long been debated, including mention in the original case series of adult patients with ARDS over 50 years ago.[1]

Use of steroids in the earliest stages of ARDS has been evaluated, but their impact on patient survival or duration of ventilation remains unclear and controversial. The earliest studies in ARDS often used high-dose steroids (>2 mg/kg/day), which were associated with increased risks for secondary nosocomial infections and should be avoided. In 2016 a combined analysis of eight small randomized trials that administered more commonly used doses of corticosteroids (methylpredisonolone or hydrocortisone) for a prolonged duration was published.[64] These compiled results suggest that ARDS resolution, liberation from mechanical ventilation, and mortality may be improved but are not sufficient to recommend use of steroids as a standard for care in early ARDS or a specific strategy for dosing. A separate randomized trial of hydrocortisone published in the same year demonstrated only improved oxygenation but survival was unchanged.[65] These studies with lower-dose steroid regimen have been associated with greater frequency of common steroid side effects (e.g., hyperglycemia) but not with increased risk of infections. Risks for prolonged weakness after critical illness have been associated with steroids and remain an unresolved question for their safety in ARDS.

Although most patients who survive ARDS have minimal residual pulmonary impairment, a small but significant number of patients require prolonged mechanical ventilatory support because of abundant fibroproliferation in the lung during recovery from ARDS. The high mortality rate among these patients seems to relate to the extent and severity of pulmonary fibrosis.[66] High-dose corticosteroids have been used to manage uncomplicated pulmonary fibrosis following ARDS, but results are mixed and controversial. In the largest multicenter trial, corticosteroids were used for patients with late fibroproliferative ARDS (>7 days' duration) and did not demonstrate a survival benefit.[67] Importantly, patients given steroids after 14 days from ARDS onset experienced a higher mortality rate than control patients, and

this has led most clinicians to conclude that steroids should be avoided after 14 days from ARDS onset.

Use of steroids in patients with ARDS for purposes other than their ARDS is common. As noted previously, the most common etiology for sepsis is sepsis, and use of steroids in septic shock has become increasingly common, despite conflicting data regarding their benefits and risks.[68] The impact on ARDS of a short course of steroids for septic shock is unknown. In addition, many patients who meet the syndrome definition of ARDS can have other pulmonary disease processes that mimic ARDS (e.g., alveolar hemorrhage, interstitial lung disease, organizing pneumonia), and many of these conditions respond to steroid therapy. In patients in whom one of these alternative diagnoses is a consideration, clinicians often will typically either perform an open lung biopsy or begin an empiric course of (high-dose) steroid therapy.

Beta-2 Agonists

In addition to their effects as bronchodilators, high doses of beta-2 agonists (e.g., albuterol, salbutamol) have been shown to accelerate clearance of alveolar edema by the epithelium of the alveolar wall in animal models.[69] However, neither of two clinical trials in humans using either aerosolized albuterol or IV salbutamol for ARDS were able to improve patient-centered outcomes.[70,71] In one of the trials, the beta-2 agonists did reduce lung water using a surrogate measurement and improved lung function (lower plateau pressures), but no change in oxygenation (i.e., P/F ratio) was observed. In the largest trial, completed by the ARDS Network, the trial was terminated early because of concern for increased mortality in the patients receiving beta-2 agonists, although the difference did not achieve statistical significance. At this time, beta-2 agonist therapy for improving alveolar fluid clearance in ARDS is not recommended.

Exogenous Surfactant Administration

Surfactant dysfunction and deficiency is a well-established component of RDS in premature infants, as well as in children and adults with ARDS. Surfactant abnormalities contribute to the development of ARDS by promoting instability of the alveolar units (airway shear trauma, atelectasis, and right-to-left shunt) and by allowing inflammatory injury to alveoli to continue unchecked. Delivery of exogenous surfactants via direct intratracheal administration has become a cornerstone of therapy in RDS since the early 1990s.[72] Multiple surfactant preparations are commercially available, including natural surfactants (harvested from lungs of animals used in the meat industry) and synthetic surfactants, which are created artificially.[73]

Unfortunately, the pathogenesis of surfactant deficiency in the ARDS of children and adults differs markedly from premature newborns. The depletion of surfactant in RDS of prematurity is secondary to the lack of lung maturation and surfactant production. In contrast, the surfactant depletion of ARDS is caused by inflammation of the alveolus and subsequent degradation of the endogenous surfactant. Numerous clinical trials have demonstrated improvement in oxygenation with intratracheal surfactant administration, including both natural and synthetic preparations.[74,75] However, the improvements in gas exchange have typically proven to be short lived (24 to 72 hours) and have not demonstrated significant impact on clinical outcomes such as mortality or duration of mechanical ventilation in survivors. These negative results in ARDS (in contrast to clear benefit in neonatal RDS) are most likely explained by degradation of the exogenously administered surfactant via the same inflammatory mechanisms that depleted the patient's native surfactant. Future studies of surfactant therapy are likely to include a combined approach that includes more prolonged courses of treatment and inhibitors of inflammation-mediated degradation.

Alternative and Rescue Ventilation Strategies

In the large majority of ARDS patients, the conventional LPV approach previously described proves to be sufficient and should be routinely used at the onset of ARDS in all patients. In patients with either severe ARDS alone or with ARDS in the setting of other chronic lung conditions, the severity of gas exchange abnormalities may progress and lead to an inability to maintain adequate oxygenation and/or ventilation to sustain the patient. In those uncommon scenarios, alternative ventilatory strategies are available and may prove beneficial in selected patients but are less well-studied or standardized. As such, these therapies are often referred to as "rescue" or "salvage" therapies. The thresholds for using alternative approaches differs across medical institutions but are typically defined by persistent markers of unsafe ventilation, such as excessive plateau pressures (e.g., >35 cm H_2O), FiO_2 (e.g., >80%), PEEP (e.g., 20 cm H_2O), or hemodynamic instability caused by positive pressure ventilation. Because the level of evidence regarding these approaches is lower, variation in practice is high and choices often depend on the local experience, expertise, and the availability of the necessary equipment.

Inverse-Ratio Ventilation

In conventional modes of mechanical ventilation, the respiratory cycle is typically characterized by I:E ratios of 1:≥2 with greater time spent during expiration than inspiration. During inverse ratio ventilation (IRV), the inspiratory time on the ventilator is prolonged so that the I:E ratio is reversed (i.e., inspiratory time now exceeds expiratory time). The mechanisms for benefit of IRV likely include some combination of increased percent of time during each respiratory cycle that alveoli remain patent to reduce V/Q mismatch and increasing mean airway pressure to recruit alveolar units. Increased mean airway pressure results from incomplete lung emptying, otherwise known as air trapping, auto-PEEP, or intrinsic PEEP. Although IRV can improve oxygenation, there are no clear advantages when compared with use of higher levels of extrinsic PEEP[76], and it can lead to increased patient discomfort and patient-ventilator dyssynchrony.

Airway Pressure Release Ventilation

Airway pressure release ventilation (APRV) is a form of pressure control intermittent mandatory ventilation with IRV (I:E ratio of ≥4:1).[77] The aim of APRV is to increase the mean airway pressure for alveolar recruitment while allowing the patient to spontaneously breathe. This mode generally features two levels of PEEP: a high PEEP (approximately 25 to 30 cm H_2O for 5 to 6 seconds) and a low PEEP (approximately 0 to 5 cm H_2O for

0.5 to 1 second). Oxygenation can often improve when APRV is used, but there are risks for large tidal volumes, leading to VILI and high transpulmonary pressures.[78,79] As a rescue therapy, use of APRV is equally unproven, but was shown, in an uncontrolled manner, to improve a small case series of patients during the H1N1 influenza pandemic.[80] Taken together, although APRV remains an alternative strategy to consider, there are no specific cases or conditions in ARDS in which its use can be formally recommended.

High-Frequency Ventilation

HFV is different from any of the conventional modes of ventilation because it uses a rapidly moving piston to create movement of air through a circuit. The device allows setting a mean airway pressure over which oscillations happen. Tidal volumes generated by HFV are typically smaller than the patient's anatomic dead space and use higher mean airway pressures to maintain alveolar patency and theoretically prevent VILI and minimize hemodynamic compromise caused by larger inspiratory pressures of conventional modes.

High-frequency ventilation (HFV) was initially devised as a method to minimize the hemodynamic effects of conventional mechanical ventilation (i.e., the large inflating pressures and volumes). Delivery of HFV requires unique expensive equipment that can differ in ability to treat children and adults and requires experienced and specifically trained personnel (MD and RT) to deliver effectively. The RT must remember that patients on HFV will be exposed to high mean airway pressures and PEEP, which may reduce cardiac output and overall O_2 delivery despite elevated arterial oxygenation.

HFV has been successfully used in ventilating neonates with RDS including both as a routine and rescue therapy, but its use is controversial due to widely differing results.[81,82] In adults with ARDS, multiple randomized trials have assessed the potential benefit of HFV versus conventional ventilation in severe ARDS. Trials conducted prior to the proven benefit and routine implementation of LPV demonstrated feasibility of supporting gas exchange and hemodynamic tolerance.[83] During and shortly after the H1N1 influenza pandemic in 2009, interest in HFV as a therapy for severe ARDS renewed, leading to two large randomized trials. The OSCAR trial showed no difference between HFV and conventional mechanical ventilation, and the OSCILLATE trial was discontinued early due to increased mortality rate in the patients treated with HFV.[84,85] Based on these results, use of HFV in routine ARDS management is not recommended. Although HFV as a rescue strategy for patients with severe refractory ARDS (P/F < 80) remains an option at some highly experienced centers, there are no multicenter trials or large single-center results to support its benefit.[86]

Extracorporeal Support

Extracorporeal membrane oxygenation (ECMO) and **extracorporeal carbon dioxide removal** ($ECCO_2R$) involve establishing a circuit for diverting a large portion of the cardiac output through an artificial gas-exchange device, or "artificial lung," to facilitate the exchange of O_2 and CO_2. More complete details on the principles and application of extracorporeal support are provided in Chapter 51. For respiratory failure, extracorporeal support is typically performed using venovenous circuits (versus venoarterial), which are able to support gas exchange without need for invasive arterial cannulas and hemodynamic support and can currently be offered through a single venous cannula.

ECMO was first introduced with a flurry of interest as a potential rescue therapy for patients with severe refractory hypoxemic respiratory failure in the 1970s. Initial trials were unsuccessful, with high rates of complications that were attributed to limitations with equipment and clinical experience. With continued improvements in equipment and delivery methods and anecdotal cases with favorable results at a large number of centers, interest and enthusiasm for the potential benefits of ECMO in severe ARDS have persisted. During the 2009 H1N1 influenza pandemic in patients with ARDS deemed refractory to conventional ventilation, ECMO was often used as rescue therapy at many highly experienced centers.[87,88]

Two randomized trials of ECMO have been completed to date. In the CESAR trial, a complex method for randomization and referral to a single ECMO center in Great Britain was used and compared groups with or without the option to be placed on ECMO with conventional ARDS ventilator approaches targeted in all patients.[89] Results demonstrated reduction of a combined outcome including death and severe disability in the ECMO option group, but interpretation of the CESAR results remains controversial due to concern regarding lower adherence to conventional LPV approach in the control group managed without an ECMO option, often at hospitals outside the ECMO center. More recently, results of the multinational EOLIA trial revealed no significant difference in mortality at 60 days in the group randomized to early ECMO. However, interpretation of the study results is also complicated by a low study population sample size (lower mortality in the ECMO arm with *P* value = .09, but only 250 patients in both groups combined) and high rate of cross over to ECMO (~25% to 30%) in the control group.[90] Unfortunately, this debate may never be fully resolved because rigorous, large randomized trials for patients with severe disease are frequently not supported by many clinicians and families in the setting of extremely high potential for mortality.

MINI CLINI

In managing patients with severe, persistent acute respiratory distress syndrome (ARDS), oxygenation (PaO_2 or SpO_2) is a readily available measure that often attracts the attention of bedside providers. In attempts to improve levels of oxygenation, providers often start additional therapies such as pulmonary vasodilators (e.g., inhaled nitric oxide [NO]) or alternative approaches to mechanical ventilation (airway pressure release ventilation [APRV], high-frequency ventilation [HFV], etc.) that can often lead to improvements in oxygenation. However, improvements in hypoxemia from these therapies have not been linked with improvements in survival. Changes or additions in therapy that improve oxygenation only slightly beyond minimum thresholds (SpO_2 >88% to 92%) are unlikely to improve the patient's outcome. Furthermore, adding inhaled vasodilators or starting more complex and unfamiliar ventilation modes leads to increased cost and risks to delivery of care based on best available evidence. These maneuvers should be reserved for patients whose oxygenation status is insufficient to meet the needs of their total body oxygen demands and leads to nonrespiratory organ dysfunction, specifically neurologic or cardiac.

Not all patients are good candidates for extracorporeal support, especially those with multisystem organ failure or advanced chronic or comorbid health conditions (e.g., metastatic cancer, severe COPD). In considering ECMO for patients with refractory severe ARDS (P/F < 80), assessment and referral to ECMO center (if needed) should be made early after optimization of conventional approaches (with or without adjunctive therapies discussed previously) and time sufficient time is allowed to confirm lack of improvement or worsening.[91] Due to the lack of rigorous randomized trials, ECMO remains an unproven option to change outcomes in severe ARDS but is the most commonly available and used option for this small subset of patients.

Nonventilatory Supportive Care

Supportive care in the ICU, including patients with ARDS, focuses on maintaining function of key organs and minimizing the complications associated with critical illnesses and spending several days in an ICU. These points of management do not directly treat the primary risk factor that triggered ARDS but are nonetheless critically important to optimize patient outcomes, both during and after their time in the ICU. Many ICUs use checklists to ensure basic supportive care measures in critically ill patients are being done consistently, all of which can apply to and improve outcomes in patients with ARDS (Table 29.1). This section will briefly review a few key aspects of supportive care related to both the lungs and other key organs. Although RTs are not always the primary provider responsible for the delivery of these priorities, the RT should be familiar with their importance and serve to encourage and support their consistent application.

Conservative fluid management. Critically ill patients receive fluids both IV and oral for a wide variety of indications: to maintain perfusion, IV medications, nutrition, hydration, and correct electrolyte imbalance. The amount of fluids taken in by critically ill patients invariably exceeds the amount of fluids that the patient loses, and patients often gain approximately 1 L of fluid per day. Recent work suggests this positive fluid balance may be associated with increased mortality in the ICU.[92] Specific to ARDS, the ARDSNet Fluids and Catheters Treatment Trial (FACTT) compared a protocol-driven ***conservative fluid management*** strategy to a so-called *liberal strategy* that closely resembled typical fluid intake seen in prior ARDSNet studies.[93] The conservative strategy was achieved essentially by eliminating maintenance IV fluids and earlier institution of and increased attention toward diuresis. Although mortality did not differ between the groups, the group managed with the conservative fluid strategy had improved oxygenation, shorter duration of mechanical ventilation, shorter ICU length of stay, and no increased frequency of other organ failures, including renal failure. In practice and in subsequent clinical trials, a simplified version of the FACTT conservative protocol has been validated and should be initiated 12 hours after the end of shock (i.e., not needing fluid boluses or vasopressors).[94]

TABLE 29.1 Nonventilatory Supportive Care Checklist

Respiratory	Fluid conservative management
	Daily spontaneous breathing trial
Neurologic/Musculoskeletal	Minimize sedation and daily awakening
	Delirium prevention and treatment
	Early mobilization
Gastrointestinal	Gastric ulcer prophylaxis
	Enteral nutrition
	Avoid excess caloric intake
Infection Prevention	Remove indwelling catheters
	Antibiotic deescalation
	Oral chlorhexidine
	Head-of-bed elevation
	Hand hygiene

Sedation and Analgesia

Over the past two decades, approaches to managing sedation and analgesia in critically ill patients have changed dramatically. Protocolized sedation and scheduled daily interruptions of sedation (awakenings) lead to shorter times on mechanical ventilation and decreased length of ICU stay.[95] Furthermore, evidence from survivors of ARDS has demonstrated that many experience persistent problems with memory and cognition and that these changes relate to the types of sedation that patients receive during their care in the ICU. In particular, using benzodiazepines (e.g., lorazepam or midazolam) carries the greatest risk for these adverse neurocognitive effects. One of the earliest neurocognitive warning signs in the ICU is the development of ICU-associated *delirium*, which can be caused by several common environmental challenges in the ICU, including lack of sleep, noise, use of restraints, and immobility. The use of benzodiazepines also has been strongly linked to the development and progression of delirium in the ICU.

MINI CLINI

Managing Hydrostatic Pressure in Patients With Acute Respiratory Distress Syndrome

Problem

A patient presented to the intensive care unit (ICU) several days ago in septic shock, and although his shock and needs for pressors have improved, he remains hypoxic and having difficulty with weaning from mechanical ventilation. Severe bilateral infiltrates persist on the daily chest x-rays, and the patient is noted to have marked peripheral edema in his legs and dependent tissues (i.e., back/sacrum), despite having resolved a mild acute kidney injury that was present when he was admitted from the emergency room.

Discussion

Patients admitted with septic shock and other critical illnesses that cause hemodynamic compromise often receive large amounts of fluids during their initial resuscitation and then continue to receive large amounts of intake (intravenous and enteral) to maintain the many aspects of their care needs while in the ICU. The use of a protocol to guide conservative fluid management leads to faster liberation from mechanical ventilation in patients with ARDS. Once patients are no longer in shock (>12 h), the protocol should be started. All care providers, including RTs, should be aware of this important intervention and encourage its application in patients to accelerate the process of liberation from mechanical ventilation and avoid unnecessary complications associated with prolonged mechanical ventilation, sedation, and immobility.

Given these concerns related to the acute and long-term adverse effects of ICU sedation, current strategies for sedation aim to minimize the exposure to all sedatives, in particular benzodiazepines.[96] Initial efforts should focus on nonpharmacologic interventions, including adjustment of ventilator to minimize dyssynchrony (when appropriate), providing necessary vision and hearing aids, and use of distracting therapy such as music or noise-canceling headphones.[97] If patients need pharmacologic agents, a validated assessment should be performed and, if positive, patient treated with analgesia. Lastly, sedative agents can be used including propofol or dexmedetomidine. Antipsychotic drugs may be given for agitation, although their role in delirium prevention remains unproven.

Emphasis on reducing sedation for patients on mechanical ventilation poses a challenge for the RT, who, along with the nursing staff, must manage more awake, restless, and agitated patients who may attempt breathing out of synchrony with LPV goals. We cannot assume that heavy sedation to optimize ventilator synchrony is the best and safest approach. The best approach must balance the short-term ventilator risks with the longer-term risks of excessive sedation with daily reassessments of care goals among all care providers.

Nutrition

Malnutrition in the ICU leads to poor outcomes, but clinicians including RTs should be aware that excess nutritional supplementation can also lead to adverse consequences. The ARDSNet EDEN trial studied whether using trophic feeds (the minimum amount of enteral nutrition to maintain protection of the mucosal lining of the gastrointestinal [GI] tract and GI motility) was equally effective to full enteral nutrition during the first 6 days of care of patients with ARDS.[98] The results of the study showed no benefit for the full nutritional approach either during the ICU stay or 1 year later.[99] Currently, there is no specific recommendation regarding nutrition in patients with ARDS, but RTs should remain aware of the potential negative impact of overfeeding, which can lead to increased CO_2 production, increased minute ventilation, and potentially delayed liberation from mechanical ventilation.

Mobility

It has long been recognized that the prolonged period patients spend lying in bed on mechanical ventilation has an adverse effect on the mass and function of muscles for patients in the ICU, including those with ARDS. Profound and persistent weakness (≥12 months) is a commonly reported long-term outcome in ARDS survivors. This severe adverse consequence of ICU care is in part attributable to inflammatory injury to the muscles and peripheral nerves, pharmacologic agents (e.g., steroids and neuromuscular blockers), and most importantly immobilization, which is most severe in patients requiring mechanical ventilation, particularly when prolonged. Numerous clinical trials have established the safety of early mobilization in patients on mechanical ventilation with endotracheal tubes including ARDS patients with severe hypoxemia.[100,101] The precise intensity and duration of mobility needed to achieve positive outcomes remains to be determined.[102] Despite these assurances, early mobilization remains a struggle in many units due to fear of adverse events, difficulty coordinating with ongoing care, and perceptions of insufficient workforce. However, with interdisciplinary cooperation, education, and sustained leadership, mobilization protocols have been implemented across a variety of ICU settings and hospital sizes.[103]

ROLE OF THE RESPIRATORY THERAPIST IN ACUTE RESPIRATORY DISTRESS SYNDROME

The RT is an essential expert in mechanical ventilation and respiratory support for the ICU team. Patients with ARDS represent some of the most challenging patients to manage on mechanical ventilation and require the greatest experience and expertise. Current therapies that have been proven (or with demonstrated potential) to improve survival in ARDS (Box 29.5) should be built-in available bedside protocols and consistently prioritized. Using the original data from the clinical trials reviewed herein, the number of patients that need to be treated for one life to be saved (i.e., number needed to treat [NNT]) can be estimated, and the impact for each of these approaches is greater than many standard therapies in other more common acute and chronic conditions (e.g., cancer, heart attack, and stroke).

The pivotal roles that RTs play in caring for patients with ARDS include ventilator setup, recommending changes and adjustments in the provision of ventilator support, monitoring and frequent equipment checks, drawing ABGs, placing arterial lines or performing hemodynamic assessments, and monitoring pulse oximetry and/or exhaled CO_2 monitors.

In multiple randomized trials, RT-driven ventilator management protocols have outperformed usual care protocols in management of ARDS, including using the most advanced techniques (e.g., ECMO) and achieving liberation from the ventilator.[95,106] The input and assistance provided by RTs in ventilator management including ventilatory strategies, adherence to LPV, oxygen titration, and technical attention to equipment is invaluable.

More specific to the management of patients with ARDS, the RT must learn and consistently apply the following key general aspects of supportive care:

1. ARDS is a diffuse injury of the lungs but is not homogenous. Despite the presence of widespread pulmonary injury on radiographs and altered gas exchange in ARDS, there are areas of the lung with near-normal mechanical characteristics.
2. Better oxygenation (in terms of PaO_2 or SpO_2) is not always linked to better survival and should not take priority over

BOX 29.5 Therapies With Proven or Potential Survival Benefit in Acute Respiratory Distress Syndrome

1. Proven
   a. Lung-protective ventilation[104]
   b. Sedation interruption[95]
   c. Prone ventilation[59]
2. Potential
   a. Extracorporeal support (ECMO)[105]
   b. Neuromuscular blockade[60]

ECMO, Extracorporeal membrane oxygenation.

optimal conventional LPV strategies in the vast majority of cases.

3. Mechanical ventilation can lead to VILI, which, when not corrected, worsens ARDS and increases mortality secondary to MODS. The RT must always remember that current evidence indicates that either excessively high tidal volumes or driving pressures may lead to VILI.
4. Initiation and maintenance of LPV, including V_T = 6 mL/kg of predicted (not actual) body weight and sufficient PEEP to exceed the LIP, should become the priority and focus of daily care. The RT should take an active role in making sure that an accurate estimate of the patient's height has been obtained so an accurate PBW can be calculated.
5. Modes of mechanical ventilation that optimize V_T and driving pressure should be preferred. Many modes are capable of maintaining V_T, and no single mode has been proven to be superior, but RTs must be familiar with how to manage each mode so that these priorities are maintained. Unnecessary transitions between multiple modes of mechanical ventilation in patients with ARDS are typically not helpful and further complicate interpretation of the patient's response to therapy.
6. Inspiratory time can be prolonged in ARDS patients to target I:E ratios as low as 1 : 1.
7. Hypercapnia can and should be tolerated (permissive hypercapnia) as long as pH remains greater than 7.15 to 7.20.
8. Adjunctive therapies, in particular prone positioning and short-term NMB, may benefit respiratory function and be warranted in patients with severe ARDS.
9. Other nonrespiratory measures of supportive care, in particular conservative fluid management and avoidance of excess sedation, improve the outcomes of patients with ARDS. RTs should be familiar with these and encourage their consistent application in all ARDS patients.
10. Pharmacologic therapies (e.g., inhaled NO, surfactant) are available and can enhance oxygenation in patients with ARDS but are expensive and do not change patient outcomes. Their routine use in ARDS is not recommended and should be limited or discouraged.
11. A small percentage of patients with ARDS will develop refractory, severe hypoxemia in which the conventional approaches fail. Alternative or "rescue" therapies are as yet unproved but are available at large referral centers. Transfer of patients with refractory hypoxemia should be considered early in the course of disease within the initial 24 to 48 hours.

SUMMARY CHECKLIST

- Pulmonary edema from both hydrostatic (e.g., CHF) and nonhydrostatic (e.g., ARDS) causes leads to acute respiratory failure and can be difficult to differentiate on initial evaluation. Pulmonary edema leads to bilateral alveolar infiltrates on the chest radiograph, restriction in lung volumes, and significant decline in gas exchange, particularly oxygenation.
- The physical examination and chest x-ray do not distinguish CHF from ARDS, whereas the clinical history and noninvasive assessment of cardiac function (e.g., echocardiography) often provide key insights. Alternative diagnostic techniques such as bronchoscopy or pulmonary artery catheterization can be helpful but are typically not required or used.
- The pathologic findings of ARDS are characterized early by acute alveolar inflammation and injury with neutrophils and cytokines, which can rapidly reverse. In severe and/or persistent ARDS, a fibrotic phase can develop and can lead to a more prolonged course of recovery.
- The clinical definition and diagnosis of ARDS is based on the presence of a syndrome of characteristics that include abnormalities on the chest x-ray, hypoxemia, and a known risk factor or trigger that generates acute inflammation. There are well-established consensus definitions for ARDS that should be used by all caregivers.
- ARDS is a common critical illness with high associated mortality and morbidity, but close attention to care protocols for patients with ARDS, in particular lung-protective lung ventilation, has improved survival and reduced recovery time for survivors.
- Early management of ARDS focuses on identifying and treating the triggering risk factor and comprehensive supportive care of vital organs, particularly ventilation.
- Ventilatory strategies for patients with ARDS are designed to minimize VILI by emphasizing low tidal volumes and driving pressures and sufficient levels of PEEP.
- The size of tidal volume selected should be based on a patient's predicted (not actual) body weight, which requires an accurate measurement of the patient's height to determine.
- Multiple modes of mechanical ventilation can be used to achieve LPV, but providers must prioritize avoiding VILI and be willing to tolerate reduced gas exchange, including lower oxygenation and higher $PaCO_2$.
- Adjunctive strategies beyond mechanical ventilation, such as prone positioning and NMB, may be beneficial in patients with severe ARDS.
- A small subset of patients with very severe ARDS fail conventional LPV ventilation strategies, and multiple alternative management strategies often called "rescue" therapies can be considered but lack proof of efficacy. Using rescue strategies should be considered early (first few days), because their potential benefits likely decline over time.
- Of all rescue therapies, ECMO is the most promising and widely available option.
- Several nonventilatory supportive care measures (e.g., conservative fluid management and minimizing sedation) have been shown to improve outcomes in ARDS, and consistent adherence to those measures should be encouraged and supported by RTs.

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30

Respiratory Management of Trauma, Obesity, Near Drowning, and Burns

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CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Discuss the clinical presentation and the differences in approach to the assessment of patients with life-threatening trauma, pulmonary and body surface burns, obesity, and near drowning.
- Discuss the specific pathophysiology that would guide the application of respiratory care to the management of patients with life-threatening trauma, pulmonary and body surface burns, obesity, and near drowning.
- List the factors affecting gas exchange in each of these patient types.
- Discuss indications for O_2 therapy, noninvasive ventilation, and invasive mechanical ventilation.
- Describe concerns associated with the application of mechanical ventilation to patients with life-threatening trauma, pulmonary and body surface burns, obesity, and near drowning.
- Discuss the application of lung protective ventilation to patients with life-threatening trauma, pulmonary and body surface burns, obesity, and near drowning.
- Discuss the use of positive end expiratory pressure, lung recruitment maneuvers, and prone positioning in patients with life-threatening trauma, pulmonary and body surface burns, obesity, and near drowning.
- Discuss the process of ventilator discontinuation in patients with life-threatening trauma, pulmonary and body surface burns, obesity, and near drowning.

CHAPTER OUTLINE

KEY TERMS

% total body surface area
blunt trauma
carbon monoxide poisoning
cold shock cardiac-respiratory reflexes
cyanide toxicity
cyanocobalamin
cytochrome oxidase
decremental PEEP trial
dry drowning
escharotomy
exudates
fluvial or brackish water
Glasgow Coma Scale
glomerular filtration rate
hydrophilic drugs
lipophilic drugs
morbid obesity
myocardial contusion
obesity hypoventilation syndrome
obstructive sleep apnea
penetrating trauma
pulmonary contusion
recruitment maneuvers
severe obesity
super obesity
tension pneumothorax
thiosulfate
thoracic flap (flail chest)
transudates
wet drowning

LIFE-THREATENING TRAUMA

Epidemiology

Trauma is the third overall cause of death in the United States and the primary cause of death for Americans between 1 and 44 years of age.[1] Each year, trauma accounts for 26.9 million admissions to emergency departments (EDs) and 2.5 million hospital admissions. In 2016 alone, 161,374 Americans lost their lives to trauma. But what exactly is trauma? In the most basic sense, trauma is an injury to the body that threatens life and limb integrity. The injury is caused by a physical agent (a force, heat, radiations, etc.) acting on one or more regions of the human body. As a result, trauma patients can have vastly different presentations and clinical manifestations and can require different levels of care. Not every trauma that involves the thorax requires intensive care and respiratory support, just as some traumas that do not involve the chest might require intensive care and respiratory support (e.g., in the setting of transfusion-related acute lung injury or head trauma). In addition, patients who suffer from trauma and require invasive mechanical ventilation (for trauma that directly involves the thorax, because of the need for an artificial airway, or as a result of massive transfusion) are at higher risk for ventilator-associated pneumonia (VAP), thus complicating these patients' clinical courses. Among patients admitted to the intensive care unit (ICU) after trauma, it has been shown that the presence of traumatic brain injury (TBI) and a poor **Glasgow Coma Scale** score (GCS < 8; Table 30.1) on admission are the main determinants of patient outcome, measured as post-ICU disability and quality of life.[2] Neurologic damage appears to be pivotal in determining patient mortality and disability; therefore the respiratory therapist must pay special attention to maintaining adequate oxygenation without compromising perfusion and hemodynamics. Because of the heterogeneous presentation of trauma, there is no overarching rule of thumb regarding patient respiratory management, and the respiratory therapist plays a key role in identifying life-threatening problems and tailoring the support to respiratory function.

TABLE 30.1 Glasgow Coma Score

Response	Score
Best Eye Response (E)	
Spontaneously	4
To speech	3
To pain	2
No response	1
Best Verbal Response (V)	
Oriented to time, place, and person	5
Confused	4
Inappropriate words	3
Incomprehensible sounds	2
No response	1
Best Motor Response (M)	
Obeys commands	6
Moves to localized pain	5
Flexion withdrawal from pain	4
Abnormal flexion (decorticate)	3
Abnormal extension (decerebrate)	2
No response	1
Total Score	*15*
Change in Mental Status	
Close monitoring is required.	14–9
Comatose. Securing the airway is required.	≤8
Totally unresponsive	3

Clinical Assessment and Specific Pathophysiologic Concerns

During the first evaluation of a trauma patient, the respiratory therapist, together with the medical team, should focus on the airway and breathing. If blunt injury is present, cervical spine injury always should be suspected, and immobilization of the cervical spine must be instituted immediately.[3]

Assessment of a victim of major trauma should start with a GCS evaluation. If a patient is fully awake, responsive (GCS = 15), and able to maintain a patent airway, close respiratory and neurologic monitoring should be instituted until the medical team completes surveillance. If a patient's GCS range is between 14 and 9, the respiratory therapist should pay extra attention to the status of the patient because the clinical condition might quickly deteriorate, requiring endotracheal intubation and invasive ventilation. A GCS lower than 8 always requires securing the airway by endotracheal intubation and further diagnostic evaluation, unless a decision has been made by an authorized party to provide only comfort care (see Chapter 58).

RULE OF THUMB Trauma victims with TBI and a GCS scores of less than 8 require endotracheal intubation and generally have poorer postinjury quality of life and greater disability (see Chapter 58).

Head, Neck, and Upper Airway Injuries

The presence of external injuries to the head should raise the suspicion of TBI. These patients are at risk for rapid neurologic deterioration as a result of an array of alterations in mental status, ranging from confusion to seizures to coma. The respiratory function of these patients can be compromised by upper airway obstruction because of loss of muscular tone or, as with seizures, to excessive muscular tone that requires immediate sedation, paralysis, and endotracheal intubation. Endotracheal intubation might be challenging because of the mandatory immobilization of the cervical spine (Fig. 30.1). Management of the upper airways is complicated by anatomic alterations of the rhino-oropharynx caused by the traumatic injury. Severe maxillofacial injuries or destructive trauma of the upper airway prompts tracheal access for definitive airway management.[4] The presence of blood, gastric contents, oral secretions, and foreign material complicates artificial airway placement and management.

Lower Respiratory Injuries

Chest trauma is usually classified either as **penetrating trauma** (i.e., high force applied to a small surface area of the body, such as with a gunshot) or **blunt trauma** (i.e., high force applied over

Fig. 30.1 (A) In trauma, cervical stabilization is generally obtained by a rigid collar that encircles the neck and supports the chin and the back of the head. The goal of cervical collars is to restrict flexion and extension while supporting the chin and the occiput. When rigid cervical collars are applied, venous outflow at the neck should always be maintained to avoid increased intracranial pressure. (B) During intubation, it may be necessary to undo the anterior part of the cervical collar while an assistant maintains in-line stabilization with the occiput held firmly in neutral position (hands are placed along the side of the head with fingertips on the mastoid holding the occiput down). When possible, another assistant applies cricoid pressure. This orientation might limit visualization of the vocal cords for the operator; however, reduction of atlantooccipital motion should be the priority. Awake or asleep fiberoptic intubation or newer airway management instrumentation should be planned before intubation of a patient with an unstable cervical spine.

a larger body surface, such as the case of a head-on-end motor vehicle accident).[5] However, most chest injuries do not fall into one of these two categories but instead represent a mix of the two. Depending on the depth of the penetrating lesions, patients can present different clinical features. An injury that penetrates the chest wall, entering the pleural space without injuring the lung, causes a decoupling of the chest wall/lung relationship. During spontaneous breathing, the chest wall tends to expand while the lung tends to collapse. This results in a physiologically negative pleural pressure. When the pleural space is exposed to atmospheric pressure, as in the case of a penetrating trauma injury, the negative pleural pressure causes air to enter the pleural space. At this point, the chest wall expands and the lung collapses, resulting in a pneumothorax. If the penetrating injury enters both the pleural space and the lung, air can enter the pleural cavity from both the chest wall and the lung. Patients with this particular injury are at high risk for developing a **tension pneumothorax**. A tension pneumothorax develops when the pleural lesion acts as a one-way valve, allowing the entrance of air into the pleural space and progressively trapping air in the expanding pleural cavity. With every breath, the volume of air increases in the pleural cavity. As volume increases, pressure increases, resulting in a force directed toward the opposite pleural cavity. The high unilateral pressure causes a shift of mediastinal structures, resulting in distortion and eventual collapse of the main vascular structures, specifically the vena cava. This phenomenon leads to rapid hemodynamic deterioration that, if unrecognized, results in cardiovascular collapse and death. Penetrating traumas may also involve one or more bronchial structures.

Bronchial injuries cause large volumes of air to rapidly enter the pleural cavity as well as the mediastinum, depending on the location of the injury.[6] The presence of bronchial injury should be suspected when, after the placement of a chest tube for pleural drainage, large amounts of air continue to exit the chest tube in a synchronized pattern with positive pressure ventilation. Tracheal lesions can be life-threatening and require prompt surgical evaluation and appropriate airway management. The chosen artificial airway should be capable of bypassing the tracheal lesion to provide adequate pressurization and mechanical ventilation to both lungs. Mechanical ventilation through a tracheal disruption leads to pneumomediastinum, hemodynamic instability, and mediastinal infection. Disruption of a large airway is one of the indications for the use of independent lung ventilation (see Chapter 49).

Esophageal rupture may result in a communicating lesion with the respiratory tract or with the mediastinum. In the first case, the main clinical features are gas leakage during mechanical ventilation and aspiration of gastric material, which can result in chemical pneumonia or full-blown acute respiratory distress syndrome (ARDS). It is vital to recognize and treat these lesions as soon as possible.[7]

Blunt trauma is the other main mechanism that can cause physical injury to the human body. The main sign that a significant blunt trauma has affected the thoracic region is the presence of rib fractures.[8] Rib fractures can be unifocal (one point of fracture per rib) or multifocal (two or more points of fracture in a single rib). This difference is fundamental in understanding the effects of rib fractures on respiratory function. Unifocal fractures can be either nondisplaced or displaced. Nondisplaced rib fractures do not usually require particular attention if the number of fractured ribs is low. However, multiple fractured ribs can be extremely painful and impair proper inspiration, leading to shallow breathing and fatigue. These patients benefit from pain medication and, eventually, pneumatic stabilization of the chest wall through continuous positive airway pressure (CPAP).[9]

RULE OF THUMB The finding of multiple and/or bilateral rib fractures, the fracture of the first rib or a flail chest is suggestive of severe, high-energy traumatic lesions. Such patients are at high risk of respiratory and/or circulatory failure.

Displaced rib fractures are even more painful, and sharp bone edges can cause pneumothorax through laceration of the visceral pleura. Pain control and pneumatic stabilization are encouraged. These patients should be routinely monitored because they can develop internal pleural bleeding, especially in the setting of anticoagulant therapy. The presence of blood in the pleural cavity (hemothorax) requires pleural drainage and close monitoring of the bleeding (total amount of blood lost and presence of active bleeding). Surgical evaluation is mandatory. Multifocal fractures of one or more ribs create a **thoracic flap (flail chest)** that is extremely painful and impairs normal respiratory mechanics. During inspiration, when pleural pressure becomes negative, the free flap will be pushed inward, whereas during exhalation, when pleural pressure is positive, it will be pushed outward. This causes extreme pain because the edges of the ribs will be subjected to continuous friction. Based on the extent of the lesion, flail chest can impair normal ventilation. The current therapeutic approach is based on pain management and CPAP. Needless to say, the presence of flail chest is associated with a high risk for pneumohemothorax, and some of these patients do require intubation and invasive ventilation.

RULE OF THUMB The presence of bronchial injury should be suspected when, after the placement of a chest tube for pleural drainage, large amounts of air continue to exit the chest tube in a synchronized pattern with positive pressure ventilation.

Blunt trauma also can cause **pulmonary and cardiac contusions**. Pulmonary contusion is characterized by acute inflammation and exudation of plasma and blood components into the alveolar space. Even though these lesions resolve spontaneously, they place the patient at high risk for bacterial or viral infection, leading to pneumonia.[10] These inflammatory processes are usually located in the regions of the lung that were subject to the traumatic force (Fig. 30.2). **Myocardial contusion** is a common finding in chest trauma, although difficult to diagnose. The severity of the condition ranges from simple bruising of the tissue to lethal damage to the valves. If a myocardial contusion is suspected or diagnosed, cardiogenic shock and arrhythmias should be anticipated, and the patient carefully monitored.

The application of a traumatic blunt force on the abdomen causes a rapid increase of intraabdominal pressure. This could

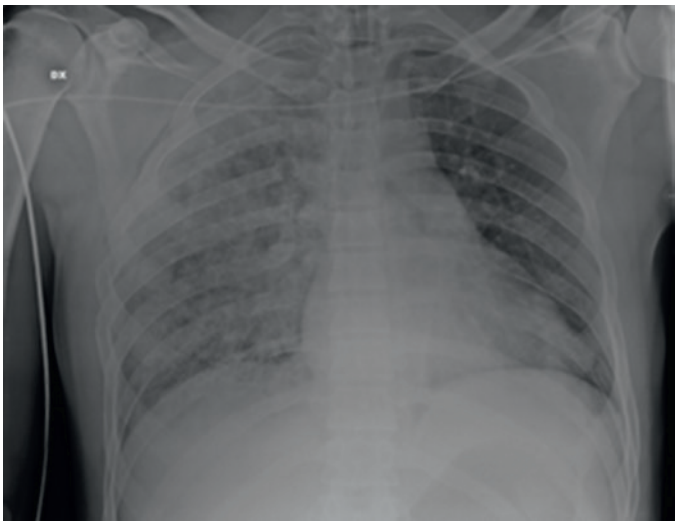

Fig. 30.2 Chest X-Ray of a 29-Year-Old Man, Victim of a Motorbike Accident. The chest x-ray was obtained at arrival in the emergency department. Extensive right lung contusion ("white" lung), pneumothorax, multiple multifocal rib fractures, and a right flail chest can be seen. (*Image courtesy Dr. Giovanni Babini.)*

lead to diaphragmatic rupture. A rupture of the diaphragm impairs normal respiratory function and represents a medical and surgical emergency. If positive pressure ventilation is not applied, the negative intrathoracic pressure during inspiration literally sucks visceral organs into the pleura, causing massive lung collapse, acute bowel obstruction, and possibly splanchnic ischemia.

RULE OF THUMB All patients with chest trauma, regardless of whether the injury is penetrating or blunt, require careful assessment for pneumothorax, airway injuries, disruption of thoracic vessels, and chest contusion leading to ARDS.

Special Considerations in Patients With Chest Trauma

All bedridden patients are at increased risk for atelectasis secondary to decreased tidal volume and residual volume. Mucus clearance is impaired by inadequate mobilization and excessive or inadequate pain control. Secretion retention might aggravate atelectasis by creating thick mucus plugs in the distal bronchial tree. This phenomenon exposes the bedridden patient to hospital-acquired pneumonia. Secretion retention is a major issue in patients with chest trauma. The pain associated with the trauma (i.e., rib fractures) further impairs the cough reflex. In addition, direct chest trauma might be complicated by lung contusion. The presence of edema and blood in the lung parenchyma represents a perfect growth medium for pathogenic bacteria. The role of the respiratory therapist is crucial in the prevention of potentially life-threatening respiratory complications. There are four interventions on which the respiratory therapist should focus (Box 30.1):

1. *Mobilization*. The patient should be assisted in changing positions periodically to help with mucus drainage and prevention of atelectasis. If tolerated, patient should be helped to move out of bed and to spend some time in a chair.[11]

BOX 30.1 Basic Respiratory Interventions in the Bedridden Trauma Patient

- Mobilization
- Humidification
- Pain control
- Incentive spirometry
- Noninvasive continuous positive airway pressure and bilevel positive airway pressure

2. *Humidification of the airways.* Regardless of mechanical ventilation, bedridden patients should receive optimal humidification of the airways to prevent the accumulation of dry secretions.
3. *Pain control.* Control of pain in the trauma patient is one of the most challenging tasks of the critical care team. Inadequate pain control generally results in minimal chest expansion as a reflex response to minimize pain associated with breathing. Excessive use of pain medications (i.e., opioids) also will decrease chest expansion and cough reflex because of sedative effects. Both scenarios exacerbate the pathophysiologic sequence of events described earlier, leading to pneumonia.[12]
4. *Incentive spirometry, positive expiratory pressure (PEP) therapy and noninvasive ventilation (NIV).* Patients should be encouraged as soon as possible to take advantage of incentive spirometry. Incentive spirometry consists of regular breathing exercises performed with the aid of a dedicated device. Regular exercise has been shown to prevent formation of atelectasis and reduces secretion retention. The use of such devices requires the full collaboration and dedication of the patient. Secretion clearance can be aided by gentle external chest percussion (i.e., chest physiotherapy), avoiding sites of injury, if tolerated. PEP therapy consists in breathing with active expiration against a positive pressure. It can be applied by a face mask or through a mouthpiece. PEP therapy promotes clearance of secretions from the lungs, improves lung ventilation, and reduces air trapping. Some devices also allow for the delivery of aerosolized drugs, such as bronchodilators. Should these interventions fail, the respiratory therapist should consider the use of NIV (CPAP or bilevel positive airway pressure) to reexpand the residual volume and assist tidal ventilation. Recruitment maneuvers should be carefully performed in patients with chest trauma. The presence of silent lesions could cause hypertensive pneumothorax under elevated airway pressures.[13]

Respiratory Management

Every trauma patient represents a case by itself, and the respiratory management of trauma patients should focus on the mechanism of chest injury. Supplemental O_2 is generally administered immediately after the trauma to prevent secondary hypoxic injury. However, any sign of pending respiratory failure should prompt endotracheal intubation and initiation of mechanical ventilation (Box 30.2). Upper airway disruption might require emergent tracheostomy. Advanced airway management such as a double-lumen endotracheal tube (ETT) may be required for injury of the trachea or for selective lung ventilation for bronchial injuries.

BOX 30.2 Mechanical Ventilation of the Trauma Patient

- Mode: Pressure or volume ventilation
- Tidal volume: 6–8 mL/kg predicted body weight
- Inspiratory time 0.6–1.0 s
- Plateau pressure: Less than 28 cm H_2O
- Driving pressure of 15 cm H_2O or less
- Rate only limited by the development of auto-PEEP
- Minute volume to maintain normal $PaCO_2$
- PEEP 5–10 cm H_2O
- FiO_2 set to maintain target PaO_2
- If ARDS, manage as any other ARDS patient

ARDS, Acute respiratory distress syndrome; *PEEP*, positive end expiratory pressure.

Injury to the lung parenchyma always should be suspected after major trauma. Extensive lung injury frequently evolves into traumatic ARDS, requiring protective lung ventilation strategies (see Chapters 29 and 49). In addition, trauma patients are at higher risk for developing lung injury resulting from the large volume of blood components that these patients may require (i.e., transfusion-related lung injury and/or transfusion-associated circulatory overload). Bronchoscopy plays a major role in the respiratory care of trauma patients. Bronchoscopy first allows removal of foreign bodies and drainage of blood clots and provides an excellent method for removal of tenacious mucus plugs. Moreover, it is the gold standard for diagnosing proximal and distal major airway lesions and is capable of providing first-line treatment. Trauma patients are at high risk for VAP, and preventive clinical bundles should be applied as soon as possible (see Chapter 24). Recent reports outlined beneficial effects of these bundles (i.e., decreased sedation, early mobilization, and improved secretion clearance) compared with early tracheostomy for patients requiring prolonged mechanical ventilation. However, it is still difficult to predict the time for liberation from mechanical ventilation.

OBESITY

Epidemiology

Obesity is defined by an excess of weight in relation to a person's height. It is mainly measured through the body mass index (BMI), which is the ratio of an individual's weight (kg) divided by the square of the individual's height (m):

$$BMI = (weight)/(height)^2 = kg/m^2$$

A normal BMI range for a healthy individual is between 20 and 25 kg/m^2, and a BMI over 30 kg/m^2 is defined as obesity. In the last decade, the prevalence of obesity progressively has increased in the U.S. population, reaching a plateau of over a third of the total population. There are differences in obesity prevalence among different ethnic groups, with non-Hispanic Asians having a lower prevalence compared to non-Hispanic whites, non-Hispanic African Americans, and Hispanic groups. Obesity is connected to a plethora of adverse health conditions and imposes considerable burdens on the U.S. healthcare system.

MINI CLINI

Trauma: Recognizing Common Life-Threatening Acute Respiratory Complications in Trauma Patients

Problem

A water-skier was sent by medical flight to the hospital after collision with a boat following a 30-foot acrobatic jump. The unknown young man was intubated with a 7.0-mm ETT at the scene for hypoxemia and GCS 6 with no lower limb movements. Vital signs at admission in the ED were heart rate 40 beats/min, blood pressure 80/40 mm Hg, O_2 saturation 99%, and body temperature 35°C. He weighs 160 lb and is 6 feet tall. The ventilator settings are as follows: volume-controlled ventilation mode, tidal volume (V_T) 500 mL, respiratory rate 14 breaths/min, and positive end expiratory pressure (PEEP) 5 cm H_2O. During central line placement, the RT notices that the peak airway pressure increased from 18 cm H_2O to 35 cm H_2O, activating the high pressure alarm, and SaO_2 declined rapidly from 99% to 90%. What are the next steps the RT should take?

Solutions

1. Immediately inform the medical team regarding the alarming acute increased peak pressure and decreased SaO_2.
2. Verify that the ETT did not migrate into the right main stem bronchus during neck positioning for central line placement by confirming tube positioning.
3. Pass a suctioning catheter to verify absence of ETT kinking or occlusion resulting from secretions or blood.
4. Visually inspect that the inspiratory and expiratory ventilator circuit is not kinked and that the water trap is not filled.
5. Auscultate breath sounds on all lung fields and inspect trachea for deviation or asymmetry in chest movements during ventilation. Tension pneumothorax should be suspected when breath sounds are absent on the affected part of the thorax and the trachea deviates away from the affected side. The thorax may also be hyperresonant with jugular venous distension. Increased intrathoracic pressure might cause hypotensive and hypoxemia. If not recognized, tension pneumothorax leads to cardiovascular collapse and death.
6. Immediate chest X-ray and arterial blood gas (ABG) analysis should be requested to confirm hypoxemia and rule out acute changes (i.e., pneumothorax, acute pleural effusion, hemothorax, bronchial mucus plug causing large lobar or entire lung collapse).
7. Until a pneumothorax is ruled out, V_T should be decreased and respiratory rate increased ideally by use of a manual ventilator. This is to ensure that limited pressure is applied to minimize the volume of gas extending the possible pneumothorax.
8. Regardless of the final diagnosis, the respiratory therapist has a key role in the care of the trauma patient in the acute setting. Common tasks of the RT are titrating the ventilator after acute changes in the patient's condition, travel to a computed tomography (CT) scan or other emergent hospital location (i.e., operating room or ICU), and assisting with procedures such as bronchoscopy, chest tube placements, or intracranial pressure monitoring.

RULE OF THUMB Among the different excesses of BMI, a BMI greater than 40 kg/m^2 is defined as **severe obesity**, a BMI greater than 45 kg/m^2 is defined as **morbid obesity**, and a BMI greater than 50 kg/m^2 is defined as **super obesity**.

Obesity is associated with increased morbidity and mortality in the context of both acute and chronic medical problems, including diabetes mellitus and related complications, hypertension, dyslipidemia, cardiovascular disease, gallstones, cholecystitis, and certain forms of cancer. Although there is now a considerable

amount of data available on the impact of obesity on ICU outcomes, there are still contradictory conclusions concerning the nature of this impact, possibly because obese ICU patients on average are younger and are affected with less severe diseases compared to nonobese ICU patients; however, obese ICU patients require the same level of intensive care.

Among people with a BMI within the range of severe obesity, the distribution of adipose tissue plays a major role in determining the risks for chronic diseases. Current guidelines concerned with the clinical care of the obese recommend measurement of waist circumference in people with a BMI greater than 25 kg/m^2 and propose that waist circumferences of 102 cm in men and 88 cm in women define abdominal adiposity. Most studies examining the association between fat distribution and mortality have shown that abdominal adiposity is an important predictor of mortality. In particular, waist circumference has been associated with mortality even in people with a normal BMI, indicating that BMI might be of limited use in assessing the severity of a person's obesity and that fat tissue distribution plays a major role in the pathophysiology of obesity.[14]

RULE OF THUMB Patients who are obese have a greater likelihood of mortality in the ICU if their waist circumference is greater 102 cm in men and 88 cm in women.

Specific Pathophysiologic Concerns

Adipose tissue is a potent source of proinflammatory molecules that induce a chronic inflammatory state mimicking critical illness and diminishing immune and metabolic reserves (Box 30.3). Moreover, an increased BMI requires additional cardiovascular, respiratory, and metabolic work, further diminishing an individual's physiologic reserves.[15]

Obesity is a risk factor for cardiovascular disease independent of diabetes mellitus and hypertension. The mechanism of obesity-related cardiovascular disease involves an increase in both preload and afterload. Adipose tissue is perfused on average by 3 mL of blood per each 100 g of tissue. The resulting expansion of blood volume increases venous return (preload), cardiac output, and cardiac work. Afterload is increased by secretion of steroids and catecholamines and through the renin-angiotensin endocrine axis. Myocardial hypertrophy and diastolic dysfunction are the results of these alterations, eventually leading to heart failure, arrhythmias, or sudden cardiac arrest. Myocardial hypertrophy and the resulting reduced heart-wall compliance, as well as reduced heart chamber volumes, are responsible for poor tolerance of intravenous fluids in these patients. In addition, the presence of diabetes mellitus and hypertension in this setting exponentially increases the risk for myocardial infarction. Moreover, the presence of diabetes mellitus increases the risk for a silent myocardial infarction being present at the time of admission or happening as a complication of critical illness. This risk is especially important at the extreme range of obese patients, whose physical activity is very limited and who may not manifest symptoms of myocardial ischemia or show signs of congestive heart failure before ICU admission.

BOX 30.3 Physiologic Concerns Associated With Obesity

- Cardiovascular disease
- Venous thrombosis and pulmonary embolism
- Chronic renal failure
- Obstructive sleep apnea
- Obesity hypoventilation syndrome
- Reduced lung volumes
- Expiratory flow resistance
- Air-trapping and auto-PEEP

PEEP, Positive end expiratory pressure.

The presence of a proinflammatory/procoagulatory state induced by adipose tissue and associated with a sedentary lifestyle and venous stasis puts these patients at high risk for venous thrombosis and pulmonary embolism. The increased cardiac output of obese patients is responsible for an increased glomerular filtration rate in patients whose obesity-related complications have not yet compromised kidney function. However, diabetes mellitus and hypertension can be responsible for chronic kidney failure. Thus, an evaluation of kidney function is mandatory in this patient population. Abnormal glomerular filtration and excess adipose tissue alter the clearance and the volume distribution of most drugs that are administered to obese paitents.

Dosing of **lipophilic drugs** should be based on the actual body weight of the patient, whereas dosing for **hydrophilic drugs** is best determined using the ideal body weight (IBW) or predicted body weight (PBW) of the patient and corrected for higher renal clearance if an abnormally high **glomerular filtration rate** is present. Because of altered clearance, distribution, and accumulation of drugs, obese patients are particularly prone to underdosage and overdosage of hypnotic medications. Because most of these drugs are lipophilic, allowing them to cross the blood–brain barrier, the accumulation of drugs in excess adipose tissue can occur and result in a slowed release into the bloodstream. Frequent spontaneous awakening trials are necessary to assess the accumulation of drugs in the adipose tissue and to determine the ability of the patient to promptly recover from sedation to avoid delaying liberation from mechanical ventilation.[16]

More than two-thirds of obese people have **obstructive sleep apnea** (OSA). OSA has been linked to daytime somnolence and higher risk of industrial and motor-vehicle accidents. However, the factors that lead to a higher incidence of OSA in obese patients are still poorly understood. It has been argued that obesity can act in different ways on the respiratory system, that it narrows the upper airway, causes upper airway collapsibility, and disrupts the normal physiologic respiratory drive. Full neuromuscular control of pharyngeal patency is of the utmost importance in these patients (see Chapter 34).

Lung volumes progressively decrease as BMI increases. Total lung capacity and residual volume decrease linearly as BMI increases, while functional residual capacity is exponentially reduced at higher BMI values, especially in patients with a central fat distribution (high waist circumference). Low functional residual capacity increases the risk for expiratory flow limitation and airway closure. This is thought to be due to an increase in pleural pressure caused by the transmission of the gravitational

weight of the abdomen. The weight of the abdomen displaces the diaphragm in a cephalad position, causing passive atelectasis in the most gravity-dependent regions of the lung. The collapsed lung tissue exerts less elastic recoil on adjacent structures, particularly on the smaller airways, reducing their diameter. The increase in pleural pressure further aggravates airway collapse. The ensuing expiratory flow limitation can lead to incomplete exhalation with air trapping, resulting in dynamic hyperinflation. Dynamic hyperinflation (auto-PEEP) is one of the most common sources of increased work of breathing and patient–ventilator asynchrony in mechanically ventilated patients.

Trapping of gas behind collapsed airways acts as a recoil pressure that needs to be released at the beginning of inspiration before the generation of a V_T, resulting in wasted work of breathing.[17,18] It has been observed that the sitting position can improve respiratory mechanics and gas exchange and lower the PEEP required to restore functional residual capacity to a normal physiologic level.[19] The presence of expiratory flow limitation and atelectasis in the dependent zones of the lung causes ventilation/perfusion ($\dot{V}/\dot{Q}$) mismatch and hypoxemia. To supplement the increased rates of O_2 consumption and carbon dioxide production, obese patients increase their minute ventilation, maintaining adequate alveolar ventilation at the expense of higher dead space ventilation. However, the most severely obese patients lose central chemosensitivity, impairing their ventilatory response to hypoxemia and hypercapnia (**obesity hypoventilation syndrome** [OHS]). These patients tend to slowly progress to hypoventilation with hypercapnic respiratory failure. Noninvasive nocturnal ventilation can be effective in restoring a more normal physiologic chemosensitivity and compensatory respiratory drive.[20]

RULE OF THUMB The majority of patients with severe obesity develop flow limitation, air trapping, and auto-PEEP, especially when ventilated in the supine position.

Clinical Assessment

Given an unstable respiratory/cardiovascular equilibrium, obese patients are particularly prone to acute respiratory failure in the setting of disease. Particular attention must be paid to gas exchange and signs of increased work of breathing (labored breathing, high respiratory rates, and use of accessory muscles), because any deterioration in their clinical status can quickly precipitate respiratory failure requiring mechanical ventilation.

BMI, body fat distribution, and history of snoring, sleepiness, and headaches should be determined or measured on admission. The degree of self-mobilization and physical daily activity should be investigated, and the risk for deep venous thrombosis or pulmonary embolism should be assessed. A plan for airway management and intubation should be discussed before the onset of respiratory failure, especially if the patient shows signs of a particularly difficult airway for intubation. The past use of and settings for home nocturnal CPAP or NIV should be investigated, and their continued use should be encouraged. In the presence of a history suggestive of OSA/OHS, intermittent/nocturnal noninvasive bilevel positive airway pressure/CPAP should be started regardless of the patient's respiratory status.

BOX 30.4 Respiratory Management of Obesity

- O_2 therapy for management of hypoxemia
- Inhalational bronchodilators for management of asthma symptoms
- Noninvasive CPAP for management of sleep apnea
- NIV for obesity hypoventilation syndrome and hypercarbic respiratory failure
- Invasive mechanical ventilation for management of hypoxemic and hypercarbic respiratory unresponsive to NIV

CPAP, Continuous positive expiratory pressure; *NIV,* noninvasive ventilation.

Respiratory Management

See Box 30.4.

Oxygen Therapy

Hypoxemia is the most common gas exchange abnormality in obese patients. It can be mild and easily corrected by O_2 supplementation, or it can be severe enough to require mechanical ventilation. However, a mild, progressive hypoxemia should prompt close monitoring of gas exchange, work of breathing, and mental status, because it might be a sign of impending respiratory failure. A sudden onset of hypoxemic respiratory failure should raise the suspicion for pulmonary embolism. If the patient's response to O_2 supplementation is inadequate but the patient's mental status is acceptable, NIV should be initiated.

Aerosolized Pharmacology

Obese patients have a higher incidence and severity of asthma, and they frequently require inhalation therapy. For a detailed discussion, see Chapter 39.

Noninvasive Ventilation

NIV should be attempted when the patient's neurologic status is relatively normal but O_2 therapy alone is ineffective at correcting hypoxemia or when hypercapnia complicates respiratory failure. By the time NIV is attempted, a plan for airway management and intubation already should have been made. NIV should be instituted immediately in the setting of hypercapnic respiratory failure. If qualified staff is available, noninvasive mechanical ventilation can be set up and begun in the ED or respiratory wards. An alert and cooperative mental status, proper mask-fitting, ability to clear secretions, and relative hemodynamic stability are essential factors that contribute to the success of NIV. Pressure-support ventilation with adequate PEEP is the preferred mode of ventilation. Vital signs, level of consciousness, respiratory pattern, oxygenation, delivered V_T, gas exchange, and circuit leaks should be frequently assessed to guarantee proper ventilatory therapy.[21] Refer to Chapter 50 on NIV for details on its application.

RULE OF THUMB If the first to second hour of NIV does not at least partially correct the patient's hypoxemia and hypercarbia, endotracheal intubation should be immediately considered.

Invasive Mechanical Ventilation

Intubation. Although airway management in obese patients can be challenging, there is no common agreement on which approach to intubation should be used in obese patients (see Chapter 22). A possible strategy is awake intubation using a flexible bronchoscope. Although this technique requires coordination, proper anesthesia of the upper airways, and complete collaboration of the patient, with this final factor being particularly important for success, even when all is ideal, intubation of the critically ill obese patient is difficult. The advent of video-laryngoscopy has significantly reduced the amount of difficulty that clinicians face in airway management, and the use of a video-laryngoscope should be strongly considered in any intubation plan for the critically ill obese patient. A kit for rapid airway access should be present at the bedside or within reach until the airway is secured. Regardless of the device or technique adopted, which should be based on patient evaluation and personal expertise, optimal positioning is mandatory to increase the chance of securing the airways. The "ramped position" consists of elevating the upper body and head of the patient to align the sternum and ear horizontally. This positioning technique results in a significantly improved laryngoscopic view. In addition, the elevated head-of-bed position improves respiratory mechanics and lung volumes during preoxygenation, increasing apnea time. The use of CPAP during preoxygenation can additionally increase the nonhypoxemic apnea time by 50%.

Tidal volume, minute volume, and respiratory rate. Pressure control ventilation or volume control ventilation are equally effective modes of mechanical ventilation in the obese patient (Box 30.5). However, regardless of mode of ventilation, ventilator settings *must not be calculated* based on actual body weight but on PBW or IBW, because an increased BMI does not reflect increased lung size. The most widely recommended formulas for determining PBW are listed as follows:

$$PBW_{MEN} = 50.0 + 0.905 * ([\text{Height in cm}] - 152.4)$$

$$PBW_{WOMEN} = 45.5 + 0.905 * ([\text{Height in cm}] - 152.4)$$

BOX 30.5 Mechanical Ventilation of the Obese Patient

- Mode: Pressure or volume ventilation
- Tidal volume: Average 6 mL/kg PBW, range 4–8 mL/kg PBW
- Inspiratory time 0.6–1.0 s
- Plateau pressure: Less than 28 cm H_2O, unless TPP measured then TPP less than 20 cm H_2O
- Driving pressure equal to or less than 15 cm H_2O
- Rate only limited by the development of auto-PEEP
- Minute volume generally 10 L/min or greater
- Lung recruitment maneuver with **decremental PEEP trial** to set PEEP
- PEEP frequently 15–25 cm H_2O dependent on the size of the patient
- FiO_2 set to maintain target PaO_2
- Position head of the bed to 30 degrees or greater elevation
- Noninvasive ventilation for 24–48 h after extubation

PBW, Predicted body weight; *PEEP,* positive end expiratory pressure; *TPP,* transpulmonary pressure.

Ventilator settings should be tailored for an adequate clearance of CO_2. In assisted partial ventilatory support, respiratory rate and volumes should be carefully monitored, especially in the setting of OHS, as central desensitization to CO_2 might result in depressed respiratory drive in the setting of normal oxygenation. It is reasonable in this context to have a lower oxygenation target (SpO_2 88% to 95%).

RULE OF THUMB V_T in obese patients always should be determined based on PBW, *not* actual body weight, because lung size is not based on weight; it is based on height and gender.

Lung recruitment and positive end expiratory pressure. It has been demonstrated in the ICU and in intraoperative settings that **recruitment maneuvers** in obese, mechanically ventilated patients are effective at improving respiratory system compliance and oxygenation without affecting hemodynamics.[22,23] This effect is due to the reversal of atelectasis that forms during induction and persists without adequate levels of PEEP during mechanical ventilation.[24] It is advisable to perform a recruitment maneuver whenever PEEP is increased or after temporary PEEP discontinuation (e.g., disconnection of the patient from the ventilator circuit in the setting of high PEEP).[25] Obese patients require higher PEEP levels to counter the pressure of abdominal weight on the lungs through the diaphragm. In obese patients with persistent hypoxemia, measurements of transpulmonary pressure and PEEP titration (whether based on best compliance or positive end-expiratory transpulmonary pressure) are highly suggested. See Chapter 49 for details on the performance of recruitment maneuvers.

Positioning. It has been shown that elevation of the head of the bed is effective at improving respiratory system compliance and oxygenation, reducing expiratory flow limitation, and reducing PEEP requirements for optimal ventilation in obese patients. This phenomenon is related to the gravitational effects of the abdomen on the diaphragm. When obese patients lie in the supine position, the abdominal content pushes against the diaphragm and displaces it in a cranial direction, resulting in increased pleural pressure and passive atelectasis in the dependent zones of the lung (see the section on pathophysiology). The adoption of a sitting position changes the vector of the gravitational forces of the abdomen, partially releasing the diaphragm from abdominal pressure. Changes in bed position in morbidly obese patients (e.g., from sitting to supine and back to sitting) should be followed by a recruitment maneuver in order to reexpand the regions of the lungs that collapsed during the transient increase in pleural pressure. In general, unless contraindicated, obese patients should be managed with the head of the bed elevated above 30 degrees.

RULE OF THUMB FiO_2 and pressure support level should always be weaned before PEEP level is decreased. When FiO_2 is approximately 0.40 and pressure support is 10 cm H_2O or less, PEEP can be decreased.

Ventilator discontinuation. One of the most challenging aspects of ventilatory management of obese patients is liberation from mechanical ventilation. Expiratory flow limitation, low

MINI CLINI

Obesity: The Role of Postoperative Noninvasive Ventilation

Problem

A 550-lb patient is recovering in the postoperative care unit after a laparoscopic cholecystectomy. The procedure was uneventful. The nurse called you because the SpO_2 decreased from 95% to 88% over the past hour despite a nonrebreather face mask at 12 L/min. You see the patient; she is calm, resting in no pain, and breathing regularly at 8 breaths/min. Other vital signs are heart rate 66 beats/min, blood pressure 128/70 mm Hg, and body temperature 36.5°C. After reviewing the nursing notes, you notice that patient required 4 mg of midazolam before surgery for anxiety, 4 mg of hydromorphone during surgery, and an additional 10 mg of morphine in the recovery room.

Solutions

Inform the medical/surgical team of the increased hypoxemia in this high-risk obese postsurgical patient. Suggest the medical/surgical team perform an ABG analysis to confirm hypoxemia and determine PCO_2 to rule out pharmacologic narcosis and request a chest X-ray to rule out postoperative atelectasis.

In this patient, NIV instead of CPAP is required because not only is there most likely marked atelectasis, but this patient's ventilatory drive has been depressed by sedatives and narcotics, requiring ventilatory support. NIV may be required for only 24 h, but considering the size of the patient and the likelihood that the patient has sleep apnea, the use of CPAP during sleep should be considered on an ongoing basis and the patient evaluated for sleep apnea once recovered from the acute episode.

respiratory system compliance, atelectasis, and impaired neurologic respiratory drive play an important role in determining increased work of breathing in morbidly obese patients. Post–critical illness muscular weakness aggravates the patient's respiratory condition. In addition, it has been shown that morbidly obese patients who undergo tracheostomy have a higher morbidity and mortality and are more prone to tracheostomy-related complications. In obese patients who required high levels of PEEP during their ICU stay, reducing PEEP in order to perform a spontaneous breathing trial can lead to dyspnea and desaturation due to a "pendelluft" effect, with air flowing within the lungs from dependent to nondependent regions of the lung, increasing work of breathing and progressing to a failed trial. In these patients, a spontaneous breathing trial can be attempted at their titrated PEEP level. If successful, they can be extubated with CPAP/NIV support.[26]

NEAR DROWNING

Epidemiology

Drowning is one of the major causes of accidental pediatric death and is more common in low-income and middle-income countries. In adults, drowning is generally associated with alcohol and drug abuse. From 2005 to 2014, there was an average of 3,536 fatal unintentional drownings annually in the United States, of which almost 700 were children younger than 14 years of age, not counting an additional 332 people who drown yearly in boating-related incidents. It has been calculated that for each drowning casualty, there are at least five times as many near-drowning–related admissions to EDs, of which half require hospitalization.

The essential feature of drowning and the primary cause of death is asphyxia leading to cardiopulmonary collapse. Permanent injuries include a spectrum of brain damage, starting with minor memory problems to severe learning disabilities, including a permanent vegetative state.[27–29]

Specific Pathophysiologic Concerns

The pathophysiologic mechanisms of drowning comprise the following two reflexes:

1. Inhalation of fluid causes irritation and cough response, resulting in fluid being either swallowed or inhaled. Laryngospasm with closure of the glottis prevents aspiration of large amounts of fluid in the lungs (**"dry drowning"**), diverting these fluids to the stomach. In general, the laryngospasm lessens with unconsciousness, leading to **"wet drowning"**—the aspiration of fluid, which is a more common occurrence.
2. **Cold shock cardiac-respiratory reflexes** occur with sudden immersion in water cooler than 25°C. The breathing pattern is characterized by gasping followed by hyperventilation and shallow breathing at almost total lung capacity. At lower water temperatures, sudden peripheral vasoconstriction can acutely increase systemic vascular resistance, leading to sudden cardiovascular collapse if the heart is unable to overcome the acute increase in preload and afterload.[30]

During "wet drowning," specific respiratory and blood chemistry dysfunction depend on whether fresh- or seawater has been inhaled.

1. Inhalation of freshwater.[31]
   a. *Inhalation of freshwater and its effects on the respiratory system*. Inhalation of freshwater rapidly depletes alveolar surfactant, leading to $\dot{V}/\dot{Q}$ mismatch. Inhaled water is quickly absorbed into the vascular system from the alveolar space by osmosis, causing alveolar collapse and worsening shunt and hypoxia. In addition, in the setting of inhaled freshwater, acute neurogenic pulmonary edema due to cerebral hypoxia has been shown to worsen alveolar flooding. However, if hypoxia is reversed, normal pulmonary function can be quickly restored.
   b. *The effects of inhalation of freshwater on other organs*. If a large volume of freshwater is inhaled, it is rapidly absorbed into the circulation, leading to electrolyte imbalance. Hyponatremia can lead to seizures, especially in pediatric patients. In addition, diluted plasma causes water to rapidly enter into erythrocytes by osmosis, causing hemolysis. The resulting hyperkalemia and hyponatremia can cause ventricular fibrillation, and the liberation of hemoglobin into the plasma can precipitate acute renal failure.
2. Inhalation of salt water.[32]
   a. *Inhalation of salt water and its effects on the respiratory system*. Seawater has a threefold higher osmolarity than blood. Hypertonic fluid inhalation therefore causes water to move from the circulation into the lungs. In experimental studies in animals, inhaled seawater accounted for less than 50% of the volume of water retrieved from the lungs at autopsy. In contrast with the inhalation of freshwater, this phenomenon explains the sustained edema and prolonged shunt after the inhalation of salt water. In addition,

BOX 30.6 Respiratory Management of Near Drowning

- Basic cardiopulmonary
- Airway clearance
  - Bronchoscopy
  - Lavage
  - Prone positioning
- Mechanical ventilation as in all ARDS patients

ARDS, Acute respiratory distress syndrome.

salt water causes direct damage to the alveolar-capillary membrane, enhancing lung injury.

b. *The effects of inhalation of salt water on other organs.* If a large volume of salt water is inhaled, the rapid loss of circulating volume into the alveolar space across the injured alveolar capillary membrane may cause hemoconcentration, hypernatremia, and hypoalbuminemia. This phenomenon, if not recognized and rapidly reversed, leads to vascular collapse and hypovolemic shock.

Despite the pathophysiologic differences and the obvious circumstantial differences between drowning in salt water versus freshwater, at autopsy, a definitive diagnosis cannot be made.[33–35]

Respiratory Management

Immediate management of patients who present with drowning or near-drowning events must follow the classic airway-breathing-circulation approach, and cardiopulmonary resuscitation should be started immediately, if needed (Box 30.6). If possible, prone positioning of the patient is preferable, because it allows optimal clearance of water from the tracheobronchial tree, especially in the case of salt water drowning. Temperature monitoring and active body temperature control should be started as soon as possible, because submersion and inhalation of water drastically reduces body temperature.

RULE OF THUMB Near-drowning victims almost always develop ARDS, and ventilator management should include all best practices regarding ARDS (see Chapter 29).

Airway Clearance Therapy

The aspiration of foreign matter occurs relatively commonly in drowning or near-drowning events, particularly events involving drowning in shallow water. The most common aspirated material is sand, mud, or dirt. This can be easily recognized if solid material is found in the upper airways or in the stomach. It has been reported that a CT scan can show distinct hyperdense "sand bronchograms" in cases of sand aspiration (Fig. 30.3). The inhalation of foreign material in the setting of drowning or near drowning is particularly harmful, because the material is usually solid, is nonsoluble, has a high density, and tends to consolidate and clog distal airways. This further worsens the onset of ARDS that follows drowning by enhancing the inflammatory response and by mechanically sealing the airways. Upper airway clearance should be performed as soon as possible. Foreign material in the distal airways can be washed after intubation through repeated bronchoscopy and bronchoalveolar lavages.[36,37]

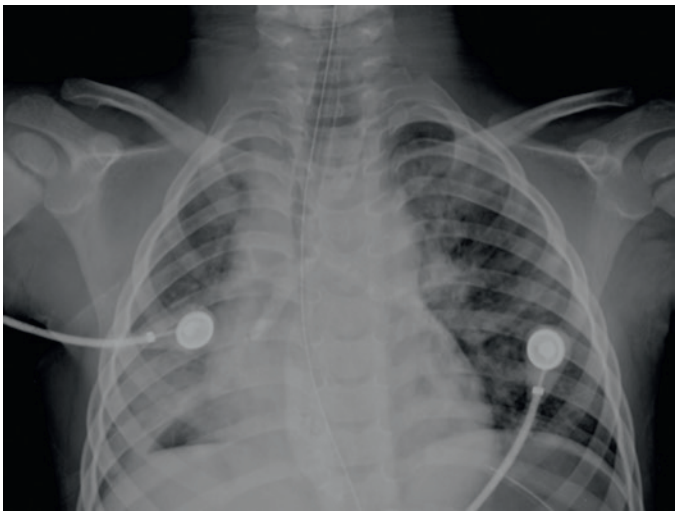

Fig. 30.3 Chest Imaging of a 4-Year-Old Child After Sand Aspiration. Radiopaque material can be seen inside the main bronchi and distal airways. Sand can cause direct mucosal injury, severe airway inflammation, and airway occlusion. (Image provided on MyPACS.net by Dr. Brenda Grabb.)

BOX 30.7 Mechanical Ventilation of the Near-Drowning Patient

- Mode: Pressure or volume ventilation
- Tidal volume: Average 6–8 mL/kg PBW
- Inspiratory time 0.6–1.0 s
- Plateau pressure: less than 28 cm H_2O
- Driving pressure equal to or less than 15 cm H_2O
- Rate only limited by the development of auto-PEEP
- Minute volume to maintain $PaCO_2$
- PEEP 5–10 cm H_2O
- FiO_2 set to maintain target PaO_2
- Prone position
- If ARDS, manage as normal for ARDS patients

ARDS, Acute respiratory distress syndrome; *PBW*, predicted body weight; *PEEP*, positive end expiratory pressure.

Mechanical Ventilation

Almost every patient who experiences drowning or near-drowning events will develop ARDS. Ventilatory management of these patients should follow ARDS ventilation guidelines as outlined in Chapters 29 and 49 (Box 30.7). Frequently, these patients develop bronchospasm as a result of the irritant effects of water in the airways. Laryngospasm and persistent upper airway closure are usually resolved by paralysis at intubation, but severe bronchospasm may persist, requiring bronchodilator therapy (see Chapter 40). Drowning in **fluvial or brackish water** or seawater is usually complicated by pneumonia caused by opportunistic pathogens inhaled at the moment of drowning. However, these bacteria usually do not show antibiotic resistance, and prompt antibiotic prophylaxis should be able to prevent pneumonia.

Positioning

Whenever feasible, prone positioning is preferable immediately after cardiovascular stabilization, especially in the case of brackish water or saltwater drowning, in which the osmotic activity of the inhaled salt causes continuous refilling of the lungs with water. The prone position allows clearance of salt-containing fluids from the lungs and might prove useful in the setting of severe ARDS.

RULE OF THUMB Once stabilized, salt-water near-drowning victims generally benefit from prone positioning, which allows better clearance of inhaled fluids from the lungs.

BURNS

Epidemiology

In the United States, each year, approximately 480,000 people receive medical treatment for burn injuries; of these patients, 40,000 are hospitalized. Over 60% of the estimated U.S. acute hospitalizations related to burn injury were admitted to 128 burn centers. Each year, 3200 patients die as a result of burn and/or smoke inhalation. In a selected case series, the reason for admission was 43% fire, 34% scald, 9% contact, 4% electrical, 3% chemical, and 7% other burn injuries.[38] The main feature characterizing the natural history of serious burns is burn shock. Burn shock can lead to death within the first hours after injury. The most important cause of mortality among those who survive burn shock is wound sepsis (Box 30.8). After recovery from the acute inflammatory phase, postburn deformities delay full functional recovery. Improved survival has been associated with early resuscitation, prevention of postburn sepsis, aggressive surgical treatment, improved perioperative care, and the development of multidisciplinary treatment teams. The first phase of the care of patients with serious burn injury is challenging in both respiratory care and hemodynamic management. Intensivists and RTs during the initial management period must work cooperatively in the management of these critically ill patients.[39]

BOX 30.8 Survival in Burn Patients

Survival in burn patients has been associated with:
- Early fluid resuscitation
- Prevention of postburn sepsis
- Aggressive surgical treatment
- Improved perioperative care
- Development of multidisciplinary teams

MINI CLINI

Near Drowning: Recognizing Life-Threatening Acute Respiratory Complications

Problem

An unresponsive 3-year-old boy is brought into the ED by his parents after he was rescued from their swimming pool. The parents were hosting a midsummer barbecue when they heard screaming kids and found their son face-down in the swimming pool. Vital signs at admission to the ED were heart rate 40 beats/min, blood pressure 50/20 mm Hg, $SatO_2$ 88%, and body temperature 33°C. What are the next steps, and how should the Respiratory Therapist (RT) respond?

Solutions

This is an emergency, and the team should be prepared for impending cardiac arrest because of near drowning. Advance Cardiac Life Support (ACLS) should be started right away without delay. While the medical team supports the circulation, the RT should be prepared for emergent and possibly difficult intubation because of aspiration, oral/pharyngeal/tracheobronchial fluids, and edema. A few pediatric ETT sizes, a pediatric intubation kit, and a difficult airway cart with an emergent tracheostomy kit should be at the bedside.

Wall suctioning should be readily available, and a pediatric flexible bronchoscope for deep suctioning and/or foreign body retrieval should be at the bedside.

In summary, a pediatric near drowning should be treated as an emergency with standard pediatric ACLS. However, immediately after recovery, the RT should focus on pulmonary toilette by body positioning, suctioning, and titration of the ventilator in anticipation of impending respiratory complications, refractory hypoxemia, and ARDS.

Clinical Assessment

During the clinical assessment of burn patients, the airway is the first priority. Burn patients always should be considered trauma patients; airway evaluation and management should follow what is described in the previous section on airway management of the trauma patient. Airways of burn patients should be monitored closely because exposure to hot gases, flames, and toxic gases causes airway obstruction as a result of acute edema. Early intubation in these patients is essential and early initiation of mechanical ventilation is required. Signs for early intubation include gradual but progressive compromise of respiratory mechanics and gas exchange and the presence of facial burns or any direct or indirect evidence of upper airway involvement.

Respiratory assessment of burn patients should focus on the following:[40]

1. Extent (**total body surface area** [TBSA]) and depth of external burns
2. Degree of involvement of lung tissue
3. Inhalation of toxic gases (carbon monoxide and cyanide)

The surface area of external burns can be easily quantified by the rule of nines, which estimates the total amount of the body surface area involved by the burns (%TBSA). The evaluation of external burns with the rule of nines is crucial to the medical team to guide fluid management during the first hours of treatment (Table 30.2). An adult patient of approximately 80 kg and with burns of 50% of TBSA would require 16 L of fluids in the first 24 hours, of which 8 L is given within the first 8 hours (1 L/h of fluid infusion). It is imperative for the RT to know the rate of fluid resuscitation and the hemodynamic response during the first critical hours after major burn. The severity of the burn depth is classified based on the anatomic planes progressively involved in the injury (Table 30.3). A first-degree burn is a superficial injury that involves only the epidermis. The second degree involves the dermis. Third-degree injury is characterized by the destruction of both the epidermis and dermis above the fascia. Fourth degree involves the muscles and the

TABLE 30.2 Quantification of Total Burn Surface Area by the Rule of Nines

Anatomic Structure	% TBSA
Adult	
Head, anterior	4.5
Head, posterior	4.5
Torso, anterior	18
Torso, posterior	18
Leg, anterior, each	9
Leg, posterior, each	9
Arm, anterior, each	4.5
Arm, posterior, each	4.5
Genitalia/perineum	1
Child	
Head, anterior	9
Head, posterior	9
Torso, anterior	18
Torso, posterior	18
Leg, anterior, each	6.75
Leg, posterior, each	6.75
Arm, anterior, each	4.5
Arm, posterior, each	4.5
Genitalia/perineum	1
Infant	
Head and neck	20
Torso, anterior	16
Torso, posterior	16
Leg, each	16
Arm, each	8
Genitalia/perineum	1

TBSA, Total burn surface area.

TABLE 30.3 Severity of Burn Depth

Degree of Burn	Depth of Injury	Level of Pain
First degree	Superficial, only involving the epidermis	Tender and sore
Second degree	Involves the dermis	Very painful
Third degree	Destruction of the epidermis and dermis above the fascia	Very little to no pain
Fourth degree	Full-thickness burns involving the fascia, muscles, and bones	Painless

bones. Surgical intervention with debridement and grafting should be considered for all burns more severe than second degree.

Extensive chest wall burns commonly lead to worsening gas exchange and increased work of breathing. The formation of thick fibrous tissue (eschar) and the accumulation of edema in the chest wall and upper abdomen lowers chest wall compliance. The deterioration of respiratory mechanics can be so severe as to require emergent **escharotomy**, a circumferential or near-circumferential surgical incision through the eschar that relieves tissue pressure and reduces chest wall stiffness.

Lung injury frequently results from inhalation of hot gases and smoke. ARDS is the typical presentation of heat-related lung injury. Fluid overload and systemic inflammatory response usually complicates the respiratory status and respiratory management of burn patients. Direct visualization of the tracheobronchial tree by flexible bronchoscopy can be extremely helpful in revealing mucosal alterations and disruptions characterized by inflammation, erythema, carbonaceous debris, and ulcerations.

BOX 30.9 Early Clinical Features of Carbon Monoxide and Cyanide Poisoning

- Anxiety
- Tachycardia
- Arrhythmias
- Tachypnoea
- Hypertension followed by:
  - Headache
  - Confusion
- Dyspnea
- Hypotension
- Bradycardia followed by:
  - Neurologic system symptoms (seizures and reduced consciousness)
  - Respiratory failure with pulmonary edema
  - Coma
  - Death

Carbon monoxide poisoning and **cyanide toxicity** are common findings in patients who have fire-related burns. The RT should be aware that CO and cyanide poisoning do not cause cyanosis. SaO_2 in blood should be measured by ABG analyses, because most SpO_2 sensors are unable to distinguish oxyhemoglobin (O_2Hb) from methemoglobin (MetHb) and carboxyhemoglobin (COHb). This phenomenon results in falsely elevated pulse oximetry readings even when the patient is severely hypoxemic. In the absence of blood gas analyses, a cooximeter can measure concentration of MetHb and COHb. CO has an affinity for hemoglobin that is 100 times greater than that for O_2, and this can shift the oxyhemoglobin dissociation curve to the left. Patients become symptomatic when COHb levels are higher than 15%; levels greater than 50% are lethal. In these patients, 100% O_2 should be administered as soon as possible, because it reduces the half-life of COHb to 74 minutes (average).[41] When feasible, hyperbaric O_2 should be considered to prevent serious neurologic sequelae.[42,43] Inhalation of cyanide-containing gas during combustion of nitrogenous materials is characterized by the presence of an adequate O_2 delivery and metabolic acidosis with anion gap. Cyanide compounds work by interfering with mitochondrial O_2 usage, blocking the final step of the oxidative phosphorylation cascade. Impaired uptake of O_2 despite normal O_2 delivery is confirmed by a high mixed venous O_2 saturation. Concentration of cyanide higher than 20 parts per million (ppm) is considered dangerous, and 100 ppm is lethal. **Thiosulfate** and **cyanocobalamin** are administered as soon as possible to reduce the half-life of this toxic compound. For both CO and cyanide poisoning, early clinical features are anxiety, tachycardia and/or arrhythmia, tachypnea, and hypertension, followed by headache, confusion, dyspnea, hypotension, and bradycardia leading to neurologic symptoms, such as seizures and reduced consciousness, respiratory failure with pulmonary edema, coma, and death (Box 30.9).[44]

RULE OF THUMB CO and cyanide poisoning do not cause cyanosis. SaO_2 in blood should be measured by ABG analyses, because most SpO_2 sensors are unable to distinguish O_2Hb from MetHb and COHb. This phenomenon results in falsely normal SpO_2 readings (100%), even when the patient is severely hypoxemic.

MINI CLINI

Carbon Monoxide Intoxication: Early Recognition and Treatment

Problem

A 46-year-old was brought to the ED after being found unconscious in his bathroom, near an improvised heater. At arrival, the patient had closed eyes, is responsive to external stimuli, and is confused when questioned. Head CT scan showed nothing remarkable. After the CT scan, his neurologic status quickly deteriorated, and the patient became unresponsive, although breathing spontaneously at a rate of 34 breaths/min. Additional vital signs were heart rate 140 beats/min with ST-segment depression on monitor, blood pressure 135/80 mm Hg, $SatO_2$ 100% with bright red skin color, and body temperature 36.7°C. Blood gas analysis reported pH 7.17, PCO_2 21 mm Hg, lactate 10.5 mmol/L, and COHb 47%. What should the RT do?

Solutions

The patient is suffering from lethal CO poisoning. His neurologic status, electrocardiographic changes, and partially compensated lactate acidosis are signs of severe hypoxemia. The emergency team should be immediately called, and the RT should be prepared for emergent rapid-sequence intubation and be prepared for possible difficult intubation. Throughout the procedure and after securing the airway, FiO_2 should be kept at 100%. Deep sedation and paralysis are helpful in reducing O_2 consumption to a minimum. Respiratory rate should be titrated to keep pH slightly acidic in order to improve O_2 delivery. Emergency hyperbaric O_2 therapy is required. After being treated with 100% O_2 at 2.8 atmospheric pressures for 90 min, COHb decreased to 1.5%, and the patient was successfully extubated 10 h after the accident.

Pathophysiology of Burn Patients

Burn injury can cause extensive tissue destruction, leading to an extensive inflammatory process, which starts with the release of inflammatory cytokines. To simplify, there is a local burn effect at the site of the burn and a systemic effect mediated by inflammatory mediators that are released. However, these two effects are interlinked and difficult to separate from each other.

It is generally better to divide burn patients according to the systemic response over time: a severe systemic response that lasts up to the first 48 hours followed by a late response starting at 48 hours, and ending at approximately 72 hours after the burn accident.[40]

1. Commonly, if TBSA exceeds 25%, a systemic inflammatory process becomes evident, and fluids from the intravascular space enter the extravascular space and develop generalized edema. Edema expands quickly within the first hours after the injury. If patients are not sufficiently hydrated, this fluid shift rapidly leads into an impairment of local and systemic perfusion with tissue and organ damage, causing ischemia, metabolic acidosis, and mixed venous desaturation, as a result of hypovolemic and distributive shock. The hematocrit gradually increases due to hemoconcentration. At the same time, the massive systemic inflammation commonly leads to cardiovascular instability followed by myocardial depression if not treated.
2. The first few hours after injury are characterized by a hyperdynamic state with high metabolic requirements with elevated CO_2 production and O_2 consumption. Massive vasodilation increases pulmonary shunt fraction, worsening hypoxemia that can develop into full pulmonary edema. However, this phase is short-lived and progresses to a catabolic state. At this stage, patients are at high risk for developing infections, with pneumonia being the most common.
3. The effects of the inhalation injury on the tracheobronchial tree and the lungs lead to edema, bronchospasm, and buildup of secretions. Different degrees of ARDS usually follow lung burn injury. When the burn circumferentially surrounds the chest, a mechanical constriction can develop, worsening chest and respiratory system compliance.

Specific Concerns

Burn-injured patients with an inhalation injury are at significantly increased risk for morbidity and mortality. Inhalation injury can complicate 20% of burn patients, and these patients often present with facial burns. Patients presenting with facial burns, burnt nasal hairs, soot in the oral and nasal pharynx, and any signs of upper airway burns should be immediately intubated, because serious airway obstruction developing over time is almost inevitable. On admission, it is difficult to identify characteristic radiographic features of inhalation injury. The effects become evident over time only when secondary complications such as inflammation, infection, or atelectasis develop. For this reason, the respiratory status and the airway patency of burn victims should be continuously monitored; they are at high risk for developing airway obstruction if an artificial airway is not already in place. Securing the airways as soon as possible should be the priority before catastrophic, irreversible airway obstruction occurs. One of the challenges in the respiratory care of severely injured burn patients is the clearance of copious and tenacious secretions. Secretions are accumulating throughout the tracheobronchial tree as a result of increased mucus secretion, buildup of toxic debris and necrotic cells, and peribronchial inflammatory **exudates** and **transudates**. In addition, mucociliary transport is severely impaired by disrupted tracheal-bronchial epithelium causing small airway plugs, worsening alveolar collapse, and predisposing to pulmonary infections. Optimization of airway humidification, careful ETT suctioning, and bronchoscope toilette are milestones of daily respiratory care for these particularly vulnerable patients.[45–47]

RULE OF THUMB Burn-injured patients with an inhalation injury have a significantly increased risk for morbidity and mortality.

Respiratory Management

Respiratory care of burn patients is complex. Hemodynamics, fluid resuscitation, %TBSA involvement and related injuries, time from the injury, and upper and lower respiratory conditions

are some of the key elements that the RT needs to know while caring for these patients.

Oxygen Therapy

The SaO_2 of burn patients has to be monitored continuously. Until proven otherwise, all victims rescued from a fire should be treated with O_2 for suspected cyanide and CO poisoning. Cyanide poisoning is treated pharmacologically. The RT should monitor continuously the level of MetHb in the blood, especially if cyanide is treated with nitrite donors. Methylene blue should be administered if levels of MetHb become symptomatic. CO poisoning treatment is focused on dislodging CO from the hemoglobin. Administering a high concentration of inspired O_2 through a nonrebreathing mask is mandatory in these patients because O_2 shortens the half-life of CO. When available, a hyperbaric chamber is used in the treatment of the most severely CO poisoned burn patients; CO is quickly dissociated from hemoglobin and **cytochrome oxidase**. Hyperbaric O_2 at three times atmospheric pressure reduces the half-life of CO to approximately 3 minutes, compared with 74 minutes for regular 100% O_2 through a nonrebreather mask. It also may reduce cerebral (and other organ) tissue ischemia by increasing O_2 transport in plasma to the brain.[48,49]

RULE OF THUMB Patients presenting with facial burns, burnt nasal hairs, soot in the oral and nasal pharynx, and any signs of upper airway burns should be immediately intubated, because the development of serious airway obstruction developing over time is almost inevitable.

Early Endotracheal Intubation

In these patients, early endotracheal intubation is generally recommended for four reasons: (1) protection of the airways from the risk for occlusion secondary to mucosal and interstitial edema, (2) the need for extensive pulmonary toilette by multiple bronchoscopies, (3) delivery of high fraction of inspired O_2 during CO poisoning, and (4) initiation of early lung-protective ventilation in patients at high risk for developing ARDS.

Flexible Bronchoscopy

Flexible bronchoscopy is often used in these patients for diagnostic and treatment purposes. Bronchoscopy is used in acute settings for clearance of foreign bodies from the airways, disrupted mucosa, and mucous debris that might cause hypoxemia by alveolar obstruction, collapse, and atelectasis (see Chapter 22). The copious and tenacious secretions and necrotic tissue often require multiple bronchoscopies over time. Clearance of the tracheobronchial tree has three purposes: (1) improving ventilation while avoiding $\dot{V}/\dot{Q}$ mismatch, (2) preventing bacterial overgrowth within the bloody-necrotic secretions and pneumonia, and (3) enhancing nebulized drug delivery that is commonly used in these patients (e.g., bronchodilators, antioxidants, and pulmonary vasodilators). Other uses of bronchoscopy in these patients includes inspection of injury and monitoring over time of major lesions and bronchoalveolar lavage for a microbiologic sample if pneumonia is clinically suspected.[50]

RULE OF THUMB Hyperbaric O_2 at three times atmospheric pressure reduces the half-life of CO to approximately 3 min, compared with 74 min for regular 100% O_2 delivered through a nonrebreather mask.

Active Humidification

Active humidification with heated humidifiers supplied by heated wire circuit should be used when possible. The aim of using continuous heated well-humidified ventilation is avoidance of mucus plugs in the distal airways and ETT while preventing body temperature loss.

Mechanical Ventilation

Mechanical ventilation should be titrated according to the underlying major respiratory condition of the patient (i.e., upper airway edema, lower airway injury, intoxication, ARDS, or pulmonary edema). In addition, the RT should be prepared to change ventilation management according to the rapid cardiovascular and respiratory changes of the patient's clinical course during hospitalization. A typical early pulmonary scenario is a combination of pulmonary edema resulting from the high rate of fluid infusion and distal atelectasis due to secretions and mucus accumulation. Often ARDS develops, complicating the multifactorial respiratory failure and worsening lung compliance and hypoxemia. An early protective lung ventilation approach with low V_T and high PEEP is especially advantageous in these patients. Neuromuscular blocking drugs are often beneficial to optimize low V_T ventilation (Box 30.10). In refractory hypoxemia, prone positioning and the use of inhaled pulmonary vasodilators might be considered an adjunct to respiratory treatment when feasible. The use of venovenous extracorporeal membrane oxygenation remains highly controversial in patients with extensive burns because of the risk for exsanguination. Early tracheostomy is often advocated because it improves secretion management by cough and suctioning, patient recovery by weaning from anesthetic medications, and wound care by patient collaboration.[51,52]

BOX 30.10 Mechanical Ventilation of Patients With Smoke Inhalation and Pulmonary Burns

- Mode: Pressure or volume ventilation
- Tidal volume: 4–8 mL/kg PBW
- Inspiratory time 0.6–1.0 s
- Plateau pressure: Less than 28 cm H_2O unless chest wall compliance decreased
- If compliance decreased, plateau pressure should exceed 28 cm H_2O
- Measure end inspiratory transpulmonary pressure to determine acceptable plateau pressure
- Driving pressure equal to or less than 15 cm H_2O
- Rate only limited by the development of auto-PEEP
- Minute volume to maintain normal $PaCO_2$
- PEEP 5–10 cm H_2O, unless ARDS
- FiO_2 1.0 initially because of concern for CO poisoning
- If ARDS, manage as any other ARDS patient

ARDS, Acute respiratory distress syndrome; *PBW*, predicted body weight; *PEEP*, positive end expiratory pressure.

MINI CLINI

Burn: Recognizing Hypoxemia in Patients After a Fire and Titrating Ventilation

Problem

A 55-year-old firefighter presents at the hospital with second- and third-degree burns on the front and back of the torso, on both arms and first-degree burns on the face after the successful rescue of an entire family from their burning house. The patient is 6 feet, 2 inches, and 240 lb. During transport to the hospital, he was intubated with an 8.0-mm ETT for increased shortness of breath and changes in mental status. Breath sounds are audible bilaterally. Ventilator settings are pressure support ventilation 15, PEEP 5 cm H_2O, and FiO_2 0.5. The patient's vital signs are heart rate 110 beats/min, blood pressure 90/50 mm Hg, respiratory rate 30 breaths/min, and SpO_2 98%. Endotracheal suctioning shows moderate dark/black secretions. The medical team started fluid resuscitation at a rate of 1 L/h of normal saline. An arterial line was placed in his right radial artery, and the medical team has been struggling for the past half hour in the emergency room to place a central line. His SpO_2 has declined to 92%, but the other vital signs are unchanged. What should the RT do?

Solutions

Immediately confirm ETT positioning by auscultation of bilateral breath sounds and suggest a chest X-ray to the medical team if it was not requested already. Confirm by ETT suctioning the dark/black secretions in the airways, which imply a severe inhalation burn and cyanide poisoning.

Obtain a blood gas sample as soon as possible to rule out CO poisoning and evaluate metabolic acidosis. It is imperative to perform a blood gas analysis as soon as possible in any burn patient with a TBSA greater than 25% admitted to the ED even when SaO_2 is 99% to 100%. It might be a falsely high reading because of MetHb and COHb. The blood gas analysis should include PaO_2, MetHb, COHb, $PaCO_2$, pH, anion gap, lactate, and base excess. If available, noninvasive continuous monitoring for MetHb and COHb should be applied to trend MetHb and COHb values and evaluate response to treatment.

This is a critically ill patient with extensive and severe burns with TBSA 58.5% (front and back torso, both arms, face), second- and third-degree burn, and inhalation injury with an ongoing massive fluid resuscitation requirement. Ventilator settings should be titrated according to the clinical scenario; however, the following should be recommended: (1) increase FiO_2 up to 100% until the presence of CO and cyanide poisoning has been ruled out; (2) increase minute volume ventilation, avoiding increased V_T and mean airway pressure to minimize effects of metabolic acidosis; (3) titrate PEEP by performing a best PEEP trial. This patient most likely will develop pulmonary edema due to inflammation and fluid resuscitation and ARDS due to inhalation injury.

SUMMARY CHECKLIST

- In trauma patients, careful assessment for injuries of the head, neck, upper airway, and chest should occur immediately on presentation.
- Obese patients are at significant risk for cardiovascular disease. In addition, lung volumes are generally decreased, with atelectasis and airflow limitation that can result in air trapping and auto-PEEP. High levels of PEEP are frequently required.
- Near-drowning victims frequently have aspirated foreign material and present with significant pulmonary edema and electrolyte imbalances.
- Patients with smoke inhalation and pulmonary burns require careful assessment of their airways. Any clinical signs of upper airway injury generally require immediate intubation and mechanical ventilation.
- Chest trauma frequently results in injuries that cause disruption of major vessels and the development of tension hemothorax or pneumothorax.
- All obese patients should be assessed for sleep apnea and OHS.
- Freshwater drowning frequently results in hyponatremia, hemolysis, hyperkalemia, and ventricular fibrillation. Salt water drowning frequently results in marked pulmonary edema, hemoconcentration, hypernatremia, and hypoalbuminemia.
- Respiratory assessment of burn patients should focus on percent of TBSA, degree of tissue involvement, and inhalation of toxic gases.
- In general, gas exchange abnormalities in trauma victims are a result of disruption of the chest wall and pulmonary contusion.
- In general, gas exchange abnormalities in obesity are a result of low lung volumes and the development of atelectasis.
- In general, gas exchange abnormalities in near drowning are a result of fluid shifts and the activation of inflammatory mediators.
- In general, gas exchange abnormalities in burns are a result of burns to the lung parenchyma and inhalation of foreign materials and toxic gases, specifically CO and cyanide.
- O_2 therapy is immediately indicated in the management of near drowning and pulmonary burns. Obese patients and trauma victims require O_2 therapy based on the severity of the patient's clinical presentation.
- Noninvasive ventilation is primarily indicated in the management of patients with sleep apnea, patients with OHS, and trauma patients with unstable chest walls.
- Invasive mechanical ventilation can be indicated in all four settings based on the severity of the injury.
- The primary concern during mechanical ventilation to trauma patients is the presence of a tension pneumothorax and hemodynamic instability.
- The primary concern with the application of mechanical ventilation to obese patients is the appropriate selection of V_T (based on PBW) and the appropriate application of PEEP.
- Near-drowning victims and pulmonary burn patients frequently and rapidly develop ARDS.
- In all four categories of patients, lung-protective mechanical ventilation should be used from the onset of mechanical ventilation.
- PEEP and lung recruitment maneuvers should be applied to the markedly obese patient and any patient who develops ARDS unless contraindicated. Prone positioning should be considered early in near-drowning patients and any patient

with refractory hypoxemia unresponsive to the lung recruitment maneuvers and the setting of PEEP by a decremental trial.
- Spontaneous breathing trials are the primary approach to liberation from ventilatory support for all of these patients.

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31

Acute Heart Failure

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CHAPTER OBJECTIVES

- To identify the epidemiology, causes, symptoms, and major therapies for acute heart failure (AHF);
- To appreciate lifesaving treatment for the most severe cases of heart failure and the role of intensive care in the treatment of these patients
- To learn to assess heart–lung interaction and realize the potential beneficial effects of ventilator therapy on the diseased cardiovascular system
- To appreciate the role of continuous positive airway pressure (CPAP) or noninvasive mechanical ventilation (NIV) as the most effective respiratory rescue therapies to treat respiratory failure during AHF
- To assess readiness and criteria for initiating CPAP and NIV, to list risk factors for failure of the latter, and to consider alternatives including invasive ventilation strategies when these rescue therapies fail
- To understand the monitoring of CPAP and NIV in patients with respiratory distress and appreciate that time at the bedside and knowledge of ventilator parameter adjustment is essential for the optimal delivery of these treatments
- To appreciate that sedation represents a therapeutic option but that it requires close monitoring.

CHAPTER OUTLINE

KEY TERMS

acute coronary syndrome (ACS)
cardiorenal syndrome
diuretic
heart failure
hypoperfusion
inotropic support
left ventricular heart failure
mechanical support
preload
pulmonary edema
right ventricular heart failure
systemic vasodilation

DEFINITION, EPIDEMIOLOGY, AND BURDEN OF CARE

Acute **heart failure** (AHF) is defined as a new onset or rapid worsening of cardiac output, leading to inadequate perfusion to meet the metabolic needs of body organs. The onset and severity of symptoms of AHF vary and depend on the nature of the underlying cardiac disease and the rate at which the syndrome develops.[1] In more economically developed countries, the most frequent cause of decompensated heart failure is myocardial infarction (MI). Between 20% and 40% of hospitalized patients with a diagnosis of MI develop AHF. The most common causes of new-onset AHF are summarized in Box 31.1.

AHF is one of the most frequent causes of unscheduled hospital admissions and high postdischarge readmission rates[2]; it is also associated with significant early and late morbidity and mortality.[3,4] A great proportion of patients admitted for AHF are diagnosed for the first time with underlying chronic HF. The 30-day mortality rate ranges from 8% to 16%, depending on patient age.

RULE OF THUMB Although primarily a cardiac disease due to inadequate blood circulation, AHF leads to a systemic disorder affecting all vital organs: the two predominant mechanisms of organ dysfunction are congestion and hypoperfusion.

PATHOPHYSIOLOGY OF ACUTE HEART FAILURE

Different classifications of AHF have been proposed based on both etiology and clinical presentation.[5] This chapter describes AHF according to the pathophysiologic characteristics that are common with any clinical cause of AHF.[6-8] AHF is responsible for a variety of symptoms that arise whenever the cardiac muscle loses its contractile force to a point where it is no longer able to maintain adequate cardiac output and blood pressure. The reduction in blood pressure triggers a catecholaminergic response aimed at improving cardiac function by increasing both the heart rate and the contractility of the remaining functional muscle tissue. Over time, both compensatory mechanisms further aggravate heart failure. Generally both the right and left ventricles are involved in the sequelae. Due to ventricular interdependence, the declining function of one ventricle may worsen the function of the other. Of note, although left ventricular dysfunction is more common, right ventricular dysfunction is predominant in patients affected by chronic lung diseases such as chronic obstructive pulmonary disease, interstitial lung disease, or pulmonary hypertension. Although AHF is primarily a cardiac disease due to inadequate blood circulation, it eventually becomes a systemic disorder affecting all vital organs. The two predominant mechanisms of organ dysfunction are congestion and **hypoperfusion**.

Congestion is the consequence of a reduced ventricular ejection fraction, which leads to increases in volume and pressure within the cardiac chambers, ventricles, atrium, and beyond.[9] Blood stasis in the venous system upstream from the failing ventricle causes increases in capillary pressure and the extravasation of plasma from the vascular space into the tissues. **Pulmonary edema** is one of the main clinical manifestations of **left ventricular AHF** (LV-AHF) and affects up to 15% of patients as the first manifestation of AHF. Increased interstitial and pleural fluid retention causes a decrease in pulmonary functional residual capacity, thus both decreasing lung compliance and increasing shunt fraction. Patients classically experience a sudden sensation of suffocation and air hunger, accompanied by extreme anxiety, cough, and the expectoration of a pink foamy liquid. As a consequence, patients place themselves in the upright sitting position and become unable to speak a full sentence. Their respiratory rate is increased, and signs of increased work of breathing are present: inspiratory retraction of the intercostal spaces and supraclavicular fossae are common. Usually inspiratory and expiratory rhonchi, wheezes, and fine crepitant rales are audible bilaterally, increasing in a craniocaudal direction. There is also hypoxemia, which may lead to an alteration of consciousness as well as signs of increased adrenergic tone (sweating, cold skin, etc.). When valvular abnormalities and/or mechanical complications after MI result in AHF, the murmurs of mitral and aortic regurgitation and ischemic ventricular septal defect are often audible. The chest x-ray may show cardiomegaly and signs of interstitial/alveolar edema.

Right ventricular AHF (RV-AHF) involves similar pathophysiologic mechanisms: venous congestion represents the main pathologic dysfunction, causing edema of the liver, splanchnic organs, and lower limbs. The size of the liver and ascites can serve as parameters for evaluating the severity and progression of RV-AHF. The presence of systemic hypoperfusion depends on the ability of the left heart to compensate for the decreased left-sided venous return. Pulmonary congestion and dyspnea are usually absent. However, due to ventricular interdependence, progressive RV failure leads to remodeling and displacement of the interventricular septum, with consequent LV diastolic and subsequent systolic dysfunction. End-stage RV-AHF causes

BOX 31.1 Causes of New-Onset Acute Heart Failure

Coronary Artery Disease
Acute coronary syndrome
Myocarditis

Acute Valve Syndromes
Acute mitral or aortic regurgitation
Thrombosed mechanical aortic or mitral valve

Progressive Valve Disease
Severe aortic or mitral valve stenosis
Severe aortic or mitral regurgitation

Cardiomyopathic States
Hypertrophic cardiomyopathy
Recent-onset dilated cardiomyopathy
Tachycardia mediated cardiomyopathy
Stress cardiomyopathy
Poorly controlled hypertension

LV-AHF, leading to biventricular failure with pulmonary edema (LV-AHF) and hypoperfusion of the distal organs (RH-AHF).

RULE OF THUMB Dyspnea secondary to *pulmonary* congestion is the main symptom in patients with LV-AHF. In patients with RV-AHF, however, *venous* congestion leads to the main symptoms of ascites, an enlarged liver, engorgement of the splanchnic organs, and edema of the lower limbs.

A rare and different clinical presentation can result from AHF due to high-output heart failure; it is commonly characterized by pulmonary congestion, tachycardia, wide pulse pressure, and warm extremities. Common causes of high-output AHF are anemia, thyrotoxicosis, advanced liver failure, and skeletal conditions such as Paget disease.

Hypoperfusion is the consequence of reduced cardiac output and of compensatory mechanisms to maintain vital organ perfusion. To cope with the reduced blood pressure due to the decline in cardiac output, the cardiovascular system increases adrenergic tone by increasing heart rate and vasoconstriction. This mounting stress on the ischemic heart causes a further increase in myocardial oxygen consumption and decreased myocardial perfusion by decreasing diastolic time and increasing myocardial wall stress (Fig. 31.1). When the heart fails to maintain adequate organ perfusion, cardiogenic shock commences, which is the most severe form of AHF. Cardiogenic shock is defined as prolonged hypotension, with systolic blood pressure (sBP) usually less than 90 mm Hg and/or a requirement for vasopressor agents to maintain sBP above 90 mm Hg in the absence of hypovolemia and signs of hypoperfusion (e.g., cold periphery or clammy skin, confusion, oliguria, elevated serum lactate).

MEDICAL MANAGEMENT OF ACUTE HEART FAILURE

In the first hours after emergency department (ED) admission, patients with AHF are at high risk for complications, including death. Indeed, patients with AHF may die in the ED before advanced treatment can be instituted in the intensive care unit (ICU).[10] Early diagnosis, triage, and the initiation of specific treatment for AHF are associated with reduced mortality as well as a shorter length of hospital stay. Rapid identification of the precipitating factor for AHF, especially if reversible (e.g., **acute coronary syndrome** [ACS]), is essential for the early initiation of specific treatments. The following stepwise approach to the management of AHF patients has been shown to be useful.[11]

RULE OF THUMB Once a diagnosis of AHF has been obtained, supportive therapies should be instituted and treatment initiated without delay.

Identifying Respiratory Distress and Hemodynamic Instability

Immediate identification of patients at higher risk of complications is associated with improved survival. Altered vital signs (heart rate, arterial pressure, respiratory rate, and peripheral oxygen saturation) together with symptoms of AHF on physical examination (respiratory distress, cool extremities, increased capillary refill time, and altered mental status) should promptly identify patients who are in need of higher-intensity care and transfer to a cardiac ICU.

Confirming the Diagnosis of Acute Heart Failure

Table 31.1 lists parameters for assessing and monitoring of heart function and hemodynamics during AHF. AHF is a clinical diagnosis based on the presence of a constellation of symptoms and signs. Respiratory fatigue is the most common cause of ED presentation in patients with AHF. Fatigue, dizziness, palpitations, and increased body weight with peripheral edema, together with decreased diuresis, are also common manifestations. Clinical examination should investigate the presence of signs of both pulmonary (increased respiratory efforts and abnormal lung sounds) and systemic congestion (increased jugular venous pressure, hepatomegaly, and peripheral edema). Signs of hypoperfusion should be sought as well (cold extremities, slow capillary refill time oliguria/anuria). A detailed history should be obtained

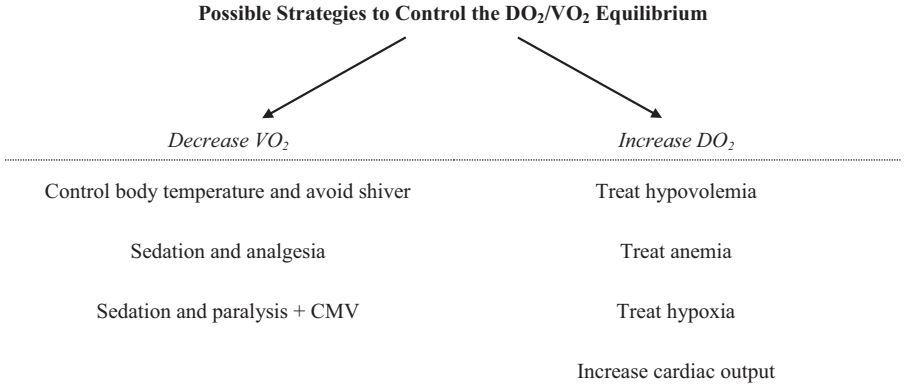


Fig. 31.1 During acute heart failure, the ultimate therapeutic goal is to maintain an energetic balance in favor of oxygen delivery *(DO_2)* versus oxygen consumption *(VO_2)*. This figure illustrates the potential therapeutic strategies aimed at improving the DO_2/VO_2 equilibrium. *CMV,* Controlled mechanical ventilation.

TABLE 31.1 Assessment and Monitoring of Heart Function and Hemodynamics During Acute Heart Failure

	Parameter	Monitoring	Explanation
Contractility	Ejection fraction	Echocardiography	Ventricular systolic emptying
	TAPSE/MAPSE		Valvular plane systolic motion
Fluid responsiveness	PPV/SVV	Arterial line	Pulse pressure/stroke volume Inspiratory excursion
Organ perfusion	Serum lactate	Blood test	Tissue anaerobic metabolism
	Urine output	Diuresis	Renal perfusion
	$SmvO_2/ScvO_2$	Central line/PAC	Tissue oxygen extraction fraction
Heart performance	Cardiac output	PAC or Calibrated pulse contour analyzers	Thermodilution
Preload	PCWP	PAC	Volumetric or pressure evaluation of cardiac preload
	GEDV	PiCCO system	
	Atrial/ventricular size	Echocardiography	
	IVC collapsibility	Echocardiography	
Afterload	SVR	CVP and mAP	Systemic and pulmonary cardiac afterload
Left ventricular	PVR	CVP and mPAP	
Right ventricular			

CVP, Central venous pressure; *GEDV,* global end-diastolic volume; *IVC,* inferior vena cava; *mAP,* mean arterial pressure; *MAPSE,* mitral annular plane systolic excursion; *mPAP,* mean pulmonary artery pressure; *PAC,* pulmonary artery catheter; *PCWP,* pulmonary capillary wedge pressure; *PiCCO,* pulse contour cardiac output; *PPV,* pulse pressure variation; *PVR,* pulmonary vascular resistance; *$ScvO_2$,* oxyhemoglobin central venous saturation; *$SmvO_2$,* oxyhemoglobin mixed venous saturation; *SVR,* systemic vascular resistance; *SVV,* stroke volume variation; *TAPSE,* tricuspid annular plane systolic excursion.

to guide the differential diagnosis: previous diagnoses of HF or prior history of coronary artery disease increase the probability of an AHF diagnosis. Plasma natriuretic peptides can be used both as adjunctive confirmation of AHF and to assess its severity. Low levels of either BNP or NT-proBNP should exclude the diagnosis of AHF; high plasma natriuretic peptides levels should identify the most severe cases.[12,13] Plasma lactate levels help to identify early cases with worsening AHF moving toward cardiogenic shock.[14]

Identifying the Causes of Acute Heart Failure

It is imperative to rapidly identify the cardiac causes of shock. A 12-lead electrocardiogram (ECG) should be obtained as early as possible. In the presence of ST-segment elevation myocardial infarction (STEMI), or non-STEMI with hemodynamic instability or persistent chest pain, transfer to the cardiac catheterization laboratory for primary revascularization is mandatory.[15]

After an ACS has been excluded, echocardiography should be done as soon as possible to exclude either cardiac tamponade or other mechanical cause of AHF and to further characterize left and right ventricular function. Pulmonary embolism should always be considered in the differential diagnosis of patients with signs of RV-AHF.

Assessing Organ Injuries

Serum troponin (T or I) levels should be obtained in any patient with possible ACS.[16] Increased levels of serum creatinine and blood urea nitrogen from before the acute event of AHF are the main criteria for the diagnosis of **cardiorenal syndrome**. In general, decreased renal function is commonly found in patients with advanced HF. Either chest x-ray or lung ultrasound can be helpful in characterizing the degree of bilateral alveolar edema. The presence of unilateral pulmonary changes should challenge the AHF diagnosis. Pleural effusion might be present but is infrequent in patients with a primary diagnosis of AHF. Liver dysfunction might be present, leading to high suspicion of right-sided heart failure. A complete blood count may help to identify the presence of infection or anemia, which may have precipitated the event.

The goal of AHF treatment is to restore adequate oxygen delivery, which is often achieved by improving perfusion pressure. Together with cardiac function and hemodynamics, distal organ function is also closely monitored. Treatment and monitoring varies according to the level of acuity and the patient's cardiac reserve. The next section of the chapter provides a detailed discussion of cardiovascular monitoring and treatment, as well as respiratory implications and treatment during AHF.

MONITORING AND ASSESSMENT OF CARDIAC FUNCTION

Monitoring of a patient with AHF is generally initiated at admission in the ED, but the level of monitoring can vary widely depending on the severity of cardiac decompensation.[17]

Hemodynamics

In the acute phase of AHF, adequate titration of vasoactive and antihypertensive drugs is commonly used to obtain adequate blood pressure and ensure coronary and distal organ perfusion while avoiding an excessive workload for the failing heart. In patients with cardiogenic shock, invasive measurement of arterial pressure is preferred. The arterial line allows obtaining serial blood gases and lactate levels to assess the effect of the

interventions performed on distal organ perfusion and oxygenation. Measurement of serum lactate levels in response to therapeutic intervention is suggested to determine improvement or worsening of tissue hypoperfusion.[18]

RULE OF THUMB The level of cardiac and hemodynamic monitoring increases according to the severity of impaired cardiac function.

Normovolemia and adequate perfusion pressure are regularly assessed. In mechanically ventilated patients, a wide variation of pulse pressure throughout a breathing cycle is considered an index of fluid responsiveness, or the heart's ability to increase cardiac output in response to a fluid load.

Unstable patients are given higher-intensity monitoring, measuring cardiac output either through a pulmonary artery catheter or other calibrated system (pulse contour cardiac output [PiCCO]). Uncalibrated systems measuring cardiac output may provide incorrect information in this setting. The measurement of cardiac output allows (1) direct measurement of the effect on cardiac performance of the therapies undertaken; (2) measurement of systemic vascular resistance, calculated as mean arterial pressure–central venous pressure divided by the cardiac output; and (3) for obtaining an estimate of cardiac **preload** either via a variation in wedge pressure or the global end-diastolic volume.[19] Fig. 31.2 exemplifies how information from advanced hemodynamic monitoring can be integrated. The use of a pulmonary artery catheter (PAC) may be indicated in patients with right heart failure to target interventions on pulmonary arterial pressure,[20,21] and the venous mixed hemoglobin oxygen saturation can be used as an index of the severity of organ hypoperfusion.[22,23] However, recent trials caution regarding the use of a PAC to determine a hemodynamic endpoint in patients with shock.[24] Whenever infusion of a vasopressor is indicated, a central venous line should be established in order to have a dedicated line for the infusion of vasoactive drugs.

Blood Tests

Serial blood tests are indicated to assess organ function—specifically hepatic and renal function. Adequate blood oncotic pressure should be maintained (serum albumin level), as should hemoglobin levels to ensure tissue perfusion and oxygen delivery.

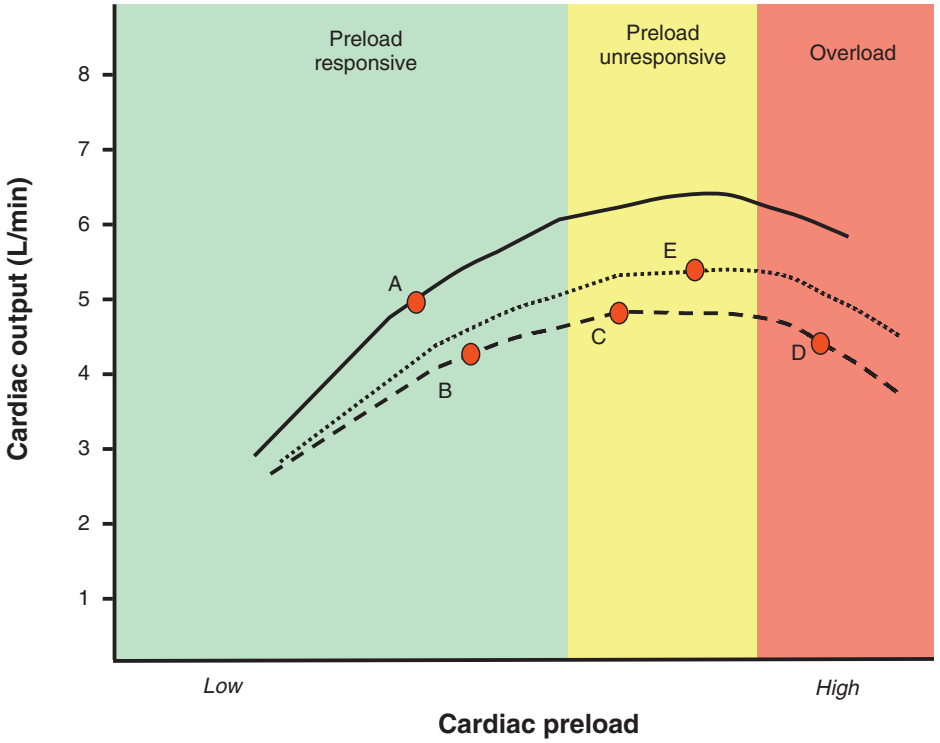


Fig. 31.2 A clinical case of acute heart failure illustrating the Frank-Starling relationship of preload to cardiac output. This figure illustrates the relationship between cardiac preload (right atrial pressure, pulmonary capillary wedge pressure, global end-diastolic volume, left ventricular end-diastolic volume) and cardiac output. The solid line represents a normally functioning myocardium *(A)*, when, despite the cause, heart function exacerbates decreases in cardiac output congestion and leads to an increase in cardiac preload *(B)*. preload increases, cardiac output may also increase *(C)* until further worsening is observed *(D)*. Various strategies *(E)* can improve heart function and decrease cardiac afterload (i.e., systemic vasodilators, intra-aortic balloon pump), decrease congestion (i.e., diuretic therapy), and improve myocardial performance (either through inotropic support or by addressing the primary heart disease). (From Guyton AC, Jones CE, Coleman TG: *Circulatory physiology: cardiac output and its regulation*, Philadelphia, 1973, W.B. Saunders.)

Whenever along the course of treatment further worsening of cardiac function occurs, an ischemic event should be suspected. In this setting, serial troponin measurements are indicated.

Monitoring of plasma electrolytes is indicated in patients receiving large-volume fluids and **diuretic** therapy: hypophosphatemia may be responsible for decreased cardiac inotropism, hypokalemia is associated with arrhythmias, diuretic therapy (particularly furosemide) may cause metabolic alkalosis, hyponatremia can occur in patients with the syndrome of inappropriate antidiuretic hormone (SIADH) due to stress, and hypernatremia is frequently seen in cases of fluid overload and secondary hyperaldosteronism.

Concurrent infections are not rare. Thus blood tests for total white blood count, C-reactive protein, and procalcitonin may be used as a guide either to trigger an infectious disease consult or the withdrawal of antibiotic therapy.

Fluid Balance and Weight Change

Because the kidneys are highly sensitive to hypoperfusion, close monitoring of a patient's diuresis is a simple but effective parameter for assessing peripheral perfusion. Diuretic therapies may represent a confounder; thus volume loss over time should be compared in similar conditions.[25]

Although the early phases of AHF are usually characterized by a positive fluid balance and increases in weight, as soon as cardiac function has improved as a consequence of therapeutic interventions, a negative fluid balance should be targeted with a progressive decrease in body weight.

Daily planning of fluid and salt input and monitoring of 24-hour urinary electrolytes and urine output should guide diuretic therapy. Transition from intravenous fluids to enteral water intake is suggested to avoid large infusions of intravenous saline solution, which favors water retention.

Electrocardiography

Daily performance of a 12-lead ECG and following any significant modification of the patient's clinical status is suggested to identify myocardial ischemia. Continuous monitoring of heart rate is required to identify cardiac arrhythmias in hemodynamically unstable patients.

Echocardiography

Noninvasive cardiac imaging obtained through both transthoracic and transesophageal ultrasound is now widely recognized as an essential exam both for monitoring cardiac function at the bedside and for the diagnosis of acute changes in cardiac performance. Due to its user-friendly characteristics, echocardiography has become a point-of-care exam available at any time at bedside in most modern hospitals.[26]

Specifically, in the case of AHF due to myocardial ischemia, echocardiography can often identify areas of reduced and/or absent wall motion and contractility in the left and right chambers of the heart. Ventricular interdependence can be investigated by analyzing the shape of the interventricular septum and its movement during the cardiac cycle.

Several parameters are usually adopted to describe heart function: first an accurate description of cardiac morphology (e.g., wall thickness, chamber size) should be reported and valvular defects or intracardiac shunt, if present, should be explored;[27] ventricular ejection fraction, defined by the ratio between the volume ejected during systole and the ventricular volume at the end of the diastole, is the parameter that is commonly used to describe cardiac systolic performance. To investigate the function of the right and the left ventricles, the tricuspid and mitral annular plane systolic excursions (TAPSEs and MAPSEs, respectively) are measured. Diastolic function is expressed as the ratio between the blood flow velocity during early passive diastole and during active atrial contraction. Whenever ventricular filling relies on the presence of atrial contraction, diastolic dysfunction is present.[28] The patient's volumetric status can also be assessed by echocardiography and analysis of variations in the inferior vena cava's diameter during the respiratory cycle. Last, during an emergency, echocardiography has a role in ruling out cardiac tamponade and pulmonary embolism.

Coronary Angiography

The direct imaging of coronary arteries represents an invasive diagnostic exam that should be reserved for cases with suspected active cardiac ischemia.[29] Some lesions identified by coronary angiography may be treated directly (reperfused) by coronary angioplasty and stent positioning. Many modern tertiary care centers have ad hoc 24/7 cardiac catheterization laboratories to guarantee the timely treatment of myocardial ischemia. Whenever intravascular treatment is not an option, the patient should be quickly referred to cardiac surgery.

Cardiac Computed Tomography and Heart Magnetic Resonance Imaging

Most modern cardiac imaging techniques, such as synchronized computed tomography or magnetic resonance imaging, have been found to have a diagnostic role in unveiling rare cardiac diseases underlying HF (i.e., myocardial amyloidosis, neoplasm) as well as in monitoring the evolution of disease (i.e., myocardial fibrosis and remodeling). However, as yet, advanced cardiac imaging has not been found advantageous in the emergent management of AHF.

Lung Imaging

Since lung function is highly sensitive to cardiac performance, congestion due to left heart failure directly determines lung interstitial edema and eventually alveolar edema. The chest x-ray (CXR) provides highly sensitive but not specific information regarding lung edema. During AHF, pulmonary edema appears as a bilateral, bibasilar (gravity dependent) infiltrate (Fig. 31.3). Although a single lung CXR might be poorly informative, a series of such x-ray images over the course of treatment is likely to be more informative.[30]

Although in the past the lung has been commonly considered "inscrutable" to ultrasound, it is now common clinical practice to take advantage of ultrasound artifacts derived from ultrasound beam interaction with lung parenchyma to measure pulmonary features. Pulmonary edema is seen on lung echography as multiple (comet tail) B-lines whose number per field of observation is proportional to the degree of lung edema.[31] Pleural effusions

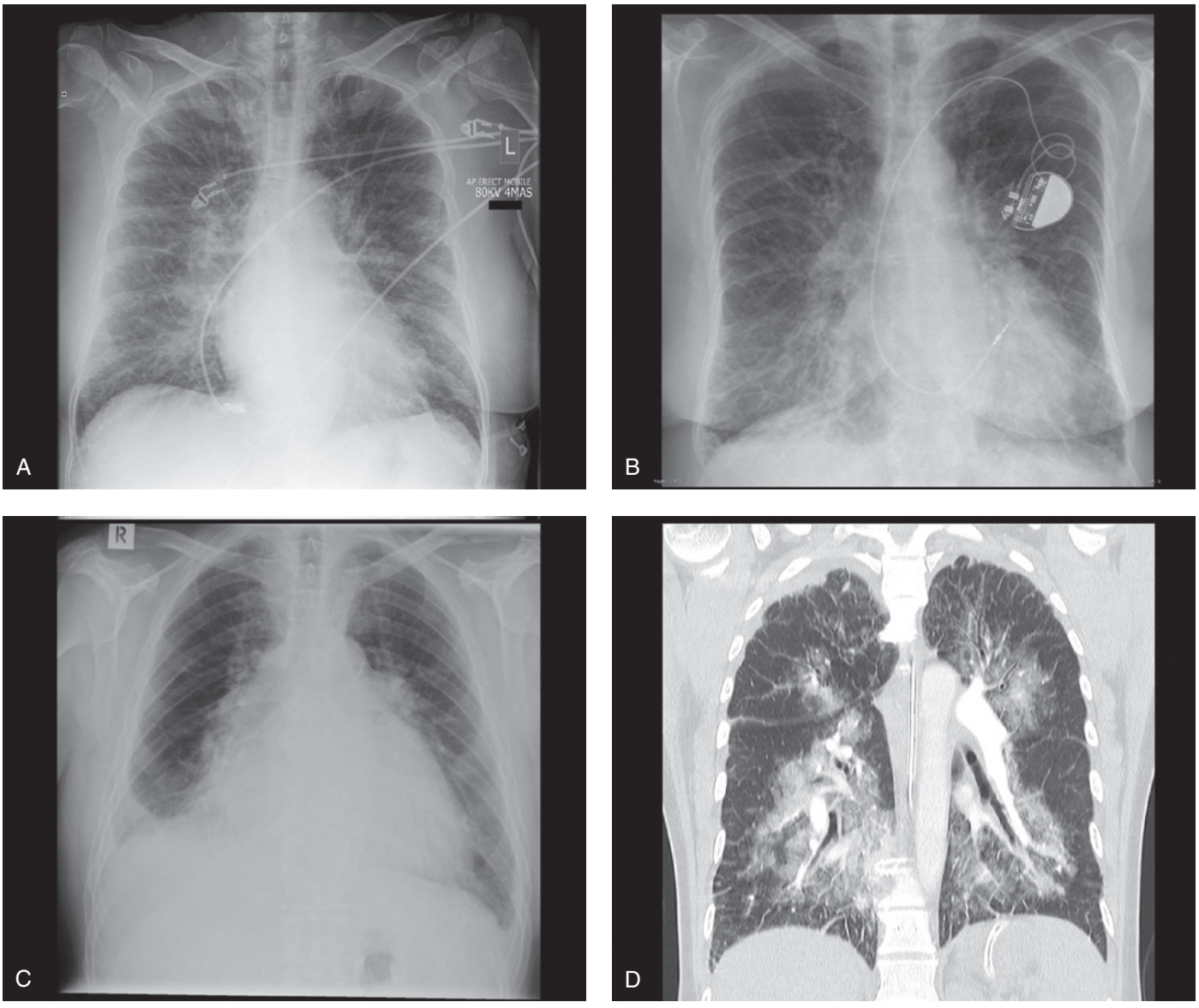


Fig. 31.3 Radiologic Images of Acute Pulmonary Edema During Acute Heart Failure. Radiography of the chest is the imaging technique most frequently used in patients admitted to the emergency department with an acute onset of dyspnea. It provides useful information to either confirm or exclude acute pulmonary edema and quantify the severity of the clinical presentation. Panel A *(upper left)* shows a mild degree of pulmonary edema characterized by increased interstitial markings throughout the lungs, vascular redistribution in the upper zone, and bilateral perihilar alveolar opacification. Panel B (upper right) is a representative case showing evidence of both interstitial (peripheral septal lines—Kerley B lines) and alveolar edema (confluent nodular opacities). Peripheral septal lines are due to thickening of the interlobular septa. It is also evident that the craniocaudal gradient in the distribution of edema is due to gravity. Panel C (lower left) is representative of bilateral pleural effusion (more pronounced in the right pleural cavity). Panels B and C are both characterized by increased size of the cardiac silhouette. Panel D (lower right) is a midthoracic chest computed tomographic image of acute pulmonary edema, which clearly illustrates the peribronchial cuffing effect. ([A] Case courtesy A. Prof Frank Gaillard," https://radiopaedia.org/cases/shenton-line-diagram. [B] Case courtesy Dr. Henry Knipe, https://radiopaedia.org/cases/acute-pulmonary-oedema-5. [C] Case courtesy A. Prof Frank Gaillard, https://radiopaedia.org/cases/acute-pulmonary-oedema-1. [D] Case courtesy Dr. Andrew Dixon, https://radiopaedia.org/cases/acute-pulmonary-oedema-on-ct.)

can be identified and easily quantified by lung ultrasound.[32] As for CXR, the degree of interstitial water retention is expected to follow a gravitational gradient; this feature helps in differentiating congestive heart failure from other causes of bilateral pulmonary infiltrates, e.g., as in acute respiratory distress syndrome (ARDS).

TREATMENT

Effective and comprehensive therapy in HF, targeting improving survival, should aim to both optimize cardiac mechanical status (decreasing preload and afterload) and prevent the excessive neurohumoral activation that can lead to myocyte dysfunction and cardiac remodeling.

In the acute setting, AHF therapy relies on the treatment of the cause of heart failure decompensation. Different pharmacologic and nonpharmacologic interventions may be adopted in order to relieve symptoms until definitive treatment can be established. Major advances in pharmacology over the past decade have decreased the mortality attributable to AHF by preventing cardiac remodeling. Most of the drugs involved are antihypertensive medications, including angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs), as well as agents used to control heart rate (i.e., β-blockers).

MINI CLINI

Acute Heart Failure: Establishing Initial Treatment in the Emergency Department

Problem

A 65-year-old man with a history of ischemic health disease is admitted to the ED for shortness of breath and chest pain. The 12-lead ECG performed during transport to the hospital showed an anterior lateral wall infarct (STEMI). On arrival at the ED the patient is in respiratory distress with preserved mental status, a respiratory rate 33 bpm, SpO_2 88%, blood pressure 135/97 mm Hg, and body temperature 36.8°C. Echocardiography confirms the presence of a hypokinetic anterolateral myocardial wall and absence of mechanical defects. An intravenous line is established to administer medical therapy (aspirin and nitrates) and to draw blood samples for lab analysis.

The ED medical team immediately transports the patient to the cardiac catheterization laboratory to perform primary angioplasty and arrange subsequent admission to the cardiac ICU for cardiac/respiratory monitoring and support. The respiratory therapist (RT) in charge is asked to set up the respiratory support necessary for the transport.

Management

On the patient's arrival at the cardiac ICU, the RT checks hiss vital signs: now SpO_2 is 93% with oxygen mask with reservoir at 10 L/min, respiratory rate is still 33 bpm, and blood pressure is 125/82 mm Hg. The RT asks for an arterial ABG, which shows respiratory acidosis (pH = 7.28 and $PaCO_2$ = 57 mm Hg). Mental status is preserved (Glasgow Coma Scale score = 15), but the patient complains of air hunger.

Noninvasive mechanical ventilation represents the first option to be tested, because oxygen therapy alone failed to relieve patient's respiratory distress and signs of respiratory failure remain present. The RT must explain to the patient that she is going to place a mask either on the patient's nose, mouth, or entire face and that communication would then be impaired but that this is necessary to improve ventilator function. An ICU ventilator is used, showing airway pressure and flow waveforms. The best-fitting interface is selected and bilevel positive airway pressure (BIPAP, or pressure support with positive end-expiratory pressure [PEEP]) is started with the following initial settings: FiO_2 60%, PEEP 5 cm H_2O, appropriate trigger level, pressure support 10 cm H_2O, and cycling-off criteria 40% of peak inspiratory flow. The rise time should be set as rapid as possible but avoiding airway pressure overshoot at the onset of inspiration. Expiratory flow should be checked to detect the presence of auto-PEEP. Air leakage should be addressed by adjusting mask fit, and/or inspiratory pressure or inspiratory ramp may decrease leak. After a few minutes of adaptation to the new ventilatory settings, vital signs should be checked and patient comfort and relief of air hunger assessed. Tidal volume and asynchrony should be monitored. It is essential to have the RT's assistance throughout transport and catheterization lab procedures to ensure the detection of problems and proper adjustment of ventilator settings. Continuous SpO_2 monitoring is mandatory.

PHARMACOTHERAPY

Vasodilators

The rationale for using **systemic vasodilation** during AHF is to decrease cardiac afterload by lowering systemic vascular resistance and reducing ventricular filling pressure by decreasing cardiac preload. In patients with mitral regurgitation (possibly due to left atrial dilation), lowering left ventricular afterload further favors effective stroke volume.

Hydralazine acts as a vasodilator by causing direct arteriolar smooth muscle relaxation; it demonstrates a benefit particularly in African-American patients.[33]

Nitrates, by releasing nitric oxide, act as both venodilators (at low doses) and arteriodilators (at higher doses), thus reducing cardiac preload and afterload.[34] Nitrate therapy represents an option particularly in the ED setting, given its rapid onset of action and effective improvement symptoms.[35] However, nitrates are contraindicated in cases of shock (sBP <90 mm Hg) and in patients with a history of clinically relevant mitral or aortic valvular stenosis. Caution should also be used in patients with suspected right ventricular failure due to the risk of reducing coronary perfusion pressure.[36]

Sodium nitropusside is a potent vasodilator with an extremely short half-life; this is useful in modulating of systemic vascular resistance in the critical care setting. A relevant side effect of sodium nitroprusside infusion is the generation of methemoglobinemia, the oxidized form of hemoglobin, which cannot transport oxygen and cyanide compounds. Use of sodium nitropusside should be limited to 24 to 48 hours to avoid methemoglobinemia.

Selective pulmonary vasodilators (i.e., inhaled nitric oxide) are indicated in selected cases of severe acute right ventricular failure due to pulmonary hypertension.[37,38]

The classes of drugs associated with the greater survival benefit in patients with cardiac failure are the ACEIs and ARBs.[39,40] Both these classes of antihypertensive drugs act by blocking the action of angiotensin II, a potent endogenous vasoconstrictor, either by lowering the production of angiotensin II or preventing its binding at the receptor site. An oral ACEI/ARB should be started once the patient is hemodynamically stable and without signs of acute kidney injury. Because initiation of these therapies is known to improve outcomes, it is recommended to start them prior to hospital discharge.

Similar to ACE inhibitors, β-blockers lower the action of catecholamines on myocardial tissue; they have been proven to reduce HF mortality regardless of the stage of disease.[41-43] By decreasing heart rate, β-blockers allow a slower relaxation, thus reducing diastolic dysfunction and increasing the time during which coronary perfusion occurs. However, they should be used cautiously, particularly in the acute phase of HF, where they have been documented to increase the risk of worsening the patient's clinical status. In patients on β-blocker therapy prior to hospitalization, withdrawal of therapy is indicated only if hemodynamic instability is present. Starting β-blocker therapy is suggested at low dosages and once euvolemia has been achieved.

Diuretics

Cardiorenal syndrome is present in 10% to 30% of patients with AHF,[44] and the severity of organ dysfunction indicates which

therapeutic approach would be most beneficial. Diuretics are frequently needed in the acute phase of AHF, and renal replacement therapy represents the ultimate therapeutic option, which may be needed in most severe cases.[45,46]

In patients with signs of congestion, administration of a challenge dose of diuretics should be attempted. Furosemide is the first-choice drug because of its venodilator and diuretic effects. Immediate symptom relief might be achieved by decreasing respiratory fatigue. The onset of diuresis typically occurs within 30 minutes, with peak diuresis achieved usually by 1 to 2 hours after intravenous administration. Repeated doses of furosemide should be carefully monitored to avoid rapid fluid and electrolyte shifts; in particular, levels of K^+ and Mg^+ should be monitored.[47] Continuous infusion of furosemide can be attempted to obtain a progressive fluid loss with a maximal dose of 800 mg over 24 hours.[48,49]

Vasopressin receptor antagonists have been proposed as adjunctive therapeutic options in patients with fluid overload and hyponatremia (serum Na^+ <120 mmol/L) despite water restriction and diuretic therapy.[50] The use of vasopressin receptor antagonists should be restricted to hospitalized patients, the duration should be time-limited, and, the drug should be avoided in patients with concomitant liver disease.

Randomized trials have demonstrated that spironolactone, an aldosterone antagonist with natriuretic properties, reduces mortality when included in the long-term management of selected patients with systolic HF while carefully monitoring serum potassium and renal function.[51-53]

Vasopressors and Inotropes

Inotropic and vasopressor support is indicated in patients with cardiogenic shock in order to support myocardial function and improve tissue perfusion. Intravenous inotropic agents such as dobutamine and/or milrinone may be required as temporizing measures in patients with severe left ventricular systolic dysfunction and low-output syndrome with diminished peripheral perfusion and end-organ dysfunction.[54] Duration of inotropic/vasopressor therapy should be limited to the shortest time required and its effects should be closely monitored until definitive therapy (e.g., coronary revascularization, mechanical circulatory support, or heart transplantation) is instituted or the acute precipitating problem has been resolved.

RULE OF THUMB Inotropic and vasopressor therapy should be guided by accurate assessment of cardiac preload and afterload together with the monitoring of cardiac function.

Among the available drugs, the two most commonly used are milrinone and dobutamine.

Milrinone is a phosphodiesterase inhibitor that increases cardiac contractility by increasing the concentration of cytosolic cyclic adenine monophosphate and decreases both afterload and preload by acting on the cyclic-guanosine monophosphate–nitric oxide pathway.[55] Because it does not act directly on β-receptors, milrinone is also efficacious in patients receiving β-blockers. The use of milrinone during AHF has been associated with an increased incidence of prolonged hypotension and atrial arrhythmias.[56]

Dobutamine is a sympathomimetic drug that increases cardiac inotropism by acting on the cardiac β1 receptors; it also causes modest vasodilation via β2 agonism.[57]

Other Drugs and Common Combinations of Drugs[58]

Levosimendan is a calcium-sensitizing agent with a duration of action of 24 hours after the drug is administered.[59] A patient-tailored approach aimed at maximizing organ perfusion may combine the inotropic effect of dobutamine/levosimendan and perfusion pressure optimized by concurrent norepinephrine infusion, to increase peripheral tone mediated by norepinephrine α1 agonism. Although dopamine has been proposed as a potential therapeutic agent combining both inotropism and vasoconstriction, it has become less popular due to its arrhythmogenic effect and the variability of patient response.[60]

Digoxin therapy represents a further therapeutic option that has been shown to decrease HF symptoms and hospitalization, thus improving quality of life but without a benefit in mortality.[61] Digoxin acts by inhibiting the Na-K-ATPase pump, thus reducing the intracellular concentration of sodium and increasing the gradient for intracellular calcium influx. The rise in intracellular calcium concentration increases myocyte contractility and contributes to digoxin's hemodynamic, neurohumoral, and electrophysiologic effects. Digoxin is not indicated for the primary stabilization of patients with an acute exacerbation of HF or whenever ejection fraction is preserved. Due to its narrow therapeutic range, careful titration is mandatory.

As discussed previously, continuous monitoring of the hemodynamically unstable patient is a cornerstone of the care of these patients. At the same time, continuous monitoring allows appropriate initiation, titration, and weaning of medications. For example, a worsening of cardiac output during inotropic therapy might be due to occlusion of the left ventricular outflow tract during systole; echocardiographic visualization of the left ventricular outflow tract enables the clinician to exclude the presence of dynamic obstruction.

Antiarrhythmic Treatment

Cardiac remodeling occurring in AHF, regardless of the baseline disease, can cause alterations in both the generation of cardiac pacing and in the conduction of electrical impulses through the myocardium. This pathophysiologic mechanism represents the substrate explaining the high incidence of malignant arrhythmias in AHF patients. Unfortunately, most of the pharmacologic agents available to either treat or prevent arrhythmic events have a negative inotropic effect, which limits their utility.[62]

In patients affected by diastolic dysfunction, the loss of an atrial contribution to ventricular preload severely decreases stroke volume. Atrioventricular resynchronization should be pursued either by pharmacologic or electrical cardioversion or catheter ablation.[63,64] Whenever the atrioventricular conduction system is irreversibly damaged, the positioning of a totally implantable pacemaker should be considered to guarantee an adequate heart rate and obtain atrioventricular synchronization.[65]

Anticoagulation

Venous thromboembolism prophylaxis—either mechanical (intermittent compression devices) or pharmacologic—is indicated in critically ill hospitalized patients due to the high risk for pulmonary embolism.[20] Specific indications for systemic anticoagulation, such as atrial fibrillation or previous thromboembolism, should be considered.

RULE OF THUMB Mechanical cardiovascular support devices represent either a bridge to transplantation or a destination therapy.

ALTERNATIVE INTERVENTIONS (OTHER THAN PHARMACOTHERAPY)

Mechanical Treatment

When medical therapy fails, **mechanical support** options such as the intra-aortic balloon pump, extracorporeal membrane oxygenation (ECMO), and ventricular assist devices (VADs; Fig. 31.4) should be considered.

The intra-aortic balloon pump is a long (approximately 15 cm) intravascular balloon introduced percutaneously and positioned in the midthoracic descendent aorta. The device is synchronized with the cardiac cycle and inflates during diastole, favoring coronary perfusion and further enhancing perfusion pressure and blood supply to distal organs. Deflation during late diastole causes a "vacuum effect," which decreases left ventricular afterload. Despite the pathophysiologic rationale, the application of an intra-aortic balloon pump during AHF shows a varying degree of success and is not currently recommended.[66,67]

Venoarterial extracorporeal membrane oxygenation (VA-ECMO) and VADs represent two possible alternatives designed to bridge patients either to recovery or to definitive treatments such as transplantation.[68-72] VA-ECMO (see Chapter 51 for details) is particularly indicated in cases of combined left and right ventricular heart failure. VADs are implantable mechanical pumps that help to pump blood from the ventricular to either the systemic or pulmonary circulation. VADs can be specifically left ventricular devices, right ventricular devices, or both. However, the most common type are the left ventricular VADs. Implantation of VADs and VA-ECMO should be done only in highly specialized centers due to the high level of care these procedures and these patients require.[73]

Surgical Treatment

A cardiac surgical consult should be obtained in all AHF patients with any of the following:

Presence of AHF secondary to coronary artery disease.

Presence of mechanical defects either due to valvular disease or wall/papillary muscle rupture requiring valvular repairs.

Requirement for miocardiectomy (i.e., the removal of part of the myocardium in hypertrophic disease)[74] and cardiomyoplasty (i.e., the transposition of an electrified skeletal muscle to surround the heart). Both treatments are potential interventions that are still being studied.

Candidates for heart transplant. The major limiting factors for the performance of cardiac transplantation are as follows: the shortage of suitable organs; management of the preoperative evaluation of the candidate for transplantation; the surgical procedure; and the postoperative follow-up, involving a multidisciplinary highly trained staff. Heart transplantation dramatically improves the quality of life of these patients, with a 5-year survival of about 70%. A survival longer than 20 years after heart transplantation has frequently been reported.[75]

MINI CLINI

Postcardiac Surgery Respiratory Failure

Problem

A 55-year-old obese (45 kg/m body mass index)[47] patient with history of unstable angina undergoes coronary bypass surgery for three-vessel disease. The procedure is performed on cardiopulmonary bypass in the absence of mechanical ventilation. When the cardiopulmonary bypass is removed at the end of surgery, the patient requires high doses of epinephrine (0.1 μg/kg per minute) to ensure adequate arterial blood pressure. Due to her hemodynamic instability, the patient remains sedated and intubated and is transported to the cardiac ICU.

Management

At arrival in the ICU, mechanical ventilation was set in volume-controlled ventilation 8 mL/kg ideal body weight, PEEP of 5 cm H_2O, respiratory rate of 12 breaths per minute, and FiO_2 100%. With this setting, the arterial blood gas analysis revealed profound hypoxemia (PaO_2 of 65 mm Hg) with modest mixed respiratory and metabolic acidosis (pH 7.32, pCO_2 of 48 mm Hg, and base excess of –6). The CXRs showed bilateral lung opacities. Due to worsening hemodynamic function (increasing adrenaline dosage with unstable arterial pressure levels), emergency transthoracic echocardiography was performed, showing a normally functioning left ventricle and dilated and hypocontractile right ventricle. A pulmonary artery catheter was placed in order to obtain a continuous measurement of right heart function. Cardiac output was 3.2 L/min, right atrial pressure was 15 mm Hg, pulmonary artery pressure was 42/24, and the pulmonary capillary wedge pressure was 10 mm Hg. Calculated pulmonary vascular resistance was about 500 dyne•s/cm^5. Recent surgery discourages the start of a VA-ECMO support due to the anticoagulation levels required, and medical management is preferred. Inhaled nitric oxide is started at 20 ppm while monitoring the levels of methemoglobinemia. Immediate improvement of hemodynamics is observed, with a drop in pulmonary artery pressure levels to 33/18 mm Hg, and cardiac output improved at 4.3 L/min with a slight increase in pulmonary capillary wedge pressure (PCWP) of 12 mm Hg. Derived peripheral vascular resistance (PVR) is now about 205 dyne•s/cm^{-5}. However, profound hypoxemia did not resolve with a modest increase in PaO_2 83 mm Hg at a FiO_2 70% (PaO_2/FiO_2 = 118 mm Hg). High levels of driving pressures (22 cm H_2O) were measured despite a reduction of tidal volume to 6 mL/kg ideal body weight to ensure protective mechanical ventilation: plateau inspiratory pressure was 27 cm H_2O and respiratory system compliance was 25 mL/cm H_2O. Lung ultrasound evidenced bilateral dependent lung consolidations with modest edema (according to the number of B-lines per field of observation). A lung recruitment maneuver was performed while carefully monitoring hemodynamic parameters, and a decremental PEEP trial identified PEEP at 15 cm H_2O associated with best respiratory system compliance (44 mL/cm H_2O). Oxygenation dramatically improved (PaO_2/FiO_2 = 277 mm Hg), allowing progressive weaning of FiO_2. Despite higher levels of intrathoracic pressure pulmonary vascular resistance did not increase, and hemodynamic stability improved, allowing the weaning of epinephrine.

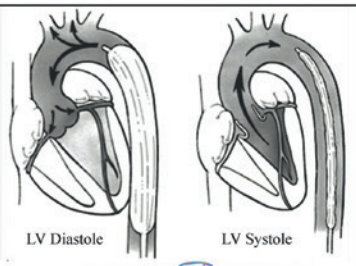
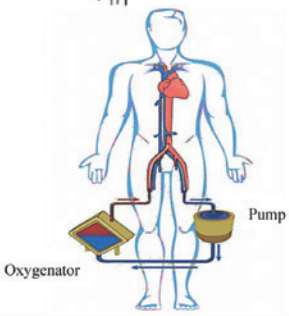
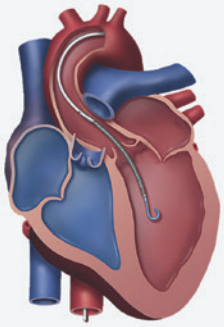
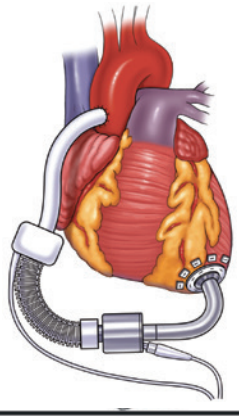
Device	Mechanism	Schema	Duration
IABP A	Counterpulsation		Days
VA-ECMO B	CBP		Days-Weeks
VAD (LVAD and BiVAD) C			Days-Weeks
Short Term			
BVS500,AB5000	Pulsatile		
Thoratec pVAD	Centrifugal		
CentriMag			
TandemHeart	Axial Flow		
Impella			
Long Term			Months
Thoratec pVAD			
Novacor	Pulsatile		
Heartmate XVE			
Abiomed TAH	Pulsatile/Pneumatic		
Berlin EXOR Pediatric			
Heartmate II	Axial Flow		
DeBakey Child D	Continuous		

Fig. 31.4 Available Types of Cardiocirculatory Mechanical Assist Devices. This figure summarizes the currently available cardiocirculatory mechanical assist devices divided according to the recommended duration of the mechanical support treatment. *BiVAD,* Biventricular assist device; *CBP,* cardio-pulmonary bypass; *IABP,* intraaortic balloon pump; *LVAD,* left ventricular assist device; *VA-ECMO,* veno-arterial extracorporeal membrane oxygenation. ([A] Image from *J Invasive Cardiol* 24(10):544–550, 2012; [C] Image from Medscape. https://www.medscape.com/viewarticle/861691. [D] From Townsend CM, et al, Sabiston Textbook of surgery: The biological basis of modern surgical practice, ed 20, Philadelphia 2017, Elsevier.)

RESPIRATORY SUPPORT AND MONITORING DURING ACUTE HEART FAILURE

Respiratory Pathophysiology of Acute Heart Failure

The failing heart tries to compensate for reduced cardiac output by increasing end-diastolic ventricular volume in order to increase myocardial contractility; when the compensatory mechanisms are exhausted, ventricular end-diastolic pressure rises, causing venous congestion in the pulmonary capillary system.[76] The main mechanism demonstrated to produce respiratory failure during AHF is a rapid increase in pulmonary capillary hydrostatic pressure and transvascular fluid filtration that exceeds the lymphatic interstitial drainage capacity, producing lung interstitial edema and alveolar flooding.[77] Two different mechanisms might be postulated to cause the increase in pulmonary artery occlusion pressure: (1) reduction in left ventricular compliance as a consequence of either left ventricular wall stiffening or ventricular compression (enlargement of the right ventricle, which compresses the left ventricle) and (2) left ventricular engorgement.[78] Pulmonary congestion results in a reduced functional residual capacity, increased intrapulmonary shunt, reduced lung compliance, and reduced distal airway diameters, resulting in increased airway resistance. Hypoxemia enhances the respiratory drive, which—together with the reduced lung compliance and the increased airway resistance—increases the energy demand of the respiratory muscles and increases oxygen consumption. Furthermore, the increased negative intrathoracic pressure negatively impacts left ventricular function by increasing left ventricular transmural pressures and thus left ventricular afterload.[79]

Ventilatory Support as Part of the Treatment of Right and Left Acute Heart Failure

The main goal of respiratory support in a patient with AHF is to increase oxygen availability and decrease work of breathing while the underlying cause of heart failure is treated. In patients with AHF admitted to the ED, oxygen therapy is the most common treatment to increase arterial oxygen content. Noninvasive ventilation (NIV), however, has further benefits for both the cardiovascular and respiratory systems.[80,81] Continuous positive airway pressure (CPAP) decreases left and right ventricular preload by increasing the gradient between peripheral venous pressure and intrathoracic venous pressure.[82] Furthermore, increased intrathoracic pressures decrease left ventricular afterload by reducing systolic wall stress.[83]

RULE OF THUMB The main goal of respiratory support in a patient with AHF is to increase oxygen availability and decrease work of breathing while the underlying cause of heart failure is treated.

Special attention should be paid to cases of predominant right ventricular failure where the application of a PEEP might worsen right heart performance due to an increase in pulmonary vascular resistance. A drop in systemic blood pressure after the initiation of NIV should prompt immediate intervention to adjust the CPAP level. The benefit for the respiratory system from the application of CPAP is attributable to the recruitment of collapsed alveoli, the dam-like effect of the positive intra-alveolar pressure against further alveolar edema, and avoidance of the development of negative intra-alveolar pressure during pronounced respiratory efforts. When an inspiratory pressure support is added during NIV (BIPAP), a further reduction of patient work of breathing may be obtained.[84] For this reason, BIPAP should be considered as first-line therapy in patients with exhausted respiratory reserve and hypercarbia.[85] On the other hand, CPAP is indicated in patients with pulmonary edema and hypoxemia but without hypercarbic respiratory failure. It is always necessary to test different NIV modalities and adjust ventilator settings to avoid the risk of patient–ventilator asynchronies.[86] The early application of both CPAP and BIPAP during acute respiratory failure due to cardiogenic pulmonary edema accelerates the improvement of PaO_2/FiO_2, resolution of hypercarbia and dyspnea; it also reduces respiratory rate and decreases the risk for endotracheal intubation.[87] The effects of NIV on outcome are not definitive.[88,89] Medical management is the key to sustained reversal of the acute respiratory failure. High-flow nasal cannula (HFNC) has recently gained popularity due to a demonstrated reduction of respiratory distress in patients with acute respiratory failure.[90] HFNC provides high-flow humidified air (with adjustable FiO_2) with a low-discomfort interface for the patient. The hypothesized benefit of HFNC is attributable to the generation of a minimal PEEP level (2 to 4 cm H_2O, when the mouth is closed) and to the reduced anatomic dead space by washout of the CO_2 in the upper airways. However, in the setting of AHF, **HFNC is *not indicated*** because higher levels of PEEP are needed to obtain its beneficial cardiovascular and respiratory effects.[91] Risk factors for NIV failure are listed in Box 31.2.

RULE OF THUMB Hemodynamic effects of respiratory support should always be considered if the patient's hemodynamic status worsens after the institution of respiratory support; potential mechanisms such as reduced cardiac preload, increased patient distress due to patient–ventilator asynchrony, or right as opposed to left heart failure should be considered.

BOX 31.2 Risk Factors for Noninvasive Ventilation Failure

Prior to initiation of NIV
- Diagnosis of lung infection
- Altered mental status
- Hypotension
- Copious and thick secretions
- Respiratory rate >40 bpm
- Severe impairment of PaO_2/FiO_2

At initiation of NIV
- Inappropriate ventilator settings
- Poorly fitting or poorly accepted patient-ventilator interface
- Patient-ventilator asynchrony

During NIV treatment
- No reduction in respiratory rate
- No improvement in pH, carbon dioxide, or oxygenation levels
- Signs of excessive respiratory effort or persistent fatigue
- Neurologic impairment
- Worsening of underlying disease

NIV, Noninvasive ventilation; *bpm,* breath per minute; *PaO_2/FiO_2,* arterial partial pressure of oxygen to inspiratory oxygen fraction ratio.

BOX 31.3 Criteria for Endotracheal Intubation During Acute Heart Failure

- Cardiac or respiratory arrest
- Altered mental status and need to protect the airway
- Progressive worsening of pH, $PaCO_2$, or PaO_2 during NIV
- Signs of fatigue despite optimization of NIV settings
- Persistent hemodynamic instability
- Agitation or intolerance to NIV with progressive respiratory failure

NIV, Noninvasive ventilation; *$PaCO_2$,* arterial carbon dioxide partial pressure; *PaO_2,* arterial partial pressure of oxygen.

Invasive mechanical ventilation should be reserved for the most acutely ill patients (Box 31.3).[92] Despite the risks associated with invasive mechanical ventilation (pulmonary infections, sedation, and the need for a critical care environment), the two main clinical reasons for initiating controlled mechanical ventilation are (1) to reduce oxygen consumption by abolishing spontaneous ventilation and (2) to take control of the patient's respiratory effort by preventing self-inflicted lung injury and excessive left ventricular afterload.

Titration of Ventilatory Support During Acute Heart Failure

The patient–ventilator interface is of critical importance when noninvasive respiratory support is initiated; different devices should be available and tested if necessary (see Chapter 50 for details). Skin protection and active heated humidification are mandatory to enhance patient compliance with respiratory therapy. When either CPAP or BIPAP is being delivered, the ventilator should allow the patient to generate up to 80 to 100 L/min of inspiratory flow to avoid drops in airway pressure throughout the respiratory cycle. Initiation of respiratory support is a critical moment: time and careful detailed communication are essential to explain to the patient the treatment and the actions that will be undertaken. Air leakage should be minimal, less than 0.4 L/s. It is advisable to start with low-level PEEP (3 to 5 cm H_2O or less, depending on the patient's initial tolerance) and inspiratory pressure support for NIV (3 to 5 cm H_2O or less, depending on the patient's initial tolerance). PEEP should then be slowly increased to 8 to 12 cm H_2O during CPAP based on patient tolerance or to lower levels of 6 to 8 cm H_2O during BIPAP. With BIPAP, the pressure support level should be titrated to obtain a tidal volume of 6 to 7 mL/kg ideal body weight. FiO_2 should be adjusted to obtain and maintain SpO_2 more than 92%[10] while avoiding hyperoxia.[93] Trigger sensitivity, inspiratory ramp, and cycling-off criteria should be titrated according to patient comfort and to avoid patient–ventilator asynchrony. Due to their respiratory distress, AHF patients usually seem to prefer high inspiratory peak flow and short inspiratory times. Intubation and pharmacologic sedation should be considered as a therapeutic option once ventilator settings have been optimized and the patient is still unable to adapt to ventilatory support. In most severe cases of pulmonary edema requiring ECMO, treatment for both cardiac and lung support, esophageal manometry can provide information on both chest wall compliance (possibly decreased due to tissue edema) and the level of PEEP required to overcome the increased lung weight.[94,95]

Close monitoring of patients undergoing NIV is necessary to ensure success of the therapy.[96] Reduction of respiratory rate and distress (dyspnea, accessory muscle use, abdominal paradoxical breathing) are the hallmarks of a successful treatment. Instead, worsening of patient's mental status and persistent respiratory distress should be immediately considered as a treatment failure and endotracheal intubation promptly performed. Monitoring the patient's respiratory drive ($P^{0.1}$ = negative inspiratory pressure developed within the first 100 ms against an occluded airway) and the patient's inspiratory effort (pressure muscle index [PMI], or inspiratory pressure developed by the patient during assisted breathing[97]), help in the early identification of patients requiring higher levels of sedation and assistance through controlled mechanical ventilation. Continuous monitoring of SpO_2 and the repeated measurement of arterial blood gases can help to tailor respiratory support. Respiratory parameters should be recorded over time, and alarms should be set carefully (apnea or high respiratory rate, low/high minute ventilation, high/low airways pressure) in order to rapidly identify a change in patient status. Visual inspection of the flow and pressure waveforms on the ventilator is recommended to detect asynchronies.

RULE OF THUMB[8] At 60–90 minutes after NIV initiation, increases in respiratory rate, $PaCO_2$, patient discomfort, and serum lactate help to identify NIV failure.

Similar to the initiation of respiratory support in AHF patients, withdrawal of respiratory support should occur as the AHF comes under control. In patients requiring either noninvasive or invasive mechanical ventilation for a period longer than 24 hours, the weaning process should be carefully monitored. Progressive lowering of inspiratory support first followed by FiO_2 and then PEEP is recommended. Once a minimal support level has been reached (FiO_2 40% and PEEP of 5 cm H_2O), a spontaneous breathing trial should be attempted. Most critical patients might deserve a transition to HFNC once FiO_2 is ≤40% and flow is ≤10 L/min using standard oxygen masks/cannulas.[98,99] Care should always be exercised during the removal of ventilatory support, as abrupt or too rapid an interruption of ventilatory support can lead to a sudden increased left-ventricular workload and a new onset of AHF.[78]

SUMMARY CHECKLIST

- AHF is defined as a new onset or increasingly rapid reduction of cardiac output leading to inadequate perfusion of the body's organs, thus failing to meet their metabolic demands.
- Between 20% and 40% of hospitalized patients with a diagnosis of MI develop AHF.
- The two predominant mechanisms of organ dysfunction are congestion and hypoperfusion.
- The goal of AHF treatment is to restore adequate oxygen delivery, which is often achieved by improving perfusion pressure.

- Critical to the management of the AHF patient is the monitoring of cardiovascular and respiratory function. The level of monitoring increases with the severity of cardiac impairment.
- In the acute setting, AHF therapy relies on treatment of the cause of the decompensated cardiac function.
- Primary pharmacotherapy for AHF includes oxygen, vasodilators, diuretics, vasopressors, inotropes, antiarrhythmics, and anticoagulants.
- Patients with severe acute right heart failure may require mechanical support with intra-aortic balloon pumps, VAD, and extracorporeal membrane oxygenation.
- Surgical treatment may be necessary if the AHF is due to coronary artery disease, valvular disease, or papillary muscle rupture.
- Patients with severe left-sided heart failure develop acute pulmonary edema.
- The primary goal of ventilatory support in AHF is to increase oxygen availability and decrease work of breathing while the underlying cause of heart failure is treated.
- Noninvasive ventilation in the form of CPAP is first-line treatment for acute pulmonary edema; however, in patients who also have severe right-sided heart failure, the increased intrathoracic pressure may worsen right heart performance due to an increase in pulmonary vascular resistance.
- CPAP should be set at 8 to 12 cm H_2O with the FiO_2 adjusted to prevent hyperoxia (SpO_2 >92% but <97%).
- Invasively ventilated patients should be managed with a lung-protective ventilatory approach ensuring the careful titration of PEEP.

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32

Lung Cancer

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CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Describe the epidemiology of lung cancer in the United States, particularly current trends.
- Identify risk factors for lung cancer.
- State the classification of lung cancer types and the cellular features of the four common types of lung cancer.
- Describe our current understanding of the pathophysiology of lung cancer.
- Identify the clinical features of the common types of lung cancer.
- Describe the diagnostic approach to lung cancer.
- State the importance of proper staging for lung cancer.
- Describe the treatment and outcomes for the common types of lung cancer by stage.
- State the role of the respiratory therapist in managing patients with lung cancer.

CHAPTER OUTLINE

KEY TERMS

adenocarcinoma
chemotherapy
computed tomography
flexible bronchoscopy
large cell carcinoma
magnetic resonance imaging
mass
nodule
non–small cell carcinoma
Pancoast syndrome
paraneoplastic syndrome
positron emission tomography (PET)
radiotherapy
screening
small cell carcinoma
squamous cell carcinoma
staging system
surgical resection
tumor, node, metastasis (TNM) staging
transbronchial needle aspiration
transthoracic needle biopsy

Lung cancer is a major public health problem. In the United States, approximately 25% of cancer deaths are caused by lung cancer.[1] Most of these deaths could be avoided if people did not smoke tobacco-related products; however, worldwide, tobacco consumption has not been declining, suggesting lung cancer will remain an epidemic for years to come. Advances in early detection and treatment have been slow but steady. The overall prognosis remains poor, with just over one in six lung cancer patients still living 5 years after diagnosis. This chapter provides an overview of lung cancer for the respiratory therapist (RT).

EPIDEMIOLOGY

New Cases

In 2018, an estimated 234,030 new cases of lung cancer were diagnosed in the United States.[1] Lung cancer is the second most frequently diagnosed cancer in men and women. The incidence of lung cancer peaked in men in 1984 and has since been declining; however, in women, the incidence increased during the 1990s, with a leveling off toward the end of the decade. These trends parallel the smoking patterns of men and women.[1] The World

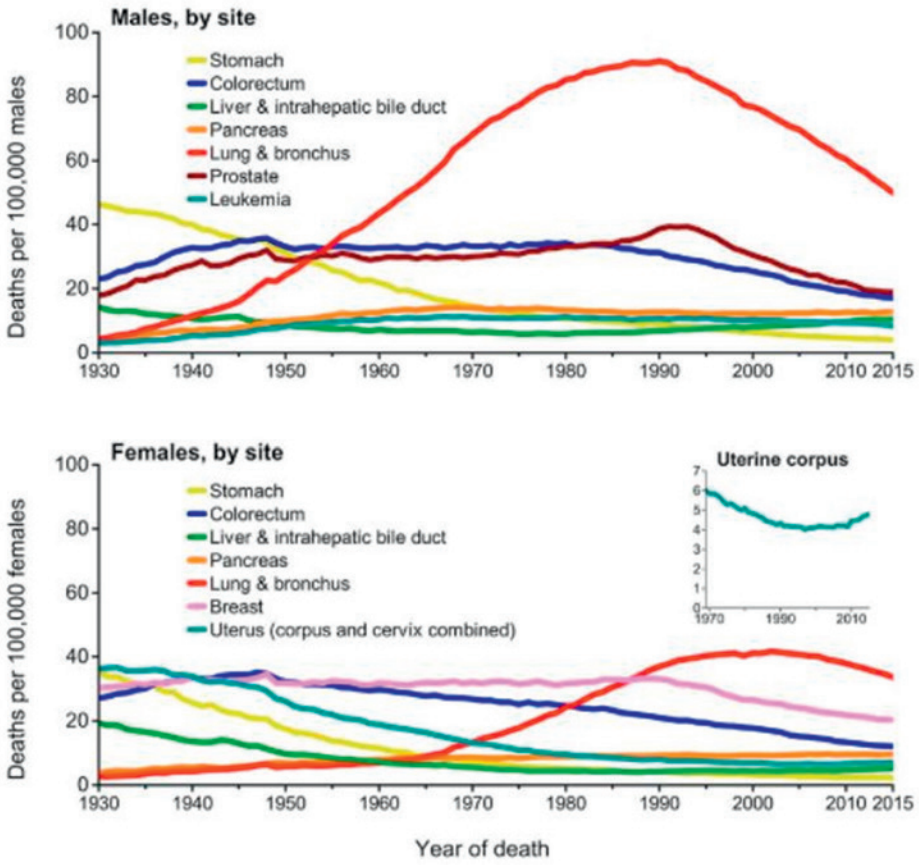

Fig. 32.1 Death Rate From Lung Cancer by Gender From 1930 to 2015. (Modified from Siegel R, Miller K, Jemal A. Cancer statistics, 2018. *CA Cancer J Clin.* 2018;68(1):7–30.)

Health Organization estimates that there are 2 million cases of lung cancer worldwide each year.

Deaths

Lung cancer is the number one cause of cancer-related death in men and women (Fig. 32.1), surpassing colon cancer in the early 1950s in men and breast cancer in the late 1980s in women. There are more deaths from lung cancer than breast, colon, and prostate cancer combined. Mortality rates in men declined significantly in the 1990s, whereas a slow increase occurred in women; these rates parallel the smoking patterns of men and women. In 2018, in the United States, an estimated 154,050 deaths were caused by lung cancer. In men, lung cancer is the leading cause of cancer-related deaths from age 40 years to the end of life, and in women, lung cancer surpasses breast cancer in the age group 60 and older.[1]

Tobacco-Related Products

Direct exposure to tobacco has occurred in 85% to 90% of individuals with lung cancer, and many tobacco-related carcinogens have been identified. The age at which smoking began, the number of cigarettes smoked per day, and the duration of smoking all influence the likelihood of developing lung cancer. Furthermore, the intensity of smoking, the depth of inhalation, and the composition of the cigarette influence the risk. All types (see later) of lung cancer are associated with smoking, with the strongest associations being with two of the cell types: *small cell* and *squamous cell carcinoma*. The risk for developing lung cancer decreases over time after smoking cessation, although it never reaches that of a lifelong nonsmoker.

There is evidence that *nicotine,* a chemical in tobacco, is highly addictive.[2] Approximately one-fifth of all adults in the United States smoke cigarettes. Progress had been made in the fight against cigarette use; in the decades from 1970 to 1990, the percentage of women who smoked declined from 33% to 25%, and the rate of smoking among men decreased from 43% to 28%. The annual decline that had occurred since the early 1970s began to slow through the 1990s despite mounting evidence associating smoking with disease and death.[3] In addition, smoking prevalence remains high in vulnerable populations (e.g., lower socioeconomic status, lower education attainment) and among sexual minorities. Cigarette smoking and other tobacco use among young people is also a major public health concern. Of young adults (18 to 24 years), 19.6% have been reported as current users of tobacco products, and 8.9% of youths (12 to 17 years) reported use within the past 30 days. In the context that a person who has not started smoking as a teenager is unlikely ever to become a smoker, the tobacco industry has focused on young people and developing countries as the primary sources of new customers.[4]

Other forms of exposure to tobacco-related products also pose risk for promoting lung cancer. Cigar smoking, which has

increased considerably over the past several years, is known to be an independent risk factor for developing lung cancer.[5] Furthermore, other non-cigarette forms of tobacco products and nicotine delivery systems (e.g., electronic cigarettes, smokeless tobacco, hookah) are more widely available and commonly used by young adults and youths. In 2013 and 2014, approximately 40% of tobacco users used multiple tobacco products, with cigarettes and e-cigarettes being the most common combination. The impact of non-cigarette nicotine delivery systems (such as e-cigarettes; "vaping") on population health is currently unknown. The small liquid pod included in most e-cigarettes contains a nicotine dose equivalent to a pack of cigarettes, and many e-cigarettes are flavored with chemicals. Exposure to the products of combustion of these chemicals may have adverse health consequences. E-cigarettes marketed to youths is a new way to get children and young adults addicted to nicotine.[4]

Exposure to *sidestream smoke,* or *passive smoking,* may also lead to an increased risk of lung cancer. The risk is generally much lower than active smoking but varies with the intensity of exposure.[6] It has been estimated that 3000 to 5000 deaths in the United States and 21,400 deaths worldwide from lung cancer occur each year because of secondhand smoke exposure.[7]

Occupational Agents and Other Risks

Many other risk factors have been identified (Box 32.1). Occupational agents are known to act as lung cancer carcinogens, with arsenic, asbestos, and chromium posing the highest risk. This risk increases when there is also exposure to tobacco products. Indoor radon exposure is also a risk factor for developing lung cancer. Radon is a naturally occurring gas produced by the breakdown of uranium ore or other rocks such as shale and granite, and indoor radon exposure generally comes from the soil underneath homes and buildings.[8] Particulates in the atmosphere (i.e., pollution) can also increase the risk for lung diseases including lung cancer.

Family members of people who develop lung cancer have an increased risk.[9-11] Women seem to have a higher baseline risk for developing lung cancer and a greater susceptibility to the effects of smoking. Differences in the metabolism of tobacco-related carcinogens and their metabolites, an effect of hormone differences, or both are thought to account for the increased susceptibility,[11] but dietary factors can also modify risks. Higher consumption of fruits and vegetables is associated with a reduced lung cancer risk, and increased dietary fat intake may lead to a higher risk.[13,14] Supplementation with vitamin A, vitamin E, or β-carotene appears not to reduce cancer risk.[14] The presence of chronic obstructive pulmonary disease (COPD) does place a person at higher risk.[15,16]

CLASSIFICATION

Lung cancers are divided into two major groups—**small cell carcinoma** and **non–small cell carcinoma**—based on pathologic features that are visible under light microscopy. The evaluation and management of a patient are guided by the type and stage (see later) of lung cancer. The non–small cell cancer category consists of **adenocarcinoma**, **squamous cell carcinoma**, **large cell carcinoma** (which has come under recent revision), and variants (Fig. 32.2). Table 32.1 presents the pathologic and epidemiologic features of the four common types of lung cancer.[17]

PATHOPHYSIOLOGY

The pathophysiology of lung cancer development is complex and incompletely understood. Damage to genetic material in lung cells is the result of exposure to chemical carcinogens such as the carcinogens contained in tobacco smoke.[16] People who develop lung cancer may have a genetic predisposition to the

BOX 32.1 Lung Cancer Risk Factors

Tobacco smoke exposure
- Active (mainstream)—cigarette, cigar
- Passive (sidestream)

Occupational and environmental exposures
- Arsenic
- Asbestos
- Chromium
- Beryllium
- Bis(chloromethyl)ether
- Cadmium
- Nickel
- Polycyclic aromatic hydrocarbons
- Radon
- Vinyl chloride

Genetic predisposition
Gender
Dietary factors
Chronic obstructive pulmonary disease
Air pollution

Courtesy Cleveland Clinic, Cleveland, OH.

TABLE 32.1 Classification of Most Common Types of Lung Cancer

Category	Cell Type	Pathologic Features (Light Microscopy)	Epidemiology
Non–small cell carcinoma	Adenocarcinoma	Formation of glandular structures; heterogeneous differentiation	Accounts for >40% of lung cancers in North America; increasing frequency in women
	Squamous cell carcinoma	Cytokeratin and intercellular bridges	Second most frequent type of lung cancer in United States
	Large cell carcinoma	Sheets and nests of cells, necrosis, lack of squamous cell or glandular features	Less common than adenocarcinoma or squamous cell carcinoma. Only labeled in surgically resected specimens.
Small cell carcinoma	Small cell carcinoma	Round to fusiform nuclei; faint to absent nucleoli; scant cytoplasm	Accounts for 13% of lung cancers

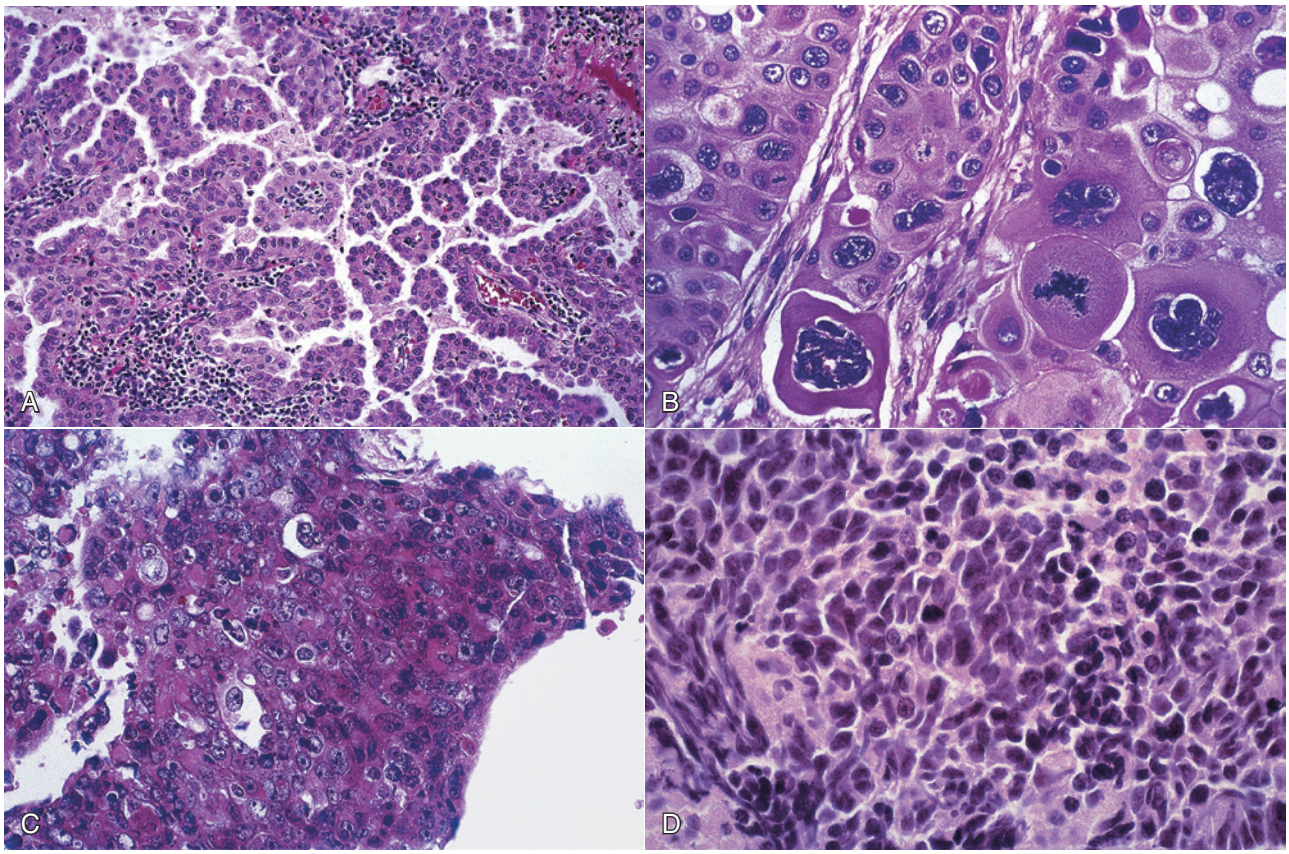

Fig. 32.2 Lung Cancer Histology. (A) Adenocarcinoma, characterized by heterogeneous differentiation in the same tumor. (B) Squamous cell carcinoma, characterized by the presence of cytokeratin differentiation with keratinization and intercellular bridges. (C) Large cell carcinoma, characterized by sheets and nest with extensive necrosis, large nuclei with prominent nucleoli, and lack of definitive evidence of squamous or glandular differentiation. (D) Small cell carcinoma, characterized by round to fusiform nuclei, nuclear molding, faint or absent nucleoli, and scant cytoplasm. (Courtesy Cleveland Clinic, Cleveland, Ohio.)

effects of these carcinogens. The genes influenced in the pathogenesis of lung cancer produce proteins involved in cell growth and differentiation, cell cycle processes, *apoptosis* (programmed cell death), *angiogenesis* (production of new blood vessels), tumor progression, and immune regulation. If enough of these pathways have been affected, the uncontrolled growth of cells that defines cancer occurs. By understanding the mechanisms that lead to genetic damage and the impact of that damage, novel means of risk stratification, prevention, early detection, and therapy could be developed.

CLINICAL FEATURES

The clinical features of lung cancer result from the effects of local growth of the tumor, regional spread through the lymphatic system, hematogenous (blood-borne) distant metastatic spread, and remote effects from tumor products or immune cross reaction with tumor antigens (Box 32.2). Some manifestations occur more commonly with a particular cell type. Only 15% of patients with a diagnosis of lung cancer do *not* have symptoms at the time of presentation.

Local growth in a central location (e.g., in a main stem bronchus) can cause a cough, hemoptysis, or features of large airway obstruction. Squamous cell carcinoma and small cell carcinoma are more likely to grow in a central location than other cell types. Adenocarcinoma occurs more commonly in the periphery of the lung. Peripheral growths may also cause cough and dyspnea; smaller tumors may not cause any symptoms. If the pleura or chest wall is involved, pain may occur.

Regional spread may lead to esophageal compression *(dysphagia),* recurrent laryngeal nerve paralysis (hoarseness), phrenic nerve paralysis with an elevated hemidiaphragm (dyspnea), and sympathetic nerve paralysis leading to Horner syndrome (ptosis [droopy eyelid], miosis [small pupils], anhidrosis [lack of facial sweating], and enophthalmos [sunken eye]). Growth at the very top of the lung may lead to a **Pancoast syndrome,** with shoulder pain radiating in an ulnar distribution as a result of involvement of the brachial plexus. The superior vena cava can become obstructed, resulting in swelling of the face, neck, and upper chest, plethora (swollen facial veins causing a ruddy complexion), and dilation of superficial veins over these areas. This is called the *superior vena cava syndrome*. Lung cancer can grow to involve the heart and pericardium. Lymphatic obstruction and spread can lead to dyspnea, hypoxemia, and pleural effusions.

Distant metastatic disease can affect most organs, with the brain, bones, liver, and adrenal glands most commonly involved.

BOX 32.2 Lung Cancer Manifestations

Local growth
- Cough
- Dyspnea
- Hemoptysis
- Pain

Regional growth
- Dysphagia
- Dyspnea
- Hoarseness
- Horner syndrome
- Hypoxemia
- Pancoast syndrome

Pericardial and pleural effusions
- Superior vena cava syndrome

Metastatic disease
- Headache
- Hepatomegaly
- Mental status change
- Pain
- Papilledema
- Seizures
- Skin or soft tissue mass
- Syncope
- Weakness

Paraneoplastic
- Cutaneous or skeletal
  - Acanthosis nigricans
  - Clubbing
  - Dermatomyositis
  - Hypertrophic osteoarthropathy
- Endocrine
  - Cushing syndrome
  - Humoral hypercalcemia
  - Syndrome of inappropriate antidiuretic hormone
  - Tumor necrosis factor (cachexia)
- Hematologic
  - Anemia or polycythemia
  - Disseminated intravascular coagulation
  - Eosinophilia
  - Granulocytosis
  - Thrombophlebitis
- Neurologic
  - Cancer-associated retinopathy
  - Encephalomyelitis
  - Lambert-Eaton syndrome
  - Neuropathies
  - Cerebellar degeneration
- Renal
  - Glomerulonephritis
  - Nephrotic syndrome

Courtesy Cleveland Clinic, Cleveland, OH.

Neurologic symptoms such as headaches, vision changes, and seizures may suggest brain metastases. Back pain and changes in strength or sensation in an extremity may indicate spinal cord compression and bone pain could indicate bone metastases. Laboratory abnormalities may point to bone marrow or liver involvement. Imaging may detect adrenal involvement.

MINI CLINI

Pancoast Tumor

Problem

A 65-year-old man who has smoked two packs of cigarettes per day for the past 40 years has had drooping of the left eyelid for the past 3 weeks. A chest x-ray reveals a mass in the apex of the left lung. Is there a link between the drooping of the eyelid and the lung mass?

Discussion

Lung tumors involving the apex of the lung (superior sulcus tumors) are also known as *Pancoast tumors*. If they involve the cervical sympathetic nerves in the neck, these tumors result in Horner syndrome, which is characterized by ptosis (drooping of the eyelid), anhidrosis (absence of sweating), and miosis (constricted pupil) on the same side as the tumor. Other manifestations of Pancoast tumor include pain and weakness in the upper extremity (caused by involvement of the brachial plexus), rib destruction, and destruction of vertebral bodies. Treatment depends on the extent of local and distant spread of the tumor.

MINI CLINI

Mediastinal Adenopathy

Problem

A 60-year-old man has been found to have small cell lung cancer on the basis of results of bronchoscopic biopsy findings, and a computed tomography scan of the chest shows extensive mediastinal adenopathy. The patient has been admitted to the oncology floor for **chemotherapy.** You are called to assess him because he cannot lie down owing to shortness of breath (orthopnea). When you arrive, the patient is sitting on the edge of the bed. You notice that his face and neck are swollen and he has dilated veins over the face, neck, chest, and arms. How do you explain these findings?

Discussion

This patient has superior vena cava obstruction caused by compression by the mediastinal adenopathy. The swelling of the face, neck, and arms is caused by impairment of the venous drainage from the upper body (the superior vena cava distribution). The dilated chest and arm veins are collateral vessels (or alternative pathway vessels) that compensate for the superior vena cava obstruction, which can be caused by various benign or malignant conditions that involve the mediastinum or the right upper lung. Treatment is usually therapy for the underlying problem.

When symptoms develop that are the result of the presence of cancer but are not related to the growth or spread of the cancer, these symptoms constitute a **paraneoplastic syndrome.** Paraneoplastic syndromes can result from the effects of proteins produced by the tumor that circulate through the body to have their effects on distant organs or result from the immune response of the body to a tumor antigen that is similar to antigens in other parts of the body, causing immune injury to the distant organ. Paraneoplastic syndromes may occur before the primary tumor can be detected or can be an indication of tumor recurrence. Examples of tumor secretion include the production of excess adrenocorticotropic hormone or its precursors (ectopic Cushing syndrome), parathyroid hormone (hypercalcemia of malignancy), and antidiuretic hormone (syndrome of inappropriate antidiuretic hormone). Immune cross-reactivity leads to

MINI CLINI

Paraneoplastic Syndrome

Problem

A 55-year-old man is brought to the emergency department by family members because of confusion and progressive generalized weakness. Examination in the emergency department shows the patient is dehydrated, lethargic, and confused. Chest x-ray reveals a cavitary lesion in the right upper lobe. Results of arterial blood gas analysis are normal. Results of chemical analysis urgently performed with the blood gas analysis reveal a sodium level of 150 mEq/L (normal 135 to 145 mEq/L) and a calcium level of 17 mg/dL (normal 9 to 10.5 mg/dL). How is the lung mass related to this patient's presentation and biochemical abnormalities?

Discussion

This patient's confusion and weakness are caused by hypercalcemia, which is a paraneoplastic presentation of lung cancer, especially squamous cell carcinoma (the cavitating mass on the chest x-ray). Paraneoplastic syndromes are systemic manifestations of lung cancer that are not caused by metastasis. Most paraneoplastic syndromes are associated with small cell lung cancer. However, hypercalcemia is more common with squamous cell carcinoma and is caused by secretion by the tumor of parathyroid hormone–related peptide. Treatment consists of hydration, diuresis, and use of medications that can reduce the levels of calcium.

paraneoplastic neurologic syndromes that can affect all parts of the neurologic system, resulting in emotional lability (limbic encephalitis), loss of balance (cerebellar degeneration), or proximal muscle weakness of the arms and legs with autonomic dysfunction (Lambert-Eaton myasthenic syndrome). Other paraneoplastic syndromes include skeletal and connective tissue syndromes (digital clubbing, hypertrophic pulmonary osteoarthropathy), coagulation and hematologic disorders, cutaneous and renal manifestations, and systemic symptoms (anorexia, cachexia, and weight loss).[18]

DIAGNOSIS

Approximately 85% of patients with lung cancer present with one or more of the previously described symptoms and in the remainder, lung cancer is detected by radiographic evaluation performed for an unrelated problem. This proportion may change in the future as **computed tomography** (CT) screening programs become widespread. Most patients have a chest x-ray and CT scan of the chest performed in their initial evaluation. These studies show a small spot (<3 cm in diameter) termed a **nodule** in the lungs or a larger spot (>3 cm in diameter) termed a **mass**. Other findings on imaging may include enlarged lymph nodes in the hila (where the bronchi and central blood vessels emerge from the mediastinum into the lung) or mediastinum, or a pleural effusion. An individual patient's clinical and radiographic presentation determines further evaluation.

The symptoms of lung cancer are nonspecific. There are many reasons that someone could have a cough or be short of breath. Similarly, an abnormality such as a lung nodule can be present on chest imaging for various reasons. Certain clinical and radiographic features make it more likely that the presentation represents lung cancer. The older the patient is and the more he or she has smoked over time, the more likely the chest finding is lung cancer. Furthermore, individuals with prior cancers are more likely to have lung cancer. Hemoptysis increases concern about cancer.

MINI CLINI

No Response to Antibiotics

Problem

A 55-year-old woman who does not smoke has a 3-month history of dyspnea on exertion, weight loss, and cough productive of copious amounts of clear, frothy sputum. She has no fever or chills. She has been treated for 2 weeks for "double pneumonia" without relief of the symptoms. Examination reveals finger clubbing and decreased air entry in both lung bases with dullness to percussion. A chest x-ray shows bilateral alveolar infiltrates. What should be done next?

Discussion

The patient has a variant of adenocarcinoma of the lung. Cough productive of copious amounts of clear, frothy sputum is characteristic of this type of lung cancer. The radiographic appearance may be indistinguishable from that of pneumonia, especially when there is sputum production. The absence of fever, the chronic presence of infiltrates, and the lack of response to antibiotic therapy should raise suspicion for this type of lung cancer. Bronchoscopy with transbronchial biopsy would be a reasonable next step to confirm the diagnosis.

Radiographic features are also used to determine the probability of cancer. The larger the lung abnormality, the more likely it is to be cancer. When the abnormality has reached the size of a mass (3 cm), it needs to be considered a cancer until proven otherwise. The rate of growth of the lesion is also helpful. If a nodule grows rapidly (doubles in size in <1 month) or grows very slowly or not at all over a couple of years, it is unlikely to be caused by cancer. If the nodule appears to be heavily calcified on imaging, it has likely been present for quite some time and is unlikely to represent cancer. If the abnormality has an irregular border, is lobulated, or is spiculated (with sharp, pointy edges), it is more likely to be a cancer than if the border is smooth and rounded. Finally, if the lesion is cavitary, the thickness of the wall of the cavity can suggest cancer. A wall thickness of 14 mm or greater is likely to represent a cancer.[19]

RULE OF THUMB A solid solitary pulmonary nodule that has not grown in 24 months is unlikely to be malignant.

After the clinical and standard imaging features are reviewed, a probability of malignancy can be determined. If the probability is very high, the potential cancer does not seem to have spread, and the individual is fit, proceeding directly to surgery would be reasonable. If the previously mentioned features suggest a very low probability of malignancy, the clinician and patient might choose to follow along with serial chest imaging over time to assess for growth. When the probability falls between these extremes, adjunctive imaging and invasive procedures can be used to help characterize the finding. The most commonly used additional imaging technique is **positron emission tomography** with fluorodeoxyglucose (FDG-PET [Chapter 21]). Owing to the fact that malignant cells are metabolically very active, they take up the glucose analogue called FDG more avidly than

non-malignant cells. The attached radioactive tracer becomes trapped in the cells, allowing it to be imaged. When this test is used to help predict the presence of lung cancer, it has a sensitivity of 89% and a specificity of 78%. PET imaging can produce false-positive results in other metabolically active conditions such as infections. It can be falsely negative if the lesion is too small (<10 mm) or if the tumor is slow growing and not very metabolically active (e.g., some adenocarcinomas, carcinoid tumor).[20]

Ultimately, tissue is obtained to confirm the diagnosis of lung cancer. **Flexible bronchoscopy** and **transthoracic needle biopsy** are invasive, nonsurgical approaches used to obtain tissue. If these procedures fail or are deemed unnecessary, a surgical approach is used.

Flexible bronchoscopy is a procedure in which a long, thin, flexible camera is passed through a patient's nostril or mouth into the lungs (see Chapter 22). The camera can be extended into the branches of the lung as far as the branches are large enough to admit it. The camera has a small channel through which very thin biopsy instruments can be passed out deeper into the lung to take samples from concerning areas. Flexible bronchoscopy has a high diagnostic yield for lesions that are endoscopically visible within the larger airways. Samples are collected by washing saline over the lesion, sending a small brush through the camera to collect cells on its bristles, and taking biopsy samples with forceps or a needle. The diagnostic yield from lesions in the periphery of the lung, beyond where the camera is able to see, is lower. Conventional sampling techniques and peripheral **transbronchial needle aspiration** complement each other. Factors that influence the diagnostic yield of flexible bronchoscopy for peripheral lesions include the size of the lesion, its location, and the presence of a 'bronchus sign' on CT (an airway leading directly into the lesion). Smaller, more peripheral lesions, without a visible bronchus within or leading directly to them, are less likely to be diagnosed by flexible bronchoscopy.[21] More recent technologic advances, such as multiplanar imaging, electromagnetic navigation of the bronchoscopy instruments, and peripheral endobronchial ultrasound, have been able to improve the yield of flexible bronchoscopy for these small peripheral lesions.[22] Not infrequently, the hilar or mediastinal lymph nodes are enlarged as a result of spread of the tumor. Diagnosis and staging can be accomplished during bronchoscopy, with endobronchial ultrasound used to guide biopsies of these lymph nodes.[23,24]

Transthoracic needle biopsy, using fluoroscopic or CT guidance, can also be used to obtain a tissue sample. With this procedure, an aspirating needle is passed through the skin into the lung lesion under the guidance of chest imaging. The yield of transthoracic biopsy is a little higher than bronchoscopy, but lymph nodes cannot be sampled during this procedure, smaller nodules in central locations have lower diagnostic rates, and there is a higher rate of pneumothorax.[23] The choice of which procedure to use is guided by the size and location of the lesion and the local expertise with each technique.

STAGING

A major factor that determines the prognosis of lung cancer and guides the selection of appropriate treatment is the extent to which the cancer has spread in the lungs and throughout the body. The extent of cancer spread is termed the *stage* of the cancer. Non–small cell lung cancer is staged using the **TNM staging** system (*T* for extent of primary tumor, *N* for regional lymph node involvement, and *M* for metastases). The eighth edition of the TNM system for non–small cell lung cancer has recently been adopted.[24]

The T component of the **staging system** is divided into T1 through T4 lesions, as follows:

- A *T1 tumor* is a small tumor confined to the lung. It must be less than 3 cm in diameter and be surrounded by lung or visceral pleura and cannot extend into a main bronchus. T1a tumors are less than or equal to 1 cm in diameter, T1b tumors are greater than 1 and up to 2 cm, and T1c is greater than 2 cm and up to 3 cm.
- A *T2 tumor* has a cut-off size of 5 cm. Any size tumor involving the mainstem bronchus or leading to partial or total atelectasis of the lung is also a T2 tumor.
- A *T3 tumor* is greater than 5 cm and up to 7 cm in size. Multiple tumor nodules in the same lobe, those involving the chest wall, phrenic nerve, and parietal pericardium regardless of size, are also considered T3 tumors.
- A *T4 tumor* is greater than 7 cm in size. Separate tumor nodules in a different ipsilateral lobe of the lung, and tumors invading the diaphragm, mediastinum, or great vessels, are also considered T4 tumors.

The N component of the staging system is determined by which lymph nodes, if any, are involved with the tumor, as follows:

- *N0 spread* indicates that the cancer has not spread to the lymph nodes.
- *N1 spread* indicates the presence of cancer in lymph nodes within the ipsilateral lung (the same side as the tumor) in hilar or peribronchial regions.
- *N2 spread* signifies cancer in lymph nodes in the mediastinum ipsilateral to the primary tumor.
- *N3 spread* signifies cancer in *contralateral* ('opposite side') mediastinal or hilar lymph nodes, *ipsilateral* or *contralateral* scalene, or supraclavicular nodes.

The M part of the staging system represents the absence *(M0)* or presence *(M1)* of metastases outside of the chest. *M1a* refers to metastasis of separate tumor nodules in the contralateral lung or the presence of a malignant pleural or pericardial effusion. *M1b* refers to a single distant site of metastatic spread, such as liver, bone, or brain lesions. *M1c* refers to multiple distant sites of metastases.

The most recent revision to this staging system occurred in 2017 (Table 32.2 and Fig. 32.3). The stages are labeled from stage IA to stage IVB based on the combination of T, N, and M features.[24,25]

For patients with small cell lung cancer, the TNM staging system was previously thought to be less useful. Instead, small cell lung cancer has been staged as limited or extensive disease. *Limited-stage* disease is present when the tumor is confined to a hemithorax (including ipsilateral mediastinal and supraclavicular lymph nodes) and can be contained within a radiotherapy port. *Extensive-stage* disease is present when the tumor extends beyond these boundaries. The recent lung cancer staging revision

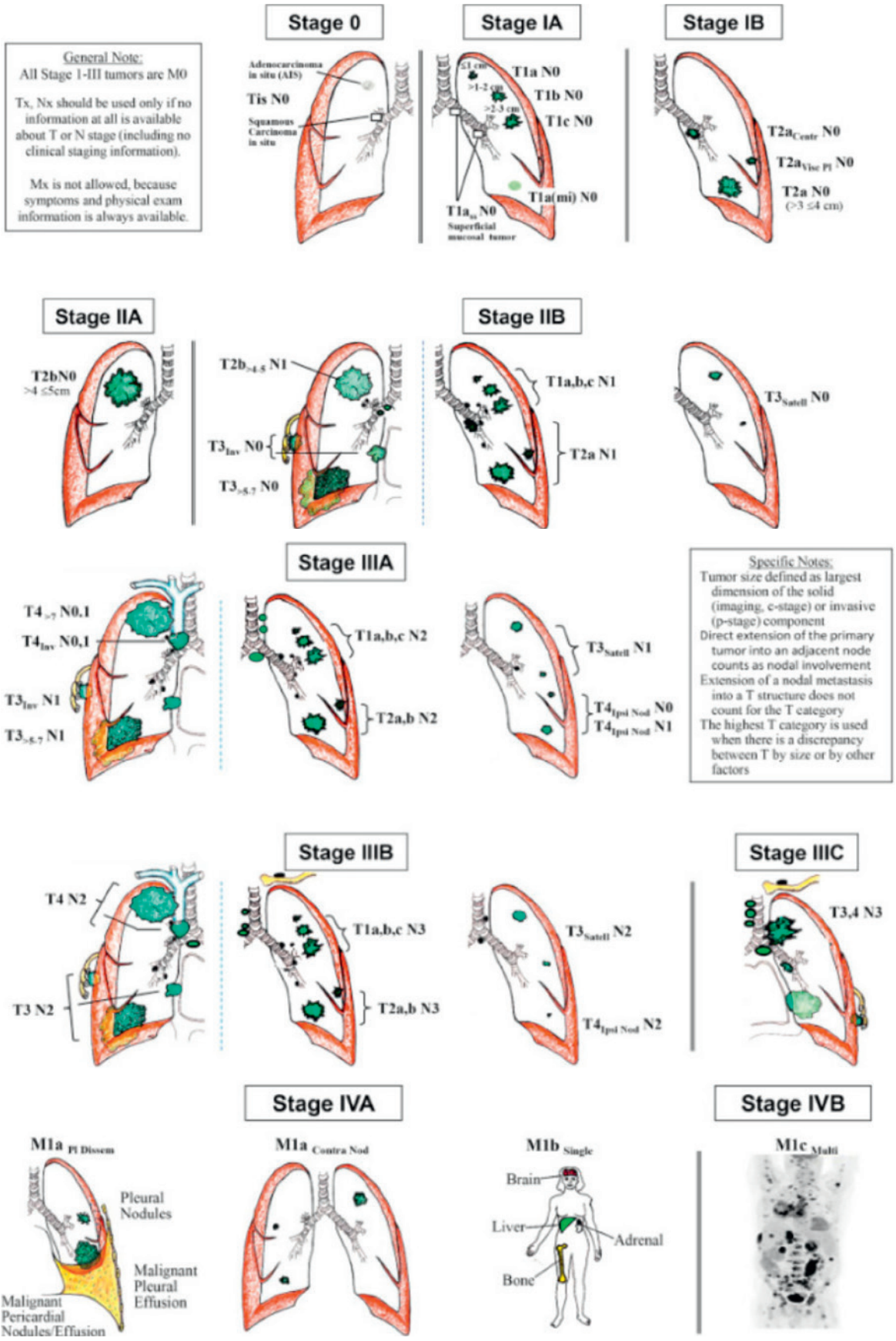

Fig. 32.3 Graphic Illustrations for Tumor, Node, Metastasis Staging of Lung Cancer. (Detterbeck FC, Boffa DJ, Kim AW, et al. The 8th edition lung cancer stage classification. *Chest*. 2017;151(1):193–203.

recognized a benefit to applying the TNM staging system used for non–small cell cancer to small cell cancer as well.[24-26]

The proper use of testing to stage a patient with lung cancer was addressed in recent guidelines.[26] The history and physical examination are important in guiding testing. The extent of spread is best evaluated using CT of the chest extending to the upper abdomen to include the liver and adrenal glands; this should be ordered in all patients. **Magnetic resonance imaging** (MRI) has not proved to be more accurate except in the setting of a Pancoast tumor. Evidence shows that integrated PET/CT scanning has better test characteristics for staging lymph node and distant disease involvement than other types of imaging (Fig. 32.4).[27-29]

Because noninvasive tests can have false-positive results, tissue confirmation is necessary. Bronchoscopy with transbronchial needle aspiration is useful to stage the mediastinum. The addition of endobronchial and endoscopic ultrasound has increased the yield of non-surgical mediastinal staging.[23,28] Surgical staging (e.g., mediastinoscopy, mediastinotomy, or thoracoscopy) is offered when lymph nodes are concerning on imaging but were negative on bronchoscopy. Despite the advances in imaging technology and sampling techniques, definitive staging with **surgical resection** and mediastinal dissection remains the gold standard in a patient with resectable disease. The assigned clinical stage (determined by the previously listed testing, including mediastinoscopy) can be lower than the pathologic staging (assigned after surgery).

The evaluation of metastatic disease also takes into consideration the history, physical examination, laboratory results (electrolytes, calcium, alkaline phosphatase, liver profile, and creatinine), and pathologic examination results.

Per guidelines, a head CT or MRI scan should be performed if symptoms or signs of metastatic disease are present or when evaluating what appears to be stage IIIA through IV disease. Although there is no proved survival benefit from CT versus MRI, many clinicians prefer to use MRI of the brain because it has greater sensitivity to detect metastatic disease.[26,29] The rest of the body is assessed by PET imaging, as is the mediastinum. PET imaging is recommended for all patients.

Along with evaluating the anatomic extent of disease, a patient's performance status is important in determining his or her prognosis and ability to tolerate any proposed treatment. The two most commonly used scales of performance status are the *Zubrod scale* and the *Karnofsky scale*. Although their definitions differ, the general principles of the two scales are the same, with ratings based on activity level, independence in daily activities, and severity of symptoms.

RULE OF THUMB Staging for lung cancer is complex and should involve a multidisciplinary team. Stage I cancers are small tumors and stage II cancers involve nearby hilar lymph nodes or are larger tumors. When mediastinal nodes are positive, the patient is at least stage III and when a malignant pleural effusion or distant sites such as the brain or bones are involved, the patient is stage IV.

PREOPERATIVE EVALUATION FOR LUNG RESECTION SURGERY

To determine if a patient would tolerate lung resection surgery, patients go through testing of their pulmonary, cardiovascular, and overall health. Reports of activity tolerance, pulmonary function testing, and exercise testing are used to assess the risk. The amount of risk is weighed against the benefit of having a traditional lung resection surgery (a lobectomy—one lobe removed, or pneumonectomy—a lung removed) versus a sublobar resection or non-surgical treatment. Traditional resection is the best chance for cure and reduces local recurrence. As would be expected, a pneumonectomy requires better preoperative lung function than a lobectomy. When a lobe is removed, patients generally have a 10% to 15% drop in lung function. With a pneumonectomy, 30% to 35% is lost.

Cardiac conditions requiring medications, or an inability to climb two flights of stairs, should prompt a cardiac evaluation.

TABLE 32.2 Tumor, Node, Metastasis Staging for Lung Cancer

Stage	
IA	T1a,b,cN0M0
IB	T2aN0M0
IIA	T2bN0M0
IIB	T1a-cN1M0, T2aN1M0, T2bN1M0, T3N0M0
IIIA	T1a-cN2M0, T2a-bN2M0, T3N1M0, T4N0-1M0
IIIB	T1a-cN3M0, T2a-bN3M0, T3N2M0, T4N2M0
IIIC	T3N3M0, T4N3M0
IVA	T(any)N(any)M1a,b
IVB	T(any)N(any)M1c

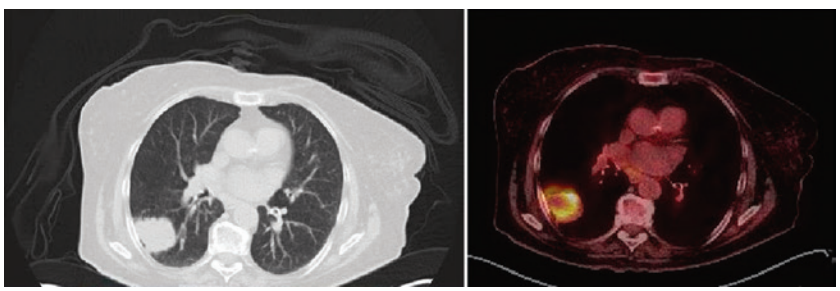

Fig. 32.4 Positron emission tomography image of right lower lobe 4.7 cm lung mass. Standardized uptake valve of 10. Corresponding computed tomography chest imaging of right lower lobe 4.7 cm lung mass. (Courtesy Cleveland Clinic, Cleveland, OH.)

BOX 32.3 To Calculate Percent Predicted Postoperative Values

The segment method

PPOFEV1 = pre-operative FEV1 × (1 − number of resected segments/19)

19 representing the total number of segments in both lungs:
Right upper lung: 3
Right middle lung: 2
Right lower lung: 5
Left upper lung: 5
Left lower lung: 4

The **thoracic revised cardiac risk index** can be used to identify patients at risk for cardiac complications. Those with any combination of the following conditions (i.e., score ≥ 2) should have noninvasive cardiac stress testing or a cardiology consultation: previous ischemic heart disease, stroke or transient ischemic attack, creatinine >2 mg/dL or planned pneumonectomy. Similarly, those with a cardiac condition requiring medication, or with a newly suspected cardiac condition, and those unable to climb two flights of stairs should be considered for noninvasive cardiac stress testing or a cardiology consultation.

The evidence shows that the volume exhaled during the first second of a forced expiratory maneuver (FEV_1) (see Chapter 20) and diffusing capacity for carbon monoxide (DLCO) are the most frequently used pulmonary function tests and the best predictors for postoperative complications, including death. Traditional preoperative cutoff values have been replaced by percent predicted postoperative (PPO) values as starting points. PPO values of FEV_1 and DLCO can be calculated by multiplying the percent predicted *pre*operative value by the fraction of the total number of lung segments that will remain postoperatively. This is the segment method (Box 32.3). Alternatively, quantitative perfusion imaging can be used to guide the calculation. If the PPO FEV_1 and DLCO are greater than 60%, the patient is considered at low risk for lung resection. If PPO values fall between 30% and 60%, an exercise test should be performed. The stair climb test, shuttle walk, and 6-minute walk tests can be used. For patients with PPO values below 30%, inadequate low-technology exercise testing results, or when measured values and predictions seem discordant with an individual's reported activity tolerance, a formal cardiopulmonary exercise test should be performed (Fig. 32.5). If the peak oxygen uptake is greater than 20 mL/kg/min (or 75% predicted), the patient is considered at low risk for any resection. If the peak O_2 uptake is less than 10 mL/kg/min (or 35% predicted), the patient is considered at high risk and conventional surgery should not be performed. Patients with a peak O_2 consumption value between these two limits are at moderate risk, and should be considered on a case-by-case basis.[31,32]

RULE OF THUMB Patients with a PPO FEV_1 and DLCO greater than 60% predicted can safely undergo surgical resection for lung cancer, even if pneumonectomy is needed.

MINI CLINI

Lung Cancer Screening

Problem

A 68-year-old man presents to the clinic with the concern of developing lung cancer in the future. He currently smokes one pack of cigarettes per day and has smoked for 45 years. He does not cough or feel shortness of breath. He has a history of high blood pressure and high cholesterol. He is otherwise in his regular state of health. Should this man have lung cancer screening?

Discussion

Based on the evidence, he meets criteria to have a low-dose CT chest to screen for lung cancer. He does not have any symptoms that also make screening appropriate. A vitally important part of the conversation with this patient should be tobacco cessation. Quitting smoking at any age reduces the risk for lung cancer and other health problems.

SCREENING

Given the poor prognosis for advanced-stage lung cancer and the high proportion of patients who present in an advanced stage, there has been great interest in **screening** for lung cancer. The earliest efforts at radiographic screening involved the analysis of mass chest x-ray screenings from the population of an individual city. Subsequently in the 1970s, there were large efforts to use chest x-ray, sputum, or a combination of the two as screening tools. Finally, a large randomized trial of chest x-ray as a screening test did not show any benefit; thus screening with chest x-ray is not recommended.[33-35]

Given the disappointing overall results from studies of chest x-ray as a screening technique, efforts have centered on the use of low-dose CT imaging as a screening tool.[36,37]

One trial, the National Lung Screening Trial, reported a 20% reduction in lung cancer-specific mortality in patients with very high risk for developing lung cancer. This finding has changed the clinical discussion regarding lung cancer screening. The U.S. Preventive Services Task Force gave low-dose CT chest screening a grade B recommendation for high-risk individuals (age 55 to 80 and at least 30 pack-years of current smoking [pack years = the number of packs per day × years smoked], or at least 30 pack-years of former smoking and quit within 15 years). The evidence shows that CT lung screening is most effective when performed in a setting where expertise in lung cancer and lung nodules is available.[38-40]

TREATMENT AND OUTCOMES

Although the respiratory therapist (RT) would not be administering the treatments for lung cancer, and the therapies change with advances over time, a brief discussion to familiarize the RT with the approach to treatment and the types of available therapy is important.

Non–Small Cell Lung Cancer (Table 32.3)

Three types of treatment are used to treat non–small cell lung cancer: surgical resection, **radiotherapy**, and **systemic therapy** (including traditional chemotherapy, targeted, and

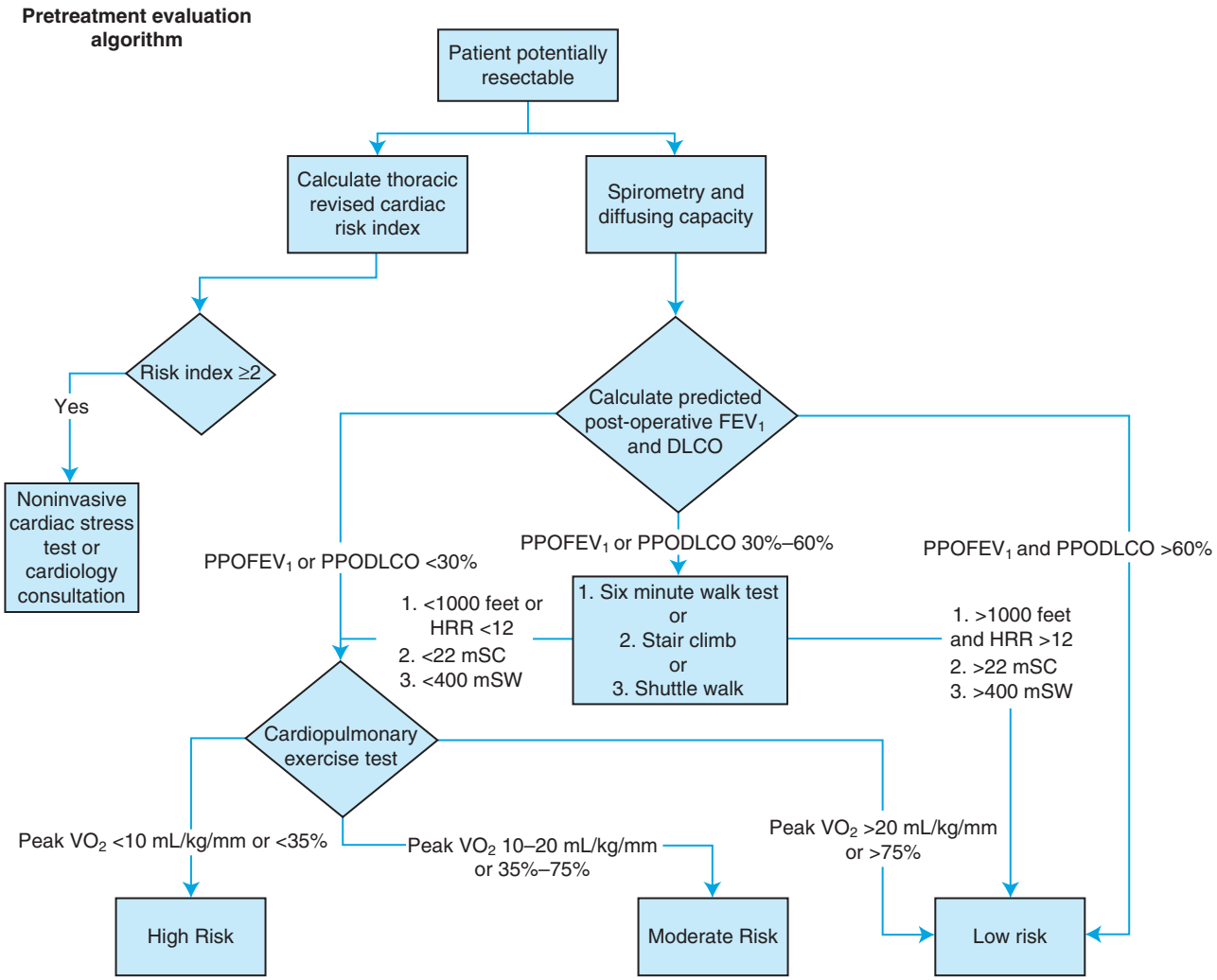

Fig. 32.5 Algorithm for Patients Considered for Lung Resection Surgery. Note 1: The algorithm represents an assessment of risk for traditional resection (lobectomy, pneumonectomy). One must consider the benefits of traditional resection over alternative therapies (sublobar resection, ablative therapies), the relative risks of the therapeutic choices and the patient's values when selecting treatment. Note 2: The 6-min walk is included in this algorithm but is not part of other guidelines owing to relatively small literature support. It is a more practical and available low-technology exercise study than the recommended tests, and we have substantial experience with this test, leading us to include it in our algorithm. Note 3: Potential modifiers of risk include smoking cessation, adequate treatment of comorbid pulmonary conditions, preresection or postresection pulmonary rehabilitation, and the surgical approach (VATS versus thoracotomy). Each of these should be considered when assessing risk. Note 4: For lobectomy, the segment method or quantitative perfusion scan can be used to calculate predicted post-operative values. For pneumonectomy, the quantitative perfusion scan should be used. Note 5: Management of cardiac disease per American College of Cardiology/American Heart Association guidelines. *DLCO*, Diffusion capacity for carbon monoxide; *FEV1*, forced expiratory volume in 1 second; *HRR*, heart rate recovery; *PPO*, predicted post-operative; *PPO*, Predicted post-operative values; *SC*, stair climb; *SW*, shuttle walk; *VO_2*, oxygen consumption; mL/kg/min, milliliters per kilogram per minute.

immune checkpoint inhibitor therapies) (Box 32.4). The first two treatments provide local control of the cancer, and the last is used to treat systemic disease. Which therapy or combination of therapies is recommended depends on the stage of the cancer, the patient's ability to tolerate treatment, and the type of cancer (or its histology). Molecular changes within the tumor now drive treatment choices for patients with advanced-stage disease.

Early Stage Non–Small Cell Carcinoma

Surgical resection offers the best chance of cure for early-stage non–small cell lung cancer (stages I and II). The surgery of choice is a *lobectomy*, in which the entire lobe of the lung containing the cancer is removed. If the tumor is very central, a pneumonectomy may be required. Sublobar resections, such as *segmentectomy*, or *wedge resection*, can be performed in patients with modest lung function to spare as much lung tissue as

TABLE 32.3 Non–Small Cell Lung Cancer: 5-Year Survival by Stage

Stage	Clinical Stage (%)	Pathologic Stage (%)
IA1	92	90
IA2	83	85
IA3	77	80
IB	66	73
IIA	3660	65
IIB	53	56
IIIA	36	41
IIIB	26	24
IIIC	13	12
IVA	10	—
IVB	0	—

Modified from Goldstraw P, Chansky K, et al. International Association for the Study of Lung Cancer International Staging Committee; IASLC Lung Cancer Staging Project: Proposals for the revision of the TNM stage groupings in the forthcoming (eighth) edition of the TNM classification of malignant tumors. *J Thorac Oncol* 2015;11:39–51.

possible. In most patients, sublobar resection leads to a slightly lower survival rate and a higher rate of local recurrence of cancer.[41,42] In the smallest cancers and in patients who are older than 70 years, a sublobar resection may be as effective as a lobectomy.[43] Recurrence usually involves distant metastases.

Radiotherapy has been used with curative intent in early-stage non–small cell lung cancer in patients who cannot tolerate surgery or in patients who elect not to undergo surgery. Stereotactic body radiotherapy is a novel radiation therapy technique in which multiple convergent beams of radiation are precisely targeted on the tumor. This targeting allows very high doses of radiation to be delivered to the tumor while sparing the normal lung tissue. Rates of local control and survival are impressive in selected groups, approaching the rates of lung resection.[44]

Adjuvant platinum-based chemotherapy leads to a significant survival benefit in selected patients with completely resected stage II lung cancers.[45] The potential benefit of adjuvant chemotherapy in patients with stage IB disease is debated.

Locally and Regionally Advanced Non–Small Cell Carcinoma

Tumors that involve the chest wall or large airways but have not spread elsewhere can frequently be treated with surgical resection. When a Pancoast tumor is present, chemoradiotherapy followed by surgical resection (lobectomy ± chest wall resection) is performed if possible. The invasion of local structures (rib, vertebral body, subclavian artery, or sympathetic chain) is a poor prognostic sign.

The approach to stage III disease caused by N2 lymph node involvement varies among institutions. Generally, the more advanced the lymph node involvement (number, extension, or location), the poorer the prognosis. Patients who have bulky lymph nodes or who require a pneumonectomy are less likely to benefit from including resection in the treatment plan. Concurrent chemoradiotherapy is the standard of care, with resection included in specialized centers. An immune checkpoint inhibitor may now be added to chemoradiotherapy.[46,47]

T4 disease without advanced nodal status (stage IIIB) may be considered for surgical treatment in only a few settings. T4 disease involving the main carina may be considered for resection at centers with expertise. The role of induction therapy in this setting has not yet been defined. Disease at the N3 level (stage IIIB) is generally considered non-surgical.[47]

Metastatic Non–Small Cell Carcinoma

In stage IV lung cancer, platinum-based chemotherapy regimens have been shown to improve survival and enhance quality of life. They are also cost-effective. This treatment is most appropriate for individuals with a good performance status. Resection

BOX 32.4 Options for Treatment of Lung Cancer

Non–Small Cell

Stages IA, IB, IIA, IIB

- Surgical resection standard of care if patient deemed able to tolerate resection
- Sublobar resection if patient is unable to tolerate larger resection
- Radiotherapy, particularly stereotactic body radiotherapy in NO disease, if patient is unable to tolerate or chooses not to undergo resection
- Adjuvant radiotherapy possibly of use if incomplete resection has occurred
- Adjuvant chemotherapy in patient with stage II disease who can tolerate it; consider in stage IB

Stage IIIA

- Concurrent chemoradiotherapy using platinum-based regimen and a PDL-1 inhibitor if performance status is reasonable
- Induction chemoradiotherapy followed by resection and adjuvant chemotherapy in selected patients

Stage IIIB

- Concurrent chemoradiotherapy using platinum-based regimen and a PDL-1 inhibitor if performance status is reasonable
- Induction chemoradiotherapy followed by resection in highly selected patients, only as part of a study protocol

Stage IV

- Platinum-based chemotherapy regimen plus a PDL-1 inhibitor in patients with adequate performance status; consider PDL-1 inhibitor alone if PDL-1 staining in > 50% of cancer cells
- Targeted therapies (e.g., EGFR and ALK inhibitors) in appropriate subgroups (where molecular testing suggests efficacy)

Small Cell

Limited Stage

- Combination chemotherapy with concurrent hyperfractionated radiotherapy if performance status is adequate
- Prophylactic cranial radiation for patients with complete response to chemoradiotherapy

Extensive Stage

- Combination chemotherapy if performance status is adequate

ALK, Anaplastic lymphoma kinase; *EGFR,* epithelial growth factor receptor; *VEGF,* vascular endothelial growth factor.
Courtesy Cleveland Clinic, Cleveland, OH.

of an isolated brain metastasis in patients with a good performance status can improve survival. Standard chemotherapy typically involves two agents administered in cycles, each approximately 3 weeks apart, for a total of four to six cycles. More recently, agents with improved tolerance have been shown to benefit patients who have shown a good response to treatment when administered as maintenance treatment, until progression is noted.[48]

Standard chemotherapy targets all growing cells, not just cancer cells (hence the common side effects seen). Chemotherapy for advanced non–small cell lung cancer (NSCLC) has progressed over the past several years to sequentially include traditional cytotoxic chemotherapies (platinum-based doublet therapy), agents that target cancer-driver mutations, and agents that improve the body's immune response to the tumor. The tumor biopsy is used to characterize the tumor, including determining the histology, identification of cancer-driver mutations, and status of the immune response to the tumor. These guide treatment choices.

Targeted therapies have been developed where the mechanism of action is more specific to the cancer cell when *driver mutations* are present. In lung cancer, inhibitors of epidermal growth factor receptors (EGFRs), vascular endothelial growth factor (VEGF), and anaplastic lymphoma kinase (ALK) translocations have been studied. EGFR and ALK inhibitors have been most successful in patients with EGFR-activating mutations and ALK translocations in their cancer tissue. Several other mutations have been identified.

Lung cancer can trick the body's immune system so that it does not attack the tumor. Immune checkpoint inhibitors have led to improved survival when combined with traditional chemotherapy in patients with advanced disease, when used alone in patients with advanced disease and high levels of programmed death-ligand 1 (PDL-1) expression, and when combined with chemoradiation in patients with N2 disease.[48-51]

Small Cell Lung Cancer

Treatment of small cell lung cancer is based on its staging (see Box 32.4). In limited-stage disease, combination chemotherapy with concurrent hyperfractionated radiotherapy is recommended. The drug etoposide and a platinum agent are standard. Prophylactic brain radiation is generally recommended for patients who have a complete response to chemoradiotherapy. Surgery is limited to cases in which the diagnosis is in doubt or in rare cases that manifest as a single lung nodule. In patients with extensive-stage disease, combination chemotherapy improves the quality of life and median survival. A poor performance status and an elevated lactate dehydrogenase level suggest a poor prognosis.[52]

RULE OF THUMB Surgery is the treatment of choice for early-stage non–small cell lung cancer. Systemic therapy (chemotherapy, target therapy, and/or immune checkpoint inhibitors) is the modality of choice for advanced non–small cell lung cancer. Chemotherapy with or without radiation therapy is used to treat small cell lung cancer.

Palliation of symptoms related to lung cancer is an important aspect of overall management. The use of analgesic agents for pain, antiemetics for nausea, and antidepressants can improve quality of life. Radiotherapy can be used to palliate bone pain related to metastatic disease, hemoptysis, or symptoms of airway obstruction. Invasive bronchoscopic procedures (e.g., laser ablation, electrocautery, stent placement) may be palliative in patients with airway obstruction. Evidence shows that in patients with end-stage non–small cell lung cancer, early integration of palliative care (see Chapter 58) can increase median survival and quality of life.[53]

FUTURE SCENARIO

The prospect of major advances in the prevention, detection, and treatment of lung cancer is strong. An attainable vision for 2038 could be as follows: Primary prevention campaigns have successfully lowered the number of individuals who are smoking to 5% of the adult population; legislation has been passed to broadly prevent exposure to tobacco smoke in public places; progress has been made in occupational exposure avoidance; and successful measures have been enacted to clean the air. Individuals who have changes in lung cells that suggest lung cancer could develop are now identified and are being treated with medication to prevent it from developing. Individuals at risk for developing lung cancer are part of a screening program that detects early-stage lung cancer with an accurate test that is inexpensive and acceptable to all. Technology has improved diagnostic abilities by making imaging more specific and biopsies more accurate. Noninvasive diagnostics have expanded, with advances in blood and breath testing, while artificial intelligence is being used to help characterize lung nodules, and population management tools are assisting clinicians and patients to be compliant with guideline and value-based recommendations. In addition to tumor appearance, researchers are identifying characteristics of tumor biology that allow more selection in choosing treatments. The best form of local control for a given tumor in a given patient (resection, radiation) is known, and means have been developed to minimize the effect of these interventions on the quality of life. Novel agents have been developed that can reach and kill tumor cells while avoiding injury to healthy tissue and stimulate our immune system to attack cancer cells without impacting healthy tissues. As evidence of successes, lung cancer is no longer the leading cause of cancer-related mortality in the United States.

ROLE OF THE RESPIRATORY THERAPIST IN MANAGING PATIENTS WITH LUNG CANCER

RTs perform many important roles in the evaluation and management of patients with lung cancer. Being among the first clinicians with which patients have contact after they are admitted, RTs are often on the front lines to help identify patients who are at risk for lung cancer. Risk factors such as smoking history or occupational exposure may be revealed to the RT as part of a formal history or in more casual conversation during an initial assessment. In the case of patients who are actively smoking, the RT has the opportunity to educate these individuals on the dangers of smoking and on the means available to help

MINI CLINI

Evaluating Surgical Risk

Problem

A 62-year-old man with a long history of smoking has a chronic, productive cough. A chest CT obtained because of a recent episode of hemoptysis reveals a lung mass in the right upper lobe. Results of transbronchial biopsy suggest the presence of adenocarcinoma. There is no evidence of metastasis. As part of the patient's evaluation for surgery, he has the following spirometry and diffusing capacity results:

Forced vital capacity (FVC) 4.2 L (80% of predicted value)
FEV_1 1.6 L (60% of predicted value)
FEV_1/FVC 0.4
DLCO 15.5 (60% of predicted)

Can he undergo surgery?

Discussion

Assessment of lung reserve is an important step in the preoperative evaluation of patients with lung cancer being considered for surgical resection. After calculating his PPO values with the segment method ($60 \times [1 - 3/19]$), he is found to have a PPO FEV_1 and PPO DLCO of 50%. This patient, similar to most patients with lung cancer, has PPO values between 30% and 60% because of underlying COPD. He needs further evaluation with exercise testing such as a stair climb or shuttle walk test to better assess his risk. Furthermore, he needs treatment optimization for his COPD. If the patient's lung function remains at moderate risk after these steps, a cardiopulmonary exercise test may help to clarify his risk.

them quit. Patients who are surgical candidates may see the RT when performing pulmonary function testing and other prescreening assessments. RTs can offer guidance on the proper use of inhaled medications, the use of supplemental O_2, and the role of pulmonary rehabilitation before and after treatment. RTs are frequently key participants in pulmonary rehabilitation programs and may also be part of the home care teams that care for patients using supplemental oxygen. Also, many RTs assist with diagnostic tests such as bronchoscopy and staff pulmonary function laboratories. Finally, in the context that the RT may spend substantial time with the patient with lung cancer, the RT may be an important source of psychologic support and help. Taken together, these various diagnostic and treatment roles establish that the RT plays a crucial role in helping to manage patients with lung cancer.

SUMMARY CHECKLIST

- Approximately 234,030 cases of bronchogenic carcinoma were newly diagnosed in the United States in 2018, making bronchogenic carcinoma a major health hazard. It is the leading cause of cancer-related mortality in the United States.
- Approximately 85% of all cases of bronchogenic carcinoma are linked to smoking.
- The major histopathologic types of bronchogenic carcinoma include adenocarcinoma, squamous cell carcinoma, and small cell carcinoma. Adenocarcinoma is the most common type, representing more than 40% of all cases.
- The clinical manifestations of bronchogenic carcinoma result from local growth of the tumor, regional spread, metastases to extrathoracic and intrathoracic organs, and paraneoplastic syndromes.
- The staging system most commonly used for non–small cell bronchogenic carcinoma is based on status of the primary tumor (T), local and regional lymph node involvement (N), and the presence of metastasis (M). The TNM classification groups patients in stages or categories that correlate with survival. Small cell lung cancer is classified in two stages, limited and extensive, although the TNM system can be used as well.
- The most commonly used treatments for patients with non–small cell lung cancer are surgical resection, radiation therapy, and systemic therapy (chemotherapy, targeted, and immunetherapies). Treatment of most patients with small cell carcinoma includes chemotherapy, with radiation therapy added when this cancer is limited stage.
- The most effective way to prevent lung cancer is to prevent smoking.

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33

Neuromuscular and Other Diseases of the Chest Wall

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CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Identify pulmonary function test results typically seen in patients with neuromuscular disease.
- List the potential respiratory complications associated with neuromuscular disease.
- Identify the clinical signs and symptoms associated with respiratory muscle weakness.
- Describe techniques for monitoring patients with respiratory muscle weakness.
- Describe general respiratory care management of patients with respiratory muscle weakness.
- Describe the clinical findings and treatment for each of the following neuromuscular disorders: Duchenne muscular dystrophy, myotonic dystrophy, polymyositis, myasthenia gravis, Lambert-Eaton syndrome, Guillain-Barré syndrome, diaphragmatic paralysis, amyotrophic lateral sclerosis, ventilator-induced diaphragm dysfunction, spinal cord injury, stroke, traumatic brain injury, and kyphoscoliosis.
- Understand the role of the RT in caring for patients with neuromuscular and chest wall diseases.

CHAPTER OUTLINE

KEY TERMS

amyotrophic lateral sclerosis
ankylosing spondylitis
bilateral diaphragm paralysis
bulbar palsy
Duchenne muscular dystrophy
dermatomyositis
Guillain-Barré syndrome
kyphoscoliosis
Lambert-Eaton syndrome
myotonic dystrophy
myasthenia gravis
neuropathy
obstructive sleep apnea
paradoxical motions
polymyositis
sleep-related hypoventilation
stroke
traumatic brain injury
unilateral diaphragm paralysis
ventilator-induced diaphragm dysfunction

Neuromuscular diseases are the group of conditions that affect the function of muscles and/or nerves. The impact of neuromuscular function on the respiratory system can be understood by splitting the respiratory system into separate components, including the lungs, the ventilatory pump, the airway, and the neural respiratory centers. In this scheme, even if the lungs are normal, diseases that affect the brain, nerves, muscles, or thoracic cage can lead to respiratory failure or hypoxemia. (See Table 33.1 for a list of respiratory system components and their functions.)

Understanding the interactions between these components is essential to understanding how their dysfunction leads to disease. The neuromuscular components of the respiratory system are shown in Fig. 33.1. Maintenance of normal respiratory function depends on intact, functional components of the neuromuscular system. The neuromuscular system contributes to

TABLE 33.1 Respiratory System Components

Lungs	Provide air-blood gas exchange.
Ventilatory pump	Composed of the rib cage, diaphragm, and other respiratory muscles. Functions to bring atmospheric air in and out of the lungs.
Upper airway	The mouth and throat are responsible for speech, swallow, cough, airway protection, prevention of aspiration, and avoidance of airway closure during sleep.
Neural respiratory centers	Control of ventilation is provided by integrated systems in the brain and the peripheral nervous system

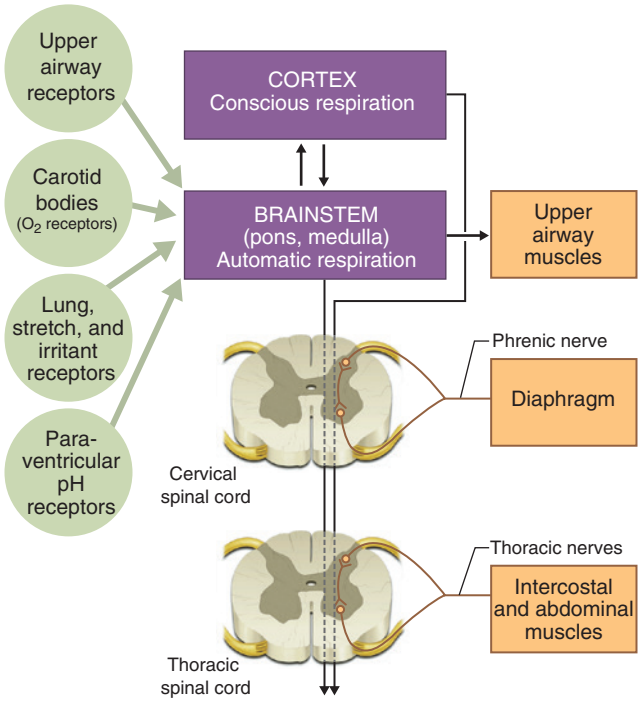

Fig. 33.1 The neuromuscular components of the respiratory system include elements of the cortex (which allow conscious alteration of breathing) and motor centers (which maintain upper airway tone). Brainstem structures receive input from peripheral O_2, pH, and stretch receptors and generate automatic respiration. Efferent nerves carry central nervous impulses to the muscles of respiration through the phrenic and spinal nerves, which drive the muscles of respiration.

respiratory function in three main ways: (1) regulation of respiratory drive, (2) ventilation, and (3) airway protection (e.g., cough). The respiratory consequences of neuromuscular disease typically develop in the following sequence:

- Atelectasis
- Impaired cough
- Airway plugging from retained secretions
- Sleep-disordered breathing
  - Obstructive sleep apnea
  - **Sleep-related hypoventilation**
- Hypoventilation while awake
- Ankylosis (stiffening) of the ribcage
- Aspiration

TABLE 33.2 Locations at Which Several Neuromuscular Diseases Affect the Respiratory System

Location	Disease
Cerebral cortex and brainstem (including the respiratory center)	Stroke and traumatic brain injury
Spinal cord	Trauma, transverse myelitis, multiple sclerosis
Motor neurons (upper and lower)	ALS, spinal muscular atrophy, progressive muscular atrophy, poliomyelitis, and postpoliomyelitis
Peripheral nerves	Guillain-Barré syndrome, neuralgic amyotrophy, Lyme disease, Diphtheria polyneuropathy
Neuromuscular junction	Myasthenia gravis, Lambert-Eaton syndrome, botulism
Muscle	Duchenne muscular dystrophy, polymyositis, acid maltase deficiency, polymyositis, and dermatomyositis
Thoracic cage	Kyphoscoliosis and ankylosing spondylitis

ALS, Amyotrophic lateral sclerosis.

- Pneumonia
- Respiratory failure
- Death

A basic understanding of the physiology of ventilation and chest wall mechanics (see Chapters 11 and 19) is needed to understand how abnormalities of the upper airway, chest wall, diaphragm, and abdominal muscles cause disease. This chapter reviews major disorders of the neuromuscular and skeletal systems that affect breathing. Disorders are grouped according to which functional unit of the neuromuscular system is affected, focusing on pulmonary manifestations of these disease processes (Table 33.2).

PATHOPHYSIOLOGY AND PULMONARY FUNCTION TESTING

Pulmonary function testing in patients with neuromuscular weakness typically reveals a restrictive ventilatory defect even if the lungs are normal (Chapter 20). Vital capacity (VC), forced expiratory volume in 1 second (FEV_1), and total lung capacity (TLC) are decreased. Functional residual capacity is normal or decreased. Residual volume (RV) may be increased, especially as weakness becomes more severe. Diffusing capacity is usually normal or near normal, representing normal lungs with preserved gas exchange function.[1] Clinically significant weakness of the diaphragm presents with orthopnea and can be identified by a decrease in VC going from the upright to the supine position. The normal decrease is 7% to 10%. A 10% to 20% decrease suggests diaphragm weakness or unilateral paralysis but can also be seen in obesity and or abdominal wall disorders. A 25% decrease has a 79% sensitivity and 90% specificity for diaphragm weakness (Table 33.3 and Fig. 33.2).[2] Whereas a decreased maximal inspiratory pressure (PImax) is generally specific for diaphragm weakness, a decreased maximal expiratory pressure (PEmax) is not specific to any single muscle group.[3]

TABLE 33.3 Pulmonary Function Testing Results From a Patient With Profound Diaphragm Weakness

	Predicted Value	Lower Limit of Normal	Sitting Position	% of Predicted	Supine Position	% Change From Sitting
FVC	4.42	3.55	1.85	42	0.89	–52
FEV_1	3.36	2.62	1.51	45	0.68	–55
FEV_1/FVC	75.88	66.20	81.75	108	75.76	–7
TLC	6.53	4.92	4.21	64		
RV	2.10	1.34	2.39	114		
DLCO	24.93	16.67	17.16	69		
Plmax	110.58	75.02	18.46	17		
PEmax	207.29	140.04	26.52	13		

DLCO, Diffusing capacity for carbon dioxide; *FEV_1,* forced expiratory volume in 1 second; *FVC,* forced vital capacity; *PEmax,* decreased maximum expiratory pressure; *Plmax,* decreased maximal inspiratory pressure; *RV,* residual volume; *TLC,* total lung capacity.

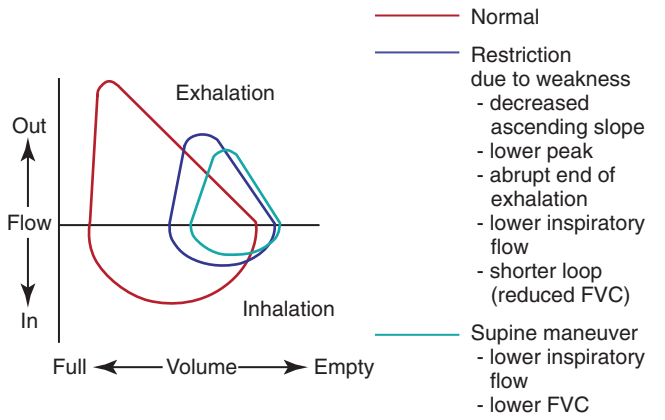

Fig. 33.2 Normal flow-volume loop compared with loops from a patient with neuromuscular weakness, showing characteristic ventilatory restriction, which worsens when the patient is placed in the supine position. *FVC,* Forced vital capacity.

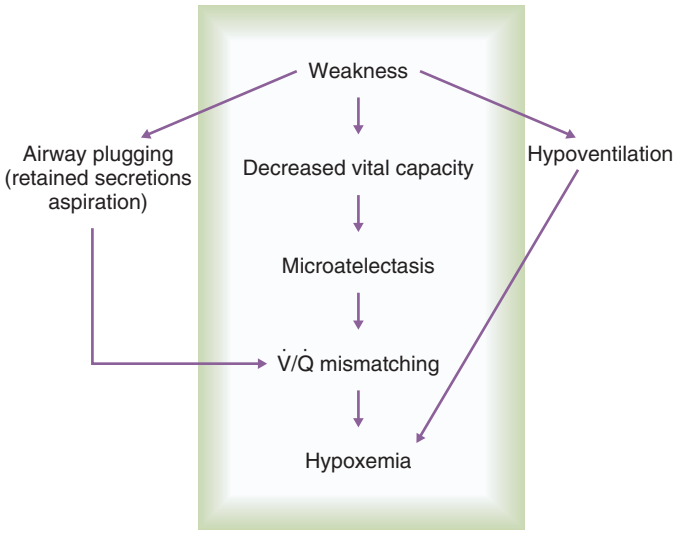

Fig. 33.3 Atelectasis as a mechanism of hypoxemia in patients with respiratory muscle weakness. V̇/Q̇, Ventilation/perfusion.

Gas exchange, which can be evaluated by arterial blood gas (ABG) analysis, is often normal in early neuromuscular pulmonary dysfunction. As the dysfunction progresses, ABGs will show hypercapnia, and, in later stages of disease, hypoxemia. Hypoxemia develops for several reasons, including hypoventilation, atelectasis, and airway plugging, each of which leads to ventilation/perfusion (V̇/Q̇) mismatching within the lung (Fig. 33.3). Supplemental oxygen (O_2) can be dangerous for patients with neuromuscular dysfunction and preexisting hypercapnia, as it can result in acute worsening of hypercapnia.[4] When starting O_2 in such patients, close monitoring with ABGs is needed to ensure safety.

Effective cough has three phases: inflation, compression, and expulsion. Inflation requires adequate inspiratory muscle strength to pull in enough volume in the lungs to generate appropriate cough pressure. The glottis must then close to allow compression, where the expiratory muscles start to pressurize the air in the lungs and narrow the central airway lumen. During expulsion, the glottis opens and air moves down the pressure gradient through the narrowed tracheobronchial tree at high velocities, thus clearing the airways. Dysfunction in any component (inspiratory muscles, glottis dysfunction, and expiratory muscles) leads to diminished peak cough flow. Although not objective, simple observation of the strength of a patient's cough can provide insight. Measuring peak cough flow is more objective; values less than 270 L/min are inadequate and should prompt consideration of cough-assist techniques (Table 33.4). A peak cough flow between 160 and 270 L/min may be adequate during periods of health but may worsen during respiratory tract infection, and so cough-assist techniques should be considered during times of illness.

RULE OF THUMB Neuromuscular weakness of the respiratory muscles may be present before any substantial decrease in VC or FEV_1 is measured. Values of PEmax may be decreased by 50% or more before any decrease in VC or FEV_1 is noticed.

CLINICAL SIGNS AND SYMPTOMS

In the early stages of neuromuscular disease, patients with respiratory muscle weakness initially report exertional dyspnea, fatigue, and poor sleep quality. The first symptoms usually start by affecting sleep. Patients with neuromuscular weakness are especially vulnerable during the night. Sleep is affected due to the effects of normal sleep stages on respiratory muscle function. This leads to nocturnal hypoventilation and interrupted sleep. The patients will often recognize a change in the quality of sleep, frequent

TABLE 33.4 Respiratory Modalities Commonly Used in Neuromuscular Weakness

Step 1: Lung Hyperinflation, Reexpansion of Atelectasis

Initiation: These therapies are generally the first respiratory support offered to patients with neuromuscular weakness and should be started when the risk of atelectasis becomes problematic, corresponding to FVC <40% predicted. Periodic hyperinflation helps manage atelectasis, increases peak cough flow aiding airway clearance, and reduces long-term risk of thoracic cage kyphosis (stiffening).

Self-inflating manual ventilation devices (e.g., Ambubag)	A simple form of hyperinflation can be achieved by delivering a single breath during inhalation. A more complex technique involves breath-stacking multiple inhalations, which requires coordination of glottis opening/closing and breath delivery.
Breath-stacking with mouthpiece ventilation	Volume-targeted ventilators with "kiss-trigger" can achieve the same breath-stacking and hyperinflation as manual breaths with a self-inflating bag.
Incentive spirometry	This device guides patients through a slow, deep inhalation. Although helpful in other conditions (postoperative, etc.) there is limited application in neuromuscular weakness.

Step 2: Cough-Assist and Secretion Clearance Modalities

Initiation: These therapies should be added when unassisted cough is not adequate to clear secretions. Indicated for regular use when peak cough flow <160 L/min or during respiratory tract infections when peak cough flow <270 L/min.

Mechanical insufflation-exsufflation	Device is applied to the airway, often with face mask, and provides brief positive pressure, followed by negative pressure to expel secretions. The insufflation component can also be used to achieve hyperinflation. When introducing the device, low pressures should be used (+10/–10 cm H_2O); if tolerable, the pressure should be titrated up (e.g., +40/–40 cm H_2O or higher). A single session should include multiple consecutive insufflation/exsufflations, and there should be multiple sessions daily. Suction may be needed to clear the mobilized phlegm.
Manually assisted cough	Somewhat similar to the Heimlich maneuver, this technique requires a second person to place their hands on the anterior chest and upper abdomen and deliver inward thrusts after the patient takes a deep inspiration.
Suction device	Helpful in patients with **bulbar** (mouth and throat) **palsy** (weakness) who have difficulty managing oral secretions.
Nebulized treatments	Albuterol or saline may help thin deep airway secretions, aiding clearance
High-frequency chest wall therapy	Manual or device-based therapy with a vest can be used to mobilize secretions in peripheral airways. Although helpful in cystic fibrosis and bronchiectasis, these therapies have limited application in neuromuscular conditions, as the airways are generally healthy, with normal mucus-clearing function.
Airway vibration device	Multiple devices apply vibration waves to the airway, intended to loosen secretions deep in the tracheobronchial tree; as with chest wall therapies above, there is limited application in neuromuscular conditions.

Step 3: Ventilatory Support Devices

Initiation: Sleep-disordered breathing (sleep hypoventilation and obstructive sleep apnea) always develops before wakeful hypoventilation; thus nighttime support is generally started prior to daytime ventilation. Hypoventilation and obstructive sleep apnea share many of the same features, including poor sleep quality, daytime drowsiness, and mood changes. Differentiating these conditions may require overnight oximetry and capnography, polysomnography, and daytime ABG or end-tidal exhaled CO_2.

Noninvasive ventilation (NIV)	Modern ventilators are more portable and functional, allowing different modes of vent support and different interfaces for daytime vs. nighttime (e.g., intermittent mouthpiece ventilation during daytime and continuous BiPAP via nasal pillows at night). In chronic stable neuromuscular disease, NIV is indicated for treatment of sleep-disordered breathing and daytime hypoventilation. In neuromuscular disease with acute worsening, NIV can be helpful for postextubation support as well as to prevent intubation (e.g., myasthenic crisis)
Interfaces for noninvasive ventilators	Nasal pillows and nasal mask are generally preferred for nighttime use, but the right interface depends mostly on patient factors, especially comfort. A mouthpiece interface for daytime ventilation has many advantages (unrestricted speech and swallow, freedom from tight-fitting masks, control over when to receive breathing assistance) but requires adequate strength to engage and disengage the mouthpiece and to achieve lip-seal.
Invasive ventilation via tracheostomy	Invasive ventilation allows higher airway pressures, while tracheostomy allows reliable clearance of airway secretions, but these advantages come at the expense of compromised speech and swallowing and increased risk of pneumonia.
Body ventilators	The "iron lung", pneumatic belt, and rocking bed ventilators are of historic interest, but there is ongoing interest in cuirass-style ventilation.
Diaphragm pacing	Stimulation of electrodes surgically implanted into the branches of the phrenic nerve within the diaphragm can provide ventilatory support. Limited but positive clinical experience with weaning spinal cord–injured patients from ventilation.
Glossopharyngeal breathing, "frog-breathing"	This technique trains patients with intact bulbar (mouth and throat) function but ventilatory pump dysfunction how to take a mouthful of air and "gulp" it into their lungs. This can be used as a rescue technique if ventilation is unexpectedly stopped (e.g., power outage) or to augment lung hyper-inflation and assist cough assist.
Supplemental O_2	Although neuromuscular patients may be hypoxic, supplemental O_2 is generally *contraindicated*, as hypoventilation can actually be worsened with administration of O_2. Occasionally, patients with both lung disease and neuromuscular weakness may benefit from cautious use of O_2.

ABG, Arterial blood gas; *BiPAP*, bilevel positive airway pressure; *FVC*, forced vital capacity.

MINI CLINI

Problem

What physical findings may suggest developing respiratory failure in a patient with neuromuscular weakness?

Discussion

Patients whose respiratory muscle strength is inadequate to meet their ventilatory needs have a *rapid, shallow breathing* pattern and use *accessory muscles* of inspiration, especially the neck strap muscles (e.g., sternocleidomastoid). The use of accessory muscles in the setting of a weak or paralyzed diaphragm pulls the diaphragm upward (cephalad) during inspiration, resulting in paradoxical inward movement of the abdomen, called ***paradoxical breathing***. Inability to complete a sentence in one breath is called *staccato speech*. Nonrespiratory signs include sweating, tachycardia, and restlessness. Any of these findings may signal the need for respiratory support.

awakenings, morning headaches, daytime sleepiness, and fatigue. As the disease process progresses, patients may complain of orthopnea and show signs of cor pulmonale (remodeling of the right ventricle, usually in response to pulmonary hypertension, which causes symptoms including dyspnea, fatigue, anorexia, chest pain, edema, and syncope). These changes occur because the muscles involved with respiration can no longer generate or maintain normal ventilation, initially during sleep and ultimately during wakefulness. The response to hypoxemia of increased respiratory drive is preserved in most patients with neuromuscular weakness.[5] Because these patients often do not have the strength to take deep breaths, they maintain minute ventilation by increasing respiratory rate and adopting a rapid, shallow breathing pattern, which requires less respiratory muscle strength but provides less efficient ventilation. Patients with poor inspiratory muscle function (especially diaphragm weakness) may have marked orthopnea and prefer to sleep in a seated position. They also may experience a decline in voice volume or quality. Muscle weakness can progress to the point that adequate ventilation is no longer maintained and hypercapnia occurs.

RULE OF THUMB When a patient complains of immediate shortness of breath on lying down, especially if one side is worse than the other, the problem is diaphragm weakness until proven otherwise.

MONITORING AND ASSESSING PATIENTS WITH NEUROMUSCULAR RESPIRATORY WEAKNESS

There are multiple important physiologic processes to monitor in patients with neuromuscular respiratory weakness, including oxygenation, ventilation, lung expansion, cough adequacy, aspiration risk, and nutrition and sleep quality.

Routine measurement of O_2 saturation (e.g., pulse oximetry) is indicated. A decrease in O_2 saturation can represent hypoventilation or development of atelectasis/pneumonia. Early on or in mild neuromuscular impairment, it often represents atelectasis and airway plugging (see Fig. 33.3), but as the disease progresses, hypoventilation and pneumonia are common causes. Hypoxemia due to atelectasis should prompt lung hyper-inflation therapy (see Table 33.4).

Cough adequacy was discussed above in the section "Pathophysiology and Pulmonary Function Testing" and is assessed with clinical observation and measurement of peak cough flows. Often, asking the patient if they feel capable of coughing effectively will yield important information.

The risk of aspiration is especially high in patients with bulbar weakness (weakness of the mouth and throat), a situation that is often worsened by ineffective cough. In these patients, the inability to clear the airway can increase the work of breathing, resulting in muscle fatigue, hypoventilation, and respiratory failure. Aspiration pneumonia is another major risk. Risk of aspiration can be assessed in several ways. A history of frequent coughing while eating or drinking should raise suspicion for aspiration. Formal evaluation with a video fluoroscopic swallow study can assess the specific risk of aspiration with different kinds of foods and drinks. A simple but informative bedside test is to watch the patient drink a small amount of water: aspiration is suspected if they cough after swallowing.

Malnutrition is a major risk in patients with neuromuscular weakness, especially with bulbar dysfunction. Weight loss is a reliable sign of malnutrition and can result in a vicious cycle, where malnutrition leads to weakness, which further exacerbates malnutrition. Once identified, malnutrition should prompt consideration of dietary supplements, or—if consistent with the patient's goals of care—a feeding tube.

Patients with neuromuscular weakness are especially vulnerable to sleep-disordered breathing, including sleep hypoventilation and **obstructive sleep apnea** (OSA). Although polysomnography is the gold standard for diagnosis and treatment of sleep-disordered breathing, home-based sleep studies (oximetry ± capnography) or nocturnal pulse oxymetry are more convenient and can be used in any patient with neuromuscular weakness who endorses symptoms of sleep-disordered breathing (e.g., poor sleep quality, daytime drowsiness).[6] In addition, modern home ventilators (both invasive and noninvasive) have sophisticated technology that records many ventilatory and physiologic parameters and allow remote access to these data through "device download" functions. These devices are both therapeutic and diagnostic, allowing care providers to review information such as the apnea-hypopnea index, inspiratory and expiratory pressures, respiratory rate, tidal volume, and minute ventilation.

Routine ventilatory function testing includes measurement of sitting and supine VC, inspiratory and expiratory pressure, and CO_2 levels (using end-tidal CO_2 or ABG). However, patients with bulbar weakness may have difficulty achieving a lip-seal on the mouthpiece of the spirometer; in this case, the sniff inspiratory pressure is sometimes more practical, as it can be done with a face mask.

MANAGEMENT OF RESPIRATORY MUSCLE WEAKNESS

Ventilatory support, initially used only during sleep, then extending into intermittent use while awake and eventually to 24-hour continuous use, is a well-recognized treatment for respiratory

MINI CLINI

Assessment of a Patient With Neuromuscular Weakness

Problem

A 50-year-old man with amyotrophic lateral sclerosis (ALS) is admitted to the hospital because of right lower lobe pneumonia. His PO_2 is 68 mm Hg on room air. ALS was diagnosed 3 years previously, and he has had progressive worsening of dyspnea since then. These symptoms first occurred with mild exertion and then with supine position, which the patient has noticed in the last 1 or 2 months. A recent measurement of VC at the physician's office was 2.1 L (50% predicted value). The patient has recently noticed difficulty with swallowing and frequent coughing at meals. What features in the patient's history may be relevant with regard to management?

Discussion

This patient has a disease that progresses slowly in most cases, now with acute deterioration probably due to aspiration pneumonia. The earliest symptom of neuromuscular weakness in the respiratory muscles is exertional dyspnea, which this patient has had for some time. A more significant finding is orthopnea, which is highly suggestive of diaphragmatic weakness. Patients with significant diaphragmatic weakness prefer an upright position, which allows the abdominal contents to shift toward the feet, thus reducing the paradoxical breathing that compromises ventilation. Although the patient may not have had a critically low VC recently, his value is low. Additional loading of already compromised ventilatory machinery can lead to fatigue and frank respiratory failure. It is important to recognize that acute diseases like pneumonia or viral illness exacerbate the weakness and will predispose a patient with stable neuromuscular weakness to respiratory fatigue and subsequent respiratory failure. The history of feeding difficulty suggests that the pneumonia is related to aspiration. The location of pneumonia in the lower lobe also favors the diagnosis if the aspiration occurred when the patient was seated upright. Noninvasive ventilation (NIV) could be considered for long-term treatment at this time.

failure from progressive neuromuscular weakness, but other respiratory support measures should be started earlier in the disease process (see Table 33.4). Lung hyperinflation (breath stacking) can be beneficial in the early stages of weakness when the risk of atelectasis becomes problematic. Breath stacking also allows patients to maintain clear airways. When breath stacking is not feasible due to bulbar disease, cough assist should be added to the therapy. Used together, these interventions can decrease hospitalizations for respiratory complications in patients with neuromuscular disease.[7] In addition to these interventions, general rehabilitation focusing on aerobic conditioning, muscle strengthening, and respiratory muscle training often can delay the need for ventilatory support and improve the overall quality of life for patients with muscle weakness.[8]

NIV is used for long-term support of patients with neuromuscular disease, as well as temporarily during episodes of acutely worsened respiratory status (see Table 33.4). Long-term NIV for stable neuromuscular weakness is started as nighttime support to treat sleep hypoventilation. If the disease progresses, NIV can be extended into daytime hours and can even be used continuously 24 h/day, but special care is needed to prevent skin breakdown at the site of mask contact. NIV can also be used as a rescue therapy for acute decompensation, such as caused by pneumonia, aspiration, or surgery. In this case, NIV should be started when the patient begins to feel fatigued by work of breathing, when there is still opportunity to recover. If NIV is delayed until frank hypercarbia has developed, it may fail simply because the patient is too severely fatigued.[9] NIV can also be used to reduce the risk of reintubation as patients are recovering from an acute illness requiring temporary invasive ventilation. Postextubation NIV is most likely to be successful when the patients tolerate NIV because of previous experience and the burden of secretions is manageable.

NIV should be considered in patients with chronic or acute neuromuscular weakness, exacerbations of myasthenia gravis (MG), postextubation support for patients intubated for transient respiratory failure, and neuromuscular patients who also have COPD or congestive heart failure. Clinical situations where NIV is not usually indicated or performs poorly include Guillain-Barré syndrome, acute spinal cord injury, severe hypercapnia, acute brain injury with coma, severe agitation requiring sedation, a large amount of respiratory secretions, hemodynamic instability (e.g., shock), and procedures requiring sedation or anesthesia.[9]

Starting NIV on a patient with chronic neuromuscular weakness is a key moment in their life: first impressions affect long-term adherence. Thus achieving comfortable settings on a device that fits in with the patient's lifestyle is crucial. Modern ventilators are small and lightweight, with a battery that allows portability. These advanced devices can also switch between separate nighttime and daytime ventilator modes, which is generally indicated as the interface and settings needed for good sleep are usually different than what is needed for daytime support. A full face mask, nasal mask, or nasal pillows are often the most comfortable for nighttime NIV. The best daytime interface is more variable; some patients may have multiple interfaces to use throughout the course of one day. A mouthpiece interface for daytime ventilation has many advantages (improved speech and swallow, freedom from tight-fitting masks, control of timing, and volume of ventilatory support) but requires adequate strength to engage and disengage the mouthpiece and to achieve lip-seal. Mouthpiece interface with a "kiss-triggered" volume-cycled ventilator can be used to breath-stack, achieving lung-hyperinflation, cough augmentation, and louder voice (even shouting!). During acute decompensation, a face mask that fits over the mouth and nose may be preferable, as it provides the most reliable positive airway pressure (PAP).

The airway pressures and mode of ventilation should be set to achieve the following: comfort/tolerance, adequate ventilatory support, avoidance of rapid shallow breathing, and elimination of OSA. The expiratory positive airway pressure (EPAP, also known as PEEP or continuous positive airway pressure [CPAP]) should be set as low as possible (<4 cm H_2O) to reduce air leaks and patient–ventilator dyssynchrony. The exception to this rule occurs in patients with sleep apnea, when EPAP needs to be set high enough to eliminate obstructive events. Inhalations can be delivered either via volume or pressure control. In volume control, the tidal volume is preset, and the machine will deliver regardless unless pressure limits or alarms are met. In pressure control, the IPAP is preset, and the delivered tidal volume varies based on patient effort and respiratory system characteristics. There are other modes of NIV, none with more evidence than simple bilevel. These modes use adaptive targeting and adjustment algorithms (e.g., volume-assured pressure support [VAPS or

MINI CLINI

Care of a Patient With Myotonic Dystrophy

Problem

A 45-year-old man has myotonic dystrophy. He has progressive dyspnea that has increased, particularly in the last year. PCO_2 determined from ABG analysis is 55 mm Hg. VC is 2.3 L (40% predicted). He has been using a mechanical insufflation-exsufflation device with good clearance of secretions and no episodes of pneumonia. The patient reports daytime drowsiness and is sleeping in a semi-recumbent position at night because of orthopnea. What interventions are indicated for this patient?

Discussion

The patient has a disease that can result in respiratory insufficiency. VC is decreased, and arterial carbon dioxide levels are increased. These factors are consistent with hypoventilation secondary to neuromuscular weakness. The patient has dyspnea on exertion and orthopnea. All these factors suggest that mechanical ventilation should be considered.

AVAPS]) to adjust the IPAP according to tidal volume or minute ventilation targets. Although studies are underway, issues with synchrony, adjustment of IPAP and how to set targets are still not standardized.[10] This highlights the importance of setting up and appropriately titrating the NIV device. Care should also be taken to choose the appropriate trigger to initiate inhalation: a threshold that is not sensitive enough could result in missed triggers (a patient breathing effort without assistance from the ventilator), whereas a threshold that is too sensitive will increase risk of auto-triggering (inappropriate delivery of a ventilator breath). A backup rate can be set to reduce the risk of hypoventilation from missed triggers.

Diaphragm pacing in patients with spinal cord injury (SCI) has been described using direct stimulation of an intact phrenic nerve to contract the diaphragm and produce negative intrathoracic pressure and inspiration, with favorable clinical experience.[11,12] A proof-of-concept study demonstrated that pacing may prevent diaphragm atrophy due to mechanical ventilation.[13] Unfortunately, despite early nonrandomized studies showing benefit of diaphragm pacing in ALS,[14] more recent randomized controlled trials demonstrated higher mortality.[15,16]

NIV may be a reasonable first choice for this patient. The patient's mental status and bulbar function are intact. He has no significant problems with secretions. (Important factors for successful application of NIV are discussed in Chapter 50.) Use of a biphasic PAP unit may be instituted and titrated to patient tolerance. NIV use overnight should be especially helpful, but it may be helpful for adjustment to start by using the device during the day. A time-triggered backup rate can be set on some ventilators to facilitate ventilation of patients who may inadequately trigger the ventilator. As long as bulbar function and secretion management are maintained, NIV is a reasonable choice for ventilatory support.

RULE OF THUMB Patient with neuromuscular weakness should generally receive the low EPAP and a relatively high inspiratory airway pressure (IPAP). The difference between IPAP and EPAP represents the pressure support that is augmenting ventilation.

SPECIFIC NEUROMUSCULAR DISEASES

Disorders of the Muscle (Myopathic Disease)

Primary muscle disease can decrease the ability of a normal neural impulse to generate effective muscle contraction. Some commonly recognized myopathies include Duchenne muscular dystrophy (DMD), myotonic dystrophy, and polymyositis. Box 33.1 presents a more complete list of myopathic diseases associated with ventilatory dysfunction.

Duchenne Muscular Dystrophy and Becker Muscular Dystrophy

Duchenne muscular dystrophy is a genetic muscle-wasting disorder caused by mutations in the dystrophin gene.[17] Because it is an X-linked recessive disorder with shortened survival, it affects essentially only males. The diagnosis is made when a dystrophin mutation is found in DNA from circulating white blood cells or when dystrophin is found to be absent or abnormal in biopsied muscle tissue.

DMD manifests early in life with proximal muscle weakness that leads to a waddling gait, exaggerated lumbar curvature (lordosis), and frequent falls. Most affected children need a wheelchair by 12 years of age. Death used to occur by 20 years of age as a result of declining respiratory muscle strength and subsequent infection. However, over the last decade, the improvement and widespread use of NIV has improved survival.

Other systemic effects of DMD include scarring of the left ventricle and decreased bowel motility (ileus). The progressive

BOX 33.1 Myopathic Diseases With Associated Respiratory Dysfunction

Muscular Dystrophies
- Duchenne muscular dystrophy
- Becker muscular dystrophy
- Myotonic dystrophy
- Facioscapulohumeral muscular dystrophy
- Limb-girdle dystrophy
- Oculopharyngeal dystrophy

Myopathies
- Congenital myopathies
- Nemaline rod myopathy
- Centronuclear myopathy
- Metabolic myopathies
- Acid maltase deficiency
- Mitochondrial myopathies (Kearns-Sayre syndrome)
- Inflammatory myopathies
- Polymyositis
- Dermatomyositis
- Hypothyroid-related and hyperthyroid-related myopathies
- Endocrine myopathies
- Steroid-induced myopathies (including critical illness myopathy)
- Miscellaneous myopathies
- Electrolyte disorders (e.g., hypophosphatemia and hypokalemia)
- Rhabdomyolysis
- Periodic paralysis
- Postneuromuscular blockade myopathy

decline in respiratory function in patients with DMD is due to global loss of muscle strength and typically manifests at the time of wheelchair dependence.

Progressive scoliosis is associated with DMD and can contribute further to respiratory insufficiency. Many patients undergo spine fusion surgery, and often the procedure allows greater comfort and ease in maintaining an upright posture. Although no randomized trials have proved any benefit of surgery on pulmonary function,[18] it appears that the rate of respiratory decline is slower after fusion surgery.[19]

OSA is present in a significant proportion of patients with DMD, but diagnosis with formal polysomnography is burdensome, and progression of the disease would require frequent retitrations of PAP support. New home-based PAP devices have advanced technologies that allow automatic adjustment of PAP to eliminate OSA events, as well as transmission of physiology and device data to care providers to aid decision making around therapy customization.

Whether to start positive pressure ventilation (PPV) is a decision that most patients will face at some point in the disease. Nocturnal PPV is indicated with signs of hypoventilation, often corresponding to forced vital capacity (FVC) less than 40% predicted.[20,21] It can be started in response to home-based oximetry showing O_2 desaturation during sleep with or without capnography showing elevations of CO_2.

Nocturnal ventilation usually improves daytime ventilatory function in patients with DMD,[22] presumably through prevention of respiratory muscle fatigue. Despite this improvement, studies of early "prophylactic" PPV for patients with DMD have shown that early PPV failed to delay the need for invasive ventilatory support.[23]

Myotonic Dystrophy

Myotonic dystrophy is the most common form of muscular dystrophy in adults, with an estimated frequency of 1 in 8000 persons.[24] *Myotonia,* or delayed muscle relaxation, is the key feature of this neuromuscular disorder. This autosomal dominant disorder causes progressive muscle weakness, abnormalities of the cardiac conduction system, endocrine dysfunction, and cataracts.

Respiratory dysfunction in myotonic dystrophy is common, usually occurring late in the course of disease, and can include respiratory muscle weakness, OSA, and bulbar muscle dysfunction leading to aspiration. Sleep-disordered breathing is common, even at an early age.[25]

Patients with myotonic dystrophy can be very sensitive to anesthesia and respiratory depressants. Both respiratory failure and prolonged neuromuscular blockade have been reported in patients with myotonic dystrophy given usual doses of these agents. NIV can be used postoperatively, especially if the patient has had the opportunity to adjust to NIV preoperatively. Prolonged monitoring after surgery is prudent.[26,27]

Nocturnal NIV is effective for these patients and should be considered if the patient has declining SaO_2 or hypercapnia despite optimal use of lung hyper-inflation and cough-assist techniques. Tracheostomy can often be avoided but may become necessary if NIV fails, often because of inability to clear secretions.

Polymyositis and Dermatomyositis

Polymyositis and **dermatomyositis** are inflammatory myopathies that occasionally involve the respiratory muscles and may also cause interstitial lung disease (e.g., scarring or other changes in the lung tissue). Respiratory muscle weakness generally parallels limb weakness, and can progress rapidly. Respiratory failure can develop within weeks to months, especially if interstitial lung disease is also present. The diagnosis of these diseases is based on clinical findings of myalgia, elevated muscle enzyme levels (creatine phosphokinase or aldolase), and compatible electromyographic or muscle biopsy results.[28,29]

Corticosteroids are important in the initial management of polymyositis and dermatomyositis, especially if interstitial lung disease is present. Other immunosuppressive and cytotoxic agents are used for aggressive disease control and to limit long-term steroid exposure. Various antisynthetase antibodies (e.g., the Jo-1 antibody) have been identified that are associated with polymyositis and dermatomyositis; when these antibodies are present, the risk of interstitial lung disease is increased.[30–32] Pulmonary vasculitis can occur with polymyositis and dermatomyositis and can lead to O_2 exchange abnormalities and pulmonary hypertension.

Ventilator-induced diaphragm dysfunction. **Ventilator-induced diaphragm dysfunction** (VIDD) is very common among critically ill patients and results in weaning failure and long-term respiratory impairment.[33] Sepsis and mechanical ventilation are definite risk factors for VIDD, while steroids and paralytics are less consistently implicated.[34] The mechanism of development is multifactorial, but disuse atrophy plays a major role, while other contributors include neuropathy, myopathy, malnutrition, and systemic inflammation. VIDD can start developing within 24 hours of ventilation.[35] Studies have demonstrated that respiratory effort by the patient impacts the development of VIDD: atrophy develops with "over-assistance" by the ventilator and minimal patient effort. Conversely, with "under-assistance" from the ventilator and excessive patient breathing efforts, the diaphragm thickens, potentially representing muscle injury, and these patients have similarly bad outcomes. Optimal assistance with mechanical ventilation that preserves a normal diaphragmatic effort has been recently proposed as a "muscle-protective ventilation" strategy, but further studies are needed.[36–39]

Disorders of the Neuromuscular Junction

Disorders of the neuromuscular junction decrease conduction of nervous system impulses to the peripheral muscles, resulting in muscle weakness. Different clinical syndromes are caused by defects in different molecules or components of the neuromuscular junction, which is represented schematically in Fig. 33.4, which compares a normal neuromuscular junction with an abnormal junction in MG. Disorders of the neuromuscular junction include MG, Lambert-Eaton syndrome (LES), and certain poisonings (organophosphate, tetanus, botulism).

Myasthenia Gravis

Myasthenia gravis is characterized by intermittent muscular weakness, which worsens on repetitive stimulation and improves with administration of anticholinesterase medications, such as edrophonium or neostigmine.[40] Muscle involvement commonly

MINI CLINI

Care of an Intensive Care Unit Patient to Minimize the Risk for Ventilator-Induced Diaphragm Dysfunction

Problem

A 60-year-old man is in the ICU with respiratory failure secondary to severe influenza pneumonia. He has developed acute respiratory distress syndrome (ARDS), and gas exchange is severely impaired, with a PaO_2/FiO_2 ratio of 90. He is requiring relatively high positive end expiratory pressure (PEEP) and FiO_2 to maintain adequate SaO_2. He has septic shock, requiring pressors immediately after intubation for the initiation of mechanical ventilation. Along with the immediate needs for stabilization, resuscitation, and supportive care, the ICU team needs to consider what impact their therapeutic choices now will have on his risk for developing ventilator-induced diaphragm dysfunction.

Discussion

This scenario is seen in high-acuity ICUs, in which patients with severe ARDS and sepsis are frequently found. This patient is at risk of poor respiratory outcome, from ARDS and VIDD, as well as long-term global outcomes from ICU-acquired weakness and neurocognitive impairment. Lung-protective ventilation using low-tidal volumes is important early in ARDS, but the deep sedation and continuous infusions of paralytics used to achieve this goal run counter to "muscle-protective ventilation" and may be detrimental for the diaphragm. The benefit of lung-protective ventilation in ARDS is time dependent; as the disease resolves, the risk-to-benefit ratio of deep sedation and paralytics will no longer be favorable. At that point, allowing the patient to resume a "normal" breathing effort, without overloading or under loading the diaphragm, may help work toward weaning from mechanical ventilation.

affects the muscles of the mouth, neck, and especially the eyes, with a presenting complaint of diplopia (double vision) or ptosis (a drooping eyelid) in more than 65% of patients (Fig. 33.5).[41] Weakness worsens with repetitive use and improves with rest, thus varying throughout the day, often worst in the evening and best in the early morning. MG is "a disease of young women and old men," as reflected by hospital admission demographics.[42]

Auto-antibodies target different elements in the neuromuscular junction in MG, often the acetylcholine receptor (ACh-R). The antibodies inactivate the ACh-R and block transmission of electrical impulses from the nerve to the muscle.[43] Antibody negative disease is confirmed with nerve studies and appropriate response to therapy.[40] Thymus abnormalities are common in MG, including hyperplasia and thymoma, and are involved in the pathogenesis of MG, as thymectomy improves the disease course.[44]

Myasthenic crisis is defined as respiratory failure or delayed postoperative extubation resulting from myasthenic weakness.[45] Triggers of myasthenia crisis include respiratory infection, aspiration, surgery, pregnancy, or new medications. Patients at risk of needing respiratory support should be monitored in an ICU. Measuring VC has limited value in predicting an impending myasthenic crisis, as muscle strength can deteriorate quickly and unexpectedly due to fatigue.[40] However, muscle strength can also recover very quickly in MG. For this reason, NIV can be very effective in providing support for an impending myasthenic crisis, provided that it is initiated before irreversible respiratory muscle fatigue has developed.[46] Multiple retrospective studies have concluded that if NIV is initiated early on during ventilatory decompensation, intubation can be avoided. NIV is likely to fail if

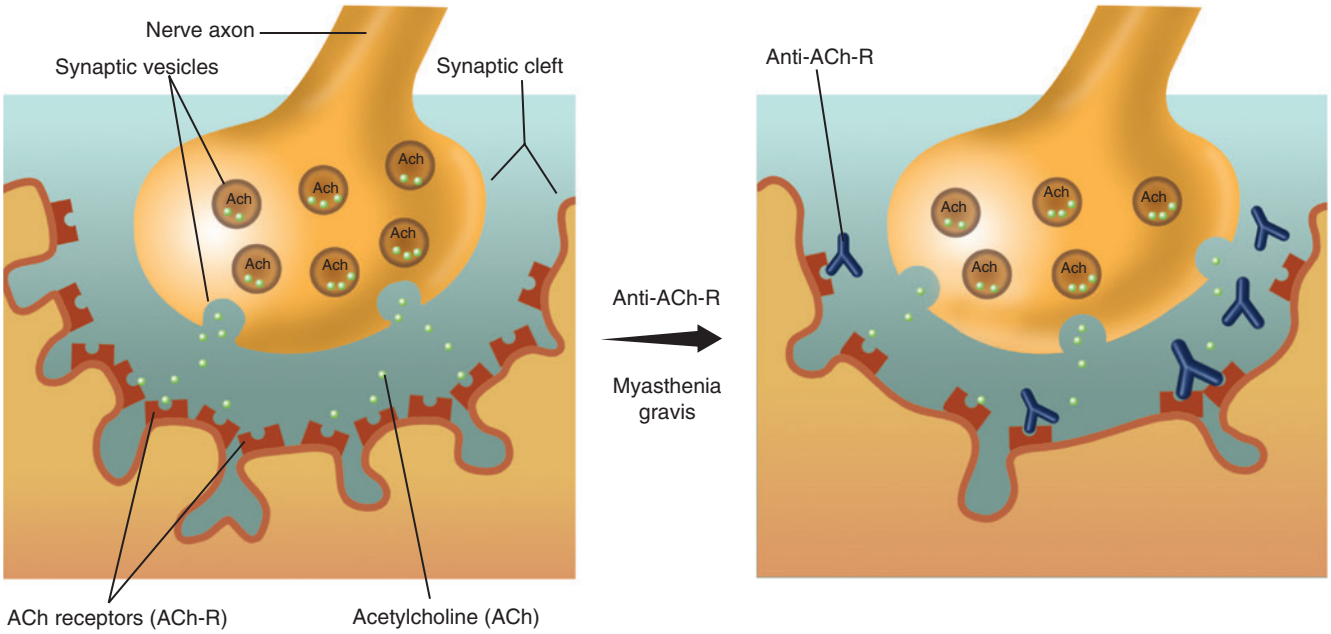

Fig. 33.4 The neuromuscular junction with acetylcholine *(ACh)* stored in presynaptic vesicles. ACh is released by exocytosis into the synaptic cleft in response to a presynaptic nerve impulse. ACh binds to its cognate *ACh-R* on the postsynaptic membrane. This process depolarizes the nerve, propagates the impulse, and causes muscle contraction. Binding of anti-ACh-R antibodies to ACh-R mediates autoimmune destruction of the receptors. This process leads to abnormal muscle activation and the weakness that occurs in patients with myasthenia gravis.

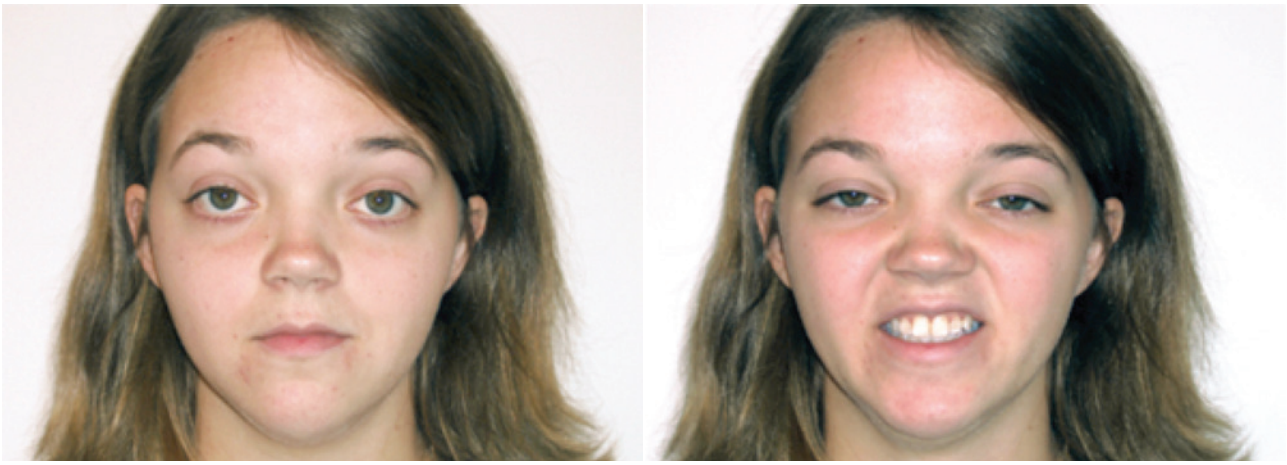

Fig. 33.5 Features of Ocular and Facial Weakness in a Patient With Myasthenia Gravis. At rest *(left),* there is slight bilateral lid ptosis, which is partially compensated by asymmetric contraction of the frontalis muscle, raising the right eyebrow. During attempted smile *(right),* there is contraction of the medial portion of the upper lip and horizontal contraction of the corners of the mouth without the natural upward curling, producing a "sneer." (From Sanders DB, Howard JF: Disorders of neuromuscular transmission. In Bradley, editor: *Neurology in Clinical Practice,* ed 5, Philadelphia, 2008, Butterworth Heinemann.)

initiation is delayed until after the onset of hypercarbia, a late sign of ventilatory failure.[9]

Lambert-Eaton Syndrome

Another syndrome of neuromuscular weakness arising from a disorder at the neuromuscular junction is **LES**. More than 50% of cases of LES are associated with cancer, especially small cell carcinoma of the lung, which accounts for 80% of malignancies causing the syndrome.[47] Autoantibodies against voltage-gated calcium channels at the nerve terminals impair the release of acetylcholine and can lead to both muscular weakness and autonomic insufficiency.[48] Increasing muscle strength with repetitive stimuli is a characteristic feature of LES, which differentiates it from MG; MG is characterized by progressive fatigue of muscular contraction with repetitive stimulation.

In comparison to MG, respiratory muscle involvement is uncommon in LES and—when it does occur—tends to be mild. Respiratory failure is rare, but can be triggered by medications (e.g., paralytics). Patients with LES usually present with weakness of the proximal muscles. The clinical course of LES tends to be one of relative stability with less fluctuation than MG. Management is aimed at treating the underlying cancer. If no malignancy is found, surveillance for lung cancer is recommended every 6 months, and LES is managed symptomatically with immunosuppressive medication or acetylcholinesterase inhibitors.[47,49]

Disorders of the Nerves

The peripheral nerves may be affected by toxic agents, inflammatory processes, vascular disorders, malignant diseases, and metabolic or nutritional imbalances. Hundreds of conditions have been associated with neuropathies leading to respiratory muscle dysfunction. Representative conditions are listed in Box 33.2.

Guillain-Barré Syndrome

Guillain-Barré syndrome (GBS) is acute inflammatory immune-mediated polyradiculoneuropathy and is the most common peripheral **neuropathy** causing respiratory insufficiency. GBS is characterized by paralysis and diminished reflexes, often with sensory symptoms and pain. The disease can be triggered by gastrointestinal or respiratory infection, which is thought to generate autoantibodies that target the myelin of the nerve sheath.[50] The diagnosis of GBS is based on a combination of clinical, laboratory, and electrophysiologic data (Table 33.5). Treatment for GBS may be beneficial when started within 2 weeks of symptom onset. Intravenous immunoglobulin or plasma exchange can be used (but not both). Corticosteroids offer little if any benefit in GBS.[51,52]

About 30% of patients with GBS will develop respiratory muscle weakness significant enough to require intubation and mechanical ventilation.[53] Median duration of mechanical ventilation is 28 days and is occasionally much longer. Tracheostomy should be considered in all patients who continue to require ventilatory support at 1 week and who are unable to lift their arms and have very abnormal nerve conduction tests.[54,55] NIV can be helpful during the recovery phase to achieve liberation from invasive ventilation, but given the prolonged course of patients who develop respiratory muscle weakness, NIV is unlikely to prevent intubation, and the delay could be dangerous.[9] Weaning trials during invasive ventilation should begin in the recovery phase, when VC is greater than 15 mL/kg and PImax greater than 30 cm H_2O.

BOX 33.2 Causes of Phrenic Nerve Dysfunction Leading to Respiratory Dysfunction

- Cardiac surgery (cold cardioplegia to arrest the heart can cause "frostbitten" phrenic nerves; ischemic injury to nerves also can complicate cardiac surgery)
- Neuralgic amyotrophy
- Diabetes
- Trauma
- Thoracic aneurysm

TABLE 33.5 Comparison of Myasthenia Gravis and Guillain-Barré Syndrome

	MG	GBS
Pattern of muscle involvement	Eye muscles are almost always involved. Weakness can be widespread or localized, usually proximal rather than distal.	Leg and arm weakness develop initially, which moves proximally with widespread muscle involvement, ("ascending paralysis"). Initial bulbar weakness is less common but can mimic MG.
Triggers	Pneumonia, aspiration, medications, surgeries, and pregnancy	Infection of gastrointestinal or respiratory tract 2–3 weeks prior to symptoms
Timeline of weakness	Weakness waxes and wanes throughout a single day. Disease responds to medical management but may require treatment for years.	A single episode of weakness steadily progressing over days to weeks, followed by recovery. (i.e., monophasic illness)
Diagnosis	Clinical impression + supportive findings: • Positive antibodies (e.g., acetylcholine receptor antibodies) • Nerve conduction studies show weakness developing with repetitive stimulation • Weakness improves with edrophonium (acetylcholinesterase inhibitor)	Clinical impression: • Bilateral weakness, especially legs • Absent reflexes • Monophasic (see "timeline" above) • Absence of alternative diagnosis Supportive findings: • Cerebrospinal fluid with high protein and low cells • Nerve conduction studies show conduction block or decreased velocities
Respiratory support	Noninvasive ventilation (NIV) is helpful when initiated early on as respiratory muscle fatigue is developing. Aggressive bronchopulmonary hygiene (lung hyperinflation, suctioning, cough assist) can be helpful.	Although ~70% of GBS patients will NOT require ventilatory support, those who do will not quickly recover and often require prolonged intubation. During the recovery phase, NIV can be helpful to prevent reintubation.
Medical treatment	Long-term treatment: cholinesterase inhibitors, steroids, and/or other immunotherapy Myasthenic crisis: plasma exchange and intravenous immunoglobulin, with high-dose steroids and rituximab for intractable disease	Intravenous immunoglobulin and plasma exchange may be helpful if given early in the disease. No long-term therapy is helpful.
Long-term outcome	Response to medical therapy is usually good. Prolonged intubation is largely avoidable.	Tracheostomy and prolonged recovery are common in patients requiring intubation. Even so, the large majority of patients will eventually regain the ability to walk.

GBS, Guillain-Barré syndrome; *MG*, myasthenia gravis.

RULE OF THUMB Patients with GBS whose vital capacity becomes less than 20 mL/kg or whose PImax is less than 30 cm H_2O and PEmax is less than 40 cm H_2O are at risk for respiratory failure and may need ventilatory support. Patients who meet the criteria of this "20-30-40 rule" are at high risk of decompensating, and intubation should be considered, especially if weakness is still progressing or if there is difficulty managing oral secretions.[56,57]

If he continues to require invasive ventilation after one week of intubation, without progress during ventilator weaning trials, then tracheostomy should be considered. Upper airway function (speech, swallow, and cough) is impaired by an oral endotracheal tube (ETT), and early tracheostomy would relieve this impairment, although full restoration of speech, swallow, and cough will be determined by neuromuscular recovery. Tracheostomy is a comfortable and secure airway compared to an oral ETT, permitting patient mobility and active rehabilitation. As his respiratory status recovers, NIV can be introduced (while deflating the cuff completely and capping the tracheostomy), especially at night, when the risk of hypoventilation for diaphragmatic weakness is greatest. If nocturnal NIV is successful, the tracheostomy can be down-sized or decannulated, as determined by his need for airway suctioning.

Phrenic Nerve Dysfunction and Diaphragm Paralysis

Each hemidiaphragm is supplied by its own phrenic nerve. The phrenic nerves emerge from the spinal cord at level C3 to C5

MINI CLINI

Respiratory Care of a Patient With Guillain- Barré Syndrome

Problem

A previously healthy 52-year-old man is admitted to the hospital with complaint of difficulty walking for the past 3 days. He reports having a diarrheal illness 2 weeks ago, which has now resolved. During the first several days of hospitalization, he experiences low-grade fever and intense pain in his legs, and his leg weakness spreads upward to involve his trunk and hands. A lumbar puncture shows elevated albumin but no inflammatory cells. Nerve conduction studies show evidence of a demyelinating process. The diagnosis of GBS is made, and he is started on intravenous immunoglobulin. Because his weakness continues to worsen, he is transferred to the ICU for closer monitoring. The next morning, he reports dyspnea with increased arm weakness.

Discussion

This patient has the typical clinical picture for GBS, with worrisome features of progression involving the respiratory muscles. Monitoring in the ICU should include serial assessment of VC, PImax, and PEmax. If he meets any of the "20-30-40" criteria, then elective intubation should be considered. Other factors that influence the decision to intubate include the tempo of his illness, ability to manage airway secretions, and autonomic lability, which can be problematic in GBS. Ideally, intubation should be performed electively, while he still has physiologic reserve. Waiting for emergency intubation can be lethal.

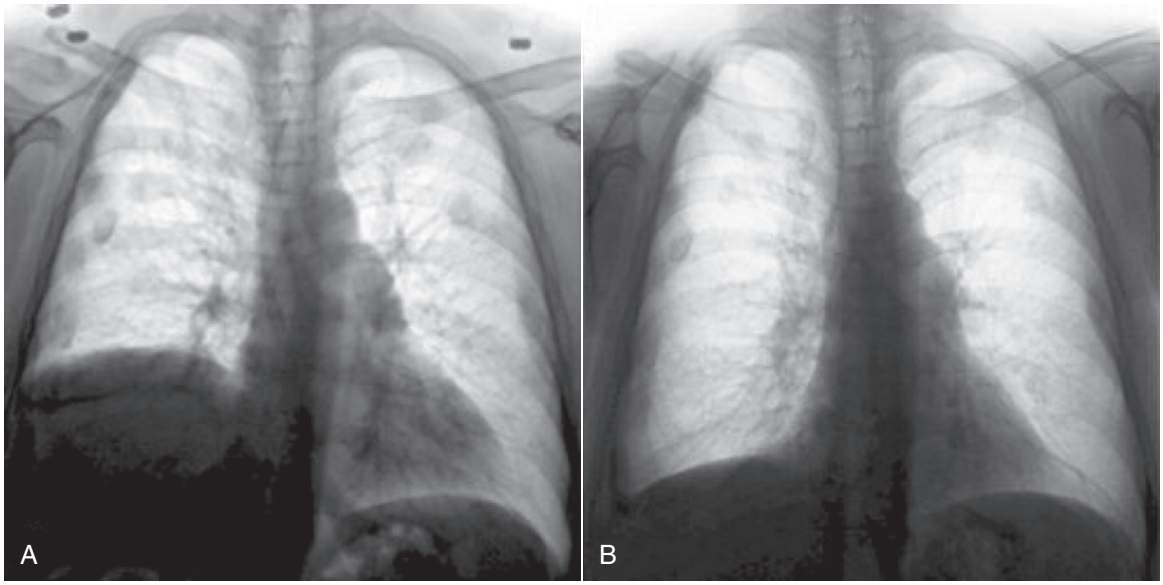

Fig. 33.6 (A) Chest X-ray showing elevation of a right hemidiaphragm. (B) Chest X-ray in the same patient 1 year after laparoscopic diaphragm plication. (From Groth SS, Andrade RS: Diaphragm plication for eventration or paralysis: a review of the literature, *Ann Thorac Surg* 89:S2146–S2150, 2010.)

and descend through the mediastinum along the great vessels of the chest and pericardium. Damage to or interruption of either phrenic nerve leads to paralysis of the ipsilateral hemidiaphragm. Bilateral involvement is seen in high SCI and causes complete diaphragmatic paralysis. Many of the other neuromuscular disorders discussed in this chapter cause respiratory impairment because of bilateral diaphragm involvement. Unilateral diaphragmatic paralysis has many causes, including trauma, brachial plexus injury, or inflammation and cardiac surgery, but in many cases, a cause cannot be determined (i.e., idiopathic).

Bilateral diaphragm paralysis generally causes significant dyspnea, especially when lying flat, bending over, or when immersed in water. Pulmonary function tests show decreased VC while upright, with values often dropping 30% to 50% further in the supine position. Sleep-disordered breathing is common, as normal ventilation is highly dependent on diaphragm function, especially during REM-sleep. For this reason, nocturnal NIV is generally helpful. Diaphragm pacing (discussed as follows in the section *Spinal Cord Injury*) is an appealing option, but clinical experience is quite limited. Because paradoxical movement of the diaphragm is not a major culprit in bilateral paralysis, diaphragm plication is not helpful.[58]

Unilateral diaphragm paralysis is usually minimally symptomatic but can contribute to respiratory impairment, especially in the presence of other comorbidities. Patients with unilateral diaphragmatic paralysis often have near-normal pulmonary function test, but VC may drop 10% to 30% in supine position. An elevated hemidiaphragm on chest X-ray is often the presenting finding (Fig. 33.6A). At fluoroscopy, the paralyzed hemidiaphragm paradoxically rises into the thorax during a sudden forceful inspiration (sniff test). Surgical plication moves the weak hemi-diaphragm downward to a more normal position (see Fig. 33.6B), minimizes paradoxical motion, and improves overall lung function.[59–62] Unilateral diaphragm weakness may slowly improve, sometimes over years, so plication should be delayed until serial testing shows that no further improvement is occurring, usually 2 years from the onset of weakness.[58]

RULE OF THUMB Unilateral diaphragm paralysis is often minimally symptomatic, but surgical plication can be offered to selected patients with significant dyspnea and respiratory impairment who are unlikely to recover (e.g., surgical transection of the nerve, or symptoms persisting >2 years from onset).

Disorders of the Spinal Cord

Upper motor neurons arise from cell bodies in the motor areas of the brain and terminate on the anterior horn cells in the spinal cord, which constitute the lower motor neurons that extend out to the skeletal muscles. Motor neuron diseases such as ALS specifically affect the neurons in the spinal cord that control movement, whereas trauma of the spinal cord can potentially damage all of the neurons (motor, sensory, autonomics, etc.) at the site of injury. Other examples of spinal cord pathology include transverse myelitis, syringomyelia, poliomyelitis, and spinal cord tumors.

Amyotrophic Lateral Sclerosis

Amyotrophic lateral sclerosis is the prototypical motor neuron disease, with progressive paralysis due to degeneration of motor neurons in the brain and spinal cord (i.e., upper and lower motor neurons). Weakness from ALS usually begins in a localized muscle group, often the arms, and spreads out progressively to involve most muscles, including the diaphragm.[63] In one quarter of cases, weakness begins in the bulbar muscles. Rarely, ALS starts as isolated diaphragm dysfunction in an otherwise intact patient. Respiratory paralysis eventually occurs in all patients with ALS and is the most frequent cause of death. There is no cure for ALS, and medications—such as riluzole and edaravone—provide limited improvement in survival.[63] NIV is the only therapy that has increased survival and quality of life in patients with ALS.[64]

The profile of respiratory impairment in ALS depends on the pattern of muscle involvement and stage of the disease. Gradual decline in respiratory muscle strength may be punctuated by acute respiratory infection or aspiration, resulting in abrupt respiratory failure. Diaphragm weakness will result in impaired cough, orthopnea, and sleep hypoventilation, deteriorating to wakeful hypoventilation. Bulbar weakness will result in malnutrition, impaired cough, aspiration, and pneumonia. Speech is also impaired, which can be socially and psychologically troubling. Limb weakness will result in functional decline and impaired mobility with eventual wheelchair dependence.

Respiratory support can be added in a stepwise fashion, as outlined in Table 33.4, tailored to each patient's specific needs. NIV is a reasonable option for many patients and has been shown to slow the rate of pulmonary decline, improve symptoms, and prolong survival.[64–66] Severe bulbar dysfunction, with poorly managed secretions and aspiration, limits the benefit of NIV. Because the disease invariably advances, patients and care providers should plan ahead and discuss invasive ventilation and tracheostomy. Many patients with ALS choose not to receive invasive mechanical ventilation and opt for palliative management. However, many patients do desire invasive ventilatory support; up to 90% of such patients report satisfaction with their decision and would choose tracheostomy and ventilation again in the same situation.[67] Conversely, caregivers of patients with ALS who receive home ventilation often report frustration and unhappiness.[68]

RULE OF THUMB The timing and type of ventilatory intervention (noninvasive or invasive) in the care of patients with ALS are the subject of much discussion. General guidelines for considering ventilatory assistance include VC less than 50% predicted, orthopnea, maximal sniff nasal inspiratory force less than 60 cm H_2O, daytime hypercapnia, and abnormal nocturnal oximetry.[69]

RULE OF THUMB ALS is a complex and devastating disease and often requires a multidisciplinary approach, with input and active participation from many clinical specialties, including pulmonology, neurology, gastroenterology, palliative medicine, respiratory care, physical therapy, occupational therapy, social work, home nursing, psychiatry, and spiritual care.

Traumatic Spinal Cord Injury

Approximately 17,500 SCIs occur in the United States each year,[71] with the majority of disability due to the cervical SCI. While young men continue to be far more likely than females to sustain a SCI, there is a recent trend towards older men being injured, often due to a fall. Complete cord injury is associated with absent motor and sensory function below the level of injury, and the patient's condition rarely improves. Patients with incomplete injury have residual function and tend to improve to varying degrees. Pneumonia and sepsis are the leading causes of death in SCI.[71]

The respiratory manifestations of SCI depend on the level of injury and extent of damage. Cervical cord injuries can be functionally divided into two classes: high cervical cord lesions (C1 to C2) and middle to low cervical cord lesions (C3 to C8). The diaphragm receives innervation from nerve roots exiting the spinal cord at levels C3 to C5. Complete injury above this level results in total respiratory muscle paralysis and death unless urgent intubation and ventilation are performed. Injury to the cord at C3 to C5 can severely reduce respiratory strength, as manifested by reductions in PEmax, PImax, FVC, and FEV_1, consistent with a restrictive ventilatory defect. Patients adopt a rapid, shallow breathing pattern and inhale with the aid of the neck strap muscles (e.g., sternocleidomastoid and scalenes), whose innervation is spared except with high cervical cord injury. Despite the serious nature of injury between C3 and C5, 80% of intubated patients with this lesion can ultimately be liberated from invasive ventilation. The muscles of expiration (muscles of the chest and

MINI CLINI

Respiratory Care of a Patient With Amyotrophic Lateral Sclerosis

Problem

A 57-year-old man was diagnosed with ALS 1 year ago, after he developed weakness in his left arm. He is now wheelchair bound because of severe weakness in all four extremities. Nocturnal NIV was started 4 months ago and has improved his orthopnea, poor sleep, and nightmares; his FVC at that time was 50% predicted, with a 30% drop while supine. He is now using NIV increasingly into waking hours, with a nasal pillow interface. He is having more difficulty speaking, especially when wearing NIV. He has lost 40 pounds in the last 6 months due to decreased appetite. He denies coughing while eating. O_2 saturation is 92% on ambient air. Cough peak flow is 160 L/min. What measures can be offered to help him maintain his respiratory function, avoid exacerbations that could lead to acute respiratory failure, and plan for the future?

Discussion

This patient is experiencing the progressive weakness involving most muscle groups, which is typical of ALS. Diaphragm and generalized muscle weakness is objectively measured by a low FVC that drops further in the supine position. His self-initiated use of daytime NIV indicates progressive ventilatory muscle weakness and a clinical opportunity to provide better daytime support. Daytime mouthpiece ventilation may be very helpful, provided he has enough bulbar function to create a good lip seal. A volume controlled mode delivering 700 to 1500 mL (adjusted to comfort) can be used for breath stacking, which cannot be done with a pressure-cycled mode. Using a "sip trigger" or "kiss trigger," multiple back-to-back inhalations will be delivered by the ventilator, which helps reexpand atelectasis (which is suggested by his mild hypoxemia), augment peak flows during cough, and possibly reduce the risk of thoracic cage kyphosis. If his "breath-stacked" cough peak flow remains less than 270 L/min, then thoraco-abdominal compressions ("quad cough") done after breath stacking will improve cough efficiency. If these do not facilitate effective cough, or if glottic closure is not effective, then a mechanical insufflator-exsufflator should be introduced for cough-assistance. The initial pressures should be low to achieve tolerance, and then titrated upward to achieve effect. Importantly, patients with ALS and bulbar (mouth and throat) weakness may not tolerate high pressures with this technique because of airway closure.[70] His 40-pound weight loss may be due to respiratory insufficiency impairing his ability to eat and might improve with daytime mouthpiece ventilation, which—compared with other ventilator interfaces—supports better swallow and speech function (even shouting). Unfortunately, even if there is a response, it will likely be short-lived, and a feeding tube should eventually be considered. Importantly, a discussion with him and his loved ones on goals of care is urgently needed, as there is high risk of acute respiratory deterioration.

abdominal wall) receive neural input from spinal levels T1 to L1 and are predominantly affected by middle to low cervical cord lesions. This condition manifests as a marked reduction in PEmax compared with PImax and a weak or ineffective cough.

There is a curious type of inverted paradoxical breathing when a low cervical SCI causes paralysis and atrophy of the chest and abdominal wall but preserves diaphragm strength. During inhalation when lying flat, the diaphragm contracts downward—which moves the abdomen outward—and generates negative intrathoracic pressure, which pulls the paralyzed and atrophied rib cage inward. Lying flat assists exhalation, because the weight of the abdomen acts as a restoring force and pushes the diaphragm upwards. Respiratory mechanics are impaired in the upright position; because the abdominal wall muscles are atrophied and highly compliant, there is no restoring force to assist exhalation, compromising ventilation and gas exchange. This leads to a rare type of positional respiratory impairment termed "platypnea-orthodeoxia syndrome": dyspnea and hypoxemia in the upright position. Abdominal binding in athletes with low cervical SCI was shown to improve respiratory mechanics.[72]

Bulbar strength is preserved in SCI, but many airway-protective behaviors (e.g., cough, sneezes, sighs) are impaired, due to disruption in the neural circuitry responsible for these reflexes.[73] There is significant functional recovery of airway-protective behaviors within 1 year of injury due to plasticity and regeneration in the nervous system.

Sleep-disordered breathing is highly prevalent in SCI, approaching 60% in complete tetraplegia.[74] A case series of adults with SCI using home-based sleep studies combined with transcutaneous capnography demonstrated OSA in 81%, nocturnal hypercapnia in 28%, and central sleep apnea in 24%.[75] The same group reported positive clinical experience in treatment of sleep-disordered breathing in SCI, using autotitrating CPAP to treat OSA and NIV with VAPS to treat nocturnal hypercapnia.[76]

Acute Brain Injury

Traumatic brain injury, **stroke**, and intracranial hemorrhage are all types of brain injury that can lead to respiratory failure through several mechanisms, most commonly failure to protect the airway often associated with decreased level of consciousness (LOC). While intubation for acute ischemic stroke is rare,[77] patients with acute severe trauma often need urgent airway management because of risk of aspiration and impaired ventilatory drive and function.[78] For more information on the initial airway and ventilation management of trauma patients, please see Chapter 30 on trauma.

The prognosis of brain-injured patients who are intubated varies significantly, with some patients quickly recovering normal function, while others will be permanently neurologically devastated. As these patients stabilize, multiple factors determine when the patient can be safely extubated, especially mental status, ability to protect the airway, resiliency, and frailty, as reflected by age and comorbidities.[79] Airway management in brain injury highlights an important concept: the ability to ventilate is separate from the ability to protect the airway. Successful ability to ventilate, as assessed by "conventional" weaning parameters such as rapid shallow breathing index and a spontaneous breathing trial, does not predict successful extubation in patients with acute brain injury. Although there is much debate around which brain-injured patients should have a trial of extubation versus proceeding straight to tracheostomy, there are a few guiding principles. First, extubation is more likely to fail when airway-protective behaviors are absent (cough, gag, and swallow).[80,81] Second, a decreased LOC, as reflected by a low Glasgow coma score, in the absence of other concerning factors, should not prevent a trial of extubation.[82,83] On the other hand, decreased LOC is a risk factor for failure of extubation and is a major factor in the decision to pursue tracheostomy.

Tracheostomy provides reliable long-term artificial airway protection and allows rescue ventilation when needed. Multiple studies have compared early versus late tracheostomy in severely brain-injured patients, with some evidence of a few modest benefits from early tracheostomy, including shorter duration of ventilation and ICU length-of-stay in brain-injured patients.[84,85] Families or decision-makers of brain-injured patient should know that 25% of patients who underwent tracheostomy after a severe stroke were alive and decannulated 12 months later, often with some functional neurologic improvement.[86]

MINI CLINI

Respiratory Dysfunction in Spinal Cord Injury

Problem

A young man who is otherwise healthy falls from a ladder and transects the spinal cord at the level of C6. Which muscles of the respiratory system will be affected, and what will be the effect?

Discussion

Transection of the spinal cord at the level of the sixth cervical vertebra paralyzes any muscle group that receives its innervation from nerve roots that exit the spinal vertebral canal below C6. A review of the innervation of the major muscles of inspiration and expiration is important:

Upper airway, tongue, palate (bulbar muscles): Cranial nerves IX, X, XI, and XII
C3 to C5: Diaphragm
C3 to C8: Neck strap and shoulder girdle muscles
T1 to T12: Intercostal muscles
T7 to L1: Abdominal muscles

The upper airway, tongue, shoulder girdle muscles, and diaphragm should be intact in this patient's injury, but the airway defense behaviors (cough, sigh, and sneeze) will be impaired because of disrupted neural networks involving the thorax. Maintenance of intrathoracic volume depends partly on continuous activation of intercostal muscles, which stabilize and expand the thoracic cage. With these muscles paralyzed, there will be inverted paradoxical breathing, with inward movement of the ribcage during inhalation while the abdomen moves outward in a normal fashion. Cough will be impaired because it depends on activation of abdominal and intercostal muscle groups, both of which are paralyzed in this injury. Although he has an intact diaphragm, this patient has a poor cough mechanics and impaired airway defense behaviors, which increases the risk of atelectasis, airway plugging, and pneumonia.

DISORDERS OF THE THORACIC CAGE

The thoracic cage contains the lungs and is composed of the ribcage and spine, which provide the framework on which the

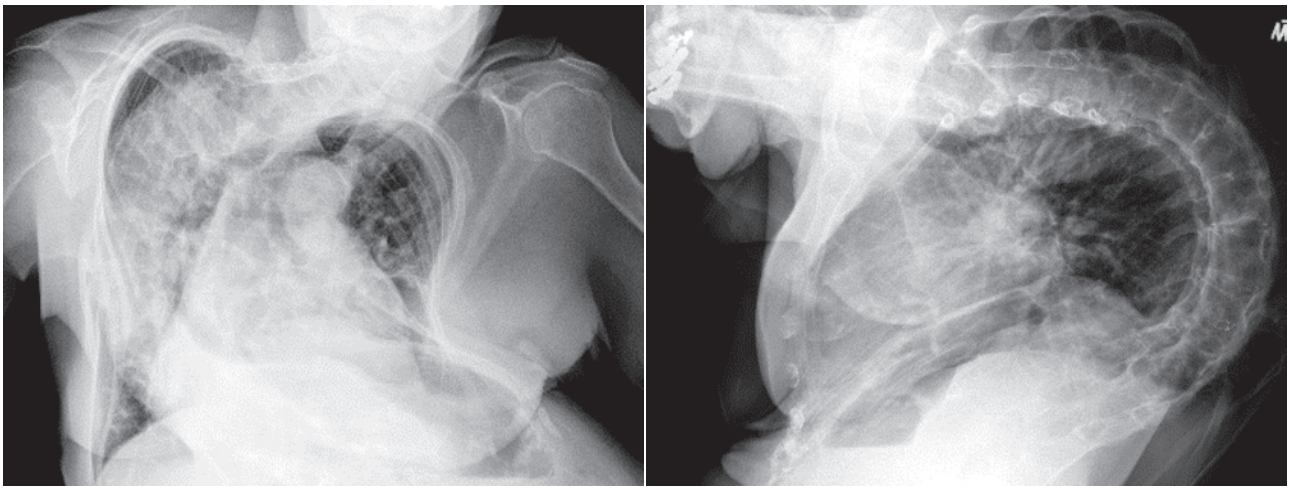

Fig. 33.7 Frontal and Lateral Chest X-Ray Views of the Same Patient, Showing Severe Scoliosis and Kyphosis.

respiratory muscles act. Normal ventilatory mechanics depend on a compliant thoracic cage with normal geometry, allowing unrestricted movement throughout the respiratory cycle. Restriction of the ribcage is usually secondary to spinal deformity and rigidity. Respiratory impairment is due to a combination of factors. First, the elastic work of breathing is increased due to the stiff thoracic cage. Second, the diaphragm and other muscles of ventilation are placed at a mechanical disadvantage from abnormal geometry. Finally, lung volumes are reduced and, in the case of children, lung growth can be limited. As with many other neuromuscular conditions, respiratory impairment first manifests with sleep-disordered breathing, particularly sleep hypoventilation, and, if untreated, progresses to daytime hypercapnia and complications of pulmonary hypertension.

Kyphoscoliosis

Kyphosis is anterior angulation of the thoracic cage. *Scoliosis* is lateral curvature of the spine (Fig. 33.7). These two deformities often occur together (called **kyphoscoliosis**) as a result of the compensatory effects of the spine in response to the primary lateral curve in scoliosis.

Idiopathic scoliosis is typically noticed during childhood and progresses during adolescence. Less commonly, scoliosis develops secondary to neuromuscular disease, such as DMD. The degree of scoliosis is measured by the *Cobb angle,* which is determined by the intersection of lines drawn between the upper and lower limbs of the primary curve in scoliosis (Fig. 33.8). Severe kyphoscoliosis (Cobb angle >90 to 100 degrees) can lead to respiratory impairment, especially sleep-disordered breathing. However, the degree of pulmonary dysfunction cannot be predicted from the Cobb angle alone.[87,88]

Surgical spine fixation can stabilize kyphoscoliosis and restore the thoracic curvature to close to normal. Fixation prevents complications resulting from progressive curvature, loss of compliance, and subsequent ventilatory dysfunction. Few options are available to restore pulmonary function to older patients with established kyphoscoliosis. Surgery to correct the deformity can be undertaken, but this treatment generally does not improve pulmonary function.[89] Better long-term results are seen when surgery or brace therapy to correct the angulation is undertaken in adolescence.[90]

Both noninvasive and invasive ventilation are used in some patients with severe kyphoscoliosis, with improvement in gas exchange, respiratory muscle strength, symptoms of dyspnea,[91] and exercise capacity.[92]

Ankylosing Spondylitis

Ankylosing spondylitis is a rheumatologic disease that affects the spine and chest wall. Chronic joint inflammation ultimately leads to fusion of the joints of the vertebrae and ribs, typically leading to a dramatic decrease in thoracic cage compliance due to kyphosis and ankylosis (stiffness due to bone and joint fusion). The most severe respiratory consequence is parenchymal lung disease, which occurs in approximately 10% of patients with ankylosing spondylitis in the form of apical fibrocystic changes that can decrease gas exchange and provide a location for chronic infection, especially fungal infection.[93]

THE ROLE OF THE RESPIRATORY THERAPIST IN CARING FOR PATIENTS WITH NEUROMUSCULAR WEAKNESS AND OTHER DISEASES OF THE CHEST WALL

Many of the diseases discussed in this chapter are chronic, progressive conditions that evolve into respiratory failure over time. Optimal management depends on the degree, rate, and specific manifestations of the disease process, and there is considerable variability. Physicians, nurses, and respiratory therapists (RTs) caring for these patients must be familiar with the course and symptoms of this progression so they can provide appropriate diagnostic testing and therapy at the right time (see Table 33.4).

RTs with expertise in caring for these patients are essential. Many patients require close monitoring of their respiratory symptoms and function, and these results must be reliable and consistent, because decisions such as when to begin a new

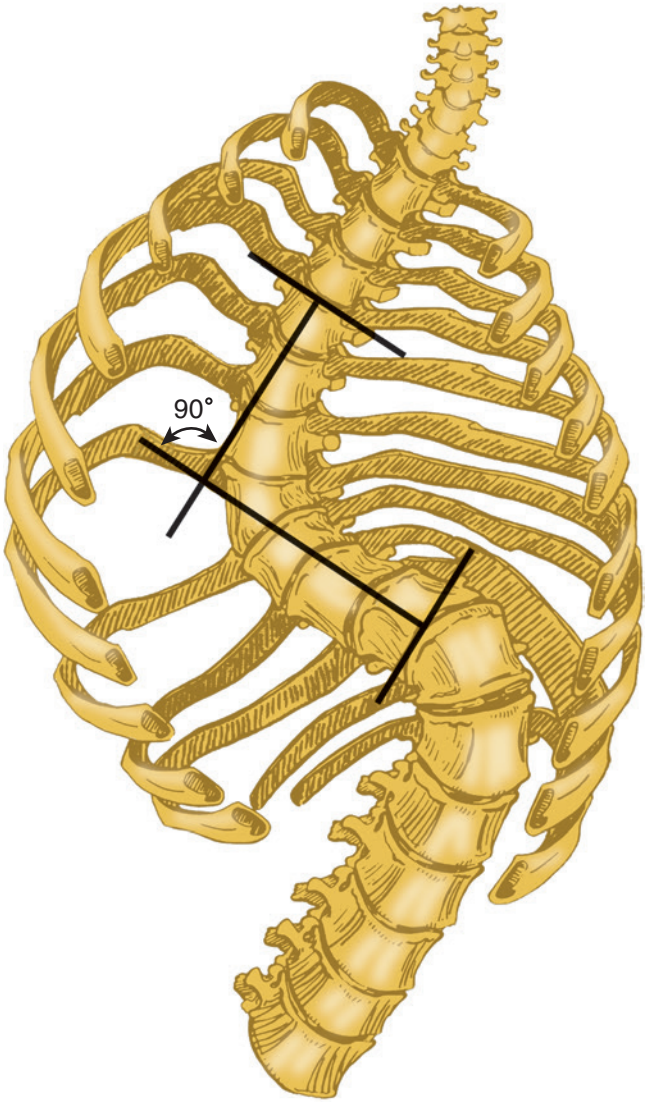

Fig. 33.8 Scoliosis Is Lateral Curvature of the Spine. The degree of scoliosis is measured by the Cobb angle, which is determined by the intersection of lines drawn between the upper and lower limbs of the primary curve in scoliosis. Respiratory insufficiency rarely occurs until the Cobb angle exceeds 90 to 100 degrees. (Modified from Fishman AP: Acute respiratory failure. In: Fishman AP, editor: *Pulmonary Disease*, New York, 1992, McGraw-Hill, p 2300.)

supportive therapy may rely heavily on them. Maneuvers such as spirometry and maximal respiratory pressures, as well as the use of respiratory devices such as NIV and cough-assist technology require explanation, education, reinforcement, and troubleshooting. Without this kind of supervision and support, many patients will use their devices improperly or not at all, which will render them of no benefit and may lead to the inaccurate conclusion that the therapies have failed.

Neuromuscular diseases also carry with them the burdens common to many chronic and progressive diseases, including depression and other psychological burdens. RTs involved in the care of these patients can provide longitudinal support, including encouragement not to give up on therapies that may be effective, and perspective when there are still additional measures that can be added to improve quality of life. The more familiar RT's are with specific disease entities as well as the diagnostic and therapeutic options, the better they can help patients understand and cope with their chronic conditions.

SUMMARY CHECKLIST

- The components of the neuromuscular system that affect respiration include the brain, spinal cord, nerves, neuromuscular junction, respiratory muscles, thoracic cage, and the upper airway.
- Respiratory failure is often the most important clinical dysfunction for many patients with neuromuscular diseases.
- Other effects of neuromuscular disease on the respiratory system include sleep hypoventilation, obstructive sleep apnea, aspiration, pneumonia, atelectasis, pulmonary hypertension, and cor pulmonale.
- Signs and symptoms that may indicate weakness of the respiratory muscles include poor sleep quality, morning headaches, daytime sleepiness, exertional dyspnea, orthopnea, weak or ineffective cough, accessory muscle use, and paradoxical breathing movements.
- Pulmonary function abnormalities in patients with inspiratory muscle weakness typically include decreases in PImax, TLC, VC, and FEV_1. Residual volume can be increased. There often is an abnormally large decrease in FVC and FEV_1 (30% to 50%) when patients repeat testing in the supine position, compared to the seated position. Diffusing capacity typically is normal.
- Common neuromuscular disorders that cause respiratory compromise include ALS, myotonic dystrophy, spinal cord injury, Guillain–Barré syndrome, Duchenne muscular dystrophy, and myasthenia gravis.
- Cervical spine injury above the C3 level results in complete paralysis of the respiratory muscles and necessitates emergency mechanical ventilation. Cervical spine injury below C5 leads to weakness of the expiratory muscles with decreased ability to cough and clear secretions.
- Unilateral diaphragmatic paralysis resulting from phrenic nerve damage usually is asymptomatic and is associated with minor reductions in respiratory function in an otherwise healthy patient, whereas bilateral diaphragmatic paralysis can have significant respiratory symptoms.
- Kyphoscoliosis is abnormal curvature of the spine. Respiratory insufficiency can occur if the curve is severe.

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34

Disorders of Sleep

Robert C. Stansbury and Patrick J. Strollo, Jr.

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Define obstructive sleep apnea (OSA).
- Identify why airway closure occurs only during sleep.
- State the long-term consequences of uncontrolled OSA.
- State how a diagnosis of OSA is made.
- Identify what groups of patients are at particular risk for OSA.
- State the treatments available for patients with OSA.
- Describe how continuous positive airway pressure (CPAP) works.
- Identify problems associated with CPAP.
- Determine when bilevel pressure is useful in the treatment of OSA.
- Define "autotitrating" CPAP.
- Identify the surgical alternatives for patients with severe OSA.

CHAPTER OUTLINE

KEY TERMS

bilevel positive airway pressure
central sleep apnea
continuous positive airway pressure
excessive daytime sleepiness
obesity hypoventilation
obstructive sleep apnea
sleep-disordered breathing
STOP-BANG Assessment Tool
uvulopalatopharyngoplasty
upper airway stimulation

Obstructive sleep apnea (OSA) syndrome is a common clinical problem that is underdiagnosed.[1] Previous prevalence estimates reported 2% to 4% of adults have OSA.[2] Recent data, in part due to the obesity epidemic, suggest that up to 14% of men and 5% of women have OSA.[3] The spectrum of disease ranges from sleep disruption related to increased airway resistance to profound daytime sleepiness in conjunction with a multitude of health consequences (Box 34.1).[4]

Sleep apnea is defined as repeated episodes of complete cessation of airflow for 10 seconds or longer. The events can be obstructive (caused by upper airway closure) or central (caused by lack of ventilatory effort). Primary central nervous system lesions, stroke, congestive heart failure, and high-altitude hypoxemia can impact respiratory control and cause central apnea events.[5] **Central sleep apnea** (CSA) is not as common as OSA. Only 10% to 15% of patients with sleep-disordered breathing are classified as having CSA.[6] Mixed sleep apnea has an initial central component followed by an obstructive component (Fig. 34.1).[7]

Hypopnea is defined as a 30% to 90% decrease in airflow in conjunction with 3% oxygen (O_2) desaturation.[7] Most investigators agree that physiologically significant hypopnea is associated with a decrease in O_2 saturation (SaO_2) and/or arousal from sleep.[8]

Respiratory therapists (RTs) are likely to encounter both OSA and CSA when treating patients. OSA is the most commonly encountered type of sleep apnea and is underdiagnosed by health professionals. The focus of this chapter is on the pathophysiology and management of OSA.

PATHOPHYSIOLOGY

Obstructive Sleep Apnea

The primary cause of OSA is a small or unstable upper (pharyngeal) airway. This condition can be caused by soft tissue factors, such as upper body obesity or tonsillar hypertrophy (rare in adults), and skeletal factors, such as a small or recessed chin.[9] During the waking state, pharyngeal patency is maintained by increased neural activity of the upper airway dilator muscles. Sleep onset is associated with a decrease in neural activity to these muscles.[10] The result is narrowing or closure of airways that are at risk due to obesity or craniofacial deficiency (e.g., a small jaw). In an unstable upper airway, narrowing and closure during sleep frequently involves multiple sites.[11]

BOX 34.1 Adverse Consequences of Obstructive Sleep Apnea

Cardiopulmonary
- Nocturnal arrhythmia
- Diurnal hypertension
- Pulmonary hypertension
- Right or left ventricular failure
- Myocardial infarction
- Stroke

Neurobehavioral
- Excessive daytime sleepiness
- Diminished quality of life
- Adverse personality change
- Motor vehicle accidents

Metabolic
- Insulin resistance
- Altered lipid metabolism

Partial or complete closure of the upper airway during sleep is associated with several serious neurobehavioral, metabolic, and cardiopulmonary consequences (see Box 34.1).[12] Compared with the general population, studies suggest patients with untreated OSA have an increased risk for mild pulmonary hypertension, stroke, nocturnal arrhythmias, heart failure, systemic hypertension, myocardial infarction, and overall mortality.[13-18] The repetitive cycle of upper airway closure and opening during sleep has deleterious effects, including recurrent arousals from sleep, profound increases in intrathoracic pressure, hypoxemia, and hypercapnia. These effects lead to an increase in inflammation, sympathetic tone, and oxidative stress that have systemic consequences, particularly to the cardiovascular system.[19]

Obesity, especially of the upper body, has been shown to correlate positively with the presence of OSA. In most instances, patients with OSA are obese with a large amount of peripharyngeal adipose tissue in addition to adipose tissue in the neck.[20] A body mass index (BMI) greater than 28 (>120% of ideal body weight normalized for height) should alert the practitioner to the possibility of OSA and the need for further assessment and referral, particularly if the patient reports excessive daytime sleepiness (EDS).[2]

Patients who are of normal body weight can be predisposed to OSA if they have an abnormal craniofacial configuration. Men may grow a beard to disguise such a craniofacial abnormality. If the chin is recessed (retrognathic) or small (micrognathic), the upper airway space may be narrow, and the risk for airway closure during sleep increases.[9,21] Patients with a deviated nasal septum or trauma to the nasal passages increase resistive load to the upper airway and contribute to the risk of upper airway closure during sleep. However, an isolated nasal abnormality is an unusual cause of OSA.

OSA also can have a genetic predisposition.[22,23] There have been reports of families in which obesity alone does not explain the increased prevalence of OSA.[24] It has been suggested that

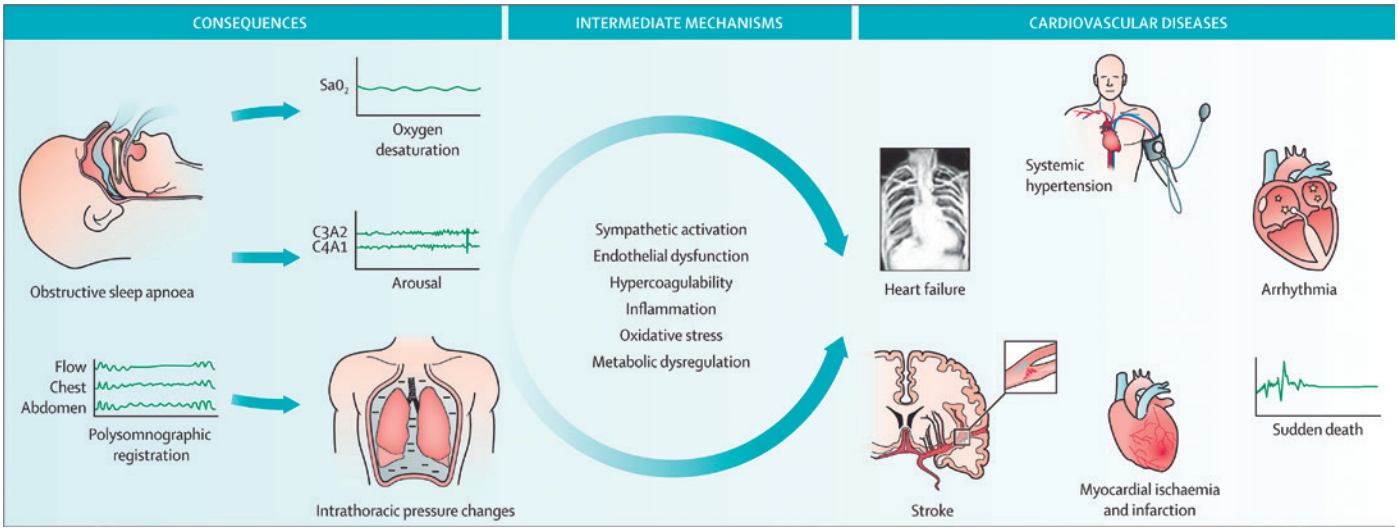

Fig. 34.1 Obstructive sleep apnea consequences and intermediate mechanisms that potentially contribute to risk of cardiovascular disease. The events associated with collapse of the upper airway lead to brain arousal, intrathoracic pressure changes, and hypoxemia and reoxygenation. Several intermediate mechanisms link obstructive sleep apnea with the initiation and progression of cardiovascular diseases. *C3A2* and *C4A1*, Electroencephalographic channels; *SaO_2*, oxygen saturation. (From Sánchez-de-la-Torre M, Campos-Rodriguez F, Barbé F: Obstructive sleep apnoea and cardiovascular disease. *The Lancet Respiratory Medicine* 1(1):61–72 2013.)

craniofacial abnormalities and/or abnormal ventilatory control may explain the increased frequency of OSA in these families.

Central Sleep Apnea

Although a detailed discussion of the pathophysiology of CSA is beyond the scope of this chapter, several concepts are important to RTs. In contrast to OSA, which represents a spectrum of the same disease related to upper airway instability, CSA is a heterogeneous group of disorders driven in part by loss of neurologic output from the respiratory centers in the brainstem that control breathing.[25] Patients have a ventilatory pattern known as periodic breathing, in which there is a waxing and waning of respiratory drive, which is reflected clinically as an increase and then a decrease in respiratory rate and tidal volume (V_T). Secondary causes of CSA typically affect the central nervous system and/or the respiratory muscles. Examples include cerebrovascular diseases such as stroke, neuromuscular diseases such as muscular dystrophy, Guillain-Barré or amyotrophic lateral sclerosis (ALS), cardiovascular disease such as congestive heart failure, chronic opiate use, and congenital abnormalities such as Chiari malformation or congenital central hypoventilation syndrome.[26] Cheyne-Stokes respiration, which often occurs in patients with congestive heart failure or stroke, is a type of periodic breathing characterized by a crescendo-decrescendo pattern of hyperpnea alternating with apnea.[27] After apnea occurs, there may be an increase in central ventilatory drive and an increase in V_T.

Overlap Syndrome

Chronic obstructive pulmonary disease (COPD) and OSA are both common respiratory disorders and coexist in many individuals. This combination is referred to as *overlap syndrome* and is associated with particularly poor outcomes including a high mortality rate.[28,29] Patients are usually obese and have a history of smoking. Patients with overlap syndrome tend to have moderate to severe nocturnal oxyhemoglobin desaturation (especially during rapid eye movement [REM] sleep) and more severe blood gas abnormalities than patients with the same degree of OSA but without COPD.[30] Undiagnosed OSA complicates the course at night with arousals, awakenings with dyspnea, and O_2 desaturation values resistant to supplemental O_2.[31]

Hypoventilation Syndromes

In addition to OSA and CSA, chronic hypoventilation syndromes are increasingly being recognized.[32,33] Patients with neuromuscular disorders such as ALS, muscular dystrophy, or spinal cord injury with diaphragm dysfunction may have underlying restrictive lung physiology. These patients may benefit from early detection of sleep-related hypoventilation. Treatment with noninvasive ventilation may result in improved breathing during sleep, quality of life, gas exchange, and mortality.[34] Alternative therapies such as placement of a diaphragmatic pacemaker also may benefit selected patients with spinal cord injuries.[35]

CLINICAL FEATURES

Classic signs and symptoms of OSA are described in Table 34.1.[20] No sign or symptom alone strongly predicts the presence of OSA. However, a combination of these signs and symptoms is predictive and useful for risk stratifying individuals for the presence of OSA.[20,36] Questionnaires and prediction rules utilizing these findings lack sufficient accuracy to detect the presence of OSA, but they are helpful in identifying patients who require screening and aid in determining appropriate diagnostic testing.[37]

TABLE 34.1 Common Signs and Symptoms in Obstructive Sleep Apnea

Signs	Symptoms
Male (gender 3× risk)	Snoring, gasping, or choking during sleep
Age greater than 40 years	Excessive sleepiness
Large neck (>42 cm in men and 40 cm in women)	Morning headaches
Obesity (body mass index >35)	Fatigue
Facial abnormalities (retrognathia)	Nocturnal GERD
Small upper airway (Mallampati ≥3, large tonsils, high arched palate)	Apneas reported by bed partner
Hypertension	Sleep fragmentation
Arrhythmias (atrial fibrillation)	Nocturia
Pulmonary hypertension	Decreased concentration and/memory loss
Stroke	Erectile dysfunction

GERD, Gastroesophageal reflux disease.

Of note, the presence of **excessive daytime sleepiness** is not found in all patients with OSA, and there is no association between apnea severity and degree of sleepiness.[38] Recent work evaluating presentations of OSA has identified three clinical phenotypes[39]: (1) asymptomatic, (2) EDS, and (3) insomnia. As a result, patients with OSA may report minimal symptoms related to OSA yet have severe disease that may require intervention.

A thorough history and physical examination are essential in identifying individuals at risk for sleep-disordered breathing. A significant proportion of occult OSA in the general population would be missed if screening or case finding were based on BMI or male gender, and breathing pauses may be particularly insensitive for identifying OSA in older adults.[40] Providers should keep a high index of suspicion for OSA, particularly in certain disease cohorts in whom treatment may impact their disease course. These disease states include pulmonary hypertension, nocturnal arrhythmias, congestive heart failure, diabetes, stroke, polycythemia, and refractory hypertension.[41-48] Providers should have a high index of suspicion for individuals undergoing preoperative assessment for bariatric surgery and high-risk driving populations.[35]

RULE OF THUMB Untreated OSA can cause daytime hypoxemia. The diagnosis of OSA should be considered when the degree of hypoxemia is out of proportion to the defect on spirometry. When the arterial partial pressure of O_2 is less than 60 mm Hg but the forced expiratory volume in 1 s (FEV_1) is greater than 30% of predicted, COPD alone is inadequate to explain the hypoxemia, and coexisting OSA should be considered. OSA in this setting is frequently associated with pulmonary hypertension and evidence of right heart failure on physical examination. Hypoxemia, pulmonary hypertension, and right heart failure can be substantially improved with management of OSA. If the patient adheres to therapy, the need for supplemental O_2 may be reduced or eliminated.

In the acute care setting, patients who present with previously undiagnosed OSA can pose a particular challenge for diagnosis and management.[49-51] Unfortunately, many patients with OSA, particularly when associated with obesity hypoventilation syndrome (OHS), come to attention during hospitalization for acute on chronic respiratory failure.[52] A high clinical suspicion for OSA in hospitalized patients is necessary because untreated or unrecognized OSA can complicate recovery from acute illness such as COPD, heart failure, stroke, and recent surgery.[53-56] Despite the potential benefit of treatment, many patients with sleep-disordered breathing are unrecognized while in the hospital.[57] Increasingly, portable testing is used to identify hospitalized patients with OSA.[58] Outpatient follow-up and evaluation are important to insure adequate adherence to therapy for effective long-term treatment. RTs should ask patients if they are treated for OSA at home, and in most instances, this therapy should be continued while hospitalized. Occasionally, patients may bring their machine from home for use during their hospital stay.

SCREENING QUESTIONNAIRES

An initial history and physical examination may be inadequate for identifying OSA. Several screening questionnaires have been developed to aid in rapidly identifying individuals with OSA. In general, screening questionnaires have good sensitivity but limited specificity for the diagnosis of OSA. The Berlin Questionnaire, the American Society for Anesthesiology (ASA) screening questionnaire, and the Sleep Apnea Clinical Score (SACS) have been validated for use as screening for OSA.[59,60] The STOP-BANG questionnaire has been used commonly because of simplicity and ease of use, particularly in patients undergoing elective surgery (Box 34.2).[61] This questionnaire has demonstrated high sensitivity using a cutoff score of ≥3 detecting sleep apnea but has a modest specificity, yielding a high false-positive rate.[61] In general, the STOP-BANG is a useful and efficient screening tool that has been validated in multiple populations but may be less useful in identifying sleep apnea in specific groups such as the veteran population and individuals with chronic renal disease.[62,63] Regardless of the questionnaire used, a diagnostic sleep study is required for diagnosing OSA.

BOX 34.2 STOP-BANG Questionnaire to Screen for Obstructive Sleep Apnea

Snore:	Do you snore loudly (louder than talking or loud enough to be heard through closed doors)?
Tired:	Do you often feel tired, fatigued, or sleepy during the daytime?
Observed:	Has anyone observed you stop breathing during sleep?
Pressure:	Do you have or are you being treated for high blood pressure?
BMI:	Greater than 35 kg/m^2?
Age:	Age older than 50 years?
Neck:	Neck circumference greater than 40 cm?
Gender:	Gender male?

One point assigned for each positive question.
Total score <3 = low probability for OSA.
Total score >3 = high probability for OSA.
Total score >5 = high probability of moderate to severe OSA.
From Chung F, Subramanyam R, Liao P, et al: High STOP-BANG score indicates a high probability of obstructive sleep apnoea, *Br J Anaesth* 108:768–775, 2012.

LABORATORY TESTING

When sleep apnea is suspected, an overnight polysomnogram (PSG) or home sleep apnea test (HSAT) should be obtained to confirm the clinical diagnosis.[37,64] Since the approval of home sleep testing by Centers for Medicare and Medicaid Services (CMS) in 2008, an increasing number of individuals are being diagnosed with OSA outside the laboratory. A full-night PSG in the sleep laboratory monitored by a sleep technologist is considered the "gold standard" method for diagnosing OSA.

In a laboratory-based sleep study, several physiologic signals are recorded to determine whether airway closure occurs during sleep and to what extent the events disturb sleep continuity and cardiopulmonary function. An electroencephalogram (EEG), electrooculogram (EOG), and chin electromyogram (EMG) are obtained for assessment of sleep stage and documentation of sleep disruption due to sleep-related breathing disturbance. Airflow (measured at the nose and mouth), ventilatory effort (using inductive plethysmography or piezoelectric belts), cardiac rhythm (with a modified lead II electrocardiogram [ECG]), tibial EMG leads, and SaO_2 (measured with pulse oximetry) are included for standard testing.

Various devices are available for HSAT. Most portable devices measure two respiratory parameters (airflow and respiratory effort), oxygen saturation, and heart rate or ECG. Newer technology for HSAT including peripheral artery tonometry has also been validated.[65] In general, HSAT has demonstrated adequate diagnostic performance compared to in-lab polysomnography in adult patients with a high pretest probability of moderate to severe sleep apnea who do not have significant cardiopulmonary comorbidities.[66]

In obstructive apnea or hypopnea, airflow is absent or decreased for at least 10 seconds in the presence of continued ventilatory effort. Asynchronous (paradoxical) movement of the abdomen and rib cage can be observed. O_2 desaturation may or may not occur (required for hypopnea). The degree of the O_2 desaturation depends on the length of the apneic event or the patient's baseline saturation (see Fig. 34.1). Respiratory effort–related arousals are characterized by increased ventilatory effort, leading to arousal from sleep that does not meet the criterion of an apneic or a hypopneic event (see Fig. 34.1).[27]

Scoring an apnea (absence of airflow for ≥10 seconds) either by laboratory or HSAT is straightforward. The diagnosis of hypopnea may be affected by the measurement technique used. In 1999, an American Academy of Sleep Medicine (AASM) task force conducted an evidence-based review of measurement techniques for detecting hypopnea.[67] The scoring system was as follows: *A,* good to excellent agreement with a reference standard (face mask pneumotachograph); *B,* limited data but good theoretical framework and clinical experience suggest the method is valid; *C,* no data, weak theoretical framework or clinical experience; and *D,* research or clinical experience suggests the method is invalid.

The measuring techniques were scored as follows: nasal pressure, B; respiratory inductance plethysmography (RIP) with sum of chest and abdominal signals, B; dual-channel RIP, C; single-channel RIP, C; piezoelectricity sensors, strain gauges, and thoracic impedance, D; breathing measurement signal with a desaturation or arousal, B; expired carbon dioxide (CO_2), D; and thermal sensors, D. A face mask pneumotachograph allows the greatest precision in measuring airflow, but it is poorly tolerated. Nasal pressure is a reliable way to detect hypopnea and is well tolerated by patients undergoing a diagnostic PSG.[67]

After the in-lab polysomnography study is completed, the sleep technologist scores it. The number of apneas and hypopneas per hour of sleep is reported as an apnea-hypopnea index (AHI) or respiratory disturbance index (RDI). The AASM has operationally defined the severity of OSA as follows: mild, AHI 5 to 15; moderate, AHI 15 to 30; and severe, AHI greater than 30. AHI less than 5 is considered within the normal range for adults. The number of arousals per hour (arousal index), percentage of each sleep stage, frequency of SaO_2, mean SaO_2, and nadir of SaO_2 also are reported (Box 34.3).

Measurement error is inevitable with HSAT compared with standard polysomnography. For instance, the AHI is calculated in HSAT by adding the total number of apneas or hypopneas divided by the total recording time rather than sleep time. Thus the index derived from the HSAT is usually lower than the index derived on polysomnography. Most of the HSAT devices do not include EEG, making identification of arousals and distinguishing from REM and non-REM sleep challenging. Sensor dislodgement and poor signal quality are additional factors that made lead to measurement error during a HSAT. If a single HSAT recording is determined to be negative (significant apnea not identified) or technically inadequate, and high suspicion remains for OSA, in-laboratory polysomnography should be performed.[37]

Since 2007, HSAT use for the diagnosis of OSA has increased dramatically. Although data interpretation at times can be troublesome, editing the data manually seems to improve the accuracy of interpretation.[68] For HSAT devices, the AHI is determined by adding up the total number of respiratory events and dividing by the total hours of valid recording time (not sleep time as done in PSG). These devices are being utilized more frequently in hospitalized patients to diagnose OSA and qualify patients for positive pressure on discharge. Challenges exist when performing these studies in the hospital, particularly when supplemental oxygen is used, which can impair the device's ability to identify respiratory events. The poor sleep patients tend to get in the hospital setting can also impact diagnostic accuracy. Despite these challenges, there is evidence that identifying OSA in the hospital and discharging patients on therapy leads to improved outcomes, including a decrease in hospital readmission rates.[53,69,70]

BOX 34.3 Key Features of Sleep Studies to Be Analyzed and Reported for Obstructive Sleep Apnea

- Apnea-hypopnea index
- Arousal index
- Sleep stage distribution
- Frequency of oxyhemoglobin desaturations
- Mean oxyhemoglobin saturation
- Nadir of oxyhemoglobin saturation

RULE OF THUMB Intermittent checks of O_2 saturation cannot reliably exclude sleep-related desaturation secondary to OSA. Placing the oximetry probe on the patient frequently awakens the patient. In addition, isolated readings may not allow sampling of all sleep stages, especially REM sleep, during which sleep-disordered breathing and nocturnal desaturation tend to be most prominent. Continuous overnight oximetry is a better assessment of the degree of oxyhemoglobin desaturation with sleep.

TREATMENT

As we enter the era of personalized medicine, management of OSA should be individualized based on disease phenotype, severity, and patient preference. Behavioral therapy should be pursued in the care of all patients. Medical and surgical therapy must be tailored to the individual patient. The likelihood of acceptance and adherence to the prescribed therapeutic intervention must be considered. The goals of treatment are to normalize SaO_2 and ventilation; eliminate apnea, hypopnea, and snoring; and improve sleep architecture and continuity, as well as improve symptoms of OSA if present (Box 34.4).

Behavioral Interventions and Risk Counseling

Patients must be informed of the risks of uncontrolled sleep apnea, particularly in severe cases. Several behavioral interventions can be beneficial, including weight loss in obese patients; avoiding alcohol, sedatives, and hypnotics; and avoiding sleep deprivation. Although weight loss clearly improves the severity of sleep apnea, it is frequently difficult to accomplish and does not lead to complete resolution of OSA in all individuals.[71,72] Involving the patient with a dietitian or nutritionist can be helpful. Alcohol should be avoided by patients believed to have sleep apnea. Alcohol decreases arousal threshold and upper airway muscle tone, making the upper airway more prone to complete or partial closure and longer periods of apnea.[73] Sedatives and hypnotics can decrease the stability of the upper airway and suppress certain stages of sleep.[74] Research suggests that the impact of these medications on indices of OSA severity are minimal.[75]

Positional Therapy

When a sleep study indicates that apnea and snoring occur only in the supine position, instruction on sleeping in the lateral position or head of bed elevation can be beneficial; however, adherence is typically poor.[76] Use of the "tennis ball" technique, in which a ball is sewn onto the back of the patient's sleeping garment, or other positional devices that discourage the patient

BOX 34.4 Goals of Treating Obstructive Sleep Apnea

- Eliminate apnea, hypopnea, and snoring
- Normalize O_2 saturation and ventilation
- Improve sleep architecture and continuity

from rolling into the supine position can be effective in treating positional OSA.[77,78]

Medical Interventions

Positive Pressure Therapy

Continuous positive airway pressure therapy. **Continuous positive airway pressure** (CPAP) therapy was introduced for management of OSA in 1981 and reduces sleep-disordered breathing by pressurizing the upper airway preventing collapse during sleep.[79] CPAP is typically delivered through a nasal or full face mask at a fixed pressure that remains constant throughout inhalation and exhalation. Positive pressure therapy to treat OSA is most often delivered using a CPAP device because it is the simplest and most extensively studied mode of therapy. The most current AASM practice parameters recommend a full montage in lab polysomnographic study (as outlined previously) to determine the optimal CPAP setting to address an individual's sleep-disordered breathing.[80] A "split-night" sleep study, in which first part of the study is dedicated to establishing a diagnosis of sleep-disordered breathing and the remainder of the study is used to titrate CPAP to effectiveness, may be used in certain scenarios.[80,81] Attempts to use an algorithms or a prediction equations as replacements for in-laboratory titrations have not been uniformly successful.[82,83] Recently, autotitrating devices (discussed later) are being used in the home setting for initiation of treatment of OSA without the need for an in-lab titration study.

CPAP therapy has been shown in numerous studies to improve daytime sleepiness, sleep-related quality of life, vigilance, and cognition and has demonstrated a modest beneficial effect on cardiovascular, psychiatric, and metabolic disease.[84-91] CPAP is the best studied treatment modality for OSA. Other positive pressure therapies have demonstrated effectiveness in controlling OSA. These modalities have less-robust outcome data compared with CPAP. Most experts agree that the positive pressure treatment modality is not the critical factor for improving outcomes in OSA. What is important, regardless of the treatment modality used, is normalization of SaO_2 and ventilation; elimination of apnea, hypopnea, and snoring; and the improvement of sleep architecture and continuity.

Bilevel positive airway pressure therapy. **Bilevel positive airway pressure** therapy was first introduced as a potential treatment for OSA in the early 1990s.[92] Bilevel differs from the continuous fixed pressure delivered by CPAP in that it allows independent adjustment of the expiratory positive airway pressure (EPAP) and inspiratory positive airway pressure (IPAP). The difference between the IPAP and EPAP is the pressure support and can provide support to the respiratory muscles and augment tidal volume. Like CPAP, bilevel PAP is typically titrated in the laboratory setting, and specific guidelines for bilevel titration are available.[81] The IPAP and EPAP are titrated together to eliminate apnea. The IPAP is increased independently to eliminate hypopneas, snoring, and arousals. Given the reduction in expiratory pressure-related discomfort with the use of bilevel therapy, one would expect improvement in adherence and other outcomes with the use of these devices. Yet, no studies to date have proven advantage to the use bilevel compared to CPAP therapy in CPAP-naive patients.[93]

MINI CLINI

Nocturnal Angina in an Obese Middle-Aged Man

History

A 45-year-old, morbidly obese nonsmoker is admitted to the coronary care unit after awakening at 4 a.m. with chest pain typical of angina pectoris. The pain has resolved by the time he reached the emergency department. The patient is unsure of the duration of the pain before he called for his wife, who sleeps in a separate bedroom because of his very loud habitual snoring. The patient reports exertional shortness of breath but no chest pain before this event. He states that he frequently gets "indigestion" that sometimes is worse at night, but that this pain was different.

Medications

- Captopril, 25 mg by mouth twice per day
- Furosemide (Lasix), 20 mg by mouth every day
- Omeprazole (Prilosec), 20 mg by mouth daily

Medical History

- Hypertension and gastroesophageal reflux
- No significant cardiac disease
- Cardiac catheterization 1 year ago showed normal left ventricular function and minimal coronary artery occlusion

Physical Examination

- *Vital signs:* Blood pressure 160/98 mm Hg, heart rate 100 beats/min, temperature 98.6°F (37°C), respiration 18 breaths/min
- *General:* Mildly diaphoretic obese white man
- *Neck:* 52 cm (20.5 inches) in circumference
- *Lungs:* Clear breath sounds bilaterally
- *Heart:* Regular rate and rhythm
- *Abdomen:* Obese; soft, normal bowel sounds
- *Extremities:* 4-mm pretibial pitting edema

Laboratory Data

- *Room air arterial blood gases (ABGs):* pH 7.36, PCO_2 37 mm Hg, PO_2 62 mm Hg, SaO_2 92%
- *Chest x-ray:* Pulmonary congestion, otherwise normal
- *ECG:* Sinus tachycardia without acute changes

Problem

Why did this patient experience angina during sleep?

Discussion

Serial cardiac enzyme values revealed no evidence of myocardial infarction. A stress test result was negative, but a submaximal effort was obtained. The patient's weight precludes an adenosine thallium stress test. A repeat cardiac catheterization demonstrated no change in the minimal coronary artery occlusion reported previously. The pulmonary consultant called to evaluate the patient's shortness of breath recommended a nocturnal PSG to rule out sleep apnea. The sleep study result is positive for severe sleep apnea (AHI 110; lowest SaO_2 70% on the oximeter during REM sleep). A CPAP titration test was performed. The patient was discharged home on CPAP 17.5 cm H_2O using a nasal mask. He returns to the pulmonary clinic 1 month after discharge. He reported no further episodes of nocturnal angina. Reflux and shortness of breath have been relieved. The patient has lost 10 lb (4.5 kg) without dieting. Lower extremity edema is markedly decreased. A download of data from his CPAP machine shows excellent CPAP adherence with use on 85% of nights, as well as good response to therapy with an average estimated AHI 3.5.

A trial of bilevel therapy is reasonable in persons intolerant of CPAP therapy. As mentioned previously, bilevel therapy can provide ventilatory support and OSA patients with concurrent respiratory disease or obesity hypoventilation syndrome may derive benefit from bilevel therapy compared with CPAP.[94,95] More advanced modes of bilevel therapy exist and are beyond the scope of this discussion. These include bilevel ST, adaptive support ventilation (ASV), and volume-assured pressure support ventilation (VAPS). These modalities are typically reserved for more complex sleep-disordered breathing or other disease processes. Due to its simplicity and lower cost, CPAP remains the initial PAP modality of choice for the treatment of uncomplicated OSA.

RULE OF THUMB Retrognathia can be the cause of OSA in young patients who are at or close to ideal body weight. CPAP therapy is highly effective for these patients, but upper airway reconstruction (phases I and II surgery) can be curative.

Autotitrating devices. A new generation of autotitrating CPAP (APAP) devices has been developed and are frequently used to address sleep apnea without the need for a formal titration study to identify a fixed CPAP pressure in the laboratory. These devices use a computer algorithm for adjusting the level of CPAP in response to dynamic changes in airflow or vibration caused by airway collapse, snoring, or both. When upper airway flow is decreased or impedance is changed, the proprietary algorithm will increase the pressure until flow is restored and/or upper airway resistance is normalized. These devices will then reduce pressure until a limitation in airflow or an increase in airway resistance is identified. Autotitrating devices have the potential to better address apnea as it adjusts when the individual's apnea becomes worse such as during REM sleep or moving into the supine position.

The initial development of APAP was prompted by a need to address issues of patient access to care, patient compliance, patient comfort, and variability of the CPAP requirement throughout the night.[96-100] Studies to date have shown little to no difference in use of fixed CPAP versus APAP in terms of improvement in AHI, subjective sleepiness, adherence, and quality of life.[101-103] Many patients are currently managed with a completely ambulatory pathway for the diagnosis and treatment of OSA. They will begin the evaluation with HSAT, and, if significant sleep apnea is identified, APAP therapy will be initiated in the home setting. Patients either remain on APAP or the APAP will be used to determine a fixed CPAP setting. This ambulatory approach to straightforward OSA in high-risk individuals has been demonstrated to be feasible and potentially an effective means of addressing OSA.[104-106] Although ambulatory treatment of OSA with APAP can be effective, it is important to note that the treatment studies have excluded several patient populations. These populations include those with congestive heart failure, COPD, central sleep apnea, neuromuscular disease, and hypoventilation syndromes. Due to lack of data in these specific populations, the most recent practice parameters do not recommend the use of APAP in individuals with these significant comorbidities.[93]

MINI CLINI

Young Man Hospitalized for Observation After a Single-Vehicle Accident in the Midafternoon

History

A 27-year-old nonsmoker is admitted to the coronary care unit for monitoring so that the diagnosis of cardiac contusion can be ruled out. The patient has been involved in a single-vehicle automobile accident. The accident occurred at 3:30 p.m. on a clear day. The patient felt drowsy immediately before the event. He became conscious after hitting the guardrail. The patient's chest hit the steering wheel. The patient reports anterior chest wall pain and denies having angina or feeling faint.

Medications

- None

Medical History

- Negative

Physical Examination

- *Vital signs:* Blood pressure 140/88 mm Hg, heart rate 100 beats/min, temperature 98.6°F (37°C), respirations 16 breaths/min
- *General:* Well-developed, well-nourished white man
- *Head, eyes, ears, nose throat:* Elongated soft palate, mild crowding of tonsillar pillars, retrognathic chin (i.e., small chin due to a posterior displaced mandible that narrows the airway)
- *Neck:* 40 cm (16 inches) in circumference
- *Chest:* Contusion on anterior portion of the chest
- *Lungs:* Clear breath sounds bilaterally
- *Heart:* Regular rate and rhythm
- *Abdomen:* Soft with normal bowel sounds
- *Extremities:* No clubbing, cyanosis, or edema
- *Skin:* Multiple small lacerations

Laboratory Data

- *Chest x-ray:* No cardiomegaly, mass, infiltrate, or effusion
- *ECG:* Sinus tachycardia
- *Troponin:* 0.4 ng/mL (normal)

Problem

What caused the patient to fall asleep at the wheel?

Discussion

The patient is found to have bradycardia during sleep on the night of admission. These episodes appeared to be associated with snoring and oxyhemoglobin desaturation on O_2 at 2 L/min through a nasal cannula. The cardiology consultant recommended a diagnostic nocturnal PSG to rule out sleep apnea. The study shows severe sleep apnea (AHI 85 with a low SaO_2 of 60%). A CPAP titration study determined that the patient requires 10 cm H_2O of CPAP delivered via nasal pillows. At follow-up 1 month later, the patient states he no longer experiences the fatigue he had previously reported. In retrospect, the patient believes that before treatment with CPAP, he was quite sleepy during the day. Despite this improvement, he wants to explore other treatment options. A surgical consultation is obtained.

Autobilevel devices use proprietary algorithms to automatically adjust the EPAP and IPAP in response to respiratory events. Research data for these devices thus far are limited, and no clear recommendations regarding their use in the treatment of OSA can be made at this time. However, these devices are commonly used in clinical practice, particularly in patients who struggle with other positive pressure modalities.

MINI CLINI

Middle-Aged Woman With Pulmonary Hypertension

History

A 59-year-old former smoker is admitted to the hospital for right and left heart catheterization. A previous ECG was compatible with pulmonary hypertension. The patient denies having angina or exertional chest discomfort. She admits to dyspnea on exertion that has been increasing over the past few months and to a chronic non-productive cough. She denies taking "diet pills."

Medications

- Nifedipine, 10 mg by mouth 3 times per day
- Furosemide (Lasix), 20 mg by mouth daily
- Potassium chloride, 20 mEq by mouth twice per day

Medical History

- Hypertension and allergic rhinitis
- No cardiac disease

Physical Examination

- *Vital signs:* Blood pressure 145/88 mm Hg, heart rate 90 beats/min, temperature 98.6°F (37°C), respirations 12 breaths/min
- *General:* Obese white woman in no acute distress
- *Neck:* 40 cm (16 inches) in circumference
- *Lungs:* Clear breath sounds bilaterally
- *Heart:* Regular rate and rhythm, increased second heart sound (P_2)
- *Abdomen:* Obese; soft, normal bowel sounds
- *Extremities:* 2-mm pretibial pitting edema

Laboratory Data

- *Chest x-ray:* Mildly enlarged heart, no mass, infiltrate, or effusion
- *ECG:* Normal sinus rhythm with P pulmonale
- *Left heart catheterization:* No significant coronary artery disease, normal left ventricular function
- *Right heart catheterization:* Pulmonary hypertension (75/25 mm Hg), pulmonary artery wedge pressure 23 mm Hg
- *Room air ABGs:* pH 7.45, PCO_2 41 mm Hg, PO_2 54 mm Hg, SaO_2 84%
- *Spirometry:* Forced vital capacity (FVC) 1.69 L (55% of predicted value), FEV_1 1.27 L (55% of predicted value), FEV_1/FVC 75, forced expiratory flow midexpiratory phase ($FEF_{25\%–75\%}$) 0.96 L/s (37% of predicted value); no significant improvement with single-dose bronchodilator

Problem

What is the cause of the pulmonary hypertension?

Discussion

The pulmonary service is consulted for evaluation for pulmonary hypertension in association with abnormal spirometry results. Results of bilateral lower extremity Doppler examinations and a ventilation/perfusion scan are normal. Because of a history of snoring, an overnight portable cardiopulmonary sleep study is performed. The study revealed evidence of snoring, nonpositional apnea and hypopnea, and desaturation to less than 60% on the oximeter for most of the monitoring period. Results of a PSG performed in the sleep laboratory confirmed the presence of moderate to severe OSA with AHI 28. The patient responded well to the application of CPAP titrated to 12 cm H_2O. Dyspnea was relieved at the time of follow-up. Repeat ABG values improved. The patient no longer required portable liquid O_2 to maintain SaO_2 greater than 90% at rest or with exercise.

It is likely this patient has pulmonary hypertension that is due to OSA, as opposed to idiopathic pulmonary artery hypertension, which generally affects younger women. Chronic thromboembolic disease should be excluded, as it was in this case. Chronic right heart failure secondary to sleep apnea can be improved with proper treatment.

Side effects and troubleshooting strategies for positive airway pressure therapy. Side effects of positive pressure therapy are frequently related to the interface and to the pressure prescribed. Feelings of claustrophobia, nasal congestion, rhinorrhea, skin irritation, and nasal dryness may be reported (Fig. 34.2). Claustrophobia and skin irritation can be managed by changing the interface to one that is more easily tolerated by the patient. Nasal congestion, rhinorrhea, skin irritation, and nasal dryness can be managed by using combinations of topical nasal steroids, antihistamines, nasal saline sprays, and lotions. An inline humidifier is standard on current machines, and the amount of humidity provided can be modified by the patient. Heated humidification has been shown to improve adherence.[100] If the patient reports a sensation of too much pressure, particularly at sleep initiation, prescribing a ramp in pressure (standard in most devices) can be beneficial. The ramp allows a gradual increase in pressure over 5 to 45 minutes. The ramp time is empirically determined by the prescribing physician. Another intervention that may be beneficial in some patients who have difficulty exhaling against pressure is the pressure release feature. This feature briefly decreases the PAP pressure by 1 to 3 cm H_2O during exhalation and then quickly returns pressure to the set CPAP pressure before the start of inspiration. There is no objective evidence that a ramp feature or pressure relief setting improves patient acceptance or compliance.[107,108]

Pressure leaks are another problem that the RT may encounter. Most interfaces involve the nose (nasal mask or nasal pillows) or the nose and mouth (oronasal mask). Some patients tend to breathe partially or mainly through the mouth. The addition of a chin strap may not resolve the problem. Changing the interface to an oronasal mask may be required for effective "pressurization" of the upper airway in these patients.[109] Leaks are important to address in patients prescribed APAP and autobilevel, because these devices can have difficulty distinguishing from leak and respiratory events, leading to excessive delivered pressure and worsening leak. Patient accommodation and long-term adherence to therapy can be impacted by available masks and devices from the home care company or medical facility. Initial optimization and acceptance of PAP therapy is of the upmost importance, as research has demonstrated long-term usage and success with PAP treatment is predicted by the usage pattern in the first few weeks of therapy.[110]

Oral Appliance Therapy

Oral appliances are devices that enlarge the airway by moving the mandible forward or by keeping the tongue in an anterior

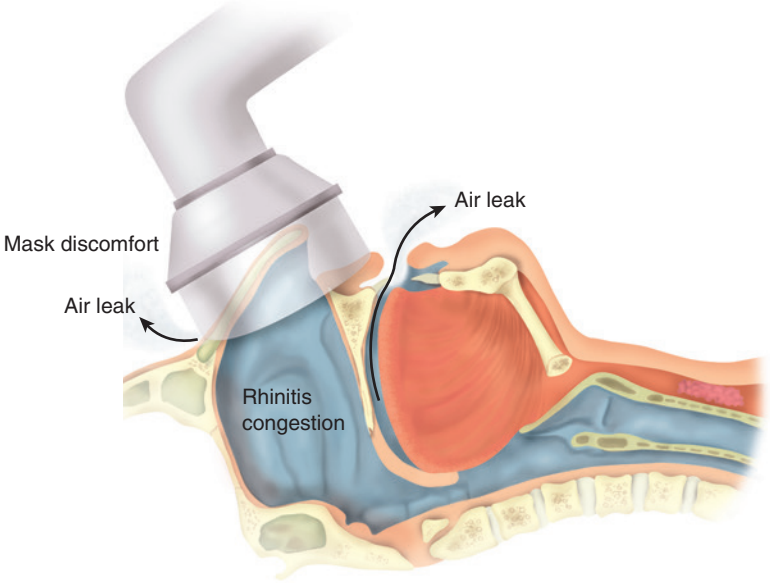

Fig. 34.2 Positive Airway Pressure Problems. Various problems can be encountered with continuous positive airway pressure.

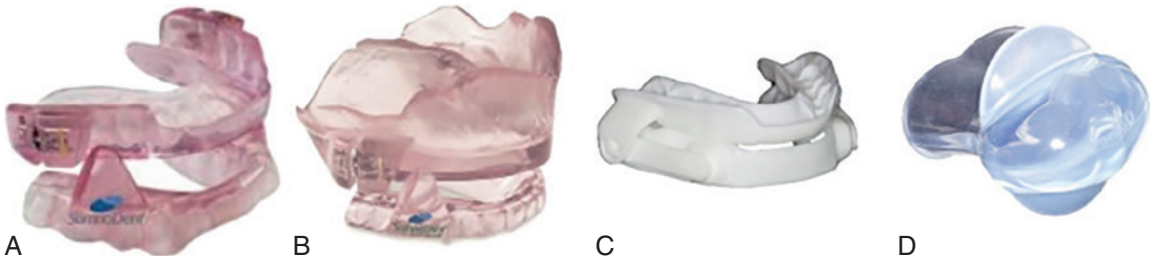

Fig. 34.3 Examples of Commercially Available Oral Appliances. (A) SomnoDent Flex, a custom-made oral appliance that moves the mandible forward (OA_m) for the dentate patient. (B) SomnoDent Edentulous, a custom-made OA_m for patients with an edentulous maxilla. (C) Narval, a custom-made OA_ms for the dentate patient. (D) AveoTSD, a prefabricated Tongue Stabilizing Device. (Modified from Hamoda MM, Kohzuka Y, Almeida FR: Oral appliances for the management of OSA. An updated review of the literature. *Chest* 153(2): 544–553, 2018.)

position (Fig. 34.3). Patients who have mild-to-moderate sleep apnea may be offered this therapeutic option up front or may be treated with an oral appliance if they are unable to tolerate PAP therapy. Oral appliances are worn only during sleep and come in various forms. The appliances are custom-fitted by dentists and are generally well-tolerated by patients. They are overall less effective in decreasing the AHI but may be of equal efficacy given higher adherence rates with oral appliance therapy compared with PAP treatment.[111,112] A few studies suggest oral appliances and PAP therapy have similar outcomes in terms of improvements in sleepiness and quality of life and at least short-term effects on blood pressure.[113-115] The role of oral appliance therapy in the acute care setting, such as patients hospitalized for acute heart failure or after elective surgery, is unclear.

Medications

Medications have proven at best minimally effective for most patients with OSA. Given the efficacy of other current treatment options, medications are currently not recommended for the treatment of OSA. The antidepressants protriptyline and fluoxetine have been used by some providers to manage mild OSA. These drugs are minimally effective in most patients.[116-118] Newer research has focused on cholinergic agents such as donepezil and cannabinoids such as dronabinol to treat OSA. Although this early work is promising, further research is necessary to evaluate the efficacy of these medications.[119-121]

O_2 therapy may be useful for patients with oxyhemoglobin desaturation who refuse positive pressure therapy. O_2 therapy can improve nocturnal desaturation but has no significant effect on ventilatory arousals and daytime sleepiness.[122] Previous work suggested O_2 therapy could lengthen apneic spells and thus potentially worsen apnea severity.[123,124] However, more recent work suggests that the effect supplemental O_2 has on apnea depends on the specific physiology underlying an individual's sleep-disordered breathing (i.e., high loop gain versus those with a more stable ventilatory control system).[125] Supplemental oxygen can be entrained into PAP devices for individuals who have persistent hypoxemia despite correction of obstructive therapy with positive airway pressure therapy. Supplemental oxygen should be used with caution in patients with significant respiratory impairment who may retain CO_2.

MINI CLINI

Worsening Right-Sided Heart Failure in a Patient With Chronic Obstructive Pulmonary Disease Who Is Using Oxygen

History

A 50-year-old former smoker previously found to have severe COPD (FEV_1 of 0.9 L [30% of predicted value]) is admitted to the hospital for evaluation and management of worsening shortness of breath and persistent bilateral leg swelling. He has been using O_2 at 2 L/min 24 h per day for the past 3 months. A chronic productive cough of clear sputum has been unchanged. He denies having chest pain.

Medications

- Ipratropium bromide by metered dose inhaler, 2 puffs 4 times per day
- O_2, 2 L/min 24 h per day
- Hydrochlorothiazide, 50 mg by mouth daily
- Roflumilast 500 mcg by mouth daily

Medical History

- Hypertension and chronic bronchitis
- No cardiac disease

Physical Examination

- *Vital signs:* Blood pressure 150/90 mm Hg, heart rate 100 beats/min, temperature 98.6°F (37°C), respirations 18 breaths/min
- *General:* Obese white man who appears short of breath
- *Neck:* 46 cm (18 inches) in circumference
- *Lungs:* Decreased breath sounds bilaterally
- *Heart:* Faint sounds but regular rate and rhythm
- *Abdomen:* Obese; soft, normal bowel sounds
- *Extremities:* "Dusky" lower extremities with 4-mm pitting edema to the knees

Laboratory Data

- *ABGs:* pH 7.36, PCO_2 44 mm Hg, PO_2 56 mm Hg, SaO_2 89% (on 2 L/min O_2)
- *Chest x-ray:* "Pulmonary congestion"; otherwise normal
- *ECG:* Sinus tachycardia without acute changes
- *Echocardiogram:* "Technically limited" but reported to be without segmental wall abnormalities or to show normal left ventricular function
- *Bilateral lower extremity Doppler examination:* Negative for deep venous thrombosis

Problem

What could be the cause of this patient's continued signs of right heart failure?

Discussion

The patient has overlap syndrome (COPD and OSA). He has been appropriately treated for COPD (bronchodilators and O_2) but has not been treated for OSA. His physician never asked and the patient never volunteered a history of nightly loud snoring with observed apnea and daytime fatigue. Subsequent evaluation with a nocturnal PSG reveals severe nocturnal desaturation to 40% on the oximeter despite treatment with O_2 at 2 L/min. A CPAP titration study is performed. The patient is discharged with CPAP set at 15 cm H_2O via a nasal mask. He returns to the outpatient clinic 3 months later and reports "feeling great." He reports that the shortness of breath has decreased and that he has much more energy during the day. Physical examination shows trace pedal edema. ABG studies on 2 L/min of O_2 reveal pH 7.40, PCO_2 40 mm Hg, PO_2 75 mm Hg, and SaO_2 93%.

BOX 34.5 Surgical Alternatives for Obstructive Sleep Apnea

- Bypass of the upper airway
- Tracheostomy
- Reconstruction of the upper airway
- Nasal surgery
- Palatal surgery
- Maxillofacial surgery

Surgical Interventions

Surgical treatments for OSA can be divided into two broad categories: procedures that bypass the upper airway and procedures that reconstruct the upper airway (Box 34.5). Before CPAP therapy became available, tracheostomy was the primary therapy for severe OSA. Because of the psychosocial and medical morbidity associated with the procedure, use of tracheostomy is currently limited to managing severe OSA when all other therapies have been exhausted.[126,127] In most instances, if a surgical approach to OSA is considered, the surgeon will perform an airway exam to identify the site(s) of airway obstruction and determine which approach will best address an individual's pattern of airway collapse. A new procedure termed drug-induced sleep endoscopy (DISE) may allow surgeons to better identify the site and mechanisms of upper airway collapse preoperatively, thus allowing the most appropriate surgical intervention for the patient.[128]

Palatal Surgery

Uvulopalatopharyngoplasty (UPPP) is palatal surgery performed with a standard "cold knife" technique or a laser. Portions of the soft palate, the uvula, and additional redundant tissue are removed in these procedures. The success rate of UPPP in 1996 was reported to be less than 50% overall.[129] Improvements in technique and the tissue-sparing modified UPPP may be more effective with less complications in the treatment of appropriately selected patients with OSA.[130]

Most patients with OSA have airway collapse at multiple levels. Thus surgical approaches such as UPPP targeting one level of obstruction typically lead to only modest improvement in OSA in most individuals. UPPP is much more commonly used nowadays as part of a multilevel approach to OSA and may be performed in conjunction with other airway procedures such as genioglossus advancement or hyoid suspension. This multilevel approach may have a greater success rate compared with standalone procedures targeting one site of obstruction.[131]

Maxillofacial Surgery

Maxillomandibular advancement surgically projects the jaw and the attached soft tissues forward, increasing the caliber of the airway and putting tension across the pharyngeal wall. This approach decreases the likelihood of airway collapse (Fig. 34.4). Maxillomandibular advancement has been shown to be effective in improving apnea severity, sleepiness, and quality of life.[132-134] These surgical procedures are a major undertaking and are performed at only a few specialized centers. A coordinated effort by a dedicated team of otolaryngologists, oral surgeons, and

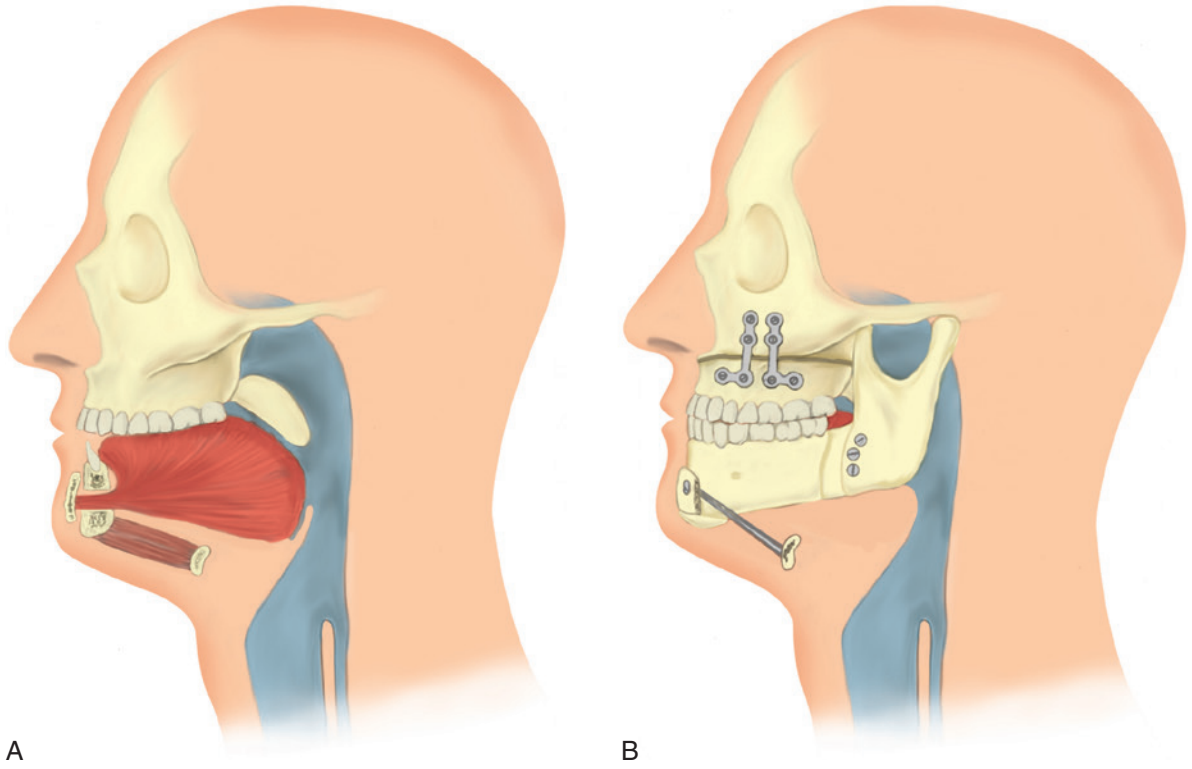

Fig. 34.4 Phase I and Phase II Upper Airway Reconstruction. (A) Phase I surgery. Lateral cutaway view of the skull shows tongue (genioglossal) and hyoid bone advancement in conjunction with uvulopalatopharyngoplasty. (B) Phase II surgery. Lateral cutaway view of the skull shows advancement of the maxilla (upper jaw) and mandible (lower jaw) in a patient who has undergone a phase I procedure.

sleep specialists is essential. Regardless of the surgical option chosen, a postoperative sleep study should be obtained to document improvement objectively.[135]

Upper Airway Stimulation

A new therapy for OSA uses a surgically implanted neurostimulator. This device stimulates the hypoglossal nerve, leading to protrusion of the tongue and bulk movement of upper airway soft tissues with the goal of maintaining airway patency. The only commercially available device was approved in 2014 based on a pivotal trial demonstrating effectiveness of this intervention in a highly selected group of 126 patients with OSA.[136] Three-year follow-up in this group has demonstrated persistent improvements in OSA and quality-of-life measures.[137] Currently, this device has very specific eligibility criteria, and its role in the management of OSA continues to evolve.

Additional Therapies

Alternative treatment options for OSA include nasal resistance devices, negative pressure oral appliances, and negative external pressure devices. These therapies can improve snoring, but their efficacy in patients with OSA, particularly moderate to severe disease, requires further evaluation.[138-140]

In addition, of interest currently is the use of combination therapy for OSA. Occasionally, patients may not have their apnea controlled optimally with PAP alone or may require a pressure that is too high for them to tolerate. The use of PAP in combination with an oral appliance may be of benefit in these situations.[141] Surgery in combination with PAP therapy may also lead to improved outcomes. Nasal procedures including turbinate reduction, septoplasty, and/or nasal valve surgeries have been minimally effective as stand-alone therapy for OSA but may lead to significant improvement in PAP adherence in those initially intolerant to PAP therapy.[142]

RULE OF THUMB Sleep symptoms may present early in patients with neuromuscular disease. Treatment with noninvasive ventilation during sleep may improve daytime symptoms.

ROLE OF THE RESPIRATORY THERAPIST IN DISORDERS OF SLEEP

RTs play a vital role in identifying high-risk patients through history and physical and either themselves doing further assessment with a STOP-BANG questionnaire or recommending referral for further assessment. As part of the multidisciplinary team, RTs prepare patients for the overnight PSG and obtain key information relating to their sleep history. During the study, RTs assess for **sleep-disordered breathing** and apply and titrate positive pressure. They are also involved with education that is important in assisting with the patient's understanding and compliance with positive pressure therapy. Some RTs pursue special certification in sleep technology.

RTs may see patients with sleep disorder–related symptoms during their clinical practice and can encourage diagnostic testing

MINI CLINI

Young Woman With Mental Status Changes After Orthopedic Surgery

History

A 37-year-old obese smoker is admitted to the hospital after elective surgical repair of a biceps tendon and ulnar collateral ligament. She initially sustained the injury after a fall when riding a bicycle. After outpatient orthopedic evaluation and preoperative cardiac clearance, an elective repair of the tendon and ligament was scheduled. She was intubated electively for the procedure, and her operative course was unremarkable. Postoperatively, she was extubated and noted to be slightly lethargic but easily arousable and in pain while in postoperative recovery. On transfer to the floor, she became increasingly lethargic and hypoxemic despite the addition of up to 6 L/min of supplemental O_2 via nasal cannula. An emergency code is called. She is transferred to a step-down bed and further testing is performed.

Medications at Home

- None

Medical History

- Hypertension, not on medications

Physical Examination

- *Vital signs:* Blood pressure 158/74 mm Hg, heart rate 68 beats/min, temperature 98.6°F (38.6°C), respirations 12 breaths/min
- *General:* Obese woman, lethargic and arousable
- *Neck:* 46 cm (18 inches) in circumference
- *Lungs:* Diminished breath sounds bilaterally
- *Heart:* Faint sounds but regular rate and rhythm
- *Abdomen:* Obese; soft, normal bowel sounds
- *Extremities:* Right arm wound intact with bandages in place, pulses equal

Laboratory Data

- *ABGs on 6 L/min O_2 via nasal cannula:* pH 7.11, PCO_2 109 mm Hg, PO_2 110 mm Hg, SaO_2 87%
- *Chest x-ray:* No mass, infiltrate, or effusion
- *ECG:* Normal sinus rhythm
- *CT scan of the head without contrast agent:* No mass, hemorrhage, or midline shift
- *CT scan of the chest with contrast agent:* No evidence of pulmonary embolism or parenchymal abnormality
- *EEG:* No seizure activity

Problem

How should this patient be managed?

Discussion

The patient requires bilevel noninvasive ventilator support intermittently for the next several days. After her work-up reveals nothing remarkable, a pulmonary and sleep consultation is obtained. Review of the medical records reveals the patient has been receiving hydromorphone (Dilaudid) frequently for pain control. After stopping opioid medication, the patient's mental status gradually returns to baseline. Repeat ABGs on room air show pH 7.39, PCO_2 62 mm Hg, PO_2 110 mm Hg, and SaO_2 93%. A diagnostic nocturnal PSG is performed, which reveals severe OSA with AHI of 55 and low SaO_2 of 72% and evidence of chronic **obesity hypoventilation**. Positive pressure titration is performed successfully with volume-assured pressure support with the goal V_T of 8 mL/kg. The patient is discharged home with a follow-up appointment in the sleep clinic.

MINI CLINI

Fatigue in a Patient With Neuromuscular Disease

History

A 54-year-old man with a recent diagnosis of ALS presents to the outpatient clinic with fatigue. He states he has been more tired and sleepy for the last few months. He had been diagnosed with ALS approximately 6 months ago but has been doing fairly well at home. He does notice that he has some difficulty sleeping at night, sometimes sleeping in a reclining chair. He denies snoring or weight gain, and in fact has lost 15 lb in the last few months. On further questioning, he reports feeling short of breath with exertion or when lying flat.

Medications

- None

Medical History

- Hypertension and gastroesophageal reflux
- No significant cardiac disease

Physical Examination

- *Vital signs:* Blood pressure 135/70 mm Hg, heart rate 80 beats/min, temperature 98.6°F (37°C), respiration 16 breaths/min
- *General:* Thin, no distress, pleasant man
- *Neck:* 52 cm (20.5 inches) in circumference
- *Lungs:* Clear breath sounds bilaterally
- *Heart:* Regular rate and rhythm
- *Abdomen:* Thin; soft, normal bowel sounds
- *Extremities:* no edema

Laboratory Data

- *Room air ABGs:* pH 7.38, PCO_2 52 mm Hg, PO_2 88 mm Hg, SaO_2 94%
- *Chest x-ray:* Normal
- *Pulmonary function tests:* FVC 1.52 L (42% predicted), FEV_1 1.41 L (53% predicted), FEV_1/FVC ratio 0.73

Problem

Why does this patient have fatigue?

Discussion

The patient's symptoms are concerning for respiratory compromise because of his neuromuscular disease. His pulmonary function tests reveal restrictive lung physiology, with decreased FVC and FEV_1 on spirometry. He also has evidence for chronic hypoventilation with elevated PCO_2 on ABG analysis. He may benefit from starting noninvasive ventilation. The patient was started on positive pressure therapy with pressure support, and his sleep quality and daytime energy improved.

by discussion with the patient or the managing physician or both. In the acute care setting, RTs and nursing staff are in a unique position to observe directly evidence of abnormal breathing during sleep or other clinical clues that may prompt further clinical action.

RTs who work for durable medical equipment companies may see patients in their home and help to manage the CPAP or bilevel PAP machines, interfaces, and supplemental O_2. In the context of rehabilitation or bariatric surgery, RTs may help to care for patients recovering from surgery or participating in rehabilitation programs for weight loss or improvement in cardiopulmonary function. The role of the RT can be key in serving

as the bridge between physician and patient to enable education, identify obstacles to therapy, and improve overall compliance. In all these ways, RTs play an invaluable role as members of the sleep medicine team.

SUMMARY CHECKLIST

- There are three types of sleep apnea: OSA, CSA, and mixed sleep apnea; OSA is the most common.
- OSA is common, underdiagnosed, and controllable.
- The major risk factor for airway narrowing or closure during sleep is a small or unstable upper airway.
- The shift in the physiologic state from wakefulness to sleep and the consequent decrease in muscle tone result in partial or complete airway closure of the upper airway in patients with OSA.
- The long-term harmful effects of OSA include poor daytime functioning, impaired metabolic function, and increased risk for cardiovascular morbidity and mortality.
- Risk factors for OSA include male sex, age greater than 40 years, upper body obesity (neck size >16.5 inches), habitual snoring, and diurnal hypertension.
- PSG is the most accurate way to make the diagnosis of OSA; however, home sleep testing is becoming increasingly common. The PSG measures several physiologic variables and allows for the staging of sleep and measurement of airflow, ventilatory effort, ECG, and SaO_2.
- First-line medical therapy for OSA is CPAP. This modality is almost always effective in the laboratory, although long-term adherence with CPAP therapy may be suboptimal.
- Bilevel PAP therapy may be useful in salvaging selected patients who have difficulty accepting or complying with CPAP.
- Autotitrating positive airway pressure devices (auto-CPAP or autobilevel PAP) are being used in managing OSA without an in-laboratory titration study.
- Oral appliances can be effective in patients with mild to moderate OSA.
- Surgical therapy including upper airway stimulation may be an option for a select group of patients who have undergone an extensive preoperative analysis of the upper airway and do not accept or comply poorly with medical therapy.
- Optimal management of OSA, regardless of the modality, requires patient education, continued monitoring, and reassessment.

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35

Neonatal and Pediatric Respiratory Disorders

Robert M. DiBlasi and Edwin L. Coombs, Jr.

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Discuss the clinical findings, radiographic abnormalities, and treatment of patients with respiratory distress syndrome.
- Describe the clinical manifestations and treatment of patients with transient tachypnea of the newborn.
- Describe the pathophysiology, presentation, and treatment of meconium aspiration syndrome.
- Identify the clinical signs and symptoms associated with bronchopulmonary dysplasia and the approaches used to manage these infants.
- State the cause and treatment of apnea of prematurity.
- Describe the pathophysiology, diagnosis, and treatment of persistent pulmonary hypertension of the newborn.
- Discuss the pathophysiology, diagnosis, and treatment of congenital diaphragmatic hernia.
- Identify the anatomic defects associated with tetralogy of Fallot.
- Describe the clinical presentation of a ventricular septal defect.
- Describe types and associated conditions for abdominal wall defects.
- Define the epidemiologic factors associated with increased risk for sudden infant death syndrome.
- Identify the respiratory problems associated with gastroesophageal reflux disease.
- State the clinical findings commonly observed in patients with bronchiolitis.
- Describe the clinical features and treatment of children with epiglottitis.
- Describe the clinical manifestations and treatment of cystic fibrosis.

CHAPTER OUTLINE

KEY TERMS

apnea of prematurity
bronchiolitis
bronchopulmonary dysplasia
croup
cystic fibrosis
ductus arteriosus
epiglottitis
gastroesophageal reflux disease
meconium aspiration syndrome
nasal flaring
persistent pulmonary hypertension of the newborn
respiratory distress syndrome
sudden infant death syndrome
tetralogy of Fallot
transient tachypnea of the newborn
transposition of the great arteries

Many perinatal disorders can affect the respiratory system. Some disorders are developmental abnormalities of the heart, lungs, or airways; some are caused by prematurity; some are caused by problems during labor and delivery; and some are caused by complications from treating the underlying disorders. Common disorders in the neonatal period with which respiratory therapists (RTs) should be familiar are respiratory distress syndrome (RDS), transient tachypnea of the newborn (TTN), meconium aspiration syndrome (MAS), apnea of prematurity, bronchopulmonary dysplasia (BPD), persistent pulmonary hypertension of the newborn (PPHN), and congenital cardiopulmonary abnormalities.

NEONATAL RESPIRATORY DISORDERS

Lung Parenchymal Disease

Respiratory Distress Syndrome

Background. Neonatal **respiratory distress syndrome** (RDS) affects approximately 40,000 infants each year in the United States.[1] Although the mortality rate has decreased dramatically over the past four decades, many infants still perish or have chronic conditions that are associated with the treatment of the syndrome (i.e., oxygen and positive pressure). RDS, previously known as *hyaline membrane disease*, is a disease of prematurity. The incidence increases with decreasing gestational age, occurring in more than 80% in neonates less than 28 weeks.[2] The major factors in the pathophysiology of RDS include surfactant deficiency, underdeveloped alveolar units and capillaries and decreased alveolar surface area, reduced lung compliance, poor gas exchange, and the presence of a **ductus arteriosus**.

RULE OF THUMB The incidence and severity of RDS, as well as incidence of chronic complications, both increase with decreasing gestational age and weight. Many of these complications can be avoided with judicious use of oxygen and positive pressure.

Surfactant production depends on both the maturity of the lung and the adequacy of fetal perfusion. Maternal factors that impair fetal blood flow, such as abruptio placentae and maternal diabetes, also may lead to RDS.

Pathophysiology. In preterm infants, adequate amounts of surfactant are present in the lung; however, the surfactant is trapped inside type II alveolar cells. In infants with RDS, type II alveolar cells do not release adequate amounts of surfactant. The surfactant that is released is incompletely formed and does not decrease alveolar surface tension. Because the surfactant molecule in the alveolus is structurally abnormal, the type II cells and alveolar macrophages have more rapid uptake for recycling. Thus there is a qualitative deficiency of alveolar surfactant.

Fig. 35.1 outlines the pathophysiologic events associated with RDS. A qualitative decrease in surfactant increases alveolar surface tension forces, which causes alveoli to become unstable and collapse and leads to atelectasis and increased work of breathing (WOB). At the same time, the increased surface tension draws fluid from the pulmonary capillaries into the alveoli. In combination, these factors impair oxygen (O_2) exchange and cause severe hypoxemia. The severe hypoxemia and acidosis increase *pulmonary vascular resistance (PVR)*. As pulmonary arterial pressure increases, extrapulmonary right-to-left shunting increases, and hypoxemia worsens. Hypoxemia and acidosis also impair further surfactant production. Steroids given to the pregnant mother before birth (antenatally) have been shown to accelerate lung maturation and surfactant function in the fetus, decrease the severity of RDS, and improve outcomes.[3,4]

Clinical manifestations. The first signs of respiratory distress in infants with RDS normally appear soon after birth. Tachypnea usually occurs first. After tachypnea, worsening retractions, paradoxical breathing, and audible grunting are observed. **Nasal flaring** also may be seen. Chest auscultation often reveals fine inspiratory crackles. Cyanosis may or may not be present. If central cyanosis is observed, it is likely that the infant has severe hypoxemia. Certain other conditions, such as systemic

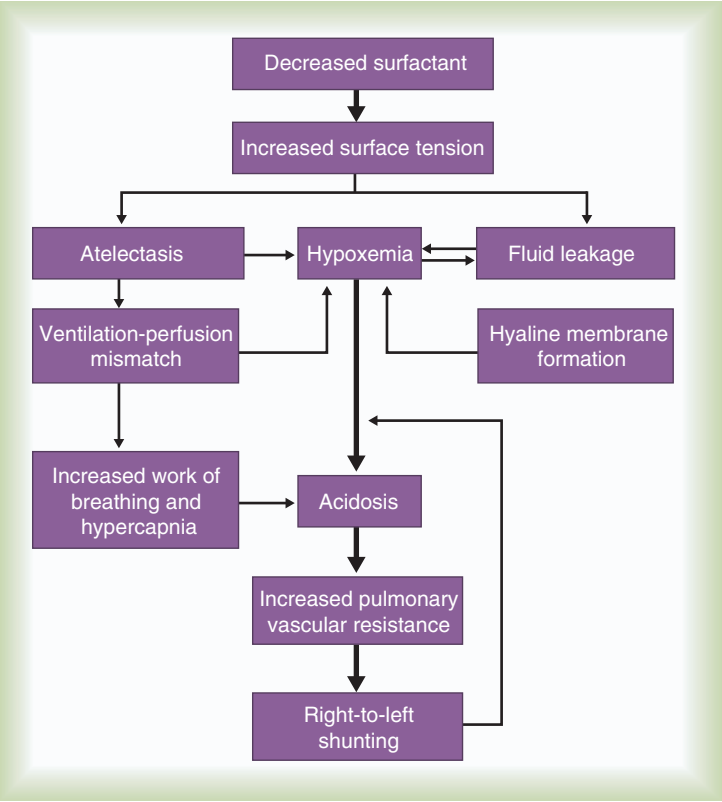

Fig. 35.1 Pathophysiology of Respiratory Distress Syndrome.

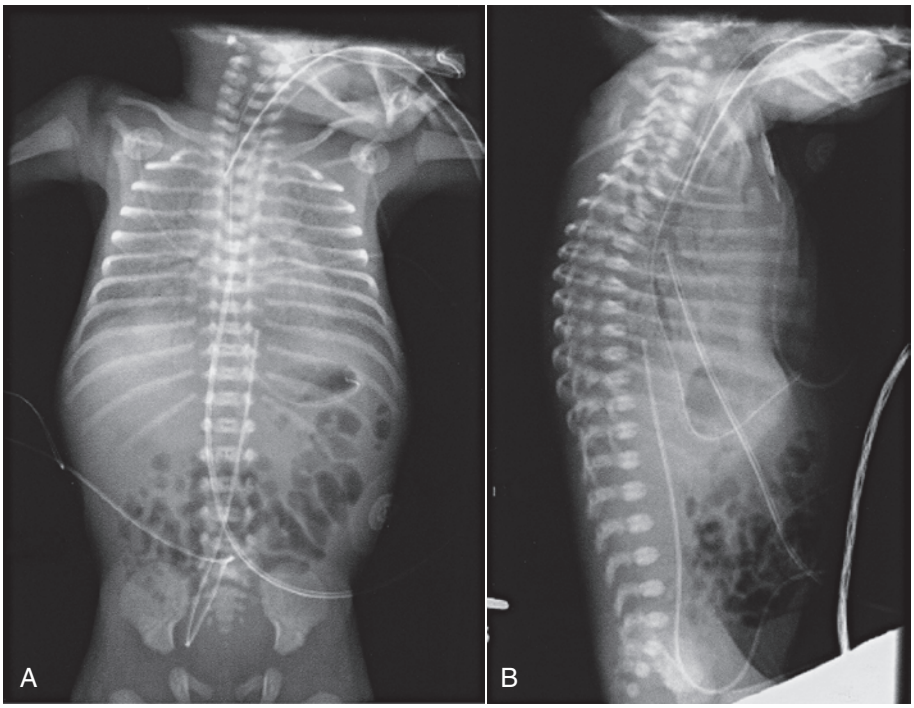

Fig. 35.2 Radiopaque Appearance of Severe Respiratory Distress Syndrome. Anteroposterior (A) and lateral (B) chest x-rays show diffuse hazy appearance with low lung volumes and air bronchograms that extend into the periphery.

hypotension, hypothermia, and poor perfusion, can mimic this aspect of RDS.

A definitive diagnosis of RDS usually is made with chest x-ray (Fig. 35.2). Diffuse, hazy, ground-glass appearance or reticulogranular densities with the presence of air bronchograms with low lung volumes are typical of RDS. The reticulogranular pattern is caused by aeration of respiratory bronchioles and widespread alveolar collapse. Air bronchograms appear as aerated, dark, major bronchi surrounded by the collapsed or consolidated lung tissue.

Treatment. *Continuous positive airway pressure (CPAP)*, surfactant replacement therapy, and mechanical ventilation with conventional or *high frequency ventilation (HFV)*, are common interventions used to manage RDS. High-flow nasal cannula (HFNC),[5] Nasal Intermittent Mandatory Ventilation (NIMV),[6] and unless the infant's condition is severe (high WOB, FiO_2 >0.4, and/or severe apnea), a trial of nasal CPAP is indicated (4 to 6 cm H_2O).[4-8] Because of the hazards of endotracheal tubes (ETTs), nasal prongs or mask are preferred. If the infant's clinical condition deteriorates rapidly, a more aggressive approach is required. Endotracheal intubation should be performed under controlled conditions as an elective procedure. Mechanical ventilation with positive end-expiratory pressure (PEEP) should be initiated if gas exchange does not improve with CPAP or if the patient's frequent apnea does not respond to stimulation.

Historically, premature infants have been intubated and placed on a ventilator in order to improve gas exchange, reduce WOB, or give surfactant to prevent RDS. However, even short-term invasive ventilation in premature infants is associated with severe complications,[9] and CPAP is gentler on premature infants' lungs.[10] If it is likely that respiratory support with a ventilator will be needed, early administration of surfactant via ETT and ventilator, followed by rapid extubation—known as INtubate, SURfactant, and Extubation to CPAP (INSURE)—is preferable to prolonged ventilation.[11,12] Early CPAP after birth and subsequent selective surfactant administration in preterm infants that develop severe RDS (high WOB, apnea, and/or FiO_2 >0.4 on CPAP) has been shown to result in lower incidence of death, development of chronic lung disease, and other complications[13] than INSURE and is now the preferred practice in preterm infants.[14]

Other forms of noninvasive support for premature RDS may include HFNC and NIMV. HFNC provides positive pressure similar to CPAP but with the added benefit of purging CO_2 from the anatomic deadspace.[15] It is unclear whether HFNC should be used as an initial form of support, like CPAP, but it appears to be as effective as and with less nasal airway pressure injuries than CPAP following extubation of premature infants.[16] NIMV is essentially "CPAP with a rate" and has been shown to provide greater support than CPAP by reducing apnea and the need for intubation in premature infants.[17,18]

RULE OF THUMB HFNC has been shown to be as clinically effective as nasal CPAP, but with fewer nasal injuries following extubation from mechanical ventilation in premature infants.

RULE OF THUMB Nasal intermittent mandatory ventilation or "CPAP with a rate" may be an effective option for avoiding intubation in infants with severe RDS that are not responding to HFNC or CPAP.

MINI CLINI

Respiratory Distress Syndrome

Problem

A woman is about to deliver at 26 weeks of gestational age. What should the RT have available for resuscitation of the infant?

Discussion

An infant at 26 weeks of gestational age is most likely going to have RDS—ranging from mild to severe disease. The RT should have equipment, supplies, and drugs necessary to support the infant. Many infants require mask-bag ventilation. It is crucial that the RT be acutely attuned to using the lowest pressures necessary to move the chest. It is very easy to injure the lung with high V_T. Most authorities recommend the use of a T-piece resuscitator that delivers manual breaths at fixed pressures, decreasing the risk for traumatic injury from high V_T. The aim of mechanical ventilation for RDS is to prevent lung collapse and maintain alveolar inflation. In severe RDS, collapse of alveoli with every breath necessitates very high reinflation pressures. To prevent the need for this high reinflation pressure, use of PEEP is necessary.

The time constant of the lungs in RDS is short, so the lung empties very quickly with each ventilator cycle. If alveolar ventilation is inadequate, either peak inspiratory pressure, tidal volume, PEEP, or rate should be increased. Modes classified as pressure control with adaptive targeting (e.g., A/C volume guarantee) have been shown to cause fewer complications than traditional pressure control breath types (with set-point targeting) in this population.[19] Such modes allow the operator to set an average tidal volume target, and the ventilator automatically adjusts inspiratory pressure to achieve the target as respiratory system mechanics change (see Chapter 47). These modes are often referred to in the pediatric literature as "volume-targeted" modes, although this term is also used to refer to volume control modes (i.e., preset tidal volume and inspiratory flow). Preset tidal volume targets of 4 to 6 mL/kg should be used, and peak inspiratory pressure limit should be kept less than 30 cm H_2O for larger premature infants, and even lower pressure is indicated for more immature infants.[20] Higher limits may be needed if the infant has an ETT leak, high airway resistance, or reduced pulmonary compliance.

RULE OF THUMB Infants receiving conventional ventilation have traditionally been supported with pressure control ventilation with set-point targeting (e.g., pressure controlled-synchronized intermittent mandatory ventilation [PC-SIMV]). Volume-targeted breath types (e.g., pressure regulated volume control) may result in fewer complications and better outcomes than pressure control, especially in preterm babies with RDS. The current standard of care is to deliver replacement surfactant to infants that have severe RDS and are not tolerating CPAP.

Surfactant replacement therapy also is used as both a rescue treatment (in infants who already have RDS) and a prophylactic therapy (in the care of infants delivered prematurely). Some centers use prophylactic surfactant replacement therapy in the care of all very small infants (<1500 g). Therapies aimed at decreasing pulmonary edema, improving cardiac output, and weaning from O_2 and high ventilator volumes are essential in successfully treating infants receiving surfactant. Recent evidence supports the use of noninvasive ventilatory support (e.g., bubble CPAP) to support even the smallest of infants.[21,22]

Surfactant proteins are important for decreasing alveolar surface tension. All of these preparations are liquid suspensions that are instilled directly into the trachea. Four surfactant preparations are currently available in the United States for managing neonatal RDS: beractant (Survanta; Abbott Laboratories, North Chicago, IL), calfactant (Infasurf; ONY, Amherst, NY), poractant alfa (Curosurf; Chiesi, Cheadle, UK), and lucinactant (Surfaxin, Discovery Labs, Warrington, PA).[23]

Animal-derived surfactants may have several advantages over synthetic surfactants and are the most commonly used.[23] Beractant and calfactant are natural bovine surfactant extracts. Poractant alfa is a natural porcine surfactant extract. When compared with Beractant, high-dose Poractant has been shown to result in better outcomes in preterm infants.[23] Lucinactant is a completely synthetic surfactant that is under investigation for use in aerosolization during CPAP. The synthetic surfactant uses an amino acid sequence that acts like surfactant protein.[24]

RULE OF THUMB Maintenance of functional residual capacity (FRC) is best supported by targeting appropriate tidal volumes and positive end-expiratory pressure (CPAP or PEEP).

All surfactants appear to be equally effective. More than a single dose has been shown to be beneficial. Each specific surfactant has different dosing volumes and intervals (Table 35.1). Multiple doses of surfactant appear to result in better clinical outcomes than a single dose.[25] Traditionally, infants are administered surfactant through the ETT and require a mechanical ventilator. If infants are intubated, it is preferable to give the surfactant early in the ventilation course rather than later.[13] The surfactant product insert describes the positioning of the infant for surfactant delivery. General practice is to position the infant with different sections of the lung dependent so that the surfactant enters that section of the lung with gravity flow. If the infant is very sick and cannot be repositioned, surfactant can be administered with the infant in the supine position.

There are many complications associated with surfactant administration, which are related to airway obstruction from the liquid in the airways.[26] Several studies are underway to evaluate aerosolized surfactant or surfactant delivered through a thin tracheal catheter delivery during CPAP, so that babies can avoid intubation, mechanical ventilation, and lung injury.[27,28]

Transient Tachypnea of the Newborn

Background. **Transient tachypnea of the newborn** (TTN), often called *type II RDS*, is probably the most common respiratory disorder of newborns.[29,30] The cause of TTN is unclear, but it is most likely related to delayed clearance of fetal lung liquid.[31] During most births, approximately two-thirds of this fluid is expelled by thoracic squeeze in the birth canal; the rest is reabsorbed through the lymphatic vessels during initial breathing. These mechanisms are impaired in infants born by cesarean section or infants with incomplete development of the lymphatic vessels (preterm or small-for-gestational-age infants). The residual lung fluid causes an increase in airway resistance and an overall decrease in lung compliance. Because compliance is low, the infant must generate more negative pleural pressure to breathe. This process can result in hyperinflation of some areas and air trapping in others. Most infants with TTN are born at term without any specific predisposing factors in common. Mothers of neonates who have TTN tend to have longer labor intervals and a higher incidence of failure to progress in labor, which leads to cesarean delivery. In many cases, however, maternal history and labor and delivery are normal.

Clinical manifestations. During the first few hours of life, infants with TTN breathe rapidly. Alveolar ventilation, as

TABLE 35.1 Surfactant Dosing

Dosing Information	Beractant (Survanta)	Calfactant (Infasurf)	Poractant Alfa (Curosurf)	Lucinactant (Surfaxin)
Dose mg/kg of birth weight	100	100	100–200	20
Dose: mL/kg birth weight	4	3	1.25–2.5	5.8
Administration	¼ dose quickly in each of four positions	½ dose slowly supine then rotated	Whole or ½ dose supine	Dose in each of four positions
Dosing interval	Every 6 h or more often	Every 12 h or more often	Every 12 h or more often	Up to 4 doses in 48 h, minimum of 6-h interval

measured by arterial pH and $PaCO_2$, usually is normal. The chest x-ray findings, which may initially be indistinguishable from pneumonia, are hyperinflation, which is due to air trapping, and perihilar streaking. The perihilar streaking probably represents lymphatic engorgement. Pleural effusions may be evident in the costophrenic angles and interlobar fissures.

Treatment. Infants with TTN usually respond readily to a low FiO_2 by nasal cannula or high-flow nasal cannula (see Chapter 42). Infants requiring a higher FiO_2 may benefit from CPAP. Because the retention of lung fluid may be gravity-dependent, frequent changes in the infant's position may help speed lung fluid clearance. Also, diuretics, bronchodilators, and fluid restriction are common therapies.[31] Because TTN and neonatal pneumonia have similar clinical signs, intravenous administration of antibiotics should be considered for at least 3 days after appropriate culture samples are obtained. Mechanical ventilation is rarely needed, and when it is, this probably indicates a complication. Clearing of the lungs evident on a chest x-ray and with clinical improvement usually occurs within 24 to 48 hours. A few infants with TTN eventually have persistent pulmonary hypertension.

RULE OF THUMB A high-flow nasal cannula is preferred to prevent nasal injury and skin breakdown versus nasal continuous positive airway pressure [NCPAP] interfaces in TTNB (see Chapter 42). If a high-flow nasal cannula is not tolerated, infants require positive pressure to support spontaneous breathing and lung clearance.

Meconium Aspiration Syndrome

Background. **Meconium aspiration syndrome** is a disease of term and near-term infants. It involves aspiration of meconium into the central airways of the lung. MAS is usually associated with perinatal depression and asphyxia.

Pathophysiology. Amniotic fluid consists mainly of fetal lung fluid, fetal urine, and transudate from the uterine wall. *Meconium,* the contents of the fetal intestine, occasionally is expelled from the fetus into the surrounding amniotic fluid. Meconium consists of mucopolysaccharides, cholesterol, bile acids and salts, intestinal enzymes, and other substances. Meconium normally is not passed until after delivery.[32] Infants who have perinatal asphyxia may pass meconium in utero. The pathophysiologic control mechanisms for the passage of meconium in utero are not completely understood. It is widely accepted that infants can have meconium aspiration in utero. Amniotic fluid stained with meconium is found in approximately 12% of all births.[32] About 5% of neonates born with meconium-stained amniotic fluid develop MAS.[33] MAS has been reported to have mortality as high as 26%.[34,35]

Meconium-stained amniotic fluid is rare among infants younger than 37 weeks of gestational age. The clinical syndrome develops in 2 of every 1000 infants. Of infants with inhaled meconium, 95% clear their lungs spontaneously.[36] Amniotic fluid infusion into the uterus before the delivery of infants with meconium-stained fluid has been shown to improve neonatal outcomes.[37]

For many years, the aspirated meconium itself was considered the primary cause of MAS. More recent evidence suggests that the real causative agent is fetal asphyxia that precedes aspiration. Fetal asphyxia causes pulmonary vasospasm and hyperreactivity of the vasculature, which lead to persistent pulmonary hypertension.[38,39]

MAS involves three primary problems: pulmonary obstruction, lung tissue damage, and pulmonary hypertension.[38] Obstruction occurs because of plugging of the airways with particulate meconium. This obstruction often is of the ball-valve type, which allows gas entry but prevents gas exit. Ball-valve obstruction causes air trapping and can lead to volutrauma (Fig. 35.3). The lung tissue injury caused by MAS is chemical pneumonitis. Persistent pulmonary hypertension with intracardiac and extracardiac right-to-left shunting frequently complicates MAS.[38]

Clinical manifestations. Before birth, thick meconium, fetal tachycardia, and absent fetal cardiac accelerations during labor are evidence that the fetus is at high risk for MAS. After delivery, if the infant has a low umbilical artery pH, an Apgar score less than 5, and meconium aspirated from the trachea, intensive care and close observation for MAS are warranted. Infants with MAS typically have gasping respirations, tachypnea, grunting, and retractions. The chest x-ray usually shows irregular pulmonary densities, which represent areas of atelectasis, and hyperlucent areas, which represent hyperinflation due to air trapping (Fig. 35.4). Arterial blood gases (ABGs) typically show hypoxemia with mixed respiratory and metabolic acidosis. In the most severe cases, there is right-to-left shunting and persistent pulmonary hypertension.[32]

Treatment. It is no longer recommended that vigorous infants with meconium-stained fluid be intubated and suctioned.[40] Traditionally, an ETT has been inserted immediately in severely respiratory-compromised (nonvigorous) infants with thick meconium, and suction applied directly to the ETT.[41] The ETT is removed and inspected for meconium. If meconium is present, the procedure is repeated with a new ETT until no further

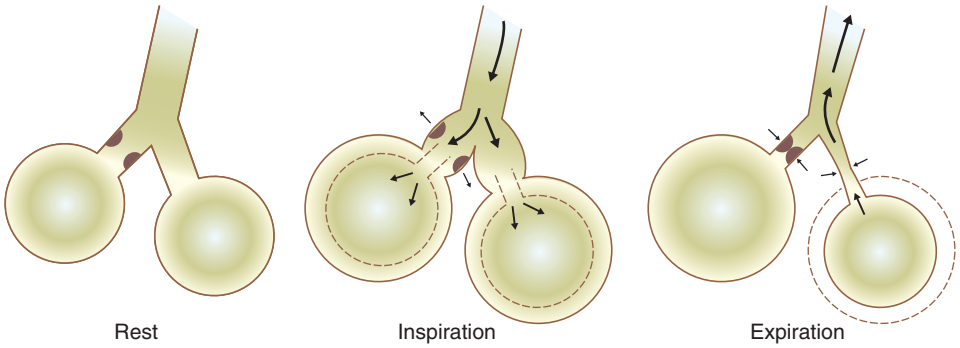

Fig. 35.3 Ball-Valve Effect. At rest, the airway lumen is partially obstructed. With inspiration, negative intrathoracic pressure opens the airway and relieves obstruction. Gas enters and expands the alveoli. With expiration, intrathoracic pressure changes to positive force, which narrows the airway and causes total occlusion. Gas cannot be expelled and is trapped within the alveoli. (Modified from Koff PB, Eitzman DV, Neu J: *Neonatal and pediatric care*, ed 2, St Louis, 1993, Mosby.)

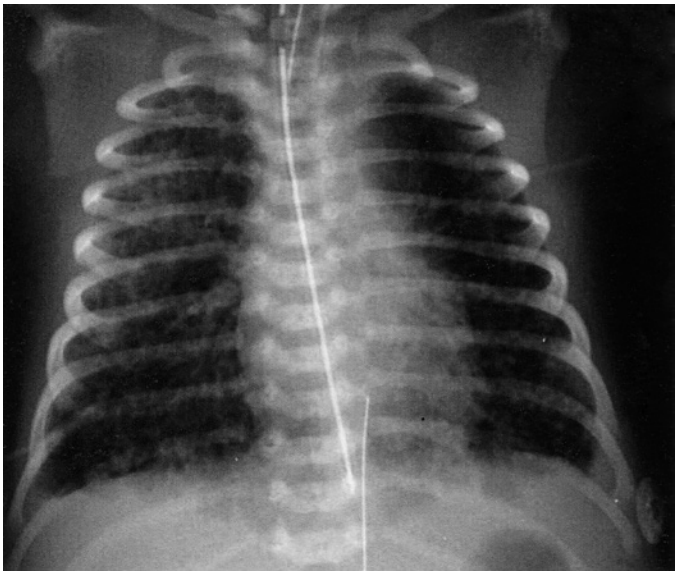

Fig. 35.4 Chest X-Ray of a Patient With Meconium Aspiration Syndrome. Anteroposterior radiograph shows diffuse patchy areas of atelectasis and emphysema.

meconium is aspirated or until two to four aspirations have been performed. The ETT should be left in place, and mechanical ventilation should be started. In 2011, that practice remained unchanged. However, it was suggested that if attempted intubation is prolonged and unsuccessful, bag-mask ventilation should be considered, particularly if there is persistent bradycardia.[41] Most recently the practice of routine endotracheal suctioning for infants with meconium aspiration has changed. Rather, the use of positive pressure ventilation is preferred to minimize any delay in initiating ventilation.[42] However, one recent study showed that this practice change has been associated with unfavorable clinical outcomes compared with the prior practice of electively intubating and suctioning depressed infants.[43] There is evidence that tracheal lavage with dilute surfactant improves the clinical course and outcome of infants with MAS.[44]

If the infant's condition worsens as evidenced by nasal flaring, substernal retractions, increased respiratory rate, and/or cyanosis, the use of NCPAP, HFNC, or mechanical ventilation may be indicated.[45] CPAP is indicated if the primary problem is hypoxemia. By distending the small airways, CPAP can sometimes overcome the ball-valve obstruction and improve both oxygenation and ventilation. If respiratory acidosis is severe or clinical assessment indicates excessive work in breathing, mechanical ventilation should be started. Inhaled nitric oxide (NO) is an extremely effective option in infants with MAS and persistent fetal circulation both with noninvasive and invasive ventilation.[46,47] Fig. 35.3 shows the ball-valve effect.[47] At rest, the airway lumen is partially obstructed. With inspiration, negative intrathoracic pressure opens the airway and relieves the obstruction. Gas enters and expands the alveoli. With expiration, intrathoracic pressure changes to a positive force, which narrows the airway and causes total occlusion. Gas cannot be expelled and is trapped within the alveoli. It is difficult to provide ventilation to infants with severe MAS. These infants often retain CO_2 and need increased ventilatory support. Because of high airway resistance, the lungs have a long time constant. High ventilator rates and pressures increase the risk for air trapping and volutrauma.

Evidence suggests that both HFV and synchronous intermittent mechanical ventilation decrease the risk for air leak.[48] Various[49] studies have shown improvement in MAS with the use of HFV and surfactant.[50] NO has become a major adjunct in managing persistent pulmonary hypertension.[51] Corticosteroids have not yet been shown to improve outcomes for infants with MAS.[52,53] High mean airway pressures may worsen pulmonary hypertension and aggravate right-to-left cardiac shunting.

Bronchopulmonary Dysplasia

Background. Preterm infants (i.e., 1000 g or less and/or 10 weeks premature) may develop a common chronic pulmonary condition called **bronchopulmonary dysplasia** (BPD). BPD is a complex disease that is characterized by lung injury/inflammation from oxygen and/or positive pressure. BPD may cause altered lung development, pulmonary emphysema, and pulmonary hypertension.[54,55] Historically, BPD has been commonly defined by the requirement for supplemental oxygen at 28 days in infants born at below 32 weeks gestation.[56] Furthermore, BPD is divided into three severity grades (mild, moderate, or severe), based on respiratory support needs at 36 weeks of postmenstrual age.

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Meconium Aspiration Syndrome

Problem

The RT is called to the delivery room to attend the delivery of a term infant with meconium-stained amniotic fluid. What should the RT have available for the resuscitation of this infant?

Discussion

The RT should have the standard resuscitation equipment available. Current recommendations for resuscitating a newborn with meconium staining do not include immediate intubation and tracheal suctioning for a vigorous infant. If the infant is depressed and not breathing, the infant should be resuscitated similar to any other depressed and apneic infant, which includes intubation. However, there is no consensus on whether the depressed infant would benefit from intubation and tracheal suctioning or not.

Most babies who have BPD get better in time, but they may need chronic respiratory support for months or even years. They may continue to have lung problems throughout childhood and even into adulthood.

Pathophysiology. The development of BPD is complex and involves many pathways. The initiating factors are related to ventilator-induced ling injury: *atelectrauma* (due to lung collapse) and *volutrauma* (due to large tidal volume, V_T). Factors such as hyperoxia and hypoxia, mechanical forces, pulmonary growth arrest, inflammation, nutrition, and genetics contribute to the abnormal development of the lung and lead to BPD.

Atelectrauma[54] is a term coined to describe the lung injury caused by repetitive opening and closure of unstable or collapsed lung units. Atelectrauma results from using inadequate PEEP and/or tidal volumes, which leads to ongoing derecruitment (e.g., areas of alveolar collapse) and inflammation in the lung. *Volutrauma* is the term used to describe local overinflation (and stretch) of airways and alveoli from excessive tidal volumes and/or PEEP. Similar to atelectrauma, volutrauma leads to damage to airways, pulmonary capillary endothelium, alveolar and airway epithelium, and basement membranes. The combination of atelectrauma and volutrauma synergistically increases lung injury and places infants at risk for developing BPD.[57,58]

Both atelectrauma and volutrauma cause a need for increased supplemental O_2 concentrations. This use of supplemental O_2 leads to overproduction of superoxide, hydrogen peroxide, and perhydroxyl radicals. Preterm infants are particularly susceptible to O_2 radicals because the antioxidant systems develop in the last trimester of pregnancy. Prolonged hyperoxia begins a sequence of lung injury that leads to inflammation, diffuse alveolar damage, pulmonary dysfunction, and death.

Chronic injury and inflammation from ventilator and oxygen-induced lung injury has been shown to delay or "arrest" pulmonary growth and development.[59,60] A "new" BPD is being described that shows decreased alveolarization rather than the prominent airway damage of the "old" BPD.[61] This change in the pathologic characteristics of BPD is thought to be related to improvements in ventilator management, the use of surfactant, judicious use of oxygen, and processes that interrupt alveolar development (e.g., postnatal steroid therapy).[62]

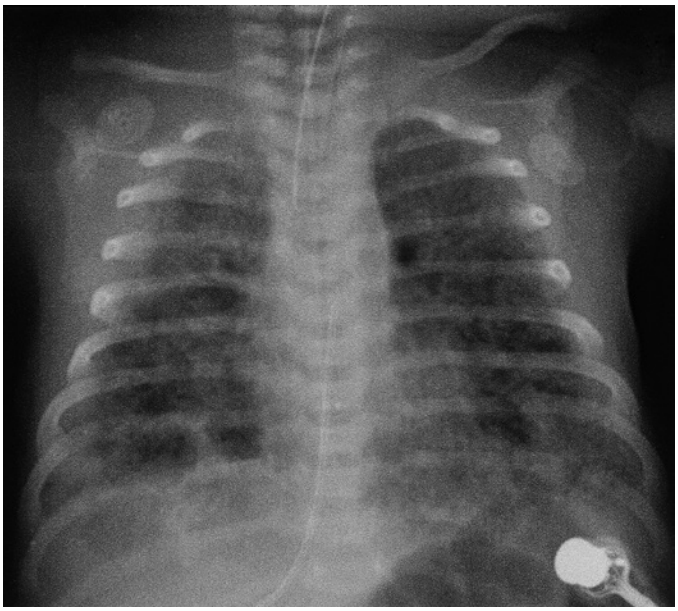

Fig. 35.5 Chest X-Ray of a Patient With Bronchopulmonary Disease. The anteroposterior chest x-ray shows areas of scarring, atelectasis, emphysema, and cysts. This film is consistent with severe bronchopulmonary disease.

Clinical manifestations. BPD has various clinical manifestations. Some infants may start with little or no O_2 requirement and little or no mechanical ventilation requirement. Progressive respiratory distress develops at approximately 2 to 3 weeks of life, and then the infant may need O_2 and/or mechanical ventilation. Other immature infants may begin with pneumonia or sepsis and need very high levels of O_2 and mechanical ventilation. In either of these scenarios, progressive vascular leakage and areas of atelectasis and emphysema develop in the lungs, and progressive pulmonary damage occurs. The chest x-ray in severe disease shows areas of atelectasis, emphysema, and fibrosis diffusely intermixed throughout the lung (Fig. 35.5). ABG measurements reveal varying degrees of hypoxemia and hypercapnia due to airway obstruction, air trapping, pulmonary fibrosis, and atelectasis. There is a marked increase in airway resistance with an overall decrease in lung compliance. Many infants with BPD may develop floppy upper airways (tracheobronchomalacia) due to prolonged ventilation of stiff lungs through relatively compliant airways.[63] This is also a major reason why infants with BPD may require chronic tracheostomy, mechanical ventilation, and longer hospital stays.[64] Infants with BPD who exhibit distress may benefit from high CPAP or PEEP levels (8 to 12 cm H_2O) to prevent airway collapse at end-exhalation.[65] Bronchodilator therapy should be used with caution, as it may relax smooth muscle and cause the airway to become floppier.[66] Approximately 10% to 20% of infants with severe BPD will have pulmonary hypertension from vascular anomalies, chronic ventilation, and poor gas exchange.[67] These infants are at greater risk than other BPD infants for tracheostomy, chronic ventilation, and mortality.

Treatment. The best management of BPD is prevention. Prevention of atelectrauma and volutrauma begins in the delivery room. Establishment of an optimal FRC without overstretching the lung requires careful attention to detail in providing manual ventilation with optimizing PEEP and avoiding large V_T.

TABLE 35.2 Evaluation of an Infant With Apnea

Possible Cause	Associated Signs	Investigation
Infection	Lethargy, respiratory distress, temperature instability	Complete blood count, sepsis evaluation
Metabolic disorder	Poor feeding, lethargy, jitteriness	Glucose, calcium, electrolyte levels
Impaired oxygenation	Respiratory distress, tachypnea, cyanosis	O_2 monitoring, arterial blood gases, chest x-ray
Maternal drugs	Maternal history, hypotonia, central nervous system depression	Magnesium level, urine drug screen
Intracranial lesion	Abnormal neurologic findings, seizures	Cranial ultrasonography
Environmental	Lethargy	Monitor temperature (infant and environment)
Gastroesophageal reflux	Feeding difficulty	Specific observation, barium swallow x-ray examination

From Stark AR: Disorders of respiratory control in infants, *Respir Care* 36:673, 1991.

Treatment of infants with BPD involves steps for rapidly weaning from mechanical ventilation to minimize additional lung damage or using CPAP over invasive ventilation whenever possible. Infants with severe disease may be dependent on supplemental O_2 or mechanical ventilation for months or years, and have symptoms of airway obstruction. Therapy usually is supportive throughout the course of the disease. Supplemental O_2 can help decrease pulmonary hypertension. Mechanical ventilation strategies to reduce hyperinflation may require larger tidal volumes (8 to 10 mL/kg), higher PIP, slower rates (20 to 25 breaths/min), and longer inspiratory times and PEEP than what is used in infants without BPD.[62]

Multiple treatments have been suggested for infants with BPD.[62] Diuretics are given as needed to decrease pulmonary edema; antibiotics are given to manage existing pulmonary infection. Bronchodilator therapy may help decrease airway resistance but should be used cautiously in patients with floppy airways. Steroid therapy with dexamethasone can produce substantial short-term improvement in lung function, often allowing rapid weaning from ventilatory support. However, steroid therapy has little effect on long-term outcome such as mortality and duration of O_2 therapy.[68-70] Steroid therapy also has been implicated in decreased alveolarization and increased developmental delay. Although steroids are still given in clinical practice, they should be used cautiously. In BPD patients with severe pulmonary hypertension, inhaled NO (INO) may be useful, but this still remains controversial.[46]

TABLE 35.3 Treatment Strategies for Infants With Apnea

Treatment	Rationale
Manage underlying cause if identified	Removes precipitating factor
Tactile stimulation	Increases respiratory drive by sensory stimulation
CPAP	Reduces mixed and obstructive apnea by splinting the upper airway
Theophylline or caffeine	Increases respiratory center output and CO_2 response, enhances diaphragm strength, adenosine antagonist
Doxapram	Stimulates respiratory center and peripheral chemoreceptors
Transfusion	Decreases hypoxic depression by increasing O_2-carrying capacity
Mechanical ventilation	Provides support when respiratory effort is inadequate

CPAP, Continuous positive airway pressure.
From Stark AR: Disorders of respiratory control in infants, *Respir Care* 36:673, 1991.

Control of Breathing

Apnea of Prematurity

Background. **Apnea of prematurity** is a common, controllable disorder among premature infants, which usually resolves over time.[71] Premature infants frequently have periodic respiration, which comprises sequential short apneic episodes of 5 to 10 seconds, followed by 10 to 15 seconds of rapid respiration. Apneic spells are abnormal if (1) they last longer than 15 seconds, or (2) they are associated with cyanosis, pallor, hypotonia, or bradycardia.

If no effort to breathe occurs during a spell, the apnea is called *central* apnea. If breathing efforts occur, but obstruction prevents airflow, the apnea is termed *obstructive.* Mixed apnea is a combination of the central and obstructive types that starts as obstructive apnea and then develops into central apnea.[72-74]

Cause. Premature infants have immature control of respiratory drive in response to O_2 and carbon dioxide (CO_2).[75] In mature animals, an increase in alveolar $PaCO_2$ elicits an increase in V_T and respiratory rate. A decrease in FiO_2 below room air also triggers an increase in V_T. Conversely, in premature animals, an increase in $PaCO_2$ temporarily increases V_T but does not increase respiratory rate. A decrease in FiO_2 below room air decreases V_T and respiratory rate. This effect can lead to apnea in a premature infant. In addition to prematurity, several other factors can cause apnea in infants. Table 35.2 summarizes the potential causes, associated signs, and diagnostic indicators.

Treatment. Infants with apnea need continuous monitoring of heart and respiratory rates. Continuous noninvasive monitoring of oxygenation by transcutaneous electrode or pulse oximetry is recommended. Most apneic episodes can be quickly ended with gentle mechanical stimulation, such as picking the infant up, flicking the sole of the foot, or rubbing the skin.[74,76] If the cause of apnea is not prematurity, treatment must be directed at resolving the underlying condition. Table 35.3 outlines current treatment strategies for infants with apnea.[77] Apnea due to prematurity responds well to methylxanthines, especially theophylline and[78] caffeine.[79,80] These agents stimulate the central nervous system and increase the infant's responsiveness to CO_2. For infants with apnea that does not respond to treatment with theophylline, doxapram may be used, but its use remains controversial, and doxapram may cause multiple toxicities.[81]

The "Back to Sleep" program initiated by the American Academy of Pediatrics has significantly decreased the incidence of sudden infant death syndrome (SIDS) from apnea.[82] It is thought that when a newborn, which has a relatively heavy head and weak neck muscles, manages to position its face into a soft surface (e.g., mattress, pillow, bunting, etc.), it will develop increased CO_2 retention and become apneic. Unlike older infants, newborns will not have a response to awaken and move; they then become apneic, then bradycardic, and then have cardiopulmonary arrest.

CPAP also can be used to manage infant apnea.[83] Although the mechanism of action is not known, CPAP probably reduces airway obstruction, increases FRC, and improves PaO_2 and $PaCO_2$. CPAP may stimulate vagal receptors in the lung, increasing the output of the brainstem respiratory centers. Severe or recurrent apnea that is unresponsive to these interventions may necessitate mechanical ventilatory support.

As the respiratory control mechanisms mature, apnea of prematurity normally resolves without intervention. Apneic spells begin to disappear by weeks 37 to 44 of postmenstrual age with no apparent long-term effects. Infants who have apnea of prematurity are not at higher risk for **sudden infant death syndrome** (SIDS) than other infants.

Sudden Infant Death Syndrome

Historically, SIDS has been a leading cause of death (40%) among infants younger than 1 year in the United States. Approximately 2500 infants die of SIDS each year in the United States.[84,85] The incidence of SIDS has decreased more than 50% in the past 20 years, largely as a result of new guidelines that place babies supine and not in a prone position to sleep.[86]

A presumptive diagnosis is based on the conditions of death in which a previously healthy infant dies unexpectedly, usually during sleep. Autopsy shows that many infants who die of SIDS have evidence of repeated episodes of hypoxemia, ischemia, and airway obstruction. Factors associated with increased frequency of SIDS are presented in Box 35.1.

Cause

The cause of SIDS is unknown. Apnea of prematurity is not a predisposing factor, and there is no evidence that immaturity of the respiratory centers is a cause. Although infants in families in which two or more SIDS deaths have occurred are at slightly higher risk, there is no evidence of a genetic link. The best knowledge of SIDS comes from population or epidemiologic studies and is summarized in Box 35.2. Risk factors for SIDS include preterm delivery, African American race, maternal age <20, and receipt of poor prenatal care. Infants 1 to 3 months old are most susceptible, and death is most likely to occur at night during the winter. The risk for SIDS also is high among infants who previously experienced an apparent life-threatening event. Such an event occurs when an infant becomes apneic, cyanotic, or limp enough to frighten the parent or caregiver. The strongest evidence supports a direct relationship between nonsupine sleeping and SIDS.[87] It is difficult to differentiate death from SIDS and death from intentional suffocation. The possibility of intentional suffocation must be investigated but with great sensitivity, especially in infants who sleep with their parent(s).

BOX 35.1 Factors Associated With Increased Frequency of Sudden Infant Death Syndrome

Maternal Characteristics
- Age <20 years
- Lower socioeconomic status
- African American, Native American, or Alaskan Native
- Previous fetal loss
- Cigarette smoking
- Narcotic abuse
- Illness during pregnancy
- Inadequate prenatal care

Infant Characteristics at Birth
- Male gender
- Premature birth
- Small for gestational age
- Low Apgar score
- Resuscitation with O_2 and ventilation at birth
- Second or third in birth order or of a multiple birth
- Sibling death from SIDS

SIDS, Sudden infant death syndrome.
From Koff PB, Eitzman DV, Neu J: *Neonatal and pediatric respiratory care*, ed 2, St Louis, 1993, Mosby.

BOX 35.2 Infant Characteristics Near the Time of Death From Sudden Infant Death Syndrome
- Age younger than 6 months (peak between 1 month and 3 months)
- Winter season
- Asleep at night
- Mild illness in week before death
- History of apparent life-threatening event
- Prone sleep position
- Mother smokes cigarettes

Prevention

Prevention of SIDS is key. Successful prevention requires that infants at high risk be identified through reviewing risk factors and monitoring or event recording. After identifying an infant at risk, the family is trained in apnea monitoring and cardiopulmonary resuscitation. The American Academy of Pediatrics (AAP) recommends placing infants in either the supine or the side-lying position for the first 6 months of life and reducing soft objects in the infant's sleeping environment.[88,89] To define the need and appropriate approach for home monitoring of infants, the AAP has developed a policy statement on infantile apnea and home monitoring (Box 35.3).

Apnea monitoring devices can allow infants who are otherwise ready for discharge but still having occasional episodes of apnea to go home (see Chapter 57).[90] However, socioeconomic factors, the home environment, and parental/family support issues must be addressed prior to discharge. A home apnea

BOX 35.3 American Academy of Pediatrics Recommendations on Home Apnea Monitoring

1. Home cardiorespiratory monitoring should not be prescribed to prevent SIDS.
2. Home cardiorespiratory monitoring may be warranted for premature infants who are at high risk for recurrent episodes of apnea, bradycardia, and hypoxemia after hospital discharge. The use of home cardiorespiratory monitoring in these infants should be limited to approximately 43 weeks postmenstrual age or after the cessation of extreme episodes, whichever comes last.
3. Home cardiorespiratory monitoring may be warranted for infants who are technology-dependent (tracheostomy, CPAP), have unstable airways, have rare medical conditions affecting regulation of breathing, or have symptomatic chronic lung disease.
4. If home cardiorespiratory monitoring is prescribed, the monitor should be equipped with an event recorder.
5. Parents should be advised that home cardiorespiratory monitoring has not been proved to prevent sudden unexpected deaths in infants.
6. Pediatricians should continue to promote proved practices that decrease the risk for SIDS, including supine sleep position, safe sleeping environments, and elimination of prenatal and postnatal exposure to tobacco smoke.

CPAP, Continuous positive airway pressure; *SIDS,* sudden infant death syndrome.
From Committee on Fetus and Newborn: American Academy of Pediatrics: Apnea, sudden infant death syndrome, and home monitoring, *Pediatrics* 111(4 Pt 1):914–917, 2003.

monitoring program must include proper training for caregivers, emergency procedures, and care of the equipment. Home monitors lack the sophistication of ICU monitors and may very frequently false alarm.[90] While there is regrettably no evidence that apnea monitoring prevents SIDS, such monitoring may well serve as an effective precaution for those babies prone to apnea of prematurity.

Pulmonary Vascular Disease

Persistent Pulmonary Hypertension of the Newborn

Background. **Persistent pulmonary hypertension of the newborn** (PPHN) is a complex syndrome with many causes.[91] The common denominator in PPHN is a return to fetal circulatory pathways, usually because of elevated PVR. This condition results in further right-to-left shunting, severe hypoxemia, and metabolic and respiratory acidosis.

Pathophysiology. In the uterus, the fetus does not use the lungs as a gas-exchange organ. PVR is high, and systemic vascular resistance (SVR) is low. This condition produces a PVR/SVR ratio greater than 1. A fetus has two anatomic shunts that are not present in older infants, children, or adults: the foramen ovale and ductus arteriosus. With a PVR/SVR ratio greater than 1 and the anatomic shunts, blood flow bypasses the lung either at the atrial level (foramen ovale) or at the pulmonary artery level (ductus arteriosus). Intrauterine total pulmonary blood flow and systemic arterial O_2 saturation (SaO_2) are low.

In the transition to extrauterine life, PVR decreases owing to gas filling the lungs and increasing PaO_2 in the pulmonary venous circulation. SVR increases with the removal of the placenta from the circulation, and this makes the PVR/SVR ratio less than 1. If PVR does not decrease to allow the PVR/SVR ratio to become less than 1, the infant has PPHN. The major cause of this condition is parenchymal lung disease (MAS, RDS) or lung hypoplasia (CDH), but PPHN may also be idiopathic.[92]

The three fundamental types of PPHN relate to vascular spasm, increased muscle wall thickness, and decreased cross-sectional area of pulmonary vessels.[93] Vascular spasm is an acute event that can be triggered by many different conditions, including hypoxemia, hypoglycemia, hypotension, and pain. Increased muscle wall thickness is a chronic condition that develops in utero in response to several different causative factors, including chronic fetal hypoxemia, increased pulmonary blood flow (e.g., intrauterine closure of the ductus arteriosus), and pulmonary venous obstruction (e.g., total anomalous pulmonary venous return with obstructed below-diaphragm return). Decreased cross-sectional area is related to hypoplasia of the lungs and occurs with congenital diaphragmatic hernia, Potter sequence (absent kidneys), and oligohydramnios syndromes (decreased amniotic fluid).

Clinical manifestations. PPHN should be suspected when an infant has rapidly changing O_2 saturation (SaO_2) without changes in FiO_2 or has hypoxemia out of proportion to the lung disease detected with chest radiography or $PaCO_2$ measurement. In infants with a significant shunt through the ductus arteriosus, there usually is a substantial gradient (>5%) between preductal and postductal O_2 saturation. Continuous pulse oximetry screening is valuable in the ongoing treatment of the newborn with PPHN, allowing the caregiver to assess the patient's oxygen saturation over time and the adequacy of oxygen delivery at the tissue level.

Oximeter probes can be placed on preductal (right hand) and postductal (feet) sites to assess for right-to-left shunting at the level of the foramen ovale and ductus arteriosus. A difference greater than 10% between preductal and postductal oxygen saturations indicates right-to-left ductal shunting. Sites on the left hand should be avoided, because it may be preductal or postductal. Significant right-to-left shunting at the level of the foramen ovale may result in lower-than-expected preductal oxygen saturations (right hand), although a significant differential should still be evident when compared with postductal oxygen saturations.

Treatment. Initial therapy for PPHN is removal of the underlying cause, such as administration of O_2 for hypoxemia, surfactant for RDS, glucose for hypoglycemia, and inotropic agents for low cardiac output and systemic hypotension. If correction of the underlying problem does not correct hypoxemia, the infant needs intubation and mechanical ventilation. Because pain and anxiety may contribute to PPHN, the infant may need sedation and, frequently, paralysis. If these measures do not improve oxygenation, the next step is HFV. This mode of ventilation allows a higher FRC without a large V_T. INO, which is a potent pulmonary vasodilator, is considered the next intervention (see Chapter 42). In fact, PPHN is the only indication for which the FDA has formally approved the use of INO therapy. INO has been shown to reduce the combined outcome of death and need for ECMO in infants with PPHN.[51] An early INO strategy (at lower oxygenation indices) is preferred over late/rescue therapy.[94] In addition, several experimental forms of aerosolized inhaled pulmonary vasodilators are being used as an alternative to INO therapy. If

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Problem

The RT is called to the bedside of a term infant who has mild respiratory distress, is receiving nasal cannula O_2 of 1 L/min, has an FIO_2 of 1.0, and has a SpO_2 of 75%. Shortly after birth, the infant's chest x-ray showed a normal-size heart and clear, slightly hyperlucent lung fields with no infiltrates. The bedside nurse describes that she has just finished taking the infant's vital signs and changing its diaper. Before her touching the infant, the infant's saturation was 96%. What is this infant's problem? What should the RT do?

Discussion

This infant is exhibiting signs of persistent pulmonary hypertension. Placing a preductal (right hand) and postductal (left hand) oxygen saturation probe and evaluating the differences in SpO2 can help determine whether ductal shunts exist. The immediate interventions potentially could include increasing the O_2 flow, lowering the lights in the room, decreasing the activity and ambient noise in the room, swaddling the infant, and minimizing physical contact with the infant. All of these interventions are aimed at getting the infant into a quiet, calm environment, allowing the infant to relax, and reducing shunting.

In addition, the RT and nurse should contact the physician who is caring for this infant and alert him or her to the possibility of persistent pulmonary hypertension. Potential additional therapies could include sedation, intubation, mechanical ventilation, and INO.

all of these modalities fail to improve oxygenation, the infant may be a candidate for extracorporeal membrane oxygenation (ECMO).[95] The use of IV sildenafil is increasingly being promoted in infants with PPHN.[96] In addition, several other experimental forms of aerosolized pulmonary vasodilators are being used as an alternative to INO therapy.[97-99] Even with all of these treatments, PPHN remains a complex disease with high morbidity and mortality.

Congenital Abnormalities Affecting Respiration

Congenital abnormalities that affect respiration can be divided into several groups: airway diseases, lung malformations, chest wall abnormalities, abdominal wall abnormalities, and diseases of neuromuscular control.

Airway Diseases

Airway abnormalities have three fundamental mechanisms: internal obstruction, external obstruction, and disruption. Internal obstruction includes common problems, such as laryngomalacia, that cause obstructive apnea. Less common problems caused by internal obstruction are tracheomalacia, laryngeal webs, tracheal stenosis, and hemangiomas. All of these diseases usually manifest as a combination of inspiratory stridor, gas trapping, expiratory wheezing, and accessory respiratory muscle activity.

External compression can be caused by hemangiomas, neck or thoracic masses, and vascular rings. These lesions are far less common than diseases caused by internal obstruction, but they are not rare. The symptoms are similar to those of internal obstruction. Neck masses usually are obvious at visual inspection. Intrathoracic masses and vascular rings must be suspected on the basis of the clinical manifestations: noise during the respiratory cycle that worsens with exertion. The infant may have difficulty with swallowing.

Airway disruptions usually are related to tracheoesophageal fistula (TEF) in a newborn. This malformation usually is associated with esophageal atresia. There are five types of TEF: esophageal atresia with a proximal fistula, esophageal atresia with a distal fistula, esophageal atresia with both a proximal and a distal fistula, esophageal atresia without either fistula, and an intact esophagus with a so-called *H fistula*.[100] The most common of these malformations is esophageal atresia with a distal fistula, which accounts for 85% to 90% of all TEFs. The least common is the H fistula. All of these malformations manifest as difficulty swallowing, bubbling and frothing at the mouth, and choking, particularly during attempts at feeding. These anomalies can occur in isolation or as part of an association of defects. The most common is the VATER or VACTERL association of vertebral anomalies, imperforate anus, TEF, and renal or radial anomalies. In VACTERL, cardiac anomalies are added, and renal and limb anomalies replace renal or radial anomalies in the acronym. These associated anomalies must be sought in any infant with TEF. TEF is managed with surgical ligation of the fistula (tying it closed) and reconnection of the interrupted esophagus.[101] Most infants with TEF have a good outcome; however, some infants have severe malformations that can cause chronic problems. Infants with TEF usually need only supportive respiratory care. They usually do not have lung disease. However, some infants need HFV because the air leak through the fistula can become larger than the airflow to the alveoli.

Lung Malformations

There is a broad spectrum of rare lung malformations that occur in the newborn period. These lesions are thought to be part of a continual spectrum of diseases that originate as defects in lung segmentation. The most common is congenital pulmonary adenomatoid malformation (CPAM); this was previously known as *cystic adenomatoid malformation of the lung*. CPAM is classified into five types on the basis of the type and size of the cyst.[102,103] The disease may affect entire lobes of the lung. The affected parts of the lung do not participate in exchange gas and can become infected. The usual treatment is surgical removal of the affected lobe. There is also the potential for malignant transformation.

Some affected fetuses can develop "hydrops." Hydrops fetalis is a serious fetal condition that is characterized by an abnormal accumulation of fluid in two or more fetal compartments. This can include ascites, pleural effusions, pericardial effusions, or skin edema while in utero. Most infants with CPAM have symptoms of lung volume loss.[104] As the mass expands, the normal surrounding lung is compressed. Some CPAMs resolve spontaneously. A few infants have severe cardiorespiratory compromise and need respiratory support and emergency surgery. However, better results are seen when surgery can be performed electively.

Other, less common lung malformations include pulmonary sequestration and lobar emphysema. Both of these diseases involve maldevelopment of lobes of the lung. Sequestration is a primitive, frequently cystic lung lobe that is not in communication with the tracheobronchial tree and frequently receives no pulmonary vascular blood flow.

Lobar emphysema is an airway malformation that causes gas trapping in a lobe of the lung. These malformations manifest

as space-occupying masses within the thorax. They usually are treated by surgical removal.

Congenital Diaphragmatic Hernia

Congenital diaphragmatic hernia is a severe disease that usually manifests in newborns as severe respiratory distress.[105] The pathophysiologic mechanism is a complex combination of lung hypoplasia, including decreased alveolar count and decreased pulmonary vasculature, pulmonary hypertension, and unusual anatomy of the inferior vena cava.[106,107] This disorder varies between asymptomatic (rare) and severe life-threatening disease (frequent). There are two types of hernia: Bochdalek hernia (lateral and posterior defect, usually on the left) and Morgagni hernia (medial and anterior, which may be on either side). Hernias that occur in the right hemidiaphragm may be less severe because the liver can block the defect and decrease the volume of abdominal contents that can enter the thorax.[107]

Some authors speculate that the diaphragmatic hernia complex is a developmental field defect and not just a simple cascade of events related to a hole in the diaphragm. This theory is partly based on long-term outcomes of survivors with diaphragmatic hernias. These survivors frequently have severe scoliosis in the direction of the diaphragm defect. They also frequently have severe esophageal reflux disease.

Most cases of congenital diaphragmatic hernia can be diagnosed in utero with ultrasonography. Physical examination may yield the following findings: scaphoid abdomen (because the abdominal contents are in the thorax), decreased breath sounds, displaced heart sounds (because the heart is pushed away from the hernia), and severe cyanosis (from lung hypoplasia and pulmonary hypertension). The diagnosis is established with chest radiography.

Initial treatment of congenital diaphragmatic hernia is insertion of an ETT, paralysis, and mechanical ventilation. A large sump tube is placed in the stomach and connected to continuous suction. These therapies allow adequate ventilation and oxygenation and prevent gas insufflation of the intestine. Most centers delay surgical repair for several days to allow the natural decrease in PVR. On day 7 to 10 of life, a surgeon closes the defect. This scenario occurs only for infants with easily correctable pulmonary hypertension. Infants with severe pulmonary hypertension may need HFV and ECMO. At some centers, the diaphragm is repaired while patients are on ECMO,[108] though most centers try to wean the infant from ECMO before performing the surgery.[109] While there is no clear consensus on whether the surgical repair should be done on ECMO or not, newer evidence supports weaning from ECMO before attempting surgical[110] repair of CDH. Despite all these advanced therapies, the mortality risk with this disease is high.[111] Survival[112] depends on many complex variables (e.g., liver herniation into the thorax, fetal head-to-lung ratio, initial PaO_2, and $PaCO_2$).[106,111]

Abdominal Wall Abnormalities

Because all newborns are primarily abdominal breathers, the abdominal wall is an intrinsic part of the respiratory system. Large defects in the abdominal wall can cause severe respiratory compromise. One of the most common of these defects is omphalocele.[113,114] An omphalocele is an abdominal wall defect that involves the insertion of the umbilical cord. The umbilical cord goes into the omphalocele. The bowel of an infant with an omphalocele is usually covered by a membrane that looks like the surface of the umbilical cord. Occasionally, the omphalocele membrane ruptures and exposes the bowel of the infant. Omphaloceles must be distinguished from gastroschisis. Gastroschisis is an abdominal wall defect that is completely separate from the insertion of the umbilical cord. The bowel of an infant with a gastroschisis is not covered by a membrane and is outside of the abdomen. Because the bowel has been out of the abdomen, the abdominal cavity is small. There are two methods of repairing gastroschisis. If the abdominal cavity is of sufficient size and the amount of bowel outside is small, a primary closure is done in which all of the bowel is returned to the abdominal cavity and the small defect is closed. However, if the abdominal cavity is too small or the amount of bowel is too large, the surgeon will place the bowel into a Silastic chimney (or silo). The open end is inserted into the defect and the closed end is suspended from the bed. Over the next several days, gravity and the gradual stretching of the abdominal wall will allow the bowel to come back into the abdomen.

Usually only large omphaloceles cause respiratory distress. When they are greater than 10 cm in diameter, these defects can cause severe respiratory distress and frequently require prolonged mechanical ventilation. Infants with gastroschisis usually have normal lungs. However, if they need to have a silo placed, this is like a water column (the height of bowel in the silo) applying pressure against the diaphragm. These infants will need PEEP to support FRC.

MINI CLINI

Delivery of an Infant With an Abdominal Wall Defect

Problem

The RT is called to the delivery room to assist in the delivery of a term infant with an abdominal wall defect. What should the RT consider for assisting this infant?

Discussion

There are many types of abdominal wall defects. The two most common are gastroschisis and omphalocele. These anomalies can be differentiated by whether the insertion of the umbilical cord into the abdomen is involved in the defect. In a gastroschisis, the umbilical cord inserts directly into the abdomen and is separate from the defect. In an omphalocele, the umbilical cord inserts directly into the defect. Although there is usually a membrane covering the bowel in an omphalocele, if the membrane has ruptured, the only means of distinguishing an omphalocele is by the umbilical cord insertion.

Most infants with these abdominal wall defects are term. Most do not have significant lung disease. An abdominal wall defect increases the intraabdominal pressure. It pushes the diaphragm up into the thorax, decreasing FRC. The RT should be aware that these patients will need support of their FRC. Typically, if the FRC can be supported with CPAP or PEEP, the infant will not need high rates or a high V_T to achieve adequate gas exchange.

Neuromuscular Control

Many diseases of poor neuromuscular control affect newborns,[115,116] including spinal muscular atrophy, congenital

myasthenia gravis, and myotonic dystrophy. These diseases frequently require respiratory support in the newborn and pediatric periods. The morbidity and mortality of these diseases are extremely variable. New technologies may allow noninvasive respiratory support of some patients.[117,118] Some diseases can be quite severe in the newborn period and improve with age. It is important to make an accurate diagnosis to be able to estimate prognosis and provide genetic counseling. Many of these diseases are inherited with known inheritance patterns.

Congenital Heart Disease

A full discussion of congenital heart disease is beyond the scope of this chapter. However, basic knowledge of the common defects is essential to good practice in pediatric and neonatal respiratory care. Congenital heart diseases usually are divided into two large categories: cyanotic and acyanotic heart disease.[119,120] Cyanotic heart diseases are diseases in which blood shunts from right to left, bypassing the lungs, and is deoxygenated. Acyanotic heart diseases are diseases in which blood shunts from left to right, causing congestive heart failure. Fig. 35.6 compares normal cardiac anatomy with the features of the five most common congenital defects.

Cyanotic Heart Diseases

The two most common cyanotic heart diseases are tetralogy of Fallot and transposition of the great arteries.

Tetralogy of Fallot. **Tetralogy of Fallot** is a defect that includes (1) obstruction of right ventricular outflow (pulmonary stenosis), (2) ventricular septal defect (VSD; a hole between the right and left ventricles), (3) dextroposition of the aorta, and (4) right ventricular hypertrophy. The severity of tetralogy of Fallot varies from mild disease, which is initially diagnosed in early childhood, to severe disease, which is diagnosed in the newborn period.[120,121] The mild form of the disease manifests as a heart murmur, intermittent severe cyanotic spells, a history of the infant squatting or entering a knee-chest position, or a combination of these features. The severe form of the disease manifests as a heart murmur and severe continuous cyanosis. Chest x-ray may reveal a "boot-shaped" cardiac silhouette. Most types of tetralogy of Fallot can be managed surgically. The type and timing of the surgical repair depend on the anatomy of the defects. Children with this defect are at increased risk for sudden death from arrhythmia later in life.

Transposition of the great arteries. **Transposition of the great arteries** is the heart disease that most frequently causes severe cyanosis.[119,122,123] It usually manifests as moderate to severe cyanosis immediately after birth. Partially oxygenated blood flow is dependent upon the infant's patent ductus arteriosus at birth until surgical correction can be made. A murmur may be present. Infants with this abnormality frequently need emergency atrial septostomy (cutting a hole in the wall between the two atria). This procedure historically has been performed in cardiac catheterization laboratories, but many pediatric cardiologists who perform invasive procedures have begun performing this procedure with ultrasound guidance in the neonatal intensive care unit. The condition of infants who need atrial septostomy usually stabilizes. The goal is to allow the PVR to decrease and then to perform the arterial switch operation in week 2 or 3 of life.

MINI CLINI

Newborn With Transposition of the Great Arteries

Problem

The RT is called to the delivery room to assist in the delivery of an infant to be born by repeat cesarean section without rupture of membranes. Fetal heart rate monitoring has been unremarkable. There is no evidence of meconium in the amniotic fluid. After delivery, the infant is breathing comfortably but fails to "pink up" (i.e., the infant is cyanotic). The transcutaneous O_2 saturation stabilizes in the low 70s, despite mask-bag ventilation with an FiO_2 of 1. What should the RT consider as the source of this problem?

Discussion

The most common reasons for a significantly cyanotic term infant immediately after delivery include pneumothorax, persistent pulmonary hypertension, and cyanotic heart disease. Spontaneous pneumothorax occurs occasionally. The infant should have decreased breath sounds in the affected hemithorax. These infants usually have a significant increase in WOB.

Excluding pneumothorax leaves persistent pulmonary hypertension and cyanotic congenital heart disease as the main differential diagnoses. The two most likely cyanotic congenital heart diseases to manifest with significant cyanosis immediately after birth are transposition of the great arteries (particularly with an intact ventricular septum) and tetralogy of Fallot (particularly with pulmonary atresia instead of pulmonary stenosis). An echocardiogram must be done as soon as possible to distinguish between these possibilities.

Infants with cyanotic heart diseases are cyanotic. Some of these infants have saturations in the low 80s. Some of them have saturations in the 40s to 50s. Because there is an anatomic right-to-left shunt, attempts to improve oxygenation with increased delivery of O_2 would be unsuccessful. Increased O_2 delivery would lead to problems with O_2 toxicity. Improvement in systemic oxygenation occurs only by developing a left-to-right shunt in the central circulation. Acutely, this shunt can be managed with administration of prostaglandin to reopen the ductus arteriosus. Long-term management requires intervention by cardiac catheterization or surgery.

RULE OF THUMB An infant with profound cyanosis at birth most likely has cyanotic heart disease or PPHN.

Hypertension of the Newborn

Acyanotic Heart Diseases

Some of the most common and most severe congenital heart diseases are acyanotic. VSD is probably the most common congenital heart disease. Hypoplastic left heart syndrome (HLHS) is one of the most severe congenital heart diseases.

Ventricular septal defect. Defects along the septum separating the right and left ventricles are quite common. VSD can occur alone or in combination with other anomalies. A simple VSD usually causes left-to-right shunting and congestive heart failure. This defect usually does not appear immediately after birth. It appears at 6 to 8 weeks of age, when the PVR has decreased enough that the shunt becomes large.

Historically, closure of VSDs has required surgery. In the last few years, many VSDs have been able to be closed during heart catheterization.[124-126]

Atrial septal defect. The most common type of atrial septal defect is a small, slit-like opening that persists after closure of

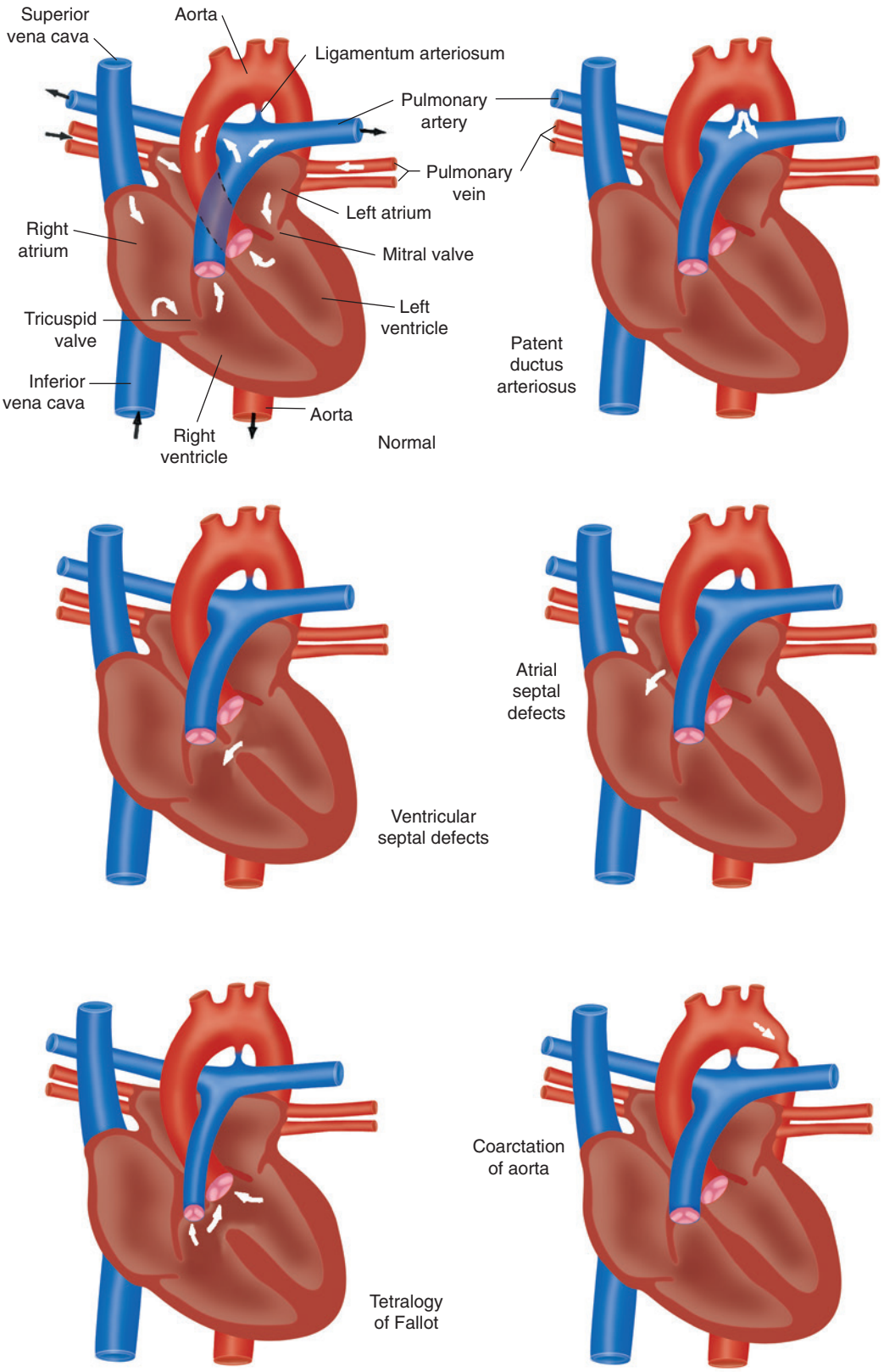

Fig. 35.6 Normal flow of blood through the heart and some congenital defects that cause abnormal flow. (Modified from Jacob S, Francone C, Lossow WJ: *Structure and function in man*, ed 5, Philadelphia, 1982, Saunders.)

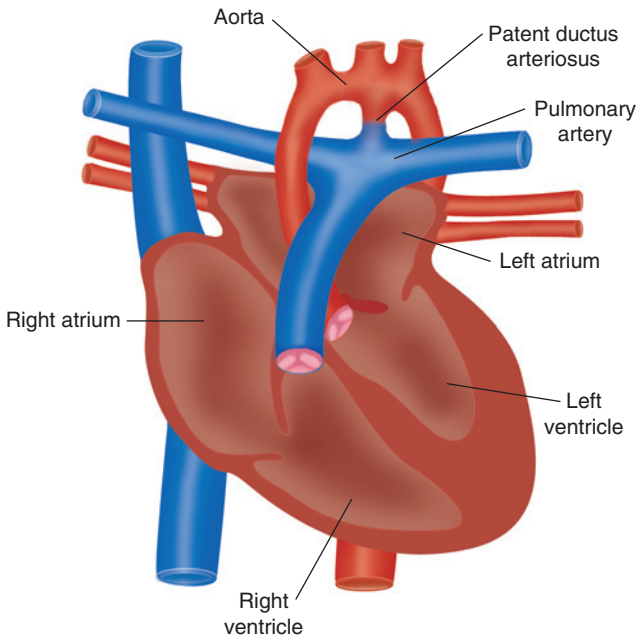

Fig. 35.7 Hypoplastic Left Heart Syndrome.

the foramen ovale.[127] An isolated atrial septal defect is of little clinical importance. As with VSDs, some ASDs can be closed during heart catheterization.[128]

Patent ductus arteriosus. In a fetus, most of the pulmonary blood flow is shunted through the ductus arteriosus to the aorta. Closure of the ductus normally occurs 5 to 7 days after birth of a term infant. Patent ductus arteriosus usually is a disease of immature, preterm infants. Factors altering pressure gradients or affecting smooth muscle contraction can cause the ductus not to close or to reopen after it has closed. Depending on the pressure gradients established, shunting through an open ductus may be either right to left (pulmonary pressure greater than aortic) or left to right (aortic pressure greater than pulmonary artery pressure). Treatment is either pharmacologic (indomethacin) or surgical (ligation). In recent years, the best timing of treatment and the treatment mechanism for PDA closure have become quite controversial, especially in premature infants (<1000 g).[129]

Left ventricular outflow obstructions. HLHS (Fig. 35.7), interrupted aortic arch, and coarctation of the aorta have in common obstruction of left ventricular outflow.[130] These conditions all manifest in the newborn period with symptoms of acute heart failure. Systemic blood flow depends on patency of the ductus arteriosus. When the ductus spontaneously closes (usually at 5 to 7 days of age), severe congestive heart failure develops. The symptoms range from moderate respiratory distress to complete cardiovascular collapse. Initial treatment is intravenous administration of prostaglandin E_1. Most infants with these defects need support with mechanical ventilation. These infants typically do not have lung disease. The pressures and rates used should be set appropriately.

There are standard surgical repairs for both interrupted aortic arch and coarctation of the aorta. Interrupted aortic arch has been classified into three types (A, B, and C) based on the site of aortic interruption. In type A interrupted left aortic arch, the arch interruption occurs distal to the origin of the left subclavian artery. In type B interrupted left aortic arch, the interruption occurs distal to the origin of the left common carotid artery. In type C interrupted left aortic arch, the interruption occurs proximal to the origin of the left common carotid artery.

Coarctation of the aorta is a narrowing of the aorta. When this occurs, the heart must pump harder to force blood through the narrowed part of the aorta.

HLHS is a birth defect that affects normal blood flow through the heart. As the baby develops during pregnancy, the left side of the heart does not form correctly. Patients with HLHS require corrective surgery or other procedures soon after birth. HLHS affects a number of structures on the left side of the heart that do not fully develop. Examples may include the *left ventricle* is underdeveloped and too small, the *mitral valve* is not formed or is very small. The *aortic valve* is not formed or is very small and the ascending portion of the *aorta* is underdeveloped or is too small.

HLHS has several accepted treatments, including a palliative surgical procedure (Norwood procedure) and heart transplantation.[131,132] The Norwood procedure usually is done within the first 2 weeks of a baby's life.[133] A "new" aorta is crafted by surgery and connects it to the right ventricle, making a tube from either the aorta or the right ventricle to the vessels supplying the lungs (pulmonary arteries). Thus the right ventricle can pump blood to both the lungs and the rest of the body.

NEONATAL RESUSCITATION

Resuscitation of the newborn is a subset of resuscitation techniques. Most infant resuscitations occur in the delivery room. Although these resuscitations can range from minimal intervention to full resuscitation, more than 90% of them can be successfully dealt with by stimulation, ensuring the presence of an airway, and providing breathing support.[40] RTs[41] are very important members of any resuscitation team. Their expertise in establishing and supporting an airway and initiating respiratory support is essential. While it is beyond the scope of this chapter to delineate the guidelines of neonatal resuscitation, the reader is referred to the neonatal resuscitation guidelines published by the American Academy of Pediatrics.

PEDIATRIC RESPIRATORY DISORDERS

Compared with the common cardiopulmonary diseases in the neonatal period, the pulmonary conditions that occur among older infants and children commonly result from airway obstruction caused by bacterial or viral infections. Other entities discussed in this section include asthma, gastroesophageal reflux disease, and cystic fibrosis.

Gastroesophageal Reflux Disease

Gastroesophageal reflux disease (GERD) is the regurgitation of stomach contents into the esophagus and is common in childhood. Some causes of GERD are not pathologic. There is general agreement that there are important interactions between GERD and various disorders of the respiratory system.[134,135] Respiratory

problems caused by gastroesophageal reflux include reactive airways disease, wheezing, aspiration pneumonia, laryngospasm, stridor, chronic cough, choking spells, and apnea.[136] GERD should be considered when an infant has faced a sudden life-threatening event and when an older child has unexplained chronic head and neck problems. GERD can be diagnosed with esophageal pH testing, upper gastrointestinal contrast studies, and gastric scintiscan. When GERD has been diagnosed, medical therapy can begin.[137,138] Occasional[139] cases that do not respond to medical management may require surgical intervention.

Bronchiolitis

Bronchiolitis is an acute infection of the lower respiratory tract, usually caused by respiratory syncytial virus (RSV). Nearly 1 in 10 infants younger than 2 years of age acquires a bronchiolitis infection. The outcome is generally good, although approximately 1% of infants hospitalized for bronchiolitis die of respiratory failure. Infants most prone to respiratory failure as a consequence of bronchiolitis are very young and immunodeficient and have a comorbidity, such as congenital heart disease, BPD, CF, or childhood asthma.[140,141]

Clinical Manifestations

The clinical manifestations of bronchiolitis are inflammation and obstruction of the small bronchi and bronchioles. Bronchiolitis commonly occurs soon after a viral upper respiratory tract infection. The infant may have a slight fever with an intermittent cough. After a few days, signs of respiratory distress develop, particularly dyspnea and tachypnea. Progressive inflammation and narrowing of the airways cause inspiratory and expiratory wheezing and increase airway resistance. A chest x-ray shows signs of hyperinflation with areas of consolidation. The diagnosis of RSV infection can be established by immunofluorescent assay the same day and assists in the implementation of a treatment plan.

Prophylaxis. In recent years, passive immunization for RSV has become available.[142,143] Initially, passive immunization was recommended only for preterm infants with BPD. However, passive immunization is now recommended for high-risk infants younger than 2 years of age who require medical therapy for chronic lung disease, infants born at less than 32 weeks of gestational age, and infants with congenital heart disease who have cardiovascular compromise (Box 35.4).[143]

Treatment. Treatment of a patient with bronchiolitis varies with the severity of the infection and the clinical signs and symptoms. Many patients can be treated at home with humidification and oral decongestants. Patients with more severe symptoms (apnea) and comorbidity usually are hospitalized, and treatment is directed at relieving the airway obstruction and associated hypoxemia. Hospitalized children frequently are treated with systemic hydration and O_2 via nasal cannula, high-flow nasal cannula, or nasal cannula, and assisted with airway clearance primarily by nasal and/or nasopharyngeal suction.[144,145] Antibiotics may be administered to control secondary bacterial infections. If bronchiolitis progresses to acute respiratory failure, noninvasive support or mechanical ventilation is required. Because of the obstructive nature of this disorder, high PEEP, low respiratory rates, and long expiratory times may be needed to prevent air trapping. Heliox has been used for severe airways disease requiring mechanical ventilation.[146,147] Bronchodilators and chest physiotherapy[148] have not been found to be effective in routine management in patients with bronchiolitis (Box 35.5).

BOX 35.4 American Academy of Pediatrics Recommendations for Respiratory Syncytial Virus Prophylaxis

Indications for RSV Prophylaxis

- Preterm infants without CLD or congenital heart disease
  - Preterm infants born before 29 weeks, 0 days gestation who are younger than 12 months at the start of the RSV season
  - Not recommended for the second year of life
- Preterm infants with CLD
  - Infants with CLD of prematurity defined as gestational age <32 weeks, 0 days, and requiring FiO_2 >21% oxygen for at least the first 28 days after birth
  - Second year of life recommendation only for those infants who continue requiring medical support during the 6-month period before the start of the second RSV season
- Infants with hemodynamically significant CHD
  - Acyanotic heart disease requiring medications to control congestive heart failure and will require cardiac surgical procedures in infants with moderate to severe pulmonary hypertension
  - Cyanotic heart defects in the first year of life
  - Infants after surgical procedures that involve cardiopulmonary bypass
    - These infants may need a postoperative dose.
  - Infants younger than 2 years of age undergoing cardiac transplantation
- Children with anatomic pulmonary abnormalities or neuromuscular disorder
- Immunocompromised children
  - Children younger than 24 months of age who are severely immunocompromised
- Children with Down syndrome
  - Routine use is not recommended unless they have qualifying heart disease, CLD, airway clearance issues, or prematurity
- Children with cystic fibrosis
  - Routine use not recommended unless other indications are present
  - Infants with CF and CLD or nutritional compromise in the first year of life
  - Infants with CF and severe lung disease requiring hospitalization, or abnormalities on chest radiograph/computed tomography, or weight for length less than 10%
- Alaska Native and American Indian infants

CF, Cystic fibrosis; *CHD,* congenital heart disease; *CLD,* chronic lung disease; *RSV,* respiratory syncytial virus.

Croup

Croup is a viral disorder of the upper airway that normally results in subglottic swelling and obstruction. Termed *laryngotracheobronchitis*, viral croup is usually caused by the parainfluenza virus and is the most common form of airway obstruction in children 6 months to 6 years old. RSV and influenza virus are less common causes. Bacterial superinfection with *Staphylococcus aureus,* group A *Streptococcus pyogenes,* or *Haemophilus influenzae* may worsen croup.

Clinical Manifestations

Symptoms become evident after 2 or 3 days of nasal congestion, fever, and coughing. A child typically has slow, progressive

BOX 35.5 American Academy of Pediatrics Recommendations for Diagnosis and Management of Bronchiolitis

Diagnosis

1a. Diagnosis and severity should be made on the basis of history and physical examination. Routine laboratory and radiologic studies are not needed.

1b. Assess for history of risk factors in patients younger than 12 weeks of age.
Prematurity
Underlying cardiopulmonary disease
Immunodeficiency

Treatment

2a. Bronchodilators should not be routinely used.

2b. A carefully monitored trial of α-adrenergic or β-adrenergic is an option. Inhaled bronchodilators should be continued only if there is a documented positive clinical response.

3. Corticosteroids should not be used routinely.

4. Ribavirin should not be used routinely.

5. Antibacterial medications should be used only with specific indications of the coexistence of a bacterial infection.

6a. Assess hydration and the ability to take oral fluids.

6b. Chest physiotherapy should not be used routinely.
Supplemental oxygen is indicated if oxyhemoglobin saturation (SpO_2) falls persistently below 90%.

7a. Supplemental O2 should be discontinued if SpO2 is ≥90% and the infant is feeding well and has minimal respiratory distress.

7b. As the child's clinical course improves, continuous measurement of SpO2 is not routinely needed.

7c. Infants with a known history of hemodynamically significant heart or lung disease and premature infants require close O2 monitoring as the O2 is being weaned.

Prophylaxis

8a. Palivizumab prophylaxis should be done according to the new AAP Guidelines (Box 35.4).

9a. Hand decontamination is the most important step in preventing nosocomial spread of RSV.
Hands should be decontaminated before and after direct contact with the patient, and after contact with inanimate objects in the direct vicinity of the patient.

9b. Alcohol-based rubs are preferred for hand decontamination.

9c. Educate personnel and family members on hand sanitation.

10a. Infants should not be exposed to passive smoking.

10b. Breastfeeding is recommended to decrease a child's risk for developing a lower respiratory tract disease.

11. Inquire about the use of complementary and alternative medicines.

- Infants with chronic lung disease
  - Infants born at younger than 32 weeks of gestational age
  - Infants born at 32–35 weeks to gestational age who are at high risk for severe infection and younger than 90 days of age
- If two or more of following risks are present
  - Childcare attendance
  - School-age siblings
  - Exposure to environmental air pollutants
  - Congenital abnormalities of the airways
  - Severe neuromuscular disease
- Infants with hemodynamically significant congenital heart disease (cyanotic and acyanotic)
- Following cardiopulmonary bypass

From American Academy of Pediatrics Subcommittee on Diagnosis and Management of Bronchiolitis: Diagnosis and management of bronchiolitis, *Pediatrics* 118:1774–1193, 2006.

inspiratory and expiratory stridor and a barking cough. As the disease progresses, dyspnea, cyanosis, exhaustion, and agitation occur. An x-ray of the upper airway is helpful in confirming the diagnosis and ruling out epiglottitis, but is usually not needed in most cases of croup. Classic croup is seen on an anteroposterior x-ray as characteristic subglottic narrowing of the trachea, called the *steeple sign* (Fig. 35.8).

Treatment

The evaluation and treatment of a child with croup must focus on the degree of respiratory distress and associated clinical findings. If stridor is mild or occurs only on exertion and cyanosis is not present, hospitalization is generally not required and the child is treated at home. If there is stridor at rest (accompanied by harsh breath sounds, suprasternal retractions, and cyanosis with breathing of room air), hospitalization is indicated. The traditional treatment of a child with mild to moderate croup has involved cool mist therapy with or without supplemental O_2. However, there is no evidence that this practice is beneficial.[149] Corticosteroids and aerosolized racemic epinephrine have been shown to have the greatest benefit for decreasing the length and severity of respiratory symptoms associated with viral croup.[150,151] The addition of budesonide has been shown to reduce the severity of symptoms in mild to moderate cases of croup.[152] Progressive

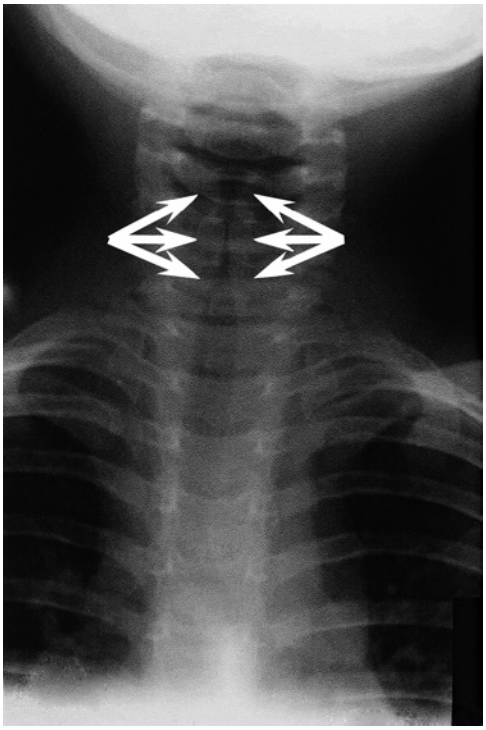

Fig. 35.8 Anteroposterior Chest X-Ray of a Patient With Croup. Subglottic narrowing typical of croup is evident *(arrows)*.

worsening of the clinical signs despite treatment indicates the need for intubation and mechanical ventilation. Heliox has been used for infants and children with severe disease (see Chapter 42). There is some evidence to show short-term benefit; however, long-term benefit has not yet been shown.[153,154]

Epiglottitis

Epiglottitis is an acute and often life-threatening infection of the upper airway that causes severe obstruction secondary to supraglottic swelling. Evidence suggests that the incidence of epiglottitis is decreasing among children and increasing in adults,[155] probably because of the use of vaccines. The most common cause is *H. influenzae* type B infection. Other organisms that are increasingly found to be causes of acute epiglottitis include group *S. pneumoniae*, *S. aureus*, *Klebsiella pneumoniae*, *Haemophilus parainfluenzae*, and β-hemolytic streptococci (groups A, B, C, and F).[156]

Clinical Manifestations

A child with epiglottitis usually has a high fever, sore throat, stridor, and labored breathing.[151,156] The presence of high-grade fever, drooling, muffled voice, and absence of a croupy bark are key features that distinguish epiglottitis from croup. Children with epiglottitis have a sickly appearance and may assume a tripod position for breathing or only tolerate certain positions that result in optimal airway patency. Older children may report a sore throat and difficulty swallowing. Difficulty swallowing may cause drooling. Lateral x-rays of the neck (Fig. 35.9) show that the epiglottis is markedly thickened and flattened (thumb sign) and the aryepiglottic folds are swollen; the vallecula may not be visualized. Visual examination of the upper airway is dangerous in these children and always should be performed in a controlled setting by personnel expert in emergency intubation. Inadvertent traction of the tongue can cause further and immediate swelling of the epiglottis and abrupt and total upper airway obstruction. Children with suspected epiglottitis should be accompanied by personnel expert in emergency intubation during any transport for diagnostic procedures.

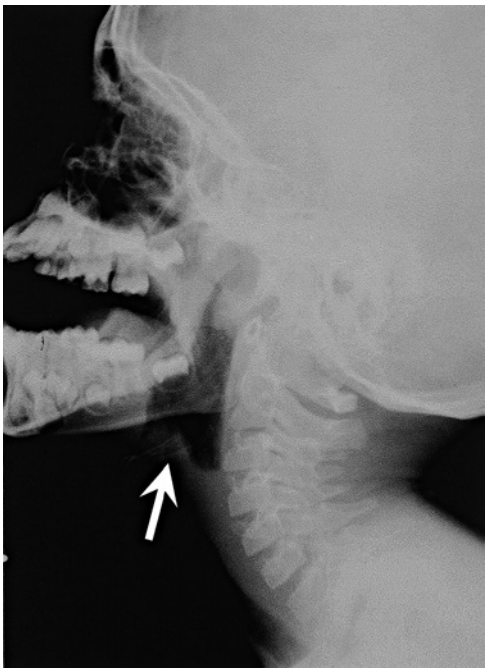

Fig. 35.9 Lateral Radiograph of the Neck of a Patient With Epiglottitis. The thumb sign is prominent *(arrow)*.

Treatment

Children with epiglottitis need elective intubation under general anesthesia in the operating room. Tracheostomy may be needed if the patient's condition warrants; however, this procedure is rarely used. There should be no attempt to lay the child down or attempts to intubate until the child is sedated. Premature attempts at intubation can precipitate acute airway obstruction and respiratory arrest. After an airway is secured, a sample for bacterial culture should be obtained and antibiotic therapy should be started. Corticosteroids may decrease the swelling.[157,158] Children with an ETT should be sedated and restrained to prevent inadvertent extubation. An upper airway leak following ET tube cuff deflation may indicate less edema but does not predict whether the extubation will be successful or not.

Cystic Fibrosis

Cystic fibrosis (CF) is one of the most common life-limiting autosomal recessive diseases, occurring in approximately 1 in every 3500 newborns in the United States.[159] There are approximately 1000 new cases of CF per year in the United States.[160] CF affects approximately 30,000 persons in the United States and 70,000 persons worldwide.[159] The prevalence varies by race and ethnicity, affecting approximately 1:3200 whites, 1:9500 Hispanics, 1:15,000 African Americans, and 1:31,000 in Asian Americans.[161] CF is caused by mutations in the gene that encodes a multifunctional protein called the *CF transmembrane conductance regulator (CFTR)*.[162] One of the main functions of this protein

MINI CLINI

Extubation

Problem

A 3-year-old child underwent emergency intubation 5 days earlier for epiglottitis. The physician asks the RT to evaluate the patient for extubation. What would the RT evaluate before making the decision to extubate? What equipment would the RT want to have at the bedside during extubation?

Discussion

Clinical examination of vital signs (e.g., body temperature), breath sounds, sensorium, and degree of airway leak should be considered. Equipment for rapid reintubation must be at the bedside, including racemic epinephrine for aerosolization.

Extubation of any patient should take into consideration the pathophysiologic condition that led to intubation. In this case, the RT should look for evidence that the infection is resolving and that the upper airway is no longer inflamed. A lack of fever for at least 12 hours and visual inspection of the throat that reveals minimal inflammation would be most helpful. After extubation, close monitoring must be performed for evidence of airway compromise. Cool mist and aerosolized racemic epinephrine may be helpful to minimize inflammation after extubation.

is to serve as an apical chloride channel in airway, intestinal, and exocrine cells.[163] The movement of chloride ions and regulation of sodium ions is important to the proper regulation of the water content of secretions.[164] The dehydrated viscous secretions that result from the *CFTR* abnormality lead to organ dysfunction, causing the clinical manifestations of the disease.[164] There are more than 1900 known *CFTR* mutations,[165] which are grouped into 6 classes that result in varying levels of *CFTR* production and dysfunction.[165] The variety of *CFTR* mutations explains some of the variability in the severity of the clinical manifestations of the disease.

RULE OF THUMB Both parents must be carriers of the mutated CF gene *(CFTR)* for a child to be born with CF. If both parents have a *CFTR* mutation associated with disease, the chance that CF will develop in their offspring is 1 in 4.

Clinical Manifestations

Patients with CF primarily experience abnormalities in the respiratory, digestive, and reproductive tracts.[166] Complications of lung disease are the leading cause of death in patients with CF.[167] The decreased airway surface liquid secondary to *CFTR* dysfunction leads to impaired mucus clearance, resulting in inflammation and infection of the airways that[168] cause a patient to have a chronic productive cough. Chronic airway infections can occur early in life, most frequently with *S. aureus*, *H. influenzae*, or *Pseudomonas aeruginosa*.[159] Certain organisms, including *P. aeruginosa*, methicillin resistant *S. aureus*, and *Burkholderia cepacia,* have been associated with more rapid rates of lung function decline.[169,170,171] Infection control guidelines aim to reduce the risk of acquiring pathogens that can be worsen the health of patients with CF.[172] As the disease progresses, the cycle of inflammation, infection, and lung damage results in lung hyperinflation and bronchiectasis.[163] Patients with end-stage CF lung disease have severe debility from respiratory failure and may develop pulmonary hypertension and cor pulmonale.[167]

Approximately 85% of patients with CF have exocrine pancreatic insufficiency.[159] *CFTR* dysfunction in the pancreas dramatically reduces the amount of digestive enzymes, leading to malabsorption of fats and proteins and less so for carbohydrates.[173] Malabsorption results in bulky, greasy, foul-smelling stools, fat-soluble vitamin deficiencies, and poor weight gain with failure to thrive. Some newborns present with a condition called *meconium ileus* due to bowel obstruction of thick and hardened meconium that sometimes causes intestinal perforation.[174] Rectal prolapse also can occur as a result of malabsorption and elimination of bulky stools.[175] Patients with pancreatic sufficiency can have recurrent bouts of pancreatitis.[176] Liver disease can result in prolonged obstructive jaundice in the newborn period.[177] Some children and adults have progressive liver disease leading to cirrhosis and portal hypertension.[178]

Males with CF have obstructive azoospermia as a result of congenital absence of the vas deferens.[179] Males and females with CF often have pubertal delays.[180] Females also have reduced fertility.[181]

As children with CF age, the risk for diabetes increases, and by adulthood, the majority of patients have abnormal glucose tolerance testing.[159]

The electrolyte composition of sweat in CF patients is abnormal because of the higher content of salt.[182] Increased salt losses in the sweat may lead to the initial presentation of some CF patients with hyponatremic hypochloremic metabolic alkalosis.[183] The sweat chloride test used for the diagnosis of CF is based on the abnormal concentration of chloride in the sweat of patients with the disease.[184]

Diagnosis

Since 2010, screening for CF in newborns indicating persistent hypertrypsinogenemia is performed in all 50 states and the District of Columbia.[159] The clinical gold standard for diagnosis is confirmed by a sweat chloride test, ideally performed at an accredited CF center. The skin is stimulated to produce sweat (pilocarpine iontophoresis), and a sweat chloride level greater than or equal to 60 mEq/L confirms the diagnosis of CF.[185] The diagnosis in some infants is challenging because they have a normal sweat chloride (<30 mEq/L in infants younger than 6 months) but two abnormal CFTR mutations.[185]

The diagnosis of CF in patients not identified by newborn screening can be made by performing a sweat test in children or adults with signs or symptoms suggestive of CF. Signs and symptoms include recurrent sinus or lung infections, bronchiectasis, nasal polyps, digital clubbing, malabsorption, failure to gain weight as expected, recurrent pancreatitis, salt-losing syndromes, and male infertility resulting from obstructive azoospermia. Testing is often conducted when there is a sibling with CF. Having two sweat chloride test results greater than 60 mEq/L confirms the diagnosis.

Monitoring

CF patients should be managed at an accredited CF center.[159] The CF Foundation recommends that newborns with CF are seen soon after a positive newborn screen result and then at least on a monthly basis until 6 months of age, then every 2 months until age 1 year, and every 2 to 3 months thereafter.[186] It is recommended that older children and adults should be seen quarterly at a minimum. Because CF lung disease is progressive, patients are closely monitored by symptom assessment, physical examination, sputum cultures to monitor airway flora, and objective measurements with spirometry and chest radiography. The nutritional status of each patient is also monitored very closely, including their growth, body mass index, protein stores, and fat-soluble vitamin levels.

Treatment

Multiple therapies are used to maintain a patient's lung health. Airway clearance has been a mainstay of therapy in CF.[187,188] There are many options for airway clearance, including percussion and postural drainage, positive expiratory pressure, autogenic drainage, autocycle of breathing technique, oscillatory positive expiratory pressure, and high-frequency chest compression. Airway clearance therapies have been shown to increase sputum production, improve exercise tolerance, and decrease the rate of lung function decline. In general, no specific airway clearance

technique is superior to another; therefore, airway clearance must be tailored to the individual patient.

As a result of the cellular debris from chronic infection and inflammation, there is free DNA in the airways that contributes to the viscosity of secretions. To treat this, inhaled recombinant deoxyribonuclease (DNase) is used to degrade the viscous DNA.[189] The routine daily use of inhaled DNase has been shown to improve pulmonary function and reduce exacerbations in patients with CF.[190] Inhaled DNase is recommended for daily use in patients 6 years of age and older.[191] Nebulized 7% hypertonic saline is thought to improve mucociliary clearance and has been shown to improve lung function and reduce exacerbations.[192,193] Nebulized 7% hypertonic saline is currently recommended for twice-daily use in patients 6 years and older.[191] High doses of the anti-inflammatory drug ibuprofen, when used at doses resulting in appropriate levels, reduce the progression of CF lung disease and are recommended for use in children 6 to 17 years of age with an FEV1 greater than 60% predicted.[191] The regular use of azithromycin helps preserve lung function and decreases the frequency of pulmonary exacerbations, possibly related to the anti-inflammatory and antimicrobial properties of azithromycin. On this basis, azithromycin is recommended in patients 6 years and older.[191] Patients taking azithromycin should be monitored for the acquisition of nontuberculous mycobacteria, at which time their azithromycin monotherapy should be discontinued.[191]

The lungs of CF patients are chronically colonized with bacteria. One of the most common organisms is *P. aeruginosa*,[159] which has been associated with more rapid decline in lung function and decreased survival.[169] Inhaled antibiotics directed against this organism are recommended for eradiation and chronic suppression. Currently two inhaled antibiotics—inhaled tobramycin and inhaled aztreonam—are available for use.[191,194,195]

More recently, developed therapies are aimed at correcting the underlying *CFTR* defect or potentiating its function. In 2012 ivacaftor, a potentiator that activates defective *CFTR*, was approved for use in the United States in patients with a specific variant of CF—the G551D *CFTR* mutation. In 2014, approval for use of ivacaftor was expanded to some other gating *CFTR* mutations. Ivacaftor has been shown to improve lung function and significantly reduce pulmonary exacerbations. Ivacaftor also was observed to significantly decrease the sweat chloride concentration and enhance antimicrobial action against *P. aeruginosa*.[196] Treatment with two CFTR modulator drugs (e.g., teazacaftor, lumacaftor) is recommended for some CF variants, and triple therapy with novel corrector molecules is being studied. In addition to treatment with corrector molecules like ivacaftor, gene therapy has been explored as a treatment for CF.[197]

Lung transplantation is an option for patients with advanced severe CF lung disease.

The malabsorption due to deficiency of pancreatic enzymes is managed with pancreatic enzyme supplementation and vitamin supplementation.[166] Some patients also require oral calorie supplements to assist with their nutritional needs.

Prognosis

The prognosis for patients with CF has steadily improved with treatment advances over the last several decades. When CF was first described in 1938, children lived approximately 6 months.[198] Survival has since significantly improved. In 2002 the median age of survival was 31.3 years, and 10 years later in 2012, the median survival of patients with CF rose to 41.1 years.[159] In the near future, the number of adults will outnumber the children with CF.[159] It has been projected based on 2016 data that the life expectancy for a baby born with CF in 2016 is 47 years of age.[199] This means that half of all babies born in 2016 are expected to live to be at least 47 years old.

ROLE OF THE RESPIRATORY THERAPIST IN NEONATAL AND PEDIATRIC RESPIRATORY DISORDERS

As in all clinical situations, the role of the RT in the special environment of neonatal and pediatric care is to use his or her expertise and knowledge to improve patient outcomes. Because there are significant differences in the diseases, pathophysiologies, and function of respiratory support equipment between adult and pediatric patients, the RT must be thoroughly familiar with all aspects of pediatric care. The old adage "children are not little adults" is true. Equally, newborns are not little children. Each of these age groups has unique characteristics that require specialized knowledge and experience. The RT is an important part of a team that is dedicated to the health and well-being of these fragile patients.

Also, the RT has an important role in providing education and emotional support, not only to the pediatric patient but also to the families and caregivers. Frequently, the RT is at the bedside of patients when the parents or caregivers are present. The RT is invaluable in helping patients and parents understand the respiratory goals of each individual patient.

SUMMARY CHECKLIST

- The incidence of RDS increases with decreasing gestational age.
- A qualitative decrease in surfactant increases alveolar surface tension forces in RDS patients. This process causes alveoli to become unstable and collapse and leads to atelectasis and increased WOB.
- The definitive diagnosis of RDS usually is made by chest x-ray. Diffuse, hazy, reticulogranular densities with the presence of air bronchograms and low lung volumes are typical of RDS.
- TTN, often referred to as type II RDS, is probably the most common respiratory disorder of the newborn. The cause of TTN is unclear but is most likely related to delayed clearance of fetal lung liquid. Infants with TTN usually respond readily to low FiO_2 by O_2 hood or nasal cannula. Infants who need higher FiO_2 levels may benefit from CPAP.
- Meconium aspiration syndrome (MAS) is a disease of term and near-term infants. It involves aspiration of meconium into the central airways of the lung. This disorder usually is associated with perinatal depression and asphyxia.
- The best management of BPD is prevention. Prevention of atelectrauma and volutrauma begins in the delivery room.

- PPHN should be suspected when an infant has rapidly changing SaO_2 without changes in FiO_2 or has hypoxemia out of proportion to the lung disease detected on the chest x-ray or on the basis of $PaCO_2$.
- Congenital diaphragmatic hernia is a severe disease that usually manifests as severe respiratory distress in the newborn period. The pathophysiologic mechanism is a complex combination of lung hypoplasia, including decreased alveolar count and decreased pulmonary vasculature, pulmonary hypertension, and unusual anatomy of the inferior vena cava.
- The cause of SIDS is unknown, but there is evidence to recommend placing infants in a supine position to sleep. Apnea of prematurity is not a predisposing factor, and there is no evidence that immaturity of the respiratory center is a cause.
- Bronchiolitis is an acute infection of the lower respiratory tract usually caused by RSV.
- Croup is a viral disorder of the upper airway that normally results in subglottic swelling and obstruction. Termed *laryngotracheobronchitis*, viral croup is caused by the parainfluenza virus and is the most common form of airway obstruction in children 6 months to 6 years old.
- Epiglottitis is an acute, often life-threatening infection of the upper airway that causes severe obstruction secondary to supraglottic swelling. Evidence suggests that the incidence of epiglottitis is decreasing among children, probably because of the use of vaccines. A child with epiglottitis usually has a high fever, sore throat, stridor, and labored breathing.
- Cystic fibrosis is the most common lethal genetic disorder among whites. It is inherited as an autosomal recessive trait that affects approximately 30,000 people in the United States. Treatment of CF lung disease requires aggressive efforts to control pulmonary infections and clear pulmonary secretions. RTs often play a key role in treating patients with CF.

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36

Airway Pharmacology

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CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Analyze the three phases that constitute the course of drug action from dose to effect.
- Describe the classes of drugs that are delivered via the aerosol route.
- Compare the mechanisms of action, indications, and adverse effects that characterize each major class of aerosolized drug.
- Compare the available aerosol formulations, brand names, and dosages for each specific drug class.
- Select the appropriate drug class for a specific patient or clinical situation.
- Assess the outcomes for each class of aerosol drug therapy.

CHAPTER OUTLINE

KEY TERMS

adrenergic
agonists
antagonists
antiadrenergic
anticholinergic
catecholamine
cholinergic
drug signaling
leukotriene
L/T ratio
muscarinic
neutropenia
pharmacodynamic phase
pharmacokinetic phase
prodrug
tachyphylaxis
vasopressor

The primary focus of respiratory care pharmacology is the delivery of inhaled aerosols to the respiratory tract for the diagnosis and treatment of pulmonary diseases. Although other drug classes are used in respiratory care, the discussion in this chapter is limited to bronchoactive inhaled aerosols. Other drug classes are discussed in standard pharmacology texts.[1,2]

PRINCIPLES OF PHARMACOLOGY

The course of drug action from dose to effect comprises three phases: *drug administration, pharmacokinetics,* and *pharmacodynamics*. These three phases of drug action can be applied to drug treatment of the respiratory tract with inhaled agents.

Drug Administration Phase

The drug administration phase describes the method by which a drug dose is made available to the body. Administering drugs directly to the respiratory tract uses the inhalation route, and the dose form is an aerosol of liquid solutions, suspensions, or dry powders. The most commonly used devices to administer orally or nasally inhaled aerosols are the metered-dose inhaler (MDI), soft-mist inhaler (Respimat), small-volume nebulizer (SVN), and dry-powder inhaler (DPI). Reservoir devices—including holding chambers with one-way inspiratory valves and simple, nonvalved spacer devices—are often added to MDIs to reduce the need for complex hand-breathing coordination and to reduce oropharyngeal impaction of the aerosol drug (see Chapter 40).

The advantages of treatment of the respiratory tract with inhaled aerosols are as follows:

- Aerosol doses are usually smaller than doses for systemic administration.
- Onset of drug action is rapid.
- Delivery is targeted to the organ requiring treatment.
- Systemic side effects are often fewer and less severe.

Disadvantages of the delivery of inhaled aerosols in treating respiratory disease include the number of variables affecting the delivered dose and lack of adequate knowledge of device performance and use among patients and caregivers.[3]

RULE OF THUMB: Increasing the L/T Ratio The higher the ratio of lung availability to total systemic availability (the L/T ratio), the greater the clinical or therapeutic effect of the bronchoactive aerosol deposited in the airway. The use of more efficient aerosol devices can increase L/T ratios. For example, the use of a spacer or valved holding chamber with a MDI can increase deposition in the lung and reduce oral impaction, leading to a higher L/T ratio.

Pharmacokinetic Phase

The **pharmacokinetic phase** of drug action describes the time course and disposition of a drug in the body based on its absorption, distribution, metabolism, and elimination. Inhaled aerosols are intended for local effects in the airway. Undesired systemic effects result from absorption and distribution throughout the body.

An inhaled aerosol distributes to the lung by inhalation and the stomach through swallowing of drug that deposits in the oropharynx. The therapeutic effect of the aerosol drug is caused by the portion in the airway, whereas systemic effects are due to absorption of the drug from the airway and gastrointestinal (GI) tract. The ideal aerosol would distribute only to the airway, with none reaching the stomach. The ratio of lung availability to total systemic availability (**L/T ratio**) quantifies the efficiency of aerosol delivery to the lung:

$$\text{L/T ratio} = \text{Lung availability}/(\text{Lung} + \text{GI availability})$$

This concept, proposed by Borgström[4] and elaborated by Thorsson,[5] is illustrated in Fig. 36.1, showing delivery of albuterol by inhalation using a MDI and a DPI.

Pharmacodynamic Phase

The **pharmacodynamic phase** describes the mechanisms of drug action by which a drug molecule causes its effects in the body. Drug effects are caused by the combination of a drug with a matching receptor. **Drug signaling** mechanisms include the following:

Signaling Mechanism	Example
Mediation by G protein (guanine nucleotide)–linked receptors	β-adrenergic agonists, antimuscarinic agents
Attachment to intracellular receptors by lipid-soluble drugs	Corticosteroids

The mechanisms of drug action are briefly described here for each class of bronchoactive drug.

Airway Receptors and Neural Control of the Lung

Pharmacologic control of the airway is mediated by receptors found on airway smooth muscle, secretory cells, bronchial epithelium, and pulmonary and bronchial blood vessels. There are *sympathetic (adrenergic)* and *parasympathetic (cholinergic)* receptors in the lung. The terminology for drugs acting on these receptors is based on the usual neurotransmitter that acts on the receptor. The usual neurotransmitter in the sympathetic system is norepinephrine, which is similar to epinephrine. The usual neurotransmitter in the parasympathetic system is acetylcholine. The receptors responding to these neurotransmitters are termed *adrenergic* and *cholinergic*. **Agonists** (stimulating agents) and **antagonists** (blocking agents) that act on these receptors are given the following classifications:

- **Adrenergic** (adrenomimetic): Drug that stimulates a receptor responding to norepinephrine or epinephrine
- **Antiadrenergic**: Drug that blocks a receptor for norepinephrine or epinephrine
- **Cholinergic** (cholinomimetic): Drug that stimulates a receptor for acetylcholine
- **Anticholinergic**: Drug that blocks a receptor for acetylcholine
- **Muscarinic**: Drug that stimulates acetylcholine receptors specifically at one of the two types of acetycholine receptors called the muscarinic receptors

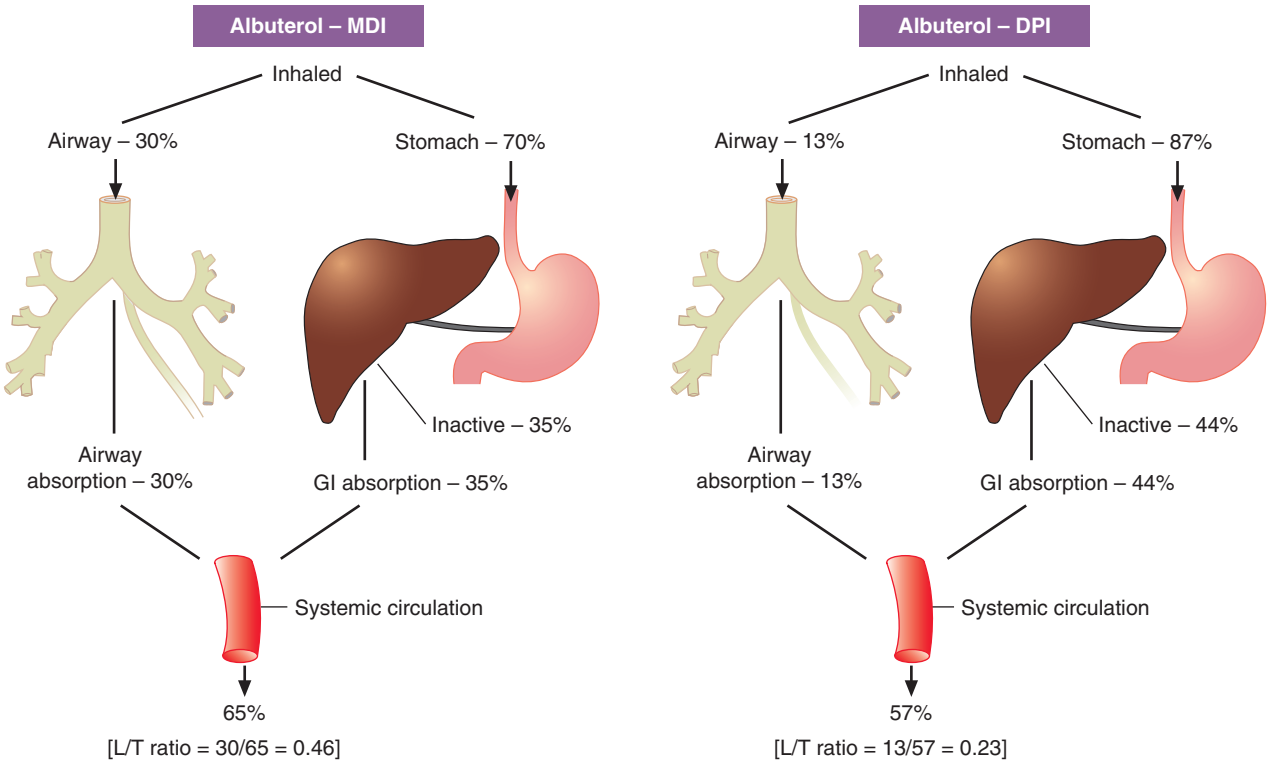

Fig. 36.1 Comparison of efficiency of aerosol delivery with MDI and DPI using the L/T availability ratio. *DPI*, Dry-powder inhaler; *GI*, gastrointestinal; *L/T*, ratio of lung availability to total systemic availability; *MDI*, metered dose inhaler. (From Gardenhire DS: *Rau's Respiratory Care Pharmacology*, ed 10, St. Louis, 2020, Elsevier.)

TABLE 36.1 Airway Receptors and Their Effects in the Cardiopulmonary System

Location	Receptor	Effect
Heart	β1-adrenergic	Increased rate, force
	M_2-cholinergic	Decreased rate
Bronchiolar smooth muscle	β2-adrenergic	Bronchodilation
	M_3-cholinergic	Bronchoconstriction
Pulmonary blood vessels	α1-adrenergic	Vasoconstriction
	β2-adrenergic	Vasodilation
	M_3-cholinergic	Vasodilation
Bronchial blood vessels	α1-adrenergic	Vasoconstriction
	β2-adrenergic	Vasodilation
Submucosal glands	α1-adrenergic	Increased fluid, mucin
	β2-adrenergic	Increased fluid, mucin
	M_3-cholinergic	Exocytosis, secretion

Adrenergic and muscarinic cholinergic receptor subtypes are indicated.
M_2, M_3, Subtypes of muscarinic *(M)* cholinergic receptors.

Because cholinergic receptors exist at autonomic ganglia and at the myoneural junction in skeletal muscle, the terms *muscarinic* and *antimuscarinic* distinguish cholinergic agents whose action is limited to parasympathetic sites. Neostigmine is a cholinergic (indirect-acting) drug that increases receptor stimulation at both the myoneural junction and the parasympathetic sites. By contrast, atropine is an antimuscarinic agent that blocks the action of acetylcholine only at the parasympathetic sites. Table 36.1 summarizes receptors and their effects on the cardiopulmonary system. A more detailed description of the autonomic nervous system and receptor subtypes is provided by Katzung and colleagues.[2]

ADRENERGIC BRONCHODILATORS

Adrenergic bronchodilators represent the largest group of drugs among the aerosolized agents used for oral inhalation. Table 36.2 lists bronchodilators in this group, with their aerosol formulations, selected brand names, and dosages.

Indications for Use

The general indication for use of an adrenergic bronchodilator is the presence of reversible airflow obstruction. The most common use of these agents clinically is to improve flow rates in asthma (including exercise-induced asthma), acute and chronic bronchitis, emphysema, bronchiectasis, cystic fibrosis (CF), and other obstructive airway states.

Indication for Short-Acting Agents

Short-acting β2 agonists (SABAs), such as albuterol and levalbuterol, are indicated for relief of acute reversible airflow obstruction in asthma or other obstructive airway diseases. Short-acting agents are termed *rescue agents* in the 2007 National Asthma Education and Prevention Program Expert Panel III (NAEPP EPR III) guidelines.[6]

TABLE 36.2 Adrenergic Bronchodilator Agents Available in the United States

Drug	Brand Name	Receptor Preference	Adult Dosage	Time Course (Onset, Peak, Duration)
Ultrashort-Acting Adrenergic Bronchodilator Agents				
Racemic epinephrine	Asthmanefrin[a]	α, β	SVN: 2.25% solution, 0.25–0.5 mL (5.63–11.25 mg) qid	*Onset:* 3–5 min *Peak:* 5–20 min *Duration:* 0.5–2 h
Short-Acting Adrenergic Bronchodilator Agents				
Albuterol	Proventil HFA, Ventolin HFA, ProAir HFA, ProAir Respiclick AccuNeb, VoSpire ER	βa-2	SVN: 0.5% solution, 0.5 mL (2.5 mg), 0.63 mg, 1.25-mg, and 2.5-mg unit dose, tid, qid MDI: 90 mcg/puff, 2 puffs tid, qid Tab: 2 mg, 4 mg, and 8 mg, bid, tid, qid DPI: 108 mcg/puff, 2 puffs tid, qid Syrup: 2 mg/5 mL, 1–2 tsp tid, qid	*Onset:* 15 min *Peak:* 30–60 min *Duration:* 5–12 h
Levalbuterol	Xopenex, Xopenex HFA	β-2	SVN: 0.31 mg/3 mL tid, 0.63 mg/3 mL tid or 1.25 mg/3 mL tid, concentrate 1.25 mg/0.5 mL, tid MDI: 45 mcg/puff, 2 puffs q4–6h	*Onset:* 15 min *Peak:* 30–60 min *Duration:* 5–8 h
Long-Acting Adrenergic Bronchodilator Agents				
Salmeterol	Serevent Diskus	β-2	DPI: 50 mcg/blister bid	*Onset:* 20 min *Peak:* 3–5 h *Duration:* 12 h
Formoterol	Perforomist	β-2	SVN: 20 mcg/2 mL unit dose bid	*Onset:* 15 min *Peak:* 30–60 min *Duration:* 12 h
Arformoterol	Brovana	β-2	SVN: 15 mcg/2 mL unit dose, bid	*Onset:* 15 min *Peak:* 30–60 min *Duration:* 12 h
Indacaterol	Arcapta Neohaler	β-2	DPI: 75 mcg/inhalation, qd	*Onset:* 5 min *Peak:* 30 min *Duration:* 24 h
Olodaterol	Stiverdi Respimat	β-2	SMI: 2.5 mcg/actuation, 2 actuations qd	*Onset:* 15 min *Peak:* 30–60 min *Duration:* 12 h

[a]Available over the counter.
DPI, Dry-powder inhaler; *MDI,* metered dose inhaler; *SMI,* soft-mist inhaler; *SVN,* small-volume nebulizer

Indication for Long-Acting Agents

Long-acting β agonists (LABAs)—salmeterol, formoterol, arformoterol, indacaterol, olodaterol, and vilanterol—are indicated for maintenance bronchodilation, control of bronchospasm, and the treatment of nocturnal symptoms in asthma or other obstructive diseases, such as chronic obstructive pulmonary disease (COPD). NAEPP EPR III guidelines consider LABAs *controllers;* their slower time to peak effect makes them poor rescue drugs. In asthma, a long-acting bronchodilator is usually combined with an antiinflammatory medication for the control of airway inflammation and bronchospasm. Although some LABAs have a rapid onset and peak effect similar to or better than that of albuterol, their prolonged activity makes them better maintenance drugs compared with an acute reliever or rescue agent.

Indication for Racemic Epinephrine

Racemic epinephrine is often used by inhaled aerosol or direct lung instillation for its strong vasoconstricting effect in order to reduce airway swelling after extubation or during epiglottitis or croup or to control airway bleeding during endoscopy.

RULE OF THUMB: Differentiating β1 From β2 β1 stimulation increase heart rate and contractility, whereas β2 stimulation results in smooth muscle relaxation. To assist in differentiating these, remember that you have one (1) heart (β1) and two (2) lungs (β2).

Mechanism of Action and Effects

Adrenergic bronchodilators can stimulate one or more of the following receptors, with the effects described:

- *α-receptor stimulation:* Causes vasoconstriction and a **vasopressor** effect (increased blood pressure)
- *β1-receptor stimulation:* Causes increased heart rate and myocardial contractility
- *β2-receptor stimulation:* Relaxes bronchial smooth muscle, stimulates mucociliary activity, and has some inhibitory action on inflammatory mediator release

Bronchodilation, through the stimulation of β2 receptors, is the desired therapeutic effect. Both α- and β-adrenergic receptors are linked with G-protein receptors. Fig. 36.2 illustrates the mechanism of action for the relaxation of airway smooth muscle

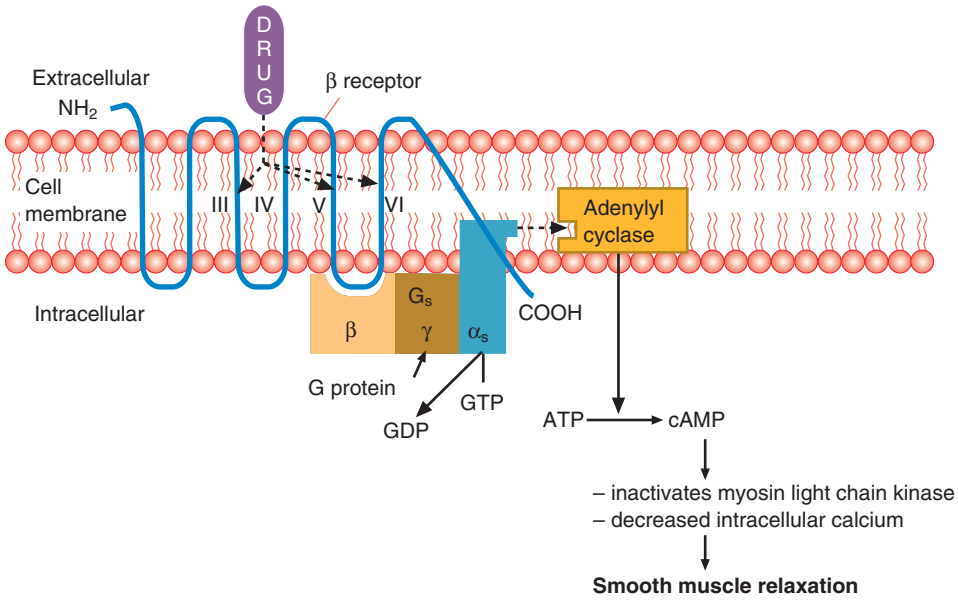

Fig. 36.2 Mechanism of action by which a β-agonist stimulates the G protein–linked β receptor to cause smooth muscle relaxation. Adrenergic agonists, such as albuterol or epinephrine, attach to β receptors, which are polypeptide chains traversing the cell membrane seven times. This causes activation of the stimulatory G protein, designated G_S, linked to the receptor. When stimulated, the receptor undergoes a conformational change, and the α subunit of the G protein attaches to adenyl cyclase. Activation of adenyl cyclase by the G_S protein causes an increased synthesis of the second messenger, cyclic adenosine monophosphate *(cAMP)*. This ultimately causes smooth muscle relaxation and bronchodilation. *ATP,* Adenosine triphosphate; *COOH,* carboxy terminus; *GDP,* guanosine diphosphate; *GTP,* guanosine triphosphate. (From Gardenhire DS: *Rau's Respiratory Care Pharmacology*, ed 10, St. Louis, 2020, Elsevier.)

when a β2 receptor is stimulated. The nature of the β receptor and its activity is presented in more detail by Chung and colleagues.[7]

Adrenergic Bronchodilator Agents

Adrenergic bronchodilator agents represent the evolution of a drug class. Although all of these agents are adrenergic agonists, the differences among individual agents are due to their receptor preference (α-adrenergic, β1-adrenergic, β2-adrenergic) and their different pharmacokinetics, as listed in Table 36.2. These differences determine the clinical application of individual agents. The adrenergic bronchodilators form three subgroups.

Ultrashort-Acting Catecholamines

Racemic epinephrine, the older agent, is a **catecholamine.** This agent lacks β2 specificity. As a result, cardiac effects, especially tachycardia and increased blood pressure, are common. Catecholamines are metabolized by the enzyme catechol *O*-methyltransferase, which causes a short duration of action. Because of a strong α1 activity and vasoconstricting effect, racemic epinephrine is used to reduce swelling in the nose (nasal decongestant) and larynx (croup, epiglottitis) and to control bleeding during bronchoscopic biopsy.

Short-Acting Noncatecholamine Agents

Because of their short duration of action and lack of β2 specificity, catecholamines were replaced by longer-acting, β2-specific agents such as albuterol and levalbuterol. Because their duration of action averages 4 to 6 hours, these drugs are better bronchodilating agents than catecholamines and can be taken on a four-times-daily schedule. However, their modest duration of action results in loss of an overnight bronchodilating effect.

Single-isomer β agonists. Levalbuterol is approved as a single-isomer β2-selective agonist. Previous inhaled formulations of adrenergic bronchodilators all were synthetic racemic mixtures, containing both the *(R)* isomer and the *(S)* isomer in equal amounts. Levalbuterol is the pure *(R)* isomer of racemic albuterol. Both stereoisomers of albuterol are shown in Fig. 36.3 with the single-isomer (*[R]* isomer) form of levalbuterol. Although the *(S)* isomer is physiologically inactive on adrenergic receptors, there is evidence that it is not completely inactive. Box 36.1 lists some of the physiologic effects of *(S)* albuterol noted in the

BOX 36.1 Effects and Characteristics of *(S)*-Isomer of Albuterol

- Increases intracellular calcium concentration in vitro[8]
- Activity is blocked by the anticholinergic atropine[8]
- Does not produce pulmonary or extrapulmonary β2–mediated effects[9]
- Enhances experimental airway responsiveness in vitro[10]
- Increases contractile response of bronchial tissue to histamine or leukotriene C_4 in vitro[11]
- Enhances eosinophil superoxide production with interleukin-5 stimulation[12]
- Slower metabolism than *(R)*-albuterol in vivo[13]
- Preferential retention in the lung when inhaled by metered dose inhaler (in vivo)[14]

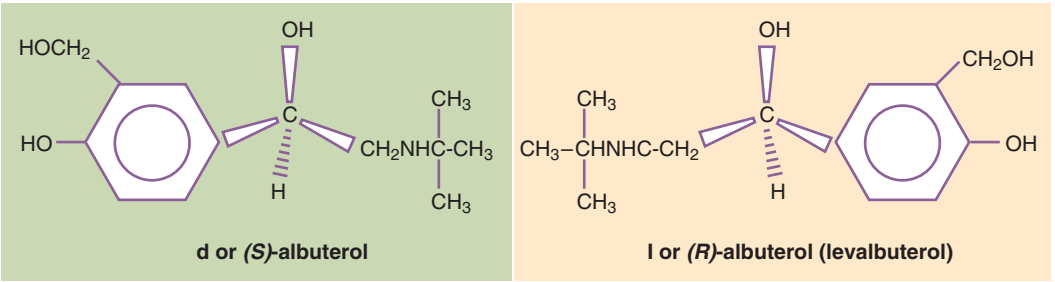

Fig. 36.3 *(R)*- and *(S)*-isomers of racemic albuterol. Levalbuterol is the single, *(R)*-isomer form of racemic albuterol and contains no *(S)*-isomer.

literature.[8–14] The effects antagonize the bronchodilating effects of the *(R)* isomer and promote bronchoconstriction. In addition, the *(S)* isomer is more slowly metabolized than the *(R)* isomer.

Levalbuterol is available in many strengths and formulas, as shown in Table 36.2. Side effects of tremor and changes in heart rate are less with the single-isomer formulation.[15] The 1.25-mg dose shows a higher peak effect on forced expiratory volume in 1 second (FEV_1) with an 8-hour duration compared with racemic albuterol. Side effects with this dose are equivalent to the side effects seen with racemic albuterol. An equivalent clinical response is seen with one-fourth of the racemic dose (0.63 mg) using the pure isomer, although the racemic mixture contains 1.25 mg of the *(R)* isomer (half of the total 2.5-mg dose).

Long-Acting Adrenergic Bronchodilators

Upon its release, salmeterol became the first LABA available in the United States. In contrast to previous agents, the duration of action of salmeterol is approximately 12 hours. The pharmacokinetics of salmeterol makes it suitable for maintenance therapy—in particular, in dealing with nocturnal asthma (although LABAs are not to be used alone in treating asthma and are best used in combination with inhaled corticosteroids). However, salmeterol should not be used for relief of acute airflow obstruction or bronchospasm because its onset is longer than 20 minutes, with a peak effect occurring by 3 to 5 hours. Although this agent is a β2 agonist, its exact mechanism of action differs from those of previous β2 agonists, allowing persistent receptor stimulation over a prolonged period (hours).

RULE OF THUMB: Onset of Action: Long-Acting β Agonists Many LABAs have a quicker onset of action and peak effect than SABAs (i.e., albuterol and levalbuterol). It is important to remember that LABAs should not be used in place of SABAs for acute exacerbations. LABAs should be used for maintenance in chronic lung conditions.

Formoterol has a duration of effect of approximately 12 hours, but in contrast to salmeterol, the onset of action and peak effect of formoterol are rapid and similar to those of albuterol.[16] Formoterol should not be used as a rescue inhaler. As with salmeterol, the extensive side chain or tail makes formoterol more lipophilic than shorter-acting bronchodilators and is the basis for its longer duration of effect.

Arformoterol, the single *(R)* isomer of formoterol, is available as a 2-mL unit-dose vial for an inhalation solution delivering 15 mcg/dose. The recommended dosage is 1 unit dose twice daily. Arformoterol is indicated for the maintenance of bronchospasm in COPD, including chronic bronchitis and emphysema.

Indacaterol (Arcapta Neohaler) a novel once-daily therapy. It has been used mainly to treat asthma; in the United States, however, it is indicated only in the treatment of COPD. Indacaterol is similar to formoterol, with a quick onset; however, it is even faster—with onset at approximately 5 minutes and a duration of 24 hours.[17]

Olodaterol is an ultra-LABA for the once-daily treatment of COPD. It has a quick onset similar to that of formoterol and indacaterol, with a change in FEV_1 at approximately 5 minutes.[18] Currently, olodaterol is not approved for the treatment of asthma; however, it has been shown to be effective as monotherapy and in combination with tiotropium.[19]

Vilanterol is an ultra-LABA that is available in fixed combinations with fluticasone (Breo Ellipta), umeclidinium (Anoro Ellipta), and fluticasone plus umeclidinium (Trelegy Ellipta). Vilanterol in not available as monotherapy but has been studied with good results in COPD.[20]

RULE OF THUMB: Metabolic Disturbances The use of SABAs and LABAs, which are often prescribed together, can produce high levels of β-agonist activity. Additionally, continuous nebulizer therapy may contribute to higher-than-normal levels of β-agonist activity. These increased levels can increase glucose and decrease serum potassium levels. With the use of β agonists, attention to lab results is needed. Moreover, it is possible that the use of high doses of an inhaled β agonist can temporarily treat hyperkalemia.

Adverse Effects

Older adrenergic agents, such as isoproterenol, commonly caused tachycardia, palpitations, and an "adrenaline effect" of shakiness and nervousness. Newer, more β2-selective agents are safer and typically cause tremor as the main side effect. Other common side effects with the inhaled agents include headache, insomnia, and nervousness. Patients should be reassured that some tolerance to these effects does occur. Potential adverse effects with the use of adrenergic bronchodilators include the following:

- Dizziness
- Hypokalemia
- Loss of bronchoprotection
- Nausea
- Tolerance (**tachyphylaxis**)

- Worsening ventilation/perfusion ($\dot{V}/\dot{Q}$) ratio (decrease in PaO_2/SpO_2)

Inhalation results in fewer and less severe side effects than oral administration. Although tolerance develops to the bronchodilating effect, this is not a contraindication to use of the drugs, and relaxation of airway smooth muscle still occurs. Desaturation resulting from a $\dot{V}/\dot{Q}$ mismatch with inhalation of the aerosol is not clinically significant and reverses quickly. The implication of β2-adrenergic agonists in deaths from asthma—termed the *asthma paradox* or the *β-agonist controversy*—remains debated.[21] There is evidence of loss of a bronchoprotective effect with use of β agonists, and patients should be cautioned to avoid asthma triggers. The increased prevalence of asthma in general remains a troublesome and unresolved issue.

Assessment of Bronchodilator Therapy

Assessment of therapy with adrenergic bronchodilators should be based on the indication for the aerosol agent (presence of reversible airflow obstruction owing to primary bronchospasm or other obstruction secondary to an inflammatory response or secretions, either acute or chronic). Basic vital signs (respiratory rate and pattern, pulse, breath sounds) should be assessed before and after treatment, especially for initial drug use, and the patient's subjective reaction (complaints of breathing difficulty). Patients should be instructed in the correct use of the aerosol device, backed up with a demonstration of correct use. Finally, the patient's subjective reaction to the treatment should be monitored for any change in breathing effort. This assessment applies to all subsequent drug groups by aerosol and is not repeated for each class. The following specific actions are suggested to evaluate patient response to this class of drugs:

- Monitor flow rates using bedside peak flowmeters, portable spirometry, or laboratory reports of pulmonary function before and after bronchodilator studies to assess reversibility of airflow obstruction.
- Assess arterial blood gases (ABGs) or pulse oximetry saturation as needed for acute states with asthma or COPD to monitor changes in gas exchange.
- β agonists increase blood glucose and decrease K^+ when high doses are used, with continuous nebulization or emergency department treatments.
- In the long term, monitor pulmonary function studies of lung volumes, capacities, and flows.
- Instruct asthmatic patients in the use and interpretation of disposable peak flowmeters to assess the severity of asthmatic episodes and provide an action plan for treatment modification.
- Emphasize in patient education that β agonists do not treat underlying inflammation and do not prevent the progression of asthma; also that additional antiinflammatory treatment or more aggressive medical therapy may be needed if there is a poor response to the rescue β agonist.
- Instruct and then verify correct use of the aerosol delivery device (i.e., SVN, MDI, reservoir, Respimat, or DPI).
- Instruct patients in the use, assembly, and cleaning of aerosol inhalation devices.

The following actions are suggested to evaluate patient response to LABA:

- Assess ongoing lung function, including predose FEV_1 over time and variability in peak expiratory flows.
- Assess the amount of rescue β-agonist use and nocturnal symptoms.
- Assess the number of exacerbations, unscheduled clinic visits, and hospitalizations.
- Assess days of absence from school or work because of symptoms.
- Assess the patient's ability to reduce the dose of concomitant inhaled corticosteroids.

Note: Death has been associated with excessive use of inhaled adrenergic agents in severe acute asthma crises. Individuals using such drugs should be instructed to contact a physician or an emergency department if there is no response to the usual dose of the inhaled agent.

Because of the ongoing safety concerns with long-acting β2 agonists, the US Food and Drug Administration (FDA) is requiring changes on how these drugs are used in the treatment of asthma. The FDA suggests that if a LABA is used, it should be done in conjunction with a corticosteroid. Once the asthma episode has improved, the LABA should be discontinued. If a child needs a LABA, it is preferred that a combination product (with a corticosteroid) be used to improve adherence.

MINI CLINI

Assessing β-Agonist Side Effects

Problem

The respiratory therapist (RT) has administered an aerosol treatment of albuterol using an MDI with a holding chamber; the patient is a 67-year-old man with newly diagnosed COPD who was admitted for an acute exacerbation and shortness of breath. When the RT returns for the second treatment that day, the patient informs the RT that he began to feel very shaky and nervous beginning about 30 minutes after the previous treatment. He also noticed a tremor when he held his water cup and took a drink. His pulse during the earlier treatment was 84 beats/min. Clinical assessment shows that he is coherent, has good color, is not diaphoretic, and is in no respiratory distress. His respiratory rate is 16 breaths/min and regular, and his pulse is 82 beats/min and regular. Auscultation reveals mild wheezing and scattered rhonchi, with little change from earlier breath sounds. A mild tremor is apparent when he holds his hand out. On questioning, he states that he is now feeling better and that the "shakiness" has subsided a bit.

Discussion

This patient's situation exemplifies a common reaction to inhaled adrenergic bronchodilators. Although albuterol is β2 preferential, it is still an epinephrine-like drug and can produce side effects secondary to sympathetic stimulation. The description of the symptoms is suggestive of common adrenergic side effects (tremor, shakiness). The timing of the symptoms coincides with the pharmacokinetics of albuterol (peak effect in 30–60 minutes). As presented in the case description, it is important to rule out other complications. The physical examination shows no changes from the earlier treatment in the patient's vital signs.

It is important to caution patients about "normal" expected side effects and to reassure them that the side effects decrease with tolerance to the medication. In addition, the RT must be alert to the possibility that a patient may have deteriorated or experienced an adverse change in his or her respiratory status.

RULE OF THUMB: Choosing an Aerosol Agent An aerosol agent to treat the respiratory tract is chosen based on the indication for the agent or class of drugs and a corresponding presence of the indication in the patient.

- *Example:* Adrenergic bronchodilator. The indication is presence of reversible airflow obstruction. The patient shows a 20% improvement in FEV_1 on spirometry with use of inhaled albuterol. Choose an adrenergic bronchodilator. (Note, the American Thoracic Society definition of reversible airflow obstruction is a 12% *and* 200 mL rise in the FEV_1 postbronchodilator. The percent alone does not define a response; if FEV_1 is very low, a small change in FEV_1 that is clinically insignificant could exceed a 20% increase.)
- *Example:* Inhaled corticosteroid. The indication is mild, moderate, or persistent asthma. The patient with asthma reports a need to use a β-agonist rescue inhaler more than a few days each week and complains of waking up at night with shortness of breath. Choose to add an inhaled corticosteroid. Additionally, a LABA may have to be added as well, depending on symptoms. Each patient should always have a rescue inhaler on hand.

ANTICHOLINERGIC BRONCHODILATORS

A second method of producing airway relaxation is through blockade of cholinergic-induced bronchoconstriction. An important difference between β agonists and anticholinergic bronchodilators is the active stimulatory action of the former versus the passive blockade of the latter. A cholinergic blocking agent is effective only if bronchoconstriction exists due to cholinergic activity.

Indications for Use

Table 36.3 lists the dosage, forms, and pharmacokinetics of anticholinergic bronchodilators available in the United States. Generally, anticholinergic agents have been found to be as effective as β agonists in airflow improvement in COPD but less so in asthma. A nasal formulation of ipratropium is also available for relief of allergic and nonallergic perennial rhinitis, including the common cold.

TABLE 36.3 Inhaled Anticholinergic Bronchodilator Agents

Drug	Brand Name	Adult Dosage	Time Course (Onset, Peak, Duration)
Ipratropium bromide	Atrovent HFA	HFA MDI: 17 mcg/puff; 2 puffs qid[a] SVN: 0.02% solution (0.2 mg/mL), 500 mcg tid, qid Nasal spray: 21 mcg; 42 mcg; 2 sprays per nostril 2–4 times qd (dosage varies)	*Onset:* 15–30 min *Peak:* 1–2 h *Duration:* 6 h
Ipratropium bromide and albuterol	Combivent Respimat	SMI: ipratropium 20 mcg and albuterol 100 mcg/puff, 1 inhalation qid SVN: ipratropium 0.5 mg and albuterol 2.5 mg	*Onset:* 15 min *Peak:* 1–2 h *Duration:* 6 h
Aclidinium bromide	Tudorza Pressair	DPI: 400 mcg/inhalation, 1 inhalation bid	*Onset:* 10 min *Peak:* 2 h *Duration:* 12
Glycopyrrolate bromide	Lonhala Magnair Seebri Neohaler	VMN: 25 mcg/1 mL bid DPI: 15.6 mcg/inhalation bid	*Onset: 15–30 min* *Peak: 1–2 h* *Duration: 12 h*
Glycopyrrolate bromide and formoterol	Bevespi Aerosphere	MDI: 9 mcg/inhalation and 4.8 mcg/inhalation bid	*Onset: 5–15 min* *Peak: 30 min–1 h* *Duration: 12 h*
Glycopyrrolate bromide and indacaterol	Ubitron Neohaler	DPI: 15.6 mcg/inhalation and 27.5 mcg/inhalation bid	*Onset: 5–15 min* *Peak: 30 min-1 h* *Duration: 12 h*
Tiotropium bromide	Spiriva; Spiriva Respimat	DPI: 18 mcg/inhalation, 1 inhalation from 1 capsule qd SMI: 2.5 mcg/inhalation, 2 inhalations qd (COPD) SMI: 1.25 mcg/inhalation, 2 inhalations qd (asthma)	*Onset:* 30 min *Peak:* 1–3 h *Duration:* 24 h
Tiotropium bromide and olodaterol	Stiolto Respimat	SMI: tiotropium 2.5 mcg/inhalation and olodaterol 2.5 mcg/inhalation, 2 inhalations qd	*Onset:* 15 min *Peak:* 1–2 h *Duration:* 24 h
Umeclidinium bromide	Incruse Ellipta	DPI: 62.5 mcg/inhalation, 1 inhalation qd	*Onset:* 5–15 min *Peak:* 1–3 h *Duration:* 24 h
Umeclidinium bromide and vilanterol	Anoro Ellipta	DPI: umeclidinium 62.5 mcg/inhalation and vilanterol 25 mcg/inhalation, 1 inhalation qd	*Onset:* 5–15 min *Peak:* 1–3 h *Duration:* 24 h

[a]A holding chamber is recommended with MDI administration to prevent accidental eye exposure.
COPD, Chronic obstructive pulmonary disease; *DPI,* Dry-powder inhaler; *HFA,* hydrofluoroalkane; *MDI,* metered-dose inhaler; *SMI,* soft-mist inhaler; *SVN,* small-volume nebulizer

Indication for Anticholinergic Bronchodilators

Anticholinergic agents are indicated as bronchodilators for maintenance treatment in COPD, including chronic bronchitis and emphysema. Additionally, tiotropium is now used as an add-on treatment for asthma when first-line agents (e.g., LABA and inhaled corticosteroids) have been less effective.

Indication for Combined Anticholinergic and β-Agonist Bronchodilators

A combination anticholinergic and β agonist, such as ipratropium bromide and albuterol (Combivent Respimat, DuoNeb), is indicated for use in patients with COPD receiving regular treatment who require additional bronchodilation for relief of airflow obstruction. Ipratropium bromide is also commonly used in severe asthma in addition to β agonists, especially in acute bronchoconstriction that does not respond well to β-agonist therapy.

Mechanism of Action

Anticholinergic or antimuscarinic agents act as competitive antagonists for acetylcholine at muscarinic receptors on airway smooth muscle. Part of the airflow obstruction in COPD may be due to vagally mediated reflex cholinergic stimulation. Airway irritation and inflammation stimulate afferent sensory C fibers in the airway, which synapse with efferent vagal (cholinergic) fibers to the airway and mucous glands. The muscarinic receptor subtype on smooth muscle and submucosal mucous glands is the M_3 receptor, which is a G protein–linked receptor. The effect of acetylcholine, the usual neurotransmitter, on the muscarinic (M_3) receptors on airway smooth muscle is bronchoconstriction.

All anticholinergic agents have affinity for M_1, M_2, and M_3 receptors; however, the main difference is how slowly they dissociate from the receptor. Ipratropium dissociates much faster; therefore it does not have as long a duration. Aclidinium, glycopyrrolate, tiotropium, and umeclidinium dissociate from the M_3 receptor much more slowly, allowing for a much longer duration of action.[22] The site of action of anticholinergic agents in reversing cholinergic-induced airflow obstruction is shown in Fig. 36.4.

Adverse Effects

Side effects of inhaled anticholinergics usually include the local topical effect of dry mouth, pupillary dilation, lens paralysis, increased intraocular pressure, increased heart rate, urinary retention, and altered mental state. Box 36.2 details the common side effects of anticholinergics.

BOX 36.2 Side Effects Seen With Anticholinergic Aerosol Agents

SVN, MDI, and DPI (Common)
- Cough, dry mouth

MDI (Occasional)
- Nervousness, irritation, dizziness, headache, palpitation, rash

SVN and DPI
- Pharyngitis, dyspnea, flu-like symptoms, bronchitis, upper respiratory tract infections, nausea, occasional bronchoconstriction, eye pain, urinary retention

PRECAUTIONS: Use with caution in patients with narrow-angle glaucoma, prostatic hypertrophy, bladder neck obstruction, constipation, bowel obstruction, or tachycardia.
Side effects were reported in a small percentage (1%–5%) of patients.
DPI, Dry-powder inhaler; *MDI,* metered dose inhaler; *SVN,* small-volume nebulizer.

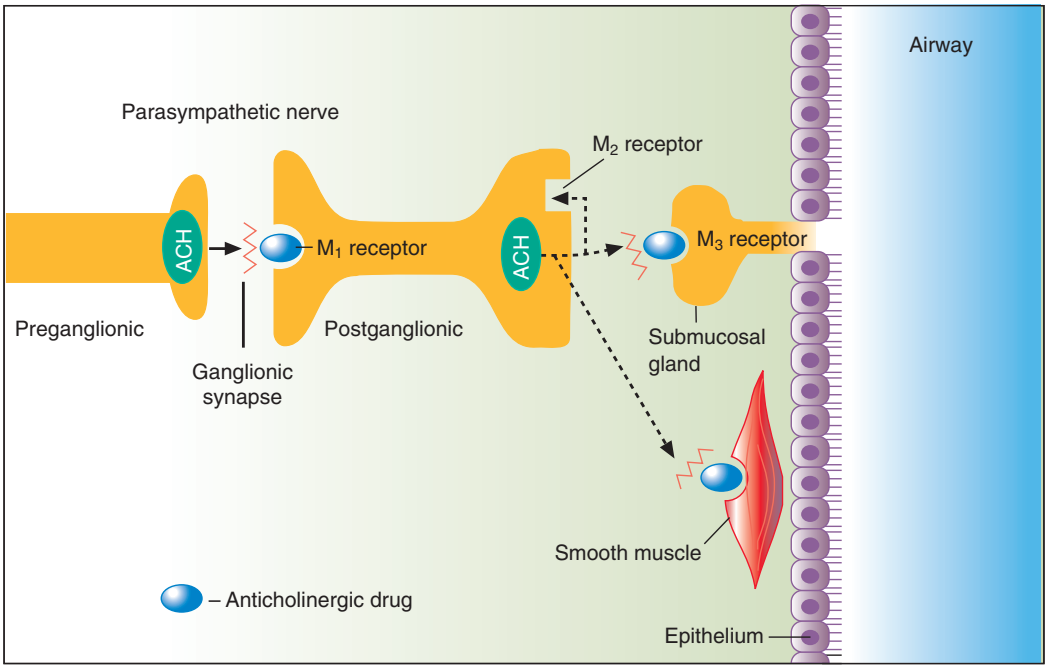

Fig. 36.4 Mechanism of action of anticholinergic agents in blocking muscarinic receptors in the airway to inhibit cholinergic-induced bronchoconstriction. *ACH,* Acetylcholine. (From Gardenhire DS: *Rau's Respiratory Care Pharmacology*, ed 10, St. Louis, 2020, Elsevier.)

The actual amount of drug delivered should be considered; for example, the nebulizer dose of ipratropium is more than 10 times greater than the MDI dose (500 vs 34 mcg). If a patient receives approximately 10% of the SVN volume in the lung, a much larger dose is given with an SVN than with an MDI. Although ipratropium is not contraindicated in patients with prostatic hypertrophy, urinary retention, or glaucoma, the drug should be used with caution and adequate evaluation for possible systemic side effects in these patients. Specifically, it is recommended that patients with certain forms of glaucoma use a mouthpiece and not a mask when they are taking ipratropium bromide via SVN. The eyes must be protected from drug exposure with aerosol use due to accidental spraying from an MDI. There is less chance for eye exposure with the MDI formulation than the SVN solution; a holding chamber is recommended with MDI use.

Assessment

Assessment of bronchodilator therapy with an anticholinergic agent is the same as assessment for adrenergic agents. In addition, preexisting conditions of narrow-angle glaucoma, prostatic hypertrophy, or urinary retention warrant caution with continued evaluation.

MUCUS-CONTROLLING AGENTS

The two agents approved in the United States for oral inhalation with an effect on mucus are *N*-acetyl cysteine (NAC) and dornase alfa. Both agents are mucolytic, although their mechanisms of action differ. Table 36.4 lists these agents along with their formulations, dosages, and bland aqueous aerosols. A review by Balsamo[23] provides additional detail.

N-Acetyl Cysteine

NAC is the *N*-acetyl derivative of the amino acid L-cysteine and is given by either nebulization or direct tracheal instillation.

Indications for Use

NAC is indicated to reduce the accumulation of airway secretions with concomitant improvement in pulmonary function and gas exchange and the prevention of recurrent respiratory infection and airway damage. Diseases of excessive viscous mucous secretions and poor airway clearance include COPD, acute tracheobronchitis, and bronchiectasis. NAC is also used to treat or prevent liver damage that can occur when a patient takes an overdose of acetaminophen.[24] Despite excellent in vitro mucolytic activity and a long history of use, no data clearly demonstrate that oral or aerosolized NAC is effective therapy for treating lung disease.[25] However, in a meta-analysis, Cazzola and colleagues suggest that patients with chronic bronchitis and COPD who were treated with oral NAC had fewer exacerbations.[26]

Mechanism of Action

NAC acts as a classic mucolytic to reduce the viscosity of mucus by substituting its own sulfhydryl group for the disulfide group in mucus, breaking a portion of the bond forming the gel structure. When NAC comes into physical contact with mucus, it begins to reduce viscosity, and mucolytic activity increases with a higher pH of 7.0 to 9.0.

MINI CLINI

Calculating Drug Doses

Problem

The dose of ipratropium bromide (Atrovent) released from the valve of the MDI is 17 mcg. With a usual dose of two actuations, this would release 34 mcg total. The SVN solution is a vial of 2.5 mL of 0.02% strength (concentration), all of which is placed in the nebulizer. Does the nebulizer dose contain the same amount of drug as the two actuations from the MDI?

Discussion

The amount of drug in milligrams or micrograms can be calculated for the nebulizer solution by using the following formula for percentage strength:

$$\%\,(\text{as decimal}) = \frac{\text{Drug solute (in g)}}{\text{Total solution (in mL)}}$$

$$0.0002 = \frac{x\ \text{g}}{2.5\ \text{mL}}$$

$$x\ \text{g} = 0.0002 \times 2.5\ \text{mL} = 0.0005\ \text{g}$$

Converting 0.0005 g to milligrams gives 0.5 mg, or 500 mcg. Two actuations of the MDI release 34 mcg, whereas the dose contained in the SVN is 500 mcg (or >10 times more). The lower-dose MDI is the reason that additional actuations of four or six are needed if a patient does not obtain relief. The SVN solution may also provide relief by giving a higher dose of the drug.

TABLE 36.4 Mucoactive Agents Available for Aerosol Administration

Drug	Brand Name	Adult Dosage	Use
N-acetylcysteine 10% N-acetylcysteine 20%	Mucomyst	SVN: 3–5 mL	Efficacy has not been demonstrated for any lung disease
Dornase alfa	Pulmozyme	SVN: 2.5 mg/ampule, 1 ampule qd[a]	CF
Aqueous water, saline		SVN: 3–5 mL, as ordered	Sputum induction
Hyperosmolar 3-7% saline	Hypersal Pulmosal	SVN: 4 mL	Airway clearance
Mannitol	Bronchitol[b]	DPI: 400 mg, bid	Airway clearance in CF

[a]Nebulizer system recommended (see package insert).
[b]Orphan designation only.
CF, Cystic fibrosis; *DPI,* dry power inhaler; *SVN,* small-volume nebulizer.

Side Effects

Because of its several side effects, NAC has come to be less used in patients with hypersecretory states. The drug is irritating to the airway and can produce bronchospasm, especially in individuals with asthma and hyperreactive airways. The general effect of airway irritation works against the goal of lessening the hypersecretion of mucus. To reduce the occurrence of bronchospasm, use of the 10% solution, which is less hypertonic than the 20% solution, is recommended. Pretreatment with an adrenergic bronchodilator, allowing adequate time for a bronchodilator effect, can prevent or reduce airflow obstruction caused by NAC.

Other side effects that can occur include the following:

- Airway obstruction secondary to rapid liquefaction of secretions
- Disagreeable odor secondary to hydrogen sulfide
- Incompatibility with certain antibiotics (sodium ampicillin, amphotericin B, erythromycin, tetracyclines, and aminoglycosides) if mixed in solution
- Increased concentration and toxicity of nebulizer solution toward end of treatment (It is recommended to dilute with equal volume of sterile water to reduce a concentration that might lead to airway irritation.)
- Nausea and rhinorrhea

MINI CLINI

Calculating Drug Doses of Differing Percent Strengths

Problem

A health care practitioner orders 4 mL of 10% Mucomyst (NAC) for her patient. The RT finds that the supplier carries only 20% Mucomyst. How would she determine the correct amount of 20% Mucomyst solution to use in order to provide 4 mL of 10% Mucomyst solution?

Discussion

When the active ingredient or solute is already diluted less than 100%, the following equation, solving for *x*, can be used:

$$\%\,(\text{as decimal}) = \frac{\text{Drug solute} \times \text{Percent strength of solute (as decimal)}}{\text{Total solution}}$$

$$0.10 = \frac{x\,(0.20)}{4\text{ mL}}$$

$$x = \frac{4(0.10)}{0.20}$$

$$x = 2\text{ mL of 20\% Mucomyst}$$

No matter the percent strength, multiplying the percent strength (in decimal form) with the amount of ordered solute and dividing by the original percent strength that is utilized will determine the amount needed. Alternatively, it can be viewed in terms of milligrams (mg) ordered. In the previous example, the ordered amount was 4 mL of 10% Mucomyst. If you know that 1% solution equals 10 mg/mL of drug, you can easily calculate that 10% = 100 mg/mL. The order is for 4 mL, so 4 × 100 = 400 mg. The order is asking to give 400 mg; therefore if you have 20% Mucomyst (200 mg/mL), you would have to provide 2 mL of 20% Mucomyst.

- Stomatitis
- Reactivity of acetylcysteine with rubber, copper, iron, and cork

Dornase Alfa

Dornase alfa (Pulmozyme) is a genetically engineered clone of the natural human pancreatic DNase enzyme, which can digest extracellular DNA material. It is a peptide mucolytic and can reduce extracellular DNA and F-actin polymers. It is occasionally referred to as *rhDNase* (recombinant human DNase). It is designated as an orphan drug. Administration and dosage are given in Table 36.4.

Indication for Use

Dornase alfa is indicated in the management of CF to reduce the frequency of respiratory infections requiring parenteral antibiotics and to improve these patients' pulmonary function.[27]

Mechanism of Action

Dornase alfa is a proteolytic enzyme that can break down the DNA material from neutrophils found in purulent secretions (Fig. 36.5). This agent is more effective than acetylcysteine in reducing the viscosity of infected sputum in CF.[28]

Side Effects

In contrast to its predecessor, pancreatic dornase (Dornavac), a natural enzyme obtained from animal preparations, dornase alfa has not been shown to produce antibodies that might cause allergic reactions, including bronchospasm. Common side effects associated with the drug include pharyngitis and voice alteration, laryngitis, rash, chest pain, and conjunctivitis. Other effects are less common but are reported as various respiratory symptoms (cough, dyspnea, pneumothorax, hemoptysis, rhinitis, sinusitis), flu syndrome, GI obstruction, hypoxemia, malaise, and weight loss. Contraindications to the drug include hypersensitivity to dornase, Chinese hamster ovary (CHO) cell products, or other components of the drug preparation.

Other Mucoactive Agents

Bland aerosols of water—including distilled water and normotonic, hypertonic, and hypotonic saline—have traditionally been nebulized to improve the mobilization of secretions in respiratory disease states. The mucous gel layer is relatively resistant to the addition or removal of water after it is formed. Bland aerosols have been found to increase the clearance of secretions, to improve sputum production, and to enable productive coughing. The effect is probably a vagally mediated reflex production of cough and secretion of mucus. Bland aerosols are more properly considered expectorants rather than mucolytic agents. Clinicians must be alert to the possibility of bronchospasm with nonisotonic solutions, in particular in patients with hyperreactive airways. Studies have confirmed that long-term use of inhaled hypertonic saline improves pulmonary function in patients with CF.[29] Additionally, hypertonic saline has been found favorable in treating bronchiectasis. Inhaled hypertonic saline is inexpensive and is recommended as part of the treatment regimen for CF.

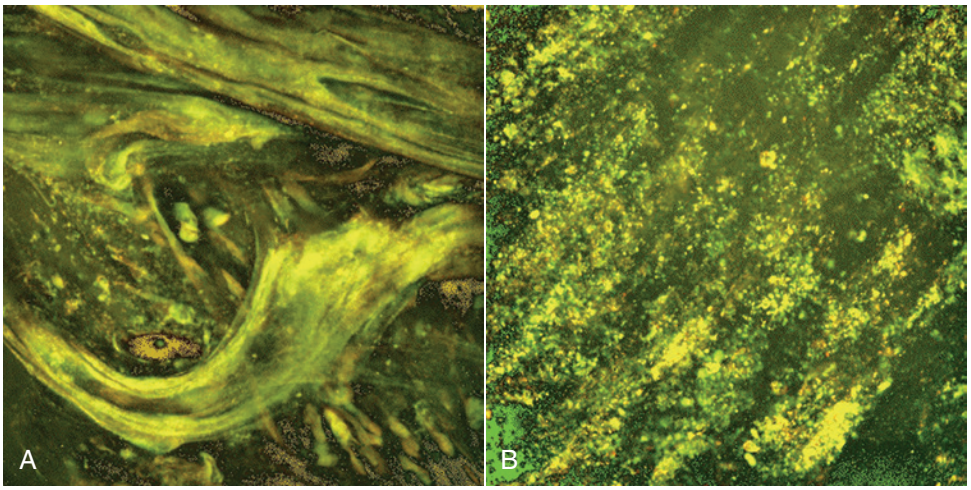

Fig. 36.5 Illustration of the mechanism of action of dornase alfa in reducing DNA polymers in cystic fibrosis (CF) sputum. Confocal micrograph showing CF sputum stained (with YOYO-1) for DNA before (A) and after (B) treatment with dornase alfa in vitro. The long DNA polymers are degraded after dornase treatment. (From Gardenhire DS: *Rau's Respiratory Care Pharmacology*, ed 10, St. Louis, 2020, Elsevier.)

Inhaled mannitol administered by DPI (Bronchitol) has been approved outside the United States. Studies have shown inhaled mannitol to be safe and well tolerated in treating patients with CF or bronchiectasis. However, because some children with CF experience bronchial hyperreactivity with inhaled mannitol,[30] it is important to pretreat with a short-acting bronchodilator before use.

Sodium bicarbonate has been aerosolized and directly instilled into the airway in intubated patients to reduce the viscosity of airway secretions. This agent is not approved for such use. The reduction in secretion viscosity is thought to be caused by the increase in topical airway pH, with degradation of bonding in the mucin polysaccharide.

Expectorants are mucoactive but stimulate the production and clearance of airway secretions rather than causing mucolysis. Examples of such agents include guaifenesin (also known as glyceryl guaiacolate), iodinated glycerol, and saturated solution of potassium iodide (SSKI). Guaifenesin is found in many over-the-counter cough and cold products.

Assessment of Mucoactive Drug Therapy

Assessment of drug therapy for respiratory secretions is difficult. FEV_1 is relatively insensitive to changes in mucociliary clearance. The rate of change in lung function over time is a better marker. In addition, during maintenance therapy, the volume of sputum expectorated varies from day to day and does not reflect effective therapy. The following assessments should be performed.

Before Treatment

- Assess the patient's adequacy of cough and level of consciousness to determine need for treatment with mechanical suctioning or adjunct bronchial hygiene (postural drainage or percussion, positive expiratory pressure therapy) to clear the airway or if treatment is contraindicated.

During Treatment and in the Short Term

- Teach and then verify correct use of aerosol nebulization system, including cleaning.
- Assess therapy based on indication for drug.
- Monitor changes in FEV_1.
- Assess the patient's breathing pattern and rate.
- Assess the patient's breathing effort or pattern.
- Discontinue therapy if the patient experiences adverse reactions.

In the Long Term

- Discontinue therapy if the patient experiences adverse reactions.
- Monitor number and severity of respiratory tract infections and need for antibiotic therapy, emergency visits, and hospitalizations.
- Monitor pulmonary function for improvement or slowing in the rate of deterioration.

General Contraindications

Mucoactive therapy should be used with caution in patients with severely compromised vital capacity and expiratory flow, as in the presence of end-stage pulmonary disease or neuromuscular disorders. Generally, if FEV_1 is less than 25% of predicted, it becomes difficult to mobilize and expectorate secretions. Theoretically, with profound airflow compromise, clearance of secretions could decline.

Gastroesophageal reflux and inability of the patient to protect the airway are risk factors for postural drainage that should be considered if postural drainage is necessary with mucoactive therapy. Mucoactive agents should be discontinued if there is evidence of clinical deterioration. Patients with acute bronchitis or exacerbation of chronic disease (CF, COPD) may be less responsive to mucoactive therapy, possibly secondary to infection and muscular weakness, which can reduce airflow-dependent mechanisms further.

BOX 36.3 Potential Hazards and Side Effects of Aerosolized Corticosteroids

Systemic

- Adrenal insufficiency[a,b]
- Extrapulmonary allergy[a]
- Acute asthma[a]
- HPA suppression (minimal, dose dependent)
- Growth retardation[b]
- Osteoporosis[b]

Local (Topical)

- Oropharyngeal fungal infections
- Dysphonia
- Cough, bronchoconstriction
- Incorrect use of MDI

[a]Following substitution for systemic corticosteroid therapy.
[b]Effect with inhaled corticosteroids alone is unclear.
HPA, Hypothalamo-pituitary-adrenocortical; *MDI,* metered dose inhaler.

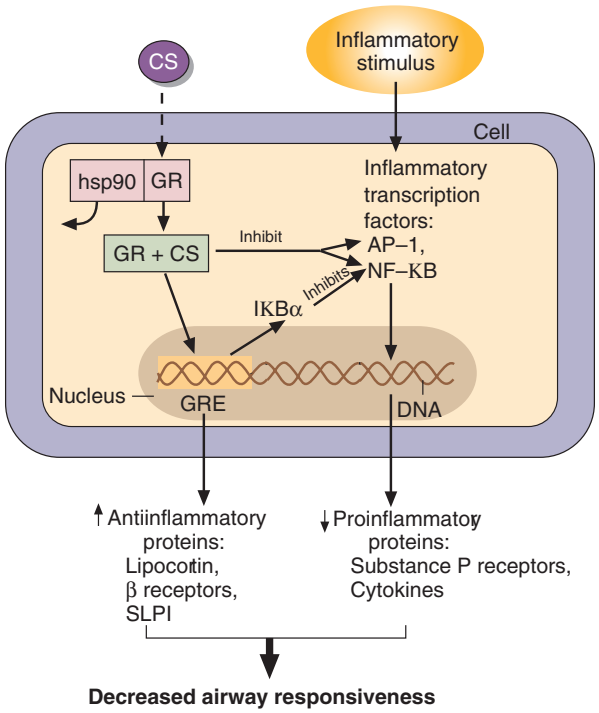

Fig. 36.6 Mechanism of action by which corticosteroids modify cell response to inhibit inflammatory response in the airway. Corticosteroids *(CS)* diffuse into the cell and bind to a glucocorticoid receptor *(GR).* When the steroid binds to the GR, a protein, heatshock protein 90 (hsp 90), dissociates from the GR, and the steroid-GR complex moves into the cell nucleus. The drug-receptor complex binds to glucocorticoid response elements *(GREs)* of the nuclear DNA to upregulate transcription of antiinflammatory substances such as lipocortin, a protein that inhibits the generation of the arachidonic acid cascade by phospholipase A_2. There is evidence that steroids also upregulate inhibitors of factors in the cell, such as nuclear factor-κB (NF-κB), which can cause transcription of inflammatory substances. There may be direct inhibition of factors such as NF-κB to limit the inflammatory process further. *AP-1,* activator protein-1; *iκBα,* inhibitor of nuclear factor-κBα; *SLPI,* secretory leukocyte protease inhibitor. (From Gardenhire DS: *Rau's Respiratory Care Pharmacology*, ed 10, St. Louis, 2020, Elsevier.)

INHALED CORTICOSTEROIDS

Corticosteroids are endogenous hormones produced in the adrenal cortex that regulate basic metabolic functions in the body and exert an antiinflammatory effect. The use of aerosolized corticosteroids is reviewed in this section. All corticosteroids used to treat asthma and COPD are glucocorticoids.

Indications and Purposes

The two general formulations of aerosolized glucocorticoids are orally inhaled and intranasal aerosol preparations. Orally inhaled preparations are listed in Table 36.5. The primary use of orally inhaled corticosteroids is for antiinflammatory maintenance therapy of persistent asthma[6] and severe COPD.[31] The use of intranasal steroids is for control of seasonal allergic or nonallergic rhinitis. With the exception of the combination drugs, most agents in Table 36.5 are available as intranasal preparations.

Mechanism of Action

Glucocorticoids are lipid-soluble drugs that act on intracellular receptors. The complex action of steroids is illustrated in Fig. 36.6.[32–33] It is important for patients to understand that inhalation of an aerosolized steroid does not provide immediate relief, as with an adrenergic bronchodilator. However, daily compliance with the inhaled medication is essential to controlling the inflammation of asthma. Oral corticosteroids may be needed initially to clear the airway or as "burst" therapy to control asthma or COPD exacerbations.

Adverse Effects

As with other classes of aerosolized drugs, the types and severity of side effects seen with inhaled aerosolized corticosteroids are much less than with systemic use of these drugs. Box 36.3 lists systemic and local effects that can occur with inhaled steroids. The systemic effect of adrenal suppression is not usually seen with inhaled doses less than 800 mcg/day in adults or less than 400 mcg/day in children. Use of a reservoir device should be routine with inhaled steroids so as to prevent the swallowed portion from adding to the systemic effect and to prevent the local effects of oral candidiasis and dysphonia.

RULE OF THUMB: Mouth Rinsing With Inhaled Corticosteroids
Instruction should be given to patients receiving inhaled corticosteroids to reduce common local effects of oral candidiasis (thrush) and dysphonia. The use of a reservoir (preferably a holding chamber) with MDI reduces impaction of corticosteroids in the oral cavity. No matter the aerosol device, a patient should *always* rinse his or her mouth with water and spit at the conclusion of therapy.

Special Considerations

The mechanisms of action of all inhaled glucocorticoids are the same with one exception: ciclesonide, a **prodrug,** is given as an inactive compound and is converted to an active metabolite, desisobutyryl ciclesonide, by intracellular enzymes. Ciclesonide is available as an intranasal formulation (Omnaris, Zetonna) and a pressurized MDI (Alvesco).

TABLE 36.5 Corticosteroids and Combination Products Available by Aerosol for Oral Inhalation

Drug	Brand Name	Formulation and Dosage
Beclomethasone dipropionate	QVAR Redihaler	MDI: 40 and 80 mcg/puff
		Adults and children ≥12 years: 40–80 mcg bid[a] or 40–160 mcg bid[b]
		Children ≥4 years: 40–80 mcg bid
Ciclesonide	Alvesco	MDI: 80 mcg/puff and 160 mcg/puff
		Adults and children ≥12 years: 80–160 mcg bid[a] or 80–320 mcg bid[b]
Flunisolide hemihydrate	AeroSpan	MDI: 80 mcg/puff
		Adults and children ≥12 years: 2 puffs bid, adults no more than 4 puffs qd[c]
		Children 6–11 years: 1 puff qd, no more than 2 puffs qd
Fluticasone propionate	Flovent HFA	MDI: 44, 110, and 220 mcg/puff
		Adults and children ≥12 years: 88 mcg bid,[a] 88–220 mcg bid,[b] or 880 mcg bid[c]
		Children 4–11 years: 88 mcg bid[d]
	Flovent Diskus	DPI: 50, 100, and 250 mcg
		Adults and children ≥12 years: 100 mcg bid,[a] 100–250 mcg bid,[b] 1000 mcg bid[c]
		Children 4–11 years: 50 mcg bid
	Armonair Respiclick	DPI: 55, 113, 232 mcg/puff
		Adults and children ≥12 years: 55–232 mcg bid
Fluticasone furoate	Arnuity Ellipta	DPI: 50 mcg/actuation, 100 mcg/actuation and 200 mcg/actuation
		Adults ≥12 years: 100 mcg or 200 mcg, qd
		Children≥5 years: 50 mcg qd
Budesonide	Pulmicort Flexhaler	DPI: 90 mcg/actuation and 180 mcg/actuation
		Adults and children ≥12 years: 180–360 mcg bid,[a] 180–360 mcg bid,[b] 360–720 mcg bid[c]
		Children ≥6 years: 180–360 mcg bid
	Pulmicort Respules	SVN: 0.25 mg/2 mL, 0.5 mg/2 mL, 1 mg/2 mL
		Children 1–8 years: 0.5-mg total dose given qd or bid in divided doses[a,b] 1 mg given as 0.5 mg bid or qd[c]
Mometasone furoate	Asmanex Twisthaler	DPI: 110 mcg/actuation; or 220 mcg actuation
		Adults and children ≥12 years: 220–440 mcg qd,[a] 220–440 mcg qd,[b] 440–880 mcg qd[c]; children 4–11 years: 110–220 mcg qd
	Asmanex HFA	MDI: 100 mcg/actuation; or 200 mcg actuation
		Adults and children ≥12 years: 100–200 mcg bid
Fluticasone propionate/ salmeterol	Advair Diskus	DPI: 100 mcg fluticasone/50 mcg salmeterol, 250 mcg fluticasone/50 mcg salmeterol, or 500 mcg fluticasone/50 mcg salmeterol
		Adults and children ≥12 years: 100 mcg fluticasone/50 mcg salmeterol, 1 inhalation bid, ~12 h apart (starting dose if not currently taking inhaled corticosteroids)
		Maximal recommended dose 500 mcg fluticasone/50 mcg salmeterol bid
		Children ≥4 years: 100 mcg fluticasone/50 mcg salmeterol, 1 inhalation bid, ~12 h apart (for patients who are symptomatic while taking an inhaled corticosteroid)[c]
	Advair HFA	MDI: 45 mcg fluticasone/21 mcg salmeterol, 115 mcg fluticasone/21 mcg salmeterol, or 230 mcg fluticasone/21 mcg salmeterol[c]
		Adults and children ≥12 years: 2 inhalations bid, ~12 h apart
	AirDuo Respiclick	DPI: 55 fluticasone/14 salmeterol, 113 fluticasone/14 salmeterol, or 232 mcg fluticasone/14 mcg salmeterol
		Adults and children ≥12 years: Respiclick, Any dose combination, 1 inhalation bid
Budesonide/formoterol fumarate HFA	Symbicort	MDI: 80 mcg budesonide/4.5 mcg formoterol and 160 mcg budesonide/4.5 mcg formoterol bid
		Adults and children ≥12 years: 320 mcg budesonide/9 mcg formoterol; or 160 mcg budesonide/9 mcg formoterol bid
Mometasone furoate/ formoterol fumarate HFA	Dulera	MDI: 100 mcg mometasone/5 mcg formoterol and 200 mcg mometasone/5 mcg formoterol
		Adults and children ≥12 years: If previously on medium dose of corticosteroids, ≤400 mcg mometasone/20 mcg formoterol qd; if previously on high dose of corticosteroid, ≤800 mcg mometasone/20 mcg formoterol qd
Fluticasone furoate/vilanterol	Breo Ellipta	DPI: 100 mcg fluticasone/25 mcg vilanterol and 200 μg fluticasone/25 mcg vilanterol
		Adults: 100 mcg fluticasone/25 mcg vilanterol qd and 200 mcg fluticasone/25 mcg vilanterol qd
Fluticasone furoate/ umeclidinium/vilanterol	Trelegy Ellipta	DPI: Adults, 100 mcg fluticasone furoate/62.5 mcg umeclidinium/25 mcg vilanterol, qd

[a]Recommended starting dose if taking only bronchodilators.
[b]Recommended starting dose if previously taking inhaled corticosteroids.
[c]Recommended starting dose if previously taking oral corticosteroids.
[d]This dose should be used regardless of previous therapy.
Individual agents are discussed in the text. Detailed information about each agent should be obtained from the manufacturer's drug insert.
HFA, Hydrofluoroalkane.

Assessment of Drug Therapy

The basic actions to evaluate an aerosol drug treatment should be followed (see Assessment of Bronchodilator Therapy, earlier). As with other drug therapy, the indications for this class of drug should be present. The NAEPP and Global Initiative on Obstructive Lung Disease (GOLD) COPD guidelines are recommended for guidance.[6,31] In addition, with inhaled corticosteroids, the following actions are suggested:

- Verify that the patient understands that a corticosteroid is a controller agent and is different from a rescue bronchodilator; assess the patient's understanding of the need for consistent use of an inhaled corticosteroid (compliance).
- Instruct the patient in the use of a peak flow meter to monitor baseline peak expiratory flow (PEF) and changes. Verify that there is a specific action plan based on symptoms and PEF results. The patient should understand when to contact a physician with deterioration in PEF or exacerbation of symptoms.

In the Long Term

- Assess severity of symptoms (coughing, wheezing, nocturnal awakenings, symptoms during exertion; use of rescue bronchodilator; number of exacerbations; missed work or school days; and pulmonary function) and modify level or dosage as recommended by NAEPP and GOLD guidelines.[6,31]
- Assess for the presence of side effects with inhaled steroid therapy (oral thrush, hoarseness or voice changes, cough or wheezing with MDI use); use a reservoir (preferably a holding chamber) with MDI use, and verify correct technique.
- Ophthalmologic assessment may be needed for long-term use of inhaled corticosteroids (ICSs), it can be associated with cataracts and glaucoma.

MINI CLINI

Patient Education

Problem

A 24-year-old patient with asthma has complained of waking up at night and being short of breath. She also reports feeling tightness in her chest and needs to use her albuterol inhaler 5–6 days/week to get relief. She is not currently on other inhaled medications. Her allergist prescribes an inhaled MDI corticosteroid and salmeterol to be taken on a daily basis. What instructions should she be given in using these agents by inhalation?

Discussion

The key points with corticosteroid inhalation should be reviewed. These are small doses and safe to take. However, it is important to take the prescribed corticosteroid dose regularly every day if the drug is to have an antiinflammatory effect in the lung. The patient should also use a reservoir device with the MDI. Rinsing her mouth with water after a treatment can reduce further the chance of oral candidiasis or dysphonia. With salmeterol, she should be instructed to follow her prescribed dose, which is usually two inhalations twice daily. Because of its pharmacokinetics, salmeterol is considered a long-term controller and not a quick reliever. It is not helpful in relieving bronchospasm if the patient experiences acute difficulty in breathing. For acute respiratory problems, she should have a quick-acting adrenergic agent such as albuterol or levalbuterol. If she experiences wheezing or chest tightness, one or two actuations of one of these agents would help. Salmeterol should be taken at the regularly prescribed time, usually every 12 h.

NONSTEROIDAL ANTIASTHMA DRUGS

Nonsteroidal antiinflammatory drugs constitute a growing class of drugs in the treatment of asthma. These include antileukotrienes, also termed **leukotriene** modifiers (zafirlukast, zileuton, montelukast) and monoclonal antibodies (benralizumab, mepolizumab, omalizumab, and relizumab). Antileukotrienes are administered orally and monoclonal antibody agents are given parenterally, but these are included as bronchoactive drugs. Table 36.6 lists the pharmaceutical details for each agent.

Indication for Use

The general indication for the clinical use of nonsteroidal antiasthma agents is prophylactic management (control) of persistent asthma (step 2 or greater asthma, using the classification in the NAEPP guidelines[6]). *Step 2 asthma* is defined as more than 2 days/week with (but not daily) symptoms and more than 2 nights/month with awakenings and FEV_1 of 80% or greater. *Step 3 asthma* is defined as daily symptoms and 3–4 nights/month with awakening and FEV_1 greater than 60% but less than 80%. *Step 4 and above asthma* is defined as symptoms throughout the day as well as night awakenings more than once per week and FEV_1 less than 60%.

The following are qualifications to the general indications for use of these agents:

- Antileukotrienes are typically recommended as alternatives to introducing inhaled corticosteroids in step 2 and 3 asthma.
- Antileukotrienes, montelukast in particular, are often used in infants and young children as alternatives to inhaled corticosteroids in step 2 asthma because of their safety profiles.
- Antileukotrienes can be useful in combination with inhaled steroids to reduce the dose of the steroid and are listed as alternatives in step 2 through 4 asthma.
- The monoclonal antibodies benralizumab, mepolizumab, omalizumab and relizumab are available for consideration in the appropriate population.[34–37]

All of the nonsteroidal antiasthma drugs described in this chapter are controllers, not relievers, and are used in asthma requiring antiinflammatory drug therapy (Box 36.4).

Mechanism of Action

Zafirlukast and montelukast act as leukotriene receptor antagonists and are selective competitive antagonists of leukotriene receptors LTD_4 and LTE_4. Leukotrienes such as LTC_4, LTD_4, and LTE_4 (previously known as *SRS-A*) stimulate leukotriene receptors termed $CysLT_1$ to cause bronchoconstriction, secretion of mucus, vascular permeability, and plasma exudation into the airway. The mechansim of action is shown in Fig. 36.7. The drug inhibits asthma reactions induced by exercise, cold air, allergens, and aspirin.

Zileuton inhibits the 5-lipoxygenase enzyme that catalyzes the formation of leukotrienes from arachidonic acid (see Fig. 36.7). Omalizumab is a recombinant DNA–derived humanized antibody that binds to immunoglobulin E (IgE). The agent inhibits the attachment of IgE to mast cells and basophils, reducing the release of chemical mediators of the allergic response.

TABLE 36.6 Nonsteroidal Antiasthma Medications

Generic Drug	Brand Name	Formulation and Dosage
Antileukotrienes		
Zafirlukast	Accolate	Tablets: 10 and 20 mg Adults and children ≥12 years: 20 mg bid, without food Children 5–11 years: 10 mg bid
Montelukast	Singulair	Tablets: 10 mg and 4-mg and 5-mg cherry-flavored chewable; 4-mg packet of granules Adults and children ≥15 years: One 10-mg tablet qd Children 6–14 years: One 5-mg chewable tablet qd Children 2–5 years: One 4-mg chewable tablet or one 4-mg packet of granules qd 6–23 months: One 4-mg packet of granules qd
Zileuton	Zyflo; Zyflo CR	Tablets: 600 mg Adults and children ≥12 years: One 600-mg tablet 4 qid; CR, 2 tablets bid, within 1 h of morning and evening meals
Monoclonal Antibody		
Omalizumab	Xolair	Adults and children ≥12 years: subcutaneous injection q 4 wk; dose dependent on weight and serum immunoglobulin E level
Benralizumab	Faserna	Adults and children ≥12 years: SQ: 30 mg, q4wk
Mepolizumab	Nucala	Adults and children ≥12 years: SQ: 100 mg, q4wk
Relizumab	Cinqair	Adults and children ≥1 years: IV: 3 mg/kg, q4wk

Detailed prescribing information should be obtained from the manufacturer's package insert.

BOX 36.4 Bronchoactive Agents Distinguished as Controllers or Relievers in Treating Asthma

Long-Term Control

- Inhaled corticosteroids
- Long-acting β2 agonists
  - Inhaled: salmeterol, formoterol
  - Oral: sustained-release albuterol
- Leukotriene modifiers
- Systemic corticosteroids
- Methylxanthines (theophylline)

Quick Relief

- Short-acting inhaled β2 agonists: albuterol, levalbuterol
- Anticholinergic (antimuscarinic): Ipratropium
- Systemic corticosteroids (oral burst therapy, intravenous therapy)

From National Asthma Education and Prevention Program, National Heart, Lung and Blood Institute, National Institutes of Health: *Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma*. NIH Publication No. 08-4051. Bethesda, MD; 2007, National Institutes of Health.

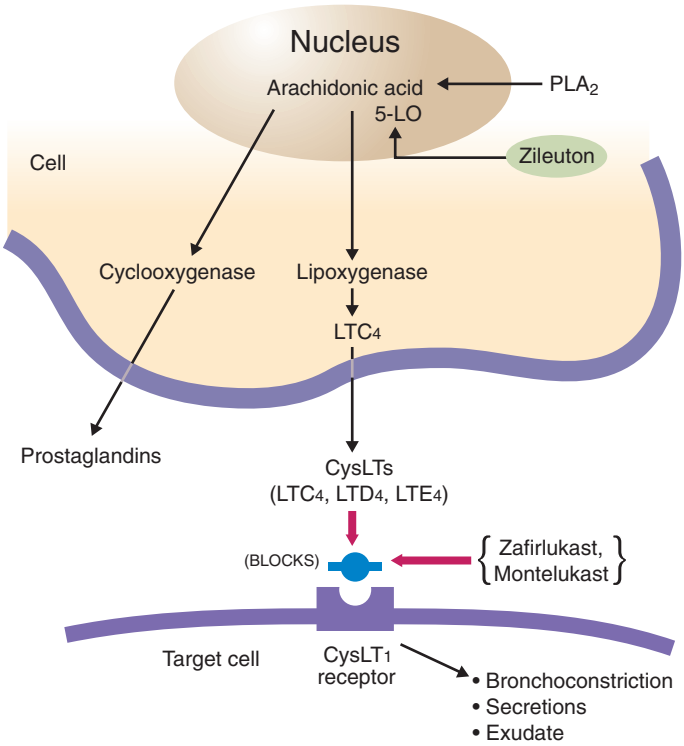

Fig. 36.7 Mechanisms and sites of action for leukotriene modifiers zileuton, zafirlukast, and montelukast. Zileuton inhibits the 5-LO enzyme, whereas zafirlukast and montelukast block the leukotriene receptor ($CysLT_1$). *LT,* Leukotriene; *PLA,* phospholipase A.

TABLE 36.7 Summary of Comparative Features of Three Available Antileukotriene Agents

Features	Zileuton	Zafirlukast	Montelukast
Brand name	Zyflo; Zyflo CR	Accolate	Singulair
Action	5-LO inhibitor	$CysLT_1$ receptor block	$CysLT_1$ receptor block
Age range	≥12 years	≥5 years	≥6 months
Dosage	600-mg tab, qid; CR: two 600-mg tab bid; 1 h within morning and evening meal	Adult: 20-mg tab bid Children 5–11 years: 10-mg tab bid	Adult: 10-mg tab hs 6–14 years: 5-mg tab hs 2–5 years: 4-mg tab hs 6–23 months: 4-mg oral granules hs
Administration	Can be taken with food	1 h before or 2 h after meal	Taken with or without food
Drug interaction	Yes (theophylline, warfarin, propranolol)	Yes (warfarin, theophylline, aspirin)	No
Side effects (common)	Headache, dyspepsia, unspecified pain, liver enzyme elevations	Headache, infection, nausea, possible liver enzyme changes	Headache, influenza, abdominal pain
Contraindications	Active liver disease or elevated liver enzyme levels, hypersensitivity to components	Hypersensitivity to components	Hypersensitivity to components

Enralizumab, mepolizumab and reslizumab block interleukin-5 (IL-5), changing the signaling of IL-5 reducing eosinophils.

Adverse Effects

A potential adverse effect with any nonsteroidal antiasthma drug is inappropriate use. These agents are not bronchodilators and offer no benefit for acute airway obstruction in asthma.

Table 36.7 summarizes information and comparative features of the three antileukotriene agents, including drug interactions, common side effects, and contraindications. The most common adverse reactions seen with monoclonal anitbodies include injection site reaction, viral infections, respiratory tract infections, headache, sinusitis, and pharyngitis.

Assessment of Drug Therapy

As with other drug therapy, the indication for this class of drug should be present.

- Verify that the patient understands that nonsteroidal antiasthma agents are controller drugs and that they differ from rescue bronchodilators; assess the patient's understanding of the need for consistent use of these agents (compliance).
- Instruct the patient in the use of a peak flow meter to monitor baseline PEF and changes. Verify that there is a specific action plan based on symptoms and PEF results. The patient should be clear on when to contact his or her physician with a deterioration in PEF or exacerbation of symptoms.

In the Long Term

- Assess the severity of symptoms—coughing, wheezing, nocturnal awakenings, symptoms during exertion, use of rescue medication, number of exacerbations, missed work or school days, pulmonary function—and modify the level of asthma therapy (up or down, as described in the NAEPP EPR III guidelines for step therapy).
- Assess for the presence of side effects with nonsteroidal antiasthma agents; refer to the particular agent and its side effects (listed previously).

AEROSOLIZED ANTIINFECTIVE AGENTS

Multiple aerosolized antiinfective agents are available. Some may be used less often than others in respiratory therapy. The antiinfective agents pentamidine, ribavirin, inhaled tobramycin, inhaled aztreonam, and zanamivir are briefly outlined here. Drug formulations and dosages are given in Table 36.8.

Pentamidine Isethionate

Pentamidine isethionate (NebuPent) is an antiprotozoal agent that has been used in the treatment of opportunistic pneumonia caused by *Pneumocystis jirovecii,* which is the causative agent of *Pneumocystis* pneumonia, or PJP (previously called PCP for *Pneumocystis carinii*). PJP is usually seen in immunocompromised patients, especially patients with AIDS with impaired immune status.

Indication for Use

General recommendations for the prophylaxis of PJP were published by the US Centers for Disease Control and Prevention (CDC) for HIV-positive children[38] and adults.[39] In the 2018 CDC recommendations, oral trimethoprim/sulfamethoxazole (TMP/SMX) is preferred for treatment and prophylaxis of PJP as long as adverse side effects from TMP/SMX were absent or acceptable.[40] Aerosolized pentamidine is recommended as an alternative therapy for primary and secondary prophylaxis of PJP; it is not recommended as a treatment.[38,39]

Adverse Effects

Possible side effects with aerosolized pentamidine include cough, bronchial irritation, bronchospasm, wheezing, shortness of breath, fatigue, bad or metallic taste, pharyngitis, conjunctivitis, rash, and chest pain. Systemic effects also have been noted with inhaled pentamidine, including decreased appetite, dizziness, rash, nausea, night sweats, chills, spontaneous pneumothoraces, **neutropenia,** pancreatitis, renal insufficiency, and hypoglycemia. Extrapulmonary infection with *P. jiroveci* can occur with prophylactic inhaled pentamidine.

TABLE 36.8 Inhaled Antiinfective Agents

Drug	Brand Name	Formulation and Dosage	Clinical Use
Pentamidine isethionate	NebuPent	300 mg powder in 6 mL sterile water; 300 mg q4wk	PJP prophylaxis
Ribavirin	Virazole	6 g powder in 300 mL sterile water (20 mg/mL solution); given q 12–18 h/day for 3–7 days by SPAG nebulizer	RSV
Tobramycin	TOBI	300-mg/5-mL ampule; adults and children ≥6 years: 300 mg bid, 28 days on/28 days off drug	*Pseudomonas aeruginosa* infection in CF
Tobramycin	Bethkis	300-mg/4-mL ampule; adults and children ≥6 years: 300 mg bid, 28 days on/28 days off drug	*P. aeruginosa* infection in CF
Aztreonam	Cayston	75 mg/1 mL; adults and children ≥7 years: 75 mg tid, 28 days on/28 days off drug	*P. aeruginosa* infection in CF
Zanamivir	Relenza	DPI: 5 mg/inhalation; adults ≥5 years: 2 inhalations (one 5-mg blister per inhalation) bid, 12 h apart for 5 days	Influenza

Details on use and administration should be obtained from manufacturer's drug insert material before use.
CF, Cystic fibrosis; *DPI,* dry-powder inhaler; *PJP, Pneumocystis jirovecii* pneumonia; *RSV,* respiratory syncytial virus; *SPAG,* small-particle aerosol generator

Assessment

When aerosolized pentamidine is being administered, an environmental containment isolation system (e.g., a booth or negative pressure room) and personnel barrier protection should be provided. Patients should be screened for tuberculosis. The drug is given using a nebulizer system with one-way valves and scavenging expiratory filters (e.g., Respirgard); this reduces environmental contamination. Nebulizer systems capable of producing a mass median diameter of 1 to 2 μm for peripheral lung deposition may reduce coughing. The patient should be monitored for onset of any of the previously described adverse reactions. In addition, the following actions are recommended:

- If coughing and bronchospasm are present, provide a short-acting β agonist or an anticholinergic bronchodilator such as ipratropium with inhaled pentamidine.
- Monitor for occurrence rate of *P. jiroveci* and rate of long-term hospitalizations.
- Monitor for presence of side effects (shortness of breath, possible pneumothorax, conjunctivitis, rash, neutropenia, dysglycemia) or appearance of extrapulmonary *P. jiroveci* infection.
- Evaluate need for prior use of a bronchodilator if symptoms of bronchospasm or coughing occur after inhalation of pentamidine.

In the Long Term

Monitor the efficacy of pentamidine prophylaxis in preventing episodes of *P. jiroveci* infection.

Ribavirin

Ribavirin (Virazole) is classified as an antiviral drug; it is active against respiratory syncytial virus (RSV), influenza viruses, and the herpes simplex virus. Recommendations for use of the drug were published in a statement by the American Academy of Pediatrics.[40] Generally, the drug is not recommended for routine RSV infection, but it may be considered for life-threatening infections. Administration of the aerosol requires use of a special large-reservoir nebulizer called a small-particle aerosol generator (SPAG). For more information on the SPAG, see Chapter 40.

Adverse Effects

Skin rash, eyelid erythema, and conjunctivitis have been noted with aerosol administration. Important equipment-related effects during mechanical ventilation include endotracheal tube occlusion and occlusion of ventilator expiratory valves or sensors. Deterioration of pulmonary function can occur. Patients or practitioners who are pregnant should not have exposure to ribavirin.

Assessment

- Monitor signs of improvement in RSV infection severity, including vital signs, respiratory pattern and work of breathing, level of FiO_2 needed, level of ventilatory support, ABGs, body temperature, and other indicators of pulmonary gas exchange.
- Monitor the patient for evidence of side effects, such as deterioration in lung function, bronchospasm, occlusion of endotracheal tube, cardiovascular instability, skin irritation from the aerosol drug, and equipment malfunction related to drug residue.

Inhaled Tobramycin

Patients with CF have chronic respiratory infection with *Pseudomonas aeruginosa* and other microorganisms. Such chronic infection causes recurrent acute respiratory infections and deterioration of lung function. With the exception of the quinoline derivatives such as ciprofloxacin, antibiotics such as the aminoglycosides (e.g., tobramycin), which are effective against *Pseudomonas* organisms, have poor lung bioavailability when taken orally. Consequently these antibiotics must be given either intravenously or by inhalation. The aminoglycoside tobramycin has been approved for inhaled administration and is intended to manage chronic infection with *P. aeruginosa* in patients with CF. Goals of therapy are to treat or prevent early colonization with *P. aeruginosa* and maintain present lung function or reduce the rate of deterioration.[41]

Adverse Effects

Side effects with parenteral aminoglycosides include possible auditory and vestibular damage with potential for deafness and

BOX 36.5 Side Effects With Aminoglycosides and Tobramycin

Parenteral Administration
- Ototoxicity (auditory and vestibular)
- Nephrotoxicity
- Neuromuscular blockade
- Hypomagnesemia
- Cross-allergenicity
- Fetal harm (deafness)

Inhaled Nebulized Tobramycin
- Voice alteration
- Tinnitus
- Nonsignificant increase in bacterial resistance

nephrotoxicity. Other possible effects are listed in Box 36.5. Risk for more serious side effects with tobramycin, whether by inhaled or parenteral routes, increases with the use of other aminoglycosides, in the presence of poor renal function and dehydration, with preexisting neuromuscular impairment, or with use of other ototoxic drugs.

The following precautions are suggested with the use of inhaled tobramycin:
- Inhaled tobramycin should be used with caution in patients with preexisting renal, auditory, vestibular, or neuromuscular dysfunction.
- Tobramycin solution should not be mixed with β-lactam antibiotics (penicillins, cephalosporins) because of admixture incompatibility, and mixing with other drugs in general is discouraged.
- Nebulization of antibiotics during hospitalization should be performed under conditions of containment, as previously described for pentamidine and ribavirin, to prevent environmental saturation and development of resistant organisms in the hospital.
- Aminoglycosides can cause fetal harm if administered to pregnant women; exposure to ambient aerosol drug should be avoided by women who are pregnant or trying to become pregnant.
- Local airway irritation resulting in cough and bronchospasm with decreased ventilatory flow rates is possible with inhaled antibiotics and seems to be related to the osmolality of the solution. Peak flow rates and chest auscultation should be used before and after treatments to evaluate airway changes. Pretreatment with a β-agonist may be needed.
- Allergic reactions in the patient, staff, or family should be considered if exposure to the aerosolized drug is not controlled. The use of a nebulizing system with a scavenging filter, one-way valves, and thumb control could reduce ambient contamination with the drug, as previously described.

In clinical trials, inhaled tobramycin was administered using the PARI LC Plus nebulizer with a DeVilbiss Pulmo-Aide compressor. Studies have reported that not all nebulizer-compressor systems perform adequately with antibiotic solutions, and higher flow rates of 10 to 12 L/min may be needed with nebulizers.[42]

Assessment
- Verify that the patient understands that nebulized tobramycin should be given after other CF therapies, including other inhaled drugs.
- Check whether the patient has renal, auditory, vestibular, or neuromuscular problems or is taking other aminoglycosides or ototoxic drugs. Consider whether tobramycin should be used for the patient based on severity of preexisting or concomitant risk factors.
- Monitor lung function to note improvement in FEV_1.
- Assess rate of hospitalization before and after institution of inhaled tobramycin.
- Assess need for intravenous antipseudomonal therapy.
- Assess improvement in weight.
- Monitor for occurrence of side effects, such as tinnitus or voice alteration; have the patient rinse and expectorate after aerosol treatments.
- Evaluate for changes in hearing or renal function during use of inhaled tobramycin.

Inhaled Aztreonam

Aztreonam was approved in December 1986 by the FDA as a monobactam, a synthetic bactericidal antibiotic; it is given as an intravenous solution. Inhaled aztreonam (Cayston) treats pulmonary symptoms in patients with CF colonized with *P. aeruginosa.*[43] Inhaled aztreonam is not indicated for patients younger than 7 years of age or patients with *Burkholderia cepacia* infection. This agent has been studied only in patients with FEV_1 greater than 25% or less than 75% of predicted. The agent is delivered by itself using the Altera Nebulizer System.

Adverse Effects

Inhaled aztreonam can cause bronchospasm and decrease FEV_1. All patients should be screened for baseline pulmonary function results and treated with a bronchodilator before inhaled aztreonam is administered.

Patients have been reported to experience severe allergic reactions with injectable aztreonam. Careful observation is warranted when first using inhaled aztreonam because it could cause an allergic reaction.

The use of antibiotics in the absence of infection may lead to the development of drug-resistant bacteria. Inhaled aztreonam should not be used in patients with CF who are not infected with *P. aeruginosa.*

Colistimethate Sodium

Colistimethate sodium (colistin) is an antibiotic used to treat sensitive strains of gram-negative bacilli, particularly *P. aeruginosa.* Colistimethate sodium is available as an inhaled formulation in Europe as Promixin; this agent is not approved by the FDA for inhalation. However, nebulization of the parenteral formulation is commonly used in patients with CF.[44]

Adverse Effects

Side effects seen with parenteral administration include neurotoxic events and nephrotoxicity. Because colistimethate sodium

is mainly eliminated by the renal system, renal insufficiency should be considered. Neurotoxic events associated with colistimethate sodium include dizziness, confusion, muscle weakness, and possible neuromuscular blockade leading to respiratory arrest. When aerosolized colistimethate sodium is used, the most common complication seen is bronchospasm. Pretreatment with a β-agonist can decrease the potential for this complication.

Inhaled Zanamivir

Zanamivir is an inhaled powder aerosol (DPI). Despite the availability of zanamivir and the oral antiinfluenza agent oseltamivir (Tamiflu), prophylactic vaccination against influenza is still recommended, especially in high-risk individuals with cardiovascular or pulmonary disease. Zanamivir and oseltamivir represent a new class of antiviral agents termed *neuraminidase inhibitors.*

Indication for Use

Inhaled zanamivir is indicated for the treatment of uncomplicated acute illness caused by influenza virus in adults and children 5 years of age or older who have been symptomatic for no longer than 2 days. The agents have an off-label use for treatment and prophylaxis of H1N1 influenza A.

Mechanism of Action

The influenza virus attaches to respiratory tract cells by binding of viral surface hemagglutinin to the cell's surface molecule of sialic acid (Fig. 36.8). The viral particle also has an enzyme, neuraminidase, on its surface. When replicated viral particles are released from the host cell after infection, the viral neuraminidase cleaves the sialic acid on both the host cell surface and other viral particle surfaces so that mature virus can be released and spread. Without neuraminidase, influenza virus would clump together and to the host cell, preventing spread. Zanamivir and oseltamivir (which is taken by pill) combine with the surface neuraminidase, preventing its action and the spread of viral particles.

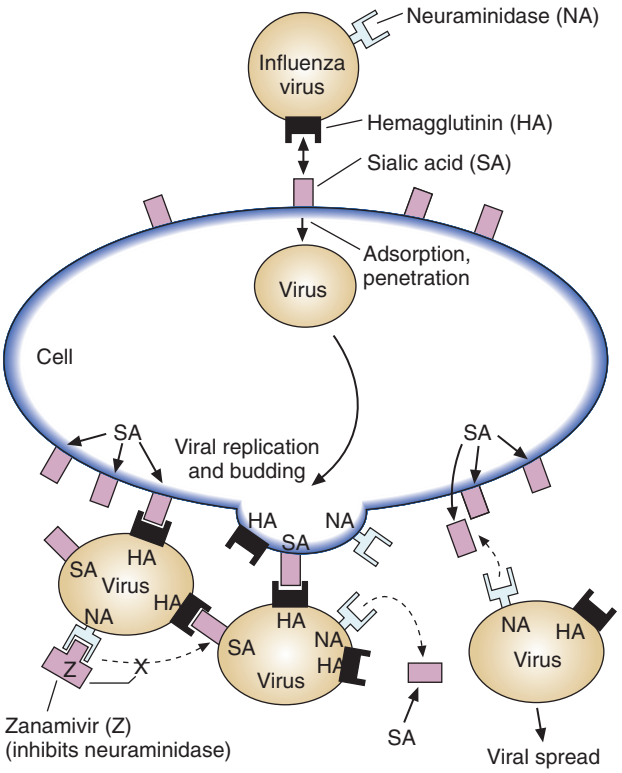

Fig. 36.8 Mechansim of action by which inhaled zanamivir exerts an antiviral effect on influenza virus. Zanamivir is a sialic acid analogue and binds to neuraminidase, the enzyme responsible for cleaving sialic acid and preventing viral binding to sialic acid. This causes viral aggregation, with binding of viral particles to each other and to the host cell, thus preventing viral spread. (From Gardenhire DS: *Rau's Respiratory Care Pharmacology*, ed 10, St. Louis, 2020, Elsevier.)

Adverse Effects

Several adverse effects can occur with inhaled zanamivir:

- Bronchospasm and deterioration in lung function, especially in patients with COPD or asthma
- Possible undertreatment of bacterial infection masquerading as a viral infection or a secondary bacterial infection in the presence of influenza
- Allergic reactions, as may occur with any drug
- Adverse reactions, such as diarrhea, nausea, vomiting, bronchitis, cough, sinusitis, dizziness, and headaches

Because of the effect on lung function in patients with respiratory disease and reports of adverse reactions, revised labeling for the drug carries a warning that zanamivir is not generally recommended for patients with underlying airways disease.[45,46]

Clinical Efficacy

In studies of clinical efficacy, the use of zanamivir resulted in shortening of the median time to alleviation of symptoms by 1 day. In subjects who began treatment within 30 hours of illness, the median time to alleviation of symptoms was reduced by approximately 3 days.[46] Zanamivir is not approved for prophylaxis of influenza, although some data suggest a preventive effect in patients exposed to influenza virus.[46] Cost-versus-efficacy issues revolve around the modest reduction in symptoms and inability to confirm the presence of influenza quickly, easily, and inexpensively as the basis for the drug treatment.

Assessment

- Assess improvement in influenza symptoms, including fever reduction, less myalgia and headache, reduced coughing and sore throat, and less systemic fatigue.
- Patients should be monitored for airway irritation and symptoms of bronchospasm, especially during initial use of the dry-powder aerosol. Provide a short-acting β agonist if needed or if the patient is at risk for airway reactivity (COPD, asthma).

INHALED PULMONARY VASODILATORS

The use of nitric oxide gas to treat neonates with persistent pulmonary hypertension is approved by the FDA and is discussed in detail in Chapters 42 and 54. In addition to this medical gas, inhaled medications are being tested and used to treat pulmonary hypertension. Several such agents are being studied, including epoprostenol (Flolan, Veletri)[47] and alprostadil (Prostin VR

Pediatric); however, only two, iloprost and treprostinil, are approved by the FDA for widespread use.

Nitric Oxide

Indications for Use

INOmax (nitric oxide) is indicated in the treatment of neonates greater than 34 weeks of gestational age with hypoxic respiratory failure.[48] INOmax should be delivered utilizing the company's delivery system with infrared technology (DS_{ir}). Nitric oxide is described in more detail in Chapters 42 and 54.

Iloprost

Indications for Use

Iloprost (Ventavis) inhalation is indicated for the treatment of pulmonary hypertension.[49] Iloprost inhalation is administered with the I-neb nebulizer.

Mechanism of Action

Iloprost is a synthetic analogue of prostacyclin (PGI_2). This agent dilates pulmonary arterial vascular beds and affects platelet aggregation. It is unknown whether platelet aggregation plays a role in the treatment of pulmonary hypertension.

Adverse Effects

Syncope and pulmonary edema may occur secondary to the vasodilatory properties of iloprost. During the 12-week clinical trial, headache and increased cough were the most noted adverse reactions.

Treprostinil

Indication for Use

Treprostinil (Tyvaso) is indicated for the treatment of pulmonary arterial hypertension to increase walking distance in patients with New York Heart Association class III symptoms.[50] It is administered using the Tyvaso Inhalation System, which is an ultrasonic pulsed-delivery device.

Mechanism of Action

Treprostinil is a prostacyclin analogue that causes vasodilation of the pulmonary and systemic arterial vascular beds and inhibits platelet aggregation. Treprostinil is available in a 2.9-mL ampule, which contains 1.74 mg of treprostinil (0.6 mg/mL). It is provided as an aerosol in the Tyvaso Inhalation System.

Adverse Effects

Treprostinil has not been studied in patients with underlying lung disease (e.g., asthma, COPD). Treprostinil may cause bronchospasm. This agent should not be mixed with any other agents.

SUMMARY CHECKLIST

- Orally inhaled aerosol drug classes include β-agonist bronchodilators, anticholinergic (antimuscarinic) bronchodilators, mucolytics, corticosteroids, nonsteroidal antiasthma drugs, antiinfective agents, and anti–pulmonary hypertension agents.
- β-agonist and anticholinergic bronchodilators are used to reverse or improve airflow obstruction; mucolytics are used to reduce mucus viscosity and improve mucociliary clearance; corticosteroids and nonsteroidal antiasthma agents are used to reduce or prevent airway inflammation in asthma; the antiinfective agent pentamidine is used to treat PJP, especially in patients with acquired immunodeficiency syndrome; ribavirin is used to treat RSV infection in at-risk infants and children; inhaled tobramycin and aztreonam are used in patients with CF to prevent or manage gram-negative *Pseudomonas* infections; and inhaled zanamivir is used to treat acute influenza.
- All aerosol treatments are assessed immediately by monitoring respiratory vital signs, which include respiratory rate and pattern, pulse, breath sounds on auscultation, general patient appearance (e.g., color, diaphoresis), and patient report of subjective reaction (e.g., chest tightness). Additional assessment should be related to the indication for the drug (e.g., monitoring of peak flow rates or bedside spirometry with bronchodilator use; frequency of exacerbation or β-agonist use with inhaled corticosteroids in asthma).
- Each class of aerosol drug has its own mechanism of action. Practitioners should be familiar with how agents they administer work. Common side effects with each class of drug include tremor and shakiness with β-agonists, dry mouth with anticholinergic agents, bronchial irritation with acetylcysteine, dysphonia and voice changes with dornase alfa, and oral fungal infections with corticosteroids.
- Agents used in asthma that provide quick relief include short-acting β agonists (albuterol, levalbuterol) and anticholinergic bronchodilators. Agents that provide long-term control include LABAs (salmeterol, formoterol, arformoterol, indacaterol, olodaterol, vilanterol), inhaled corticosteroids, and nonsteroidal antiasthma drugs (cromolyn, montelukast, and other leukotriene antagonists). Systemic corticosteroids are used for both quick relief (intravenously) and long-term control (orally).
- Newer inhaled medications within a class known as *aerosolized prostacyclins* are being introduced to help treat pulmonary hypertension. Several agents are being studied, including epoprostenol (Flolan, Veletri) and alprostadil (Prostin VR Pediatric); however, only treprostinil (Tyvaso) and iloprost (Ventavis) are approved by the FDA for use in aerosols

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37

Airway Management

Carolyn J. La Vita

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Describe how to perform endotracheal and nasotracheal suctioning safely.
- Describe how to obtain sputum samples properly.
- Assess the need for and select an artificial airway.
- Identify the complications and hazards associated with insertion of artificial airways.
- Describe how to perform orotracheal and nasotracheal intubation of an adult.
- Assess and confirm proper endotracheal tube placement.
- Describe how to use alternative airway appliances.
- Describe the rationale and the methods for performing a tracheotomy.
- Identify the types of damage that artificial airways can cause.
- Describe how to maintain and troubleshoot artificial airways properly.
- Describe techniques for measuring and adjusting tracheal tube cuff pressures.
- Identify when and how to extubate or decannulate a patient.

CHAPTER OUTLINE

KEY TERMS

decannulation
endotracheal tubes
extubation
fenestrated
intubation
laryngectomy
obturator
pharyngeal airways
radiopaque
stenosis
suctioning
tracheoesophageal fistula
tracheoinnominate artery fistula
tracheomalacia
tracheostomy
tracheostomy tubes
tracheotomy

Respiratory therapists (RTs) are an important part of the health-care team whose aim is to optimize patient ventilation and gas exchange. Because adequate ventilation and gas exchange are impossible without a patent airway, RTs often assume responsibility for airway management of patients in both the acute care and the post–acute care settings. RTs must develop skills in three broad areas of airway care. First, the RT must be proficient in airway clearance techniques, including methods designed to ensure the patency of the patient's natural or artificial airway. Second, the RT must be able to insert and maintain artificial airways designed to support patients whose own natural airways are inadequate. Third, the RT must be able to assist physicians in performing special procedures related to airway management. This chapter explores each of these areas.

SUCTIONING

Airway obstruction can be caused by retained secretions, foreign bodies, and structural changes such as edema, tumors, or trauma. Retained secretions increase airway resistance and the work of breathing and can cause hypoxemia, hypercapnia, atelectasis, and infection. Difficulty in clearing secretions may be due to the thickness or amount of the secretions or to the patient's inability to generate an effective cough.

RTs can remove retained secretions or other semiliquid fluids from the airways by suctioning. **Suctioning** is the application of negative pressure (vacuum) to the airways through a collecting tube (flexible catheter or suction tip). Removal of foreign bodies, secretions, or tissue masses beyond the mainstem bronchi requires bronchoscopy, which is generally performed by a physician; however, an increasing number of centers have trained RTs to perform therapeutic bronchoscopy. RTs often assist physicians in performing bronchoscopy (refer to Chapter 22). Other suctioning adjuncts include mechanical in-exsufflation, chest physiotherapy, and positive expiratory pressure (PEP) therapy are discussed in Chapter 44. These techniques raise secretions from lung periphery and small airways to large airways, allowing for removal via suctioning.

Suctioning can be performed by way of either the upper airway (oropharynx) or the lower airway (trachea and bronchi). Secretions or fluids also can be removed from the oropharynx by using a rigid tonsillar or Yankauer suction tip (Fig. 37.1). Access to the lower airway is by introduction of a flexible suction catheter (Fig. 37.2) through the nose (nasotracheal suctioning) or artificial airway (endotracheal suctioning). Tracheal suctioning through the mouth should be avoided because it causes gagging.

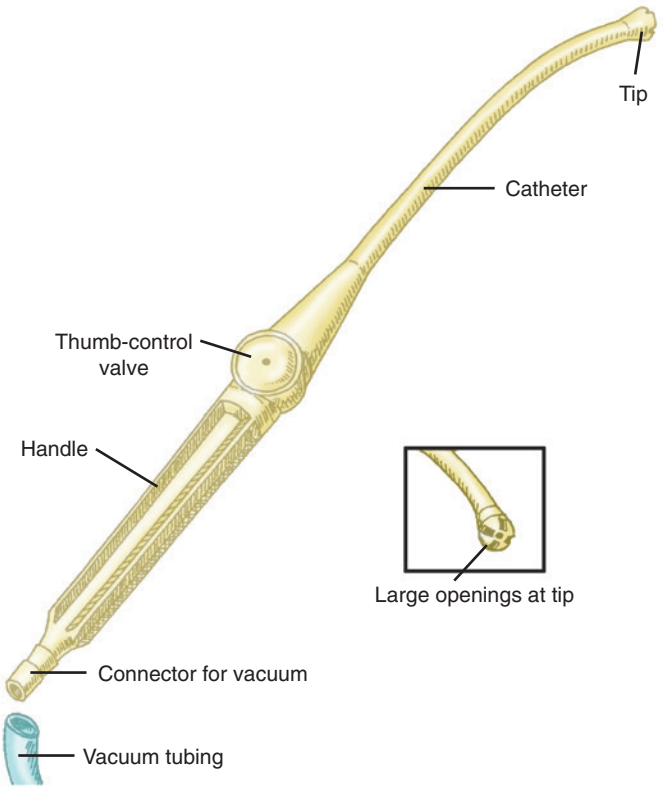

Fig. 37.1 Rigid tonsillar, or yankauer, suction tip. (Modified from Sills JR: *The comprehensive respiratory therapist exam review, entry and advanced levels*, ed 5, St. Louis, 2010, Mosby.)

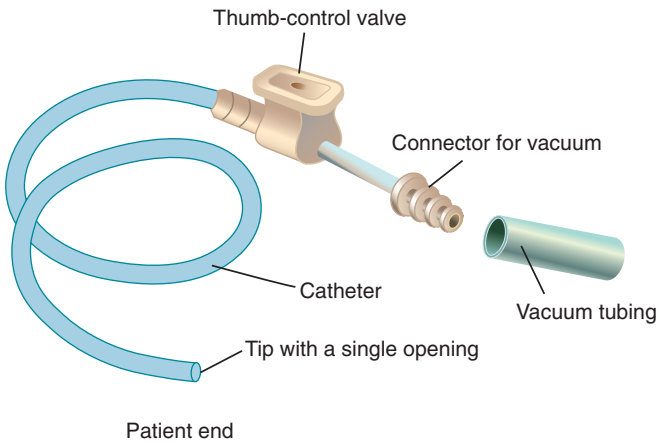

Fig. 37.2 Flexible suction catheter for lower airway suctioning.

Endotracheal Suctioning

Equipment and Procedure

There are two techniques for endotracheal suctioning: open and closed. The open, sterile technique requires disconnecting the patient from the ventilator. This technique is often used when the patient with a tracheostomy is receiving humidified gas via tracheostomy collar and not receiving mechanical ventilation support. The closed technique uses a sterile, closed, in-line suction catheter that is attached to the ventilator circuit so that the suction catheter can be advanced into the patient's endotracheal airway without disconnecting the patient from the ventilator.

There are also two methods of suctioning based on how deep the suction catheter is inserted in the artificial airway: deep suctioning and shallow suctioning. Deep suctioning is when the catheter is inserted until resistance is met and then withdrawn approximately 1 cm before applying suction. Shallow suctioning is when the catheter is advanced to a predetermined depth, which is usually the length of the airway plus the adapter.[1] Using shallow suctioning rather than deep suctioning is recommended in infants and children,[2] and in adults the use of deep tracheal suctioning is being questioned because of its effects on lung volume and oxyhemoglobin saturation.

Step 1: Assess Patient for Indications.

In general, a patient should never be suctioned according to a preset schedule. Although very thick secretions may not move with airflow and may not create any adventitious sounds, the patient should be assessed for clinical indicators, such as rhonchi heard on auscultation, which suggest the need for suctioning. Suctioning done with lack of clinical indication can lead to unnecessary complications including hypoxemia, bronchospasm, mucosal irritation, and patient discomfort.

Step 2: Assemble and Check Equipment.

The equipment needed for endotracheal suctioning is listed in Box 37.1. The suction catheter, gloves, and cup are often prepackaged together in disposable sterile kits for use during

BOX 37.1 Equipment Needed for Suctioning

- Vacuum source
- Calibrated, adjustable regulator
- Collection bottle and connecting tubing
- Disposable gloves: sterile (open suction) or clean (closed suction)
- Sterile suction catheter
- Sterile water and cup (open suction), if needed to clear catheter
- Goggles, mask, and other appropriate equipment for standard precautions
- Oxygen (O_2) source with a calibrated flowmeter (open suction) or ventilator (closed suction)
- Pulse oximeter
- Manual resuscitation bag equipped with O_2-enrichment device for emergency backup use
- Stethoscope

Optional Equipment

- Electrocardiograph
- Sterile sputum trap for culture specimen

MINI CLINI

Indication for Endotracheal Suctioning

Problem

The respiratory therapist is called to the bedside to assess an adult patient exhibiting moderate respiratory distress, with respiratory rate of 32 breaths per minute, heart rate of 115 beats per minute, and O_2 saturation (SpO_2) of 91%. The patient has amyotrophic lateral sclerosis (ALS) and underwent tracheostomy tube placement to aid in secretion clearance. Upon assessing bilateral breath sounds, the RT notes the patient has rhonchorous breath sounds throughout the left lung and absent breath sounds in the right lung. The most recent chest x-ray demonstrates complete opacification of the right hemithorax. The care team asks for the RTs clinical assessment.

Discussion

Coarse rhonchi indicate airflow through retained secretions. Absent breath sounds with complete opacification on chest x-ray in a patient with an impaired cough could indicate a mucus plug in the mainstem bronchus and is likely the reason for the increased work of breathing. The RT should increase the FiO_2, suction the patient, and suggest a trial of cough assist for prevention of additional problems. If no clinical improvement is seen, the RT could suggest a flexible bronchoscopy to remove the secretions.

the open suctioning technique. Suction pressure should always be checked by occluding the end of the suction tubing before attaching the suction catheter. The suction pressure should be set at the lowest effective level. Negative pressures of 80 to 100 mm Hg in neonates and less than 150 mm Hg in adults are generally recommended.[3]

Suction catheters are available in various designs, most with side ports to minimize mucosal damage. Most suction catheters for adult are 22 inches long (sufficient to reach the main stem bronchi) and sized in French units (external circumference). A curved-tip catheter, or catheter coudé, is available to help direct access to the left mainstem bronchus. The size of the catheter may be more important than its design. A catheter that is too large can obstruct part or all of the airway by occupying too much of its opening. Too large a suction catheter combined with negative pressure quickly evacuates lung volume and can cause atelectasis and hypoxemia. To avoid this problem, the diameter of the catheter should be less than 50% of the internal diameter of the artificial airway in adults.[4,5] In infants and small children, the diameter of the suction catheter should be less than 70% of the internal diameter of the artificial airway.[6]

RULE OF THUMB To estimate quickly the proper size of suction catheter to use with a given tracheal tube, first multiply the tube's inner diameter by 2. Then use the next smallest size catheter.

Example: 6-mm endotracheal tube: 2×6 = 12;
next smallest catheter is 10 F

Example: 8-mm endotracheal tube: 2×8 = 16;
next smallest catheter is 14 F

An in-line suction catheter can be used for patients receiving ventilatory support (Fig. 37.3) and is recommended over open suction because ventilation is continued during suctioning regardless of the level of ventilatory support provided.[7-10] These systems are incorporated directly into the ventilator circuit and used repeatedly. In addition, cross contamination is less likely with in-line catheter systems. The use of in-line suction catheters is cost-effective because they need to be changed only if soiled or malfunctioning and not on a daily basis.[11] However, in-line suction catheters have no effect on risk for ventilator-associated pneumonia (VAP).[12] The extra weight an in-line catheter adds to a ventilator circuit may increase tension on the endotracheal tube (ETT), so care should be taken to support the ventilator tubing appropriately.

Basic indications for the use of closed suction catheters are listed in Box 37.2.[13] Routine instillation of sterile normal saline to aid secretion removal before suctioning is not recommended because there is no evidence that this practice is beneficial, and it may increase infection risk and destabilize the patient. If the secretions are extremely tenacious, instillation of acetylcysteine or sodium bicarbonate (2%) may be more effective than normal saline; this generally requires a physician's order. The use of these medications is discussed in more detail in Chapter 36.

After connecting the catheter to the suction source, the level of suction pressure should be checked by closing the catheter thumb port and aspirating some sterile water or saline from the basin. If no vacuum is generated, it is necessary to check for leaks in the tubing, at the collection container, or at the suction regulator. In addition, if the collecting bottle is full, the float-valve closes and prevents vacuum transmission.

RULE OF THUMB Set suction pressure 120–150 mm Hg for adults, 100–120 mm Hg for children, and 80–100 mm Hg for infants.

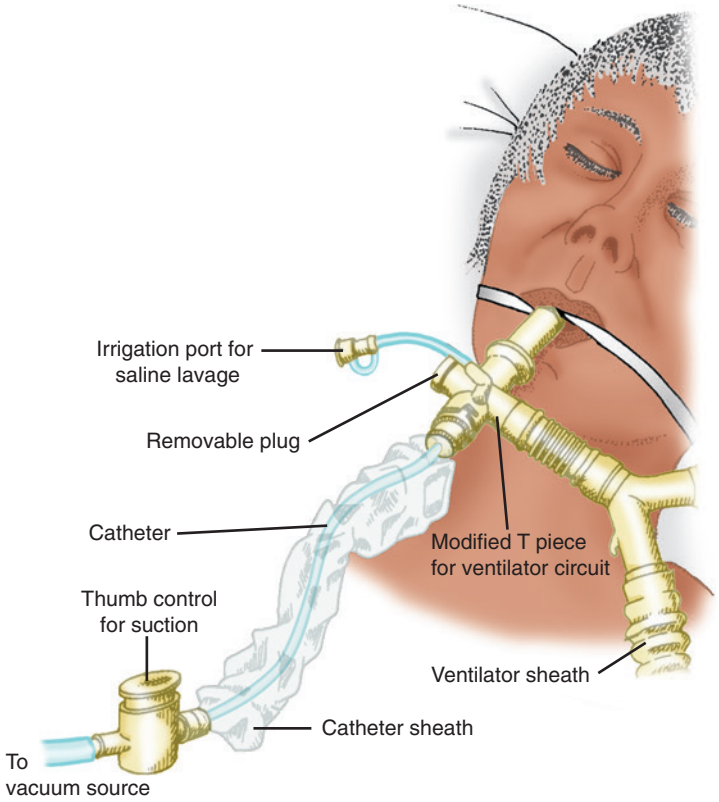

Fig. 37.3 In-line, closed-system multiuse suction catheter. (Modified from Sills JR: *The comprehensive respiratory therapist exam review, entry and advanced levels*, ed 5, St. Louis, 2010, Mosby.)

BOX 37.2 Indications for Use of Closed Suctioning Technique

Mechanically ventilated patients, especially neonates and patients with:

- Positive end expiratory pressure ≥10 cm H_2O
- Mean airway pressure ≥20 cm H_2O
- Inspiratory time ≥1.5 s
- FiO_2 ≥0.60
- Frequent suctioning (≥6 times/day)
- Hemodynamic instability associated with ventilator disconnection
- Respiratory infections requiring airborne or droplet precautions (see Chapter 4)
- Inhaled agents that cannot be interrupted by ventilator disconnection (e.g., nitric oxide, helium/oxygen mixture)

Step 3: Assess Patient for Hyperoxygenation.
Before suctioning, delivery of 100% oxygen (O_2) for 30 to 60 seconds to pediatric and adult patients is suggested, especially to patients who are at risk for hypoxemia.[14] In addition, the O_2 concentration should be increased by 10% in neonates before suctioning[15]; this may be done by increasing the set FiO_2 or activating the temporary 100% setting on microprocessor ventilators. Manual ventilation before suctioning is not recommended since derecruitment occurs whenever the ventilator is disconnected from the patient and high pressure is normally applied to the airway potentially causing lung injury.[16] However, if there is no other alternative to hyperoxygenating the patient, positive end-expiratory pressure (PEEP) should be maintained by adding a PEEP valve to the manual resuscitator during manual ventilation with 100% O_2.

Step 4: Insert Catheter.
To prevent tracheal mucosal trauma, especially in infants, the shallow suction method should be used, advancing the catheter just to the end of the artificial airway.

Step 5: Apply Suction and Clear Catheter.
Suction is applied while withdrawing the catheter. Total suction time should be kept to less than 15 seconds.[17,18] After removing the catheter, it should be cleared using sterile water or saline. The closed suction catheter has an adapter for saline vials to be placed in line with the device. The catheter is cleared by squeezing the saline vial and applying suction at the same time. Caution must be used to ensure that saline is being drawn into the catheter and not entering the airway. If any untoward response occurs during suctioning, the catheter should be immediately removed and the patient should be oxygenated.

Step 6: Reoxygenate Patient.
The patient should be hyperoxygenated by the same method used in Step 3 for at least 1 minute. Routine hyperventilation is not recommended. If there are indications of derecruitment, lung recruitment maneuvers may be used.

Step 7: Monitor Patient and Assess Outcomes.
Steps 3 through 7 are repeated as needed until improvement is seen or an adverse response is observed. Any necessary corrective steps should be taken.

Minimizing Complications and Adverse Responses

Careful adherence to procedure is the best way to avoid or minimize complications of endotracheal suctioning. Potential complications are as follows:

- Hypoxemia
  - Minimized by preoxygenating the patient, preferably without disconnecting patient from the ventilator.[19]
  - Minimized by using closed suction technique, especially in neonates and adults requiring high FiO_2 or PEEP, or both or at risk for lung derecruitment.
- Cardiac dysrhythmias
  - Bradycardia may occur secondary to vagal nerve stimulation.
  - Tachycardia may occur as a result of agitation and/or hypoxemia.
  - If either occurs, stop suctioning, administer O_2 and ventilation.
- Hypotension or hypertension
  - May occur as a result of cardiac dysrhythmia, hypoxemia, anxiety, stress, pain, or coughing.
  - If either occurs, stop suctioning, administer O_2 and ventilation.
- Atelectasis (collapse of alveoli)/lung derecruitment
  - Limit amount of negative suction pressure used (see Rule of Thumb).
  - Keep duration of suctioning less than 15 seconds.
  - Use appropriate-size catheter (see Rule of Thumb).
  - Avoid disconnection from ventilator by using closed suction technique, especially in neonates and adults who require high FiO_2 or PEEP.
- Mucosal trauma
  - Limit amount of negative suction pressure used (see Rule of Thumb).
  - Use shallow suctioning method.
- Increased intracranial pressure (ICP)
  - Usually transient and returns to baseline within 1 minute.
  - For patients who already have increased ICP, administer aerosolized topical anesthetic (lidocaine) 15 minutes before suction to minimize cough, discomfort, and increased ICP.[20]
- Bacterial colonization of lower airway
  - Use sterile technique during open suctioning.
  - Do not routinely instill normal saline; only instill normal saline to help mobilize very thick secretions.
  - Use closed suction technique to avoid disconnection from ventilator.

RULE OF THUMB To minimize hypoxemia and lung derecruitment when suctioning a mechanically ventilated patient, preoxygenate and suction the artificial airway with a closed-system in-line catheter to avoid disconnecting the patient from the ventilator.

Nasotracheal Suctioning

Nasotracheal suctioning is indicated for patients who have retained secretions but do not have an artificial airway. The nasal passages are highly vascularized. Mucosal trauma and bleeding can occur with repeated suctioning, adding to difficulty managing secretions. The use of soft suction catheters and/or a nasopharyngeal airway/trumpet is recommended to prevent these complications.

MINI CLINI

Suctioning Complications

Problem

A patient in the intensive care unit is intubated following a cardiac arrest. The RT notices the patient coughing and attempts to suction the ETT using a closed suction catheter system and the deep method. When the RT meets resistance, the patient's heart rate precipitously drops, oxygen saturation decreases, and blood tinged secretions are noted in the catheter.

Discussion

This patient's cardiac status is tenuous, and the bradycardia is likely a result of stimulation of the vagus nerve. The hypoxemia is most likely due to alveolar derecruitment and/or decreased perfusion. Blood-tinged secretions can be a result of mucosal trauma. To minimize these complications, the RT should consider using the shallow suction method, limiting the suction duration and suction pressure used, and preoxygenating the patient before the procedure.

Equipment and Procedure

The equipment and procedure for nasotracheal suctioning are similar to the equipment and procedure for endotracheal suctioning. Only the key differences are highlighted here. In addition to the equipment and supplies used for endotracheal suctioning (see Box 37.1), sterile water-soluble lubricating jelly is needed to aid catheter passage through the nose. Use of a nasopharyngeal airway should be considered to help reduce mucosal trauma in the nose of patients who require repeated, long-term nasotracheal suctioning.

The key aspect of the nasotracheal suctioning procedure is catheter insertion. After lubricating the catheter, the RT inserts it gently through the nostril, directing it toward the septum and floor of the nasal cavity without applying negative pressure. The catheter is gently twisted if any resistance in the nose is felt. If twisting does not help, the catheter is withdrawn and inserted through the other nostril.

As the catheter enters the lower pharynx, the patient should assume a "sniffing" position (Fig. 37.4). This position helps to align the opening of the larynx with the lower pharynx, making catheter passage through the larynx more likely. The catheter is continually advanced until the patient coughs or a resistance is felt.

Minimizing Complications and Adverse Responses

Complications of nasotracheal suctioning are as follows:

- Gagging and/or regurgitation
  - To minimize this risk, avoid suctioning soon after a meal or tube feeding; coordinate with nurse.
  - If this occurs, reposition patient and suction oropharynx if necessary.
- Airway trauma (bleeding)
  - To avoid, before suctioning, assess patient for any bleeding disorder (check platelet count and/or bleeding studies and anticoagulation medications).

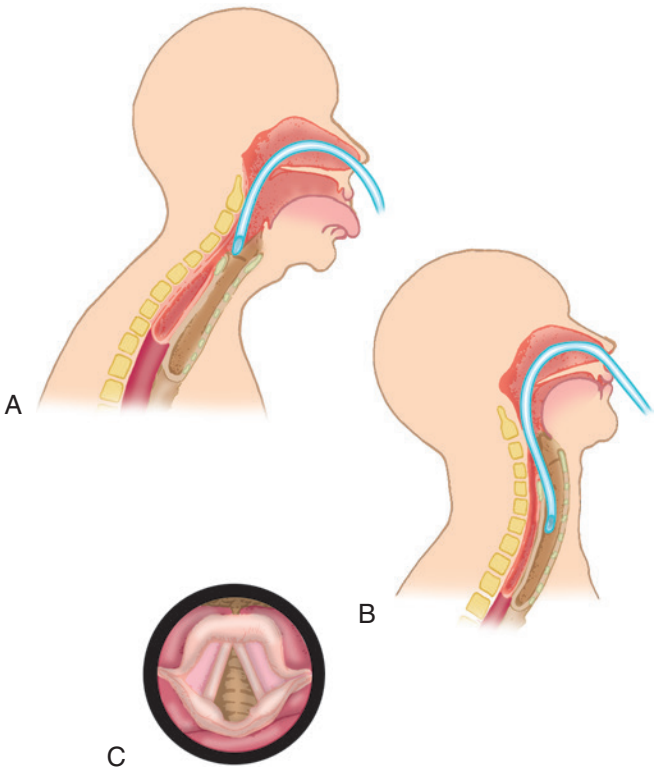

Fig. 37.4 Nasotracheal Suctioning Technique. (A) Optimal position of the head to insert catheter into the trachea. The neck is flexed, and the head is extended. The tongue is protruded (and held by a 4 × 4 gauze pad). (B) After catheter has advanced into the trachea, the tongue is released, and the patient's head is allowed to assume a comfortable position. (C) View of vocal cords from above. The cords are most widely separated during inspiration. (Modified from Sanderson RG: *The cardiac patient: a comprehensive approach*, Philadelphia, 1972, Saunders.)

  - To minimize, do not use excessive force when advancing catheter.
  - To minimize, lubricate catheter.
  - To minimize, use nasopharyngeal airway or soft suction catheters to protect nasal mucosa.
- Contamination of the lungs
  - Immunosuppressed patients are especially at risk.
  - To avoid, use sterile technique and gentle insertion of catheter.
- Bronchospasm or laryngospasm
  - These incidents may be stimulated by the catheter in the lower airway.
  - Patients with hyperactive airway disease are especially at risk.
  - If these occur, stop suctioning and administer aerosolized bronchodilator if needed.

RULE OF THUMB A nasopharyngeal airway may be left in the patient's nares to prevent mucosal trauma from repeated suctioning.

Sputum Sampling

Sputum samples are often collected to identify organisms infecting the airway. To obtain the sample, the suctioning procedures described previously should be followed. In addition to the usual equipment, a sterile specimen container is needed. This device consists of a plastic tube or cup with flexible tubing on one end to attach to the suction catheter. The other outlet is a stiff plastic nozzle that connects to the suction tubing from the wall vacuum unit (Fig. 37.5).

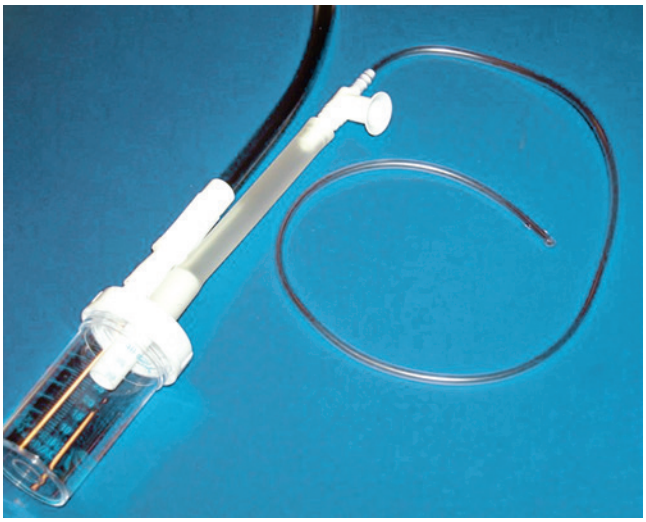

Fig. 37.5 Specimen container placement between the suction catheter and wall suction source.

It is important to maintain sterile technique when touching the connection points on the trap. If a closed suction system is being used, a new catheter should be placed just before suctioning the patient for the sample. When an adequate sample is obtained, the container is removed from the suction catheter and suction tubing. The flexible tubing on the container is attached to the open nozzle; this creates a closed container. The container should be labeled according to hospital or facility policy. The suctioning procedure is completed as previously described.

ESTABLISHING AN ARTIFICIAL AIRWAY

Routes

Artificial airways are inserted for various reasons and involve varying degrees of invasion into the upper airway. **Pharyngeal airways** extend only into the pharynx. Artificial airways that are placed through the mouth or nose into the trachea are called **endotracheal tubes (ETTs)**. The process of placing an artificial airway into the trachea is referred to as **intubation.** When the ETT is passed through the nose first, the procedure is referred to as *nasotracheal intubation*. When the tube is passed through the mouth on its way into the trachea, the procedure is called *orotracheal intubation*.

Pharyngeal Airways

Pharyngeal airways prevent airway obstruction by keeping the tongue pulled forward and away from the posterior pharynx. This type of obstruction is common in an unconscious patient as a result of a loss of muscle tone.

A *nasopharyngeal airway* (Fig. 37.6) is most often placed in a patient who requires frequent nasotracheal suctioning. Although

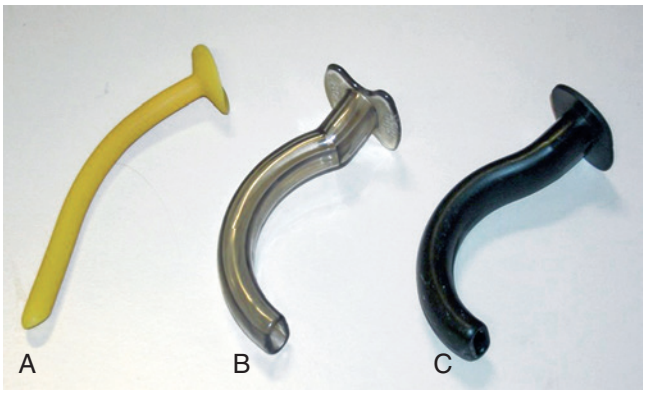

Fig. 37.6 Pharyngeal Airways. (A) Nasopharyngeal airway. (B and C) Oropharyngeal airways.

it does not ensure entry into the trachea, it minimizes damage to the nasal mucosa that can be caused by the suction catheter. A nasopharyngeal airway also may be placed in a patient who was recently extubated after facial surgery. The nasopharyngeal airway helps to maintain the patency of the upper airway despite swelling.

Oropharyngeal airways (see Fig. 37.6) are inserted into the mouth over the tongue. Use of oropharyngeal airways should be restricted to unconscious patients to avoid gagging and regurgitation. These airways maintain a patent airway when the tongue would otherwise obstruct the oropharynx. The airway also can be used as a bite block for patients with oral tubes.

Pharyngeal airways are used mainly in emergency life support. Further details on their use, insertion techniques, and size selection are provided in Chapter 38.

Tracheal Airways

Tracheal airways extend beyond the pharynx into the trachea. The two basic types of tracheal airways are *endotracheal (translaryngeal) tubes* and *tracheostomy tubes (TTs)*. ETTs are inserted through either the mouth or the nose (orotracheal or nasotracheal), through the larynx, and into the trachea. **Tracheostomy tubes** are inserted through a surgically created opening in the neck directly into the trachea. Table 37.1 summarizes the advantages and disadvantages of each of these three approaches.

Artificial Airways

Endotracheal Tubes

ETTs are semirigid tubes most often composed of polyvinyl chloride or related plastic polymers.[21] Fig. 37.7 shows a typical ETT, its key components, and a stylet used for insertion. The proximal end of the tube is attached to a standard adapter with a 15-mm external diameter. The curved body of the tube usually has length markings, indicating the distance (in centimeters) from the beveled tube tip. In addition to the beveled opening at the tip, there is a side port, or "Murphy eye," that ensures gas flow if the main port should become obstructed. The angle of the bevel minimizes mucosal trauma during insertion. The tube cuff is permanently bonded to the tube body. Inflation of the cuff seals off the lower airway, either for protection from gross aspiration or to provide positive pressure ventilation. A small

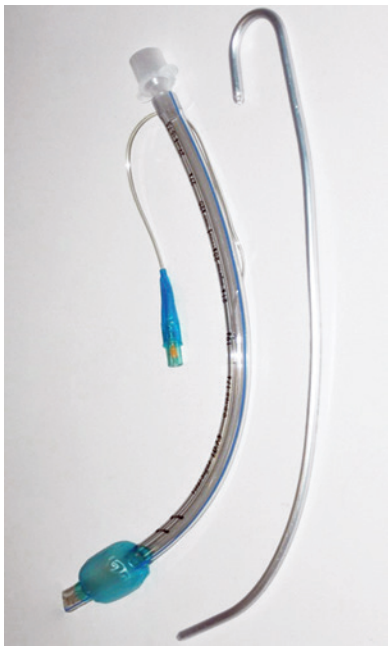

Fig. 37.7 Typical endotracheal tube and stylet.

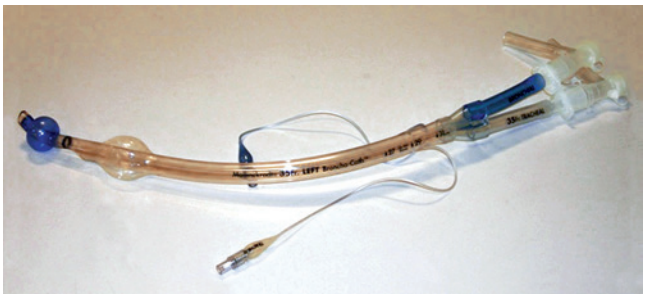

Fig. 37.8 Double-lumen endotracheal tube for independent lung ventilation.

filling tube leads from the cuff to a pilot balloon, used to monitor cuff status and pressure when the tube is in place. Finally, a valve with a standard connector for a syringe allows inflation and deflation of the cuff. Although not shown in Fig. 37.7, included with most modern ETTs is a **radiopaque** indicator that is embedded in the distal end of the tube body. This indicator allows for easy identification of tube position on chest x-ray.

Specialized endotracheal tubes. Some standard ETTs have been modified for specific uses, including special ventilation methods, lung pathologic conditions, and surgical procedures. Some more common tubes, including double-lumen tubes, tubes with special adapters for jet ventilation, tubes with subglottic suction ports, and laryngeal mask airways (LMAs), are discussed.[22] Advantages and disadvantages of the double-lumen tube and LMA are summarized in Table 37.2.

Special mechanical ventilation techniques may require unique types of ETTs. When unilateral lung disease occurs, independent lung ventilation may be needed. This ventilation requires the use of a double-lumen ETT (Fig. 37.8). This tube has two proximal ventilator connectors (15-mm adapter), two inner lumens for gas flow, two cuffs, and two distal openings. The larger cuff

TABLE 37.1 Advantages and Disadvantages of Tracheal Airway Routes

Route	Advantages	Disadvantages
Oral intubation	Insertion is faster, easier, less traumatic, and more comfortable	Esthetically displeasing, especially long term
	Larger tube is tolerated	Greater risk for self-extubation or inadvertent extubation
	Easier suctioning	Greater risk for main stem intubation
	Less airflow resistance	Risk of tube occlusion by biting or trismus
	Decreased work of breathing	Risk of injury to lips, teeth, tongue, palate, and oral soft tissues
	Easier passage of bronchoscope	
	Reduced risk for tube kinking	May require additional use of oral airway
	Avoidance of nasal and paranasal complications, including epistaxis and sinusitis	Great risk for retching, vomiting, and aspiration
		Pain and discomfort, especially with inadequate preparation
Nasal intubation	Less retching and gagging	Nasal and paranasal complications, including epistaxis, sinusitis, otitis
	Greater comfort in long-term use	
	Less salivation	More difficult to perform
	Improved ability to swallow oral secretions	Spontaneous breathing required for blind nasal intubation
	Improved communication	Smaller tube is necessary
	Improved mouth care and oral hygiene	Greater suctioning difficulty
	Avoidance of occlusion by biting or trismus	Increased airflow resistance
	Easier nursing care	Increased work of breathing
	Avoidance of oral route complications	Difficulty passing bronchoscope
	Less posterior laryngeal ulceration	Smaller risk for transient bacteremia
	Better tube anchoring, less chance of inadvertent extubation	
	Reduced risk for main stem intubation	
	Some patients can swallow liquids, providing a means of nutritional support	
	Blind nasal intubation does not require muscle relaxants or sedatives	
	May avert "crash" oral intubation	
Tracheotomy	Avoidance of laryngeal and upper airway complications of translaryngeal intubation	Greater expense
		Requirement for use of operating room in most cases
	Greater comfort	Need for general anesthesia in most cases
	Aids feeding, oral care, suctioning, speech	Permanent scar
	Psychologic benefit (improved motivation)	More severe complications
	Easier passage of flexible bronchoscope	Greater mortality rate
	Easier reinsertion	Delayed decannulation
	Esthetically less objectionable	Increased frequency of aspiration
	Facilitation of weaning from ventilator	Greater bacterial colonization rate
	Elimination of risk for main stem intubation	Persistent open stoma after decannulation, reducing cough efficiency
	Reduced work of breathing	
	Better anchoring (reduced risk for decannulation)	
	Improved ability to place curve-tipped suction catheter in left bronchus	
	Improved mobility (transfer out of intensive care unit to ward or extended-care facility)	

From Stauffer JL, Silvestri RC: Complications and consequences of endotracheal intubation and tracheostomy, *Respir Care* 27:417, 1982.

seals the tracheal lumen and allows gas to flow into one bronchus. The smaller cuff seals the opposite bronchial lumen (Fig. 37.9).

There are important points to consider when using double-lumen ETTs. These tubes are stiffer and bulkier to insert than standard tubes and must be rotated during insertion to align with the proper bronchus. Flexible bronchoscopy should be performed to ensure proper placement. The resistance to flow through each tube is increased because each lumen is smaller than the same-size single-lumen tubes. Tube position must also be regularly assessed.

The double-lumen airway (Combitube) is designed to be inserted blindly through the oropharynx and into the trachea or the esophagus (Fig. 37.10).[23] Its external design is similar to that of a double-lumen ETT with two external openings, two 15-mm adapters, two lumens, and two cuffs. One cuff seals the oropharynx. The second seals the trachea or the esophagus.

If the tube is placed into the esophagus and the cuffs are inflated, ventilation is accomplished by air passing through a series of holes in the area of the hypopharynx and into the trachea. The pharyngeal cuff prevents air from leaving through the mouth. The distal cuff in the esophagus helps to decrease regurgitation. If the tube is placed in the trachea, it functions like an ETT. To assess placement, the RT can manually ventilate through the external adapters and determine which gives the best breath sounds.

High-frequency jet ventilation uses a special ETT adapter (Fig. 37.11). This adapter replaces the standard ETT adapter. There is a jet port for the injection of high-flow pulses from the

TABLE 37.2 Advantages and Disadvantages of Alternatives to Endotracheal Intubation for Maintaining Upper Airway Patency

Device	Advantages	Disadvantages
Oral and nasal airways	Little training required	Does not guarantee airway patency
	No special equipment necessary	May worsen obstruction
	Inexpensive	Poorly tolerated by awake patient
	Can be quickly placed	Does not prevent aspiration
		Short-term use
		Does not facilitate positive pressure ventilation
Double-lumen airway (Combitube) placement	Less skill than bag-valve-mask or intubation	Difficulty distinguishing tracheal vs. esophageal insertion
	No special equipment necessary	Short-term use
	Protection against aspiration	Aspiration during removal
	Facilitates positive pressure ventilation	Cannot suction in esophageal position
		Only one size (adult)
		Potential for esophageal injury
Laryngeal mask airway (LMA)	Easy to insert	Short-term use
	No special equipment necessary	Aspiration not avoided
	Can intubate without removing LMA	Cannot provide high ventilation pressures if needed
	Avoids laryngeal and tracheal trauma	

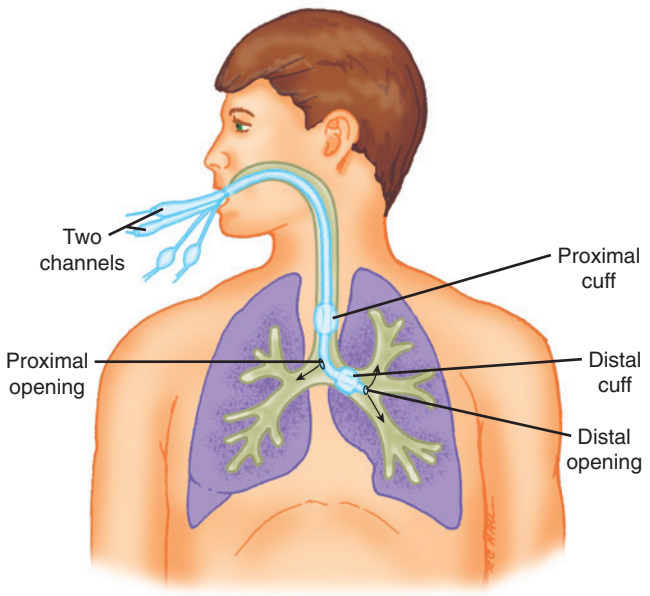

Fig. 37.9 Correct positioning of double-lumen endotracheal tube.

jet ventilator and a 15-mm connection for conventional ventilation. A pressure monitoring tube also is available for monitoring airway pressures.

A specialized ETT with a subglottic suction port has been designed to allow for removal of secretions that often accumulate above the cuff (Fig. 37.12). A separate channel in the wall of the tube attaches to a wall suction source. The suction source is run continuously at negative pressures of 20 to 30 cm H_2O or aspiration is preformed intermittently. Every 4 hours, a small amount of air should be injected into the suction port to ensure the port and tubing are not clogged. Due to the removal of subglottic secretions, use of this tube has been reported to decrease the incidence of VAP, in conjunction with head of bed elevation greater than 30 degrees, use of medications for stress ulcer prophylaxis, and timely removal of the artificial airway.[24,25]

The algorithm created by the American Society of Anesthesiologists for management of a difficult airway has been modified to show the various uses of the LMA.[26] The LMA consists of a short tube and a small mask that is inserted deep into the oropharynx (Fig. 37.13).[23,26] The open surface of the mask faces the laryngeal opening, and the tip of the mask is just above the esophageal sphincter. The short tube has a 15-mm adapter that can be connected to a manual resuscitator bag. A small tube is used to inflate a cuff when the device is in place. LMAs range in size from size 5 for adults to size 1 for infants.

Compared with bag and mask ventilation, a greater amount of ventilation is directed to the lungs by the LMA. The ease and speed of insertion offer an advantage over intubation when the intubator is inexperienced, the patient cannot be positioned for intubation, or the intubation is difficult.

The insertion of the LMA does not require any equipment (Fig. 37.14).[23] Before insertion, the posterior surface of the mask must be lubricated, and the cuff must be fully deflated. The index finger is used to guide insertion of the mask along the palate and down into the oropharynx. When the cuff is in place, it is inflated to a maximum of 60 cm H_2O. Inflation causes the mask to rise slightly out of the mouth.

Use of the LMA has two major limitations.[23] First, it cannot be used in a conscious or semicomatose patient because of stimulation of the gag reflex. Second, if ventilating pressures greater than 20 cm H_2O are needed, gastric distension may occur. This device does not protect against aspiration should regurgitation occur.

The classic LMA can be used to facilitate intubation because the opening faces the glottis. However, because of the small size of the ventilating tube on the mask, a small ETT is needed. A specially designed LMA with a small handle facilitates intubation (Fig. 37.15).

RULE OF THUMB The cuff on an LMA tube requires a large volume of air to inflate to 60 cm H_2O to seal the airway. The RT should be prepared with a large syringe when using this type of alternative airway.

Tracheostomy Tubes

TTs are generally made from polyvinyl chloride or silicone, although some are still made from metal.

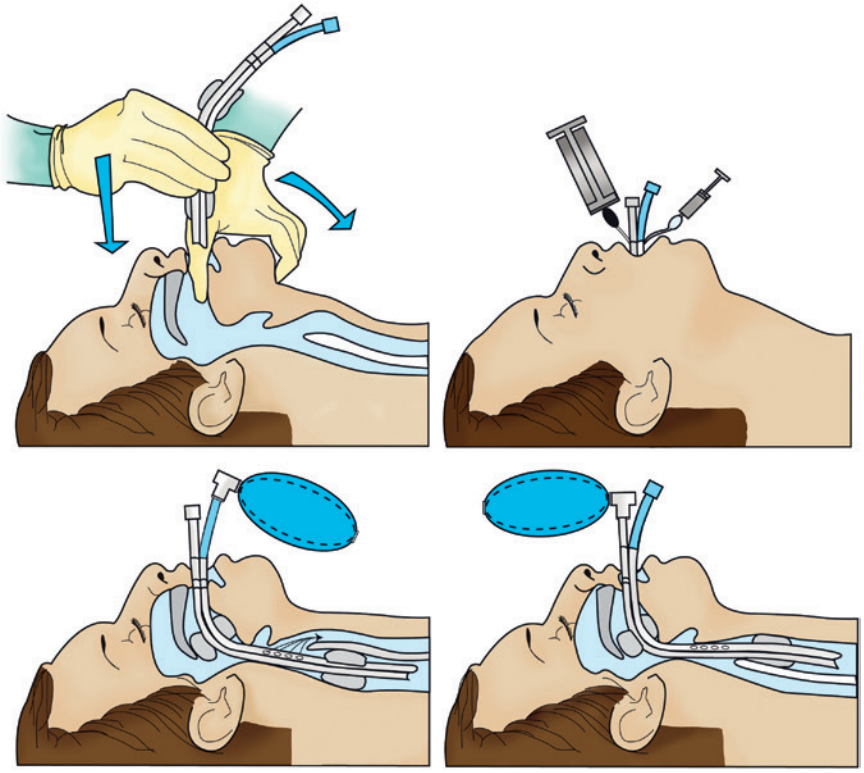

Fig. 37.10 Insertion of a double-lumen airway (combitube). (Modified from Cairo JM, Pilbeam SP: *Mosby's respiratory care equipment*, ed 8, St. Louis, 2010, Mosby.)

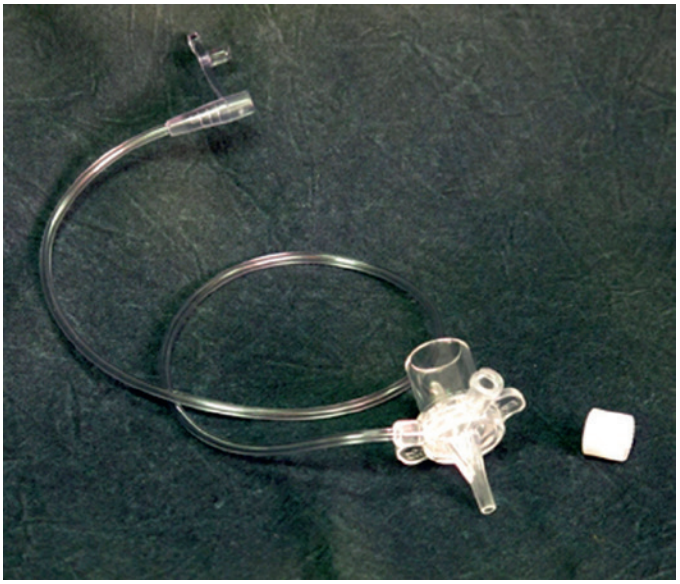

Fig. 37.11 Endotracheal tube adapter for jet ventilation. LifePort adapter. (Courtesy Bunnell Incorporated, Salt Lake City, Utah.)

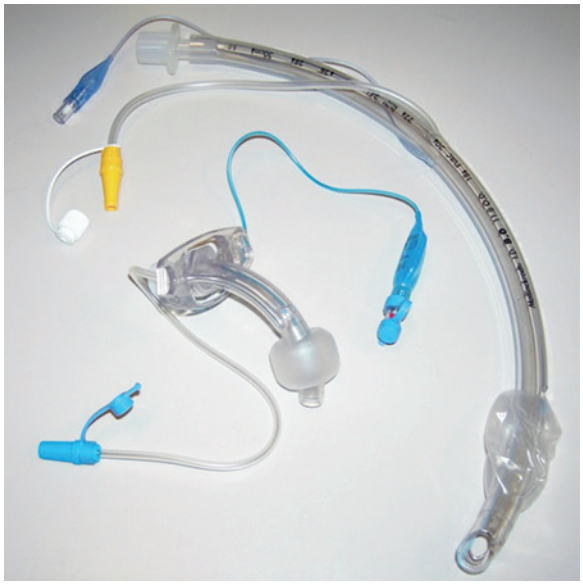

Fig. 37.12 Endotracheal and tracheostomy tubes with subglottic suction ports.

Fig. 37.16 shows a typical TT and its key components. The outer cannula forms the primary structural unit of the tube, to which the cuff and a flange are attached. The flange prevents tube slippage into the trachea and provides the means to secure the tube to the neck. There are single-cannula and double-cannula TTs. The double-cannula tube has a removable inner cannula with a standard 15-mm adapter. It is normally kept in place within the outer cannula. To prevent accidental removal, the inner cannula can be locked in place at the proximal end of the outer cannula. The inner cannula may be disposable or nondisposable. If the tube becomes occluded with very thick secretions or blood clots, the inner cannula can be easily removed and cleaned or replaced to establish a patent airway. This prevents emergently changing of the entire TT when obstructed. Double-cannula tubes are

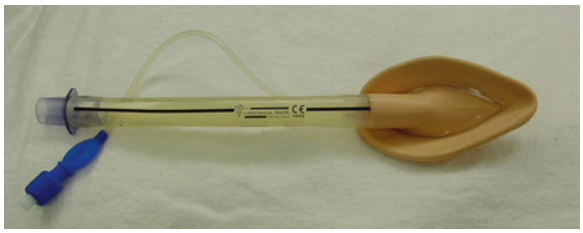

Fig. 37.13 Laryngeal mask airway. (From Gartsman G: *Shoulder arthroscopy*, ed 2, Philadelphia, 2009, Saunders.)

especially recommended for patients who are going home with a TT or in situations in which the humidity delivered to the airway is less than optimal. However, the inner cannula in some TTs can decrease the inner diameter of the tube, causing some patients to have difficulty breathing through the tube because of the increased airway resistance. In other double-cannula tubes the outer diameter is larger than the outer diameter of the same-size single-cannula tube. This can decrease the room around the tube with the cuff deflated so that a patient may not be able to

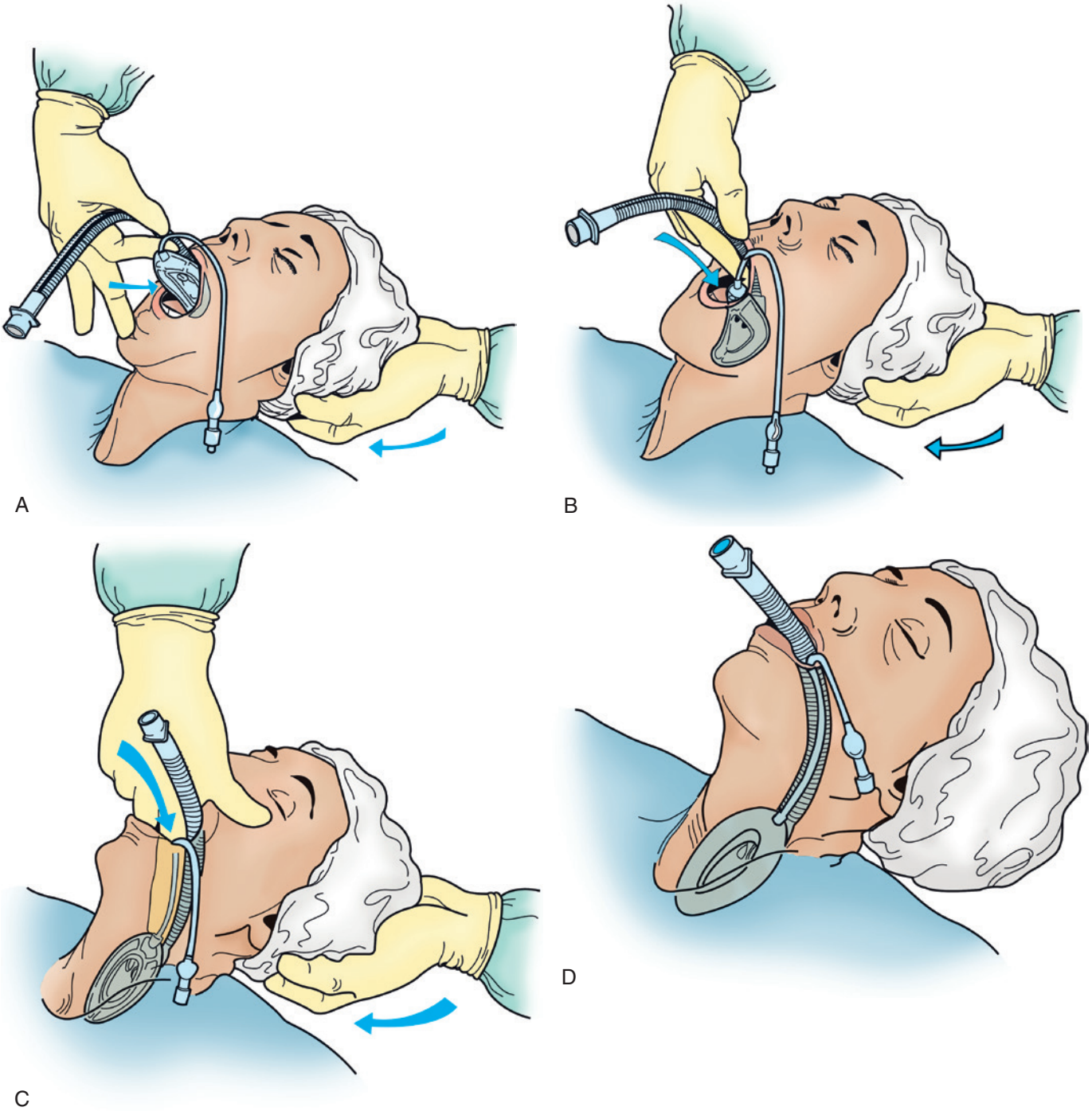

Fig. 37.14 **Insertion of Laryngeal Mask Airway.** (A) Initial positioning of the LMA. (B) Beginning of insertion using index finger as a guide. (C) Movement of the LMA to above the larynx. (D) Proper position of the LMA. (Modified from Cairo JM, Pilbeam SP: *Mosby's respiratory care equipment*, ed 8, St. Louis, 2010, Mosby.)

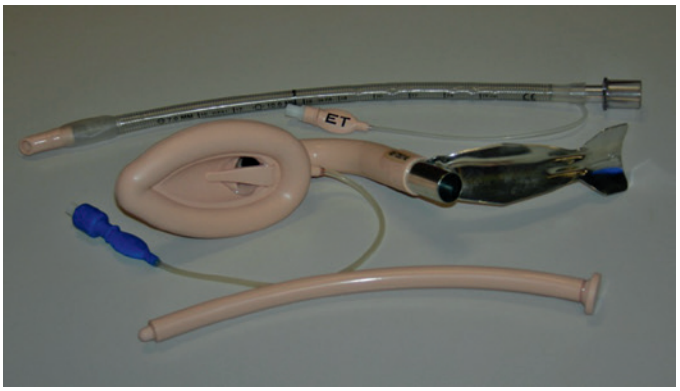

Fig. 37.15 Intubating laryngeal mask airway.

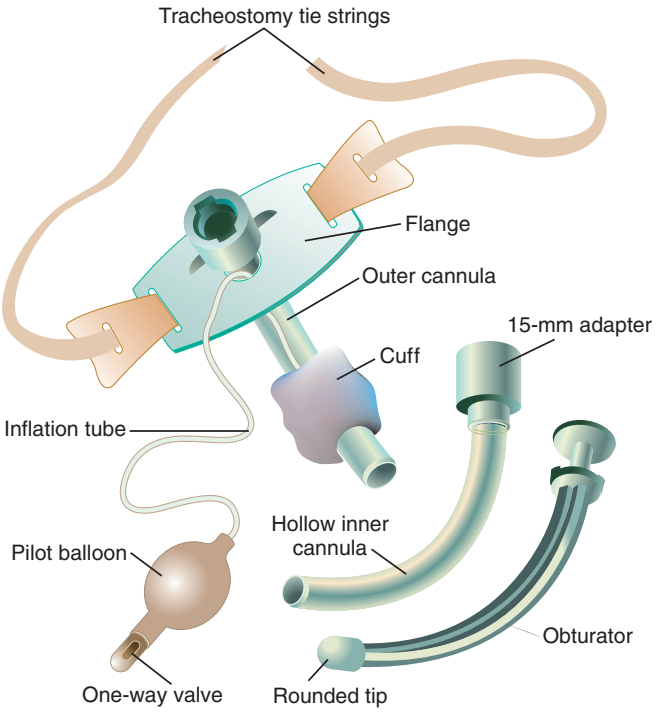

Fig. 37.16 Parts of a tracheostomy tube.

breathe around it with a speaking valve or cap on the tube. In this case the tube would need to be changed to a one with a smaller outer diameter.[27]

As with an ETT, an inflation tube leads from the cuff to a pilot balloon and valve. The tube is stabilized at the stoma site with cotton tape, which attaches to the flange and is tied around the neck or, more frequently, a soft TT holder with Velcro fasteners. An **obturator** with a rounded tip is used for tube insertion. Before insertion, the obturator is placed within the outer cannula, with its tip extending just beyond the far end of the tube; this minimizes mucosal trauma during insertion. Finally, as with ETTs, a radiopaque indicator in the distal end of the tube helps to confirm tube position on a chest x-ray.

As with ETTs, various modified TTs are available. Extra-long TTs may be used in patients who require extra proximal or distal length because of anatomic considerations, such as a thick neck. Some extra-long tubes have an adjustable flange so that the tube,

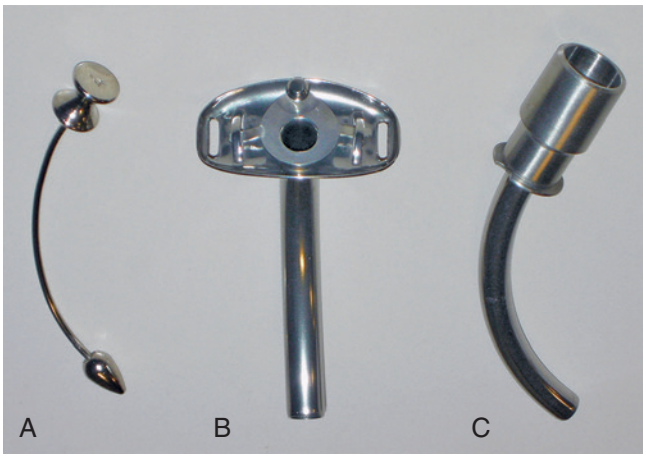

Fig. 37.17 Jackson Tracheostomy Tube Made From Stainless Steel. It has no cuff and no 15-mm adapter. (A) Obturator. (B) Outer cannula. (C) Inner cannula.

Fig. 37.18 Laryngectomy tubes.

under direct vision with a bronchoscope, can be placed past an abnormality in the trachea, such as a tumor or tracheal stenosis. Other modifications address cuff design. Cuffless TTs are used in patients without high risk of aspiration or need for mechanical support. These promote airflow over the vocal cords and increase speech. Tight-to-shaft (TTS) cuffs conform to the outer cannula of the TT when deflated. These are also used to aid in speech. The cuff material is more porous than a standard cuff, so must be filled with sterile water instead of air.

The metal Jackson TT is made of stainless steel with an inner and outer cannula (Fig. 37.17). There is no cuff at the distal end or 15-mm adapter at the proximal end. This TT is generally used in patients with a long-term need for an airway but who do not require a seal to protect the airway from aspiration or to facilitate positive pressure ventilation. If the patient requires manual ventilation, a 15-mm adapter should be inserted into the proximal opening. If the patient requires a sealed airway, the tube needs to be changed to the standard cuffed tube described earlier. A laryngectomy tube is a shorter tube without a cuff inserted into the stoma after a laryngectomy. The tube keeps the stoma open until it heals. There are several different types, some with a flange that can be secured with a fastener around the patient's neck and some without a flange (low profile). The tube may be easily removed to be cleaned and then reinserted (Fig. 37.18).

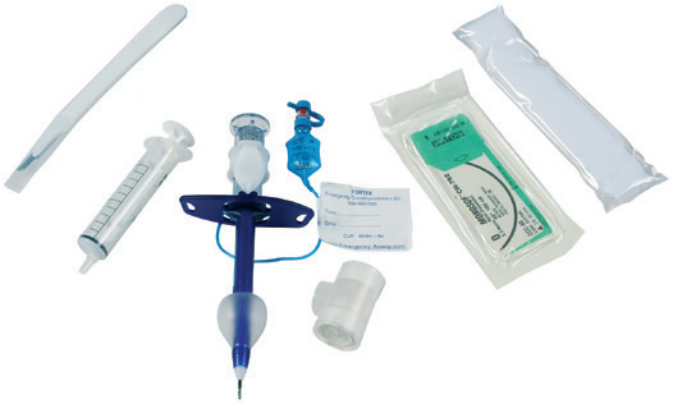

Fig. 37.19 Commercially available cricothyroidotomy kit. (Courtesy Smith's Medical International, Kent, United Kingdom.)

Surgical Emergency Airways

Despite various alternatives to establish ventilation, occasionally the problem of "cannot intubate/cannot ventilate" occurs.[28] In these situations, a surgical transtracheal airway must be established. Cricothyroidotomy and percutaneous transtracheal ventilation are options. Commercial kits are available, or a series of available supplies can be used (Fig. 37.19).[29]

Complications include bleeding, subcutaneous emphysema due to inspiratory airway resistance through a small lumen, and air trapping secondary to expiratory flow resistance. Nevertheless, cricothyroidotomy and percutaneous transtracheal ventilation are the preferred routes over emergent tracheotomy until a more definitive airway can be placed after the emergency has passed. Surgical placement of a TT should be accomplished in 48 to 72 hours.[29,30]

MINI CLINI

Alternative Airway Devices

Problem

A female patient is admitted to the emergency room after suffering an intracranial hemorrhage. She is unconscious and not breathing. Intubation attempts are unsuccessful and a clinician skilled at intubation is not present. What alternative airway device could be used?

Discussion

A laryngeal mask airway (LMA). The LMA offers ease and speed during insertion for the inexperienced intubator. The airway can be secured quickly and mechanical ventilation commenced. This patient was unconscious, so the LMA is appropriate. The patient was admitted with a neurologic injury and likely has normal respiratory system resistance and compliance. Ventilating pressures greater than 20 cm H_2O will likely not be needed. The patient should be stabilized, and once appropriate personnel are present, the LMA should be exchanged for an ETT.

Procedures

Orotracheal Intubation

Orotracheal intubation is the preferred route for establishing an emergency tracheal airway because the oral passage is the quickest and easiest route in most cases. Orotracheal intubation can be safely performed by an appropriately trained physician, RT, nurse, or paramedic.[28] Typically, this training involves manikin practice and application on anesthetized patients under the guidance of an anesthesiologist or other appropriately skilled individual. The basic steps in orotracheal intubation are described here.[31] Proficiency in this technique can be developed only with extensive training and experience.

BOX 37.3 Equipment Needed for Endotracheal Intubation

- Oxygen flowmeter and tubing
- Suction apparatus
- Flexible sterile suction catheters
- Sterile gloves for endotracheal suctioning
- Yankauer (tonsillar) tip suction
- Manual resuscitation bag and mask
- Colorimetric carbon dioxide detector
- Oropharyngeal airways
- Laryngoscope (two) with assorted blades (size 2 or 3 for adults, size 1 or 2 for children, size 0 or 1 for infants)
- Endotracheal tubes (three appropriate sizes)
- Tongue depressor
- Stylet
- Stethoscope
- Tape or endotracheal tube holder
- 10- or 12-mL syringe
- Water-soluble lubricating gel
- Magill forceps
- Local anesthetic (spray)
- Towels (for positioning)
- CDC barrier precautions (gloves, gowns, masks, goggles, or face shields)

CDC, U.S. Centers for Disease Control and Prevention.

Step 1: Assemble and Check Equipment.

Box 37.3 lists the equipment necessary for intubation. All suction equipment is assembled, and the vacuum pressure is checked before intubation because vomitus or secretions may obscure the pharynx or glottis. The appropriate-size laryngoscope blade (see Box 37.3) is attached to its handle, and the light source is checked for secure attachment and brightness. If the light does not function, the bulb first should be checked to see if it is tight. If the scope still does not light, the batteries should be checked or the bulb should be replaced.

An appropriate-size tube should be selected, and other tubes should be available that are at least one size larger and one size smaller. Table 37.3 lists recommended orotracheal tube sizes according to patient weight or age. ETTs are sized by their internal diameter (in millimeters). Tube lengths given in Table 37.3 are averages after insertion, confirmed placement, and fixation (incisor teeth to tube tip).

RULE OF THUMB In general, a woman is intubated with a No. 7 or No. 7.5 orotracheal tube and a man is intubated with a No. 8.0 or No. 8.5 orotracheal tube.

After selecting the correct size of tube, the RT inflates the tube cuff and checks for leaks. The RT must be sure to deflate the cuff before insertion. To ease insertion, the outer surface

TABLE 37.3 Guideline for Infant, Pediatric, and Adult Oral Endotracheal Tube Sizes

Age	Tube Size (mm internal diameter)	Distance (in cm) From Incisors (lip in infants) to Tip of Tube
Infant, <1 kg	2.5	6.5–8
Infant, 1–2 kg	3.0	7–8
Infant, 2–3 kg	3.5	8–9
Infant, 4 kg	3.5–4.0	9–10
6 months	3.5–4.0	10–11
18 months	3.5–4.5	11–13
3 years	4.5–5.0	12–14
5 years	4.5–5.0	13–15
6 years	5.5–6.0	14–16
8 years	6.0–6.5	15–17
12 years	6.0–7.0	17–19
16 years/small women	6.5–7.0	18–20
Women (average)	7.5–8.0	19–21
Men	8.0–9.0	21–23

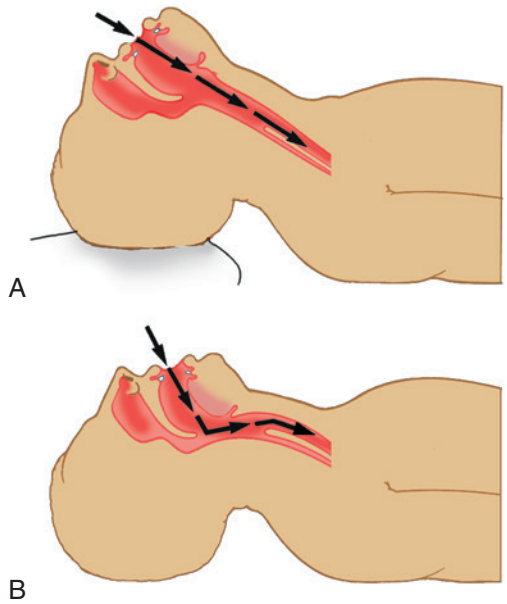

Fig. 37.20 (A) Correct head position before intubation. (B) Incorrect head position before intubation.

of the tube should be lubricated with a water-soluble gel. Finally, many clinicians insert a stylet into the tube to add rigidity and maintain shape during insertion. The tip of the stylet must never extend beyond the ETT tip.

Step 2: Position Patient.

To visualize the glottis and insert the tube, the RT aligns the patient's mouth, pharynx, and larynx. This alignment is achieved by combining moderate cervical flexion with extension of the atlantooccipital joint. Placement of one or more rolled towels under the patient's shoulders helps. Next the RT flexes the patient's neck and tilts the head backward with his or her hand, placing the patient into the sniff position (Fig. 37.20).

MINI CLINI

Indications for Endotracheal Intubation

Problem

A woman is admitted to the emergency department after sustaining chest trauma during a motor vehicle accident. The patient is unconscious, cyanotic, and tachypneic and has blood in the mouth and pharynx. Breath sounds are diminished on both sides. The physician requests that the RT immediately perform orotracheal intubation. Why?

Discussion

This patient exhibits several indications for insertion of an artificial airway. First, being unconscious, the patient is probably unable to protect her lower airway adequately. With blood in the mouth and pharynx, there should be increased concern for protecting her lungs from aspiration. The blood also may indicate partial airway obstruction; the breath sounds, cyanosis, and respiratory distress contribute to that conclusion. Finally, the cyanosis and chest trauma indicate potential hypoxemic respiratory failure, which may require positive pressure ventilatory support through, a cuffed ETT.

Step 3: Preoxygenate and Ventilate Patient.

A patient in need of intubation is often apneic or in respiratory distress. Providing ventilation and oxygenation by manual resuscitator bag and mask with 100% O_2 before intubation helps to ensure the patient tolerates the intubation procedure. In many, continuous positive airway pressure (CPAP) or high-flow nasal cannula are also being used during preoxygenation. No more than 30 seconds should be devoted to any intubation attempt. If intubation fails, immediate ventilation and oxygenation of the patient for 3 to 5 minutes before the next attempt should occur.

Step 4: Insert Laryngoscope.

The RT should use the left hand to hold the laryngoscope and the right hand to open the mouth (Fig. 37.21). The laryngoscope is inserted into the right side of the mouth and moved toward the center, displacing the tongue to the left. The tip of the blade is advanced along the curve of the tongue until the epiglottis is visualized.

RULE OF THUMB A No. 3 curved Macintosh or straight Miller laryngoscope blade is commonly used to intubate adults.

Step 5: Visualize Glottis.

As the laryngoscope blade reaches the base of the tongue, the RT looks for the arytenoid cartilage and epiglottis (Fig. 37.22). If these structures are not visible, the blade is probably advanced too far and may be in the esophagus. If this is the case, the RT should maintain upward force on the laryngoscope and slowly withdraw the blade until the larynx is seen.

Step 6: Displace Epiglottis.

The technique used to displace the epiglottis depends on the type of blade chosen (Fig. 37.23). With the curved or MacIntosh blade, the epiglottis is displaced indirectly by advancing the tip of the blade into the vallecula (at the base of the tongue), and the laryngoscope is lifted up and forward (see

Fig. 37.23A). With the straight or Miller blade, the epiglottis is displaced directly by advancing the tip of the blade over its posterior surface and the laryngoscope is lifted up and forward (see Fig. 37.23B).

One should avoid levering the laryngoscope against the teeth while lifting the tip of the blade because this can damage the teeth and gums. This problem can be avoided by keeping the wrist fixed and moving the handle of the laryngoscope in the direction it is pointing when visualizing the epiglottis.

Step 7: Insert Tube.

When the epiglottis is displaced and the glottis is visualized, the tube is inserted from the right side of the mouth and advanced without obscuring the glottic opening (Fig. 37.24). When the tube tip is seen passing through the glottis, it is advanced until the cuff has passed the vocal cords. When the tube is in place, the RT stabilizes it with the right hand and uses the left hand to remove the laryngoscope and stylet. The cuff is inflated to seal the airway, and ventilation and oxygenation are immediately provided.

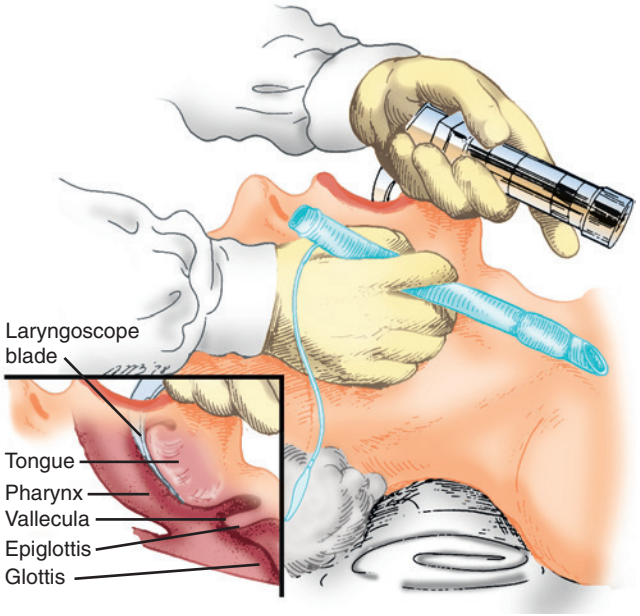

Fig. 37.21 To achieve orotracheal intubation, the respiratory therapist holds the laryngoscope in the left hand, introduces the blade into the right side of mouth, and displaces the tongue to the left. (Modified from Ellis PD, Billings DM: *Cardiopulmonary resuscitation: procedures for basic and advanced life support*, St. Louis, 1980, Mosby.)

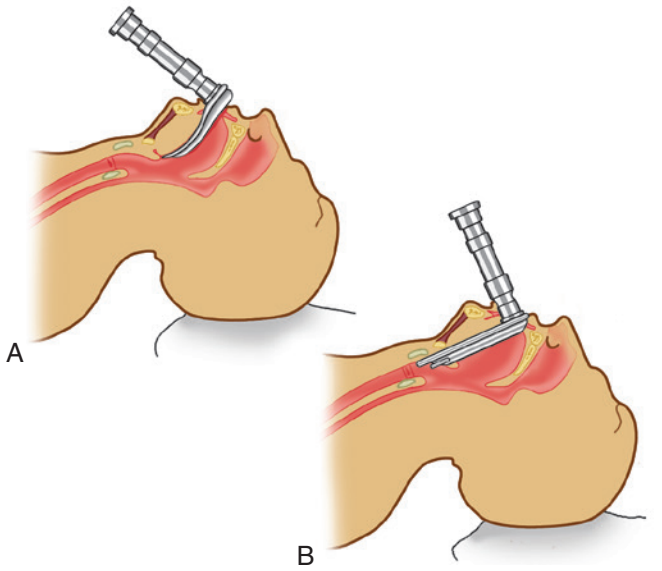

Fig. 37.23 Placement of curved (A) versus straight (B) laryngoscope blade.

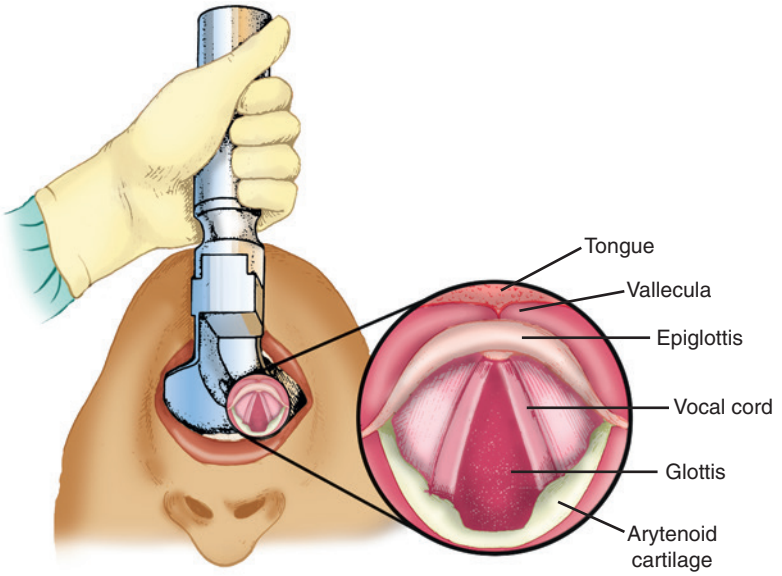

Fig. 37.22 Visualization of vocal cords is achieved with a laryngoscope. (Modified from Ellis PD, Billings DM: *Cardiopulmonary resuscitation: procedures for basic and advanced life support*, St. Louis, 1980, Mosby.)

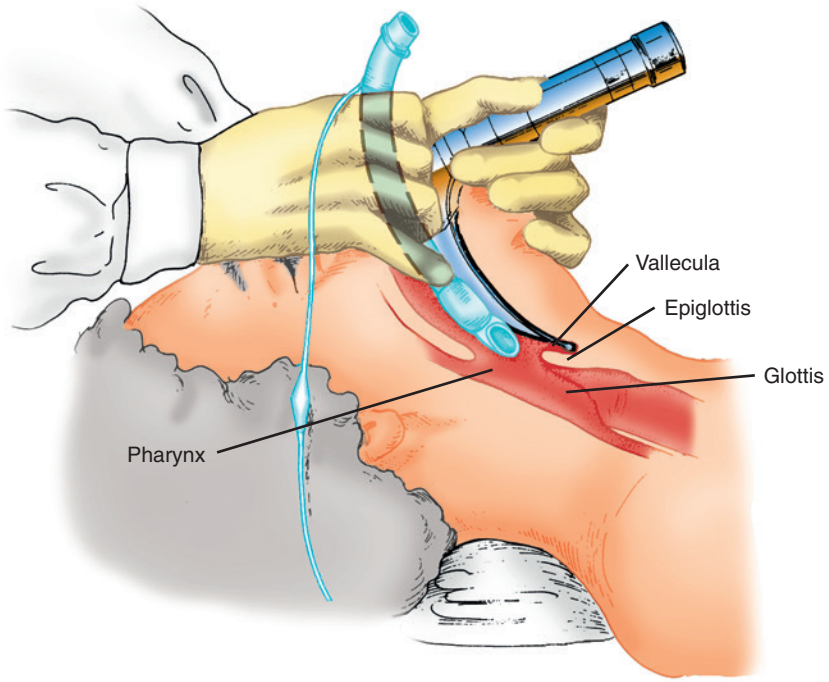

Fig. 37.24 Insertion of endotracheal tube. (Modified from Ellis PD, Billings DM: *Cardiopulmonary resuscitation: procedures for basic and advanced life support*, St. Louis, 1980, Mosby.)

BOX 37.4 Bedside Methods to Assess Endotracheal Tube Position

- Auscultation of chest and abdomen
- Observation of chest movement
- Tube length (centimeters to teeth)
- Light wand
- Capnometry
- Colorimetry
- Flexible laryngoscopy or bronchoscopy
- Videolaryngoscopy
- Ultrasound

Step 8: Assess Tube Position.

Ideally, the tip of an ETT should be positioned in the trachea approximately 3 to 5 cm above the carina.[32] One or more of several bedside methods can be used to assess positioning of the ETT before stabilization (Box 37.4). With the exception of direct laryngoscopy and bronchoscopy, none of these methods can absolutely confirm proper tube placement. Use of bedside ultrasound technology for evaluation of ETT placement is increasing. Ultrasound machines are more readily available and provides clinicians with immediate assessment.

After tube passage and cuff inflation, the RT listens for equal and bilateral breath sounds as the patient is being ventilated. Air movement or gurgling sounds over the epigastrium indicate possible esophageal intubation. In addition, the chest wall is observed for adequate and equal chest expansion. These movements, combined with good breath sounds, are reinforcing. The combination of decreased breath sounds and decreased chest wall movement on the left side may indicate right main stem intubation. Right mainstem intubation is corrected by slowly withdrawing the tube while listening for the return of left-side breath sounds. Other conditions may cause decreased breath sounds in the left lung (e.g., atelectasis, pleural effusion).

The depth of tube insertion (length from incisor teeth to tip) is useful to help determine tube position. As indicated in Table 37.3, the average length from the teeth (incisors) to the tip of a properly positioned oral ETT in men is 21 to 23 cm. For women, this distance is approximately 2 cm less. Tube length alone cannot confirm proper placement; a tube with the 23-cm mark positioned at the teeth could just as well be in the esophagus as in the trachea. A light wand is a flexible stylet with a lighted bulb at the tip. If a light wand is used during intubation, as the stylet and ETT pass into the larynx, a characteristic glow is seen under the skin, just above the thyroid cartilage.[33] This glow is not as bright or focused if the tube is in the esophagus.

Esophageal intubation is best assessed using exhaled carbon dioxide (CO_2) analysis (capnometry) and should be performed after every intubation. Because inspired air contains only approximately 0.04% CO_2 and end-tidal gas contains approximately 5% CO_2, placement of an ETT in the respiratory tract causes CO_2 levels to increase abruptly during expiration. This increase is evident on a capnographic display (Fig. 37.25). If the tube is in the esophagus, CO_2 levels remain near zero.[34] However, of concern is patients who may have recently consumed carbonated fluids, because CO_2 may be released via the esophagus.

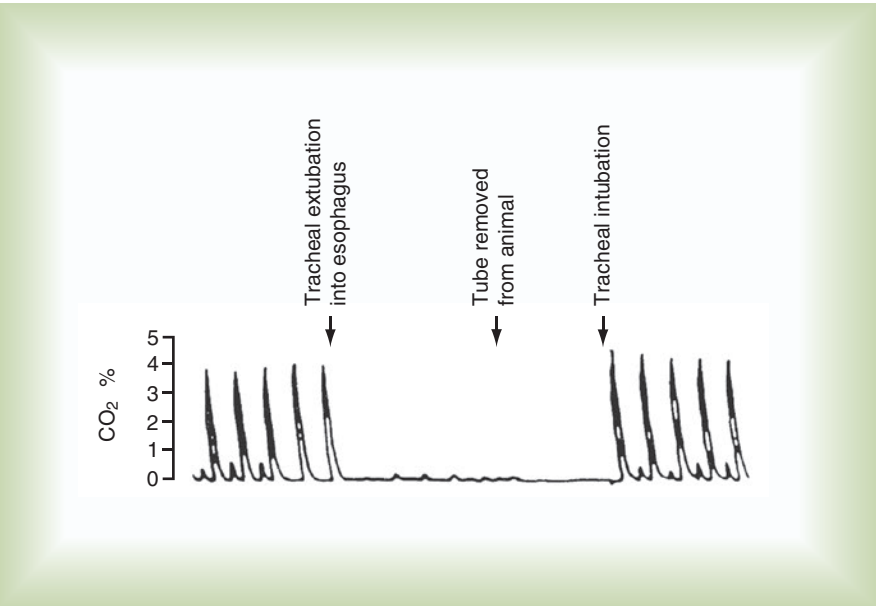

Fig. 37.25 Capnogram tracing showing changes in expired percent carbon dioxide with proper and improper placement of endotracheal tube in test animals.

Fig. 37.26 Disposable colorimetric carbon dioxide detector for confirming tracheal intubation. (Used by permission from Nellcor Puritan Bennett LLC, Boulder, Colorado, doing business as Covidien.)

Colorimetric CO_2 analysis is an inexpensive alternative to capnometry. Functioning similar to pH paper, a colorimetric system has an indicator that changes color when exposed to different CO_2 levels.[35] Fig. 37.26 shows a disposable colorimetric system designed specifically to confirm tube placement during intubation. Colorimetric devices are portable and disposable and are commonly used in hospitals.

Both devices are effective in detecting most esophageal intubations. However, in patients with cardiac arrest, expired CO_2 levels may be near zero because of poor pulmonary blood flow, yielding a false-negative result.[33-35] Waveform capnography can also be used to assess the effectiveness of chest compressions during cardiopulmonary resuscitation. If the exhaled CO_2 begins to fall, chest compressions are inadequate and compressors should be rotated. In general, expired CO_2 levels increase with the return of spontaneous circulation due to the significant increase in amount of CO_2 returned to the lungs. CO_2 analysis, colorimetric or waveform, is an unreliable indicator of mainstem bronchial intubation.

RULE OF THUMB In general, an orotracheal tube initially should be inserted to the 21- to 23-cm mark at the teeth in men and to the 19- to 21-cm mark at the teeth in women and adjusted based on the results of the patient assessment (bilateral breath sounds) and chest x-ray findings after intubation.

Proper tube placement in the trachea can be confirmed without a chest x-ray by using a flexible laryngoscope or bronchoscope (Fig. 37.27).[36] After ensuring patient reoxygenation, a flexible bronchoscope can be inserted directly into the ETT. Visualization of the carina distal to the tip of the ETT ensures proper placement in the trachea. More precise placement is possible by moving the bronchoscope from the tube tip to the carina, while measuring this distance.

A videolaryngoscope can also be used to ensure proper placement of the ETT, especially in anticipated difficult intubations. It provides a better view of the airway, especially when there is limited mobility of the patient's neck or mouth. A camera is incorporated into the distal tip of the laryngoscope. The image is projected onto a mobile screen, allowing other clinicians to see the airway and help if needed.[37]

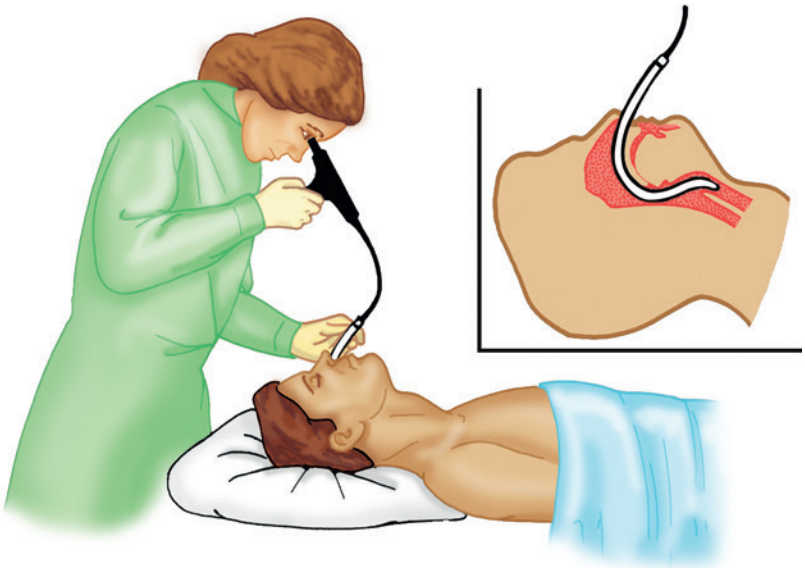

Fig. 37.27 Flexible laryngoscopy used to confirm endotracheal tube placement.

MINI CLINI

Capnometry and Endotracheal Tube Placement

Problem

At a code blue in the emergency department, a patient is intubated by the RT. A capnometer is attached to the ETT to confirm placement in the trachea. The end-expired CO_2 reads 0% as the patient is ventilated with a manual resuscitator. At this time, no one is performing cardiac compressions. Should the RT conclude that the ETT is not in the trachea?

Discussion

No. If the patient is in cardiac arrest, no blood is perfusing the alveoli and no CO_2 is entering the alveoli. The result is an end-tidal CO_2 of 0%. When cardiac compressions begin (and they should begin immediately in confirmed cardiac arrest) and if compressions are effective, one should see an increase in end-tidal CO_2 as blood begins to perfuse the alveoli and CO_2 diffuses from the blood.

There are other simple ways to assess ETT placement in the trachea, such as bilateral breath sounds on auscultation and chest excursions.[38] However, an increase in end-tidal CO_2 is a sure indication that the ETT is in the lungs because the only source of CO_2 is in the alveoli.

Step 9: Stabilize Tube and Confirm Placement.

The tube should not be secured until correct placement has been assessed by using one or more of the previously mentioned methods. After assessing placement and while holding the tube in position, the RT secures the tube to the skin above the lip and on the cheeks using tape or an ETT holder. A bite block, oropharyngeal airway, or similar device may be needed to prevent the patient from biting down on the tube (Fig. 37.28). After the tube is stabilized, a chest x-ray should be taken to confirm its position.

The most common complication of emergency airway management is tissue trauma. The most serious complications are acute hypoxemia, hypercapnia, bradycardia, and cardiac arrest.[39,40] These problems can be minimized by using proper technique, providing the patient with adequate ventilation and oxygenation (before, during, and after), and strictly adhering to intubation time limits. In addition, sedation and anesthesia can reduce complications and facilitate intubation in a semicomatose or combative patient.[28] Muscle-relaxing or muscle-paralyzing agents can be used in a combative patient who cannot be controlled by sedation. A paralyzed patient has no ability to compensate for hypoxemia or hypercapnia. It is imperative that the patient can be adequately ventilated by bag and mask. Rapid-sequence induction is used with the administration of a sedative-hypnotic medication and a muscle-relaxing or -paralyzing agent. Difficult intubations occur because of inability to open the patient's mouth, inability to position the patient, or unusual airway anatomy. Special intubation equipment (e.g., laryngoscope blades, videolaryngoscopy, or specialized stylets) or alternative techniques can be used.[28,38] A thin soft guide, referred to as a bougie, can be used if a clinician encounters difficulties passing an ETT through the glottic opening. Under direct laryngoscopy, a bougie can be passed first, with an ETT fed over the proximal end. Placement of a bougie ensures access to the trachea. Additional details of these techniques are beyond the scope of this chapter.

Nasotracheal Intubation

Nasotracheal intubation is not the preferred route of intubation, but it is the route of choice in certain clinical situations. Examples include intubation of patients when the oral route is unavailable, such as patients with maxillofacial injuries or undergoing oral surgery.

Nasotracheal intubation is performed either blindly or by direct visualization.[39] The direct visualization approach requires either a standard or a flexible laryngoscope. For the blind technique to

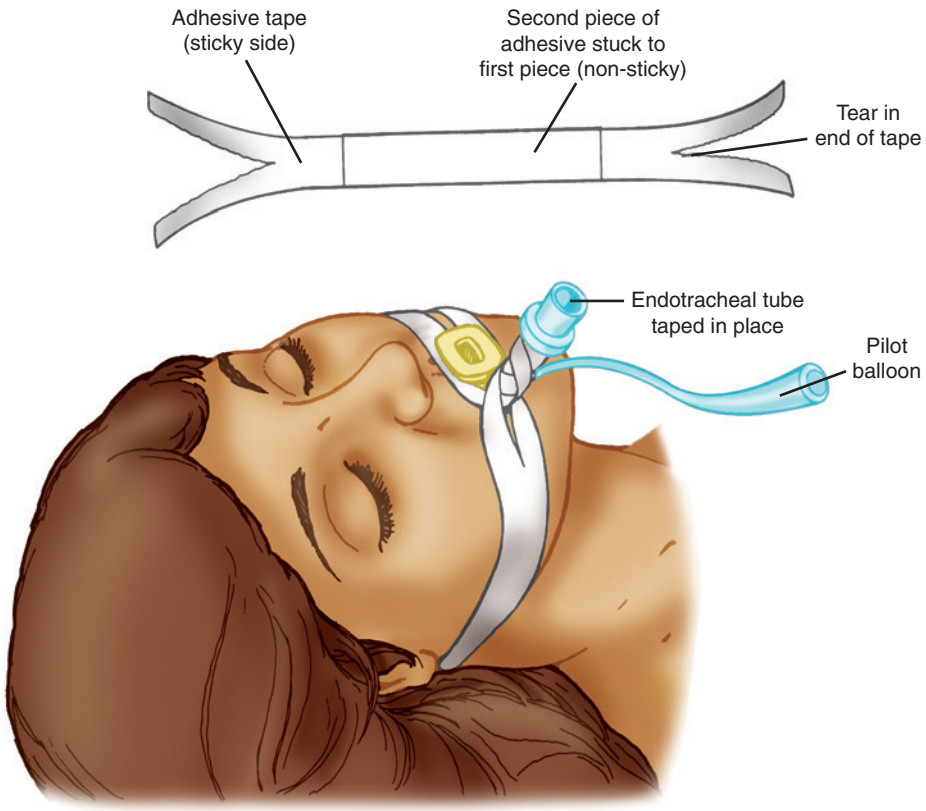

Fig. 37.28 Securing the endotracheal tube.

work, the patient must be breathing spontaneously. Equipment assembly, patient positioning, and preoxygenation are essentially the same as with oral intubation. A mixture of 0.25% phenylephrine and 3% lidocaine may be applied to the nasal mucosa with a long cotton-tipped swab to provide local anesthesia and vasoconstriction of the nasal passage.

Direct visualization. The equipment needed for nasal intubation by direct visualization is the same as for oral intubation, with the addition of Magill forceps. A smaller ETT also may be needed. The tube should be prelubricated with water-soluble gel to aid passage. To insert the tube, the bevel is positioned toward the septum and advanced along the floor of the nasal cavity (inferiorly). When the tip of the tube is in the patient's oropharynx, the RT opens the patient's mouth, inserts the laryngoscope (with the left hand), and visualizes the glottis. The RT uses the Magill forceps with the right hand to grasp the tube just above the cuff and direct it between the vocal cords (Fig. 37.29). To help advance the tube past the vocal cords, the neck may need to be flexed. Confirmation of position and stabilization follows, as with the oral route.

Alternatively, a flexible bronchoscope or laryngoscope can be used to guide tube passage.[36] With the bronchoscopic method, the distal end of the scope is passed through the ETT and directly into the trachea. When placement is ensured, the RT slides the ETT down over the scope into proper position. The procedure is similar with a flexible laryngoscope. However, because directional control of the scope is limited, the RT may have to reposition the patient's head and neck to help guide the tube.

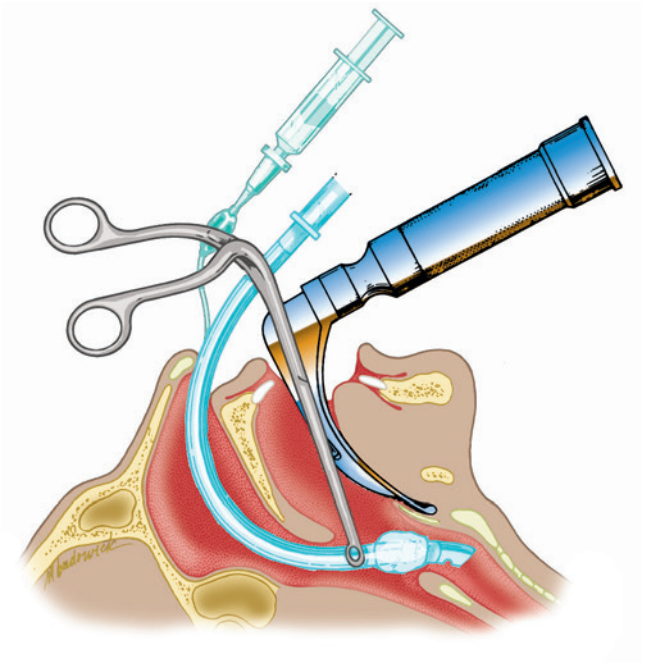

Fig. 37.29 Nasal intubation using Magill forceps. (Modified from Finucane BT, Santora AH: *Principles of airway management*, Philadelphia, 1988, FA Davis.)

RULE OF THUMB Nasotracheal intubations are beneficial for patient with maxillofacial trauma or undergoing oral surgery.

Blind passage. For blind nasal intubation, the patient is placed in either the supine or the sitting position. As with direct visualization, the tube is inserted through the nose. As the tube approaches the larynx, one can listen through the tube for air movement. The breath sounds become louder and more tubular when the tube passes through the larynx. Successful passage of the tube through the larynx usually is indicated by a harsh cough, followed by vocal silence. If the sounds disappear, the tube is moving toward the esophagus. A malpositioned tube can be corrected by manipulating the tube and repositioning the patient's head and neck. Confirmation of tube placement and stabilization should follow. As previously indicated, a light wand can help to ensure proper tracheal placement during blind nasotracheal intubation.

Tracheotomy

Tracheotomy is the procedure of establishing access to the trachea via a neck incision. The opening created by this procedure is called a **tracheostomy.** Tracheotomy may be performed as a regular surgical procedure or by a percutaneous dilation procedure.

Tracheotomy is the preferred, primary route for overcoming upper airway obstruction or trauma and for patients with poor airway protective reflexes. Another indication for tracheotomy is the continuing need for an artificial airway after a prolonged period of oral or nasal intubation. If the patient still needs an artificial airway after approximately 7 to 14 days, a tracheostomy is commonly considered. The benefits of a tracheostomy versus oral or nasal intubation are elimination of vocal cord injury, increased patient comfort, less need for deep sedation, easier removal of secretions, decreased work of breathing, and potentially shorter weaning time.[40] The decision when to switch from an ETT to a TT should be individualized. Pertinent factors that should be considered in making this decision are summarized in Box 37.5. Fig. 37.30 is a decision-making algorithm useful for timing tracheotomy in critically ill patients.

BOX 37.5 Factors to Consider in Switching From Endotracheal Tube to Tracheostomy

- Projected time the patient will need an artificial airway
- Patient's tolerance of endotracheal tube
- Patient's overall condition (including nutritional, cardiovascular, and infection status)
- Patient's ability to tolerate a surgical procedure
- Relative risks of continued endotracheal intubation vs. tracheostomy

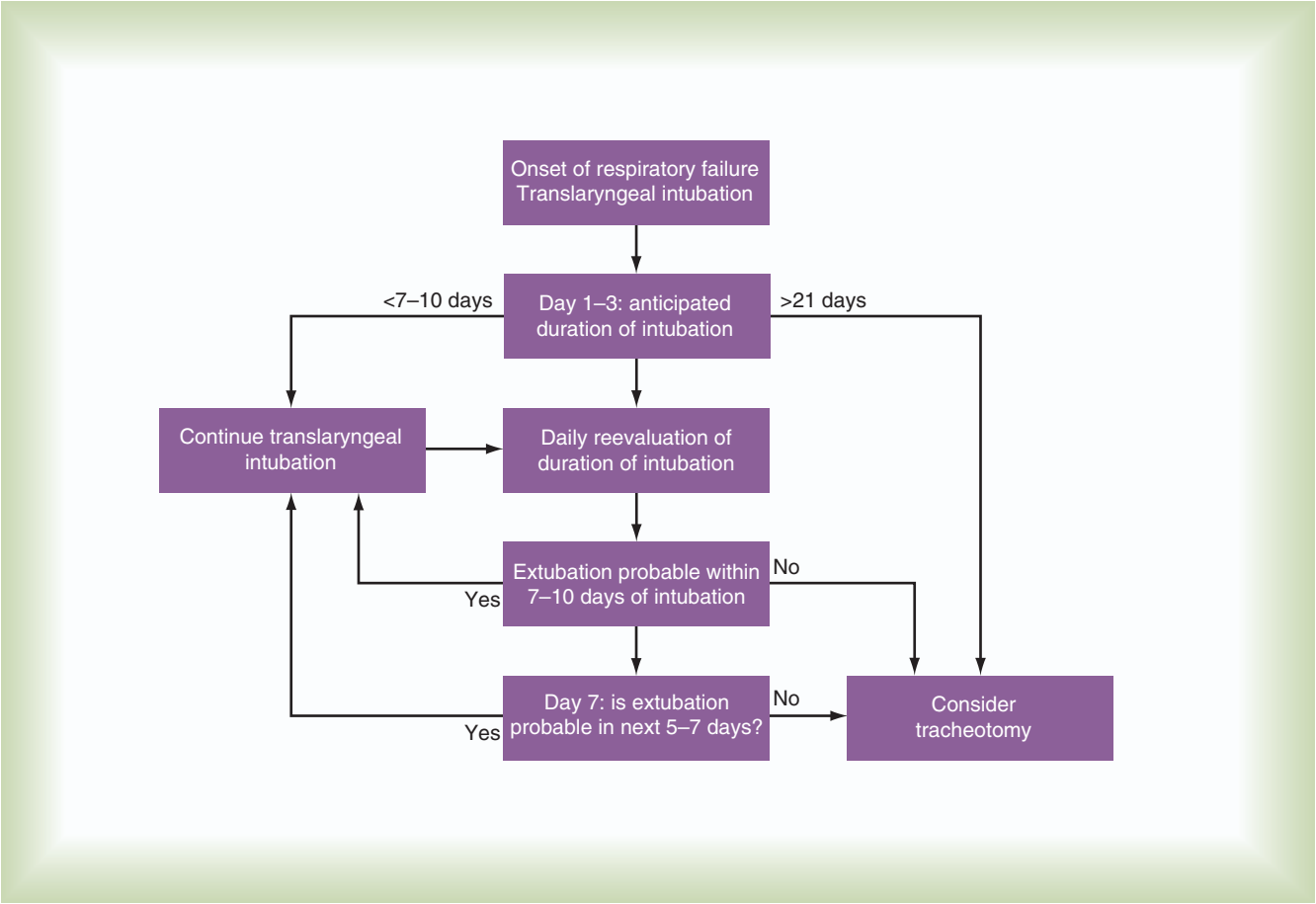

Fig. 37.30 Approach to timing tracheotomy in patients intubated and mechanically ventilated for respiratory failure. (From Heffner JE: Timing of tracheostomy in ventilator-dependent patients, *Clin Chest Med* 12:611–625, 1991.)

Procedure. Tracheotomy should be performed as an elective procedure by a skilled physician or surgeon after the patient's airway is stabilized. Mortality and morbidity are greater when the procedure is performed on an emergency basis. The RT may be asked to assist in tracheotomy, especially if performed at the bedside. For this reason, we briefly describe both the traditional surgical procedure and the percutaneous dilation method.[40]

A local anesthetic is used, and the patient is mildly sedated if conditions permit. If an ETT is in place, it should not be removed until just before the insertion of the TT. Keeping the ETT in place this way ensures a patent airway and provides additional stability to the trachea during the procedure.

In traditional surgical tracheotomy, the surgeon makes an incision in the neck over the second or third tracheal ring. After the skin and subcutaneous tissue have been incised, the surgeon divides the superficial muscles and locates the underlying thyroid gland. The surgeon divides and ligates the thyroid isthmus, which overlies the second and third tracheal rings. The surgeon then enters the trachea through either a horizontal incision between rings or a vertical incision through the second and third rings. As little cartilage as possible should be removed to promote better closure after decannulation.

In percutaneous dilation tracheotomy, the initial steps to prepare the patient are similar to the steps in the traditional tracheotomy procedure. After dissection to the anterior tracheal wall, the ETT is retracted to keep the tip of the tube inside the larynx. A bronchoscope can be used to reassess placement for the ETT for the duration of the procedure. A large leak around the ETT may develop, requiring adjustment of mechanical ventilation. If the patient is unable to tolerate the large leak, and adjustments to ventilatory support cannot compensate for the leak, a surgical procedure may be indicated for that patient.

The physician inserts a needle and sheath into the trachea between the cricoid and first tracheal ring or between the first and second rings. The physician then inserts a guidewire through the sheath, the sheath is removed, and a dilator is passed over the guidewire. Increasingly larger dilators are introduced until the stoma is large enough for a standard TT. The physician slips the TT over the last dilator used. An alternative to the use of multiple dilators is to use a single dilator with increasing diameter from the proximal to the distal end.

The procedure may be performed under direct vision with a bronchoscope passed through the ETT or an LMA. Compared with the traditional surgical procedure, a percutaneous dilation tracheotomy is rapid, with fewer complications from the surgical site, and has a better cosmetic appearance after decannulation. Contraindications for percutaneous tracheotomy are listed in Box 37.6.

Insertion of the tube, inflation of the cuff, and securing the tube follow both methods. TT ties should be secure enough to prevent movement of the tube but not so tight as to cause skin ulceration. The role of the RT in the procedure may include managing the ETT, making ventilator changes as needed, assisting with the bronchoscope, and monitoring the patient. Advantages and disadvantages of percutaneous and open surgical tracheotomy are listed in Table 37.4.

In general, the tube size is correct if it occupies two-thirds to three-quarters of the internal tracheal diameter. TTs come in various sizes, lengths, and shapes depending on the manufacturer. The size marked on the flange usually indicates the internal diameter, but some TTs with inner cannulas use Jackson sizing. Table 37.5 lists the sizes, internal diameter, external diameter, and length of commonly used brands and styles of adult TTs. Table 37.6 provides guidelines for selecting a TT according to a patient's age. Within an age category, the exact size of tube chosen depends on the patient's height, weight, and airway anatomy. To choose a TT that fits a patient properly, it is important to consider not only the internal and external diameter of the tube but also the length and shape of the tube.

BOX 37.6 Contraindications for Percutaneous Dilation Tracheostomy

Absolute
- Need for emergent surgical airway

Relative
- Children younger than 12 years of age
- Poor landmarks secondary to body habitus, abnormal anatomy, or occluding thyroid mass
- Positive end expiratory pressure less than 15 cm H_2O
- Coagulopathy
- Pulsating blood vessel over tracheotomy site
- Limited ability to extend cervical spine
- History of difficult intubation
- Infection, burn, or malignancy at tracheotomy site

From Park S, Goldenberg D: Percutaneous tracheotomy: Griggs technique, *Op Tech Otolaryngol* 18:95, 2007.

TABLE 37.4 Comparison of Percutaneous and Open Surgical Tracheotomy

Procedure	Advantages	Disadvantages
Percutaneous tracheotomy	May be done in intensive care unit	Not done in children younger than 12 years
	Sedation and local anesthetic given	
	Stoma usually stabilizes in 5 days	May be difficult to insert because of calcified cartilaginous rings
Open surgical tracheotomy	Done in patients with poor landmarks because of abnormal anatomy or body habitus	Usually done in operating room
	May be done emergently	General anesthesia given
	Done in children younger than 12 years	Stoma usually takes longer to stabilize (7–10 days)

Laryngectomy

Total **laryngectomy,** removal of the larynx (voice box), is usually done to treat laryngeal cancer. It also may be done to treat severe trauma, such as from a gunshot wound to the neck or damage to the larynx from radiation (radiation necrosis). Besides removing the larynx, the surgeon creates a hole in the neck (stoma) and attaches the trachea to the stoma. The patient will now

TABLE 37.5 Comparison of Commonly Used Brands of Adult Tracheostomy Tubes

PORTEX FLEX DIC: SIZED BY ID; ALSO AVAILABLE CUFFLESS OR FENESTRATED

ID (mm)	OD (mm)	Length (mm)[a]
6.0	8.2	64
7.0	9.6	70
8.0	10.9	74

SHILEY SCT: SIZED BY ID; ALSO AVAILABLE CUFFLESS

ID (mm)	OD (mm)	Length (mm)[a]
6.0	8.3	67
7.0	9.6	80
8.0	10.9	89

SHILEY DOUBLE CANNULA (LPC, DC, CFS, CFN, FEN, PERC) WITH DISPOSABLE OR NONDISPOSABLE INNER CANNULA: SIZED BY JACKSON SCALE; ALSO AVAILABLE CUFFLESS OR FENESTRATED

Size (Jackson)	ID (mm)	OD (mm)	Length (mm)
4	5.0	9.4	65
6	6.4	10.8	76 (PERC 74)
8	7.6	12.2	81 (PERC 79)

JACKSON DOUBLE CANNULA STAINLESS STEEL TUBE; AVAILABLE CUFFLESS ONLY; AVAILABLE FENESTRATED

Size (Jackson)	ID (mm)	OD (mm)	Length (mm)
4	5.3	8.0	62
6	7.2	10.0	69
8	9.2	12.0	69

EXTRA LENGTH TUBES: SHILEY TRACHEOSOFT XLT PROXIMAL OR DISTAL EXTENSION WITH DIC: SIZED BY ID

ID (mm)	OD (mm)	Length (mm)
6.0	11	95
7.0	12.3	100
8.0	13.3	105

BIVONA MID-RANGE AIRE-CUF EXTRA LENGTH FIXED OR ADJUSTABLE NECK FLANGE: SIZED BY ID

ID (mm)	OD (mm)	Length (mm)
6.0	8.7	100 (adjustable 110)
7.0	10.0	110 (adjustable 120)
8.0	11.0	120 (adjustable 130)

BIVONA TTS: SIZED BY ID; CUFF INFLATED WITH STERILE WATER NOT AIR

ID (mm)	OD (mm)	Length (mm)
6.0	8.7	70
7.0	10.0	80
8.0	11.0	88

[a]The main difference between these tubes is the length.
CFN, Cufffless fenestrated tracheostomy tube; *CSF,* cuffless tracheostomy tube; *DCT,* Disposable cannula tracheostomy; *DIC,* disposable inner cannula; *FEN,* fenestrated low pressure cuffed tracheostomy tube; *ID,* inner diameter; *LPC,* low pressure cuffed tracheostomy tube; *OD,* outer diameter; *PERC,* percutaneous tracheostomy tube; *SCT,* single-cannula tracheostomy tube; *TTS,* tight to shaft tracheostomy tube.

TABLE 37.6 Guideline for Infant, Pediatric, and Adult Tracheostomy Tube Sizes

Age/Weight[a]	ID (mm)
Premature <2 kg	2.5 cuffless neonatal
Infant	3.0–3.5 cuffless neonatal
6–18 months	3.5–4.0 neonatal or pediatric
18 months to 4–5 years	4.0–4.5 pediatric
4–5 years to 10 years	4.5–6.0 pediatric
10–14 years	5.0–6.5 pediatric or adult
14 years to adult	6.0–9.0 adult

[a]Typical pediatric size = (16 + age) / 4 or (age / 4) + 4.
NOTE: The difference between the same size (ID) neonatal and pediatric tube or pediatric and adult tube is the length; that is, the adult tube is longer than the pediatric tube, and the pediatric tube is longer than the neonatal tube.
ID, Inner diameter.

breathe through this permanent stoma. A laryngectomy tube may be inserted into the stoma to keep it open while it heals.

The surgeon may also do a tracheoesophageal puncture (TEP), which is a small opening between the posterior wall of the trachea and esophagus. The surgeon will insert a small device (prosthesis) that has a one-way valve. This prosthesis allows the patient to speak when the patient occludes the stoma during exhalation once the patient has been trained by a speech and language pathologist (Fig. 37.31). Some patients with TEP use their thumb, and others use an attached tracheostoma adjustable valve to occlude the stoma during exhalation to be able to speak. Another way a laryngectomy patient can speak is by holding an electrolarynx against the throat. This is a battery-operated device that creates vibrations that are transmitted through the pharynx and mouth to produce a voice.[41]

The risks associated with this surgery are hematoma, wound infection, fistulas, stomal stenosis (narrowing), leaking around tracheoesophageal prosthesis, difficulty swallowing and eating, and problems speaking.

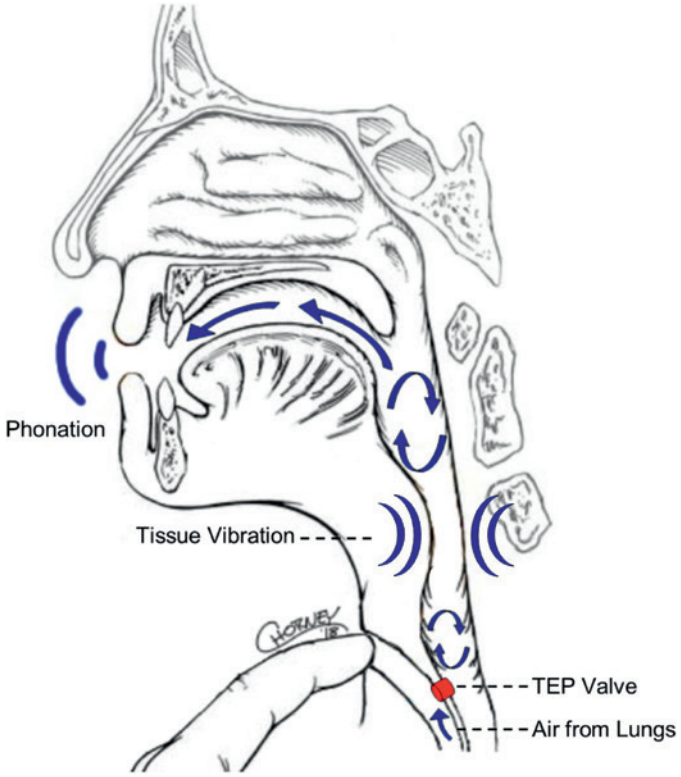

Fig. 37.31 Laryngectomy with tracheoesophageal voice prosthesis. (From Chorney MA, Dubin RM, Levine MS: Tracheobronchial foreign body aspiration in laryngectomized patient with tracheoesophageal voice prosthesis. Clinical Imaging 49:181–183, 2018.)

Sometimes the surgeon will perform only a partial laryngectomy. A tracheotomy is also done and a TT is inserted while the surgical site is allowed to heal. There is still communication between the pharynx and trachea, so the patient should eventually be able to breathe using the normal upper airway and may even be able to speak once the TT is removed.[42]

It is important to know whether a patient has had a total or partial laryngectomy, in case the patient accidentally loses the artificial airway and requires manual ventilation. In the case of a total laryngectomy the RT would apply bag-mask ventilation over the stoma, ideally using a small pediatric mask that would fit more closely over the stoma than an adult mask. In a partial laryngectomy the RT would cover the stoma with a gauze pad and apply bag-mask ventilation over the nose and mouth with the standard adult mask because there is still communication between the trachea and upper airway.

AIRWAY TRAUMA ASSOCIATED WITH TRACHEAL TUBES

Artificial airways do not conform exactly to patient anatomy, which may result in pressure on soft tissues that can result in ischemia and ulceration.[43] In addition, artificial airways tend to shift position as the patient's head and neck move or as the tube is manipulated. This shifting can result in friction-like injuries. Occasional reaction to the materials composing the tube also may cause problems.

Depending on the type of tube, damage to the patient's airway can occur anywhere from the nose down into the lower trachea. Because TTs do not pass through the larynx, structural injury resulting from these airways is limited to tracheal sites. Laryngeal dysfunction may occur secondary to a lack of stimulation from airflow or restricted movement due to equipment.[15]

Because injury often cannot be assessed while an artificial airway is in place, the patient's airway should always be evaluated carefully after extubation. Techniques commonly used to diagnose airway damage include physical examination, air tomography, fluoroscopy, laryngoscopy, bronchoscopy, magnetic resonance imaging, and pulmonary function studies.[44]

Laryngeal Lesions

The most common laryngeal injuries associated with endotracheal intubation are glottic edema, vocal cord inflammation, laryngeal or vocal cord ulcerations, and vocal cord polyps or granulomas. Less common and more serious injuries are vocal cord paralysis and laryngeal stenosis.[32,43]

Glottic edema and vocal cord inflammation are transient changes that occur as a result of pressure from the ETT or trauma during intubation.[43] The primary concern with glottic edema and vocal cord inflammation occurs after extubation. Because swelling can worsen over 24 hours after extubation, patients should be evaluated periodically for delayed development of glottic edema.

The primary symptoms of glottic edema and vocal cord inflammation are hoarseness and stridor. Hoarseness occurs in most extubated patients and usually resolves quickly. Stridor is a more serious symptom than hoarseness, indicating a significant decrease in diameter of the airway. Stridor is often treated with epinephrine (2.25% racemic solution or levoepinephrine 1:1000) via aerosol.[43] The treatment goal is to reduce glottic or airway edema by mucosal vasoconstriction. A steroid also may be added to the aerosol to reduce inflammation further. Both of these techniques are more commonly used in children than in adults.

To reduce laryngeal edema in patients who have had prolonged intubation or patients who have failed prior extubation because of glottic edema, intravenous steroids, and/or diuretics may be given 24 hours before extubation.[43] If stridor continues and is unresponsive to treatment, structural changes that narrow the airway should be suspected.

Laryngeal and vocal cord ulcerations may cause hoarseness soon after extubation. Symptoms usually resolve spontaneously, and no treatment is indicated. Vocal cord polyps and granulomas develop more slowly, taking weeks or months to form. Symptoms include difficulty in swallowing, hoarseness, and stridor. If symptoms are severe or persistent, the polyps or granulomas may have to be removed surgically.

Vocal cord paralysis is likely in extubated patients with hoarseness and stridor that does not resolve with treatment or time. In some patients, symptoms may resolve within 24 hours, and

full movement of the vocal cords can return over several days. If the obstructive symptoms continue, tracheotomy may be indicated.

Laryngeal **stenosis** occurs when the normal tissue of the larynx is replaced by scar tissue, which causes stricture and decreased mobility. The symptoms of laryngeal stenosis are similar to symptoms of vocal cord paralysis—stridor and hoarseness. Because laryngeal stenosis does not resolve spontaneously, surgical correction is usually required. Some patients require a permanent tracheostomy.

Tracheal Lesions

Although laryngeal lesions occur only with oral or nasal ETTs, tracheal lesions can occur with any tracheal airway. These tracheal lesions include granulomas, **tracheomalacia,** and tracheal stenosis.[45] Less common but more serious complications are tracheoesophageal and tracheoinnominate artery fistulas.

Tracheomalacia and tracheal stenosis can occur either separately or together. *Tracheomalacia* is the softening of the cartilaginous rings, which causes collapse of the trachea during inspiration and expiration. *Tracheal stenosis* is a narrowing of the lumen of the trachea, which can occur as fibrotic scarring, causing the airway to narrow. In patients with ETTs, this type of damage most often occurs at the cuff site. In patients with TTs, stenosis may occur at the cuff, tube tip, or stoma sites; the stoma site is the most common. Stenosis at the stoma site is associated with too large a stoma, infection of the stoma, movement of the tube, frequent tube changes, and advanced age.[46]

Signs of possible tracheal damage before extubation include difficulty in sealing the trachea with the cuff and evidence of tracheal dilation on chest x-ray.[43] Signs and symptoms of postextubation problems include difficulty with expectoration, dyspnea, and stridor. Although these findings may appear acutely, they may develop over several months and may not be present until the radius is reduced by 50% to 75%. Dyspnea at rest may not be seen until the diameter of the trachea is less than 5 mm. Symptoms are often incorrectly attributed to the development of asthma or chronic lung disease.

Tomography, fluoroscopy, and pulmonary function studies (especially flow-volume loops) may be helpful in quantifying the severity of the damage. Flow-volume loops are also helpful in distinguishing between tracheomalacia and tracheal stenosis. Tracheomalacia appears as a variable obstruction with different inspiratory and expiratory patterns. As an example, with variable extrathoracic obstruction (e.g., when the extrathoracic trachea is floppy or malacic), the flow-volume loop shows flattening of the inspiratory limb and the expiratory limb is normal. Tracheal stenosis appears as a fixed obstructive pattern, with flattening of both the inspiratory and the expiratory limbs of the flow-volume loop (Fig. 37.32).

Treatment depends on the severity of the lesion, especially the length and circumference of the damage.[44] Laser therapy may be useful if the lesion is small. Resection and end-to-end anastomosis may be indicated when the damage involves fewer than three tracheal rings. More involved damage may require staged repair. Stents may be placed to maintain the patency of the airway.

A **tracheoesophageal fistula** is a direct communication between the trachea and the esophagus. Tracheoesophageal fistula is a rare complication of both tracheotomy and endotracheal intubation. If it occurs soon after a tracheotomy, incorrect surgical technique may be the cause. Later development is related to sepsis, malnutrition, tracheal erosion from the cuff and tube, and esophageal erosion from nasogastric tubes.[43] The diagnosis can be made based on a history of recurrent aspiration and abdominal distension as air is forced into the esophagus during positive pressure ventilation. The diagnosis is also made by direct endoscopic examination of the trachea and esophagus. Treatment involves surgical closure of the defect.

A **tracheoinnominate artery fistula** can occur when a TT causes tissue erosion through the innominate artery. The result

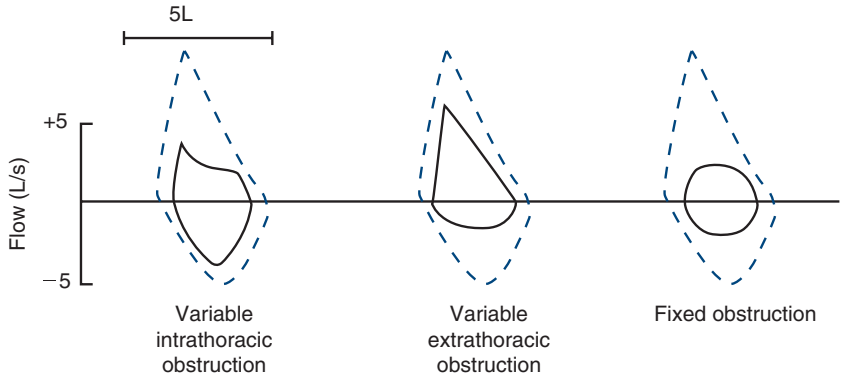

Fig. 37.32 Patterns of Pulmonary Dysfunction Revealed by Flow-Volume Loops. *Dashed lines* are normal values for comparison. Tracheomalacia is typically seen as a variable obstruction, whereas stenosis most often manifests with a fixed obstruction pattern. (From Mottram C: *Ruppel's manual of pulmonary function testing,* ed 10, Mosby, 2013, St. Louis.)

is massive hemorrhage and, in most cases, death. Tracheoinnominate artery fistula is a rare complication, probably caused by improper low positioning of the stoma or excessive movement of the tube.[44] Pulsation of the TT may be the only clue before actual hemorrhage. When hemorrhage begins, hyperinflation of the cuff may slow the bleeding, but the patient still needs surgical intervention.[44] Even with proper corrective action, only 25% of patients who develop this serious complication survive.

Prevention

Several actions can minimize the trauma caused by tracheal airways. Many studies suggest that tube movement is a primary cause of injury.[43,44] Several methods can be used to limit tube movement. Sedation can help keep patients comfortable and decrease the likelihood of self-extubation. Nasotracheal tubes are easier to stabilize and may move less than orotracheal tubes. Swivel adapters can be used to minimize tube traction whenever respiratory therapy equipment is attached to patients with tracheostomies. If a patient with a tracheostomy requires O_2 therapy, tracheostomy collars are preferred to T-tubes or Briggs adapters.

Selection of the correct airway size is also important. Once in place, endotracheal and TTs should not be changed unless necessary. To minimize vocal cord closure around ETTs, patients should be discouraged from unnecessary coughing or efforts to talk. Tracheal wall injury from the endotracheal or TT cuff can be reduced by maintaining pressures of 20 to 30 cm H_2O.[13,45] If the airway is in place solely for suctioning or to bypass an obstruction, a cuff may not be needed.

Infected secretions have been implicated in the development of tracheitis and mucosal destruction, and infection of the tracheotomy stoma has been linked to tracheal stenosis.[44] Sterile techniques should be used when cleaning or suctioning TTs. Good tracheostomy care, including aseptic cleaning of the stoma with sterile normal saline, should be carried out routinely, and soiled tracheostomy dressings should be changed as needed. If there is significant drainage from the stoma, it is better to use a foam dressing, which will absorb the drainage away from the skin, rather than a standard gauze dressing, which when wet will keep the skin moist. (See discussion of tracheostomy care procedure later in the chapter.) When sutures are used to secure the TT flange to the patient's neck, it can be very difficult to properly clean around the stoma. So, if sutures are present, it is recommended to remove them as soon as possible, ideally by day 5 to 7 after the tracheostomy was performed. If there are any signs of pressure injury from the trach flange, place a hydrocolloid dressing under the flange. Sometimes because of a patient's neck anatomy, changing the TT to another type with a different style of flange as soon as it is safe to do so may also prevent further skin injury.

RULE OF THUMB In adults, tracheal tube cuff pressure should be maintained at 20–30 cm H_2O to minimize tracheal mucosal injury and aspiration of oral secretions.

AIRWAY MAINTENANCE

The RT must attend to several aspects of airway maintenance when a tracheal airway is in place. Critical responsibilities in this area include: (1) securing the tube and maintaining its proper placement, (2) providing for patient communication, (3) ensuring adequate humidification, (4) minimizing the possibility of infection, (5) aiding in secretion clearance, (6) providing appropriate cuff care, and (7) troubleshooting airway-related problems.

Securing the Airway and Confirming Placement

The most common way to secure ETTs is with tape. The tape is secured to one side of the face and then wound around the tube and airway once or twice before the end is secured to the skin again (see Fig. 37.28). Silk tape is adequate if the period of intubation is short, such as during surgery; however, silk tape is easily loosened by oral secretions. Cloth tape seems to be better for longer use and may adhere better if the skin is prepared with a nonirritating medical liquid adhesive. Instead of using tape to secure the tube, practitioners can choose among several commercial ETT stabilizers. Case reports indicate that use of these stabilizers can result in less skin damage, tube movement, and self-extubations than with traditional taping. However, these stabilizing devices cannot prevent airway or skin trauma, so the skin around the mouth or nose should be checked regularly. If there is evidence of skin irritation, the tube should be moved to the other side of the mouth or the other nares and then resecured. Alternation of securing sites for ETTs should be done on a routine basis to prevent skin breakdown. However, consensus does not exist on the exact interval.

A TT can be secured by threading cloth ties through the tube flange and tying them together on the side of the patient's neck. Alternatively, a commercial TT holder made of soft foam with Velcro attachments threaded through the tube flange can be used. This soft TT holder is easier to change and does not cause skin ulceration as often as cloth ties. Whichever tube holder is used, skin damage can be minimized by keeping the ties loose enough to slip one finger underneath easily.

Proper placement of an ETT or TT normally is confirmed by chest x-ray. The tube tip should be approximately 3 to 5 cm above the carina in adults, or between the second and fourth tracheal rings.[32,46] Keeping the tube position in this range minimizes the chance of the tube moving down into the main stem bronchi or up into the larynx. Even so, the ETT position changes with movement of the head and neck (Fig. 37.33).[47] Flexion of the neck moves the tube toward the carina, whereas extension pulls the tube toward the larynx.[48,49] When reviewing a chest x-ray for tube placement, the clinician should also check the position of the head and neck. If the tube is malpositioned, the old tape should be removed and the tube repositioned, using the centimeter markings as a guide. This maneuver usually requires two people to prevent extubation.

As an alternative to using chest films to confirm tube placement, a practitioner trained in flexible laryngoscopy or bronchoscopy may confirm the position of the tube visually.[50] With

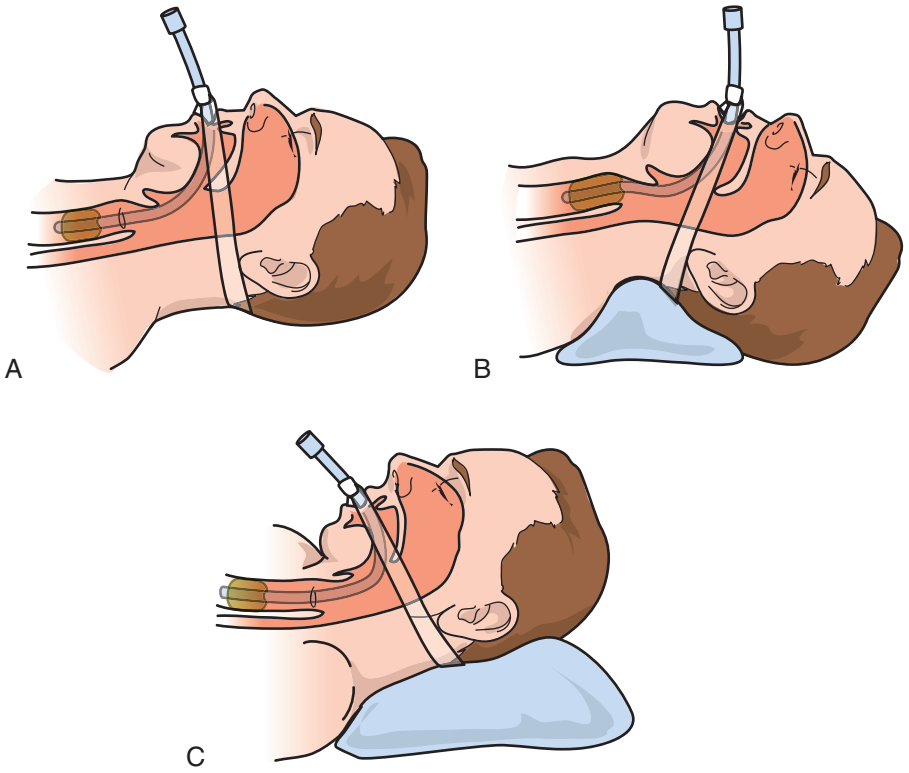

Fig. 37.33 (A) Properly positioned and secured endotracheal tube, with the head and neck in the neutral position. The tip of the tube is in the middle third of the trachea. Extension of the head and neck (B) causes the tip of the tube to rest in the upper third of the trachea, while flexion (C) of the head and neck moves the tip of the tube to the lower third of the trachea.

this method, the flexible scope is inserted into the tube and the carina is directly visualized. By moving the scope from the tube tip to the carina and measuring the distance of bronchoscopy displacement, the exact distance of insertion can be determined.

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Securing the Artificial Airway and Confirming Location

Problem

A male patient in the intensive care unit was recently intubated following drug overdose and ventilated in the AC/PC mode. The ventilator is alarming for low exhaled minute ventilation, and a cuff leak is audible. Attempts to seal the airway with addition of air to the cuff are unsuccessful. Upon further inspection, the RT notes the silk tape used to secure the ETT has become loose and the tube is resting at 19 cm mark at the teeth. The most recent chest x-ray report does not comment on the ETT.

Discussion

The ETT in this patient has partially migrated out and is at risk of dislodging. The silk tape that was used to secure the ETT was not sufficient. The cuff leak could not be rectified by adding air as the cuff is likely in the hypopharynx. It is difficult to see this ETT on x-ray, because the distal tip is likely just at the thoracic inlet. The RT should call the nurse and doctor immediately and advance the ETT. An alternative securing method, such as commercial tube holder, should be used. A follow-up chest x-ray is important to document proper location.

Providing for Patient Communication

One of the most frustrating aspects of caring for a patient with a tracheal tube is his or her inability to talk. Phonation requires moving vocal cords, resulting in airflow between them. ETTs prevent vocal cord movement and airflow through the cords. Standard TTs allow vocal cord movement but prevent airflow. Without the ability to speak, the patient cannot easily inform the healthcare providers of changes in symptoms or make basic requests. This situation may lead to agitation and stress in the patient. If that agitation is treated with sedatives, a patient on a ventilator may wean more slowly.[51]

An experienced practitioner may use lip reading, but this technique is very difficult in patients with orotracheal tubes. Alternatively, an alert patient may write messages on paper or some other writing surface. However, for many patients, restricted hand movement because of restraints or vascular catheters makes writing impossible. Some critically ill patients simply cannot hold up their heads. A better solution is a letter, phrase, or picture board.[51] These devices allow patients to communicate by simple pointing. Large and simple drawings are particularly important for patients who cannot see print clearly. Some patients may choose to use special electronic devices to communicate, especially patients who have a TT because of the need for chronic mechanical ventilation. Speech-language pathologists often work with these patients to figure out which device will work best so an individual patient can communicate.

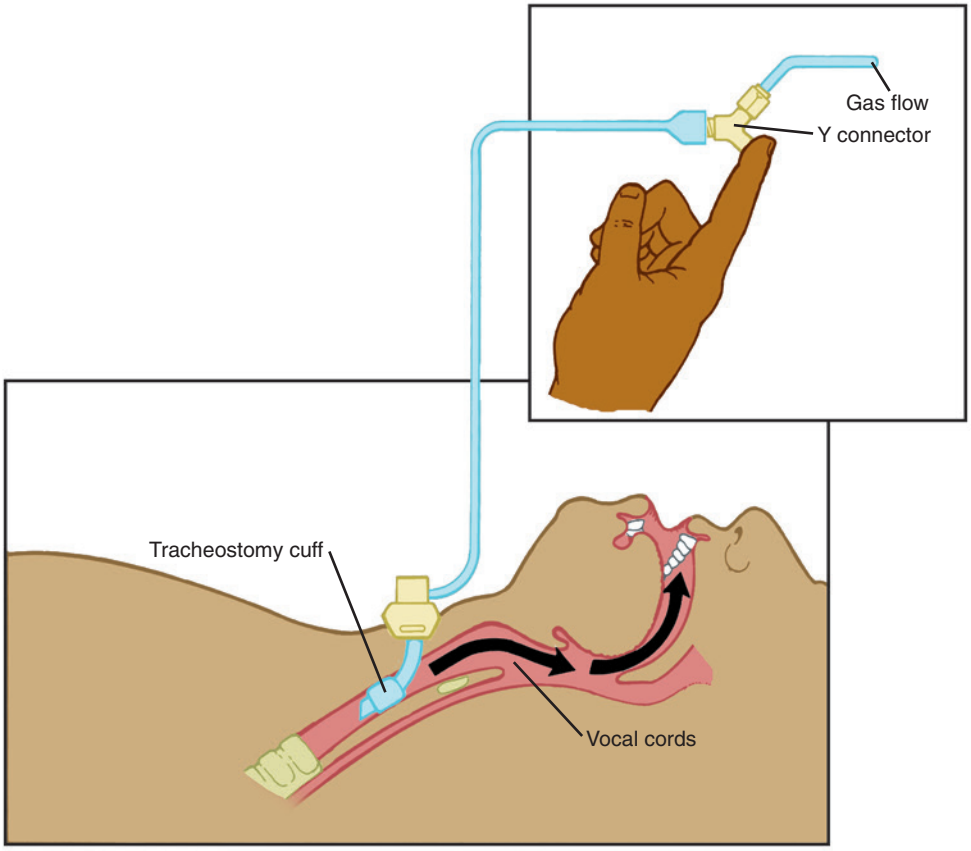

Fig. 37.34 "Talking" tracheostomy tube.

For conscious patients with a long-term tracheostomy who are ventilator-dependent, communication can be enhanced with a "talking" TT (Fig. 37.34).[31] These special airways provide a separate inlet for compressed gas, which escapes above the tube, allowing phonation. However, there are some problems associated with these tubes. The continuous gas flow through a new tracheostomy may cause air leaks. High flow rates may cause mucosal drying and irritation. Finally, secretions may occlude the speaking gas outlets. Although not life threatening, these problems can be frustrating for both the patient and the practitioner.

Another TT, the Blom fenestrated TT, has a special speech cannula that allows ventilator-dependent patients to speak with the cuff fully inflated. With the speech cannula inserted during inhalation, the flap valve opens and the flexible bubble valve expands, blocking the fenestrations. During exhalation the flap valve closes and the bubble valve collapses, which allows air to pass through the fenestrations, so the patient can speak (Fig. 37.35).[31]

Fig. 37.35 Blom fenestrated trach tube with speech cannula.

An alternative to a speaking TT is to place a one-way valve (speaking valve) on the external opening of the TT.[31] With this device in place and the TT cuff deflated, the patient inhales around and through the tube and exhales only around the tube through the larynx. Speech is coordinated with exhalation through the larynx. A patient who is a good candidate for a speaking valve is one who is medically stable, is able to communicate, and has a low risk for aspiration. Several types of speaking valves are available, as shown in Fig. 37.36. They can be used with spontaneously breathing or ventilator-dependent patients. When using the speaking valve, the cuff on the tube must be completely deflated to allow airflow around the tube. This deflation of the cuff causes a leak on inspiration and a decrease in tidal volume (V_T) delivery during mechanical ventilation. However, an increase in the set V_T on the ventilator during initial trials of the valve should compensate for this.

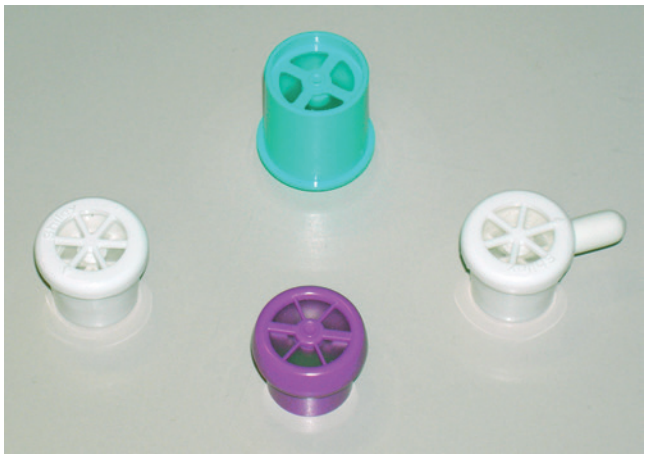

Fig. 37.36 Speaking valves.

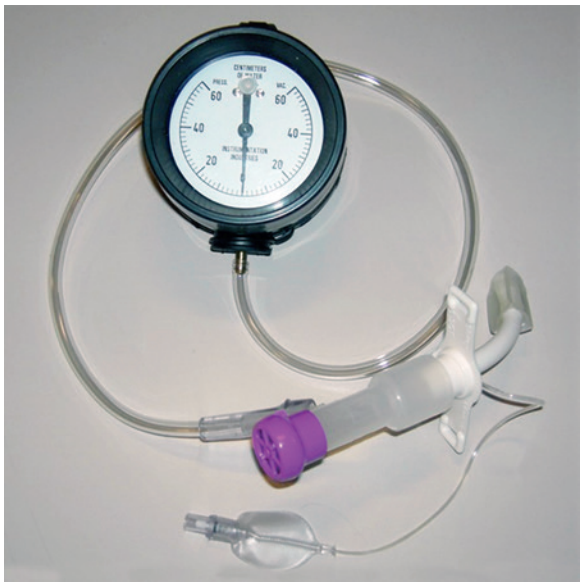

Fig. 37.37 Setup to measure transtracheal pressures with speaking valve on tracheostomy tube.

During the initial placement of the speaking valve, the patient's ability to exhale around the TT should be assessed by measuring the tracheal pressure during exhalation with the valve in place as shown in Fig. 37.37. If the tracheal pressure is greater than 5 cm H_2O, it may indicate that there is increased resistance during exhalation. The most common causes of this problem are the size of the TT relative to the size of the trachea, tube position, inadequate cuff deflation, or an upper airway abnormality.[31] The tube may need to be changed to a smaller size, to a cuffless tube, or to a tube with a TTS cuff. The speaking valve then can be placed and the tracheal pressure measured again. If an upper airway abnormality is suspected, an otolaryngologist should be consulted. A speech-language pathologist may be consulted to assist in the assessment of the patient's risk for aspiration and tolerance of the speaking valve.

RULE OF THUMB A speaking valve can aid in communication and can safely be used if transtracheal pressures are less than 5 cm H_2O.

BOX 37.7 Why Tracheal Airways Increase the Incidence of Pulmonary Infection

- Bypassed upper airway filtration
- Increased aspiration of pharyngeal secretions
- Contaminated equipment or solutions
- Impaired mucociliary clearance in trachea
- Increased mucosal damage owing to tube or suctioning
- Ineffective clearance via cough

Assessment of heart rate, respiratory rate, and saturation should follow initial placement of the valve for all patients. In addition to facilitating communication, other benefits of airflow over the upper airway include better function of the vocal cords, better sense of smell, and fewer secretion problems. Improved swallowing function and less aspiration have been reported with the speaking valve.[50,52]

RULE OF THUMB The tracheostomy tube cuff must be completely deflated before a speaking valve is placed on the tracheostomy tube.

Ensuring Adequate Humidification

Although tracheal tubes provide an artificial airway to conduct gas to and from the lungs, they do not function as well as natural airways. Specifically, artificial tracheal airways bypass the normal humidification, filtration, and heating functions of the upper airway. The decreased humidity in the inspired air can cause secretions to thicken. Cool air also can decrease ciliary function. These conditions may impair mucociliary clearance and cause retention of secretions. Several devices that provide artificial heat and humidification are available.

The selection of a humidification device ultimately should be based on patient needs and assessment of the airway and include the volume and thickness of secretions and the history of mucous plugging or tube occlusions. More details on humidification are provided in Chapter 39.

Minimizing Nosocomial Infections

Patients with tracheal airways are very susceptible to bacterial colonization and infection of the lower respiratory tract. The presence of infection is suggested by changes in the patient's sputum (color, consistency, or amount), breath sounds (wheezes, crackles, or rhonchi), or chest radiograph (infiltrates or atelectasis).[53] Additional changes associated with bacterial infection include fever, increased heart rate, and leukocytosis.

There are several reasons why tracheal tubes increase the incidence of pulmonary infection (Box 37.7).[53,54] To guard against infection, the clinician first should avoid introducing organisms into the airway. The clinician does this by (1) adhering to sterile technique during suctioning, (2) ensuring that only aseptically clean or sterile respiratory equipment is used for each patient, and (3) consistently performing hand hygiene between patient contacts (see Chapter 4).[55]

In addition, efforts should be made to prevent retention of secretions. Suctioning, chest physiotherapy, and adequate

humidification are useful to this end. Closed suction systems may be preferred to open suction systems in preventing infection.[55] Routinely cleaning or changing the inner cannula on TTs also may help to minimize bacterial contamination and infection. Techniques to decrease the consequences of pharyngeal aspiration include: (1) use of medications for stress ulcer prophylaxis, such as sucralfate, that maintain normal gastric pH; (2) positioning of patients with the head of the bed elevated 30 degrees or more to decrease reflux; and (3) continuous aspiration of subglottic secretions.[56]

Facilitating Secretion Clearance

The most common cause of airway obstruction in critically ill patients is retained secretions. To remove retained secretions, blood, or other semiliquid fluids from the large airways, the patient is suctioned as described previously in this chapter. Suctioning involves application of negative pressure to the large airways through a catheter. This method may be used alone or in combination with noninvasive techniques described in Chapter 44. One noninvasive technique is the mechanical insufflator-exsufflator (Cough Assist, J. H. Emerson, Cambridge, MA). The mechanical in-exsufflator (MIE) is primarily used to facilitate secretion clearance in patients with impaired cough, especially due to neuromuscular disease, such as ALS, spinal muscular atrophy (SMA), and muscular dystrophy (MD).[57]

Providing Cuff Care

Tracheal tube cuffs are used to seal the airway for mechanical ventilation or to prevent or minimize aspiration. As previously mentioned, tracheal stenosis and tracheomalacia are associated with cuff use. The pathogenesis of these problems is related to the amount of cuff pressure transmitted to the tracheal wall, impeding the flow of blood and lymphatic fluid. If cuff pressure exceeds the mucosal perfusion pressure, ischemia, ulceration, necrosis, and exposure of the cartilage may result (Fig. 37.38).

Importance of Cuff Pressure

In the past, high-pressure tracheal tube cuffs were a major cause of airway damage. Since the 1970s, high-residual-volume, low-pressure cuffs have become the norm (Fig. 37.39). The fully inflated diameter of these cuffs is greater than the diameter of the trachea. This means that the cuff does not have to be fully inflated to seal the airway, and less internal cuff pressure is needed. When properly used, these cuffs transmit less pressure to the tracheal wall than the older high-pressure designs. Although low-pressure cuffs have reduced the incidence of tracheal damage, they have not eliminated the problem entirely.

Cuff Inflation and Measuring and Adjusting Cuff Pressure

Key aspects of airway care are cuff inflation and cuff pressure measurement and adjustment. The goal is to keep cuff pressures less than the tracheal mucosal capillary perfusion pressure, estimated to range from 20 to 30 mm Hg.[45] Higher pressure cuts off mucosal blood flow and causes tissue damage. However, if the cuff pressure is too low, it does not prevent silent aspiration of pharyngeal secretions, which can contribute to the development of VAP. It is recommended to inflate the cuff to 20 to 30 cm H_2O, which should prevent tracheal mucosal injury. Minimal occluding volume and minimal leak inflation techniques are no longer recommended because they increase the risk for silent aspiration.[45]

Cuff pressure can be measured with various devices designed for this purpose. These devices measure the pressure and allow air to be added or withdrawn from the cuff. There are two key considerations when making these adjustments. First, most manometers are calibrated in centimeters of water, with the "acceptable range" of pressure 20 to 30 cm H_2O.[44] Second, attaching the measurement system to the pilot tube evacuates some volume from the cuff (and decreases its pressure). For this reason, the clinician should always adjust the pressure to the desired level and never just measure it.

High cuff pressures are a result of the need to overinflate the cuff to seal the airway. This problem is common if the tube chosen is too small for the patient's trachea or positioned too high in the trachea or if the patient has developed tracheomalacia (softening of the tracheal tissue). Another cause of high cuff pressures is high airway pressures generated by mechanical ventilation, which may require adding air to the cuff to maintain an adequate tracheal seal. Intracuff pressure measurements should be done regularly to maintain the cuff pressure in the safe range to avoid tracheal wall injury and minimize risk for aspiration of oral secretions.

Devices are currently available to continuously monitor intracuff pressures via tubing connected directly to the pilot line. A target pressure is set by the RT. The machine will add or withdraw air to maintain that set pressure. In addition, proprietary ETTs include a subglottic suction line. Periodic irrigation and removal of contaminated secretions above the cuff are associated with decreased rates of ventilator associated pneumonia.[58] Additional care must be given to the tubing connecting the pilot line of the artificial airway to the controller box. The tubing depresses the spring-loaded valve in the pilot line. Upon disconnection at the proximal attachment point, the volume within the cuff will escape, potentially leading to frank aspiration of subglottic secretions.

Alternative Cuff Designs

Some different types of cuffs have been designed to minimize mucosal trauma. The foam cuff is one, which is designed to seal the trachea with atmospheric pressure in the cuff (Fig. 37.40). Before insertion, the foam cuff must be deflated by actively withdrawing air from the cuff with a cuff pressure device or syringe. When in position, the pilot tube is opened to the atmosphere, and the foam expands against the tracheal wall. Expansion of the cuff stops when the tracheal wall is encountered. If too much air leak and volume loss occur around the tube, the pilot tube can be placed in line with the ETT. Foam cuff tubes are not commonly used except in patients who have already developed tracheal injury. This cuff can minimize tracheal mucosal trauma but does not minimize the risk for aspiration of oral secretions and may make mechanical ventilation difficult.

Another cuff design is the TTS cuff on some TTs (Fig. 37.41). This is a low-volume, high-pressure cuff designed to maximize airflow around the tube when it is deflated. It should be inflated

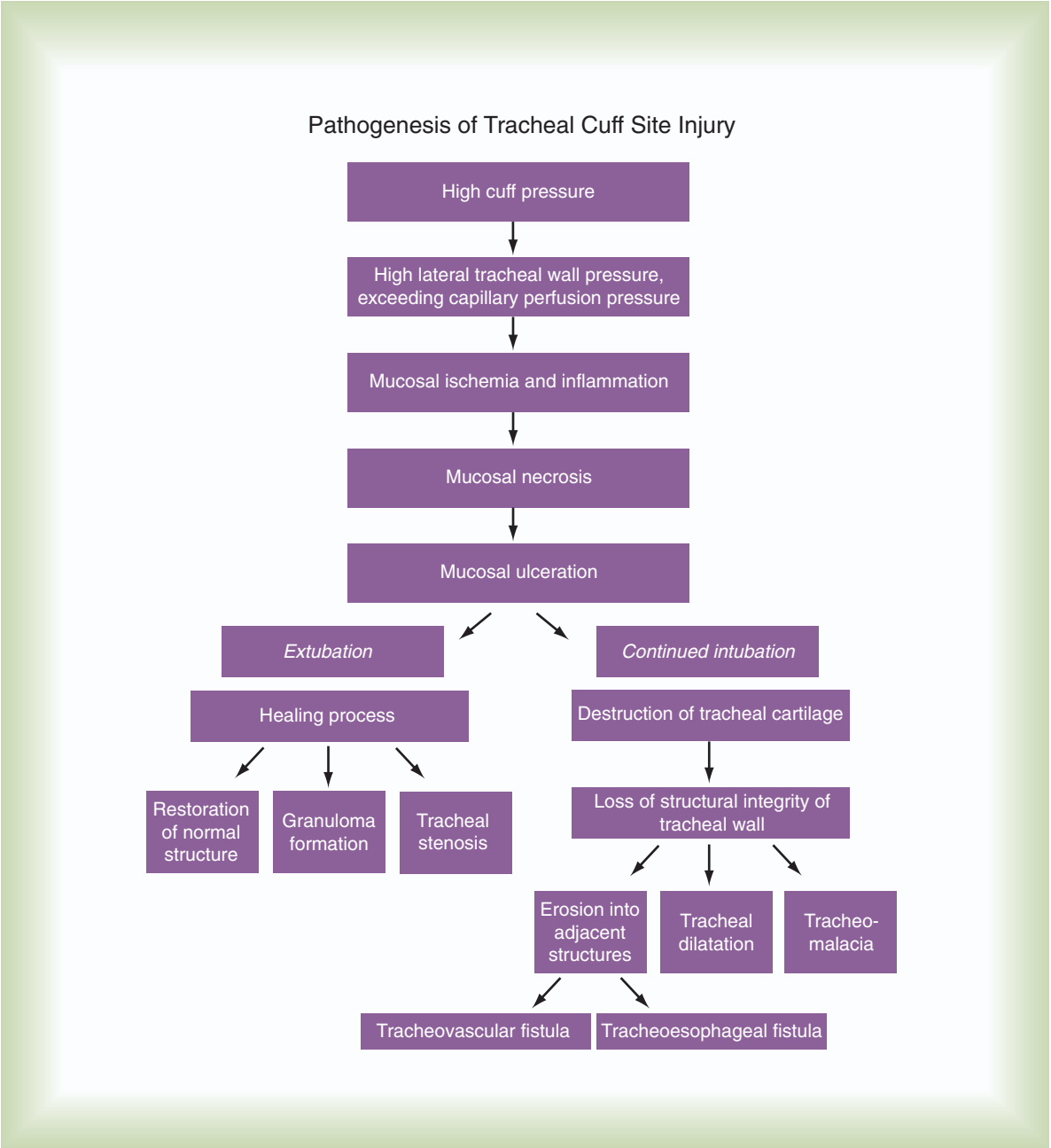

Fig. 37.38 Tracheal injury may occur secondary to trauma from the cuff. (Modified from Stauffer JL: Complications of endotracheal intubation and tracheostomy, *Respir Care* 44:828, 1999.)

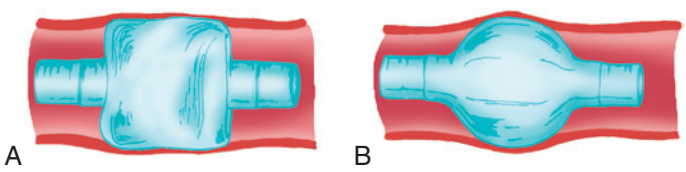

Fig. 37.39 Comparison of shapes of high-residual-volume, low-pressure cuff (A) and low-residual-volume, high-pressure cuff (B). (Modified from McPherson SP: *Respiratory therapy equipment*, ed 4, St. Louis, 1989, Mosby.)

only intermittently for airway protection or short-term ventilation. Because the cuff is made of a porous silicone material, it can be inflated only with sterile water and not air.

Prevention of silent aspiration is difficult because the current generation of cuffs when inflated properly create channels along the cuff in which secretions from above the cuff move by capillary action. Newer tubes with longer length ultrathin polyurethane cuffs form a cylinder shape or an inverted pear shape when inflated so that they do not form channels. These newer cuff designs and material seem to minimize silent aspiration that has been implicated in the development of VAP.[59]

Minimizing Likelihood of Aspiration

When judging the adequacy of a tracheal seal, the potential for aspiration should be taken into account. Keeping the cuff pressure between 20 and 30 cm H_2O helps to minimize aspiration and injury. In addition, aspiration is reported to be more common in spontaneously breathing patients than in patients receiving positive pressure ventilation; this may be due to the movement of pharyngeal secretions past the cuff during the negative pressure phase of a spontaneous inspiration.

A simple swallowing test can help to determine whether aspiration is occurring. These tests can be performed by various clinicians, including speech therapists, nurses, and RTs. To perform this test, blue food coloring is added to the patient's feedings or the patient swallows a small amount of blue food coloring in water. The patient's trachea is suctioned through the artificial airway. If blue-tinged secretions are obtained when performing suctioning, some aspiration is occurring. However, false-negative results can occur; the patient may still be aspirating despite no sign of blue coloring in suctioned secretions. For this reason, a modified barium swallow test may be needed to determine conclusively whether a patient is aspirating.[60]

If aspiration is confirmed, efforts must be made to minimize the aspiration. Ideally, the patient should be switched to a tube that continually aspirates subglottic secretions (see the previous section on Specialized Endotracheal Tubes). If it is impossible to make this switch, oropharyngeal suctioning (above the tube cuff) should be performed as needed. To decrease the possibility of aspiration with feedings, the head of the bed should be elevated 30 degrees or more when possible.[56] In addition, the feeding tube can be inserted into the duodenum, with its position confirmed by imaging. The use of slightly higher cuff pressure during and after feedings may minimize aspiration.

Care of Tracheostomy and Tube

TTs require daily care to clean the site and change the tie or holder securing the tube. The tubes also may be removed and replaced for routine cleaning or in an emergency, such as obstruction of the tube. The procedures for tracheostomy care and changing a TT are described in the following section.[61-63]

Tracheostomy Care

Step 1: Assemble and Check Equipment.

Box 37.8 lists the equipment needed for routine tracheostomy care. The equipment needed is for cleaning through the tube, around the tube, and the tube itself. Personal protective

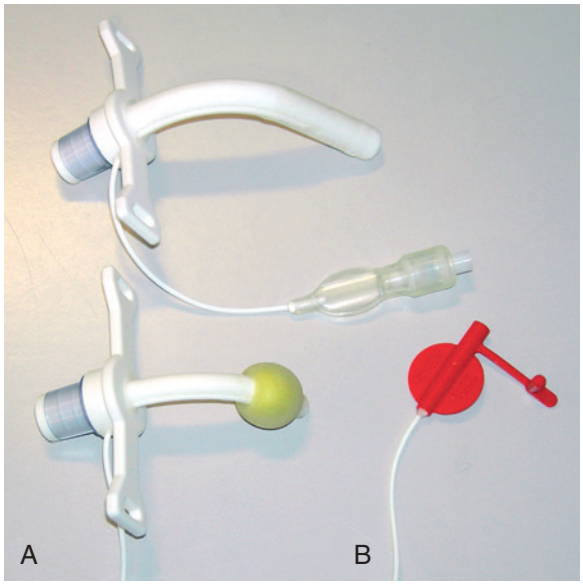

Fig. 37.40 Tracheostomy Tubes With Different Types of Cuffs. (A) Tight-to-shaft cuff. (B) Self-inflating foam cuff.

BOX 37.8 Equipment for Tracheostomy Care

- Personal protective equipment: Goggles and mask or face shield
- Sterile gloves
- Suction equipment
- Resuscitation bag
- Oxygen
- Tracheostomy care kit (basin and brush)
  - Spare inner cannula
  - Disposable inner cannula (if appropriate)
  - Hydrogen peroxide and sterile water
  - Cotton-tipped applicators
  - Precut gauze pad or precut foam dressing (to absorb excessive drainage)
  - New tracheostomy tube tie or Velcro tracheostomy tube (TT) holder
  - Another TT of the same size as backup
  - Additional equipment needed if changing TT
  - New TT with component parts and another tube one size smaller
  - Water-soluble lubricant
  - 10- or 12-mL syringe

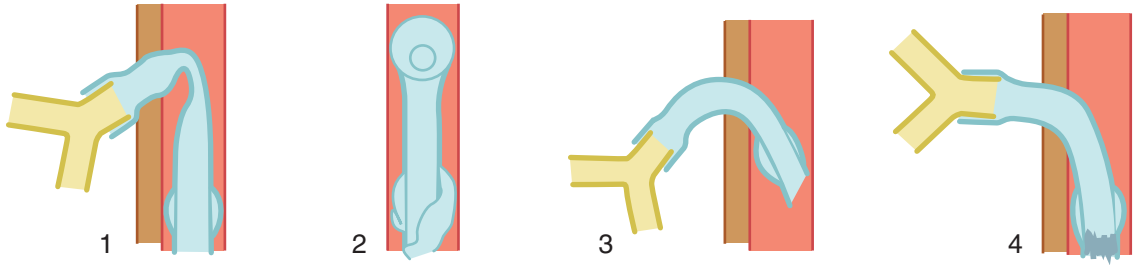

Fig. 37.41 Causes of Tube Obstruction. (See Text for Details.) (1) Kinked TT. (2) Cuff herniated over tip of TT. (3) Malpositioned TT where tip of tube is against posterior tracheal wall. (4) Properly positioned TT. (Modified from Sykes MK, McNichol MW, Campbell EJM: *Respiratory failure*, Philadelphia, 1969, FA Davis.)

equipment (face shield or mask and goggles) for the clinician is needed because stimulation of the trachea may result in coughing and expectorated secretions. Use of suction equipment to remove secretions from the tube before the procedure can decrease the possibility of secretions contaminating the environment. O_2 and a manual resuscitator are needed for the suctioning procedure and in case any problems such as desaturation occur. To clean around the tube, sterile water, cotton-tipped applicators, and tracheostomy sponges are needed along with a new tie or TT holder to secure the tube. A TT kit includes a basin and brush to clean the inner cannula of the tube. Alternatively, a disposable inner cannula may be used. The function of the manual resuscitator, O_2 flow, and suction control must be checked before starting.

Step 2: Explain Procedure to Patient.
Explain the procedure and confirm the patient understands what will be done.

Step 3: Suction Patient.
The procedures previously described for endotracheal suctioning are appropriate for this situation. A TT is much shorter than an ETT. The catheter is inserted just to the end of the TT to avoid causing mucosal injury to the carina.

Step 4: Clean Inner Cannula (If Present and Nondisposable).
The inner cannula is removed and placed in the basin. If appropriate, such as in the case of a ventilator-dependent patient, the spare inner cannula is inserted. Patients with certain types of TTs can be mechanically ventilated without an inner cannula in place. If the patient is not mechanically ventilated, the O_2 therapy device is reapplied as necessary. Sterile water is added to the basin, and the cannula is left to soak. A brush is used to remove any dried secretions from the inner lumen or the outside of the cannula. The cannula is rinsed with sterile water and allowed to air dry on sterile gauze.

Step 5: Clean and Examine Stoma Site.
The dressing (if present) is removed and disposed. Applicators that have been dipped in sterile normal saline are used to clean around the stoma site. After cleaning liquid, a skin barrier should be applied to protect the skin from moisture. A clean dressing, if needed to absorb drainage, is placed under the flange of the tube. An absorbent foam dressing, especially if there is excessive drainage around stoma, should be used. If the stoma site appears red or swollen, has pus around it, or is emitting a foul smell, the physician and nurse should be notified.

RULE OF THUMB Skin assessment around and underneath artificial airways should be completed frequently to prevent breakdown.

Step 6: Change Tie or Holder.
The clinician cuts the old tie or loosens the Velcro holder. One hand is kept on the flange of the TT to keep it secure. The old tie or holder is removed and discarded. The clinician replaces the tie or holder, keeping one finger-width of space between the neck and tie or holder.

Step 7: Replace Clean Inner Cannula (if present).
If the inner cannula is marked disposable and is not to be reused, a new one is inserted.

Step 8: Reassess Patient.
The clinician checks for adequate breath sounds, vital signs, and oxygenation and confirms no adverse effects.

RULE OF THUMB An extra tracheostomy tube of the same size and another, one size smaller, should be kept readily available in or near the patient's room in case of an accidental decannulation.

Changing a Tracheostomy Tube

A TT may need to be replaced in the case of long-term mechanical ventilation; if the current tube develops a problem, such as a mucous plug or damage to the cuff; or if a different size or type of tube is needed.[63] If a tube needs to be replaced before the stoma heals (7 to 10 days), it is best done by a physician. Intubation equipment should also be available. Because a single-cannula tube has no inner cannula to remove for cleaning, it may need to be replaced periodically.

Step 1: Assemble and Prepare Equipment.
In addition to the equipment described previously, the new tube, an extra tube one size smaller, and water-soluble lubricant are necessary. An additional TT that is one size smaller is necessary in the event of partial closure of the stoma site and difficulty reinserting initial size tube.

Step 2: Explain Procedure to Patient.

Step 3: Prepare Equipment.
Sterile technique must always be maintained for the distal portion of the cannula, which goes into the trachea. The inner cannula is removed and placed on a sterile surface. The obturator is inserted. The tie or TT holder is attached to one side of the flange of the tube. The clinician inflates the cuff, checks for leaks, and deflates the cuff. Lubricant is applied to the distal portion of the cannula.

Step 4: Prepare Patient.
The patient should be placed with the neck extended so that the tracheal stoma is accessible. The patient is suctioned and hyperoxygenated.

Step 5: Remove Old Tube.
The tie is cut, or the Velcro TT holder is opened. The cuff is deflated. The clinician removes the tube by following the curve of the tube. The clinician grasps the outer portion of the TT with one hand and rotates the wrist toward the chest. The stoma is inspected for any bleeding or other problems, such as granuloma or ulceration.

Step 6: Insert New Tube, Confirm Placement, and Assess Patient.
The new tube is picked up by the proximal portion. The surface that enters the trachea should not be touched. The tip of the obturator is inserted into the stoma, and the tube is advanced following the curve of the tube. While holding the flange of the tube against the neck, the clinician immediately removes the obturator. The clinician assesses for airflow through the tube. Coughing may reflect pressure on the outside of the trachea. The patient is assessed for proper tube placement and tolerance of the procedure. If extreme difficulty is encountered

inserting the new tube, insertion of the "stand-by" tube, which is one size smaller, is attempted.

Step 7: Secure Tube.

While still holding onto the flange, the clinician secures the TT tie or holder without overtightening. The inner cannula, if present, is inserted. If a cuff is present, it should be inflated to the appropriate pressure with the appropriate medium (air or sterile water, in the case of TTS cuff). The clinician reassesses for airflow and reapplies the O_2 therapy device or ventilator.

Step 8: Reassess Patient.

Suctioning may be required again. The clinician checks vital signs and SpO_2 and assesses the patient's overall tolerance of the procedure.

Troubleshooting Airway Emergencies

The areas discussed so far are routine aspects of airway care. Three emergency situations that may occur are tube obstruction, cuff leaks, and unplanned extubation. Clinical signs frequently encountered under these circumstances include various degrees of respiratory distress; changes in breath sounds; air movement through the mouth; or, if the patient is mechanically ventilated, changes in pressures.

Decreased breath sounds are a common finding in airway emergencies. The RT must try to identify specific indications of decreased breath sounds, such as the inability to pass a suction catheter (obstruction, occluded tube) or airflow around the tube (leaking cuff). Replacement airways, a manual resuscitator, mask, and gauze pads (for patients with tracheostomies) should be kept at the bedside.

Tube Obstruction

Obstruction of the tube is one of the most common causes of airway emergencies. Tube obstruction can be caused by: (1) the kinking of the tube or the patient biting on the tube, (2) herniation of the cuff over the tube tip,[64] (3) obstruction of the tube orifice against the tracheal wall, and (4) mucous plugging (see Fig. 37.41).

Different clinical signs are present depending on whether the tube obstruction is partial or complete.[41,65] A spontaneously breathing patient with partial airway obstruction exhibits decreased breath sounds and decreased airflow through the tube. If the patient is receiving volume-controlled ventilation, peak inspiratory pressures increase, often causing the high-pressure alarm to sound; during pressure-controlled ventilation, delivered V_Ts decrease. With complete tube obstruction, the patient exhibits severe distress, no breath sounds are heard, and there is no gas flow through the tube.

If the tube is kinked or positioned against the tracheal wall, the obstruction can be reversed by moving the patient's head and neck or repositioning the tube.[41] If this action does not relieve the obstruction, a herniated cuff may be blocking the airway. Deflating the cuff relieves the obstruction in such cases. If these steps fail to overcome the obstruction, the clinician can try to pass a suction catheter through the tube. The distance the catheter inserts before stopping helps to determine the site of obstruction. If the catheter does not travel much beyond the tube tip and insertion does not cause coughing, the likely problem is a herniated cuff or a mucous plug. In the case of mucous plugging, the clinician can attempt to remove the plug by suctioning the tube before considering more drastic action. Although instillation of sterile normal saline into the tube is not routinely needed during suctioning, it may facilitate mobilizing the mucous plug so that it can be more easily removed by suctioning. In addition, a mucus-shaving device may be used to clear thick, dried secretions from the inner lumen of the ETT. This device has a balloon at the end of the catheter. Once the catheter is inserted into the ETT, the balloon is inflated. When the catheter is withdrawn, the balloon scrapes the thick, dried mucus from the inside of the tube (Fig. 37.42).[66]

When the patient has a TT with an inner cannula, it should be removed and checked to see if the plug is lodged in the tube. O_2 should be provided to the patient through the outer cannula, or the inner cannula should be replaced with a spare one to facilitate manual ventilation.

If the obstruction cannot be cleared by using these techniques, the airway should be removed and replaced. In patients who have undergone recent tracheotomy (4 or 5 days earlier), the stoma may not be well established and may close when the tube is removed. If suture ties were left in place by the surgeon, they can be used to pull open the stoma.

After the obstructed airway is removed, the clinician should immediately try to restore adequate ventilation and oxygenation. For a patient with a tracheotomy stoma, the stoma may need to be covered with a gauze pad and the patient may need to be manually ventilated with a mask. Airway reinsertion by a properly trained RT or physician should be undertaken only after adequate ventilation and oxygenation are restored.

RULE OF THUMB If the patient exhibits respiratory distress and the cause is thought to be an obstructed tracheostomy tube, the inner cannula, if possible, should be promptly assessed for patency.

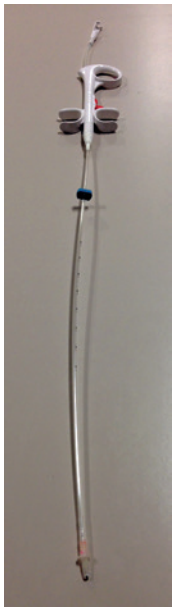

Fig. 37.42 Mucus-shaving device.

Cuff Leaks

A leak in the cuff, pilot tube, or one-way valve is a problem mostly for patients receiving mechanical ventilation. This leak causes a system leak, with a resultant loss of delivered volume or decreased inspiratory pressure or both.

A small cuff leak can be detected by noting decreasing cuff pressures over time. A large leak, such as occurs with a ruptured cuff, generally has a more rapid onset. Breath sounds are decreased, but a spontaneously breathing patient has air movement through the tube. With positive pressure breaths, airflow often is felt at the mouth. Under such circumstances, the RT should try to reinflate the cuff while checking the pilot tube and valve for leaks.[13] If the pilot tube or valve is leaking, the tube needs to be changed as soon as possible. However, a pilot valve (pilot balloon) repair kit, which permits the insertion of a replacement valve into the pilot tubing, can offer a safe and effective alternative until a replacement tube can be inserted.

A ruptured cuff requires extubation and reintubation emergently if the patient is being mechanically ventilated. This procedure can be done via the standard reintubation procedure or by using an ETT exchanger, which is a semirigid guide over which the damaged tube can be removed and the new tube promptly inserted. An ETT exchanger should be used only by an individual trained in its use, and all necessary intubation equipment and personnel should be available to perform a standard intubation if problems occur. An ETT that is positioned too high in the trachea and near the glottic opening can mimic a cuff leak. Before presuming a cuff leak, the RT should check the tube depth by noting the markings, and if the tube appears shallow, the RT should attempt to advance the tube slightly and reassess the leak. A leak around a tracheal tube can occur from a tube or cuff problem. Fig. 37.43 is a diagram of the process to investigate the source of a leak around a tube.[13]

MINI CLINI

Airway Cuff Problems

Problem

The RT is called to assist with a 220-lb, 6-ft 2-inch, male patient who is intubated with a 7-mm ETT and receiving positive pressure ventilation. The patient's nurse reports to the RT that over the past week it has been increasingly difficult to get a good seal with the tube cuff and that she has had to add "more and more air" to prevent gross leakage. When asked if the cuff pressures have been monitored, she says no. What is the likely problem and solution?

Discussion

"Low-pressure" cuffs can exert high pressure at high inflation volumes. The need for high volumes to get a good seal usually indicates that the ETT or tracheostomy tube is too small for the patient. This large man probably should have been intubated with at least an 8-mm tube. In addition, because cuff pressures were not monitored, it is possible that tracheal damage has already occurred. The fact that the nurse reports having to add "more and more air" to get a seal suggests tracheomalacia, which could be confirmed by radiographic or bronchoscopic examination.

Tracheomalacia can cause a vicious cycle in which high pressure causes more tracheal dilation, which requires higher pressures to seal the cuff, and so on. If tracheomalacia is confirmed and the patient still needs an artificial airway, the smaller tube should be replaced with a larger one that allows a good seal at acceptable cuff pressures. It also may be necessary to reposition the tube so that the cuff is not the original site of damage.

Unplanned Extubation

Partial displacement of an airway out of the trachea can be detected by noting decreased breath sounds, decreased airflow through the tube, and the ability to pass a catheter to its full length without meeting an obstruction or eliciting a cough. With positive pressure ventilation, airflow through the mouth or into the stomach may be heard and a decrease in delivered volumes or pressures occurs. In these cases, the tube should be completely removed and ventilatory support should be provided by manual resuscitator and mask as needed until the patient can be reintubated or the TT reinserted. To monitor trends and optimize quality outcomes associated with unplanned extubations, hospitals often require certain details of such incidents to be recorded.

RULE OF THUMB Resuscitation efforts differ greatly in patients with a tracheostomy tube versus a laryngectomy.

Tracheostomy—cover stoma with gauze; provide manual ventilation to upper airway.

Laryngectomy—provide manual ventilation via a small mask to the stoma site because there is no longer communication between the upper and lower airway.

Partial laryngectomy—may be able to ventilate via the upper airway because the separation was not complete. Attempts at both routes maybe necessary to determine which approach results in the best ventilation.

EXTUBATION OR DECANNULATION

For most patients, tracheal intubation is a temporary measure. The artificial airway should be removed when it is no longer needed. The process of removing an artificial tracheal airway is called **extubation** (ETT) or **decannulation** (TT). Although most patients eventually undergo extubation, a few need to maintain a permanent artificial route, usually by tracheostomy. Permanent tracheostomies are common among patients with surgically treated throat or laryngeal cancer and patients requiring long-term positive pressure ventilation. Advances in noninvasive mechanical ventilation have reduced the need for permanent tracheostomies in the latter group.

Assessing Patient Readiness for Extubation

A patient is ready to be extubated when the original need for the artificial airway no longer exists. Because artificial airways are inserted for many different reasons, several different criteria to establish readiness for extubation need to be considered. Some basic assessments include the ability to maintain adequate oxygenation and ventilation without mechanical support, ability of

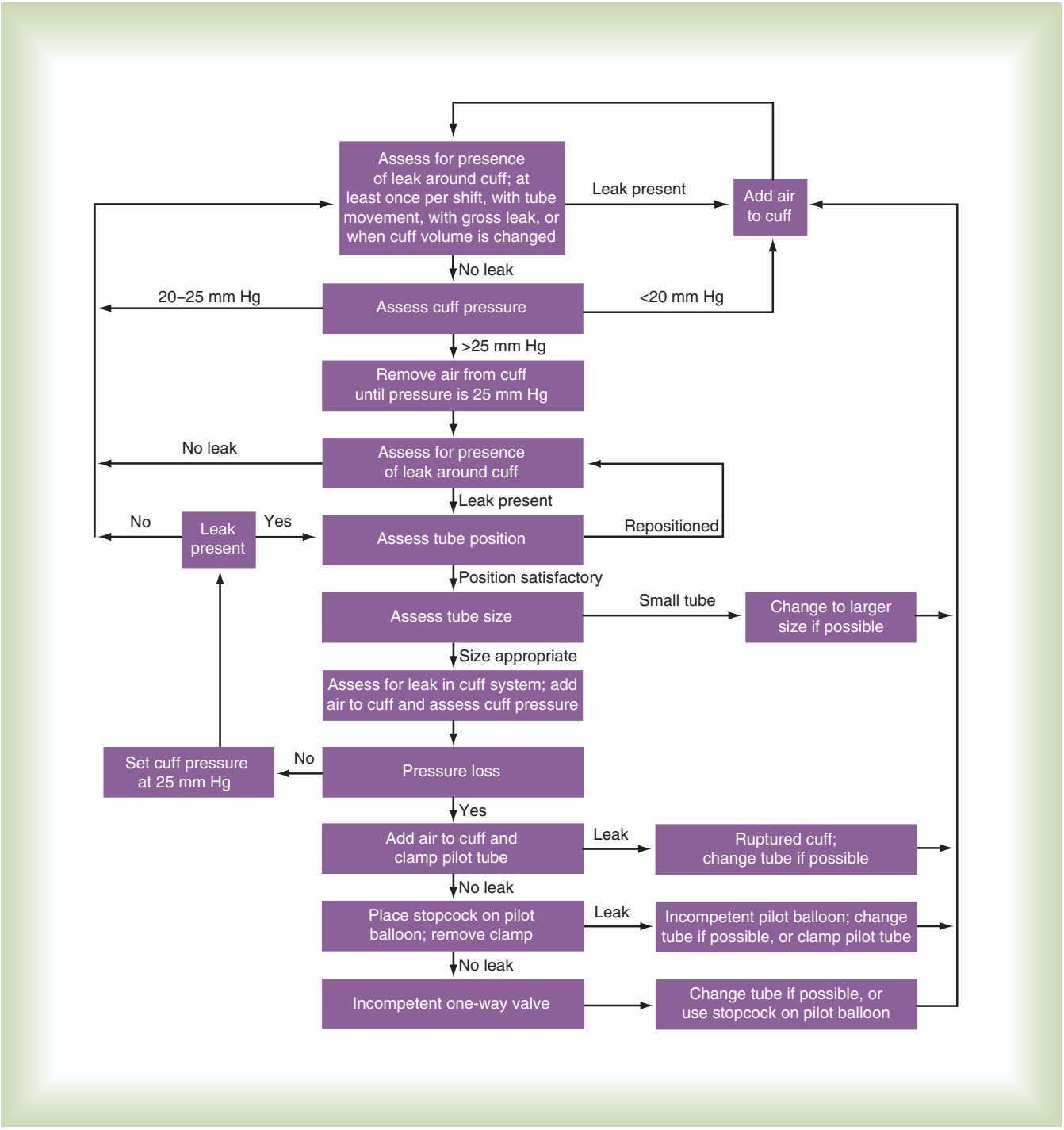

Fig. 37.43 Algorithm for solving leaking cuff problems. (From Hess D: Managing the artificial airway, *Respir Care* 44:759, 1999.)

the patient to protect the airway by the presence of a gag reflex, the ability to manage secretions based on cough strength, the quantity and thickness of secretions, and the patency of the upper airway.

The decision to remove the airway may not be the same as the decision to discontinue mechanical ventilation. The ventilator and airway may be removed simultaneously in the case of patients with normal lungs intubated for surgery. If a patient was intubated because of respiratory failure and has improved, but the upper airway problems remain (e.g., no gag reflex), the ventilator may be discontinued before extubation. In this scenario, it is customary to place a tracheostomy tube to assist with airway protection.

The cuff-leak test is designed to help predict the occurrence of glottic edema or stridor after extubation.[67,68] The clinician totally deflates the tube cuff and assesses the leak around the

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Extubation Assessment

Problem

A physician informs the RT that a patient recently removed from a ventilator is maintaining adequate oxygenation and ventilation via spontaneous breathing through an oral ETT. She requests that the RT evaluate the patient for extubation. What would the RT assess and why?

Discussion

Because the patient is maintaining adequate oxygenation and ventilation off the ventilator, two key criteria for extubation have already been met. Further assessment is needed to determine (1) the risk for upper airway obstruction after extubation, (2) the level of protection against aspiration, and (3) the ability of the patient to clear secretions after extubation. First, the RT should perform a leak test to assess for upper airway edema. Second, the RT should determine the patient's level of consciousness and neuromuscular function by assessing the gag reflex or having the patient try to raise and hold his or her head off the bed. Third, the RT should determine the patient's ability to cough, using either subjective assessment (on suctioning) or measurement of maximum expiratory pressure or peak cough flow. Extubation should be recommended only if all three areas yield positive results.

tube during positive pressure ventilation in a volume-controlled mode. The percent of the cuff leak should be approximately 15% or greater, as determined by the difference between the measured expiratory V_T with the cuff inflated and then deflated.[67] If the exhaled volume is 500 mL with the cuff inflated and 400 mL with the cuff deflated, the difference is 100 mL. The percent cuff leak is 20% (100 mL divided by 500 mL), which suggests that there is no significant upper airway edema or obstruction. However, some data suggest that this test may not always be predictive of the presence of upper airway obstruction or edema.[68] This test may be most useful in patients who are at greatest risk for postextubation stridor, such as children, women, and patients intubated for more than 6 days.[69] Some patients who fail the test or who have questionable results may still be extubated, but they must be closely monitored with the appropriate personnel and equipment available to reestablish the airway if needed.

Procedures

Because RTs play a key role in extubation and decannulation and the techniques differ, the procedures for removing orotracheal or nasotracheal (extubation) and TTs (decannulation) are reviewed separately.

Orotracheal or Nasotracheal Tubes

The procedure for orotracheal or nasotracheal extubation is as follows.

Step 1: Assemble Needed Equipment.
Needed equipment includes suctioning apparatus; two suction kits with correct size sterile suction catheters and gloves; tonsillar suction tip (Yankauer); 10-mL or 12-mL syringe; O_2 and aerosol therapy equipment; manual resuscitator and mask; aerosol nebulizer with racemic epinephrine and normal saline (if concerns regarding postextubation edema); and intubation equipment (laryngoscope blades, handle, ETTs, stylets, water-soluble lubricant, syringe to inflate cuff, tape or holder to secure tube).

Step 2: Suction ETT and Pharynx Above Cuff.
Suctioning before extubation helps to prevent aspiration of secretions after cuff deflation. After use, the first suction kit should be discarded, and another should be prepared for use, or a rigid tonsillar (Yankauer) suction tip should be prepared to suction the oropharynx.

Step 3: Oxygenate Patient Well After Suctioning.
Extubation is a stressful procedure that can cause hypoxemia and unwanted cardiovascular side effects. To help avoid these problems, 100% O_2 should be administered for 5 minutes.

Step 4: Deflate Cuff.
The 10- or 12-mL syringe is attached to the pilot tubing. All the air is withdrawn from the cuff while applying positive pressure to direct any pooled secretions above the cuff up into the oropharynx, where they can immediately be suctioned with the tonsillar suction tip. The RT should listen for an audible leak around the tube. If no audible leak is present, the RT should reinflate the cuff and discuss with the physician how to proceed.

Step 5: Remove Tube.
The tape or holder that is securing the tube is removed. The technique used to remove the tube should help to avoid aspiration of pharyngeal secretions and maximally abduct the vocal cords. Clinicians use one of two different techniques to accomplish these goals. In the first method, a large breath is given with the manual resuscitator, and the tube is removed at peak inspiration (when the vocal cords are maximally abducted). In the second method, the patient coughs and the tube is pulled during the expulsive expiratory phase. This technique also results in maximal abduction of the vocal cords.

Step 6: Apply Appropriate Oxygen and Humidity Therapy.
Patients who have been receiving mechanical ventilation may still require O_2 therapy, usually at a higher FiO_2. Other patients may require some O_2 because this is a stressful procedure. If humidity or aerosol therapy is indicated, apply a cool mist immediately after extubation.

Step 7: Assess or Reassess Patient.
After extubation, auscultation is performed to check for good air movement. Stridor or decreased air movement after extubation indicates upper airway problems. Next, the patient's respiratory rate, breathing pattern, heart rate, blood pressure, and SpO_2 are checked. Mild hypertension and tachycardia immediately after extubation are common and resolve spontaneously in most cases. The patient should be monitored for nosebleed after nasotracheal extubation. The patient is encouraged to cough, with assistance as needed. Because laryngeal edema may worsen with time and stridor may develop, racemic epinephrine for nebulization should be available. Arterial blood gas (ABG) values should be sampled and analyzed as needed.

The most common problems that occur after extubation are hoarseness, sore throat, and cough.[43] These problems are benign and improve with time. A rare but serious complication associated with extubation is laryngospasm. Postextubation

laryngospasm is usually a transient event, lasting several seconds. If laryngospasm occurs, oxygenation can be maintained with a high FiO_2 and the application of positive pressure. If laryngospasm persists, a neuromuscular blocking agent may need to be given, which necessitates manual ventilation or reintubation.

Because the vocal cords have had limited function during the intubation period, they may not close fully as needed when the airway has been removed. To avoid aspiration, oral feedings, especially liquids, should be withheld for 24 hours after extubation. Patients may aspirate liquids even with an intact gag reflex.[50]

Extubation failure, defined as the sudden need for reinsertion of the airway because of airway problems, often occurs within 8 hours of extubation. Aspiration and edema are the most common problems. If the patient also is mechanically ventilated, reintubation may be required for work of breathing issues unrelated to the airway.

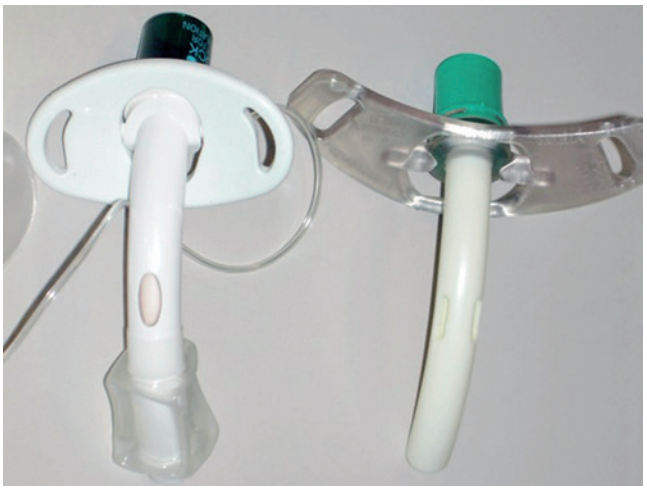

Fig. 37.44 Fenestrated tracheostomy tubes.

Tracheostomy Tube Removal (Decannulation)

Decannulation refers to removal of the TT. Several approaches exist to remove TTs. Patients who received a tracheostomy because of upper airway obstruction that has been resolved may have their tube removed in one step. Patients who have been on mechanical ventilation for an extended time may have problems with muscle weakness, problems adjusting to the increase in anatomic dead space, and upper airway problems with secretions and glottic closure. For these patients, a weaning process is used rather than abrupt removal of the tube. Weaning is accomplished by using fenestrated tubes, progressively smaller tubes, or tracheostomy buttons.[70]

Before decannulation, a comprehensive patient assessment is required. The patient should have sufficient muscle strength (peak expiratory pressure >40 cm H_2O) to generate an effective cough. Ideally, there should be no active pulmonary infection, and the volume and thickness of secretions should be acceptable. Patency of the upper airway can be assessed by bronchoscopy.[68] An adequate swallow must be present to decrease the risk for aspiration. After removal of the tube, the stoma closes on its own in a few days. After cleaning around the stoma, a sterile occlusive dressing should be applied over the stoma until it closes. The particular decannulation technique used depends on the patient's needs.

Fenestrated Tracheostomy Tubes

A **fenestrated** TT is a double-cannulated tube that has an opening in the posterior wall of the outer cannula above the cuff (Fig. 37.44). Removal of the inner cannula opens the fenestration, allowing air to pass into the upper airway. Capping or placing a speaking valve on the proximal opening of the tube's outer cannula, accompanied by deflation of the cuff, allows for assessment of upper airway function. Removal of the cap or speaking valve allows access for suctioning. If mechanical ventilation is needed, the inner cannula can be reinserted and the cuff reinflated.

One problem associated with this type of TT is malposition of the fenestration, such as between the skin and stoma or against the posterior wall of the larynx.[45] Customizing the fenestration or trying a fenestrated tube of a different size or by a different manufacturer can help to avoid this problem. Proper placement can be confirmed by using flexible bronchoscopy.

Case reports have shown granular tissue formation in some patients using a fenestrated TT. Granular tissue tends to form on the posterior tracheal wall, above the tube fenestration. This granular tissue may occlude the fenestration, cause bleeding (especially with tube changes), or result in airway obstruction on decannulation. Given the location of this granular tissue, these problems may be due to poor positioning of the fenestration within the airway.

Progressively Smaller Tubes

A second airway weaning technique is to use progressively smaller TTs. Similar to fenestrated tubes, this approach maintains the airway, but it allows for increasing use of the upper airway. This technique is also indicated in patients whose airway is too small for the available fenestrated tubes. The use of progressively smaller tubes may also allow for better healing of the stoma.

The problem with these techniques is the continued presence of a tube within the lumen of the airway.[69] The presence of the tube (cuffed or uncuffed) increases airway resistance. In patients with preexisting obstructive disorders, this added airway resistance may be too high to sustain spontaneous breathing, resulting in failed decannulation. These tubes also can impair coughing by preventing full compression of the inspired thoracic volume. The last factor to consider when using smaller tubes is the fit of the tube within the trachea. Smaller tubes have not only a smaller diameter but also a different length and angle of curvature; this may result in the tip of the tube impacting the posterior tracheal wall or the distal tip migrating into the subcutaneous space in the neck.

Tracheal Buttons

The tracheal button also may be used to maintain a tracheal stoma.[45] In contrast to the fenestrated tube, the tracheal button fits through the skin to just inside the anterior wall of the trachea

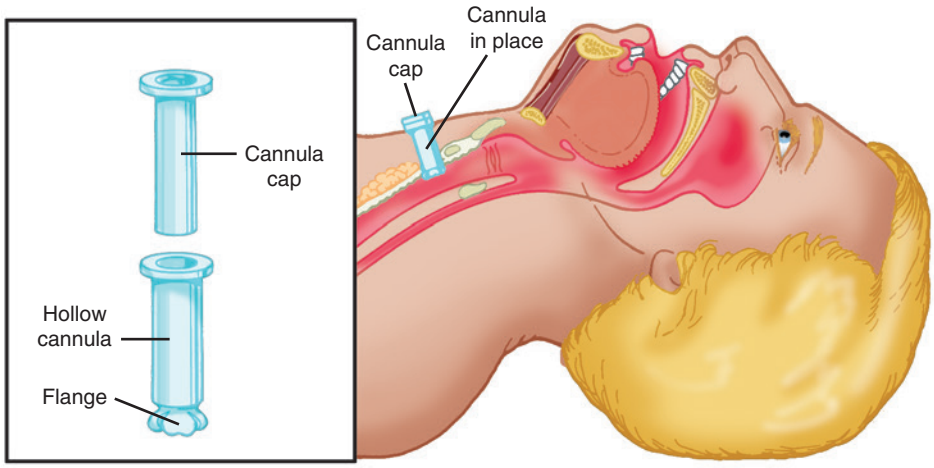

Fig. 37.45 Tracheostomy button.

(Fig. 37.45), which avoids the problem of added resistance. Because the tracheal button has no cuff, its use is limited to relieving airway obstruction and aiding the removal of secretions. When the inner cannula is removed, the clinician can suction through the outer cannula. However, when the inner cannula is removed, the clinician needs to hold the outer cannula in place to prevent it from being coughed out during suctioning.

Assessment After Tracheostomy Decannulation

After tracheostomy decannulation, the patient should be assessed for vocal cord responses.[69] Vocal cord abnormalities can result in either aspiration or acute airway obstruction. Symptoms such as stridor, retractions, and inability to feel airflow through the upper airway indicate upper airway obstruction. A replacement TT and suctioning equipment should be available in case the patient develops any of these symptoms of obstruction.

SUMMARY CHECKLIST

- Retained secretions or other semiliquid fluids are removed from the large airways via suctioning. Removal of foreign bodies or tissue masses beyond the mainstem bronchi requires bronchoscopy.
- To avoid or minimize the complications of suctioning, the RT needs to: (1) preoxygenate, (2) limit negative pressure and suction time, and (3) use sterile technique.
- The primary indications for an artificial tracheal airway are: (1) to relieve airway obstruction, (2) to facilitate secretion removal, (3) to protect against aspiration, and (4) to provide positive pressure ventilation.
- There are two basic types of tracheal airways: endotracheal (translaryngeal) tubes and TTs.
- Orotracheal intubation is the preferred route for establishing an emergency tracheal airway.
- Before intubation, adequate ventilation and 100% O_2 by manual resuscitator and mask should be provided.
- No more than 30 seconds should be devoted to any intubation attempt.
- There are many ways to assess ETT position; only laryngoscopy or bronchoscopy can definitively confirm positioning in the trachea.
- Serious complications of emergency airway management include acute hypoxemia, hypercapnia, bradycardia, and cardiac arrest.
- Nasotracheal intubation is the preferred route for intubation of patients with maxillofacial injuries.
- An LMA or a double-lumen airway (Combitube) can be used in a difficult intubation.
- The primary indication for tracheotomy is the continuing need for an artificial airway after a prolonged period of oral or nasal intubation; the decision when to switch from ETT to TT should be individualized.
- Cricothyroidotomy is performed when a patient cannot be intubated or ventilated.
- The most common laryngeal injuries associated with endotracheal intubation are glottic edema, vocal cord inflammation, laryngeal or vocal cord ulcerations, and vocal cord polyps or granulomas.
- Although laryngeal lesions occur only with oral or nasal ETTs, tracheal lesions can occur with any tracheal airway. The most common tracheal lesions are granulomas, tracheomalacia, and tracheal stenosis.
- To minimize or prevent trauma secondary to tracheal airways, the RT needs to: (1) select the correct size of airway, (2) avoid tube movement or traction, (3) maintain appropriate cuff pressures, and (4) use sterile techniques.
- To minimize the risk for infection, the RT needs to: (1) use closed suction devices, (2) use passive humidification, (3) monitor cuff pressure carefully, (4) use subglottic suction, and (5) keep the head of the bed elevated.
- ETT obstruction can be caused by: (1) kinking of or biting on the tube, (2) herniation of the cuff over the tube tip, (3) obstruction of the tube orifice against the tracheal wall, and (4) mucous plugging.
- If a tracheal airway appears to be completely obstructed, the RT needs to perform the following steps in order until the obstruction is relieved: (1) Reposition the patient's head and

neck, (2) deflate the tube cuff, (3) try passing a suction catheter, (4) try removing the inner cannula of the TT, and (5) remove the airway and provide bag-valve-mask ventilation and oxygenation.

- A patient is ready for extubation if the patient: (1) can maintain adequate spontaneous oxygenation and ventilation, (2) is at minimal risk for upper airway obstruction, (3) has adequate airway protective reflexes, and (4) can adequately clear secretions.
- Tracheostomy decannulation can be accomplished by using fenestrated tubes, progressively smaller tubes, or tracheostomy buttons.

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38

Emergency Cardiovascular Life Support

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CHAPTER OBJECTIVES

After reading this chapter you will be able to

- List the causes of sudden cardiac arrest (SCA)
- List the signs of SCA, heart attack, and foreign body airway obstruction
- Describe how to perform cardiopulmonary resuscitation (CPR) on adults, children, and infants
- Describe how use a bag-valve-mask device without causing gastric inflation
- Describe how to perform defibrillation with automated external defibrillators and manual defibrillators
- State how to administer synchronized cardioversion
- Describe how to evaluate the quality and effectiveness of CPR
- List the complications that can occur as a result of resuscitation from SCA
- State when not to initiate CPR
- Describe how to apply key adjunct equipment during Advanced Cardiac Life Support (ACLS)
- State common drugs and drug routes used during ACLS
- Describe how to monitor patients before cardiac arrest, during CPR, and after cardiac arrest

CHAPTER OUTLINE

KEY TERMS

abdominal thrust
active compression/decompression (ACD)
active compression/decompression device
Advanced Cardiovascular Life Support (ACLS)
automated external defibrillators (AEDs)
Basic Life Support (BLS)
cardiopulmonary resuscitation
cardioversion
defibrillation
gastric inflation
impedance threshold device
Pediatric Advanced Life Support (PALS)
synchronized cardioversion

Respiratory therapists (RTs) play a vital role in emergency cardiovascular life support. In hospitals, RTs serve as key members of medical emergency teams, also known as *rapid response teams.* In addition to managing the airway, RTs often provide ventilatory and circulatory support; drug and electrical therapy; and monitoring immediately before, during, and after a cardiac arrest.

In the community, RTs also may be certified **cardiopulmonary resuscitation** (CPR) instructors, extending their knowledge to lay people through organizations such as the American Heart

Association (AHA) and the American Red Cross. Mastery of an extensive knowledge base and the development of various, sometimes difficult manual skills are required for teaching and performing CPR. The practitioner is encouraged to obtain further competencies by completion of formal courses in CPR, **Advanced Cardiovascular Life Support (ACLS)**, **Pediatric Advanced Life Support (PALS)**, and a neonatal resuscitation program.

CAUSES AND PREVENTION OF SUDDEN DEATH

Sudden cardiac arrest (SCA) is a leading cause of death among adults over the age of 40 in the United States and many other parts of the world.[1,2] In the United States, approximately 500,000 people per year experience SCA and receive an attempted resuscitation. Pulseless ventricular rhythms are the first manifestation of 23% of emergency medical services (EMS)–treated out-of-hospital cardiac arrests.[3] Each year, approximately 209,000 people are treated for in-hospital cardiac arrest.[4] In 2011, approximately 326,200 people experienced emergency medical services–assessed out-of-hospital cardiac arrests in the United States.[4] Successful resuscitation depends on immediate CPR and the delivery of a shock before pulseless ventricular rhythms deteriorate into asystole. In cases of SCA related to asphyxia due to trauma, drug overdose, or upper airway obstruction, CPR with chest compressions and ventilation before the shock is critical.

BASIC LIFE SUPPORT

The goal of **Basic Life Support (BLS)** is to restore ventilation and circulation to victims of airway obstruction and respiratory or cardiac arrest. These skills can be used by a single practitioner to restore ventilation and circulation until the victim is revived or until ACLS equipment and personnel are available. The steps for administering BLS by a single health care practitioner are as follows:

1. Check for lack of movement or response and no normal breathing or only gasping.
2. Activate the emergency response system (get and use an **automated external defibrillator [AED]** if available close to your location).
3. If no AED is available, start chest compressions and rescue breathing for adult cardiac arrest (use cycles of 30 compressions to 2 ventilations).
4. Open airway and check breathing.
5. If the person is not breathing, give two breaths that produce chest rise.
6. Immediately resume chest compressions (push hard and deep with a minimum depth of 2 inches [5 cm] and a rate of 100 to 120 per minute. Do not exceed 120 compressions/min because depth of compression and release of pressure during chest compression will be affected).
7. AED arrives with response team.

Steps 3 through 6 are referred to as the *CABDs* of resuscitation—circulation, airway, breathing, and defibrillation. Table 38.1 summarizes the CABDs of CPR for adults, children (1 year old to puberty), and infants (younger than 1 year).

Determining Unresponsiveness

BLS begins with immediate recognition of SCA and activation of the emergency response system based on assessment of unresponsiveness, not moving, and no normal breathing (only gasping). Check for a do-not-intubate/do-not-resuscitate (DNI/DNR) advanced directive if the resuscitative effort is in a medical setting or hospice at home and proceed accordingly.

Whatever the location, the victim's level of consciousness should be assessed quickly by checking for signs of life (e.g., movement and normal breathing). The rescuer should call for help and activate the emergency medical services (EMS) system if the patient is not moving or breathing or only gasping. Outside the hospital, someone may have to call 911 or the emergency number for the local EMS system. Within the hospital, specific protocols exist for "calling a code." All RTs must be familiar with the protocols of their institution for handling these emergency situations.

Restoring Circulation

Determining Pulselessness

For ease of training, the lay rescuer should be taught to assume that a cardiac arrest is present if the unresponsive victim is not breathing or only gasping; he or she should not take time to check for a pulse. Health care workers may also take too long for a pulse check and have difficulty determining whether a pulse is present. For this reason, if no pulse is found within 10 seconds, health care rescuers should immediately proceed with chest compressions.

RULE OF THUMB Assessment of the pulse of an unresponsive patient by health care providers should be limited to 10 s to avoid delaying chest compressions. Pulse checks are difficult to accomplish with any fidelity. Pulse and rhythm checks should not be done after a shock until five cycles of CPR have been completed. Pulse checks should not be done by lay rescuers.[5]

Pulselessness is evaluated by palpating a major artery. In adults and children older than 1 year, the carotid artery in the neck or femoral artery should be palpated. To locate the carotid artery, the rescuer should maintain the head-tilt with one hand while sliding the fingers of the other hand into the groove created by the trachea and the large neck muscles (Fig. 38.1). The carotid artery area must be palpated gently to avoid compressing the artery or pushing on the carotid sinus. Because the pulse may be slow, weak, or irregular, the artery may have to be assessed for approximately 10 seconds in order to confirm the presence or absence of a pulse.

For infants, the brachial artery is preferred for assessing pulselessness. To palpate the brachial artery, the rescuer must grasp the infant's arm with two or three fingers and, the thumb outward, slide his or her fingers down toward the antecubital fossa and press gently for 5 to 10 seconds to feel for a pulse (Fig. 38.2). The femoral artery can also be palpated; this may be done for an adult, a child, or an infant.

TABLE 38.1 Steps for Cardiopulmonary Resuscitation in Adults, Children, and Infants

Procedure	Adult[5]	Child[14]	Infant[11]
Compressions			
Where to check pulse (limit pulse check to <10 s)	Carotid artery	Carotid or femoral artery	Brachial artery
Hand placement	Heel of one hand on sternum in center of chest, between nipples. Second hand on top of first with hands overlapped and parallel	Lower half of sternum with heel of one hand or with two hands (for larger children). Do not compress over xiphoid	Sternum with two fingers placed just below nipple line in center of chest
Compression-to-ventilation ratio	One or two rescuers, 30:2	One rescuer, 30:2; two rescuers, 15:2	Neonatal: One rescuer 3:1 ratio of compressions to ventilation, with 90 compressions and 30 breaths to achieve approximately 120 events per minute to maximize ventilation at an achievable rate; 15:2 for cardiac origin
Cycles of compression-to-ventilation	5	5	n/a
Depth of compressions (push in hard and fast, allow chest to recoil fully)	Minimum of 2 in (5 cm)	At least one-third anteroposterior diameter of chest or 2 inches (5 cm)	At least one-third anteroposterior diameter of chest or 1½ inch (4 cm)
Compression rate	100–120/min (do not exceed 120/min)	100–120/min (do not exceed 120/min)	120/min
Breathing			
Obstructive procedure	*Responsive:* If mild, allow victim to clear the airway by coughing. If severe, repeat abdominal thrusts until foreign body is expelled or the choking victim becomes unresponsive. Consider chest thrusts if abdominal thrusts are ineffective, if rescuer is unable to encircle victim's abdomen, or if victim is in the late stages of pregnancy *Unresponsive:* Carefully move victim to the ground, immediately activate EMS system, and begin CPR (compressions first), then look into the mouth before giving breaths. If a foreign body is seen, it should be removed. Follow ventilation with chest compressions	Same as for adult	*Responsive:* If mild, allow infant to clear the airway by coughing. If infant is unable to make a sound (severe obstruction), deliver five back blows (slaps) followed by chest thrusts repeatedly until object is expelled or infant becomes unresponsive. Abdominal thrusts should not be done on infants because they may damage the largely unprotected liver *Unresponsive:* Activate EMS system and begin CPR, 30 chest compressions first, then look into the mouth before giving breaths. If a foreign body is seen, it should be removed. Follow ventilations with cycles of 30 chest compressions and 2 ventilations
Rescue Breathing (Pulse Present)			
Palpable pulse but no spontaneous breaths or inadequate breathing	10–12/min, 1 breath every 5–6 s	12–20/min, 1 breath every 3–5 s; if palpable pulse ≥60/min	40–60/min, 1 breath every 1–1.5 s; if palpable pulse ≥60/min to <100/min

In critical care settings within the hospital, bedside monitoring equipment may provide supporting or confirming information regarding the respiratory or circulatory status of a patient. However, information obtained from these devices should never be a substitute for careful clinical assessment.

If the patient has a pulse but is not breathing, ventilation must be started immediately at the appropriate rate of 8 to 10 breaths/min (every 6 to 8 seconds). If no pulse is palpable, external chest compressions must be interposed with ventilatory support. Deliver cycles of 30 compressions and 2 ventilations until an advanced airway is placed; then deliver uninterrupted chest compressions with asynchronous ventilations at a rate every 6 to 8 seconds (8 to 10 per minute) (see Table 38.1).

Providing Chest Compressions

Adequate circulation can be restored in a pulseless victim using external chest compressions. The rescuer manually compresses the lower half of the sternum (for an adult patient) at a minimum rate of 100 compressions/min without exceeding 120 per minute as a maximum recommended frequency of compressions. The duty cycle for downstroke and upstroke (release) is a 1:1 downstroke-to-upstroke ratio. It is very important to have a complete upstroke so as not to increase intrathoracic pressure during the diastolic phase. The best way to ensure that the upstroke is complete is for the rescuer to take his or her hand slightly off the chest between compressions and avoid leaning on the chest.[5-7] Cardiac output produced by external chest

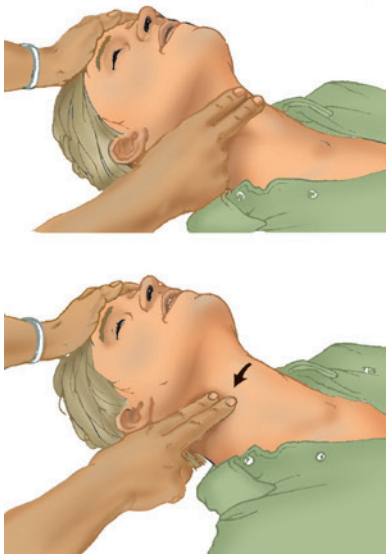

Fig. 38.1 Determining Pulselessness.

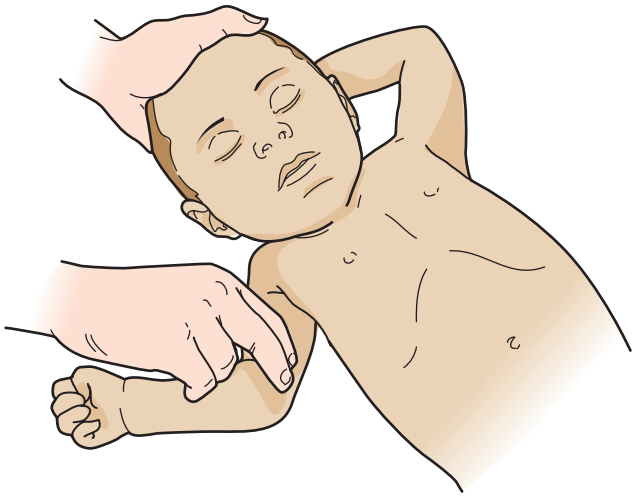

Fig. 38.2 Determining Pulselessness in an Infant.

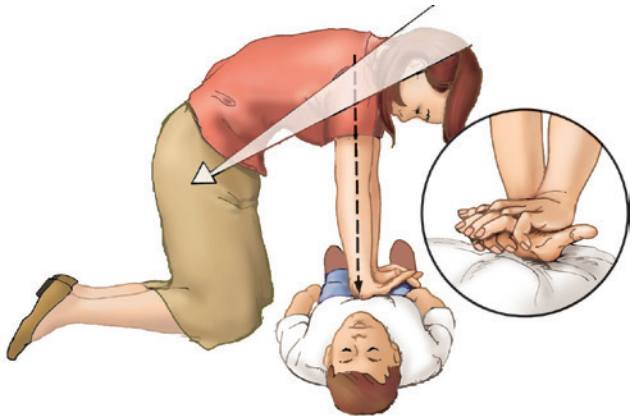

Fig. 38.3 Position of Practitioner for External Cardiac Compression. Note interlocked fingers to prevent pressure on rib cage.

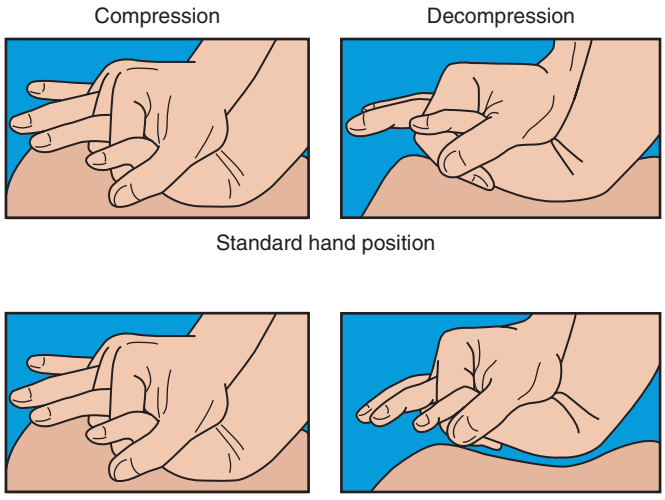

Fig. 38.4 Techniques for Hand Position.

compressions is approximately one-fourth of normal cardiac output, with arterial systolic blood pressures between 60 and 80 mm Hg. Blood flow during chest compression probably results from changes in the intrathoracic pressure. The American Heart Association (AHA) states that it is "reasonable to use physiologic parameters such as quantitative waveform capnography, arterial relaxation diastolic pressure, arterial pressure monitoring, and central venous O_2 saturation when feasible to monitor and optimize CPR quality, guide vasopressor therapy, and detect ROSC."[5] Quantitative capnography might be particularly beneficial. A persistent end-tidal PCO_2 less than 10 mm Hg during resuscitation is associated with a poor outcome. A sharp increase in end-tidal PCO_2 suggests return of spontaneous circulation (ROSC). A decreasing end-tidal PCO_2 suggests a worsening quality of CPR and the need to switch to a new person to perform compressions. An abrupt increase in end-tidal PCO_2 ≥40 mm Hg indicates ROSC.[8]

Adults. The procedure for providing chest compressions to adults is as follows (Figs. 38.3 and 38.4):

1. Place the victim in a supine position on a firm surface, because chest compressions are more effective when the victim is on a firm surface.
2. Choose a position close to the patient's upper chest so that the weight of your upper body can be used for compression. If the patient is on a bed or stretcher, stand next to it with the patient close to that side. If the bed is high or you are short, you may have to lower the bed, stand on a stool or chair, or kneel on the bed next to the victim. If the patient is on the ground, kneel at his or her side.
3. Identify the lower half of the victim's sternum, in the center of the chest between the nipples; place the heel of your hand on the sternum with your other hand on top and lock your elbows.[5]
4. Perform compression with the weight of your body exerting force on your outstretched arms, elbows held straight. Your shoulders should be positioned above the patient so that the thrust of each compression goes straight down onto the

sternum, using your upper body weight and the hip joints as a fulcrum (see Fig. 38.3). It is acceptable to let your hands leave the victim's chest ever so slightly to ensure a complete upstroke (see Fig. 38.4).

5. Compress the sternum 2 inches (5 cm) at a minimum rate of 100 compressions/min; however, do not exceed a rate of 120 per minute. The compression phase of the cycle should be equal in duration to the upstroke phase.
6. If CPR must be interrupted for transportation or advanced life support (ALS) measures, resume chest compressions as quickly as possible. Advanced airway placement presumes that the provider has the initial training, needed skills, and current experience to insert the airway and verify its proper position with minimal interruption in chest compressions.[8]

Children. Children who have reached puberty should receive chest compressions as outlined for adults. The procedure for younger children (1 year old to puberty) is as follows:

1. Place the victim in the supine position on a firm surface. Small children may require additional support under the upper body; this is particularly true when chest compressions are given with mouth-to-mouth ventilation because extension of the neck raises the shoulders. The head should be no higher than the body.
2. As with an adult, identify the lower half of the sternum. Because the liver and spleen of younger children lie higher in the abdominal cavity, take special care to ensure proper positioning as described previously. However, use only one hand to compress. Use the other hand to hold the head in position and maintain the airway.
3. Compress the chest at a rate of at least 100 compressions/min. Push with enough force to depress the chest one-third of the anteroposterior diameter, approximately 1½ inch (4 cm) in infants or at least 2 inches (5 cm) in children. Generally the heel of one hand is sufficient to achieve compression. Because children and rescuer hands come in all sizes, one or two hands can be used to deliver chest compressions to ensure that adequate compression depth and complete release occur. The use of two hands to compress the chest of a child will result in better release (less leaning) and less fatigue.[9,10] As with adults, compression and relaxation times should be equal in length and delivered smoothly.

Infants. The procedure for infants (1 year of age or younger) is as follows (Fig. 38.5):

1. Use the lower half of the sternum for compression in an infant. Proper placement is determined by imagining a line across the chest connecting the nipples. Place your index finger along this line on the sternum. Then place your middle and ring fingers next to the index finger. Raise your index finger and perform compressions with the middle and ring fingers. Use the other hand to maintain the infant's head position and airway.
2. Compress the sternum approximately 1.5 inch (4 cm) at a rate of at least 100 compressions/min. Compression and upstroke phases should be equal in length and delivered smoothly. Your fingers should remain on the chest at all times.

Neonates. Chest compressions are indicated if the neonate's heart rate decreases to less than 60 beats/min despite adequate ventilation with supplemental oxygen (O_2). Before starting chest compressions, the rescuer should ensure that the neonate is being ventilated optimally.[11] The oxygen concentration should be increased to 100% when chest compressions are provided.[11] To reduce the risk of complications associated with hyperoxia, the higher oxygen concentration should be weaned as soon as the heart rate improves. Neonatal chest compressions are delivered on the lower third of the sternum to a depth of approximately one-third of the anteroposterior diameter of the chest to achieve a 3:1 ratio of 90 compressions and 30 breaths for 120 events per minute; rescuers may consider using higher ratios (e.g., 15:2) if the arrest is believed to be of cardiac origin.[11] Coordinated chest compressions and ventilations should continue until the spontaneous heart rate is greater than 60 beats/min. The current measure for verifying progress in neonatal resuscitation is to assess the heart rate response.[11] Two methods have been described. The first method uses a "wraparound" technique (Fig. 38.6). To

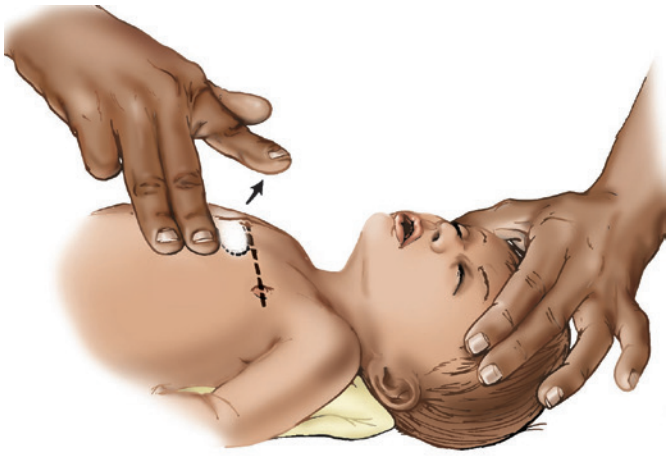

Fig. 38.5 Position for Chest Compression in Infants.

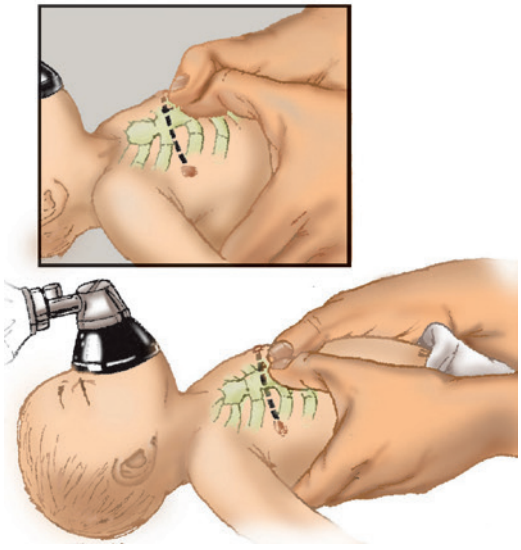

Fig. 38.6 Neonatal Chest Compression Using the Wraparound Technique.

use this method, the rescuer encircles the neonate's chest with both hands and compresses the sternum with two thumbs, using the other fingers of both hands to support the neonate's back. The rescuer should position the thumbs just below the victim's intermammary line, taking care not to compress the xiphoid process. Compression should be performed smoothly, with downstroke and upstroke times approximately equal. In all infants, the chest should be allowed to expand fully after a compression. After every third compression, the neonate should receive a breath of 100% O_2; this should be coordinated with compressions to avoid simultaneous delivery. The second method, the two-finger technique (see Fig. 38.4), may have advantages when access to the umbilicus is required.

Chest Compressions Under Special Circumstances

Two unique circumstances—near drowning and electrical shock—require modification of the normal procedures for applying cardiac compressions.

Near drowning. **Because of the hypoxemia caused by near drowning, use the ABC approach instead of CAB.** When cardiac arrest occurs as a result of drowning, the victim must be moved as quickly as possible to a firm surface. Cardiac compressions are difficult to perform while a victim is in the water and may be ineffective. Mouth-to-mouth ventilation in shallow water may be helpful when administered properly. Stabilization of the cervical spine is unnecessary unless circumstances leading to the incident indicate that trauma is likely. Manual cervical spine and spine immobilization equipment may restrict adequate opening of the airway and may delay the delivery of adequate ventilation.[5,12]

Suspected opioid-related life-threatening emergency. Isolated opioid toxicity is associated with central nervous system (CNS) and respiratory depression, which can advance to respiratory and cardiac arrest. For a patient with known or suspected opioid overdose who has a pulse but no normal breathing or only gasping should receive standard BLS care, and it is sensible for BLS health care providers to administer intramuscular or intranasal naloxone. Standard resuscitation, including activation of emergency medical services, should not be delayed for naloxone administration. For patients in cardiac arrest, medication administration is ineffective without concomitant chest compressions for drug delivery to the tissues, so naloxone administration should be considered only after initiation of CPR if there is high suspicion for opiate overdose.[5,13]

Restoring the Airway

After calling for help and activating the EMS system, the lay rescuer providing "hands only" CPR should not use a passive airway, such as hyperextending the neck. There is insufficient evidence indicating that a passive airway improves ventilation when chest compressions are being administered.[5,12]

After activating the emergency response system and sending someone for an automatic external defibrillator, the health care provider should deliver 30 chest compressions and use the head-tilt/chin-lift or jaw-thrust maneuver to open the airway (Figs. 38.7 and 38.8). The victim should quickly be inspected for any neck or facial trauma. If spinal cord trauma is suspected, the neck must be carefully positioned in a neutral in-line position and procedures requiring hyperextension must be avoided. In

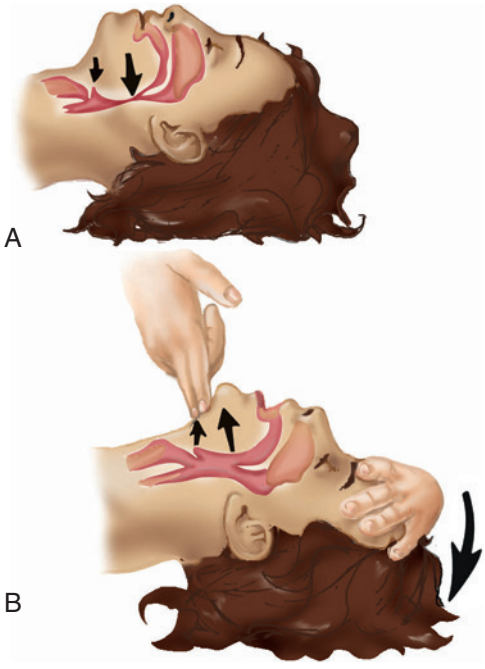

Fig. 38.7 Opening the Airway. (A) Airway obstruction produced by tongue and epiglottis. (B) Relief by head-tilt/chin-lift method.

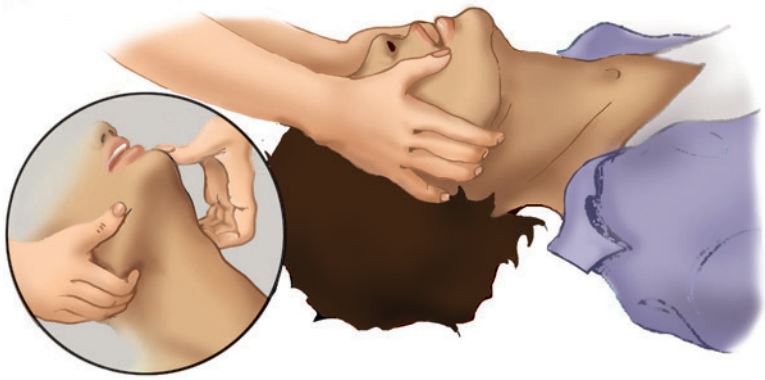

Fig. 38.8 Jaw-Thrust Maneuver.

addition, when a victim is found lying on his or her side or stomach, he or she should be moved to a supine position before airway procedures are begun. Manual in-line spinal motion restriction should be employed when the patient is being moved. The rescuer must ensure that the victim is positioned on a hard flat surface.[5]

One of two procedures can be used: (1) The head-tilt/chin-lift method is the primary procedure recommended when spinal trauma is not suspected. (2) The jaw thrust is used mainly by trained clinicians when spinal neck injuries are suspected. Health care providers should use the head-tilt/chin-lift procedure if the jaw-thrust maneuver does not open the airway.[5] After the airway is cleared and opened, the rescuer must immediately deliver two breaths.

Restoring Ventilation

Before attempting to provide artificial ventilation, the rescuer should assess for breathing. To determine breathlessness, the rescuer places his or her ear over the victim mouth and nose while simultaneously observing for spontaneous chest movement. Breathlessness exists if no chest movement or normal breath sounds are present or only gasping is present. This evaluation should take no longer than 3 to 5 seconds to complete. Delivery of chest compressions should always precede attempts to ventilate the patient using a ratio of 30 compressions to two breaths. Health care providers should provide chest compressions and ventilation for all adult patients in cardiac arrest from either a cardiac or noncardiac cause.[5]

RULE OF THUMB It is rational for health care providers to provide chest compressions and ventilation for all adult patients in cardiac arrest from a cardiac or noncardiac cause.[5] However, it is important to **restore circulation first,** with chest compressions, before attempting airway control. The sequence of rescue actions should be determined by the most likely cause of arrest. For example, if a lone health care provider sees an adolescent collapse, the provider may assume that the victim has had a sudden arrhythmic arrest; the provider should then call for help, get a nearby AED, and return to the victim to use the AED. Next, he or she should provide CPR starting with chest compressions at a 30:2 compression-to-ventilation ratio.

A team of highly trained rescuers may use an approach that undertakes multiple steps and assessments simultaneously rather than in the consecutive manner used by a single rescuer (e.g., one rescuer activates the EMS while retrieving a defibrillator, the second begins chest compressions, and a third provides airway control and ventilation with a bag-mask device for rescue breaths).[5]

Providing Artificial Ventilation

During respiratory arrest, the victim must be provided with O_2 within 4 to 6 minutes or biologic death will follow. The lay rescuer can restore O_2 supply to the victim's lungs by exhaling into the victim's mouth, nose, or tracheal stoma. These procedures can be used for any victim, with appropriate modification for the patient's age. Health care providers should provide ventilation with bag-mask ventilation that delivers 100% O_2. The routine use of passive oxygen administration without positive pressure during conventional CPR for adults is not recommended.[5] After placement of an advanced airway, it may be reasonable for the provider to deliver 1 breath every 6 seconds (10 breaths/min) while continuous chest compressions are being performed.[8]

Mouth-to-mouth ventilation. **Untrained lay rescuers should be encouraged to deliver hands-only (chest compression only) CPR** (i.e., continuous chest compression over the middle of the chest). Trained rescuers can restore adequate oxygenation through mouth-to-mouth ventilation. To do this, the rescuer should take a normal breath (500 to 600 mL) and exhale directly into the victim's mouth over 1 second to produce visible chest rise. Exhaled air provides approximately 16% O_2, which is sufficient to achieve an arterial O_2 tension (PaO_2) of 50 to 60 mm Hg. A tidal volume (V_T) of 500 mL should be delivered when chest compressions are being administered. Children require proportionally smaller volumes.

During resuscitation of a victim of cardiac arrest, two breaths should be given over a period of 1 second each. Excessive volumes (>500 mL) or an inspiratory rate that is too fast (>10 breaths/min) must be avoided because this can push air into the stomach, causing **gastric inflation,** and increase intrathoracic pressure. Increased intrathoracic pressure can decrease coronary and cerebral perfusion. Visible chest rise should be used to gauge the V_T needed in children and adults.

Adults. Thirty chest compressions should be delivered to unresponsive victims with apnea or abnormal breathing (gasping) before attempting mouth-to-mouth breathing. The exception would be a hypoxic event such as a near-drowning. The procedure for mouth-to-mouth ventilation of adults with spontaneous circulation (i.e., strong palpable pulses) is as follows (Fig. 38.9).[12]

1. Place the person on his or her back on a hard flat surface.
2. Kneel at the person's side, and open and clear the airway as previously described. Pinch the person's nose with your thumb and index finger close to the nares to prevent air from escaping during ventilation.
3. Take a normal breath and deliver 500 mL over 1 second while making a seal over the person's mouth and watching for chest

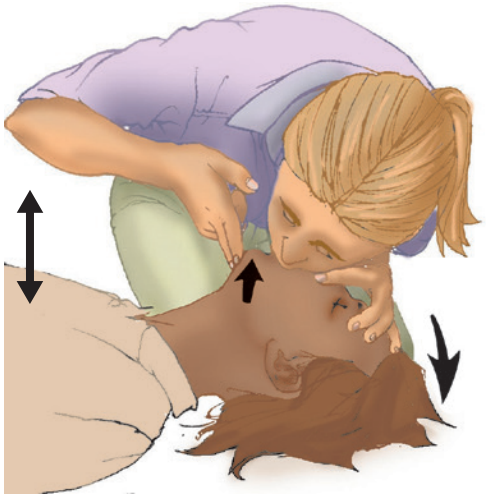

Fig. 38.9 Adult Mouth-to-Mouth Ventilation.

rise. A good seal over the person's mouth is essential. If a good seal cannot be obtained using this method, attempt mouth-to-nose ventilation.
4. Remove your mouth from the person's mouth and allow him or her to exhale passively. Provide a second breath after exhalation is complete.
5. After successfully delivering two breaths, immediately assess the circulatory status (take <10 seconds to accomplish this).
6. Should the initial attempt to ventilate fail, reposition the person's head and repeat the effort. If a second attempt at ventilation fails, the person may have foreign body airway obstruction (FBAO) and the procedures for handling such situations described elsewhere in this chapter should be followed.
7. Assuming that mouth-to-mouth ventilation is successful and the person remains apneic, continue the effort at a rate of 1 breath every 5 to 6 seconds to maintain the adult rate of 10 to 12 breaths/min.

Infants and children. Airway opening maneuvers for children and infants are similar to maneuvers for adults, but with several key differences. Anatomic differences in the infant's airway make it especially susceptible to occlusion by the tongue. The infant's head should be extended only slightly, or it should be tilted back gently into a neutral position when the head-tilt/chin-lift maneuver is used. The procedure for children and infants is as follows:
1. If the child is an infant (younger than 1 year), create an airtight seal by placing your mouth over the infant's nose and mouth (Fig. 38.10).
2. If the patient is a child between 1 year old and puberty, ventilate the child's lungs using the same technique as would be used for an adult (Fig. 38.11).
3. Provide an initial breath (over 1 second) sufficient to cause a visible rise in the chest. In infants, small puffs of air from the rescuer's cheeks are usually sufficient to achieve adequate ventilation.
4. Remove your mouth and allow the child to exhale passively. Provide a second breath after this deflation pause.
5. After successfully delivering two breaths, immediately assess the pulse (<5 seconds). Provide chest compressions if the pulse is less than 60 per minute despite adequate oxygenation and ventilation.
6. If the initial attempt to ventilate fails, reposition the child's head and repeat the effort. A child's head may have to be moved through a wide range of positions to secure an open airway. Hyperextension of a child's neck can cause obstruction and should be avoided. If a second attempt at ventilation fails, the victim may have FBAO, and the appropriate procedures outlined elsewhere in this chapter should be followed.
7. Assuming that mouth-to-mouth ventilation is successful and the child remains apneic, continue to provide one breath every 3 to 5 seconds to maintain a rate of 12 to 20 breaths/min. Recheck the pulse every 2 minutes.[14]

Mouth-to-nose ventilation. Mouth-to-mouth ventilation cannot be performed in some situations; these include trismus (involuntary contraction of the jaw muscles, also known as *lockjaw*) and traumatic jaw or mouth injury. Also, it is sometimes difficult to maintain a tight seal with the lips using the mouth-to-mouth method. In these situations, mouth-to-nose ventilation should be used. The procedure is as follows (see Fig. 38.11):
1. Place the person in a supine position.
2. Use the head-tilt/chin-lift maneuver to establish the airway, taking care to close the mouth completely.
3. Inhale normally and exhale into the person's nose. Greater force may have to be applied than would be used with mouth-to-mouth ventilation because the nasal passageways are smaller.
4. Remove your mouth from the person's nose to allow the person to exhale passively. If the person does not exhale through the nose (because of nasopharyngeal obstruction from the soft palate), open the mouth or separate his or her lips to facilitate exhalation.
5. If the person remains apneic, maintain ventilation at the rate appropriate for his or her age.

Mouth-to-stoma ventilation. Patients with tracheostomies or laryngectomies can be ventilated directly through the stoma or

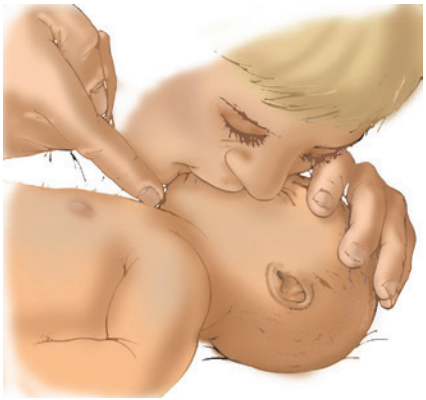

Fig. 38.10 Mouth-to-Mouth and Nose Seal for Infants.

Fig. 38.11 Mouth-to-Nose Ventilation.

tube. These patients can be identified by an obvious stoma or a tracheostomy or laryngectomy tube in place. Some patients wear a medical alert tag or bracelet indicating that a stoma is present. The procedure for mouth-to-stoma ventilation is as follows:

1. Place the person on his or her back with the neck in vertical alignment. Usually, the neck does not need to be extended and the nose or mouth does not need to be sealed because oropharyngeal structures are bypassed by the stoma.
2. Ensure that the stoma is clear of any obstructing matter and breathe directly into the stoma (or tube). If the person has a cuffed tracheostomy tube in place, inflate the cuff to prevent air from escaping around the tube. If the tube is uncuffed, the mouth and nose may have to be sealed off with your hand or a tight-fitting face mask. A pediatric face mask may be used to create an adequate peristomal seal for bag-mask ventilation to persons with stomas without artificial airways.
3. After delivering two breaths, immediately assess circulatory status.
4. If the person remains apneic, maintain ventilation at the rate appropriate for his or her age.

One-Rescuer Versus Two-Rescuer Adult Cardiopulmonary Resuscitation

Outside the hospital, one-rescuer CPR is common. In such cases, the rescuer must assess the victim, call for help, and begin CPR without assistance from others. The rescuer must remain calm and remember the steps of one-rescuer CPR. The technique for performing chest compressions, opening the airway, and giving mouth-to-mouth breaths is the same regardless of the number of rescuers.

When CPR is being performed by only one rescuer, the lay rescuer must remember to give only compressions for adults, children, and infants until an AED arrives. When two rescuers are available, the second rescuer ventilates and evaluates the effectiveness of CPR. The other rescuer administers cardiac compressions. To facilitate movement, each rescuer should assume the appropriate rescue position on opposite sides of the victim.

RULE OF THUMB Lay rescuers should be taught to do 100 to 120 compressions/min (and not to exceed 120 per minute) for all age groups until the AED arrives because it is easier to remember.[5] Emphasis should be placed on teaching lay rescuers to "push hard and fast" on the sternum.

RULE OF THUMB Health care providers should use a 30:2 compression-to-ventilation ratio on adults and children.[5,14] For infants younger than approximately 1 year of age, use a 3:1 ratio of compressions to ventilation, with 90 compressions and 30 breaths to achieve about 120 events per minute in order to maximize ventilation at an attainable rate.[11] A 3:1 compression-to-ventilation ratio is used for neonatal resuscitation, where poor gas exchange is almost always the primary cause of cardiovascular failure, but rescuers may consider using 15:2 if the arrest is believed to be of cardiac origin.[11] When two health care providers work together to resuscitate a child or infant, the compression-to-ventilation ratio should be 15:2.[11,14] Use AED as soon as it is available.

When two health care providers resuscitate an adult patient, the individual providing compressions briefly pauses after 30 compressions so that the other person can administer two ventilations. The cycle is repeated without interruption of compressions to check for signs of circulation or response until an AED arrives or until the hospital code team takes over CPR. Health care providers should limit interruptions in chest compressions to no longer than 10 seconds.

To provide rest for the individual delivering cardiac compressions, the rescuers should change positions every five cycles (approximately 2 minutes). The individual doing cardiac compressions calls for the change, saying "we will change next time" in sequence with compressions. The switch should be accomplished in less than 5 seconds. The cycle continues with the two rescuers in their new positions. Alternatively, to avoid fatigue, teams of three health care providers can be assigned to do chest compressions, switching every five cycles of the 30:2 compression-to-ventilation ratio. The goal is to push "hard and fast" without letting fatigue diminish that rate.

RULE OF THUMB The person doing chest compressions should be changed every 2 minutes. Doing chest compressions is tiring, and fatigue occurs within a few minutes, leading to a compression rate less than 100 to 120 compressions/min, shallow chest compressions less than 1.6 inches or 4 cm, and incomplete chest recoil.[5] Health care providers should perform chest compressions to a depth of at least 2 inches or 5 cm for an average adult while avoiding chest compression depths that are greater than 2.4 inches or 6 cm.[5]

Rescue attempts continue until advanced life support is available, the rescuers note spontaneous pulse and breathing, or a physician pronounces the victim dead. A cardiopulmonary emergency is a crisis for the victim and his or her family, and appropriate support and intervention should be provided to all individuals affected. Victims who survive CPR should be transported quickly to tertiary care facilities, ideally only after advanced life support is instituted.

Automated External Defibrillation

Early Defibrillation

Since 1990 the AHA has recommended adding a fourth step to the treatment of cardiac arrest. This step involves early **defibrillation** after CPR has been initiated. The rationale is as follows:

1. The most common initial rhythm in witnessed sudden cardiac arrest is VF.
2. The treatment for VF is electrical defibrillation.
3. The probability of successful defibrillation diminishes rapidly over time.
4. VF tends to convert to asystole within a few minutes.

Studies have shown that survival rates are highest when immediate bystander CPR is provided and defibrillation occurs within 5 minutes after SCA.[15,16]

The AHA recommendation is that AEDs be made available to individuals expected to respond to emergencies, such as police, security personnel, ski patrol personnel, flight attendants, and first-aid volunteers (Fig. 38.12). Fig. 38.13 demonstrates how

Fig. 38.12 Automated External Defibrillator With Pads Attached. (From Chapleau W: *Emergency first responder, making the difference*, revised ed 2, St. Louis, 2011, Mosby JEMS.)

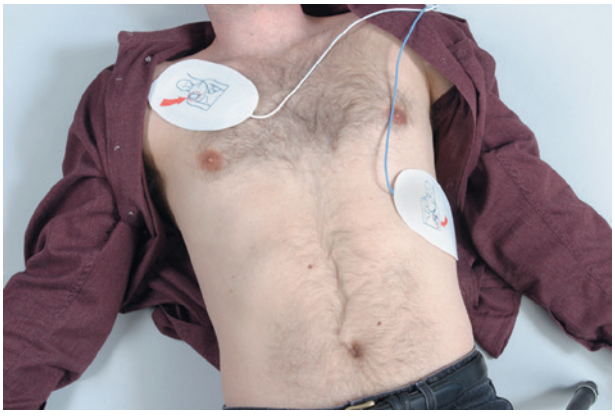

Fig. 38.13 Placement of Pads When Using Automated External Defibrillator. (From Chapleau W: *Emergency first responder, making the difference*, revised ed 2, St. Louis, 2011, Mosby JEMS.)

the AED is attached to the victim. Early defibrillation has already proved effective in saving lives of people who otherwise may not have been successfully resuscitated.[15,16] After appropriate training and implementation of the circulation, airway, and breathing (CAB), this last step is inserted as the letter *D*, for defibrillation. This step should be initiated within 2 minutes of beginning CPR. If the EMS provider witnesses the collapse or for in-hospital situations, the rescuer should use the defibrillator as soon as it is available.

Personnel employed at high-acuity hospitals may not be equipped with AEDs because access to ACLS is readily available, usually within minutes of the code being called. However, low-acuity hospitals, skilled nursing facilities, and other medical facilities that do not have a code team on the premises would benefit from AEDs. RTs working at such facilities should inquire whether an AED is on the premises; if so, they should determine where it is located and how it functions. If an AED is not present, a recommendation should be made to the administration of the facility to purchase one. RTs should know where AEDS are located in the hospitals and outpatient clinics where they work and know how to use them. The AHA recommends that an AED be available wherever CPR is likely to be performed. AEDs should be deployed in locations where there is a high incidence of witnessed SCA, such as airports, casinos, and sports facilities.

Ventricular fibrillation (VF) cardiac arrest is less common in children than in adults, accounting for 5% to 15% of pediatric and adolescent arrests.[12] The AHA recommends using an AED for children older than 1 year who are in cardiac arrest and recommends the use of a pediatric dose-attenuator system if one is available. If such a system is unavailable, a standard AED is recommended.[17] For infants, a manual defibrillator is chosen when a shockable rhythm is identified by a trained health care provider. The recommended first energy dose for defibrillation is 2 J/kg; a second dose should be doubled to 4 J/kg. If a manual defibrillator is not available, an AED equipped with a pediatric attenuator is preferred for infants.[17]

MINI CLINI

Problem

Health care colleagues are unsure whether, for adult patients, to deliver several stacked monophasic shocks at escalating higher energy levels to convert VF to sinus rhythm and what energy level should be used for each shock.

Solution

Research has shown that lower-energy (120 to 200 J) biphasic waveform shocks have equivalent or higher success in terminating VF than three stacked monophasic waveform shocks delivering escalating energy of 200, 300, and 360 J. The incremental benefit of another shock is low, and resumption of CPR is likely to confer a greater value than another shock.[18] There is no evidence indicating the superiority of one biphasic waveform or energy level for the termination of VF with the first shock (termination is defined as absence of VF at 5 s after shock).[8] All published studies support the effectiveness (consistently in the range of 85% to 98%) of the first biphasic shock using 200 J or less.[19] Biphasic waveforms are reported to be uniformly more effective in terms of first-shock success than monophasic across energy levels in a stacked-shock protocol.[19] An automated external defibrillator administering a high peak current at 150 J biphasic fixed energy can terminate initial and recurrent VF with a high rate of success.[8,20]

Automated External Defibrillators

AEDs function in a semiautomatic fashion; the device only recommends that a shock be delivered; it does not initiate one automatically. AEDs have pads that are placed on the chest in positions guided by diagrams (see Fig. 38.13). When all of the equipment is hooked up, the "Analyze" button should be pressed to begin. A rhythm recognition program then analyzes the patient's rhythm. If it detects VT or VF, it advises the rescuer through voice and visual prompts that a shock should be delivered. If a shock is indicated, the rescuer should "Clear" (all hands off to avoid being shocked) the patient and press the "Shock" button. Having done this, the rescuer should deliver five cycles of CPR beginning with chest compressions.

The rescuer should not delay chest compressions by stopping to recheck the rhythm or pulse. The rhythm is checked by the AED after five cycles (approximately 2 minutes) of CPR have been completed. The rescuers should be prepared to initiate another five cycles of CPR immediately after a second shock has

been delivered. The rescuer administering chest compressions should be changed every 2 minutes. The rescuer providing 2 minutes of chest compressions should be prepared to deliver a shock immediately after having removed his or her hands from the victim's chest. The second rescuer should be in position to start chest compressions as soon as the shock has been delivered. If no shock is advised by the AED, the AED voice prompt should instruct the rescuer to resume CPR immediately, starting with chest compressions. If the message reads "No shock indicated," CPR should be performed for 1 to 2 minutes and then the rhythm analysis should be repeated. A 1- to 2-minute period of CPR after a no-shock prompt from the AED delivers O_2 and metabolic substrates to the myocardium, increasing the probability that a perfusing rhythm will occur. The rescuer should not be concerned that chest compressions might trigger the return of VF in the presence of a postshock organized rhythm.[21]

RULE OF THUMB Patients in VF or pulseless VT cardiac arrest should receive only one shock followed immediately by five cycles of CPR before the next shock is delivered. Time should not be taken to check for a pulse or to ventilate the patient before delivering the second shock if needed. Biphasic AEDs have a 90% conversion rate of VF on the first shock, so it is unlikely that a second shock will be needed. Chest compressions immediately after the first shock increase O_2 delivery as well as the chance of VF converting to a normal rhythm.[8]

Evaluating the Effectiveness of Cardiopulmonary Resuscitation

CPR providers must continuously judge both the effectiveness of CPR and the victim's response. Ventilation can be evaluated by observing visible rise and fall of the victim's chest during mouth-to-mouth resuscitation. Air that is escaping can be heard and felt during exhalation.

Hazards and Complications

The most common complications that occur with CPR are worsening of existing neck or spine injuries, gastric inflation and vomiting, trauma to internal structures during chest compressions, and problems associated with the removal of foreign objects to clear an obstructed airway.

Neck and Spine Injuries

Health care providers can aggravate neck or spinal injuries by inappropriately moving the victim's head. However, only approximately 2% to 5% of victims with blunt trauma have a spinal injury. Spinal injury risk is greatest if the victim has craniofacial injury or a Glasgow Coma Scale score of less than 8 (see Chapter 52).[22] The victim should be carefully assessed for head, neck, or spinal injuries. If this type of injury is apparent, the head should be carefully supported and side-to-side motion avoided. In such situations, using the jaw-thrust maneuver rather than the head-tilt/chin-lift method to open the airway is recommended by the AHA.[5,12] If jaw thrust is unsuccessful in establishing an airway, the rescuer should try a slight head-tilt.[12]

Gastric Inflation

During prolonged mouth-to-mouth ventilation, air may enter the esophagus and stomach.[23,24] Severe gastric inflation puts pressure on the diaphragm, restricting lung expansion.[25]

RULE OF THUMB The best way to avoid gastric inflation during bag-mask ventilation is to deliver breaths with low to moderate flow (<30 L/min) over 1 second.[23,24,26] V_T size should be only large enough to cause visible chest rise. The health care provider should not ventilate and compress the chest simultaneously with a bag-mask device.

However, most important is the fact that severe gastric inflation prompts regurgitation. Because an unconscious patient lacks normal upper airway reflexes, regurgitated stomach contents can easily be aspirated into the lungs. Aspiration of stomach contents into the lungs may cause death by making ventilation virtually impossible or lead to severe lung injury such as aspiration pneumonia, which may cause death days or weeks later.

Internal Trauma

External cardiac compression is hazardous, and every attempt should be made to minimize trauma by using the correct technique. Complications associated with chest compression include rare incidents of gastric perforation, laceration of the liver, pneumothorax, hemothorax, cardiac tamponade, and soft tissue emphysema. More common complications are contusion of the lung and fractured ribs or sternum.[27] These complications are most often linked to improper hand position. Placement of the hands too far to either the left or the right can cause fractured ribs or a lacerated lung. Incorrect placement on the left can injure the heart. Placing the hands too high on the sternum can fracture the sternum; placing the hands too low can cause a fractured xiphoid process or a lacerated liver. Correct identification of landmarks and proper hand placement will minimize the likelihood of these complications.

Foreign Body Airway Obstruction

Manual removal of a foreign body from the upper airway also can be hazardous because of the possibility of forcing the object deeper into the airway or traumatizing the airway. This hazard can be minimized by attempting to remove foreign body only when the provider can see solid material obstructing the airway in an unresponsive patient and using extreme care in removing it.[12]

Contraindications to Cardiopulmonary Resuscitation

A pulseless apneic patient dies within 4 to 6 minutes without intervention. Fear of further harm should never influence the decision to begin CPR. CPR is contraindicated only when the patient is obviously biologically dead (as noted by such findings as rigor mortis). In the hospital, CPR is contraindicated when a valid do-not-resuscitate order is in effect or when a properly executed living will (advance directive) specifically requests that CPR not be initiated.

Health Concerns and Cardiopulmonary Resuscitation

The actual risk for disease transmission during mouth-to-mouth ventilation is very small. However, the reluctance to initiate CPR poses a clear threat to the effectiveness of early intervention in life-threatening emergencies. A bystander should provide hands-only (chest compression only) CPR, with an emphasis on "push hard and fast" or follow the directions of the emergency medical dispatcher.[5]

RULE OF THUMB Rescuers of adult VF cardiac arrest should provide chest compressions at a rate of 100–120 per minute with an emphasis on "push hard and fast." Periodic gasps and chest recoil in victims of adult cardiac arrest may provide some ventilation if the airway is open. Most children and infants with cardiac arrest require both prompt ventilations and chest compressions.

Health care providers with a duty to provide CPR should follow the guidelines established by the US Centers for Disease Control and Prevention (CDC) and the Occupational Safety and Health Administration (OSHA). These recommendations include the use of latex gloves, masks, and goggles. Mechanical barrier aids to ventilation (e.g., masks, filters, valves, bag-mask device) have also been suggested to allay fear and protect the rescuer. However, these devices require training to be used properly.[28]

Equipment contaminated with blood or other body fluids during a resuscitation effort should always be discarded in appropriate receptacles or thoroughly cleaned and disinfected according to hospital protocols.

Treating Foreign Body Airway Obstruction

Early recognition of FBAO is critical. Foreign bodies may cause partial or complete obstruction. Partial obstruction may allow nearly adequate air exchange, in which case the patient remains conscious and coughing. If air exchange is present, the patient should be reassured and allowed to clear his or her own airway by coughing. If partial obstruction persists or air exchange worsens, the EMS system should be activated. Poor air exchange exists when the patient has a weak or ineffective cough, increased inspiratory difficulty, or cyanosis.

With a completely obstructed airway, the patient commonly clutches at his or her throat. This is known as the *universal distress signal for foreign body obstruction.* A person with a complete obstruction cannot talk, cough, or breathe and is in dire need of emergency intervention using abdominal thrusts, chest thrusts, back blows, or a combination of two or more such maneuvers.[12]

Several procedures can be used to obtain a clear passageway if attempts to open a victim's airway are unsuccessful or if a foreign body is observed but cannot be removed from the mouth or pharynx. For adults and children, the procedure for health care providers for clearing a foreign body is the *abdominal thrust.* The rescuer should attempt back blows first for infants with an obstructed airway; if these are unsuccessful, the rescuer should try chest thrusts.[17] *Chest thrusts* may be used in place of abdominal thrusts on women in advanced stages of pregnancy and on markedly obese individuals. Both abdominal thrusts and chest thrusts are normally followed by a visual check and manual removal of any observed obstructing foreign material.[12]

Abdominal Thrusts (Heimlich Maneuver)

Forceful thrusts applied to the epigastrium can dislodge an obstruction caused by a food bolus, vomitus, or other foreign body. Quick thrusts to the abdomen rapidly displace the diaphragm upward, increasing intrathoracic pressure and creating expulsive expiratory airflow. As with a normal cough, this expulsive airflow may be sufficient to expel the foreign body from the airway. The procedure for performing abdominal thrusts on adults and children is as follows (Fig. 38.14): (1) If the victim is sitting or standing, stand behind the victim and wrap your arms around his or her waist. (2) Make a fist with one hand and place the thumb side midline on the abdomen slightly above the navel and well below the tip of the xiphoid process (see Fig. 38.14). (3) Grasp the fist with the other hand and deliver a quick upward and inward thrust. Each thrust should be a separate and distinct movement. (4) Repeat the process until the obstruction is removed or the victim loses consciousness.

If an adult victim with FBAO becomes unresponsive, the rescuer should move the patient to the ground, activate the EMS system, and begin CPR. Each time the mouth is opened during cycles of compressions and ventilation, the rescuer should look into the victim's mouth for the foreign body and remove it; this should be done without increasing the time to deliver 2 breaths (~6 seconds). The routine use of blind finger sweeps to remove foreign bodies in adults, children, and infants is not recommended by the AHA.[12,17]

A conscious victim who is alone can attempt to dislodge the foreign body with self-administered abdominal thrusts, performed by pressing his or her fist into the abdomen or pushing the abdomen against a firm surface such as a countertop, sink, chair back, railing, or tabletop.

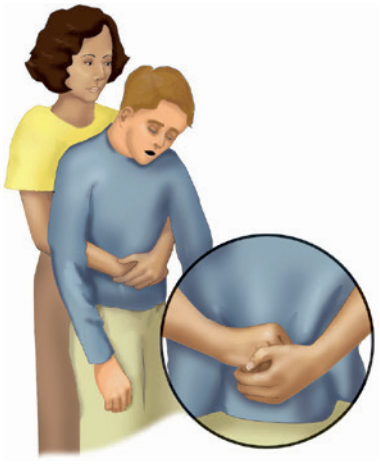

Fig. 38.14 Abdominal Thrusts, Adult Victim Standing. (From Chapleau W: *Emergency first responder, making the difference*, revised ed 2, St. Louis, 2011, Mosby JEMS.)

Vomiting

Vomiting is another complication associated with **abdominal thrusts and gastric inflation;** it is impossible to avoid in some victims. The hazard is the aspiration of vomitus into the lung. Aspiration can be prevented by using advanced airway devices such as an endotracheal tube, laryngeal mask airway, or esophageal-tracheal double-lumen airway (Combitube, Medtronic, Minneapolis, MN). During bag-mask ventilation, vomiting and aspiration can be lessened by limiting gastric inflation. Using a 1-second inspiratory time and tidal volumes limited to 500 mL may reduce the incidence of gastric inflation and the aspiration of vomitus.[23,24]

Internal organ damage. The major hazard associated with abdominal thrusts that are performed when an individual has choked and lost consciousness is possible damage to internal organs, such as laceration or rupture of abdominal or thoracic viscera.[29] The body of clinical data regarding choking is largely retrospective and anecdotal. Abdominal thrusts have been recommended for the relief of FBAO in adults and children since 1975, based mostly on early anecdotal case reports. Abdominal thrusts are recommended by the AHA and several other resuscitation councils for use for *unresponsive* adult and child (but not infant) victims. Abdominal thrusts are not recommended for infants younger than 1 year of age because of their relatively unprotected abdomens and large livers. Rational conjecture and common practices suggest that back blows may loosen an obstruction, so that subsequent abdominal or chest thrusts may relieve obstruction. The risk for internal organ damage from abdominal thrusts in a conscious patient can be minimized by the rescuer placing his or her arms and fist below the victim's xiphoid process and the lower margin of the ribs.

Back Blows and Chest Thrusts

Because an abdominal maneuver can easily cause abdominal injury when applied to infants, a combination of back blows and chest thrusts should be used to clear foreign bodies from the upper airway. Back blows alone may create sufficient force to dislodge trapped objects, but if this is ineffective, the back blows should be followed with five chest thrusts. The rescuer should continue inspecting the airway until it has been cleared. This procedure is as follows:

1. Back blows can be administered to infants more efficiently if the child is held straddled over one arm with the head lower than the body (Fig. 38.15).
2. Use the flat portion of your hand to deliver gently but quickly five back blows between the shoulder blades.
3. If the back blows do not clear the infant's airway, turn the infant over and institute a series of five chest thrusts (see Fig. 38.15). Similar to abdominal thrusts, chest thrusts create a rapid increase in intrathoracic pressure, aiding expulsion of the foreign body. Chest thrusts for infants are performed in the same manner and at the same location as cardiac compressions but at a slower rate.
4. Try to clear the airway between attempts to expel the foreign body. Visually inspect the oral cavity and remove any foreign matter that can be seen.

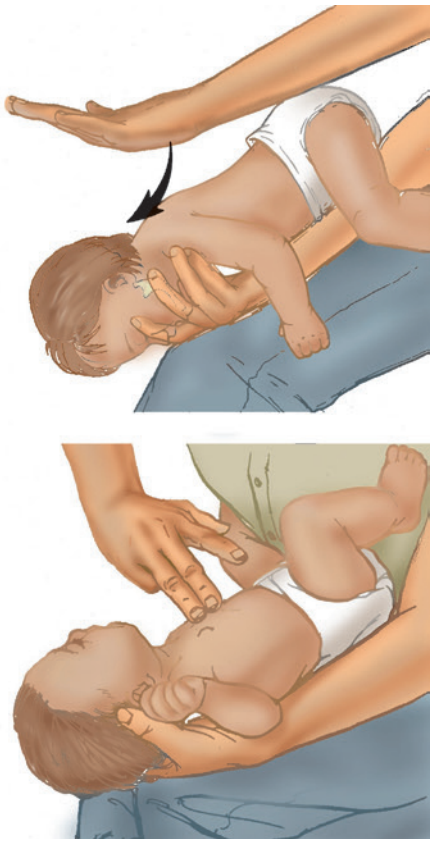

Fig. 38.15 Use of Back Blows and Chest Thrusts to Clear Foreign Bodies From Infant Airway.

Evaluating the Effectiveness of Foreign Body Removal

After each airway restoration maneuver, the rescuer must determine whether the foreign body has been expelled and the obstructed airway cleared. If the foreign body has not been dislodged, the appropriate sequence (abdominal thrusts or chest thrusts for adults and children, back blows and chest thrusts for infants) should be repeated until they have succeeded. Successful removal of an obstructing body is indicated by the following:

- Confirmed expulsion of foreign body
- Clear breathing and ability to speak
- Return of consciousness
- Return of normal color

If successive attempts to clear the airway fail, more aggressive techniques are indicated if available. These include direct laryngoscopy and foreign body removal with Magill forceps, transtracheal catheterization, cricothyrotomy, and tracheotomy. These methods require specially trained health care professionals and equipment, and they are aptly categorized as advanced life-support techniques. Transtracheal catheterization and cricothyrotomy are discussed later in this chapter, and laryngoscopy, bronchoscopy, and tracheotomy are described in Chapter 37.

ADVANCED CARDIOVASCULAR LIFE SUPPORT

ACLS extends BLS capabilities by providing additional measures beyond immediate ventilatory and circulatory assistance. These measures include using accessory equipment to support ventilation

and oxygenation, monitoring the electrocardiogram (ECG), establishing an intravenous route for drug administration, and applying selected pharmacologic agents and electrical therapies (Fig. 38.16). The AHA claims that "the foundation of ACLS is good BLS care, beginning with prompt high-quality bystander CPR and, for pulseless ventricular rhythms, attempted defibrillation within minutes of collapse."[30]

During ACLS in the hospital, the RT assumes primary responsibility for supporting oxygenation, establishing and maintaining the airway, and providing ventilation. RTs must demonstrate high levels of proficiency in these advanced life support skills and other ACLS skills that may be assigned by the resuscitation team leader.

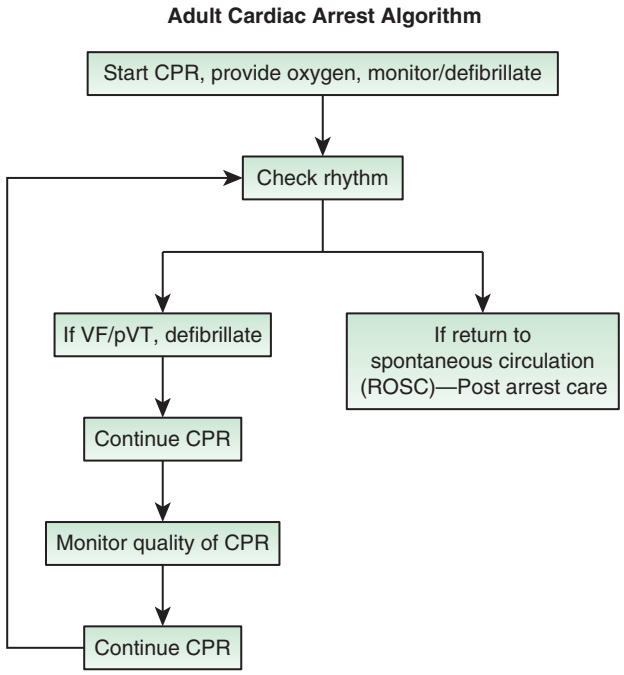

Fig. 38.16 Adult Cardiac Arrest Algorithm. (Information from Link MS, Berkow LC, Kudenchuk PJ, et al. Part 7: Adult advanced cardiovascular life support. 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation* 132(18 suppl 2):S444–S464, 2015; Wyckoff MH, Aziz K, Escobedo MB, et al. Part 13: Neonatal resuscitation: 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation* 132(18 Suppl 2):S543–560, 2015.)

Support for Oxygenation

Although expired air ventilation provides an acceptable level of oxygenation, other factors—including low cardiac output, pulmonary shunting, and abnormalities during CPR—may lead to hypoxia. Hypoxia results in anaerobic metabolism and metabolic acidosis. Metabolic acidosis impedes the action of certain drugs and can diminish the effectiveness of electrical therapies. For these reasons, the highest possible concentration of O_2 should be administered as soon as possible to adults and children.[8] Concerns about O_2 toxicity are not valid during this period of resuscitation. Less than 100% O_2 may be used during neonatal resuscitation at birth.[11]

During ACLS, supplemental O_2 is normally given through accessory devices designed to support ventilation. The ability of these devices to provide high fractional inspired O_2 (F_iO_2) is a key factor in judging their performance.[31,32]

Airway Management

Accessory equipment designed to provide airway management during ACLS includes a variety of masks and artificial airways.

Pharyngeal Airways

Pharyngeal airways can help to restore airway patency and maintain adequate ventilation, in particular when using a bag-mask device. A properly placed pharyngeal airway may also help to provide access for suctioning. Pharyngeal airways should be used only after BLS methods have opened and cleared the airway.

Pharyngeal airways restore airway patency by separating the tongue from the posterior pharyngeal wall. Two types of pharyngeal airways are used in clinical practice: the oropharyngeal airway and the nasopharyngeal airway.

Oropharyngeal airways come in many different sizes to fit adults, children, and infants. Fig. 38.17 shows the two most common oropharyngeal airway designs: the Guedel airway (Flexicare, Irvine, CA; see Fig. 38.17A) and the Berman airway

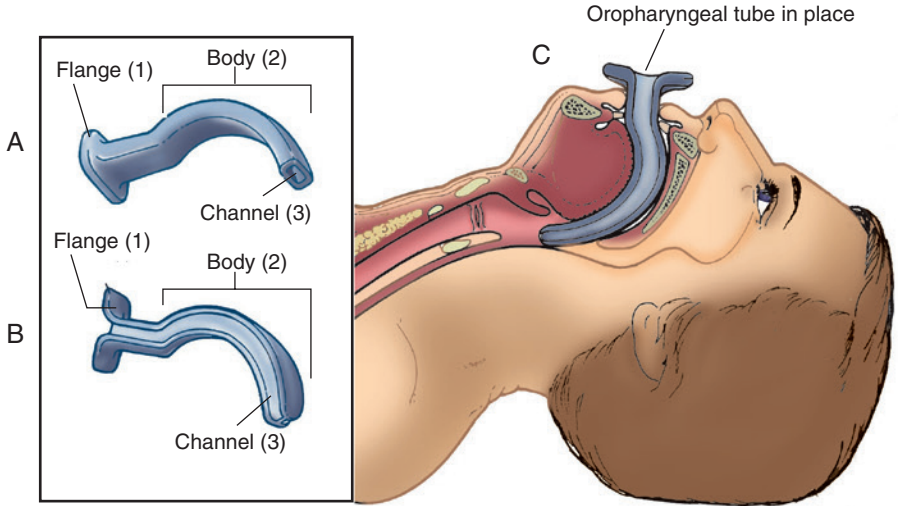

Fig. 38.17 Oropharyngeal Airways. (A) Guedel airway. (B) Berman airway. (C) Airway in place.

(Medline, Mundelein, IL; see Fig. 38.17B). Both types have an external flange, a curved body that conforms to the shape of the oral cavity, and one or more channels. The Guedel airway has a single center channel, whereas the Berman airway uses two parallel side channels.

To choose an airway of the correct size, the clinician should place the devices on the side of the patient's face with the flange even with the patient's mouth. The correct size airway measures from the corner of the patient's mouth to the angle of the jaw following the natural curve of the airway.

Because insertion of an oropharyngeal airway can provoke a gag reflex, vomiting, or laryngeal spasm, these devices are generally contraindicated for conscious or semiconscious patients. They also are contraindicated when there is trauma to the oral cavity or the mandibular or maxillary areas of the skull. These airways should never be placed when either a space-occupying lesion or a foreign body obstructs the oral cavity or pharynx.

Two techniques may be used to insert an oropharyngeal airway. In the first method, the tongue is displaced away from the roof of the mouth with a tongue depressor. The curved portion of the airway is slipped over the tongue, following the curve of the oral cavity.

In the second approach, the jaw-lift technique is used to help displace the tongue. The oropharyngeal airway is rotated 180 degrees before insertion. In this manner, the airway itself helps separate the tongue from the posterior wall of the pharynx. As the tip of the airway reaches the hard palate, it is rotated 180 degrees, aligning it in the pharynx.

In either approach, incorrect placement can displace the tongue, pushing it farther back into the pharynx and worsening the obstruction. Oropharyngeal airways must be inserted carefully and by trained personnel only. As shown in Fig. 38.17C, when properly inserted, the tip of an oropharyngeal airway lies at the base of the tongue above the epiglottis, with the flange portion extending outside the teeth. Only in this position can the device properly maintain airway patency.

Nasopharyngeal Airways

Nasopharyngeal airways are inserted through the nose instead of the mouth. A properly inserted nasopharyngeal airway provides a passageway from the external nares to the base of the tongue. As with the oropharyngeal airway, the nasopharyngeal airway helps restore airway patency by separating the tongue from the posterior pharyngeal wall.

The nasopharyngeal airway is generally indicated when placement of an oropharyngeal airway is impossible. The nasopharyngeal airway is also used when the jaws of a victim cannot be separated, as may occur with seizures. A nasopharyngeal airway should not be used when there is trauma to the nasal region or when a space-occupying lesion or foreign object blocks the nasal passages. Because the nasal passageway in children and infants is small, the use of nasal airways is generally limited to adults.

Most nasal airways are made from either rubber or plastic polymers and sized by external diameter according to the French scale, with 26F to 32F being the usual range for adults. Anatomically, the length of the airway is more critical than the diameter. The appropriate length can be estimated by measuring the distance from the patient's earlobe to the tip of the nose.

To insert a nasopharyngeal airway, the victim's head is tilted slightly backward. The airway is lubricated with a water-soluble agent to ease insertion, and it is positioned perpendicular to the frontal plane of the victim's face. The airway is advanced slowly through the inferior meatus of either the right or left nasal cavity, with the bevel edge facing the septum. If an obstruction is felt during insertion, gentle twisting may facilitate placement. If the resistance continues, the most likely cause is a deviated nasal septum. In this case, an attempt may be made to insert the airway through the other naris or a smaller-diameter tube may be tried.

After the airway has been inserted, the rescuer must try to visualize and confirm its correct position quickly, using a tongue depressor if necessary. When properly positioned, a nasopharyngeal airway is usually stabilized by its own flange.

Masks

A mask that fits the patient is a useful tool for the application of artificial ventilation by appropriately trained rescuers. An ideal mask should be made of transparent material, be capable of sealing tightly against the face, provide an inlet for supplemental O_2, and have a standard 22-mm port for connection to a bag-mask device. Masks should be available in various sizes to accommodate adults, children, and infants. Infant masks often have a 15-mm male connector instead of a 22-mm port. The use of masks to support ventilation presumes that the airway can be maintained by conventional BLS techniques. Which mask should be used in a given situation depends on careful assessment of the status of the victim and an in-depth knowledge of the capabilities and limitations of the equipment on hand.

Endotracheal Intubation

An advanced airway allows the rescuer to achieve one or more of the following goals:

1. Deliver ventilations that are not synchronous with chest compressions
2. Restore airway patency
3. Maintain adequate ventilation
4. Isolate and protect the airway from aspiration
5. Provide access for clearance of secretions

Endotracheal intubation is used for securing the airway during CPR. When positioned properly, endotracheal tubes can maintain a patent airway, prevent aspiration of stomach contents, permit suctioning of the trachea and mainstem bronchi, facilitate ventilation and oxygenation, and provide a route for drug administration.

Attempts to intubate the trachea must never interfere with providing adequate ventilation and oxygenation by other means, such as a bag-mask resuscitator. Advanced airway placement presumes that the provider has the initial training and skills as well as current experience to insert the airway and verify its proper position with minimal interruption in chest compressions.[8] Bag-mask ventilation also requires skill and proficiency. The choice of a bag-mask device versus advanced airway insertion, then, will be determined by the skill and experience of the provider. Only highly trained personnel should perform endotracheal intubation, and each attempt ideally should not exceed 10 seconds, because chest compressions will not be possible during the procedure.

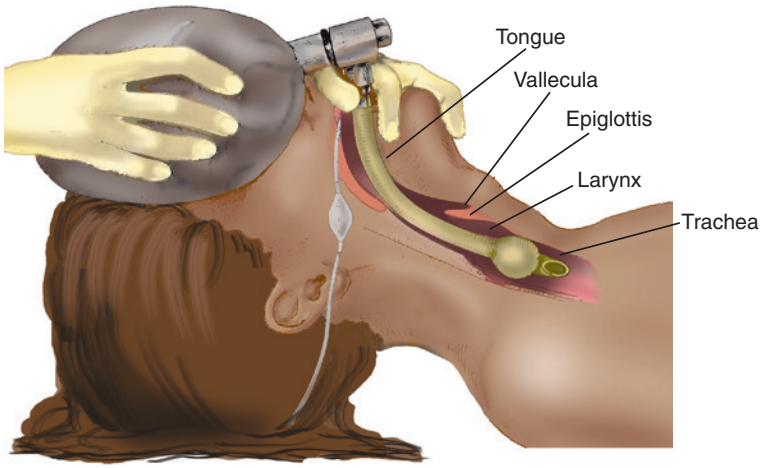

Fig. 38.18 Orotracheal Tube in Place, Being Used With a Bag-Valve Resuscitator.

Continuous waveform capnography is recommended by the AHA guidelines in addition to physical assessment as the initial method for confirming and monitoring correct placement of an endotracheal tube.[8] When capnometry is not available, auscultation and direct visualization should be used to confirm the position of the endotracheal tube. Adequate ventilation and oxygenation must be provided between attempts. Fig. 38.18 shows a cuffed orotracheal tube properly positioned in the trachea. It is being used with a manual bag-mask device to provide ventilation and oxygenation. Adequate ventilation and oxygenation can be provided with 10 to 12 breaths/min.

RTs should be trained in endotracheal intubation techniques as applied in both emergency life support and mechanical ventilation situations. Details about the necessary equipment, procedures, and short- and long-term complications of endotracheal intubation are provided in Chapter 37.

Accessory equipment used to support ventilation in advanced life support includes manual and O_2-powered resuscitators. Bag-mask devices, also called manual resuscitators, are available for adults, children, and infants. Conversely, O_2-powered resuscitators are strictly limited to adult application and are not discussed in this chapter.

Bag-Mask Devices

One-way valves on bag-mask devices should be simple, dependable, and jam-free. All health care professionals responding to a cardiac arrest call should be familiar with and skilled in the use of such a device for the support of ventilation and oxygenation. Application of the bag-mask device is best performed with the practitioner positioned at the head of the victim, using the head-tilt maneuver to maintain the airway (Fig. 38.19). The rescuer delivers V_T adequate to produce visible chest rise (6 to 7 mL/kg predicted body weight or 400 to 500 mL) over 1 second. Using this smaller V_T decreases airway pressure and minimizes the risk for gastric inflation.

After an advanced airway replaces the face mask, the ventilatory rate should be 10 breaths/min during CPR. Slower rates of 6 to 8 breaths/min might be needed for patients with chronic obstructive pulmonary disease (COPD) to prevent air trapping and the development of auto-positive end expiratory pressure (auto-PEEP). Ventilatory rates greater than 12 breaths/min are not recommended during CPR because they lead to increased intrathoracic pressure, impeding venous return to the heart during chest compressions and hyperventilation.[33]

Fig. 38.19 Ventilation Using a Bag-Mask Device and Head-Tilt/Chin-Lift Method to Open the Airway. (From Henry MC, Stapleton ER: *EMT prehospital care*, revised ed 4, St. Louis, 2009, Mosby.)

The rescuer delivers a breath every 6 seconds with a 1 second inspiratory time and should not attempt to synchronize ventilations with the chest compressions. Nonsynchronized delivery of ventilation and compressions allows the number of chest compressions delivered per minute to increase to 100 to 120 per minute and breaths delivered to 10 per minute. After restoration of a perfusing rhythm, the ventilation rate should be 10 to 12 breaths/min delivered with a 1 second inspiratory time.

RULE OF THUMB

Rescuers should not hyperventilate victims of cardiac arrest. Once an advanced airway is placed, ventilations should be delivered with a 1 s inspiratory time at a rate of 10 breaths/min (every 6 s). Do not attempt to synchronize ventilations with chest compressions. Ventilation for patients with a perfusing rhythm should be at a rate of 10–12 breaths/min (1 breath every 5–6 s). Patients with COPD may need ventilation rates of 6–8 breaths/min to prevent auto-PEEP.

Bag-mask devices combine a mask with a self-inflating bag and a nonrebreathing valve mechanism. These devices may be used to ventilate patients by applying the mask over the patient's mouth and nose or by attaching the self-inflating bag directly to an endotracheal tube or other advanced airway. All devices can provide ventilation with air or with supplemental O_2. Bag-mask devices provide 100% O_2 when properly applied. Although initially designed as adjuncts for emergency life support, they are used extensively in other respiratory care settings, particularly in the areas of airway management and continuous mechanical ventilation.

Design

Fig. 38.20 is a schematic of a typical bag-mask device, showing gas movement and valve action during both the inhalation-compression and exhalation-relaxation phases. The key components shown in this schematic are the nonrebreathing valve *(left)*, the bag itself, the O_2 inlet and bag inlet valve *(to the right of the bag)*, and the O_2 reservoir tube *(far right)*.

During exhalation (see Fig. 38.20A), gas flows out from the patient's lungs through the nonrebreathing valve into the atmosphere. At the same time (while the bag expands), the intake valve opens and 100% O_2 flows into the bag from both the reservoir and the O_2 inlet.

During the inhalation phase (see Fig. 38.20B), the bag is compressed manually, causing bag pressure to increase. This increase in bag pressure simultaneously closes the inlet valve and opens the nonrebreathing valve, forcing gas into the patient. While the bag inlet valve is closed, O_2 coming in through the O_2 inlet goes into the reservoir tube, where it is stored for the next breath.

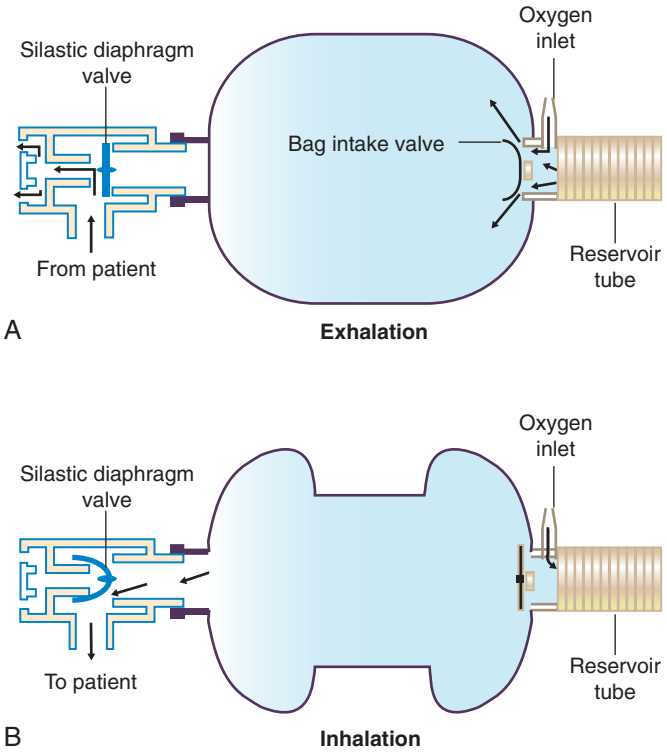

Fig. 38.20 Components of Bag-Mask Device.

Use

To use a bag-mask device, the health care provider is positioned at the head of the patient's bed. Ideally, an oral airway is inserted, and the head-tilt method is used to keep the airway open (assuming that there are no neck injuries). While using one hand to keep the patient's head extended and the mask tightly sealed to the patient's face, the health care provider uses the other hand to compress the bag (see Fig. 38.19).

In addition to providing adequate ventilation, bag-mask devices can provide high FiO_2. Theoretically, all such devices on the market can deliver 100% O_2; however, the actual FiO_2 provided at the bedside depends on several factors, including O_2 input flow, reservoir volume, delivered volume and rate, and bag refill time. As a guideline to achieve the highest possible FiO_2 with a bag-mask device, the following always should be done:

1. Use an O_2 reservoir of adequate size.
2. Set the O_2 input flow at 10 to 15 L/min.
3. Deliver appropriate V_T for a 1-second period (when using a mask).
4. Ensure the longest possible bag refill time.

Hazards and Troubleshooting

Bag-mask devices are simple and safe advanced life support devices. However, several major hazards are associated with their use. The first and most common problem is unrecognized equipment failure. Knowledge of how such devices operate can help clinicians understand the operational testing of and troubleshooting for these devices. Gastric inflation is another common hazard encountered when using a bag-valve device with a face mask. Gastric inflation can be minimized by providing low to moderate inspiratory flows (<30 L/min).[23,24,26] For an adult, a full 1 s should be used to deliver V_T of 500 mL.[23,24]

MINI CLINI

Ventilation During Cardiopulmonary Resuscitation

Problem

A student is observing a code blue in progress in the intensive care unit. The patient has had a cardiac arrest, and CPR is being administered. The student notices that the RT is ventilating the patient's lungs with a bag-valve device through an endotracheal tube at a considerably higher rate and minute ventilation than would normally be established on a mechanical ventilator for a patient of this size. Is this increased minute ventilation needed?

Solution

No, it is not. The ventilation rate should be 10 breaths/min, and V_T should be limited to achieve no more than a visible chest rise so as to avoid excessive ventilation.[34,35] Ventilation rates greater than 12 breaths/min and large V_T (>6 to 7 mL/kg) increase intrathoracic pressure and impede venous return to the heart during chest compressions.[33] During CPR, hyperventilation reduces cardiac output and decreases coronary and cerebral perfusion and markedly decreases coronary perfusion pressure and survival rates.[33] Overzealous ventilation with high rates (>12 breaths/min) during resuscitation of cardiac arrest increases intrathoracic pressure, impedes venous return, decreases cardiac output, decreases coronary artery perfusion pressure, increases gastric inflation, and provides more ventilation than is needed.

MINI CLINI

Problem

Inadequate refilling of the heart during the decompression phase of CPR.

Solution

If the depth of chest compression for adults is not 2 inches (5 cm), chest recoil can be impaired.[5] Chest wall recoil creates a relative negative intrathoracic pressure that promotes venous return and cardiopulmonary blood flow. Incomplete recoil could increase intrathoracic pressure and reduce venous return, coronary perfusion pressure, and myocardial blood flow and could potentially influence resuscitation outcomes.[10] It has been demonstrated that when compressions are too rapid, the compression depth is too shallow. When CPR is performed according to the AHA's recommendations, at 100–120/min, using either both hands or an **active compression/decompression device (ACD)** CPR device (Fig. 38.21), the addition of the **impedance threshold device** (ITD) (Fig. 38.22) provides important hemodynamic and survival benefits.[5,36,37] The small negative intrathoracic pressure generated within the thorax during the chest wall recoil phase is critical for refilling the heart during the decompression phase of CPR.[38] The ITD is designed to enhance venous return and cardiac output during CPR by increasing the amount of negative intrathoracic pressure.[39,40] The ITD (ResQPOD) (see Fig. 38.22) prevents the influx of respiratory gases into the chest during the chest wall recoil (relaxation or decompression) phase, which lowers the intrathoracic pressure and draws more venous blood back to the heart. Improved blood return to the heart (preload) results in improved blood flow out of the heart (cardiac output) during the subsequent compression. The ITD cannot function to enhance negative intrathoracic pressure during the decompression phase of CPR without adequate chest wall recoil. Active compression-decompression CPR uses a handheld device with a suction cup (ACD device) to perform closed-chest cardiac massage. The ACD is applied to the midsternum to compress the chest and then to actively decompress the chest after each compression. This differs from traditional manual CPR, where the chest can recoil passively. A meta-analysis review comparing ACD and standard chest compression techniques reported active chest compression-decompression to have no advantage and some drawbacks compared with standard CPR.[41] To the contrary, a large study found strong evidence that the application of ACD plus ITD in a wide spectrum of patients with out-of-hospital cardiac arrest can significantly increase long-term survival with restoration of baseline neurologic function at 1 year after arrest.[42] The 2015 ACLS guidelines recommend that the combination of ITD with active compression decompression CPR may be an acceptable alternative to conventional CPR in settings with available equipment and properly trained personnel.[36]

Increases in central venous pressure, because of increased intrathoracic pressure, can decrease cerebral blood flow. Increased airway pressures and auto-PEEP generated by hyperventilation should be avoided. The AHA consensus statement, "Cardiopulmonary Resuscitation Quality: Improving Cardiac Resuscitation Outcomes Both Inside and Outside the Hospital," recommends avoiding excessive ventilation during and after cardiac arrest.[34] Methods have been developed that decrease ventilation rate using electronic metronomes.[35] However, methods to limit excessive tidal volume and inspiratory pressure are less well developed but may include the use of smaller resuscitation bags, bags with manometers, and direct observation of chest rise.

Barotrauma has long been recognized as a potential hazard when a bag-mask device is used. However, with the full-bag volume of adult-size devices (generally ≤2000 mL), the potential for barotrauma is small if the nonrebreathing valve is working properly and a bronchial intubation has not occurred. The average mask leak with bag-mask devices ranges from 20% to 40% of stroke volume and substantially reduces the risk for barotrauma, especially if no more than visible chest rise is used to determine adequate V_T. Some pediatric bag-mask devices have bag volumes of more than 500 mL, and rescuers may cause barotrauma to small children or infants if they do not adjust stroke volume by squeezing the bag so that only half to one-third of the volume is delivered to the mask.

Restoring Cardiac Function

Perfusion support techniques, such as chest compressions, can restore circulation only temporarily. ACLS must go beyond simple perfusion support to identify, remove, or relieve the underlying cause of cardiac failure; this is done by combining ECG monitoring with pharmacologic and electrical therapies.

Fig. 38.21 Active Compression-Decompression Device. (Courtesy Zoll.)

Electrocardiogram Monitoring

Because most cases of cardiac arrest are caused by arrhythmias, ECG monitoring should be started as soon as the necessary equipment and personnel arrive. Monitoring may be done with either standard ECG equipment or the quick-look paddles now available on most defibrillators.

Given their important role in ACLS, RTs must be skilled in recognizing arrhythmias. Although an RT may be able to quickly

interpret gross arrhythmias appearing on ECG monitors at the bedside, these skills develop only after much practice with actual rhythm strips. Chapter 18 presents a review of ECG interpretation. The reader should focus on the following arrhythmias:

- VT
- VF
- Sinus tachycardia
- Sinus bradycardia
- Sinus arrest
- Premature atrial contractions
- Supraventricular tachycardia (SVT)—a classification of arrhythmias including but not limited to sinus tachycardia, atrial flutter, and atrial fibrillation
- Atrioventricular blocks—first degree, second degree types I and II, and third degree
- Premature ventricular contractions (PVCs)
- Pulseless electrical activity (PEA)
- Systole

Fig. 38.22 Impedance Threshold Device (ZOLL, Chelmsford, MA). (Courtesy ResQPOD.)

This section briefly discusses the arrhythmias closely associated with CPR conditions, including SVT, VT, VF, and PEA.

Supraventricular tachycardia. The term *supraventricular tachycardia* is commonly used to describe any tachycardia not of ventricular origin. This grouping can include sinus tachycardia, atrial tachycardia, junctional tachycardia, atrial flutter, and atrial fibrillation (with rates >100 beats/min). These individual supraventricular arrhythmias are identified by ECG and treated accordingly (Fig. 38.23).

A more specific form of SVT involves rapid impulse formation caused by a reentry mechanism that develops in the atria or atrioventricular junction. Normally, a single impulse from the sinoatrial node traverses the atria and continues down into the ventricles, causing depolarization and contraction. In reentry, an ectopic focus disrupts this normal conduction. The impulse not only moves down to the ventricles but also returns to the atria. This pattern repeats in a self-perpetuating, or circular, manner.

Typically, this form of SVT results in heart rates between 160 and 220 beats/min. The rhythm is regular, which distinguishes it from rapid atrial fibrillation. However, because of its rapid rate, P waves may not be seen. If identifiable, the P waves appear abnormal. In addition to the rate and regular rhythm, SVT is characterized by a normal QRS complex. At very high rates, the ventricles may not have enough time to fill completely. Incomplete ventricular filling can result in decreased cardiac output, congestive heart failure, and tissue hypoxia. SVT may deteriorate to VT if it is not recognized and treated in a timely manner.

The treatment of SVT varies according to the clinical situation (Fig. 38.24). If a patient with SVT is ill or unstable, the treatment of choice is immediate synchronized electrical **cardioversion**, as described elsewhere in this chapter. If the patient is stable, other interventions are tried before cardioversion is considered. The most common nonelectrical treatment for SVT is vagal stimulation by carotid artery massage or Valsalva maneuver. If these attempts are ineffective and the patient remains stable, drugs such as adenosine, diltiazem, verapamil, or β blockers (as a second-line agent) may halt SVT. These drugs work primarily on the nodal tissue by slowing ventricular response to atrial arrhythmias, or they block the reentry SVT that travels through the atrioventricular node.[30]

Ventricular tachycardia. VT occurs when one or more irritable foci within the ventricle discharge at rapid rates, creating the appearance of a prolonged chain of PVCs. Rates typically range from 140 to 220 beats/min and are usually regular (Fig. 38.25). Although VT may come and go in brief episodes, or *paroxysms,* it is always a sign of a serious underlying pathologic

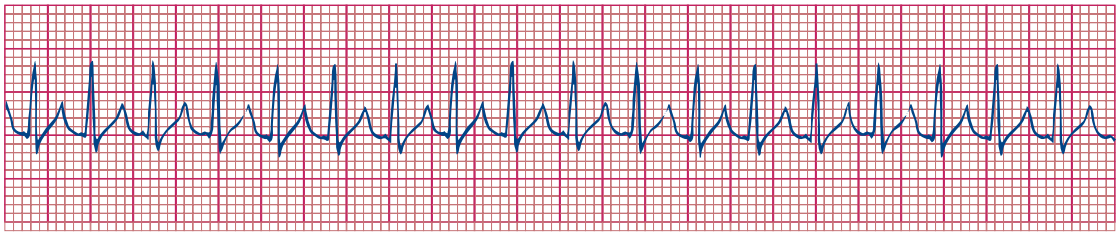

Fig. 38.23 Supraventricular Tachycardia, Lead II.

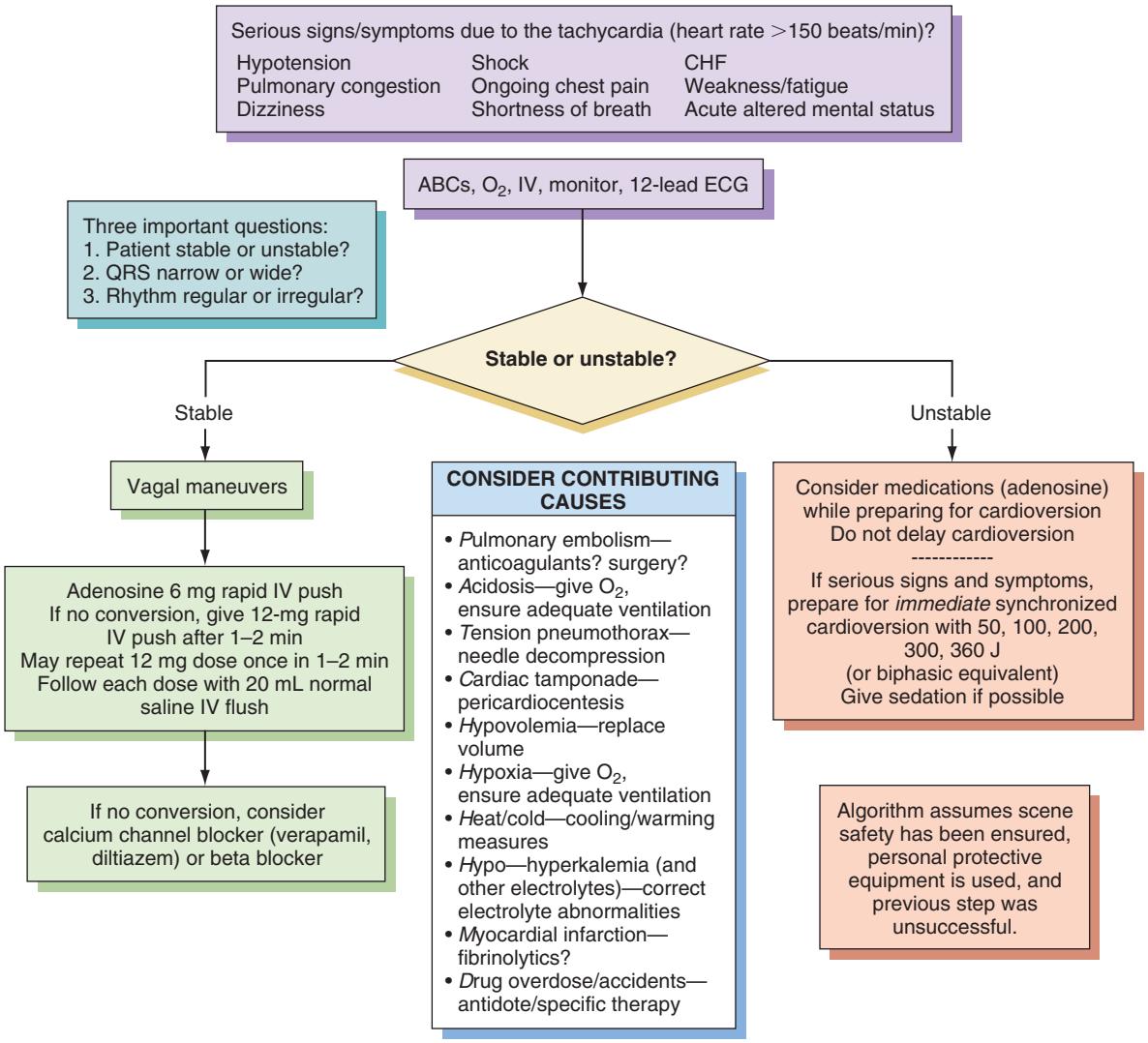

Fig. 38.24 Narrow-Complex QRS Tachycardia Algorithm. (From Aehlert B: *ACLS study guide*, ed 5, St. Louis, 2017, Mosby.)

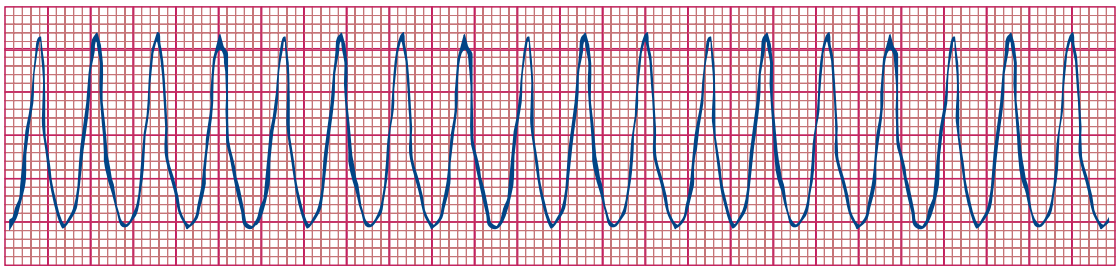

Fig. 38.25 Ventricular Tachycardia, Lead II (St. Louis, 2017, Mosby.)

condition and should be treated immediately. In stable patients, VT is managed with amiodarone, procainamide, and/or sotalol.[30] Procainamide and sotalol should be avoided in patients with a prolonged QT.[30] For patients with sustained VT who exhibit hypotension, ischemic chest pain, shortness of breath, decreased consciousness, or signs of pulmonary edema, immediate **synchronized cardioversion** is indicated (Fig. 38.26). Patients with sustained VT in full cardiac arrest are treated similarly to patients with VF.

Ventricular fibrillation. VF is a rapid, sustained, uncontrolled depolarization of the ventricles. During VF, the ECG is characterized by irregular, widened, poorly defined QRS complexes, known as *coarse* VF (Fig. 38.27A). These complexes widen farther and lose amplitude, resembling a coarse asystole, which now is defined as *fine* VF (see Fig. 38.27B). Rather than exhibiting coordinated contractions, the ventricles quiver in a totally disorganized manner. Cardiac output during VF is zero. The rapid decrease in cardiac output produces acute cerebral hypoxia, often

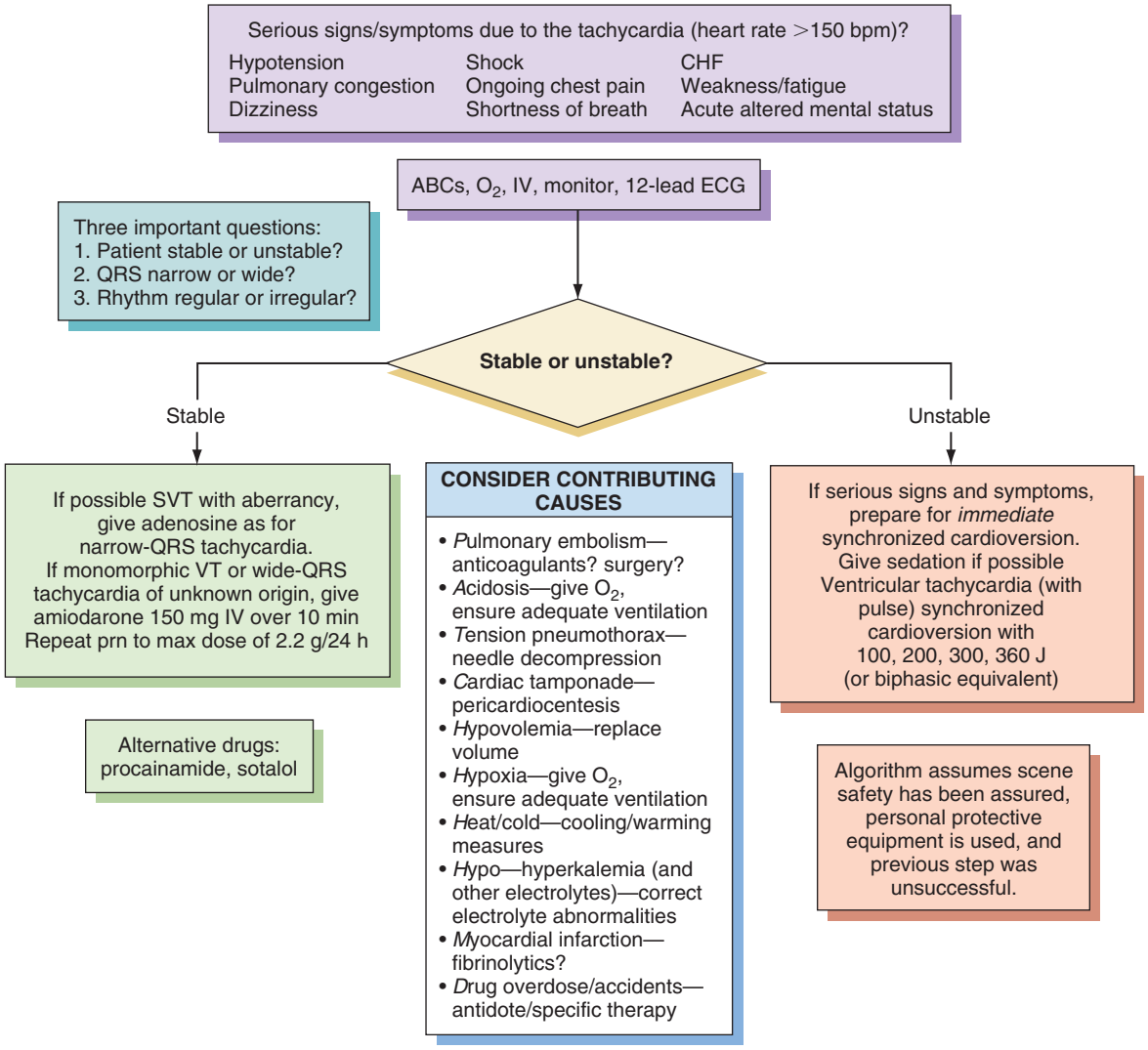

Fig. 38.26 Wide-Complex QRS Tachycardia Algorithm. (From Aehlert B: *ACLS study guide*, ed 5.)

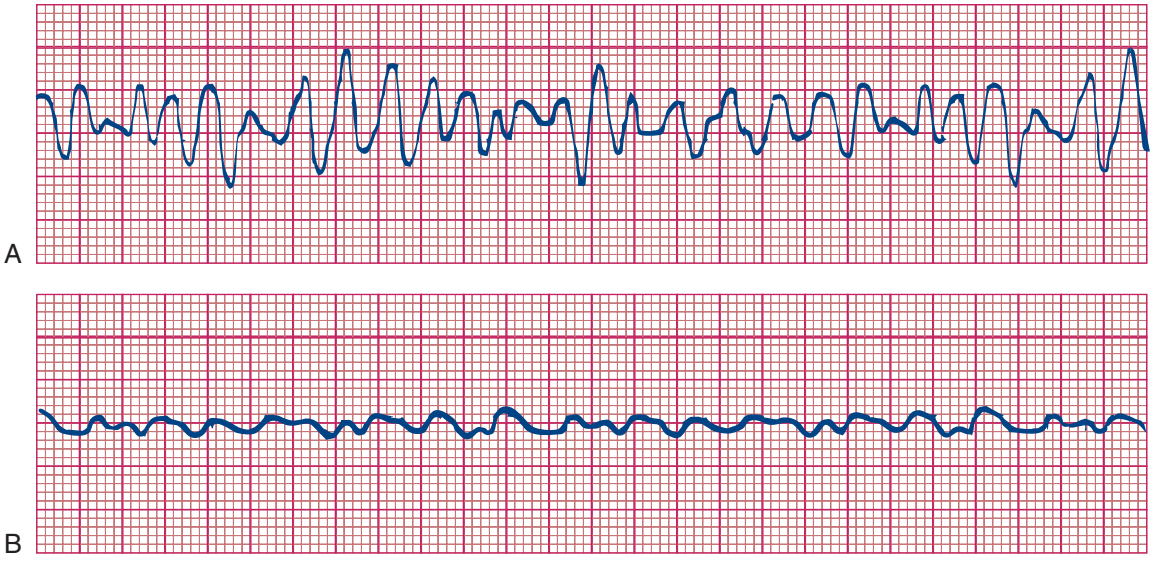

Fig. 38.27 Ventricular Fibrillation. (A) Coarse VF. (B) Fine VF, lead II.

manifested by seizures. VF is uniformly fatal if not corrected immediately.

Many conditions cause VF. The most common causes include hypoxemia, hypovolemia, acidosis, hypokalemia and hyperkalemia, hypothermia, toxins, cardiac tamponade, tension pneumothorax, pulmonary thrombosis, and coronary thrombosis.[30] Regardless of the cause, VF constitutes a true emergency. Patient survival depends on immediate provision of ACLS, especially electrical defibrillation. Early defibrillation is the major determinant of survival in cardiac arrest caused by VF.

Pulseless electrical activity. PEA that is not shockable can result from several reversible causes (Fig. 38.28). The immediate primary treatment is uninterrupted CPR for approximately 2 minutes with epinephrine administered as soon as feasible after the onset of cardiac arrest due to an initial nonshockable rhythm.[8] The best secondary approach is to identify and treat reversible causes (e.g., for hypovolemia, replace volume; for tension pneumothorax, use needle decompression).

Pharmacologic Intervention

Although the full range of drug use in ACLS is beyond the scope of this chapter, RTs must have a general knowledge of both the various drug categories and the specific agents used in emergency situations.[43] Table 38.2 summarizes the major drug categories and primary agents currently used in ACLS.

Routes of administration. Unless a central vein is already cannulated, the ideal route for drug administration in emergency situations is a peripheral intravenous line. Intravenously administered drugs should be given by rapid bolus injection, followed by a 20-mL bolus of intravenous fluid and elevation of the extremity.

Selected drugs—such as epinephrine, lidocaine, and atropine—may also be given through intraosseous access when intravenous access is not readily available.[44]

The intraosseous route is always an option, especially in small children or infants.[44] Chapter 36 provides information about some pharmacologic agents often used in ACLS.

Electrical Therapy

The following three general types of electrical therapy are used in emergency cardiac care: (1) unsynchronized countershock, or defibrillation; (2) synchronized countershock, or cardioversion; and (3) electrical pacing.

Unsynchronized countershock (defibrillation). When an electrical shock of appropriate strength is applied to the myocardium, all myocardial fibers depolarize simultaneously. Theoretically, when all cells depolarize, the cells that fire spontaneously at the fastest rate should be able to regain control and pace the heart. Normally, the sinus node spontaneously depolarizes most rapidly. After electrical shock, the sinus node should discharge first and capture all parts of the myocardium as the depolarization wave travels through the still silent heart.

Defibrillation is an unsynchronized shock used to depolarize all the myocardial fibers simultaneously. It is the definitive treatment for both VF and pulseless VT. If one of these arrhythmias is present and the proper equipment and trained personnel are available, defibrillation of the patient should be performed immediately.

MINI CLINI

Route of Drug Administration During Advanced Cardiovascular Life Support

Problem

An RT working in a small rural hospital is called to the emergency department, where a patient is in cardiac arrest. The RT is able to intubate and ventilate the patient, using a bag-valve device with 100% O_2.

Nurses are performing cardiac compressions and attempting unsuccessfully to start a peripheral intravenous line. The ECG monitor reveals a fine VF pattern. Electrical defibrillation is unsuccessful on the first attempt, and five cycles of 30 compressions to 2 ventilations are in progress. Immediate administration of epinephrine without interrupting CPR is indicated before or after the next shock. Attempts to secure an intravenous line continue to be unsuccessful. What action is appropriate at this time?

Solution

Because of its strong inotropic and α-adrenergic effects, epinephrine should be the first drug administered during resuscitation from cardiac arrest, and it should be administered as soon as possible. Drugs given via a peripheral vein take 1 to 2 minutes to reach the central circulation. Epinephrine can convert fine VF to coarse VF and improves the chance for successful electrical defibrillation. In this case, because intravenous routes are unavailable, epinephrine should be administered by the intraosseous route, which can quickly be established with minimal complications by providers with varied levels of training.[44,45]

If a biphasic defibrillator is available, the AHA recommends an initial energy level of 120 to 200 J for the defibrillation of adults and 2 to 4 J/kg for the defibrillation of children and infants.[8,17,20] For children older than 1 year, if a shockable rhythm persists after five cycles of CPR, the rescuer should give one shock (4 J/kg) and resume compressions immediately. For adults, a 360-J shock should be used with monophasic defibrillators for the first and subsequent shocks with 2 minutes of CPR between shocks.[8] If VF recurs, and compressions should be resumed immediately.

The size and placement of electrode paddles are important to ensure that the full energy of the countershock is applied. Many AEDs have pads that are placed on the chest in positions guided by diagrams. Such pads are connected to the defibrillator, so that paddles are not actually used in this circumstance (see Fig. 38.12). For adults, paddles should be 8 to 12 cm in diameter to decrease resistance; adult paddles are of adequate size for children older than 1 year. Normally, one paddle is placed below the clavicle and just to the right of the upper portion of the sternum with the other positioned on the midaxillary line to the left of the left nipple. Alternatively, one paddle may be placed on the left precardium with the other positioned posteriorly under the patient, behind the heart. Paddles should be prepared with conducting gel and applied with firm pressure (approximately 25 lb).

Synchronized countershock (cardioversion). **Cardioversion** is like defibrillation with two major exceptions. First, the countershock is synchronized with the heart's electrical activity (the R wave). Synchronization is necessary because electrical stimulation during the refractory phase (part of the T wave) can cause

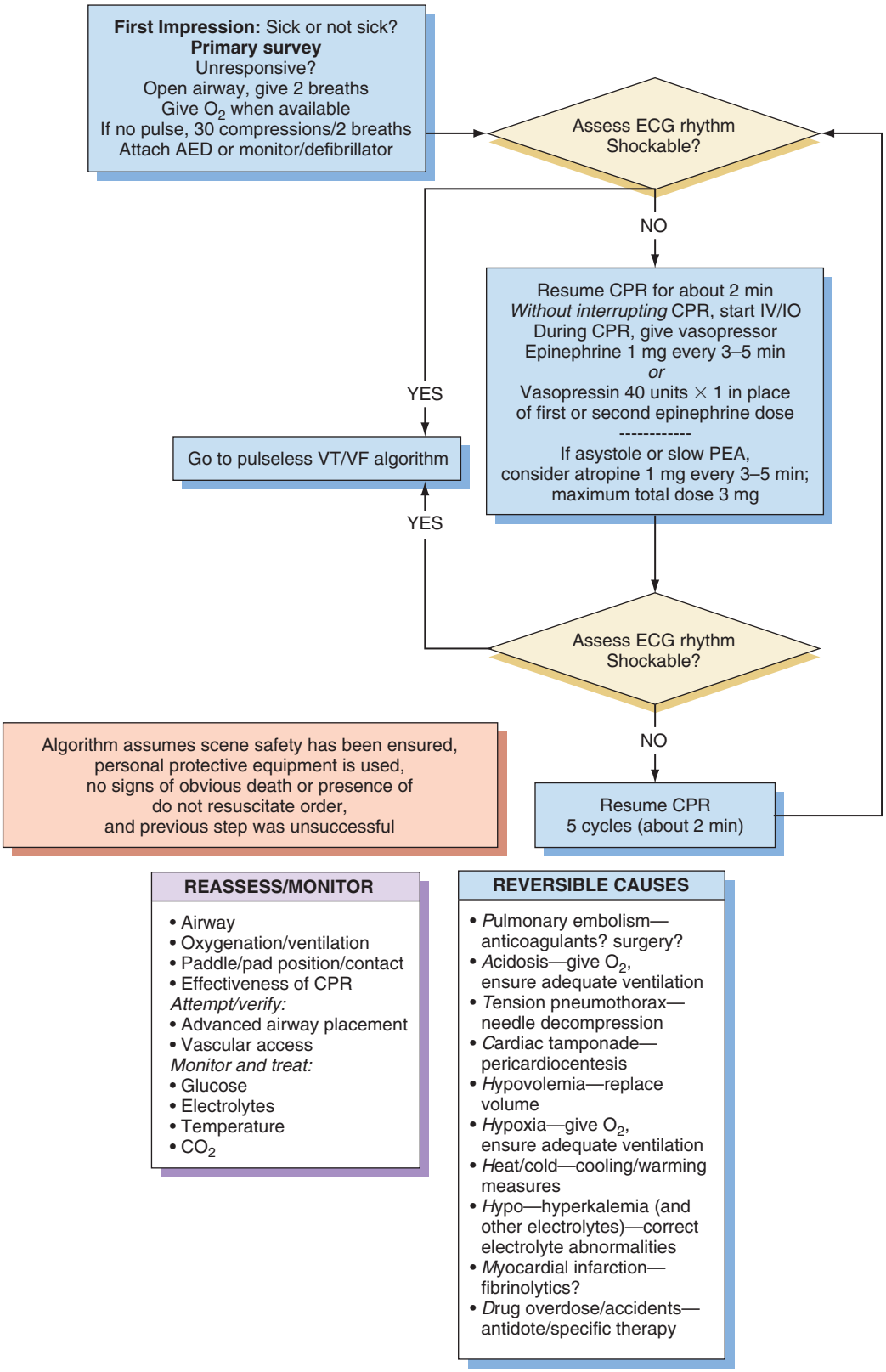

Fig. 38.28 Asystole or Pulseless Electrical Activity Algorithm. (From Aehlert B: *ACLS study guide*, ed 5, St. Louis, 2017, Mosby.)

TABLE 38.2 Drugs Used in Advanced Cardiovascular Life Support

Drug	Indications	Contraindications	Route	Dosage[8]	Pharmacologic Effects
Adenosine	PSVT; recommended as a safe and potentially effective therapy in the initial management of stable undifferentiated regular monomorphic wide-complex tachycardia	Use with caution if patient has asthma; may precipitate atrial fibrillation; poison-induced or drug-induced tachycardia; second-degree or third-degree heart block	IV bolus	6 mg IV for 1–2 s followed by 20-mL saline bolus; repeat twice with 12 mg in 1–2 min if needed	Decrease in AV node conduction
Amiodarone	Stable regular narrow-complex tachycardia to control rapid ventricular rate secondary to accessory pathway conduction in preexcited atrial arrhythmias	Prolonged QT interval	IV; IO	First dose: 300 mg bolus. Second dose: 150 mg	Multichannel blocker (calcium, potassium); inhibited α- and β-adrenergic responses
Atropine sulfate	Acute symptomatic bradycardia	Sinus, atrial, and ventricular tachycardia; hypothermic bradycardia; infranodal (type II) AV block; new third-degree with wide QRS complexes	IV bolus; IO	0.5–1 mg IV repeated every 3–5 min to total dose of 3 mg	Increased heart rate; increased force of atrial contractions
Dopamine	Hypotension with signs and symptoms of shock; second-line drug for symptomatic bradycardia	Use with caution in cardiogenic shock with accompanying CHF	IV infusion	2–20 mcg/kg/min	Increased renal and splenic flow at low doses (1–5 mcg/kg/min); β-adrenergic effects at moderate doses (5–10 mcg/kg/min); α-adrenergic effects at high doses (>10 mcg/kg/min)
Epinephrine	Cardiac arrest; VF; pulseless tachycardia; asystole; PEA; symptomatic bradycardia; severe hypotension; anaphylaxis; severe allergic reaction	VT and frequent PVCs	IV bolus; IO; endotracheal[a] use only if IV or IO cannot be established; IV infusion	1 mg every 3–5 min in cardiac arrest, up to 0.2 mg/kg; High-dose epinephrine is not recommended for routine use in cardiac arrest	Increased heart rate; increased force of contractions; vasoconstriction; increased coronary perfusion pressure; increased myocardial irritability; increased myocardial O_2 consumption
Isoproterenol	Alternative when a bradyarrhythmia is unresponsive to or inappropriate for treatment with atropine, or as a temporizing measure while awaiting the availability of a pacemaker. Refractory torsade de pointes[b] unresponsive to magnesium sulfate	Cardiac arrest; VT; frequent PVCs	IV infusion	2–10 mcg/min, titrate to adequate heart rate	Increased heart rate; increased force of contractions; vasodilation
Lidocaine	Second-line prophylactic antiarrhythmic therapy for monomorphic VT; lidocaine may be considered immediately after ROSC from cardiac arrest due to VF/pVT	Signs of lidocaine toxicity; prophylactic use in acute MI	IV bolus; IV infusion; IO; endotracheal[c]	1–1.5 mg/kg bolus every 5–10 min up to 3 mg/kg	Increased electrical stimulation threshold; depressed ventricular electrical activity
Propranolol	Suspected MI and unstable angina; SVTs	Bronchospastic disease; severe bradycardia; hypotension; second-degree or third-degree heart block; cocaine-induced acute coronary syndrome	IV	Total dose: 0.1 mg/kg by slow IV push, divided into 3 equal doses at 2- to 3-min intervals. Do not exceed 1 mg/min, repeat in 2 min to a total dose of 0.1 mg/kg if required	Reduce heart rate; decreased stroke volume; decreased myocardial O_2 consumption; increased LVEDP

Continued

TABLE 38.2 Drugs Used in Advanced Cardiovascular Life Support—cont'd

Drug	Indications	Contraindications	Route	Dosage[8]	Pharmacologic Effects
Verapamil, diltiazem	Alternative drug (after adenosine or vagal maneuvers) to terminate PSVT with narrow QRS complex, adequate blood pressure, and preserved left ventricular function; control ventricular rate in patients with atrial fibrillation or atrial flutter	Wide-complex QRS tachycardias of uncertain origin, Wolff-Parkinson-White syndrome and AF, sick sinus syndrome, second-degree or third-degree block without pacemaker, concurrent IV administration with IV β blockers	IV bolus	*First dose:* Verapamil: 2.5–5-mg IV bolus over 2 min (over 3 min in older patients) *Second dose:* 5–10 mg, if needed, every 15–30 min; maximum dose 20 mg *Alternative:* 5-mg bolus every 15–30 min to a total dose of 20–30 g *Diltiazem:* initial dose 15–20 mg (0.25 mg/kg) IV over 2 min; an additional 20–25 mg (0.35 mg/kg) IV in 15 min if needed; 5–15 mg/h IV titrated. Maintenance infusion titrated AF heart rate (if given for rate control)	Decreased sinoatrial node automaticity; slowed AV node conduction

[a]Endotracheal tube dosage is usually double the intravenous dosage.
[b]*Torsade de pointes* is a specific form of ventricular tachycardia in patients with a long QT interval. It is characterized by rapid and irregular QRS complexes, which may cease spontaneously or degenerate into ventricular fibrillation; In *Wolff-Parkinson-White* (WPW) syndrome, an extra electrical pathway between the heart's atria and ventricles causes a rapid heartbeat. The extra pathway is present at birth and the condition is rare.
[c]Dose of lidocaine via an endotracheal tube is 2.0–2.5 times the normal intravenous dose diluted in 10 mL of normal saline or sterile water to be used only when intravenous and intraosseus access is unavailable.
AF, Atrial fibrillation; *AV,* atrioventricular; *CHF,* congestive heart failure; *IO,* intraosseous; *LVEDP,* left ventricular end-diastolic pressure; *MI,* myocardial infarction; *PSVT,* paroxysmal supraventricular tachycardia; *PEA,* pulseless electrical activity; *PVC,* premature ventricular contraction; *SVT,* supraventricular tachycardia; *VF,* ventricular fibrillation; *VT,* ventricular tachycardia.

VF or VT. Second, the energy used during cardioversion is usually less than the energy applied during defibrillation.

Cardioversion is considered when a patient with an organized arrhythmia producing a high ventricular rate exhibits signs or symptoms of cardiac decompensation. These so-called *tachyarrhythmias* include SVT, atrial flutter, atrial fibrillation, and monomorphic VT with pulses. Cardioversion is ineffective for the treatment of junctional tachycardia or multifocal atrial tachycardia.[18]

If the arrhythmia is not causing serious signs or symptoms, drug therapy is used first. However, if the patient is hypotensive, exhibits signs of decreased consciousness or pulmonary congestion, or complains of chest pain, cardioversion is indicated.

Electrical pacing. Another application of electrical therapy uses intermittently timed low-energy discharges to replace or supplement the natural pacemaker of the heart. There are two primary types of electrical pacing. First, the electrical discharge can be delivered from an external power pack through wires inserted into the patient's chest wall (transcutaneous, or transthoracic, pacing). Alternatively, wire electrodes may be floated through the large veins and implanted directly inside the heart (transvenous pacing). Because it can be started quickly, transcutaneous pacing is the method used most often in emergency cardiac care.

Pacemaker therapy is used to treat sinus bradycardias that produce serious signs and symptoms and that do not respond to atropine (Fig. 38.29). Electrical pacing is also used to manage second-degree type II and third-degree heart block.

Because defibrillation can cause damage to permanent pacemakers, care should be taken not to place the electrode paddles or AED pads near these devices. After a patient with a permanent pacemaker undergoes either cardioversion or defibrillation, the device should be checked for proper functioning. Pacing is not recommended by the AHA for patients in asystolic cardiac arrest because it is ineffective and may delay or interrupt the delivery of chest compressions.[18]

The ECG is the most common and one of the most useful types of monitoring used during ACLS. The ECG provides the basis for selecting various drug and electrical therapies during CPR and helps to indicate patient response to these interventions. However, an acceptable ECG rhythm does not mean that cardiac output is adequate. Other indices of perfusion—such as pulse, blood pressure, and skin temperature—are needed to confirm adequate cardiac output.

Few criteria can predict the effectiveness of continued resuscitation. Considering this doubt, all pediatric and adult patients who experience cardiac arrest in the hospital setting should have resuscitative attempts initiated unless the patient has a valid

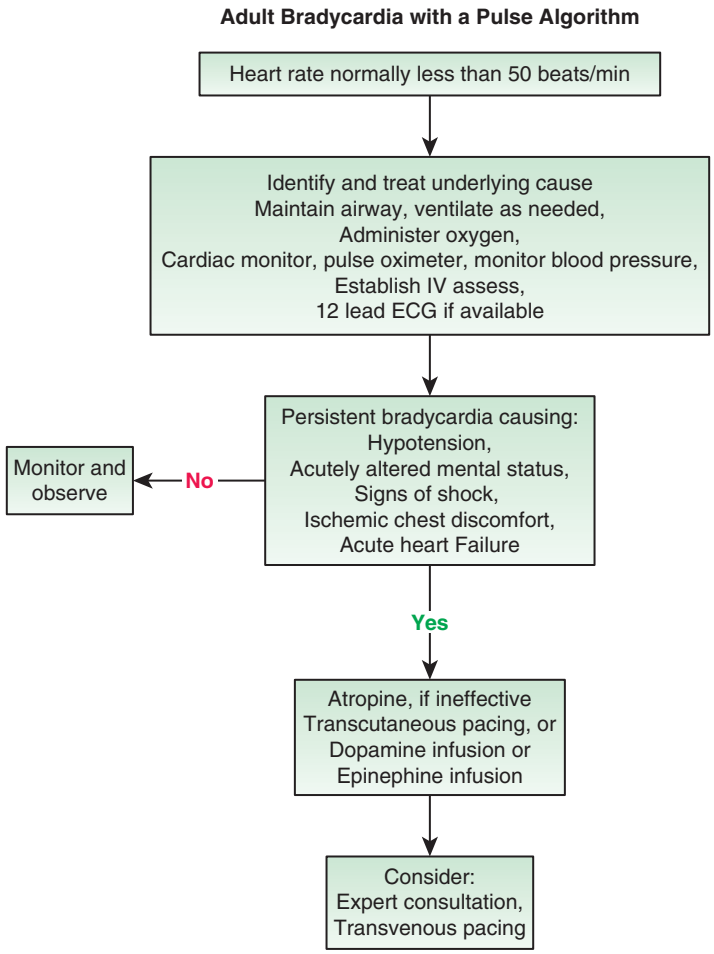

Fig. 38.29 Symptomatic Bradycardia Algorithm. (From Aehlert B: *ACLS study guide*, ed 5, St. Louis, 2017, Mosby.)

MINI CLINI

Problem

The code team is unsure when to discontinue resuscitation of a pediatric or adult cardiac arrest victim and whether family members should be allowed into the room.

Solution

First understand the principle of futility:

> "Patients or families may ask for care that is highly unlikely to improve health outcomes. Health care providers, however, are not obliged to provide such care when there is scientific and social consensus that the treatment is ineffective. If the purpose of a medical treatment cannot be achieved, the treatment can be considered futile."[46]

DNR order or has objective signs of irreversible death (e.g., hypostasis of the blood following death, which causes a purplish red discoloration of the skin).[46] In the hospital the decision to terminate resuscitative efforts rests with the treating physician and is based on attention to many factors including witnessed versus unwitnessed arrest, time to CPR, initial arrest rhythm, time to defibrillation, comorbid disease, prearrest state, and whether there is ROSC at some point during the resuscitative efforts.[46] In pediatric in-hospital cardiac arrest the clinician should consider stopping resuscitation using the following arrest characteristics: duration of CPR, witnessed event, number of doses of epinephrine, etiology of arrest, first and subsequent rhythm, and age.[46] Multiple variables should be considered in attempting to predict outcomes during cardiac arrest. Although there are factors associated with better or worse outcomes, no single factor studied predicts outcome with sufficient accuracy to recommend termination or prolongation of CPR.[47]

It may be helpful to offer limited family members the opportunity to be present during a resuscitation (assuming that the patient, if an adult, has not raised a prior objection).[46] Parents and other family members should be encouraged to do so by health care providers. Resuscitation team members should be sensitive to the presence of family members during resuscitative efforts, assigning a team member to remain with the family to answer questions, clarify information, and otherwise offer comfort (see "end of life," discussed in Chapter 58).[46]

Patient Care After Resuscitation

The key principles of postarrest care are (1) to identify and treat the core etiology of the cardiac arrest, (2) to lessen ischemia-reperfusion injury and avert secondary organ injury, and (3) to

make accurate appraisals of prognosis to guide the clinical team and to advise the family when they are selecting goals for continued care.[36]

After cardiac arrest, a patient may exhibit an optimal response, in which case the patient regains consciousness, is responsive, and breathes spontaneously. More often, however, the patient requires support of one or more organ systems. Acidemia associated with cardiac arrest usually improves when normal ventilation and perfusion are restored.

If the patient is conscious and breathing spontaneously after resuscitation, supplemental O_2, maintenance of an intravenous infusion, and continuous cardiac and hemodynamic monitoring may be all that is necessary. A 12-lead ECG, chest x-ray, arterial blood gas (ABG) analysis, and clinical chemistry profile should be performed as soon as possible. Providers of care after cardiac arrest should do the following to optimize survival and neurologic recovery:

> *"(1) maintain constant body temperature between 32°C and 36°C for at least 24 hours after achieving target temperature; (2) actively prevent fever in comatose patients after targeted temperature management.; (3) identify and treat acute coronary syndromes; (4) avoid and immediately correct hypotension and hypoxemia by using the highest available oxygen concentration until the arterial oxyhemoglobin saturation or the partial pressure of arterial oxygen can be measured; (5) optimize mechanical ventilation to minimize lung injury; (6) reduce the risk for multiorgan injury and support organ function if required; (6) objectively assess prognosis for recovery; and (7) assist survivors with rehabilitation services when required."*[36,48]

The patient should be closely supervised in an intensive care or coronary care unit, especially during the first 24 hours after a cardiac arrest.

Only in this setting can underlying organ system insufficiency or failure be properly identified and managed. The organs most likely to exhibit failure after resuscitation are the lung, heart, vasculature, and kidneys. Central nervous system failure is an ominous sign and generally indicates a failed resuscitation attempt.

Respiratory Management

If the patient remains apneic or exhibits irregular breathing after resuscitation, mechanical ventilation is instituted through a properly positioned endotracheal tube with an initial O_2 concentration of 100%. ABGs, preferably obtained through an arterial line, are analyzed as needed until the oxygenation and acid-base status of the patient stabilize. ABG analysis also helps differentiate between pulmonary and nonpulmonary (or cardiac) causes of hypoxemia and tissue hypoxia. Mechanical ventilation is adjusted to maintain a normal $PaCO_2$ level. Hyperventilation is detrimental and should be avoided. Higher ventilatory rates and larger V_T may cause hyperventilation. This hyperventilation may generate increased airway pressures and auto-PEEP, leading to an increase in cerebral venous and intracranial pressures and a decrease in coronary artery and cerebral arterial pressures.[49] If hyperventilation results in increased intrathoracic pressure, cerebral blood flow may decrease, causing increased brain ischemia. For details of the selection and use of mechanical ventilators and appropriate patient monitoring procedures, see Chapters 46 to 49, 52, and 53.

Cardiovascular Management

The 12-lead ECG, chest x-ray, clinical chemistry profile, cardiac enzyme results, and current and past drug histories should be reviewed. Invasive hemodynamic monitoring may be needed to monitor blood pressure and cardiac output. Such monitoring provides needed data on the adequacy of vascular volumes, left ventricular performance, and overall tissue perfusion. Based on these data, judgments can be made regarding the need for fluid therapy and the selection and use of appropriate drugs.

SUMMARY CHECKLIST

- The most common cause of sudden death in adults is coronary artery disease; accidents are the most common cause of death in young people.
- The fundamental steps of basic CPR implemented by health care providers for a witnessed cardiac arrest are as follows:
  1. Confirm unresponsiveness.
  2. Call for help and activate the EMS system.
  3. Check for a pulse (<10 seconds).
  4. Perform 30 cardiac compressions.
  5. Give two 1-second breaths to produce visible chest rise.
  6. Initiate automated external defibrillation immediately (perform defibrillation as soon as possible).
- In CPR for adults, five cycles of 30 compressions to 2 ventilations should be given between attempts at defibrillation using only one shock followed immediately by chest compressions.
- Evaluating the effectiveness of CPR is important and requires rescuers to watch for visible chest rise and fall with ventilation and to push hard and fast when they are delivering chest compression.
- Complications of CPR include worsening of potential neck injuries, gastric inflation and vomiting, and internal trauma during chest compressions. Correct technique minimizes the risk for such complications.
- The RT is most often called on to establish an airway and ventilation with elevated FiO_2 during ACLS of hospitalized patients. Most often, knowledge and skill with bag-valve devices and oropharyngeal airways is required. Special care should be taken not to hyperventilate the patient during or after cardiac arrest.
- Common pharmacologic agents used during ACLS include atropine for bradycardia, epinephrine and amiodarone or lidocaine (less effective than amiodarone) for ventricular arrhythmias, and epinephrine for cardiac arrest and hypotension.
- The RT is often involved in the care of a patient after cardiac arrest who has responded favorably to CPR. In the postresuscitative phase, the RT may have to maintain normal ventilation and oxygenation and assist the physician and nurses in monitoring the patient's condition.

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39

Humidity and Bland Aerosol Therapy

James B. Fink and Arzu Ari

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Describe how airway heat and moisture exchange normally occurs
- State the effect dry gases have on the respiratory tract
- State when to humidify and warm inspired gas
- Describe how various types of humidifiers work
- Describe how to enhance humidifier performance
- State how to select and use humidifier heating and feed systems safely
- Identify the indications, contraindications, and hazards that pertain to humidification during mechanical ventilation
- Describe how to monitor patients receiving humidity therapy
- Describe how to identify and resolve common problems with humidification systems
- State when to apply bland aerosol therapy
- Describe how large-volume aerosol generators work
- Identify the delivery systems used for bland aerosol therapy
- Describe how to identify and resolve common problems with aerosol delivery systems
- Describe how to perform sputum induction
- State how to select the appropriate therapy to condition a patient's inspired gas

CHAPTER OUTLINE

KEY TERMS

American Society for Testing and Materials
absolute humidity
baffling
body humidity
heat and moisture exchangers
humidifier
hydrophobic
hygrometer
hygroscopic
hypothermia
inspissated
International Organization for Standardization
isothermic saturation boundary
nebulizer
piezoelectric crystal
servo-controlled heating system
ultrasonic nebulizer

Vapors and mists have been used for millennia to treat respiratory disease. Modern respiratory care still uses these treatments at the bedside in the form of water vapor (humidity) and bland water aerosols. Concepts of absolute and relative humidity are essential for understanding humidity therapy; they are covered in Chapter 6. This chapter reviews the principles, methods, equipment, and procedures for using these concepts appropriately.

HUMIDITY THERAPY

Humidity therapy involves adding water vapor and (sometimes) heat to the inspired gas. Simply put, humidity is water in its gaseous or molecular form and its quantity depends on the temperature of the gas and is expressed as **absolute humidity** (AH) and relative humidity (RH).

AH, the amount of water in a given volume of gas, is usually expressed in milligrams per liter (mg/L). RH, the amount of water vapor in a volume of gas, is expressed as a percentage of the amount of water vapor required to fully saturate that gas at the same temperature and pressure. To understand the need for humidity therapy, clinicians must understand the normal control of heat and moisture exchange (HME).

Physiologic Control of Heat and Moisture Exchange

HME is a primary function of the upper respiratory tract, mainly the nose.[1-4] The nose heats humidifies gas on inspiration; it cools the gas and reclaims water the gas that is exhaled. The nasal mucosal lining is kept moist by secretions from mucous glands, goblet cells, transudation of fluid through cell walls, and condensation of exhaled humidity. The nasal mucosa is very vascular, actively regulating temperature changes in the nose and serving as an active element in promoting effective heat transfer. Similarly, the mucosa lining the sinuses, trachea, and bronchi aid in heating and humidifying inspired gases.

During inspiration through the nose, the tortuous path of gas passing through the turbinates increases surface area contact between the inspired air and the mucosa. As the inhaled ambient air enters the nose, it warms to 28.5°C *(convection)* and picks up water vapor from the moist mucosal lining *(evaporation),* cooling the mucosal surface to 30.2°C at the end of inspiration.[5]

During exhalation, the expired gas (34.1 7°C) transfers heat back to the cooler tracheal and nasal mucosa, which is 32.2°C at the end of expiration. As the saturated gas cools, it holds less water vapor. Condensation occurs on the mucosal surfaces during exhalation, and water is reabsorbed by the mucus *(rehydration).* In cold environments, the formation of condensate may exceed the ability of the mucus to reabsorb water (resulting in a "runny nose").

The mouth is less effective at HME than the nose because of the low ratio of gas volume to moist and warm surface area and the less vascular squamous epithelium lining the oropharynx and hypopharynx. When a person inhales through the mouth at normal room temperature, pharyngeal temperatures are approximately 3°C less than when the person breathes through the nose, with 20% less RH. During exhalation, the RH of expired gas varies little between mouth breathing and nose breathing, but the mouth is much less efficient in reclaiming heat and water.[2]

As inspired gas moves into the lungs, it achieves body temperature and pressure saturated (BTPS) conditions (i.e., body temperature, 37°C; barometric pressure; saturated with water vapor [100% RH at 37°C]) (Fig. 39.1). This point, normally approximately 5 cm below the carina, is called the **isothermic saturation boundary** (ISB).[6] Above the ISB, temperature and humidity decrease during inspiration and increase during exhalation. Below the ISB, temperature and RH remain constant (BTPS).

Numerous factors can shift the ISB deeper into the lungs. The ISB shifts distally when a person breathes through the mouth rather than the nose; when the person breathes cold dry air; when the upper airway is bypassed (breathing through an artificial tracheal airway); or when the minute ventilation is higher than normal. When this shift of ISB occurs, additional surfaces of the airway are recruited to meet the heat and humidity requirements of the lung. This recruitment of airways that do not typically provide this level of heat and humidity can have a negative impact on epithelial integrity. These shifts of the ISB can compromise the body's normal HME mechanisms, in which case humidity therapy is indicated.

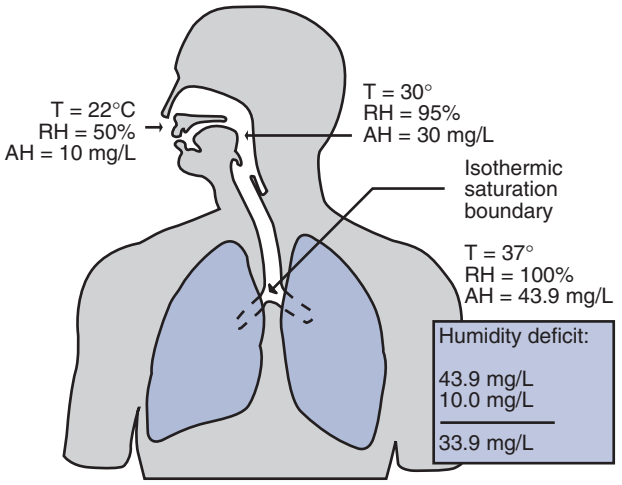

Fig. 39.1 As a person breathes typical ambient air, the upper airway adds 20 mg/L of water vapor and the lower airway adds 13.9 mg/L. If all of that humidity were exhaled, it would represent a humidity deficit of 33.9 mg/L. *AH,* Absolute humidity; *RH,* relative humidity; *T,* temperature. (From Fink J: Humidity and aerosol therapy. In Cairo J, Pilbeam S, editors: *Mosby's respiratory equipment*, ed 8, St. Louis, 2010, Mosby.)

RULE OF THUMB

The heat and humidity (AH) of a medical gas should be targeted to match conditions found in normal airways at the part of the airway where the gas is being introduced.

Indications for Humidification and the Warming of Inspired Gases

The primary goal of humidification is to maintain normal physiologic conditions in the lower airways. Proper levels of heat and humidity help to ensure normal function of the mucociliary transport system. Humidity therapy is also used to treat abnormal conditions. Box 39.1 summarizes the indications and contraindications for humidity therapy.

Administration of dry medical gases at flows greater than 4 L/min to the upper airway causes immediate heat and water loss and, if prolonged, causes structural damage to the epithelium. As the airway is exposed to relatively cold dry air, ciliary motility is reduced, airways become more irritable, mucus production increases, and pulmonary secretions become **inspissated** (thickened and dried, owing to dehydration).[7]

As listed in Box 39.2, the hazard of breathing dry gas is even greater when the normal heat- and water-exchange capabilities

BOX 39.1 Indications for Humidification Therapy

Primary

- Humidifying dry medical gases
- Overcoming humidity deficit created when the upper airway is bypassed

Secondary

- Treating bronchospasm caused by cold air
- With thick, copious, or bloody secretions.
- With an expired tidal volume (V_T) less than 70% of the delivered V_T (e.g., patients with large bronchopleural fistulas or incompetent or absent endotracheal tube cuffs).
- With a body temperature below 32°C.
- With high spontaneous minute volumes (>10 L/min).
- Receiving noninvasive ventilation with large mask leaks, because the patient does not exhale enough V_T to replenish heat and moisture to adequately condition the inspired gas. Also, the resistance and dead space of the HME may negate the effects of the noninvasive positive pressure and add additional work of breathing.
- Receiving lung-protective ventilation strategies, as in acute respiratory distress syndrome (the additional dead space of HME may increase the ventilation requirement and $PaCO_2$).
- Receiving in-line aerosol drug treatments (a standard HME must be removed from the patient circuit during treatments. An HME designed for aerosol delivery must be switched to the aerosol bypass mode).

HME, Heat and moisture exchanger.

BOX 39.2 Hazards and Complications for Humidification Therapy

Hazards and complications associated with use of HH and HME units during mechanical ventilation include the following:

- Potential electrical shock (HH)
- Potential for burns to caregivers from hot metal (HH)
  - Hypothermia (HME unit or inadequately set HH)
  - Hyperthermia (HH)
  - Thermal injury (HH)
- Underhydration and mucous impaction (HME unit or HH)
  - Hypoventilation and/or alveolar gas trapping, resulting from mucus plugging of airways (HME unit or HH)
  - Hypoventilation secondary to hypercapnia caused by the increase in dead space (HME unit)
  - Increased work of breathing (HME unit)
  - Possible hypoventilation resulting from hypercapnia caused by the increase in dead space (HME unit)
  - Inadvertent overfilling or pooled condensate, resulting in unintentional tracheal lavage (HH)
  - High flow rates during disconnect, which can aerosolize contaminated condensate (HH)
  - Elevated airway pressures caused by condensation (HH)
  - Ineffective low-pressure alarm during disconnection (HME unit)
  - Patient–ventilator dysynchrony and improper ventilator function caused by condensation in the circuit (HH)
  - Airway burns or tubing meltdown if heated-wire circuits are covered or incompatible with humidifier (HH)

HH, Heated humidifier; *HME,* heat and moisture exchanger.

BOX 39.3 Clinical Signs and Symptoms of Inadequate Airway Humidification

- Atelectasis
- Dry, nonproductive cough
- Increased airway resistance
- Increased incidence of infection
- Increased work of breathing
- Patient complaint of substernal pain and airway dryness
- Thick, dehydrated secretions

TABLE 39.1 Recommended Heat and Humidity Levels

Delivery Site	Temperature Range (°C)	Relative Humidity (%)	Absolute Humidity (mg/L)
Nose/mouth	20–22	50	10
Hypopharynx	29–32	95	27–32
Trachea/carina	32–35	100	34–40
Lungs (ISB)	37	100	44

ISO, Isothermic saturation boundary.

of the upper airway are lost or bypassed, as occurs with endotracheal intubation. Breathing dry gas through an endotracheal tube (ETT) can cause damage to tracheal epithelium within minutes. However, as long as the inspired humidity is at least 60% of BTPS conditions, no injury occurs in normal lungs. Prolonged breathing of improperly conditioned gases through a tracheal airway can result in **hypothermia** (reduced body temperature), inspissation of airway secretions, mucociliary dysfunction, destruction of airway epithelium, and atelectasis.[6-8] Delivery of inspired gas at 30°C or even 34°C with 100% RH may not be sufficient to prevent epithelial damage occurring during a 6-hour exposure.[7]

Box 39.3 summarizes the signs and symptoms associated with breathing cold dry gases. A reduction of 20 mg/L below BTPS (44 mg/L) is less than 60% RH at BTPS.

The amount of heat and humidity that a patient needs depends on the site of gas delivery (e.g., nose or mouth, hypopharynx, trachea). Table 39.1 summarizes the recommended levels based on current standards.

RULE OF THUMB

Despite minimal levels in the standards, delivery of inspired gas to the lower airways at 30°C or even 34°C with 100% RH may not be sufficient to prevent the occurrence of epithelial damage during a 6-hour exposure.[7]

Warmed, humidified gases are used to prevent or treat various abnormal conditions. In the treatment of hypothermia, heating and humidifying the inspired gas is one of several techniques used to raise core temperatures back to normal.[8-10] Heated humidification is used to reduce intraoperative hypothermia.[9]

MINI CLINI

Stabilization of Preterm Infants at Birth With Conditioned or Unconditioned Gas

Problem

A preterm infant is delivered and requires oxygen, bagging, and continuous positive airway pressure (CPAP) during stabilization and transport to the nursery, but heated humidified gas is not ready. What is the risk of using unconditioned gas?

Solution

Use of heated humidity from delivery to arrival at the nursery improves admission temperatures, whereas inadequate humidification and heating of inspired gases increases heat loss and can lead to mild hypothermia. Cold inspired gases can also cause distal airway and alveolar damage, and even a brief exposure to dry and cold respiratory gases can decrease lung compliance and increase work of breathing (WOB).

However, transient use of dry cold gases during resuscitation did lower temperature, but no detectable differences in acute or longer-term respiratory outcomes—including level of respiratory support, bronchopulmonary dysplasia or mortality—were reported. Although transient administration of unconditioned gas did no apparent harm, additional studies are required to support a practice change.

Of possibly greater clinical significance, warming and humidifying the inspired gas can help to alleviate bronchospasm in patients who develop airway narrowing after exercise or when they breathe cold air. Although the cause of this condition is not known for certain, the primary stimulus is probably a combination of airway cooling and drying, which leads to the hypertonicity of airway lining fluid and the release of chemical mediators.[11] The incidence of cold air–induced bronchospasm can be reduced by wearing a scarf over the nose and mouth in cold weather; the scarf becomes a crude passive HME device.

The delivery of cool humidified gas is used to treat upper airway inflammation resulting from croup, epiglottitis, and postextubation edema. This technique is used most often in conjunction with bland aerosol delivery (see the later section titled "Bland Aerosol Therapy").[12]

Equipment

A **humidifier** is a device that adds molecular water to gas. This process occurs by evaporation of water from a surface to a gas that is not 100% saturated with water vapor (see Chapter 6), whether the water is in a reservoir, a wick, or a sphere of water in suspension (aerosol).

Physical Principles Governing Humidifier Function

The following four variables or principles affect the performance of a humidifier: (1) temperature, (2) surface area, (3) time of contact, and (4) thermal mass.[13] These factors are exploited to various degrees in the design of humidification devices (Box 39.4).

Temperature. Temperature is an important factor affecting humidifier performance. The higher the temperature of a gas, the more water vapor it can hold (increased capacity). As gas expansion and evaporation cool water in unheated humidifiers to 10°C below ambient temperature, the humidifiers become less efficient.

Fig. 39.2 shows this concept, where—owing to evaporative cooling—the unheated humidifier on the left is operating at 10°C. Although the humidifier fully saturates the gas, the low operating temperature limits total water vapor capacity to approximately 9.4 mg/L, equivalent to approximately 21% of **body humidity**. Simply heating the humidifier to 40°C (see Fig. 39.2, right) increases its output to 51 mg/L, which is sufficient to meet BTPS conditions.

Surface area. The greater the area of contact between water and gas, the more opportunity there is for evaporation to occur. Pass-over humidifiers pass gas over a large surface area of water. More space-efficient ways to increase the ratio of water to gas surface area include bubble diffusion, aerosol, and wick technologies.

Bubble-diffusion directs a stream of gas under water, where it is broken up into small bubbles. As the gas bubbles rise to the surface, evaporation increases the water vapor content within the bubble. The smaller the bubble, the greater the ratio of water to air surface area.

An alternative to dispersing gas bubbles in water is spraying water particles (aerosol) into the gas. The higher the aerosol density (number of particles per volume of gas), the greater the gas-to-water surface area available for evaporation.

Wicks use porous water-absorbent materials to draw water (similar to a sponge) into its fine honeycombed structure by means of capillary action. The surfaces of the wick increase the area of contact between the water and gas, which aids evaporation.

Contact time. The longer a gas remains in contact with water, the greater the opportunity for evaporation to occur. For bubble humidifiers, contact time depends on the depth of the water column; the deeper the column, the greater the time of contact as the bubbles rise to the surface. In pass-over and wick-type humidifiers, the flow rate of gas through the humidifier is inversely related to contact time, with high flow rates reducing the time available for evaporation to occur. Aerosols suspended in a gas stream have extended contact time (and opportunity for evaporation) as the aerosol and gas travel to the patient.

Thermal mass. The greater the amount of water in a humidifier, the greater the thermal mass. Increased thermal mass equates to increased capacity to hold and transfer heat to therapeutic gases. Larger-reservoir humidifiers can provide more consistent heat and humidification with a broader range of gas flow.

BOX 39.4 Physical Principles Governing Humidifier Function

Temperature: The higher the temperature of a gas, the more water vapor it can hold (increased capacity), and vice versa.

Surface area: The greater the surface area of contact between water and gas, the more opportunity for evaporation to occur.

Contact time: The longer a gas remains in contact with water, the greater the opportunity for evaporation to occur.

Thermal mass: The greater the mass of water or the core element of a humidifier, the greater its capacity to hold and transfer heat.

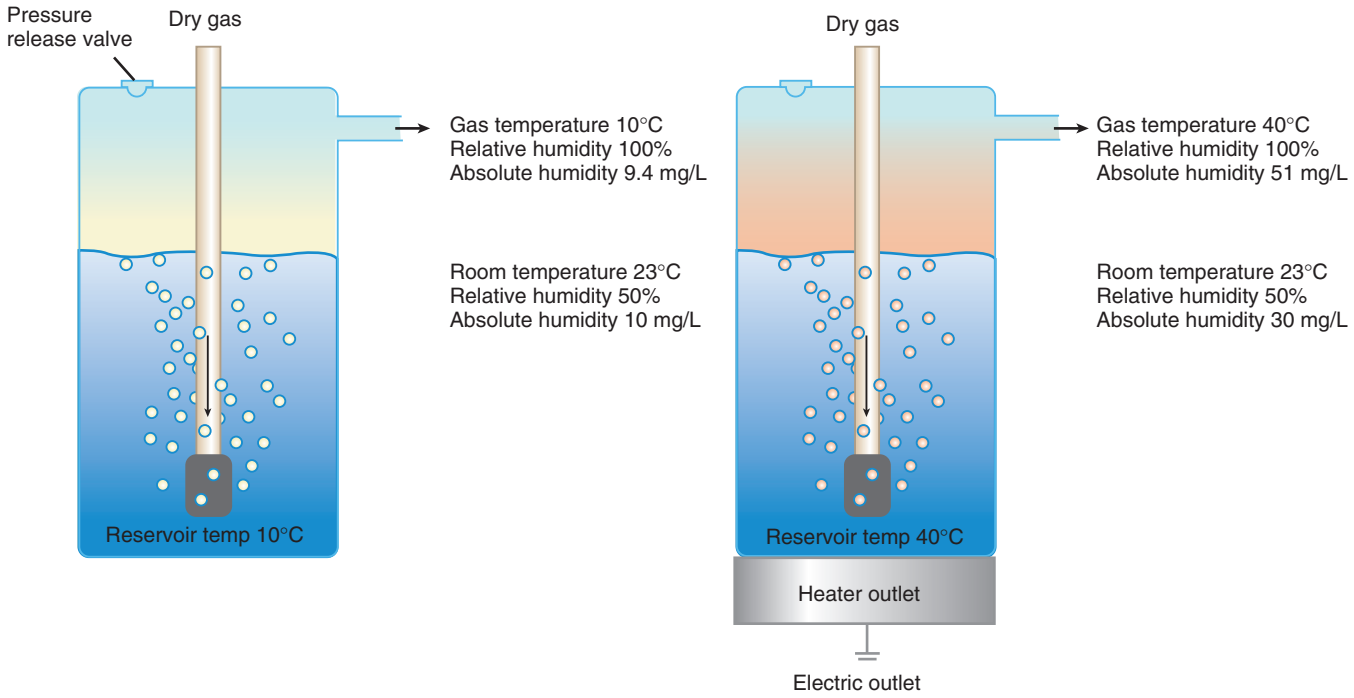

Fig. 39.2 Effects of reservoir temperature on humidity output with unheated *(left)* and heated *(right)* bubble-type humidifiers. (Modified from Fink J, Cohen N: Humidity and aerosols. In Eubank D, Bone R, editors: *Principles and applications of cardiorespiratory care equipment*, St. Louis, 1994, Mosby.)

Types of Humidifiers

Humidifiers are either *active* (actively adding heat, water, or both to the device–patient interface) or *passive* (recycling exhaled heat and humidity from the patient). Active humidifiers typically include (1) bubble humidifiers, (2) pass-over humidifiers, (3) nebulizers of bland aerosols, and (4) vaporizers. Passive humidifiers are typical **heat and moisture exchangers**. Specifications covering the design and performance requirements for medical humidifiers are established by the **American Society for Testing and Materials** (ASTM).[14]

Active humidifiers

Bubble. A bubble humidifier breaks (diffuses) an underwater gas stream into small bubbles (Fig. 39.3). Use of a foam or mesh diffuser produces smaller bubbles than an open lumen, allowing greater surface area for gas–water interaction. Unheated bubble humidifiers are commonly used with oxygen (O_2) delivery systems (see Chapter 41) to raise the water vapor content of the gas to ambient levels.

As indicated in Table 39.2, unheated bubble humidifiers can provide AH levels between approximately 15 and 20 mg/L.[13,14] At room temperature, 10 mg/L AH corresponds to approximately 80% RH but only approximately 25% body humidity (see Chapter 6). As gas flow increases, the reservoir cools and contact time is reduced, limiting effectiveness at flow rates greater than 10 L/min. Heating the reservoirs can increase humidity content, but this is not recommended because cooling produces a condensate that obstructs small-bore delivery tubing.

To warn of flow-path obstruction and prevent bursting of the humidifier bottle, bubble humidifiers incorporate a simple pressure-relief valve, or *pop-off*. The pop-off is commonly a gravity- or spring-loaded valve that releases pressures greater than 2 psi. Humidifier pop-offs should provide both an audible and a visible alarm and resume normal position when pressures return to normal.[14] The pop-off can be used to test an O_2 delivery system for leaks by obstructing delivery tubing at or near the patient interface. If the pop-off sounds, the system is leak free; failure of the pop-off to sound may indicate a leak (or a faulty pop-off valve).

As gas flow increases, bubble humidifiers can produce aerosols. Although invisible to the naked eye, these water droplet suspensions can transmit pathogenic bacteria from the humidifier reservoir to the patient.[15] Because any device that generates an aerosol poses a high risk for spreading infection, strict infection-control procedures must be followed when these systems are used (see Chapter 4).

TABLE 39.2 Types, Mechanisms, and Absolute Humidity Range of Passive Heat and Moisture Exchangers

	Mechanism	Absolute Humidity Range
HME	Hydrophobic	10–14 mg H_2O/L
HMEF	Hydrophobic + filter	18–28 mg H_2O/L
HHME	Hydrophobic + hygroscopic	22–34 mg H_2O/L
HHMEF	Hydrophobic + hygroscopic + filter	23–35 mg H_2O/L

HME, Heat and moisture exchanger; *HMEF,* heat and moisture exchanging filter; *HHME,* hydrophobic hydroscopic heat and moisture exchanger; *HHMEF,* hydrophobic hydroscopic heat and moisture exchanging filter.

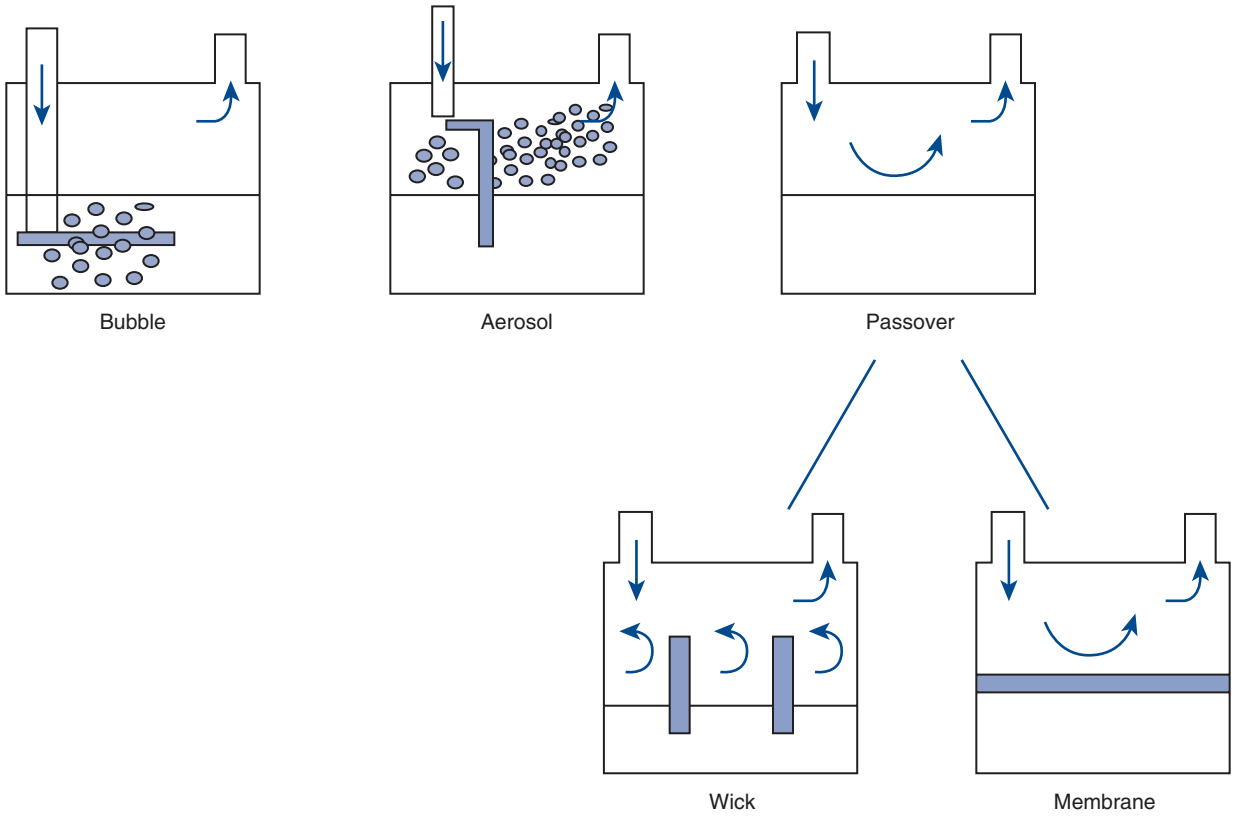

Fig. 39.3 Primary Types of Active Humidifiers. Gas passes through the water *(bubble)*, around drops of water *(aerosol)*, or over the surface of water *(pass-over)*, a saturated material *(wick)*, or a semipermeable membrane *(membrane)*. (From Fink J: Humidity and aerosol therapy. In Cairo J, Pilbeam S, editors: *Mosby's respiratory equipment*, ed 8, St. Louis, 2010, Mosby.)

RULE OF THUMB

Jet, bubble, and ultrasonic humidifiers produce aerosols that can carry bacteria from the reservoir to the patient. Minimize contamination of the reservoir by draining condensate away from the humidifier, and rinse, wash, sterilize, or replace frequently.

Pass-over. Pass-over humidifiers direct gas over a surface containing water. There are three common types: (1) simple reservoir type, (2) wick type, and (3) membrane type (see Fig. 39.3).

The simple reservoir device directs gas over the surface of a volume of water (or fluid). The surface for gas–fluid interface is limited. Typically used with heated fluids during invasive mechanical ventilation, room-temperature fluids may be used with noninvasive ventilatory support (nasal CPAP or bilevel ventilation).

A wick humidifier uses an absorbent material to increase the surface area for dry air to interface with heated water. Typically a wick is placed upright with the gravity-dependent end in a heated water reservoir. Heating elements might be below or surrounding the wick. Capillary action draws water up from the reservoir and keeps the wick saturated. As dry gas enters the chamber, it flows around the wick, quickly picking up heat and moisture and leaving the chamber saturated with water vapor. No bubbling occurs, so no aerosol is produced.

Membrane-type humidifiers separate heated water from the gas stream by means of a **hydrophobic** membrane. Hydrophobic

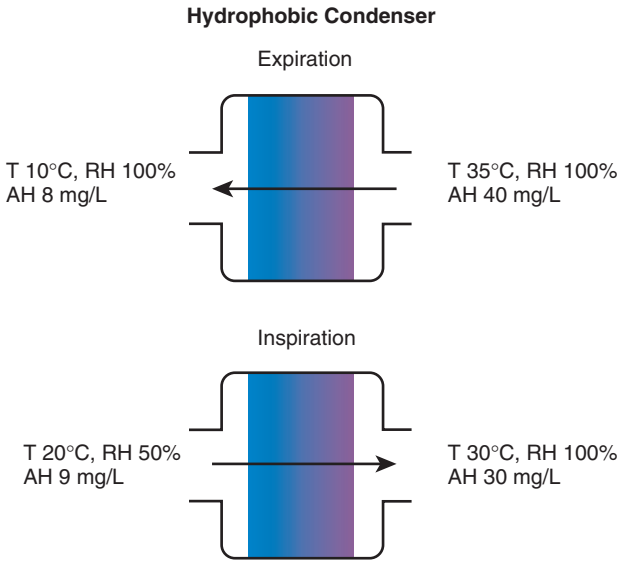

Fig. 39.4 Process of Humidification With a Hydrophobic Condenser Humidifier. *AH,* Absolute humidity; *RH,* relative humidity; *T,* temperature.

("water hating") membranes have little or no tendency to absorb water, typically having a nonpolar surface that repels water (Fig. 39.4). Water vapor (molecules) pass through the pores in the membrane, but liquid water (and pathogens) cannot.

Compared with bubble humidifiers, pass-over, wick, and membrane humidifiers offer several advantages.[15,16] First, they

maintain heat and saturation at higher flow rates than bubbling or jet humidifiers. Second, they add little or no flow resistance to spontaneous breathing circuits.[16,17] Third, they do not generate any aerosols and pose minimal risk for spreading infection.[15]

Vaporizer humidifiers. Simple vaporizers heat water to the point of expansion as a gas. Simple room vaporizers have been used in ambulatory settings for years as room humidifiers. A capillary force vaporizer is a thin-film, high-surface-area boiler that combines capillary force and phase transition to impart pressure onto an expanding gas (water vapor) and ejects it into the gas stream.

Heat and moisture exchangers. Heat and moisture exchange (HME) units typically comprise a passive humidifier, also described as an "artificial nose." Similar to the nose, such a device captures exhaled heat and moisture and returns up to 70% of the heat and humidity to the patient during the next inspiration. In contrast to the nose, with its rich vasculature and endothelium, most HME units do not actively add heat or water to the system.[13]

Traditionally, HME units have been mainly used to provide humidification to patients receiving ventilatory support via endotracheal or tracheostomy tubes. More recently, they have been used successfully in meeting the short-term humidification needs of spontaneously breathing patients with tracheostomy tubes[16-19] and long-term needs with laryngectomies where a significant decrease in the frequency of coughing, forced expectoration, and stoma cleaning were reported with a decrease in pulmonary symptoms and improvement of speech and sleeping regardless of country or climate.[20]

Reports of an increased incidence of blocked tracheal tubes associated with the long-term use of HME deices in the intensive care unit[21] are in contrast to evidence supporting their long-term use in spontaneously breathing patients.[22-25]

The three basic types of HME units are (1) simple condenser humidifiers, (2) hygroscopic condenser humidifiers, and (3) hydrophobic condenser humidifiers. Simple condenser units contain a condenser element with high thermal conductivity; the latter usually consists of metallic gauze, corrugated metal, or parallel metal tubes. Inspired air cools the condenser element, and expired water vapor condenses directly on its surface and rewarms it. On the next inspiration, cool dry air is warmed and humidified as it passes over the condenser element. Simple condenser humidifiers can recapture only some 50% of a patient's exhaled moisture.

Hygroscopic materials absorb moisture from the air. Hygroscopic condenser HME units use materials that (1) incorporate a condensing element of low thermal conductivity (e.g., paper, wool, or foam) and (2) impregnate this material with a hygroscopic salt (calcium or lithium chloride). By using an element with low thermal conductivity, hygroscopic condenser HME units can retain more heat than simple condenser systems, while hygroscopic salt helps capture extra moisture from the exhaled gas. The lower water vapor pressure in the inspired gas liberates water molecules directly from the hygroscopic salt without cooling. Fig. 39.5 depicts the overall process of humidification with a hygroscopic condenser humidifier, showing the changes in temperature and the RH and AH occurring during the cycle of breathing. As shown, these units typically achieve approximately 70% efficiency (40 mg/L exhaled, 27 mg/L returned).

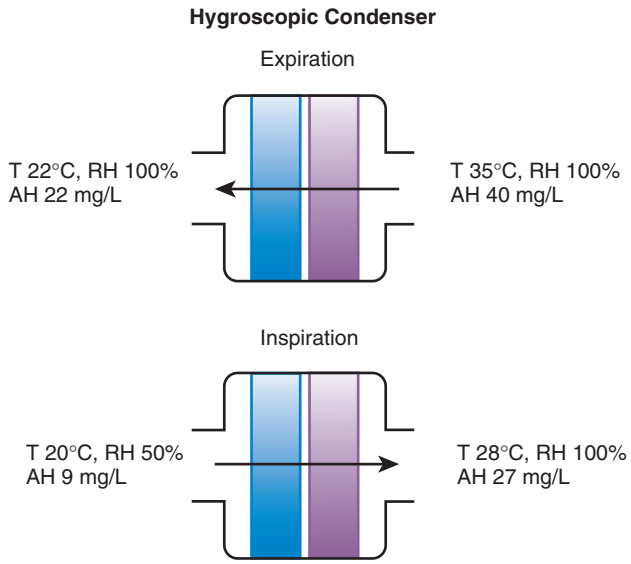

Fig. 39.5 Process of Humidification With a Hygroscopic Condenser Humidifier. *AH,* Absolute humidity; *RH,* relative humidity; *T,* temperature

Hydrophobic condenser HME units use a water-repellent element with a large surface area and low thermal conductivity (see Fig. 39.4). During exhalation, the condenser temperature increases to approximately 25°C because of conduction and the latent heat of condensation. On inspiration, cool gas and evaporation reduce the condenser temperature down to 10°C. This large temperature change results in the conservation of more water to be used in humidifying the next breath. The efficiency of these units is comparable to that of hygroscopic condenser HMEs (approximately 70%). However, some hydrophobic HMEs that provide bacterial filtration may reduce the risk for pneumonia but be unsuitable for patients with limited respiratory reserve or those are prone to airway blockage because they may increase artificial airway occlusion.[26] HME units that deliver at least 30 mg H_2O/L should be used because they are associated with a lower incidence of ETT occlusion.[21]

Design and performance standards for HME units are set by the **International Organization for Standardization** (ISO).[27,28] The ideal HME unit should operate at 70% efficiency or better (providing at least 30 mg/L water vapor); use standard connections; have a low compliance; and add minimal weight, dead space, and flow resistance to a breathing circuit.[29] HME performance varies from brand to brand and may differ from manufacturers' specifications.[21] Insufficient heat and humidification can occur with some HME units, causing complications. Table 39.3 compares performance of several commercially available HME units according to their moisture output, flow resistance, and dead space.[21]

RULE OF THUMB

As many as 50% of HME units do not provide the recommended inspired AH of 30 mg H_2O/L. Check manufacturing performance specifications and independent bench studies before adopting an HME unit for clinical use.

As shown in Table 39.4, the moisture output of HME units tends to decrease with high volumes and rates of breathing. In addition, high inspiratory flows and high FiO_2 levels can decrease the efficiency of such a device.[30] Flow resistance through the HME also is important. When they are dry, resistance across most devices is minimal. However, because of water absorption, flow resistance increases after several hours of use.[31] For some patients, the increased resistance imposed by the HME may not be well tolerated, particularly if the underlying lung disease has already increased WOB. An increase in WOB through the HME may lead to elevated airway pressures and a possible disconnect.[32]

Because HME units eliminate the problem of condensation in the breathing circuit, many clinicians consider these devices (especially hydrophobic filter HME units) to be helpful in preventing nosocomial infections and ventilator-associated pneumonia (VAP).[33-38] Compared with active humidification systems, HME units reduce bacterial colonization of ventilator circuits.[34] However, if usual maintenance precautions are applied, circuit colonization plays a minor role in the development of nosocomial infections.[35] Further, there is no evidence of an overall difference between HME units and heated humidifiers in preventing mortality and other complications in patients who are mechanically ventilated,[26] and previous research indicates no difference in the incidence of ventilator-associated infections with HME units versus heated humidifiers.[26,29,33-40] The position of the HME relative to the patient's airway can affect its ability to heat and humidify inhaled gas. Secretions can foul HME units attached directly to the airway. The use of devices such as closed suction catheters and airway monitor ports requires placement of the HME closer to the ventilator. Previous research has tested the performance of HME units placed directly at the airway, 10 cm away from the ETT, and proximal to the ventilator circuit.[41] It was then reported that the performance of the HME unit was best when placed directly at the airway (Fig. 39.6).[41] Clinicians should select HME units that perform adequately when placed at the intended position. Although use of these devices has been associated with a thickened and increased volume of secretions in some patients, the incidence of ETT occlusion when HME units are used is equivalent to that with heated humidifiers.[37,42]

HME units are not recommended for use with infants and small children because they add 5 to 90 mL of mechanical dead space, exceeding the tidal volume of the preterm infant. In addition, infants are commonly ventilated through uncuffed ETTs, which allow exhaled gas to leak around the tube and bypass the HME, thus reducing recovered heat and humidity. Similarly, for other populations, HME units are not recommended for patients requiring lung-protective ventilation. The greater dead space frequently results in hypercapnia in patients with small tidal volumes.[43]

Active heat and moisture exchangers. Active HME units add humidity, heat, or both to inspired gas by chemical or electrical means.[44] The Humid-Heat (Louis Gibeck AB, Upplands Väsby, Sweden) consists of a supply unit with a microprocessor, water pump, and humidification device, which is placed between

TABLE 39.3 Comparison of Active Heated Humidity Units With Passive Heat and Moisture Exchangers

Humidifier	Advantages	Disadvantages
Active heated humidity	Wide application	Cost—setup
	Reliability	Water use
	Temperature monitoring and alarms	Condensation
	Control over range of temperatures	Risk of contamination
	Optimal absolute humidity	Risk of burns or electrical shock (low)
Passive—heat and moisture exchanger	Cost—low per unit	Limited applications—not for all patients
	No power required	Added mass at airway
	No added water	Increased dead space
	Minimal condensation	Increased resistance and work of breathing
	Ease of use	Potential occlusion
		Limited temperature and absolute humidity
		Breaking circuit to change and administer aerosol

TABLE 39.4 Representative Range of Measured Absolute Humidity and Resistance of Heat and Moisture Exchangers

Device	Manufacturer	Measured AH (mg H_2O/L)	Dead Space mL/AH/mL	Resistance 60 L/min cm H_2O
Hygrobac	Mallinckrodt	31.7 ± 0.7	84 mL/0.33	2.1
Hygrobac S	Mallinckrodt	31.2 ± 0.2	49 mL/0.69	2.3
Humid Vent Filter	Hudson	30.8 ± 0.3	35 mL/0.88	2.3
BB100E	Pall	27.2 ± 0.7	85 mL/0.32	1.4
Iso-Gard Hepa Light	Hudson	23.6 ± 0.3	80 mL/0.47	2.4
BB25	Pall	19.6 ± 1.4	35 mL/0.56	2.6
Barrierbac S	Mallinckrodt	13.2 ± 0.2	35 mL/0.38	2.1

AH, Absolute humidity; *NA,* not available.
Modified from Lellouche F, Taille S, Lefrancois F, et al: Humidification performance of 48 passive airway humidifiers: comparison with manufacturer data, *Chest* 135:276, 2009.

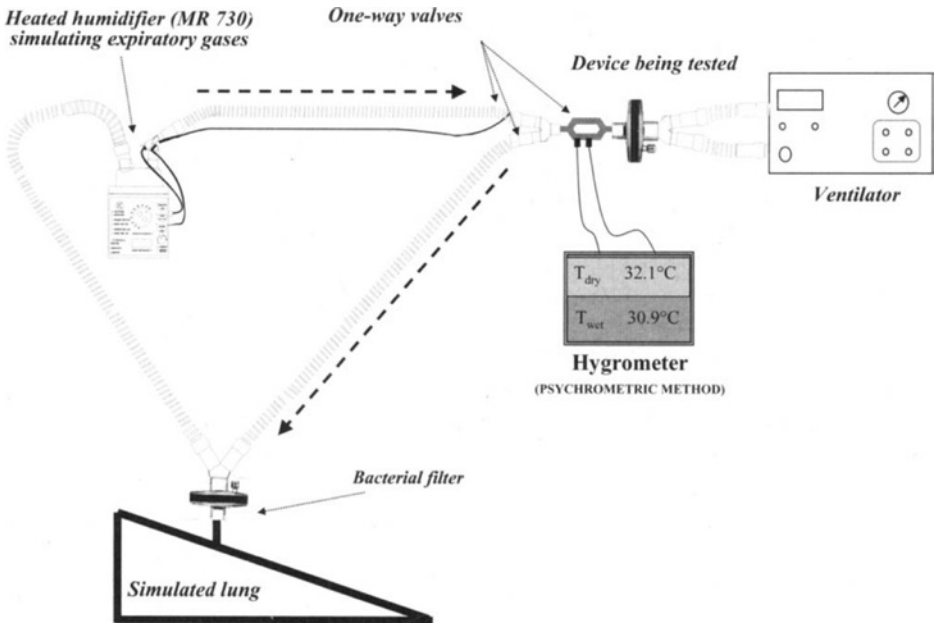

Fig. 39.6 Hygrometric bench test apparatus to measure humidification performance of heat and moisture exchange. A ventilator delivered controlled cycles (respiratory rate of 20 breaths/min with a tidal volume of 500 mL and a positive end-expiratory pressure of 5 cm H_2O). A heated humidifier *(MR 730)* was connected to the expiratory limb of the model and was set to deliver gases with a water content of 35 mg H_2O/L at the Y piece. A circuit with heated wire was used after the humidification chamber. The room temperature was kept constant between 24.5°C and 25.5°C. (From Lellouche F, Taillé S, Lefrançois F, et al: Humidification performance of 48 passive airway humidifiers: comparison with manufacturer data, *Chest* 135(2):276–286, 2009.)

TABLE 39.5 Attributes of Humidifiers

Attribute	Bubble, Unheated	Pass-over, Heated	Nebulizer, Unheated	Nebulizer, Heated	HME
Output (mg/L)	15–20	30–50	15–30	20–40	10–35
Temperature (°C)	10–20	30–40	10–20	22–28	22–30
Flow limits	Yes	No	Yes	Yes	Yes
Retain body heat	No	Yes	No	Yes	Yes
Infection risk	Yes	No	Yes	Yes	No
Possible overheating	No	Yes	No	Yes	No
Risk of underhydration	High	Low	High	Moderate	Moderate
Increased work of breathing	Low	Low	Moderate	Moderate	High
Electrical hazard	None	Possible	None	Possible	None

HME, Heat and moisture exchange.

the Y piece and the ETT. The humidification device is based on a hygroscopic HME unit, which absorbs the expired heat and moisture and releases it into the inspired gas. External heat and water are added to the patient side of the unit in order to increase temperature. The external water is delivered to the humidification device via a pump onto a wick and evaporated into the inspired air by an electrical heater. The microprocessor controls the water pump and heater by an algorithm using the minute ventilation (which is fed into the microprocessor) and the airway temperature measured by a sensor mounted in the flex-tube on the patient side of the humidification device. The HME Booster (King Systems, Noblesville, IN) has a T piece containing an electrically heated element designed for use as an adjunct to a passive HME. The heating element heats water, so that water vapor passes into the airway between the artificial airway and ETT via a Gore-Tex membrane and aluminum. Using gravity feedbag via a flow regulator that limits flow to 10 mL/h, water is fed to the heater, which operates at 110°C and adds 3 to 5.5 mg/L of humidity and 3°C to 4°C to inspired gas compared with the HME alone. The Humid-Booster was designed for patients with minute volumes of 4 to 20 L and is not appropriate for use with pediatric patients or infants. Active HME units add weight and complexity at the patient airway (Table 39.5).

The Performer (StarMed, Mirandola, Italy), similar to a common hygroscopic-hydrophobic HME unit, has the ability (in active mode) to add water and heat to the inspired gas circuit. The water is continuously added from an external source, wetting the hygroscopic-hydrophobic membrane; the membrane is heated,

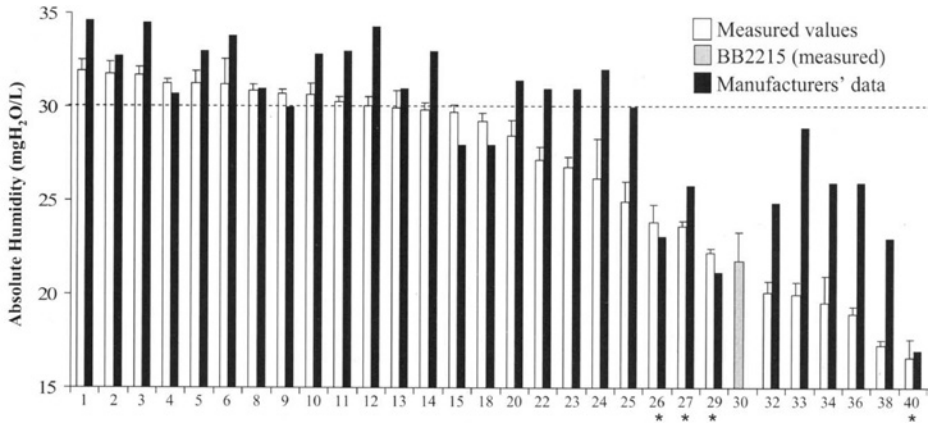

Fig. 39.7 Inspired absolute humidity values obtained using the bench test apparatus compared with manufacturer data when available (29 devices). Results of the hydrophobic heat and moisture exchange Pall BB2215 are also displayed. The asterisks indicate the devices that are proposed as antimicrobial filters. (From Lellouche F, Taillé S, Lefrançois F, et al: Humidification performance of 48 Passive Airway Humidifiers: comparison with manufacturer data, *Chest* 135(2): 276–286, 2009.)

yielding water from evaporation. In passive mode, it produced AH 28.9 ± 0.9 mg H_2O/L in vitro during normothermic conditions and 30.7 ± 1.6 mg H_2O in vivo. In active mode, AH ranged from 30 to 36 mg H_2O/L, independent of minute ventilation and expiratory AH without loss of efficiency after 12 hours, reaching a steady state of temperature and humidity after only 15 minutes of use (Fig. 39.7). Although active heat moisture exchangers can increase the temperature and AH of the inspired gases compared to the commonly used heat moisture exchangers, the use of active heat moisture exchangers should be restricted in patients with variable minute ventilation or in presence of thickened secretions or hypothermia (Fig. 39.8).

RULE OF THUMB

HME units should be replaced if secretions have contaminated the filter and/or if flow resistance has increased, causing an increase in the WOB.

Heated Humidifiers

Heat improves the water output of humidifiers. Heated humidifiers are used to increase the heat and water content of inspired gas for patients with bypassed upper airways and those receiving noninvasive mechanical ventilatory support.[12] Humidifier heating systems generally have a controller that regulates the power to the heating element by monitoring it, which matches a preset or adjustable temperature. They also may use a thermistor placed at the outlet of the humidifier, with a heater set to control output temperature. Servo-controlled heating systems monitor the temperature at the humidifier's outlet and at the patient's airway using a thermistor probe. The controller adjusts the heater power to reach the desired airway temperature and incorporates alarms and an alarm-activated heater shutdown function.[13]

An electrical heating element provides the needed energy. Five types of heating elements are common: (1) a hotplate element at the base of the humidifier; (2) a wraparound type that surrounds the humidifier chamber; (3) a yoke, or collar, element that sits between the water reservoir and the gas outlet; (4) an immersion-type heater, with the element placed in the water reservoir; (5) a heated wire in the inspiratory limb warming a saturated wick or hollow fiber; and (6) a thin-film high-surface-area broiler.

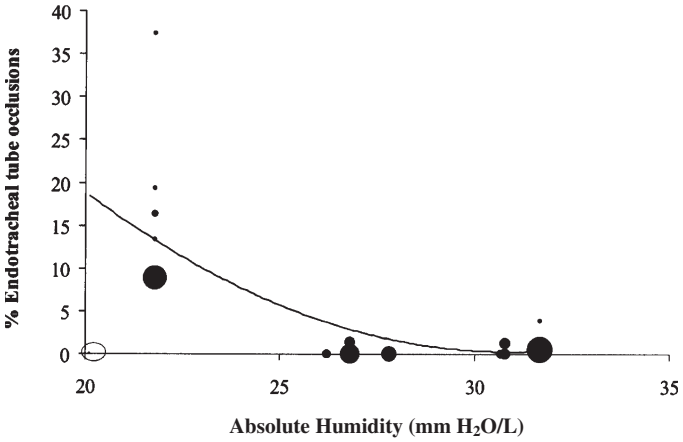

Fig. 39.8 Reported incidence of airway occlusion *(circles)* correlated with absolute humidity determined from in vitro testing of the same heat and moisture exchangers (HME units). A hydrophobic HME unit that delivered an absolute humidity of 21.8 ± 1.5 mg H_2O/L in the bench study was associated with high rates of endotracheal tube occlusion in five published studies. (From Lellouche F, Taillé S, Lefrançois F, et al: Humidification performance of 48 Passive Airway Humidifiers: comparison with manufacturer data, *Chest* 135(2):276–286, 2009.)

Humidifier heating systems have a controller that regulates the element's electrical power. In the simplest systems, the controller monitors the heating element, varying the delivered current to match either a preset or an adjustable temperature. In these systems, the temperature of the patient's airway has no effect on the controller. Conversely, a **servo-controlled heating system** monitors temperature at or near the patient's airway using a thermistor probe. The controller adjusts heater power to achieve the desired airway temperature. Systems usually have alarms and alarm-activated heater shutdown. Box 39.5 outlines key features of modern heated humidification systems.

BOX 39.5 Key Features of Heated Humidification Systems

- Gas temperature delivered to the patient should not be greater than 40°C. When temperatures greater than 40°C are reached, audible and visual alarms should indicate an overly high temperature condition and interrupt power to the heater.
- Audible and visual alarms should indicate when remote temperature sensors are disconnected, absent, or defective, and power to the heater should be interrupted to prevent overheating.
- Temperature overshoot should be minimized. Overshoot can occur when servo-controlled units warm up without flow through the circuit, when the temperature probe is not inserted in the circuit (or becomes dislodged), or when flow changes during normal operation. Non–servo-controlled units can overshoot when temperature controls are set too high or when gas flow is abruptly reduced.
- Indicators for delivered gas temperature should be accurate to ±3°C of the indicated value.
- Humidifier temperature output should not vary more than 2°C from the set value (proximal to the patient).
- Warmup time should not exceed 15 min.
- The water level should be readily visible in either the humidifier or the remote reservoir.
- Humidifiers should be able to withstand ventilation pressures greater than 100 cm H_2O.
- Internal compliance should be low and stable so that changes in the water level do not significantly alter the delivered tidal volume.
- The exposed surface of a humidifier should not be too hot to touch during operation. Readily accessible surfaces should not be warmer than 37.5°C. A warning label is needed for hotter surfaces.
- Operator, or feed, systems must not be able to overfill the humidifier to the point that water can block gas flow through the humidifier or ventilator circuit. Humidifiers should not be damaged by spilled fluids.
- Electromagnetic interference from other devices should not affect humidifier performance. The unit should not be damaged by 95–135 volts.
- Fuses or circuit breakers should be clearly labeled and easily reset or replaced. The unit should have adequate overcurrent protection to prevent ventilator shutdown or loss of power to other equipment on the same branch circuit because of internal equipment failures.
- It should be impossible to assemble the unit in a way that would be hazardous to the patient. The direction of gas flow should be indicated on interchangeable components, for which proper direction is essential.
- The humidifier should be assembled and filled in a manner that minimizes the introduction of infectious materials or foreign objects.
- Service and operation manuals should be provided with the humidifier and should cover all aspects of its use and service.

Modified from Emergency Care Research Institute: Heated humidifiers, Health Devices. 1987. http://www.fda.gov/oc/po/firmrecalls/Vapotherm2000i_01_06.html. Accessed March 2, 2011.

RULE OF THUMB

Place heated humidifier thermistor probes in the inspiratory limb of a ventilator circuit far enough from the patient's Y adaptor to ensure that warm exhaled gas does not fool the controller system. Never place a thermistor probe in an isolette or a radiant warmer, where the probe is warmed externally and the humidifier is fooled into shutting down, reducing the humidity available to the patient.

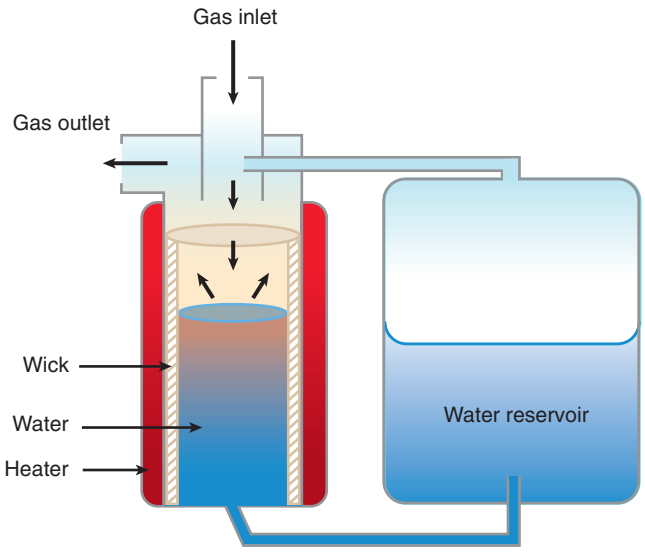

Fig. 39.9 Schematic of the Concha-Column wick-type humidifier with a level-compensated reservoir feed system (Hudson RCI, Temecula, CA). (Modified from Fink J, Cohen N: Humidity and aerosols. In Eubank D, Bone R, editors: *Principles and applications of cardiorespiratory care equipment*, St. Louis, 1994, Mosby.)

Reservoir and Feed Systems

Heated humidifiers operating continuously in breathing circuits can evaporate more than 1 L of water per day. An ideal reservoir or feed system should be safe, dependable, easy to set up, and allow continuity of therapy, even when the reservoir is being replenished.

Manual systems. Simple large-reservoir systems are manually refilled (with sterile or distilled water). If a manual system is used, momentary interruption of humidifier operation and mechanical ventilation is required for refilling. Because the system must be "opened" for refilling, cross contamination can occur. Water levels in manually filled systems are constantly changing, and changes in the humidifier fill volume alter the gas compression factor and the delivered volume during mechanical ventilation.

A small inlet that can be attached to a gravity-fed intravenous bag and line allows refilling without interruption of ventilation. Such systems still require constant checking and manual replenishment by opening the line valve or clamp. If not checked regularly, the reservoir in these systems can go dry, placing the patient at considerable risk.

Automatic systems. Automatic feed systems avoid the need for constant checking and manual refilling. The simplest type of automatic feed system is the level-compensated reservoir (Fig. 39.9). In these systems, an external reservoir is aligned horizontally with the humidifier, maintaining relatively consistent water levels between the reservoir and the humidifier chamber.

With flotation-type systems (Fig. 39.10), a float rises and falls with the water level. As the water level falls below a preset value, the float opens the feed valve; as the water rises back to the set fill level, the float closes the feed valve. Alternatively, optical sensors can be used to sense water level, driving a solenoid valve to allow refilling of the humidifier reservoir.

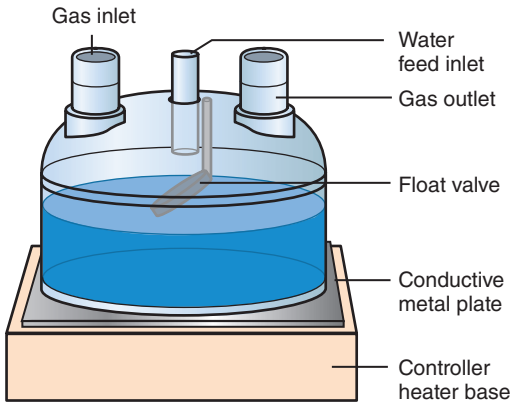

Fig. 39.10 Schematic of a pass-over heated humidifier with water autofeed valve and heater base.

MINI CLINI

Selecting the Appropriate Therapy to Condition a Patient's Inspired Gas: Hypothermia

Problem

A survivor of near drowning has just been intubated and placed on mechanical ventilatory support. Her body temperature is 31°C and her minute ventilation is high. What would be the appropriate humidification system to recommend for this patient?

Solution

Normally, patients without chronic obstructive pulmonary disease supported by mechanical ventilation can be started with an HME unit unless its use is contraindicated. Using an HME unit with this patient is contraindicated because (1) she is hypothermic and (2) she has a high minute ventilation. Based on this assessment, the best choice is a heated humidifier, preferably with servo-controlled airway temperature. A gas temperature above 41°C may lead to a potential thermal injury to the patient; high-temperature alarms protect the patient from thermal injury.

Membrane-type humidifiers require no water-feed control system because the liquid water chamber feeding the membrane cannot overfill, so only an open gravity feed system is required. The Vapotherm humidifier (Vapotherm, Stevensville, MD; Fig. 39.11) utilizes a membrane cartridge system whereby blended gas passes through the lumens of hundreds of parallel hollow fibers made of a polymer that allows molecules of heated water surrounding the fibers to pass to the air within the fibers with no direct contact with the water. The warmed humidified gas enters the center of a triple-lumen heated delivery tube, where it is surrounded by two outer lumens circulating warmed water to maintain the temperature of the inner lumen and minimize rain-out. There are separate cartridges for infants (delivering up to 8L/min) and children/adults (delivering up to 5 to 40 L/min) with a temperature range from 33°C to 43°C.

RULE OF THUMB

Humidification of inspired gas is critical for mechanically ventilated patients with ETTs or tracheostomy tubes. During noninvasive ventilation (NIV), active humidification is suggested to improve patient comfort.

Setting Humidification Levels

The American National Standards Institute (ANSI) recommends *minimum* levels of humidity for intubated patients (>30 mg/L). However, optimum humidity targets the temperature and humidity for normal conditions at the point that the gas is entering the airway. For example, the humidity of air entering the carina is typically 37 to 40 mg/L. When humidifiers run too cold (<32°C), humidity can be reduced to the point of increased airway plugging. Not all active heated humidifiers perform the same under all conditions. Previous research emphasizes the need to set humidifiers to maintain airway temperatures between 35°C and 37°C.

Controversy exists regarding the appropriate temperature and humidity of inspired gas delivered to mechanically ventilated patients with artificial airways. The current clinical practice guideline of the American Association for Respiratory Care (AARC) recommends 33°C, within 2°C, with a minimum of 30 mg/L of water vapor.[1] In a comprehensive review, Williams[45] suggested that inspired humidity be maintained at an optimal level, 37°C with 100% RH and 44 mg/L, to minimize mucosal dysfunction. Theoretically, optimal humidity offers improved mucociliary clearance. The benefits of this strategy are based on theory and have yet to be demonstrated conclusively in the clinical setting. Further controlled studies are needed to better support the need for optimal humidity.

MINI CLINI

Selecting the Appropriate Therapy to Condition a Patient's Inspired Gas: Noninvasive High Gas Flow

Problem

A patient is prescribed to receive high-flow oxygen at greater than 30 L/min via face mask. What temperature would be most comfortable for the patient?

Solution

Gas applied to an intact upper airway, whether via mask or nasal cannula, should be conditioned to normal ambient temperature and RH. Normal room temperature at 50% to 55% RH approximates an AH of 20 mg/L. However, patients receiving high-flow gas for extended periods may complain of airway dryness and discomfort. However, patients receiving gas with an AH of 40 mg/L also complain of discomfort (too warm or claustrophobic). An AH of 30 mg/L has been reported to be more comfortable.

MINI CLINI

When Is Sterile Water Essential?

Problem

Sterile water is back ordered. Your department is running low and there is not enough to support all of the humidifiers in use, but your hospital does have an unlimited supply of distilled water.

Solution

Pass-over, wick, and membrane humidifiers produce water vapor, or molecules, that are too small to carry bacteria, so distilled water would be fine for those humidifiers. In contrast, bubbling and jet humidifiers produce aerosols that *can* carry bacteria, so sterile water should be used in those.

Caution: Tap water should not be used with any humidifier, as chemicals used in public water supplies may vaporize and irritate patients' airways.

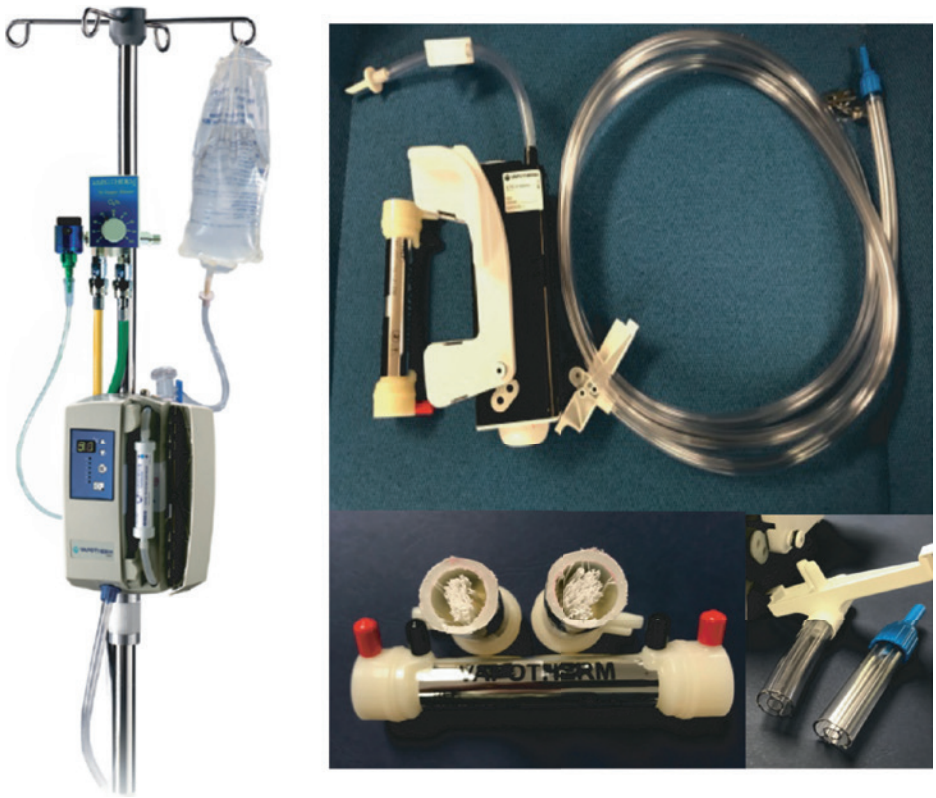

Fig. 39.11 Example of a membrane humidifier—Vapotherm humidifier with cartridge. Single-patient disposable circuit with heating block, cartridge, and circuit. Cartridge and cross section showing bundle of fibers that carry blended gas and space between the fibers where warm water heats and humidifies the gas in the fibers. Cross section of circuit with triple lumen. The central lumen carries heated humidified gas; the other two lumens carry warm water, increasing thermal mass of circuit and reducing condensate formation. (Left, Courtesy of Vaportherm.)

Problem Solving and Troubleshooting

Common problems with humidification systems include condensation, avoiding cross contamination, and ensuring proper conditioning of the inspired gas.

Condensation

In standard heated humidifier systems, saturated gas cools as it leaves the point of humidification and passes through the delivery tubing en route to the patient. As gas cools, water vapor capacity decreases, resulting in condensation or "rain out." Factors influencing the amount of condensation include (1) the temperature difference across the system (humidifier to airway); (2) the ambient temperature; (3) the gas flow; (4) the set airway temperature; and (5) the length, diameter, and thermal mass of the breathing circuit.

Fig. 39.12 illustrates the condensation process. Because cooling occurs as gas transits the circuit, the humidifier is set to a higher temperature (50°C) than desired at the airway. At 50°C, saturated gas has an AH level of 84 mg/L of water. As cooling occurs along the tubing, the capacity of the gas to hold water vapor decreases as temperature decreases to 37°C, holding only 44 mg/L of water vapor. Although BTPS conditions have been achieved at 40 mg/L, half the total output of the humidifier (84 mg/L to 44 mg/L = 40 mg/L) condenses in the inspiratory limb of the circuit.

This condensation poses risks to patients and caregivers and can waste a lot of water. Condensation can disrupt or occlude gas flow through the circuit, potentially altering ventilator function. Because condensate can enter the patient's airway and be aspirated, circuits must be positioned to drain condensate away from the patient and checked often, with condensate drained from breathing circuits regularly.

Patients contaminate ventilator circuits within hours; thus condensate colonized with bacteria poses a risk for infection.[45] Health care personnel should treat all breathing circuit condensate as infectious waste. See Chapter 4 for more detail on control procedures used with breathing circuits, including the AARC's Clinical Practice Guideline on changing ventilator circuits.

RULE OF THUMB

Always treat breathing circuit condensate as infectious waste. Use standard precautions, including wearing gloves and goggles. Always drain the tubing away from the patient's airway into an infectious waste container and dispose of the waste according to the policies and procedures of the institution.

A common method to minimize problems with condensate is to place water traps at low points in the circuit (both the inspiratory and expiratory limbs of ventilator circuits) to collect

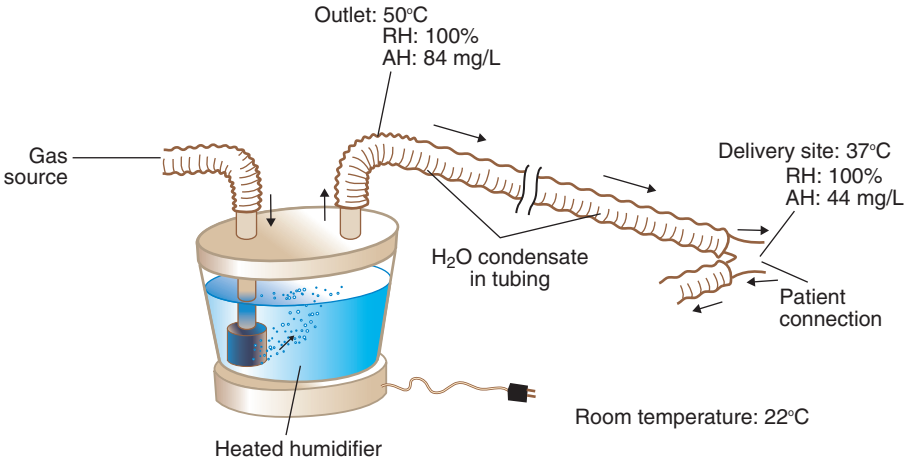

Fig. 39.12 Gas leaving a standard bubbling heated humidifier is cooled en route to the patient. Although the gas remains saturated (100% relative humidity *[RH]*), cooling reduces its water vapor capacity and condensation forms. Almost half of the original water (500 mL/d) is lost to condensation. The temperature at the patient connection (37°C) shown here is for illustrative purposes only. Heated humidifiers should be set to deliver inspired gas at 35°C ± 2°C. *AH,* absolute humidity.

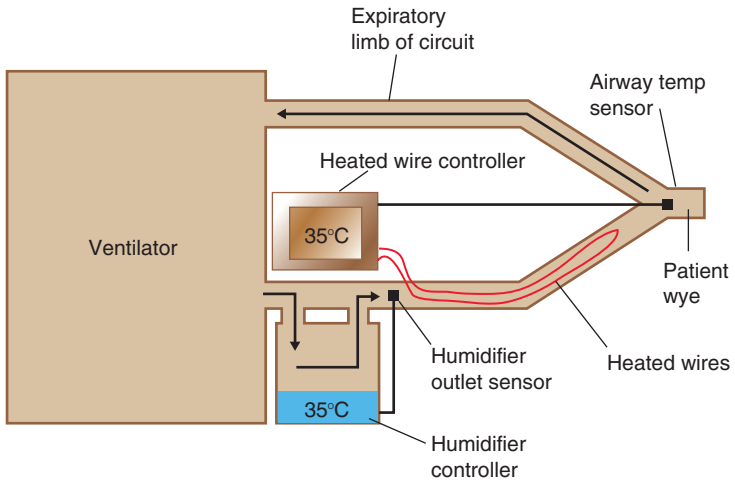

Fig. 39.13 Heated-wire humidifier system. The dual sensor system keeps the temperature constant throughout the inspiratory limb of the ventilator circuit, minimizing condensation. Cooling of exhaled gas in the expiratory limb can cause condensation unless it also is heated.

condensate and reduce the likelihood of gas flow obstruction. Water traps should have little effect on circuit compliance, allow emptying without disrupting ventilation, and not be prone to leakage.

A nebulizer, with a medication reservoir positioned below the ventilator circuit, can act as a "water trap," collecting contaminated condensate. This creates a risk that contaminated aerosols can be generated and pathogens delivered to deep into the lung. To minimize this risk, nebulizers should be placed in a superior position so that any condensate travels downstream from the nebulizer. In addition, nebulizers should be rinsed and air dried, washed and sterilized, or disposed of and replaced between treatments.

One way to avoid condensation problems is to prevent condensation from forming. Because the decrease in temperature in gas traveling from the humidifier to the airway causes condensation, maintenance of heat in the circuit can prevent the formation of condensate. Several methods, such as insulation or increasing the thermal mass of the circuit, can reduce circuit cooling by keeping the circuit at a constant temperature. The most common approach uses wire heating elements that are inserted into the ventilator circuit.

Most heated-wire circuits use dual controllers with two temperature sensors: one monitoring the temperature of gas leaving the humidifier and the other placed at or near the patient's airway (Fig. 39.13). The controller regulates the temperature difference between humidifier output and patient airway. When heated-wire circuits are used, the humidifier heats gas to a lower temperature (32°C to 40°C) than with conventional circuits (45°C to 50°C). Reduction in condensate in the tubing results in less water use, reduced need for drainage, and less infection risk for patients and health care workers.

RULE OF THUMB

Heated humidifiers should be set to deliver an inspired gas temperature of 34°C or greater but less than 41°C at the inspiratory limb near the Y adaptor during invasive mechanical ventilation. Gas temperatures in patients receiving NIV should be selected based on patient comfort, tolerance, adherence, and the underlying pulmonary condition.

Unwanted levels of condensate can still occur with heated wires. Absorptive material in the inspiratory limb of the ventilator circuit acts as a wick warmed by the heated wire system (Fisher & Paykel Healthcare, Irvine, CA).

Use of heated-wire circuits in neonates is complicated by incubators and radiant warmers.[46] Incubators provide a warm environment surrounding the infant and radiant warmers use radiant energy to warm objects that intercept radiant light. In both cases, a temperature probe placed in the heated environment would affect humidifier performance, resulting in reduced humidity received by the patient. Fig. 39.14 shows the impact of temperature probe placement, in or out of the incubator, on AH delivered to the neonate. Consequently temperature probes should always be placed outside of the radiant field or incubator (Fig. 39.15).

Cross Contamination

Aerosol and condensate from ventilator circuits are known sources of bacterial colonization.[45] However, advances in both circuit and humidifier technology have reduced the risk for nosocomial

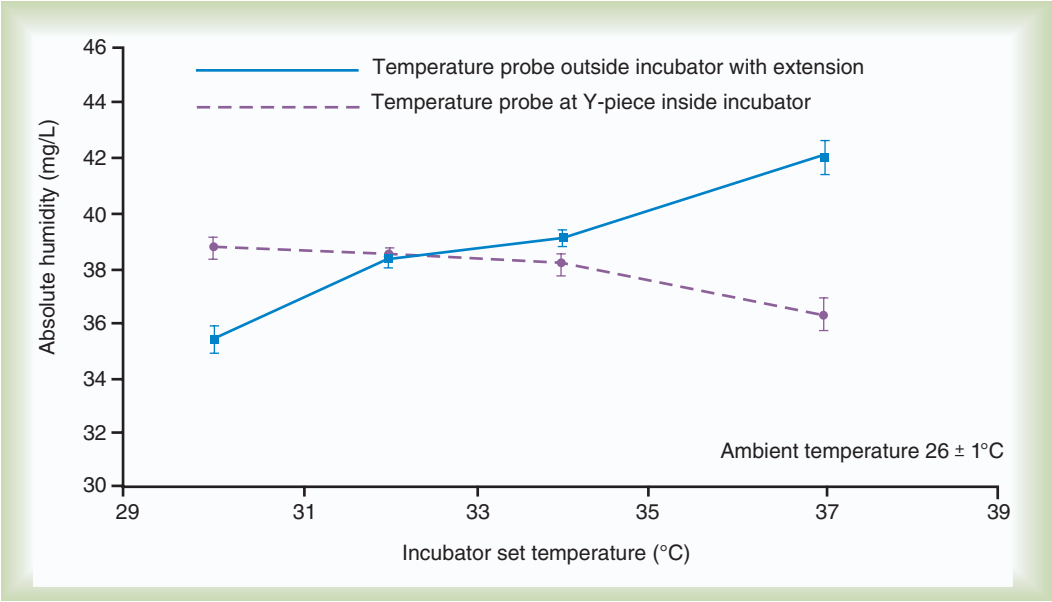

Fig. 39.14 Humidity achieved at the Y piece of a neonatal humidification system when used inside an incubator *(dotted line)* and outside or under an incubator *(solid line)*.

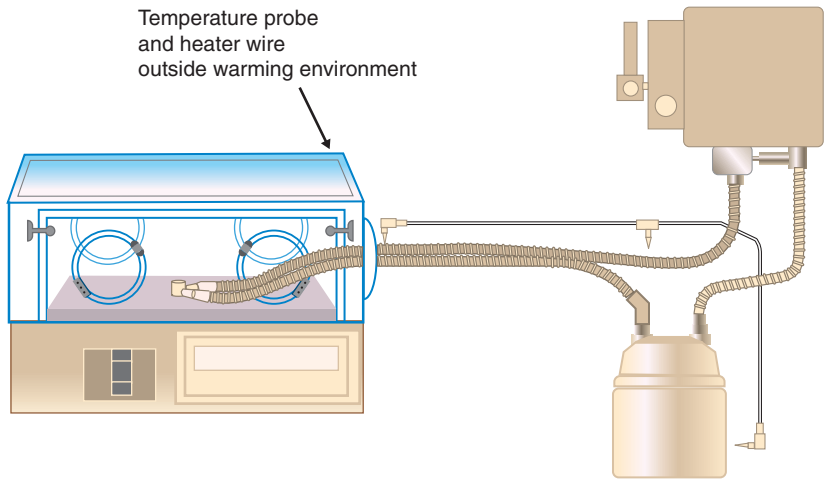

Fig. 39.15 Neonatal breathing circuit configuration used with an incubator, with the temperature probe placed outside of the warming environment and an unheated portion of the inspiratory circuit delivering the gases to the Y piece.

infection when these systems are used. Wick-type or membrane-type pass-over humidifiers prevent the formation of bacteria-carrying aerosols. Heated-wire circuits reduce the production and pooling of condensate within the circuit. In addition, the high reservoir temperatures in humidifiers tend to be bactericidal. In ventilator circuits using wick-type humidifiers with heated wire systems, circuit contamination usually occurs from the patient to the circuit rather than vice versa.

For decades, the traditional way to minimize the risk for circuit-related nosocomial infection in critically ill patients receiving ventilatory support was to change the ventilator tubing and its attached components daily. It is now known that such frequent changes increase the risk for nosocomial pneumonia.[47] There is minimal risk for VAP with weekly circuit changes, and there may be no need to change circuits at all unless they are visibly soiled. In addition, substantial cost savings can accrue with fewer circuit changes.

Proper Conditioning of Inspired Gas

All respiratory therapists (RTs) are trained to measure patient inspired FiO_2 levels regularly and, in ventilatory care, to monitor selected pressures, volumes, and flows. However, few clinicians take the steps needed to ensure proper conditioning of the gas to be inspired by the patients.

The most accurate and reliable way to ensure that patients are receiving gas at the expected temperature and humidity level is to measure these parameters. Portable battery-operated digital **hygrometers**, which measure temperature and RH, are available for less than $300 and are invaluable in ensuring proper conditioning of the inspired gas. When high-humidity environments are being assessed, hygrometers become saturated and nonresponsive over time and so should be used for spot checks only.

Many heated wire humidification systems have a humidity control. This control does not reflect either AH or RH but only the temperature differential between the humidifier and the airway sensor. If the heated wires are set warmer than the humidifier, less RH will be delivered to the patient. To ensure that the inspired gas is being properly conditioned, clinicians should always adjust the temperature differential to the point at which a few drops of condensation form near the patient connection, or "wye." Lacking direct measurement of humidity, observing this minimal condensate is the most reliable indicator that the gas is fully saturated at the specified temperature. If condensate cannot be seen, there is no way of knowing the level of RH without direct measurement—it could be anywhere between 99% and 0%. An HME unit's performance can be evaluated in a similar manner.[48]

RULE OF THUMB

You can estimate whether an HME unit is performing well at the bedside by visually confirming condensation in the flex tube or HME housing between the device and the patient's airway. Lack of condensate may be a clue that humidification is inadequate and that an alternative system may be more appropriate for use with the patient. This can be applied to heated humidifiers as well.

BLAND AEROSOL THERAPY

Humidity is simply water in the gas phase, whereas a bland aerosol consists of liquid particles suspended in a gas (see Chapter 40 for details on aerosol physics). Bland aerosol therapy involves the delivery of sterile water or hypotonic, isotonic, or hypertonic saline aerosols. Bland aerosol administration may be accompanied by O_2 therapy.[49]

Equipment

The equipment needed for bland aerosol therapy includes an aerosol generator and a delivery system. Devices used to generate bland aerosols include large-volume jet nebulizers and **ultrasonic nebulizers** (USNs). Delivery systems include various direct airway appliances and enclosures (mist tents).

Aerosol Generators

Large-volume jet nebulizers. A large-volume jet nebulizer is the most common device used to generate bland aerosols. As depicted in Fig. 39.16, these devices are pneumatically powered, attaching directly to a flowmeter and compressed gas source. Liquid particle aerosols are generated by passing gas at a high velocity through a small "jet" orifice. The resulting low pressure at the jet draws fluid from the reservoir up to the top of a siphon tube, where it is sheared off and shattered into liquid particles. The large unstable particles fall out of suspension or hit on the internal surfaces of the device, including the fluid surface; these act as **baffles** (surfaces that affect aerosol by removing large particles from suspension). The remaining small particles leave the nebulizer carried in the gas stream through the outlet port.

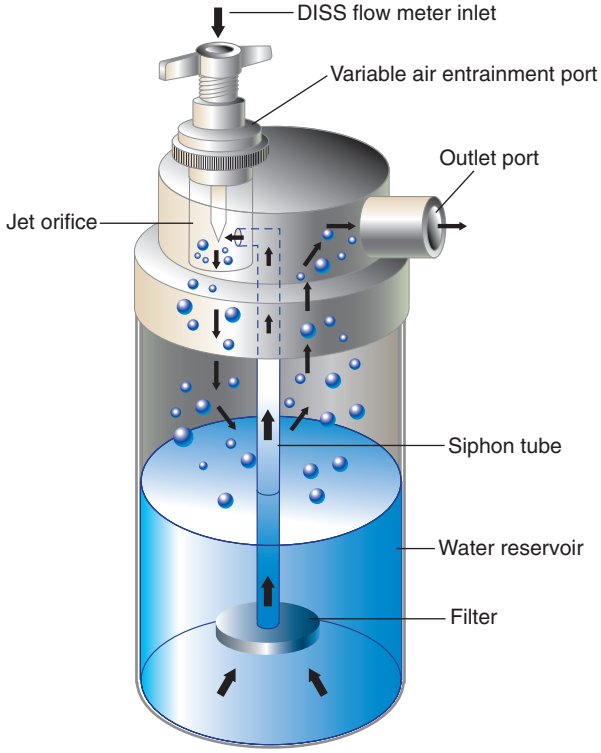

Fig. 39.16 All-Purpose Large-Volume Jet Nebulizer.

A variable air-entrainment port allows air mixing to increase flow rates and to alter FiO_2 levels (see Chapter 42).

If heat is required, as in the case of humidifiers, a hot plate, wraparound, yoke collar, or immersion element can be added (Fig. 39.17). These devices rarely have sophisticated servo-controlled systems to control delivery temperature. They may not shut down when the reservoir empties, resulting in the delivery of hot, dry gas to the patient. Failure of the heating element can also cause a loss of heating capacity without warning to the clinician.

Depending on the design, input flow, and air-entrainment setting, the total water output of unheated large-volume jet nebulizers varies between 26 and 35 mg H_2O/L. When heated, output increases to between 33 and 55 mg H_2O/L, mainly because of increased vapor capacity. Larger versions of these devices (with reservoirs holding 2 to 3 L of water) are used to deliver bland aerosols into mist tents. These enclosure systems can generate flow rates greater than 20 L/min, with water outputs of 5 mL/min (300 mL/h). Because heat buildup in enclosures is a problem, these systems are always run unheated.

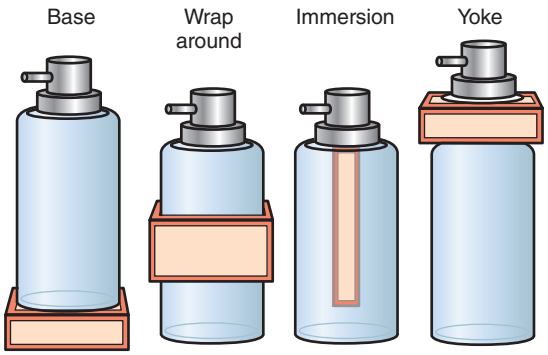

Fig. 39.17 Methods used to heat jet and bubble humidifiers with placement of electrical heating elements.

Ultrasonic nebulizers. A USN is an electrically powered device that uses a **piezoelectric crystal** to generate an aerosol. This crystal transducer converts radio waves into high-frequency mechanical vibrations (sound), which are transmitted to a liquid surface. There the intense mechanical energy creates a cavitation in the liquid, forming a standing wave, or "geyser," that sheds aerosol droplets. Fig. 39.18 is a schematic view of a large-volume USN. Output from a radiofrequency generator is transmitted over a shielded cable to the piezoelectric crystal. Vibrational energy is transmitted either indirectly through a water-filled couplant reservoir or directly to a solution chamber. Gas entering the chamber inlet picks up the aerosol particles and exits through the chamber outlet.

The properties of the ultrasonic signal determine the characteristics of the aerosol generated by these nebulizers. The frequency at which the crystal vibrates, preset by the manufacturer, determines the size of the aerosol particles. Particle size is inversely proportional to signal frequency. A USN operating at a frequency of 2.25 MHz may produce an aerosol with a mass median aerodynamic diameter (MMAD) of approximately 2.5 µm, whereas another nebulizer operating at 1.25 MHz produces an aerosol with MMAD between 4 and 6 µm. Signal amplitude directly affects the amount of aerosol produced; the greater the amplitude, the greater the volume of aerosol output. In contrast to frequency, signal amplitude can be adjusted by the clinician.

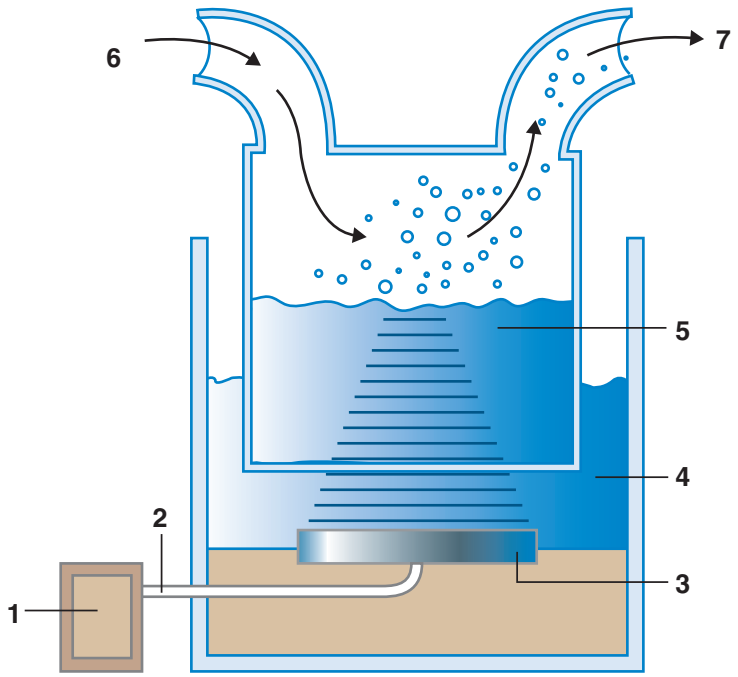

Fig. 39.18 Functional schematic of a typical large-volume ultrasonic nebulizer. *1,* Radiofrequency generator; *2,* shielded cable; *3,* piezoelectric crystal transducer; *4,* water-filled couplant reservoir; *5,* solution chamber; *6,* chamber inlet; and *7,* chamber outlet. (Modified from Barnes TA: *Core textbook for respiratory care practice*, ed 2, St. Louis, 1994, Mosby.)

Particle size and aerosol density delivered to the patient are also affected by the source and flow of gas through the aerosol-generating chamber. Some large-volume USNs have built-in fans that direct room air through the solution chamber conducting the aerosol to the patient. The airflow may be adjusted by changing the fan speed or using a simple damper valve. Alternatively, compressed anhydrous gases can be delivered to the chamber inlet through a flowmeter. For precise control over delivered O_2 concentrations, clinicians can attach a flowmeter with an O_2 blender or air-entrainment system to the chamber inlet.

The flow and amplitude settings interact to determine aerosol density (mg/L) and total water output (mL/min). Amplitude affects water output. At a given amplitude setting, the greater the flow through the chamber, the less the density of the aerosol. Conversely, low flows result in aerosols of higher density. Total aerosol output (mL/min) is greatest when both flow and amplitude are set at the maximum. With these settings, some units can achieve total water outputs of 7 mL/min.

Particle size, aerosol density, and output are also affected by the RH of the carrier gas (see Chapter 40). In contrast to jet nebulizers, the temperature of the solution placed in a USN increases up to 10°C during use. Although this increase in temperature affects water vapor capacity, its impact on aerosol output is minimal.

RULE OF THUMB

To produce a high-density aerosol using a USN (useful for sputum induction), set the amplitude high and the flow rate low. To maximize aerosol delivery per minute (in trying to help mobilize secretions), set the flow rate to match and slightly exceed the patient's inspiratory flow rate and set the amplitude at the maximum.

Although USNs have some unique capabilities, their relative advantages over jet nebulizers in most cases of bland aerosol administration are outweighed by their high cost and erratic reliability. Exceptions include the use of a USN for sputum induction, where the high output (1 to 5 mL/min) and aerosol density seem to yield sputum specimens of higher quantity and quality, although at some cost in increased airway reactivity.[50,51] Although a major manufacturer of USNs (DeVilbiss, Scottsdale, AZ) has discontinued this product line, other companies in both the United States and Europe still manufacture USNs for clinical use.

Commercially available USNs (usually marketed as "cool-mist" devices) have found a place in the home, being used as room humidifiers. As with any nebulizer, the reservoirs of these devices can easily become contaminated, resulting in the airborne transmission of pathogens. Care should be taken to ensure that these units are cleaned according to the manufacturer's recommendations and that water is discarded from the reservoir periodically between cleanings. In the absence of a manufacturer's recommendation, these units should undergo appropriate disinfection at least once daily. Generally, pass-over and wick-type humidifiers present less risk than USNs as room humidifiers.

Airway Appliances

Airway appliances used to deliver bland aerosol therapy include the aerosol mask, face tent, T tube, and tracheostomy mask (Fig. 39.19). The aerosol mask and face tent are used for patients with intact upper airways. The T tube is used for patients who are orally or nasally intubated or have a tracheostomy. The tracheostomy mask is used only for patients who have a tracheostomy. In all cases, large-bore tubing is required to minimize flow resistance and prevent occlusion by condensate.

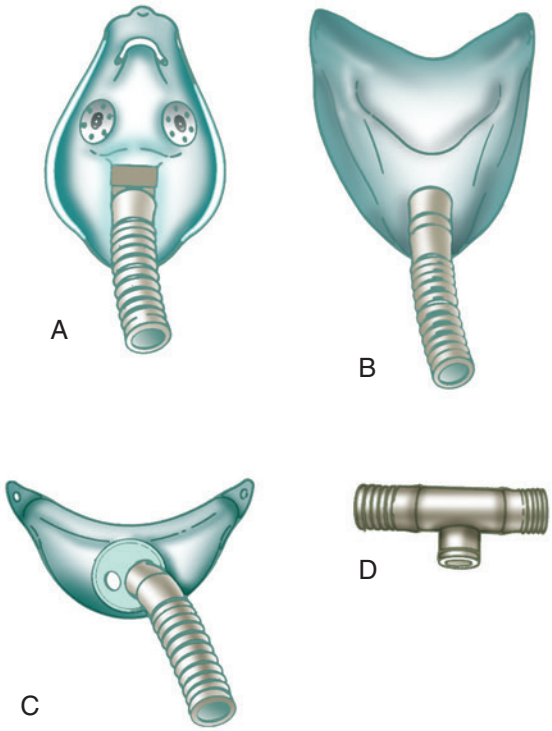

Fig. 39.19 Airway Appliances Used to Deliver Bland Aerosol Therapy. *A,* Aerosol mask. *B,* Face tent. *C,* Tracheostomy mask. *D,* T tube.

For short-term therapy to patients with intact upper airways, the aerosol mask is the device of choice. However, some patients cannot tolerate masks and may do better with a face tent. No data support preferential use of an open aerosol mask versus a face tent.

Although the T tube is the most common application for tracheostomy patients, a tracheostomy mask is a better choice unless moderate to high FiO_2 levels are needed. In contrast to T tubes, tracheostomy masks exert no traction on the airway and allow secretions and condensate to escape from the airway, thus reducing airway resistance.

Enclosures (Mist Tents and Hoods)

Infants and small children may not readily tolerate direct airway appliances such as masks, so enclosures such as mist tents and aerosol hoods are used to deliver bland aerosol therapy to these patients. More recent studies have shown that aerosol hoods can provide aerosol delivery with efficiency similar to that of a properly fitted aerosol mask in infants, and with less patient discomfort.[52]

Mist tents were used for more than 40 years mainly to treat croup and thus were called *croup tents*. The cool aerosol provided through these enclosures promotes vasoconstriction, decreases edema, and reduces airway obstruction.

All body enclosures pose two problems: carbon dioxide (CO_2) buildup and heat retention. CO_2 buildup can be reduced by providing sufficiently high gas flow rates. These high flows of fresh gas circulate continually through the enclosure and "wash out" CO_2 while helping to maintain the desired O_2 concentrations. Heat retention may be handled with high fresh gas flows to prevent heat buildup or use of a separate cooling device such as a simple ice compartment to cool the aerosol.[53,54] The Ohmeda Ohio Pediatric Aerosol Tent (Ohmeda Ohio, Gurnee, IL) and other similar units use electrically powered refrigeration units to cool the circulating air.

The cooling produces a great deal of condensation, which must be drained into a collection bottle outside of the tent. Units such as the Mistogen CAM-3M (Mercury Medical, Clearwater, FL) have overcome some of these problems with a thermoelectric cooling system in which an electrical current passing through a semiconductor augments heat absorption and release. As warm air is taken from the tent, heat is transferred and released into the room, and cool air is returned to the tent.

Problem Solving and Troubleshooting

The most common problems with bland aerosol delivery systems are cross contamination and infection, environmental safety, inadequate mist production, overhydration, bronchospasm, and noise.

Cross Contamination

Rigorous adherence to the infection control guidelines detailed in Chapter 4, especially guidelines covering solutions and equipment processing, should help to minimize the cross contamination and infection risks involved in using these systems. In addition, the water should be changed regularly, and the couplant compartments and nebulizer chambers of USNs should be disinfected or replaced regularly.

Environmental Exposure

Environmental safety issues from secondhand and exhaled aerosol arise mainly when aerosol therapy is prescribed for immunosuppressed patients or for patients with tuberculosis. A survey suggested that RTs may be at increased risk for developing asthma-like symptoms attributed partly to secondhand exposure to aerosols such as ribavirin or albuterol.[55] To minimize problems in this area, all clinicians should strictly follow the standards and airborne precautions published by the US Centers for Disease Control and Prevention, including precautions specified for the control of exposure to tuberculosis (see Chapter 4). Additional methods for dealing with the environmental control of drug aerosols are described in Chapter 40.

Inadequate Aerosol Output

Inadequate mist production is a common problem with all nebulizer systems. With pneumatically powered jet nebulizers, poor mist production can be caused by inadequate input flow of driving gas, siphon tube obstruction, or jet orifice misalignment. With the exception of inadequate driving gas flow, these problems require unit repair or replacement. If a USN is not functioning properly, the electrical power supply (cord, plug, and fuse or circuit breakers) should be checked first. The clinician next should check to confirm that (1) carrier gas is flowing through the device and (2) the amplitude, or output, control is set above minimum. If there is still no visible mist output, the clinician should inspect the couplant chamber to confirm proper fill level and the absence of any visible dirt or debris. Finally, the clinician must ensure that the couplant chamber solution meets the manufacturer's specifications (most units do not function properly with distilled water).

Overhydration

Overhydration is a problem with the continuous use of heated jet nebulizers and USNs. With USNs capable of such extraordinarily high water outputs, they should never be used for continuous therapy. The risk for overhydration is highest for infants, small children, and patients with preexisting fluid or electrolyte imbalances. Even if used only to meet BTPS conditions, bland aerosol therapy effectively eliminates insensible water loss through the lungs and should be equated to a daily water gain (approximately 200 mL/d for an average adult). In addition to overhydration of the patient, inspissated pulmonary secretions can swell after high-density aerosol therapy, thus worsening airway obstruction. Careful patient selection and monitoring can prevent most potential problems with overhydration. Box 39.6 lists variables that should be recorded during the inspection and monitoring of humidification devices.

Bronchospasm

Bland water aerosols are irritating and can cause bronchospasm in some patients. Ultrasonic nebulization of distilled water is used in some pulmonary function laboratories to provoke bronchospasm and assess bronchial hyperactivity.[56] The patient's history and diagnosis should always be carefully reviewed before any bland aerosol, especially a hypotonic water solution, is administered. Patients receiving continuous bland aerosol therapy should initially be monitored carefully (including breath sounds and subjective responses) and reevaluated every 8 hours or with any change in clinical condition.[57] If bronchospasm occurs during therapy, treatment must be stopped immediately, O_2 provided, and appropriate bronchodilator therapy initiated as soon as possible. If the physician still requests bland aerosol therapy, pretreatment with a bronchodilator may be needed. Isotonic solutions (0.9% saline) instead of water may be better tolerated by these patients.

A problem unique to large-volume air-entrainment jet nebulizers is the noise they generate, especially at high flows. The American Academy of Pediatrics recommends that sound levels remain below 58 dB to avoid hearing loss in infants being cared for in incubators with O_2 hoods. Because many commercial nebulizers exceed this noise level, careful selection of equipment is necessary. However, the best way to avoid this problem and minimize infection risks further is to use heated pass-over humidification instead of nebulization.

SELECTING THE APPROPRIATE THERAPY

Fig. 39.20 provides a basic algorithm for selecting or recommending the appropriate therapy to condition a patient's inspired

BOX 39.6 Sputum-Induction Procedure

- Gather the necessary equipment: Ultrasonic nebulizer, aerosol mask, large-bore tubing, specimen container, 3% sterile saline, and stethoscope.
- Check the chart for order or protocol, diagnosis, history, and other pertinent information.
- Wash your hands and follow applicable standard, airborne, and tuberculosis precautions.
- Introduce yourself and identify your department, verify the patient's identity, and explain the procedure and verify that the patient understands it.
- Have the patient assume an upright, seated position if possible.
- Have the patient rinse his or her mouth with water, blow his or her nose, and clear any excess saliva.
- Perform pretreatment assessment, including vital signs, muscle tone, ability to cough, and auscultation.
- Assemble the nebulizer, fill the couplant chamber with tap water, plug the unit into a grounded electrical outlet, and attach the delivery tubing and mask.
- Aseptically fill the medication chamber of the nebulizer with 3% sterile saline.
- Turn the unit on and adjust the output control to achieve adequate flow and high density.
- Place the mask comfortably on the patient's face and instruct the patient to take slow, deep breaths, with an occasional inspiratory hold as tolerated.
- Periodically reassess the patient's condition (including breath sounds) throughout the application.
- Modify the technique and reinstruct the patient as needed based on his or her response.
- Terminate the treatment after 15–30 min, if significant adverse reactions occur, or when a sputum specimen has been obtained.
- Encourage the patient to cough and expectorate sputum into a specimen cup; observe for volume, color, consistency, odor, and the presence or absence of blood.
- Label the specimen container with patient identification and other required information and deliver it to the appropriate personnel.
- Chart the therapy according to departmental and institutional protocol.
- Notify the appropriate personnel of any adverse reactions or other concerns.

Modified from Butler TJ: *Laboratory exercises for competency in respiratory care*, ed 2, Philadelphia, 2009, FA Davis.

gas. Key considerations include (1) gas flow, (2) presence or absence of an artificial tracheal airway, (3) character of the pulmonary secretions, (4) need for and expected duration of mechanical ventilation, and (5) contraindications to using an HME unit.

Regarding delivery of O_2 to the upper airway, the American College of Chest Physicians advises against using a bubble humidifier at flow O_2 rates of 4 L/min or less because the entrained ambient gas provides sufficient humidity.[48] As O_2 flow increases, inhaled humidity decreases. For the occasional patient who complains of nasal dryness or irritation when he or she is receiving low-flow O_2, a humidifier should be added to the delivery system. Conversely, the relative inefficiency of unheated bubble humidifiers means that the clinician may have to consider heated humidification for patients receiving long-term O_2 at higher flow rates (>10 L/min without air entrainment).

HME units provide an inexpensive alternative to heated humidifiers when used for ventilation of patients who do not have complex humidification needs. However, passive HME units may not provide sufficient heat or humidification for long-term management of certain patients. When an HME unit is to be used, it should be selected based on the individual patient's needs and ventilatory pattern and the unit's performance, efficiency, and size. All patients using HME units should be reevaluated regularly to confirm the appropriateness of continued use.

RULE OF THUMB

HME units are better suited for short-term use and during transport, whereas heated humidifiers should be used for patients requiring long-term mechanical ventilation (>96 h) or for patients for whom the use of an HME unit is contraindicated.

MINI CLINI

Heat and Moisture Exchange Versus Heated Humidifier and Ventilator Outcomes

Problem

Do HME units reduce the incidence of ventilator-associated infections?

Solution

As HME units became more common in the ICU, some studies reported a lower incidence of infections associated with their use among hospital care workers than those associated with HHs. Comprehensive reviews and meta-analysis report no significant differences in the use of HHs and HME units on the incidence of VAP, ventilator days, days of ICU stay, and overall mortality rate. It was concluded that there is insufficient evidence to recommend the use of HME units for the prevention of hospital-acquired infections.

The following table compares illustrative costs associated with three humidification strategies in terms of circuit setup costs, water usage, and labor for a typical patient requiring 12 days of mechanical ventilation at a large acute-care hospital. Labor costs were calculated as the time required to perform setup or maintenance multiplied by the average salary. This example assumes no circuit changes for a patient over 14 days and that the HME unit is changed daily.

Components of Circuit Setup and Operating Costs	Heated Humidifier With Standard Circuit	Heated Humidifier With Heated-Wire Circuit	Heat Moisture Exchanger
Vent circuit	$3.00	$11.00	$3.00
Humidifier/water feed system	$12.00	$12.00	—
HME unit filter	—	—	$5.00
Setup cost (labor)	$18.00	$23.00	$8.00
Daily cost (labor)	$11.00	$1.50	$5.00
Total costs (5 days)	$62.00	$29.00	$28.00
Total costs (12 days)	$139.00	$39.50	$63.00

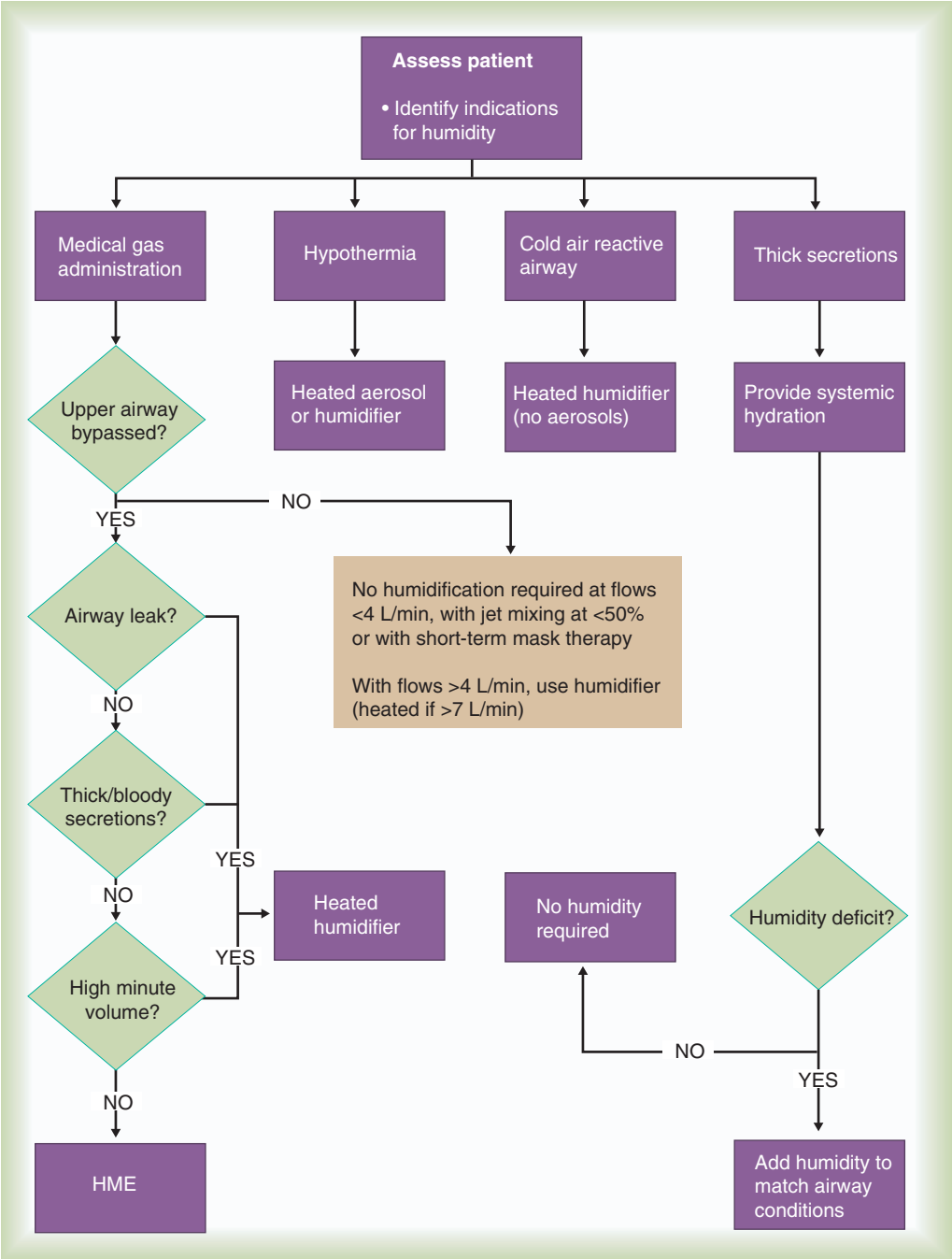

Fig. 39.20 Selection Algorithm for Humidity and Bland Aerosol Therapy. *HME,* Heat and moisture exchanger.

In this example, the standard circuit costs less than the heated-wire circuit but has twice the daily water usage, with an additional labor cost of $9.50 per day for adding and removing water from the system. The HME unit has the lowest setup cost, but after ventilator day 5, the total cost of daily filter replacement exceeds the cost associated with operation of the heated-wire circuit. However, most modern ventilator humidification systems require the purchase of their prepackaged water. This can markedly increase the cost of both unheated and heated-wire circuits. Although different component costs may shift the analysis, in general, there is no significant cost difference associated with the use of an HME, unheated-wire, and heated-wire systems. The final decision is generally based on the patient's clinical needs.

Mechanical Ventilation

Consideration of humidification device selection is patient specific. Reducing dead space with the use of a HH decreases $PaCO_2$; more importantly, if isocapnic conditions are maintained by

reducing tidal volume (V_T), this strategy improves respiratory system compliance as well as plateau airway pressure.

With heated humidity, maintaining temperature at one point in the inspiratory circuit (e.g., the Y piece), does not ensure adequate delivery of water vapor. Other factors (humidification system, expired minute volume [VE], gradient setting) are critical. At a given temperature, humidification may be significantly higher or lower than expected. Higher AH has been correlated to increased secretion volume, suggesting optimization of mucocilliary transport. This would support using a HH for patients with inspissated secretions.

Noninvasive Ventilation

NIV is often applied with a single-limb circuit with a fixed leak between the gas source and the patient's airway, typically with a mask interface. Analysis of the need for humidification during noninvasive mask ventilation (NIMV) should take into account the following parameters: air leaks, NIV interface, mechanical ventilator type, room temperature, inhaled gas temperatures and chamber vaporization, airflow and inlet pressure of the humidification system, and humidification system type. In addition, histopathologic changes in the nasal mucosa during NIV without a humidification system dictates that humidification should be considered even when short-term NIV use is expected.

The question becomes which to use: an HME or a HH during NIV? The increased dead space of an HME can affect ventilatory function and gas exchange negatively. The effect of the HME's dead space may decrease the efficiency of NIV in patients with autorespiratory failure (ARF).

When the use of HME units was randomly compared with that of HHs, minute ventilation was higher with HME units than with HHs despite similar PaCOs. The use of HME units was associated with a greater increase in WOB and other indexes of patient effort. NIV with an HME unit failed to decrease WOB compared with baseline. The addition of PEEP reduced the level of effort, but similar differences between the HME unit and HH were observed.[58] Use of an HME unit decreased CO_2 elimination during NIV despite increased minute ventilation, especially in hypercapnic subjects.[59-61] However, a multicenter randomized controlled trial reported no differences in intubation rates from NIV with HME units versus HHs (Fig. 39.21).[60]

The AH delivered to an oronasal mask during NIV is affected by gas flow and the amount of leak; moreover, it varies among patients at equivalent humidifier settings.[56] With a HH, the presence of condensate in the mask was associated with improved oral moistness and patient comfort. AH varied among the subjects, and some complained of oral dryness even with a HH. Oral breathing decreased oral moistness and worsened the feeling of dryness.[55]

High-Flow Nasal Oxygen

High-flow nasal oxygen (HFNC) use has been described in infants as well as in pediatric and adult patients. The need for heated humidity is even clearer than with NIV, as the high flow is directed into the nares, and use of an HME would not be practical. Use of heated high-flow gas in children has been reported to be more comfortable than MNIV or standard unheated nasal cannula.[62]

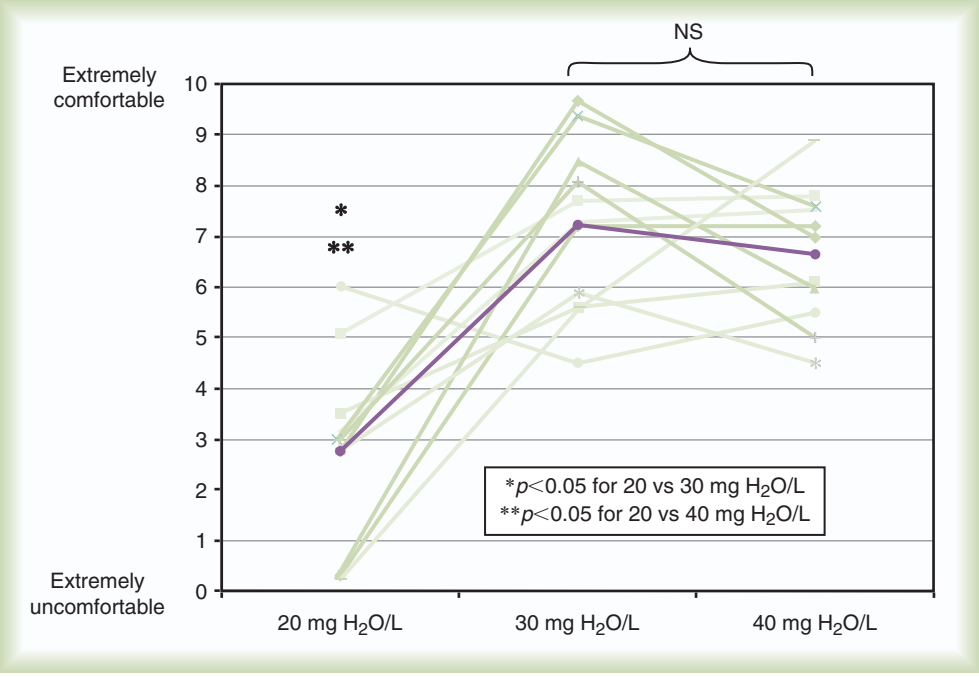

Fig. 39.21 Comfort levels with the administration of heated humidified noninvasive high-flow gas vary with absolute humidity. *NS,* Not significant. (Redrawn from Lellouche F, Bouchard PA: Hygrometry of gas delivered with different high flow oxygen humidifiers and impact on comfort of the level of hygrometry, *Intensive Care Med Exp* 3(Suppl 1):A805, 2015.)

In contrast, use of dry air has been reported to cause flow-dependent cooling of the brain in porcine models simulating adult conditions. The mechanism of cooling appears to be evaporation of nasal mucus as cooling is mitigated by humidifying the air at flows as low as 40 L/min.

Sputum Induction

As a diagnostic procedure, sputum induction (see Box 39.6) warrants separate attention from other modes of bland aerosol therapy. Sputum induction is a useful, cost-effective, and safe method for diagnosing tuberculosis, pneumocystis pneumonia (caused by *Pneumocystis jirovecii,* formerly *Pneumocystis carinii*), and lung cancer.[50,51]

The success rate of sputum induction and analysis is about 80%. Sputum induction involves short-term application of high-density hypertonic saline (3% to 10%) aerosols to the airway to help mobilize pulmonary secretions for evacuation and recovery. These high-density aerosols are often made using ultrasonic nebulization. Box 39.7 outlines a procedure for sputum induction using a 3% saline solution.[56]

To ensure a good sputum sample, every effort must be made to identify saliva from true respiratory tract secretions. Some protocols have patients brush their teeth and tongue surface thoroughly and rinse their mouths before sputum induction. Although the distinction between saliva and sputum can be made in the diagnostic laboratory, care during the collection procedure reduces the need for repeat inductions.

BOX 39.7 Monitoring

The humidifier should be inspected during the patient–ventilator system check and condensate should be removed from the circuit as needed. HMEs should be inspected and replaced if secretions have contaminated the insert or filter. The following should be recorded during equipment inspection:

- *Humidifier settings*: During routine use on an intubated patient, a HH should be set to deliver inspired gas at 34°C or greater but less than 41°C at the Y adapter in the circuit and should provide a minimum of 33 mg/L of water vapor.
- *Inspired gas temperature*: This should be monitored at or near the patient's airway opening (HH).
- *Location of probe:* For heated-wire circuits used with infants, the probe must be placed outside the incubator or away from the radiant warmer.
- *Temperature:* The high-temperature alarm should be set no higher than 41°C, and the low-temperature alarm should be set no lower than 2°C below the desired temperature at the circuit Y piece.
- *Water level and feed system:* Water level and function of automatic feed system (if applicable) should be monitored.
- *Quantity and consistency of secretions:* Quantity, consistency, and other characteristics of secretions should be noted and recorded., If secretions become copious or appear increasingly tenacious while an HME unit is being used, an HH should replace the unit.
- *Airway obstruction:* The presence of copious secretions increases the resistance of airflow through the HME unit. This may even increase peak pressures and induce changes of the flow waveforms consistent with those observed with airway obstruction. If these changes persist after changing the HME unit because of copious secretions, an HH should be used instead.

HH, Heated humidifier; *HME,* heat and moisture exchanger.

SUMMARY CHECKLIST

- Conditioning of inhaled and exhaled gas is accomplished primarily by the nose and upper airway. Bypassing the upper airway without providing similar levels of heat and humidity to inhaled gas can cause damage to the respiratory tract.
- Gases delivered to the nose and mouth should be conditioned to 20°C to 22°C with 10 mg/L water vapor (50% relative humidity).
- When being delivered to the trachea, gases should be warmed and humidified to 35°C to 40°C with 40 to 45 mg/L water vapor (>90% relative humidity).
- A humidifier is a device that adds invisible molecular water to gas.
- A nebulizer generates and disperses liquid particles in a gas stream.
- Water vapor cannot carry pathogens, but aerosols and condensate can do so.
- Temperature is the most important factor affecting humidifier output. The higher the temperature, the greater the water vapor content of the delivered gas.
- Bubble humidifiers, pass-over humidifiers, wick humidifiers, and HME units are the major types of humidifiers. Active humidifiers incorporate heating devices and reservoir and feed systems.
- At high flow rates, some bubble humidifiers can produce microaerosol particles, which can carry infectious bacteria.
- Most HME units are passive, capturing both heat and moisture from expired gas and returning it to the patient at approximately 70% efficiency. HME are not recommended for use with infants because of the increased mechanical dead space and use of uncuffed ETTs, which allow some exhaled gas to bypass the HME.
- HME are also not recommended for use in patients requiring lung-protective ventilation strategies because of the small tidal volume and increased levels of hypercapnia.
- Common problems with humidification systems include condensation, cross contamination, and ensuring proper conditioning of the inspired gas.
- Breathing circuit condensate must always be treated as infectious waste.
- Bland aerosol therapy with sterile water or saline is used to (1) treat upper airway edema, (2) overcome heat and humidity deficits in patients with tracheal airways, and (3) help obtain sputum specimens.
- Large-volume jet nebulizers and USNs are used to generate bland aerosols. Delivery systems include various direct airway appliances and mist tents.
- Common problems with bland aerosol therapy are cross contamination and infection, environmental safety, inadequate mist production, overhydration, bronchospasm, and noise.

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40

Aerosol Drug Therapy

James B. Fink and Arzu Ari

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Define the term *aerosol*.
- Describe how particle size, motion, and airway characteristics affect aerosol deposition.
- Describe how aerosols are generated.
- List the hazards associated with aerosol drug therapy.
- Describe how to select the best aerosol drug delivery system for a patient.
- Describe how to initiate and modify aerosol drug therapy.
- State the information patients need to know to self-administer drug aerosol therapy properly.
- Describe how to assess patient response to bronchodilator therapy at the point of care.
- Describe how to apply aerosol therapy in special circumstances.
- Describe how to protect patients and caregivers from exposure to aerosolized drugs.

CHAPTER OUTLINE

KEY TERMS

aerosol
aerosol output
aging
atomizer
baffle
breath-actuated nebulizer
breath-enhanced nebulizer
brownian diffusion
chlorofluorocarbons (CFCs)
deposition
emitted dose
fine-particle fraction
geometric standard deviation (GSD)
heterodisperse
hydrofluoroalkane (HFA)
hygroscopic
inertial impaction
inhaled mass
mass median aerodynamic diameter (MMAD)
monodisperse
nebulizer
propellant
residual drug volume
respirable mass
scintigraphy
sedimentation
therapeutic index
volume median diameter (VMD)

An **aerosol** is a suspension of solid or liquid particles in gas. Aerosols occur in nature as pollens, spores, dust, smoke, smog, fog, and mist. The upper airway and respiratory tract filter out larger particles to protect the lungs from invasion by these aerosols. In the clinical setting, medical aerosols are generated with **atomizers**, **nebulizers**, and inhalers. An atomizer convert liquid into droplets. Early atomizers were used for perfumes and later medical aerosol on a limited basis, using low volume gas pumps to draw liquid from a reservoir and disperse relatively large particles as individual puffs. Nebulizers produce finer aerosol particles from liquid-based formulations over greater periods of time using compressed gas (often with baffles) or electricity. Inhalers generate aerosolized medication from liquids or dry powders for a single inhalation. Aerosols can be used to deliver bland water solutions to the respiratory tract (see Chapter 39) or to administer drugs to the lungs, throat, or nose for local and systemic effect. This chapter focuses on the principles of medical aerosol drug therapy.

The aim of aerosol therapy is to deliver a therapeutic dose of the selected drugs to the desired site of action such as nose, throat, airways, or deep lung. The indication for any specific aerosol is based on the need for the specific drug.[1] Administration of drugs by aerosol offers higher local drug concentrations in the lung with lower systemic levels compared with other forms of administration. Improved therapeutic action with fewer systemic side effects provides a higher **therapeutic index** (TI).[2] A drug's TI identifies the margin of safety of the drug and is a ratio between the effective therapeutic dose (emergency department [ED]) and the toxic dose (TD) in 50% of humans. TI = TD50/ED50.

CHARACTERISTICS OF THERAPEUTIC AEROSOLS

Effective use of medical aerosols requires an understanding of the characteristics of aerosols and their effect on drug delivery to the desired site of action. Key concepts include aerosol output, particle size, deposition, and changes in the aerosol over time.

Aerosol Output

Aerosol output is the mass of fluid or drug produced by an aerosol generator per actuation or unit of time. Output varies greatly among different nebulizers and inhalers. For drug delivery systems, **emitted dose** describes the mass of drug exiting the mouthpiece of a nebulizer or inhaler as aerosol.

Aerosol output can be measured by collecting the aerosol that leaves the nebulizer on filters and measuring either their weight (gravimetric analysis) or quantity of drug (assay). Gravimetric measurement of aerosols is easier but less reliable than drug assay techniques because weight changes with water evaporation, whereas drug mass does not. A drug assay provides the most reliable measure of aerosol output.

A large proportion of particles that leave a nebulizer may never reach the lungs. The ability of aerosols to travel through the air, enter the airways, and become deposited in the lungs is based on many variables ranging from particle size to breathing pattern. Understanding and skillful manipulation of these variables can greatly improve pulmonary delivery of aerosols.

Particle Size

Aerosol particle size depends on the substance for nebulization, the method used to generate the aerosol, and the environmental conditions surrounding the particle.[3,4] It is impossible to determine visually whether a nebulizer is producing an optimal particle size. The unaided human eye cannot see particles less than 50 to 100 μm in diameter (equivalent to a small grain of sand). The only reliable way to determine the characteristics of an aerosol suspension is laboratory measurement. The two most common laboratory methods used to measure medical aerosol particle size distribution are cascade impaction and laser diffraction.[4] *Cascade impactors* are designed to collect aerosols of different size ranges on a series of stages or plates. The mass of aerosol deposited on each plate is quantified by drug assay, and a distribution of drug mass across particle sizes is calculated. In *laser diffraction,* a computer is used to estimate the range and frequency of droplet volumes crossing the laser beam.

Because medical aerosols contain particles of many different sizes (**heterodisperse**), the average particle size is expressed with a measure of central tendency, such as **mass median aerodynamic diameter (MMAD)** for cascade impaction or **volume median diameter (VMD)** for laser diffraction. These measurement techniques of the same aerosol may report different sizes, so it is important to know which measurement is used. The MMAD and VMD both describe the particle diameter in micrometers (μm). In an aerosol distribution with a specific MMAD, 50% of the particles are smaller and have less mass, and 50% are larger and have greater mass.

The **geometric standard deviation (GSD)** describes the variability of particle sizes in an aerosol distribution set at 1 standard deviation above or below the median (15.8% and 84.13%, respectively). Most aerosols found in nature and used in respiratory care are composed of particles of different sizes, described as heterodisperse. The greater the GSD, the wider the range of particle sizes and the more heterodisperse is the aerosol. Aerosols consisting of particles of similar size (GSD ≤1.2) are referred to as **monodisperse**. Nebulizers that produce monodisperse aerosols are used mainly in laboratory research and in nonmedical industries.

Deposition

When aerosol particles leave suspension in gas, they deposit on (attach to) a surface. Only a portion of the aerosol generated and emitted from a nebulizer (emitted dose) may be inhaled (inhaled dose). A fraction of the inhaled dose is deposited in the lungs (respirable dose). **Inhaled mass** is the amount of drug inhaled. The proportion of the drug mass in particles that are small enough **(fine-particle fraction)** to reach the lower respiratory tract is the **respirable mass**. Not all aerosol particles delivered to the lung are retained or deposited. A small percentage (1% to 5%) of inhaled drug may be exhaled. Whether aerosol particles that are inhaled into the lung are deposited in the respiratory tract depends on the size, shape, and motion of the particles and on the physical characteristics of the airways and breathing pattern. Key mechanisms of aerosol **deposition**

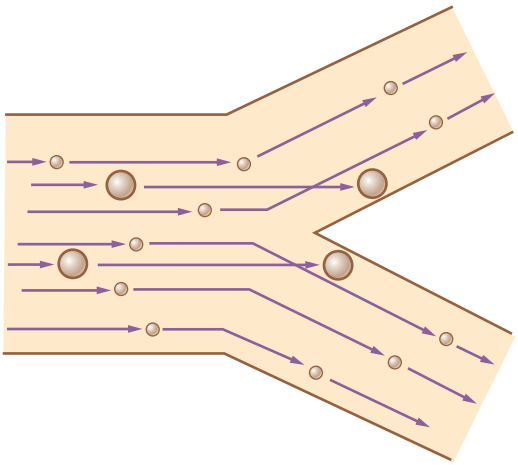


Fig. 40.1 Inertial impaction of large particles, the masses of which tend to maintain their motion in straight lines. As airway direction changes, the particles are deposited on nearby walls. Smaller particles are carried around corners by the airstream and fall out less readily.

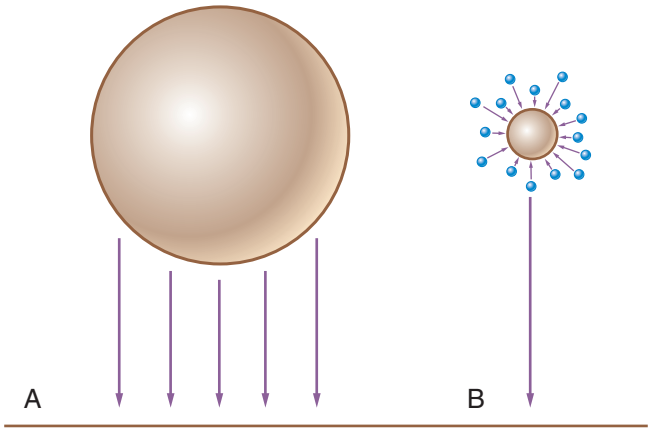


Fig. 40.2 Effect of Mass on Particle Size. Large particles (A) are more susceptible to the force of gravity than smaller particles (B), which are more affected by the bombardment of molecules deposited by diffusion.

include inertial impaction, gravimetric sedimentation, and **brownian diffusion**.[3,5]

Inertial Impaction

Inertial impaction occurs when suspended particles in motion collide with and are deposited on a surface; this is the primary deposition mechanism for particles larger than 5 µm. The greater the mass and velocity of a moving object, the greater its inertia and the greater the tendency of that object to continue moving along its set path (Fig. 40.1). When a particle of sufficient (large) mass is moving in a gas stream and that stream changes direction, the particle tends to remain on its initial path and collide with the airway surface.

Because inertia involves both mass and velocity, the higher the flow of a gas stream, the greater the tendency for particles to impact and be deposited in the airways. Turbulent flow patterns, obstructed or tortuous pathways, and inspiratory flow rates greater than 30 L/min are associated with increased inertial impaction. Turbulent flow and convoluted passageways in the nose cause most particles larger than 10 µm to impact and become deposited. This process produces an effective filter that protects the lower airway from particulates such as dust and pollen. However, particles 5 to 10 µm tend to become deposited in the oropharynx and hypopharynx, especially with the turbulence created by the transition of air as it passes around the tongue and into the larynx.

Sedimentation

Sedimentation occurs when aerosol particles settle out of suspension and are deposited owing to gravity. The greater the mass of the particle, the faster it settles (Fig. 40.2). During normal breathing, sedimentation is the primary mechanism for deposition of particles 1 to 5 µm. Sedimentation occurs mostly in the central airways and increases with time, affecting particles 1 µm in diameter. Breath holding after inhalation of an aerosol increases the residence time for the particles in the lung and enhances distribution across the lungs and sedimentation.

Diffusion

Brownian diffusion is the primary mechanism for deposition of small particles (<3 µm), mainly in the respiratory region, where bulk gas flow ceases and most aerosol particles reach the alveoli by diffusion. These aerosol particles have very low mass and are easily bounced around by collisions with carrier gas molecules. These random molecular collisions cause some particles to contact and become deposited on surrounding surfaces. Particles of size 1 to 0.5 µm are so stable that most remain in suspension and are cleared with the exhaled gas, whereas particles smaller than 0.5 µm have a greater retention rate in the lungs.

RULE OF THUMB Aerosol particle size ranging from 1 to 0.5 µm is so stable that most remain in suspension and may be cleared with the exhaled gas, whereas particles smaller than 0.5 µm have a greater retention rate in the lungs.

Fig. 40.3 summarizes the relationships between particle size and aerosol deposition in the respiratory tract. The depth of penetration and deposition of a particle in the respiratory tract tend to vary with size and tidal volume (V_T).[5] With this knowledge, it may be possible to target aerosol deposition to specific areas of the lung by using the proper particle size and breathing pattern.

RULE OF THUMB The site of deposition in the respiratory tract varies with the size of the particle. Use of nebulizers that produce particles in a specific size range improves the targeting of aerosols for deposition to a desired site in the respiratory tract, as follows:

Desired Location	Recommended MMAD
Upper airway: nose, larynx, trachea	5 to >50 µm
Lower airways	2–5 µm
Parenchyma: alveolar region	1–3 µm
Parenchyma	<0.1 µm

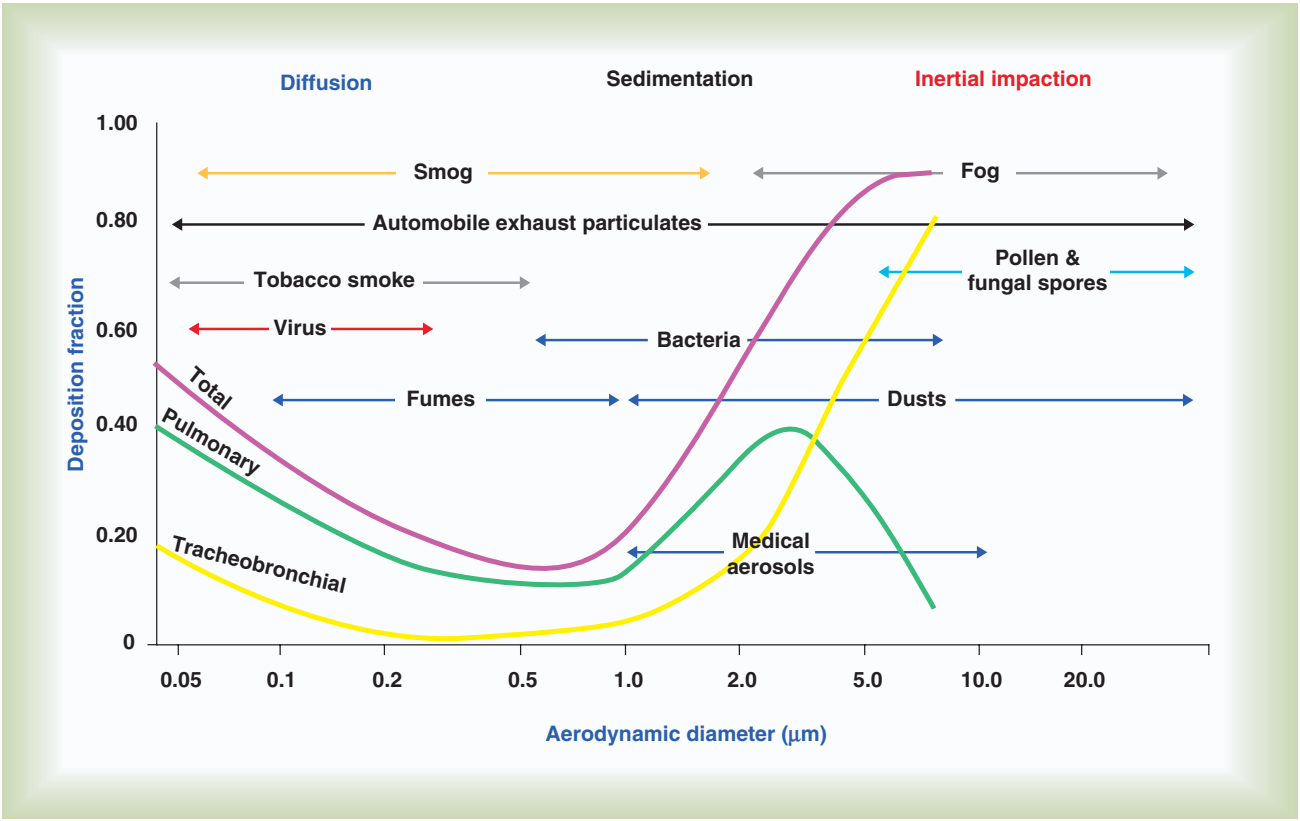


Fig. 40.3 Range of particle size for common aerosols in the environment and the influence of inertial impactions, sedimentation, and diffusion.

Aging

Aerosols are dynamic suspensions. Individual particles constantly grow, shrink, coalesce, and fall out of suspension. The process by which an aerosol suspension changes over time is called **aging**. How an aerosol ages depends on the composition of the aerosol, the initial size of its particles, the time in suspension, and the ambient conditions to which it is exposed.

Aerosol particles can change size as a result of either evaporation or **hygroscopic** water absorption. The relative rate of particle size change is inversely proportional to the size of a particle, so small particles grow or shrink faster than large particles. Small water-based particles shrink when exposed to relatively dry gas. Aerosols of water-soluble materials, especially salts, tend to be hygroscopic, absorbing water and growing when introduced into a high-humidity environment.[5]

Particle size is not the only determinant of deposition. Inspiratory flow rate, flow pattern, respiratory rate, inhaled volume, ratio of inspiratory time to expiratory time (I:E ratio), and breath holding all influence where a particle of any specific size is deposited. The presence of airway obstruction is one of the greatest factors influencing aerosol deposition. It has been shown that total pulmonary deposition is greater in smokers and patients with obstructive airway disease than in healthy persons (Fig. 40.4). Similarly, when inspiratory flow rates are constant, the deposition fraction of monodisperse aerosols increases with increased V_T, length of inspiration, and particle size.

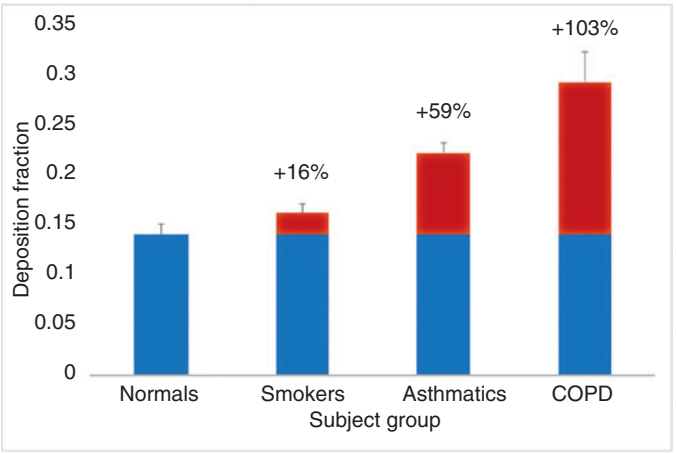


Fig. 40.4 Total lung deposition of a fine aerosol of particles 1 μm in diameter in healthy adults and in subjects with obstructive airway disease. The *red bars* indicate the percentage increase greater than normal value. *COPD,* Patients with chronic obstructive pulmonary disease.

These dynamic variables make it difficult to intuitively predict exactly what occurs to aerosol particles when they enter a gas stream and are inhaled. For this reason, prediction of actual aerosol deposition for an individual patient requires extensive computational analysis and testing.

Quantifying Aerosol Delivery

As mentioned in the preceding sections, many characteristics of aerosols can account for the variances in quantity of aerosolized medication delivered to the patient. Although the precise amount of drug delivered to the patient's airways can be difficult to determine, it can be measured in terms of the patient's clinical response to aerosol drug therapy, including the desired therapeutic effects and any unwanted adverse effects. The amount of aerosol deposited to a patient's airways can be quantified using specialized equipment and tests.

One approach used to quantify aerosol deposition involves **scintigraphy**, in which a drug is "tagged" with a radioactive substance (e.g., technetium), aerosolized, and inhaled. A scanner like those used in nuclear medicine counts the radiation distribution and intensity across the patient's head and thorax and the aerosol device. The result is a map of aerosol deposition in the upper airway, the stomach, and the lungs and device. Radiation counts are used to calculate the percentage of drug retained by the device and delivered to various areas in the patient.[6-8]

A less direct approach relates the systemic pharmacokinetic profile of a drug delivered by aerosol to an assay of the drug in a patient's blood or urine over time. This method does not directly estimate lung delivery but provides insight into systemic drug levels achieved after aerosol administration. Care must be taken to differentiate drug absorbed through the lungs from drug absorbed through the gastrointestinal tract. Simple laboratory bench, or in vitro, models, which simulate a range of V_T values, inspiratory flow rates, I:E ratios, and respiratory rates, have been useful in predicting inhaled mass of drug and relative performance of nebulizers.[9,10]

HAZARDS OF AEROSOL THERAPY

The primary hazard of aerosol drug therapy is an adverse reaction to the medication being administered (see Chapter 36). Other hazards to the patient include infection, airway reactivity, systemic effects of bland aerosols, drug concentration, and eye irritation. Care providers and bystanders risk these hazards as a result of exposure to secondhand aerosol drugs.

Infection

Aerosol generators can contribute to nosocomial infections by spreading bacteria by the airborne route.[11] The most common sources of bacteria are patient secretions, contaminated solutions (i.e., multiple-dose drug vials), and caregivers' hands. Various procedures can help to reduce contamination and infection associated with respiratory care equipment. Guidelines from the U.S. Centers for Disease Control and Prevention (CDC) state that nebulizers should be sterilized between patients, frequently replaced with disinfected or sterile units, or rinsed with sterile water (not tap water) and air dried between treatments (see Chapter 4). In addition, some recommend one nebulizer for one treatment. The Cystic Fibrosis Foundation recommends that standard small volume nebulizers (SVNs) should be discarded after each treatment to prevent infection in cystic fibrosis patients.

RULE OF THUMB Jet and ultrasonic nebulizers with medication reservoir open to the connection to the patient are susceptible to contamination. Therefore, they should be rinsed with sterile water and air dried between treatments. Tap water should not be used to clean jet nebulizers.

Airway Reactivity

Cold air and high-density aerosols can cause reactive bronchospasm and increased airway resistance, especially in patients with preexisting respiratory disease.[12] Medications such as acetylcysteine, antibiotics, steroids, ribavirin, and distilled water have been associated with increased airway resistance and wheezing during aerosol therapy. Administration of bronchodilators before or with administration of these agents may reduce the risk or duration of increased airway resistance.

The risk of inducing bronchospasm always should be considered when aerosols are administered. Monitoring for reactive bronchospasm should include auscultation for adventitious breath sounds; observation of the patient's breathing pattern before and after therapy; and most importantly, communication with the patient during therapy to determine the perceived work of breathing.

Pulmonary and Systemic Effects

Pulmonary and systemic effects are associated with the site of delivery and the drug being administered. Preliminary assessment should balance the need versus the risk of aerosol therapy, especially among patients at high risk, such as infants, patients who are prone to fluid and electrolyte imbalances, and patients with atelectasis or pulmonary edema. For patients unable to clear their own secretions, suctioning or other airway clearance techniques may be indicated as an adjunct to aerosol therapy. Care must be taken to ensure that patients are capable of clearing secretions when the secretions are mobilized by aerosol therapy. Appropriate airway clearance techniques should accompany any aerosol therapy designed to help mobilize secretions (see Chapter 44).

RULE OF THUMB Patients should be monitored continuously during aerosol treatment to avoid hazards such as reactive bronchospasm and accumulation of secretions and obstructing the airway. Patient monitoring should include auscultation for adventitious breath sounds; observation of the patient's breathing pattern and overall appearance before and after therapy; and, most essential, communicating with the patient during therapy to determine the perceived work of breathing.

Drug Concentration

During nebulization, the evaporation, heating, baffling, and recycling of drug solutions undergoing jet or ultrasonic nebulization increase solute concentrations.[9] This process can expose the patient to increasingly higher concentrations of the drug

over the course of therapy and result in a higher concentration of drug remaining in the nebulizer at the end of therapy. This increase in concentration is often time-dependent with the greatest effect occurring during nebulization over extended periods, as in continuous aerosol drug delivery.

Eye Irritation

Aerosol administration via a face mask may deposit drug in the eyes and cause eye irritation. In very rare cases, anticholinergic medications (see Chapter 36) have been suspected to worsen preexisting eye conditions, such as forms of glaucoma. Caution should be exercised when a face mask is used during aerosol drug therapy. In addition, special mask designs that have been shown to reduce drug deposition in the eyes or mouthpieces should be considered for at-risk patients.[13,14]

Secondhand Exposure to Aerosol Drugs

Workplace exposure to aerosols may be detectable in the plasma of bystanders and healthcare providers. Repeated secondhand exposure to bronchodilators is associated with increased risk of occupational asthma. Institutions should develop and implement an occupational health and safety policy to minimize the risk of secondhand aerosol exposure for care providers and bystanders.[15-17] Implementation of an occupational health and safety policy should include using systems that introduce less fugitive emissions of aerosol to the atmosphere generated by both aerosol devices and patients. These include filtering exhalation to contain aerosol, producing aerosol only during inspiration and using environmental controls. Up to 70% of aerosol generated by SVNs directly enter the environment. Unless filters are placed in the expiratory limb, 40% of aerosols produced during mechanical ventilation are exhausted to the air of the intensive care unit (ICU).[18]

AEROSOL DRUG DELIVERY SYSTEMS

Effective aerosol therapy requires a device that quickly delivers sufficient drug to the desired site of action with minimal waste and at a low cost.[19] Aerosol generators in use include pressurized metered dose inhalers (pMDIs) with or without spacers or valved holding chambers (VHCs), dry powder inhalers (DPIs), small and large volume (jet) nebulizers, hand-bulb atomizers and nasal spray pumps, ultrasonic nebulizers (USNs), and vibrating mesh (VM) nebulizers, as well as numerous emerging technologies.[2]

Pressurized Metered Dose Inhalers

The pMDI is the most commonly prescribed method of aerosol delivery in the United States (Fig. 40.5). The pMDI is portable, compact, and easy to use and provides multidose convenience. A uniform dose of drug is dispensed within a fraction of a second after actuation and is reproducible throughout the canister life. The pMDI and actuator are designed for the specific drug formulation, propellants, and dose volume to be delivered. The pMDI is used to administer bronchodilators, anticholinergics, and steroids. More formulations of these drugs are available for use by pMDIs than for use with nebulizers. When properly used, pMDIs are at least as effective as other nebulizers for drug delivery. For this reason, pMDIs often are the preferred method for delivering bronchodilators to spontaneously breathing patients and patients who are intubated and undergoing mechanical ventilation.[20-22]

Fig. 40.5 An Example of a Commonly Used Pressurized Metered Dose Inhaler.

Although pMDIs have relatively easy-to-use design, patients commonly misuse them during therapy. Most pMDIs are "press and breathe," but there is increasing presence of a variation known as *breath-actuated pMDIs*. The basic components of pMDI are similar regardless of type, manufacturer, or active ingredient; commonly used pMDIs are shown in Fig. 40.6.

The pMDI appears to be a simple device, but it represents sophisticated technology and engineering. A pMDI is a pressurized canister that contains the prescribed drug (a micronized powder or aqueous solution) in a volatile **propellant** combined with a surfactant and dispersing agent. Propellant is defined as a compressed inert gas that helps to dispense aerosolized medications when the pressure is released. When the canister is inverted (nozzle down) and placed in its actuator, or "boot," the volatile suspension fills a metering chamber that controls the amount of drug delivered. Pressing down on the canister aligns a hole in the metering valve with the metering chamber. The high propellant vapor pressure quickly forces the metered dose out through this hole and through the actuator nozzle.

Aerosol production takes approximately 20 ms. As the liquid suspension is forced out of the pMDI, it forms a plume, within which the propellants vaporize. Initially, the velocity of this plume is high (approximately 15 m/s). However, within 0.1 second, the plume velocity decreases to less than half its maximum as the plume moves away from the actuator nozzle. At the same time, propellant evaporation causes the initially large particles (35 μm) generated at the actuator orifice to decrease rapidly in size.

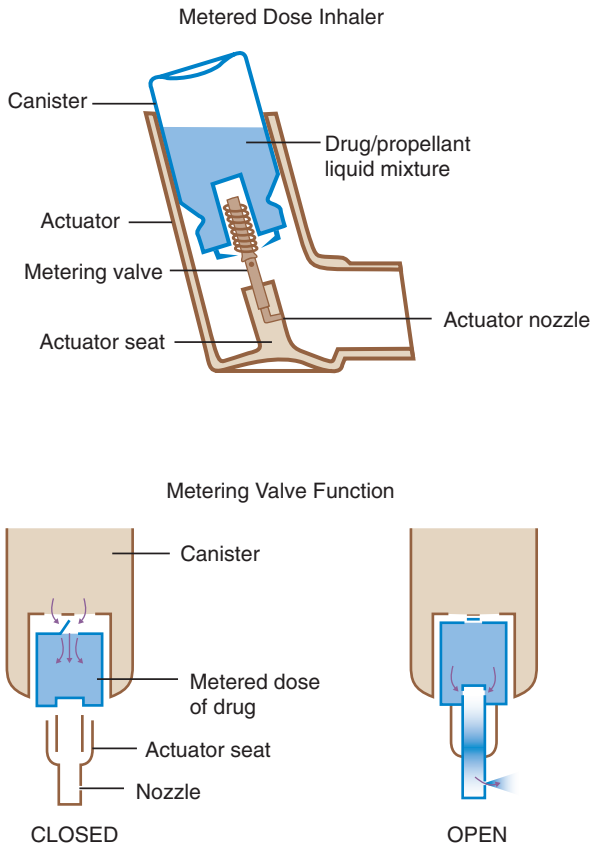


Fig. 40.6 Components of a Pressurized Metered Dose Inhaler, Including Function of the Metering Valve. (From Gardenhire DS: *Rau's respiratory care pharmacology*, ed 8, St. Louis, 2012, Mosby.)

The output volume of pMDIs ranges from 30 to 100 mcL. Approximately 60% to 80% by weight of this spray consists of the propellant, with only approximately 1% being active drug (50 mcg to 5 mg, depending on the drug formulation). For a chlorofluorocarbon (CFC) pMDI used in a standard actuator, loss of drug in the valve stem housing and on the actuator mouthpiece amounts to 10% to 15% of the nominal dose from the metering valve.

From their inception in the mid-1950s to the beginning of the 21st century, **chlorofluorocarbons (CFCs)** such as Freon were the propellants used in pMDIs. Manufacture of CFCs for most applications has now been prohibited because of the effect of these compounds on global warming, with a period of transition provided for pMDIs. A consortium of eight pharmaceutical companies developed **hydrofluoroalkane (HFA)**-134a to be more environment friendly and possibly clinically safer than CFCs.[23] Redesign of key components of the pMDI has resulted in improved performance.[23,24]

In addition to the propellant, pMDIs use dispersal agents to improve drug delivery by keeping the drug in suspension. The most common dispersal agents are surfactants, such as soy lecithin, sorbitan trioleate, and oleic acid. These agents help to keep the drug suspended in the propellant and lubricate the valve mechanism but may also cause adverse responses (coughing or wheezing) in some patients.[25,26]

Every pMDI should be primed by shaking and actuating the device to atmosphere one to four times (see label for the specific device) before initial use and after storage. Without priming, the initial dose actuated from a new pMDI canister contains less active substance than subsequent actuations.[25,26] This "loss of dose" from a pMDI occurs when drug particles rise to the top of the canister over time ("cream"). A reduction in emitted dose with the first actuation commonly occurs with a pMDI after storage, particularly with the valve pointed in the downward position. Loss of prime is related to valve design and occurs when propellant leaks out of the metering chamber during periods of nonuse (e.g., 4 hours). The result is reduced pressure and drug released with the next actuation.[25,26] Improved designs of metering valves developed for use with HFA propellants reduce these losses. It is recommended that a single dose be wasted before the next dose is inhaled when a CFC pMDI has not been used for 4 to 6 hours. An HFA pMDI requires no wasting of dose for periods exceeding 2 days.

Breath-Actuated Pressurized Metered Dose Inhaler

A variation of a pMDI is a **breath-actuated nebulizer**, which incorporates a trigger that is activated during inhalation. The trigger theoretically reduces the need for the patient or caregiver to coordinate pMDI actuation with inhalation.[26] Evaluation of the efficacy of breath-actuated pMDIs in children younger than 6 years is limited, and their use should be restricted to older children and adults. Oropharyngeal deposition of steroids using these devices is still very high.

RULE OF THUMB

- A pressurized metered dose inhaler (pMDI) has a press-and-breathe design; a breath-actuated pMDI incorporates a trigger that is activated with inspiration.
- Before initial use and after storage, every pMDI should be primed by shaking and actuating the device to atmosphere one to four times, depending on the label.

Dose Counters

A serious limitation of multidose inhalers is the lack of a "counter" to indicate the number of doses remaining in the canister. After the number of label doses has been administered, the pMDI may appear to give another 20 to 60 doses, which may deliver little or no medications as the doses "tail off." The *tail-off effect* refers to variability in the amount of drug dispensed toward the end of the life of the canister. The result of tail-off is swings from normal to almost no dose emitted from one breath to the next with no reliable indicator to the user. Without a dose counter, there is no viable method to determine remaining drug in a pMDI other than manually keeping a log of every dose taken. The US Food and Drug Administration (FDA) is requiring all new pMDIs to have counter technology to track pMDI actuations remaining. Third-party dose counters may be added to older pMDI models but may not have the accuracy of built-in technology (Fig. 40.7).

Fig. 40.7 Dose counters may be mounted on the top of a pressurized metered dose inhaler canister integrated in the actuator boot.

MINI CLINI

Using Universal Pressurized Metered Dose Inhaler Actuator or Boot

Problem

The association of CFCs with degradation of the earth's atmosphere and the ozone layer has resulted in an international treaty banning use of these compounds. As HFAs become the propellants of choice, a problem arises. If the CFC and HFA drug formulations are bioequivalent, can these compounds be used with the same (universal) pMDI actuator, or boot?

Discussion

In the case of HFA-based albuterol (e.g., Proventil HFA), the operating pressure and stem orifice differ from those used for the CFC formulation. The result is different plume geometries. When HFA albuterol is used in a universal adapter designed for CFC albuterol, the MMAD and GSD are greatly increased. The result is that significantly less drug is available to the patient. When possible, accessory devices that are used in the manufacturer's boot with the pMDI should be selected. If these devices are unavailable, the universal adapter device that is available should be evaluated to determine how much additional dose may be required to provide an equivalent dose through a third-party adapter.

Factors Affecting Pressurized Metered Dose Inhaler Performance and Drug Delivery

Temperature. Low temperature (<10°C) decreases the output of CFC pMDIs. Patients with cold air–induced bronchospasm who keep their pMDIs in outer coat pockets when outside in cold winter weather may receive only a small percentage of drug compared with that administered with the same pMDI at 25°C. This problem has been less serious with the newer HFA pMDIs.[25,26]

Nozzle size and cleanliness. Aerosol drug delivery is influenced by nozzle size and cleanliness. Nozzle size is pMDI specific. As debris builds up on the nozzle or actuator orifice, the emitted dose is reduced.[27,28] Manufacturer recommendations should be followed for cleaning. pMDI canisters should never be placed under water.

BOX 40.1 Optimal Technique for Use of a Pressurized Metered Dose Inhaler

1. Warm the pMDI canister to hand or body temperature and shake it vigorously.
2. Before first use of a new pMDI and when the pMDI has not been used for several days, prime the pMDI by pointing it into the air (away from people) and actuating a couple of times.
3. Assemble the apparatus and uncap the mouthpiece, ensuring there are no loose objects in the device.
4. Open-mouth technique: Open your mouth wide, keeping tongue down. Hold the pMDI with the canister oriented downward and the outlet aimed at your mouth. Position the pMDI approximately 4 cm (two fingerbreadths) away from your mouth.
5. Closed-mouth technique: Place mouthpiece between lips, with tongue out of the path of the outlet.
6. Breathe out normally.
7. As you slowly begin to breathe in (<0.5 L/s), actuate the pMDI.
8. Continue inspiration to total lung capacity.
9. Hold your breath for up to 10 s. Then relax and breathe normally.
10. Wait 1 min between puffs.
11. Disassemble the apparatus, and recap the mouthpiece.

pMDI, Pressurized metered dose inhaler.

Priming. Priming is defined as shaking the device and releasing one or more sprays into the air when the pMDI is new or has not been used for a while. It is done to mix the drug and the propellant, which can separate in the canister over time. Priming is required to provide an adequate dose, according to the manufacturer's guidelines.

Timing of actuation intervals. Manufacturers recommend 30 seconds to 1 minute between actuations. When propellants are released, the device cools, changing aerosol output. The pause allows the device to return to room temperature and recover normal output. However, previous research[29] showed that pMDI output is similar at 15-second intervals. Very rapid actuation of multiple puffs per breath reduces inhaled drug per puff.

Aerosol Delivery Characteristics

Although pMDIs can produce particles in the respirable range (MMAD 2 to 6 μm),[26] the initial velocity and dispersion of the aerosol plume generate larger particles that decrease in size as they leave the pMDI, resulting in approximately 80% of the dose leaving the actuator to impact and become deposited in the oropharynx. A significant proportion of this oropharyngeal deposition is swallowed and may be a factor in systemic absorption of some drugs. Pulmonary deposition ranges from 10% to 20% in adults and larger children (less in infants).[30] The exact amount of drug delivered to an individual patient is unpredictable because of high variability between patients and because pMDI drug administration is technique dependent.

Technique

The successful administration of aerosol drugs by pMDI is highly technique dependent. Two-thirds of patients and healthcare professionals who teach pMDI use do not perform the procedure properly.[31] Box 40.1 outlines the recommended steps for

self-administering a bronchodilator by pMDI. Patient instruction requires 10 to 30 minutes and should include demonstration, practice, and confirmation of patient performance (demonstration pMDIs with placebo are available from manufacturers for this purpose). Repeated instruction improves performance; repeat instruction is done most appropriately with follow-up clinic or home visits. Demonstration and return demonstration must occur several times for best patient adherence to device use.

For best effect, the pMDI should be actuated once at the beginning of inspiration. Common hand–breath coordination problems include actuating the pMDI before or after the breath. Some patients, especially infants, young children, elderly adults, and patients in acute distress, may be unable to coordinate actuation of the pMDI with inspiration. Some patients exhibit a "cold Freon effect," which occurs when the cold aerosol plume reaches the back of the mouth and the patient stops inhaling. All of these problems reduce aerosol delivery to the lung to the point that the patient does not benefit from the medication, but they can be corrected entirely or in part by use of the proper pMDI accessory device.

Most pMDI labels call for placing the mouthpiece between the lips. However, positioning the outlet of the pMDI approximately 4 cm (two finger lengths) in front of the mouth improves lung deposition by decreasing oropharyngeal impaction.[32] Holding the canister outside the open mouth (at two finger lengths) provides a space for the particles to decelerate while evaporating, allowing particle size to reduce to respirable size. Using the open-mouth technique with a low inspiratory flow rate can result in a doubling of the dose delivered to the lower respiratory tract of an adult from approximately 7% to 10% to 14% to 20%. However, this technique is more difficult for patients to perform reliably than the closed-mouth technique. Although it may reduce oropharyngeal deposition, the technique has not been shown to improve the clinical response to pMDI bronchodilators.

MINI CLINI

High Oral Deposition With Pressurized Metered Dose Inhalers

Problem

High oral deposition with pMDIs.

Discussion

The manufacturer labels for pMDIs call for placing the mouthpiece between the lips. However, positioning the outlet of the pMDI approximately 4 cm (two finger widths) in front of the mouth improves lung deposition up to twofold in adults from approximately 7%–10% to 14%–20% by decreasing oropharyngeal impaction.[32] Holding the canister outside the open mouth provides a space for the particles to decelerate while evaporating, allowing particle size to reduce to a more respirable size. Although it may reduce oropharyngeal deposition, the technique is more difficult for some patients and has not been shown to improve the clinical response to pMDI bronchodilators.

Concerns have been raised about use of the open-mouth technique with ipratropium bromide because poor coordination can result in drug being sprayed into the eyes. Use of anticholinergic agents has been associated with increased ocular pressure, which could be dangerous for patients with glaucoma. For avoidance of ocular exposure, the drug manufacturer recommends that patients use the closed-mouth technique with ipratropium.

The high percentage of oropharyngeal drug deposition with use of steroid pMDIs can increase the incidence of oral yeast infection (thrush) and changes in the voice (dysphonia). Rinsing the mouth after steroid use can help to avoid this problem, but most pMDI steroid aerosol impaction occurs deep in the hypopharynx, which cannot be easily rinsed with gargling. For this reason, steroid pMDIs should not be used alone but always in combination with a spacer or VHC. See Box 40.2 for instructions for determining dosage left in the pMDI.

BOX 40.2 Determining Dose Left in Pressurized Metered Dose Inhaler

Tracking the number of actuations (puffs) remaining in a pMDI can be done with or without dose counters (see Fig. 40.7).

With Dose Counters

The user should:[29]

1. Determine how many puffs of drug the pMDI has when full.
2. Learn to read the counter display, because each dose counter has a different way of displaying doses left in the canister.
3. Check the counter display to track the pMDI actuations remaining in the canister.
4. Reorder the pMDI when there are a few days of drug remaining.
5. Dispose of the pMDI properly, after the last dose is dispensed.

Without Dose Counters

The user should:[29]

1. Read the label to determine how many puffs of drug the pMDI has when full.
2. Calculate how long the pMDI will last by dividing the total number of puffs in the pMDI by the total puffs used per day. If the pMDI is used more often than planned, it will run out sooner.
3. Identify the date that the medication will run out, and mark it on the canister or on a calendar.
4. For drugs that are prescribed to be taken as needed, track the number of puffs of drug administered on a daily log sheet and subtract them from the remaining puffs to determine the amount of medication left in the pMDI.
5. Keep the daily log sheet in a convenient place, such as taped to the bathroom mirror.
6. Refill the pMDI prescription when there are a few days of use remaining in the pMDI.
7. Dispose of the pMDI properly when the last dose is dispensed.

pMDI, Pressurized metered dose inhaler.

Pressurized Metered Dose Inhaler Accessory Devices

Various pMDI accessory devices have been developed to overcome the two primary limitations of these systems: hand–breath coordination problems and high oropharyngeal deposition. Accessory devices include spacers and VHCs.

Spacers and valved holding chambers. Spacers and VHCs are designed to reduce both oropharyngeal deposition and the need for hand–breath coordination. A spacer is a simple valveless extension device that adds distance between the pMDI outlet and the patient's mouth. This distance allows the aerosol plume

Fig. 40.8 Pressurized metered dose inhaler and accessory devices consisting of spacer and holding chambers. All of the accessory devices reduce oropharyngeal deposition. Small volume spacers such as (A) the unidirectional spacer (RTC 15-D) (Courtesy Instrumentation Industries, Bethel Park NC) and (B) the bidirectional spacer (Dual Spray Mini Spacer) (Courtesy Thayer Medical, Tucson, AZ) offer no additional advantage, but the large volume spacers, (C) Aerovent (Courtesy Monaghan/Trudell Medical) and (D) Aerochamber Plus Z Stat (Courtesy Monaghan/Trudell Medical, London, Canada), improve inhaled aerosol with delay between actuation and inspiration. Different colors of AeroChamber Plus Z Stat represent different patient populations. For instance, *orange* is for infants, while *yellow* is for children and *blue* is for adults.

to expand and the propellants to evaporate before the medication reaches the oropharynx. Larger particles leaving the pMDI tend to impact on the spacer walls. In combination, this phenomenon reduces oropharyngeal impaction and increases pulmonary deposition. VHCs incorporate one or more valves that prevent aerosol in the chamber from being cleared on exhalation. This allows patients with a small V_T to empty the aerosol from the chamber over two or more successive breaths. In general, holding chambers provide less oropharyngeal deposition, higher respirable drug dosages, and better protection from poor hand-breath coordination than simple spacers. VHCs protect the patient from poor hand–breath coordination, with exhaled gas venting to the atmosphere, allowing aerosol to remain in the chamber, available to be inhaled with the next breath. VHCs allow infants, small children, and adults who cannot control their breathing pattern to be treated effectively with pMDIs.

Types of accessory devices. Basic concepts for spacer devices include: (1) small volume adapters, (2) open tube designs, (3) bag reservoirs, and (4) VHCs (Fig. 40.8). More than a dozen different devices with volumes ranging from 15 to 750 mL have been developed over the past 30 years. Despite differences in design, all spacers add distance between the pMDI and the mouth, reducing the initial forward velocity of the pMDI droplets, which occurs with partial evaporation of propellant in the time the aerosol traverses the length of the spacer. The reduction in initial forward velocity decreases the number of nonrespirable particles reaching the airway. The same drug used with different accessory devices may produce differences in MMAD, GSD, and fine-particle fraction. The quantity of respirable drug available at the spacer or VHC depends on spacer volume and design and formulation. The placement of a valve between the pMDI, the chamber, and the mouthpiece works like a baffle, reducing the size of particles inhaled. A simple tube spacer may reduce oral deposition by 90%, whereas a VHC can reduce oral deposition by 99%.

It is increasingly common practice to provide asthmatic patients an accessory device to use with the pMDI and to teach them how to use the pMDI with and without the accessory device. Patients are instructed to use the device with the pMDI whenever they feel short of breath. Many of these patients find that they get much better relief from the pMDI with an accessory device than with the pMDI alone.

Proper use of a simple open-tube spacer still requires some hand–breath coordination because a momentary delay between triggering and inhaling the discharged spray results in a substantial loss of drug and reduced lung delivery. Exhalation into a simple spacer after pMDI actuation clears the aerosol from the device and wastes most of the dose to the atmosphere. This reduction in dose also occurs with small volume reverse-flow design spacers if there is no provision for "holding" the aerosol in the device.[33]

The MMAD of the aerosol emitted from the pMDI exiting a spacer decreases approximately 25%, whereas the fraction containing particles less than 5 μm in diameter increases. This change is largely due to rapid evaporation of propellant in the spacer. With VHCs, in addition to evaporation of the plume, the valves act as baffles of larger particles, increasing the respirable fraction further.

VHCs produce a finer, slower moving, more "respirable" aerosol with less impaction of drug in the oropharyngeal area (1% of dose) than simple spacers (10%) or a pMDI alone (80% of dose). Research suggests that a properly used pMDI and aerochamber can significantly reduce oropharyngeal deposition versus an

open-mouth technique while maintaining drug dose delivery to the lungs. This finding was true for both healthy subjects and patients with chronic obstructive pulmonary disease (COPD).[34] The advantage of reduced oropharyngeal deposition is fewer side effects from steroid aerosols. Multiple actuations of one or more drugs into a spacer reduce both the total dose and the respirable dose of drug available for inhalation. The extent of these losses may vary for different drugs and spacer designs.[35,36]

VHCs with masks are available for use in the care of infants, children, and adults. These units allow effective administration of aerosol from a pMDI to patients who are unable to use a mouthpiece device (because of their size, age, coordination, or mentation). VHCs are helpful in administering pMDI steroids because deposition of the drug in the mouth is largely eliminated, and systemic side effects can be minimized.

Even with a VHC, respirable particles containing drug settle out and become deposited within the device, causing a whitish buildup on the inner chamber walls. This residual drug poses no risk to the patient but should be rinsed out periodically. Plastic spacers decrease drug output due to the presence of an electrostatic charge. With these devices, a buildup of material can be seen on the walls of the chamber. As more material builds up on the wall of the chamber, the charge is dissipated, and more drug is inhaled by the patient. Washing the chamber with water (without soap) causes the electrostatic charge to be reestablished, making the device less effective for the next few puffs, until the static charge in the chamber (which attracts small particles) is again reduced.[37] Optimal technique is outlined in Box 40.3.

Use of conductive metal or nonelectrostatic plastic chambers or washing the plastic chamber periodically with deionizing detergent (liquid dishwashing soap) can overcome the loss of fine-particle mass owing to electrostatic charge and increase the inhaled mass from 20% to 50% of the emitted dose of the pMDI, even in children.[1] The effect of washing the chamber with conventional dishwashing soap reduces this static charge for up to 30 days. All manufacturers recommend that VHCs and spacers should be cleaned regularly, typically monthly, using dilute liquid dishwashing soap, with or without rinsing, and allowing them to air dry.

The addition of a one-way valve to convert an open tube into a reservoir for the aerosol, the incorporation of the actuator in the pMDI, the shape of the device, flow of air through the device, edge effects, masks, and manufacturing materials all affect aerosol characteristics. The inhalation valve, which is used to contain the aerosol, also acts as a baffle to reduce oropharyngeal deposition. This valve must be able to withstand the initial pressure from the pMDI when the device is triggered to retain aerosol and have sufficiently low resistance to open readily when the user inhales, in particular when the user is a child or an infant. Exhalation valves in a face mask attached to a spacer device must also provide low resistance. Issues of spacer volume, V_T, frequency of breathing, and mechanical dead space between the spacer and mouth are of particular concern when these devices are used by children.[37] There are twofold to threefold differences in the amount of drug available at the mouth when different spacers are used to treat infants. Clinicians should determine the delivery efficiencies of spacer devices before using the device in a particular population.

Accessory devices are used with either the manufacturer-designed boot that comes with the pMDI or with a "universal adapter" that triggers the pMDI canister. Formulations of pMDI drugs operate at varying pressures and have a different-sized orifice in the boot that are specifically designed by the manufacturer for use exclusively with that pMDI. The output characteristics of a pMDI change when an adapter with a different-sized orifice is used. With HFA pMDIs, the diameter of the actuator orifice is smaller and the spray is predictably finer. When the HFA pMDI is used in an actuator designed for use with CFC pMDIs, output is reduced. When these HFA formulations are used with any particular spacer, it is important to know how comparable the available dose and particle size distribution are to the dose and particle size from an existing CFC pMDI.

BOX 40.3 Optimal Technique for Use of a Metered Dose Inhaler With a Valved Holding Chamber

1. Warm the pMDI to hand or body temperature.
2. Assemble the apparatus, ensuring there are no objects or coins in the chamber that could be aspirated or obstruct outflow.
3. Hold the canister vertically and shake it vigorously. Prime if necessary.
4. Place the pMDI in the holding chamber inlet, position chamber outlet in the mouth (or place the mask over nose and mouth), and encourage the patient to breathe through the mouth. Visually inspect for proper valve function.
5. With normal breathing, actuate the pMDI once and have the patient breathe through the device for three to seven breaths (three breaths for adults and seven breaths for infants).[a]
6. Allow 30 to 60 s between actuations.

[a]For a cooperative patient, synchronizing actuation at the beginning of larger breaths with breath holding may be encouraged. However, this maneuver has not been shown to increase clinical response to inhaled bronchodilators.

pMDI, Pressurized metered dose inhaler.

Cost

Many hospitals are moving away from the use of HFA pMDIs because of the high cost of these devices. Regardless of drug delivered, these devices cost between $200 and $300 in the United States compared with pennies a dose for the same drug in a liquid preparation to be used in a nebulizer. The use of these less expensive preparations with a VM nebulizer (see later discussion) has now become the norm in many hospitals because of cost.

Dry Powder Inhalers

A DPI is typically a breath-actuated dosing system. With a DPI, the patient creates the aerosol by drawing air though a dose of finely milled drug powder with sufficient force to disperse and suspend the powder in the air. DPIs are inexpensive, do not need propellants, and do not require the hand–breath coordination needed for pMDIs. However, dispersion of the powder into respirable particles depends on the creation of turbulent flow in the inhaler. Turbulent flow is a function of the ability of the

patient to inhale the powder with a sufficiently high inspiratory flow rate (Fig. 40.9). In terms of both lung deposition and drug response, DPIs are as effective as pMDIs.[38,39]

RULE OF THUMB

- Unlike pMDIs, DPIs do not require hand–breath coordination but require patients to generate a high inspiratory flow to disaggregate and disperse drug powder into respirable particles.

Equipment Design and Function

Most passive dry powder–dispensing systems require the use of a carrier substance (lactose or glucose) mixed into the drug to enable the drug powder to disaggregate more readily and flow out of the device. Reactions to lactose or glucose seem to be fewer than reactions to the surfactants and propellants used in pMDIs, even though the amount of these substances is substantially greater than the amount of the drug and can represent 98% or more of the weight per inhaled dose in some formulations.

As shown in Fig. 40.10A to C, there are numerous DPIs on the market, which can be divided into three categories based on the design of their dose containers: (1) unit-dose DPI, (2) multiple unit-dose DPI, and (3) multiple-dose drug reservoir DPI.

Unit-dose DPIs, such as the Aerolizer (Schering-Plough, Kenilworth, NJ), Arcarta Neohaler (Sunovion Pharmaceuticals Inc, Marlborough, MA), and the HandiHaler (Boehringer Ingelheim, Ingelheim am Rhein, Germany), dispense individual doses of drug from punctured gelatin capsules. Multiple unit-dose DPIs (Diskhaler; GlaxoSmithKline, Philadelphia) contain a case of four or eight individual blister packets of medication on a disk inserted into the inhaler. Multiple-dose DPIs include the Twisthaler (Schering-Plough), Flexhaler (AstraZeneka, London, UK), and the Diskus (GlaxoSmithKline). The Twisthaler and Flexhaler have a multidose reservoir powder system preloaded with a quantity of pure drug sufficient for dispensing 120 doses of medication, and the Diskus incorporates a tape system that contains up to 60 sealed single doses (Fig. 40.11).

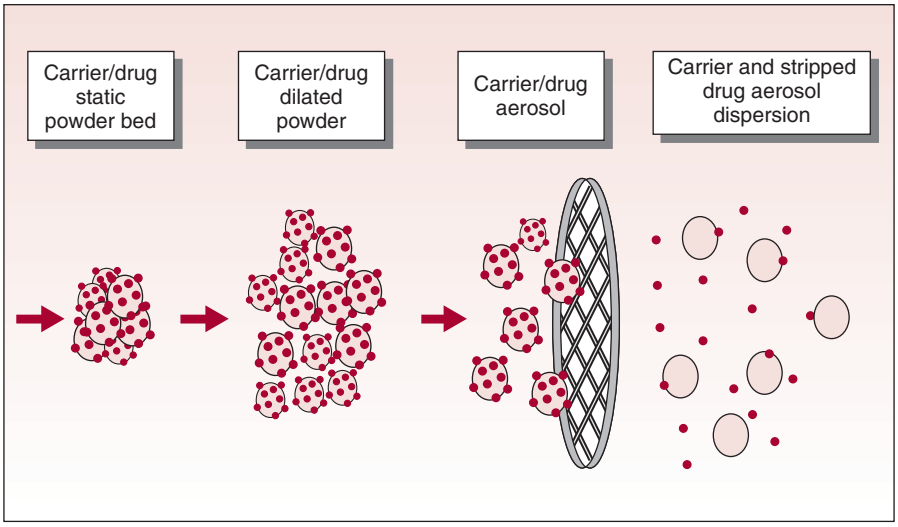


Fig. 40.9 Aerosolization of Dry Powder.

Fig. 40.10 Some currently available dry powder inhalers *(DPIs)*: (A) unit-dose DPI (Courtesy Arcapta Neohaler, Sunovion Pharmaceuticals), (B) multiple unit-dose DPI (Dishaler) (Courtesy GlaxoSmithKline), and (C) multiple-dose DPI (Discus) (Courtesy GlaxoSmithKline).

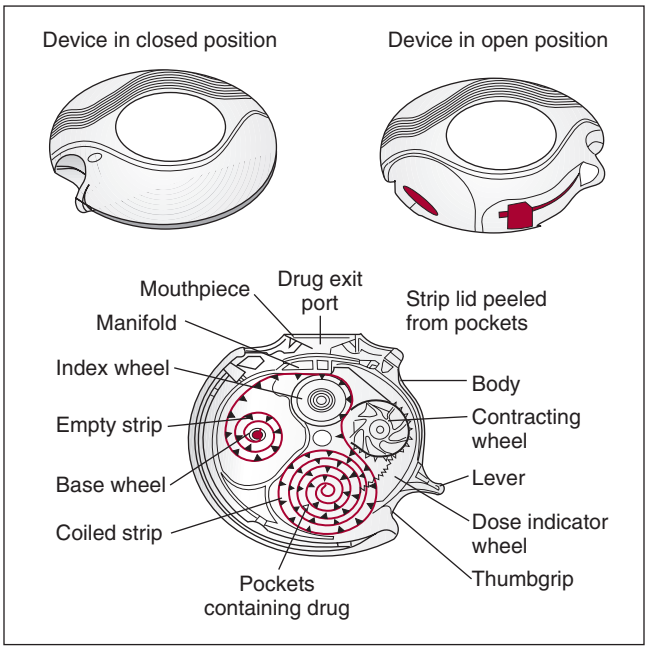


Fig. 40.11 Diskus Dry Powder Inhalers (Modified from Dhand R, Fink J: Dry powder inhalers. Resir Care 44:940, 1999).

The particle size of the dry powder particles of drug ranges from 1 to 3 µm. However, the size of the lactose or glucose particles can range from approximately 20 to 65 µm, so most of the carrier (≤80%) is deposited in the oropharynx.

Factors Affecting Dry Powder Inhaler Performance and Drug Delivery

Intrinsic resistance and inspiratory flow rate. Optimal performance for each DPI design occurs at a specific inspiratory flow rate. The fine-particle fraction of respirable drug from existing DPIs ranges from 10% to 60% of the nominal dose. The amount varies with inspiratory flow and device design. The higher the resistance or the greater the flow requirement of a DPI device, the more difficult it is for a compromised or young patient to generate inspiratory flow sufficient to obtain the maximum dose of drug from the device.

Exposure to humidity and moisture. The emitted dose of DPI decreases in a humid environment, likely because of powder clumping. The longer the exposure and the greater the level of absolute humidity, the lower the dose emitted. New DPIs with multiple unit-doses minimize the effects of moisture on the powder as long as individual doses are inhaled as soon as the seal is broken.

Patient's inspiratory flow ability. High peak inspiratory flow rates (>60 L/min) are required to dispense the drug powder from most current DPI designs and result in a pharyngeal dose comparable with the dose received from a typical pMDI without an add-on device. If a patient does not inhale at the optimal inspiratory flow rate for a particular device, delivery to the lung decreases as the dose of drug dispensed decreases and the particle size of the powder aerosol increases.[39,40]

Passive, or patient-driven, DPIs rely on the patient's inspiratory effort to dispense the dose. The result is differences in lung delivery and clinical response. Active or powered DPI devices, which disaggregate the powder before inhalation, are independent of patient effort. Active DPIs use an energy source to disaggregate the powder and suspend the powder into an aerosol, allowing the dose to be suspended independent of patient inspiratory flow rates.

BOX 40.4 Optimal Technique for Use of a Dry Powder Inhaler

1. Assemble the apparatus.
2. Load dose, keeping device upright.
3. Exhale slowly to functional residual capacity.
4. Seal lips around the mouthpiece.
5. Inhale deeply and forcefully (>60 L/min). A breath hold should be encouraged but is not essential.
6. Repeat the process until dose is completed.
7. Monitor adverse reactions.
8. Assess beneficial effects.

Modified from Pedersen S: How to use a Rotahaler, *Arch Dis Child* 61:11, 1986; and Hansen OR, Pedersen S: Optimal inhalation technique with terbutaline, *Turbuhaler Eur Respir J* 2:637, 1989.

Technique. Proper technique is essential to derive the maximum benefit from a DPI. Box 40.4 outlines the basic steps for ensuring optimal drug delivery. The most critical factor in using a passive DPI is the need for high inspiratory flow. Patients must generate an inspiratory flow rate of at least 40 to 60 L/min to produce a respirable powder aerosol. Because infants, small children (<5 years old), and patients who are unable to follow instructions cannot develop inspiratory flows this high, these patients cannot use DPIs. Because patients with severe airway obstruction may be unable to achieve the required flow, they should not use DPIs during acute bronchospasm.

Exhalation into a DPI before inspiration can result in loss of drug delivery to the lung. Some DPIs also require assembly, which can be cumbersome or difficult for some patients, especially in an emergency. It is important that patients receive demonstrations with their inhalers and have the opportunity to assemble and use the DPI (return demonstration) before self-administration. Although the DPI may require cleaning in accordance with the product label, the device should never be submerged in water. Moisture in the device dramatically reduces available dose. Table 40.1 provides methods to determine the dose of the different types of DPI.

RULE OF THUMB

- DPIs should be used for patients who can generate an inspiratory flow rate at least 40 to 60 L/min in order to produce a respirable powder aerosol.

New Dry Powder Inhaler Technologies

As shown in Fig. 40.12, new DPI technologies include the Easyhaler, Ellipta, Podhaler, Tudorza Pressair, and Spiromax.

Easyhaler. The Easyhaler (Orion Corporation, Espoo, Finland) is approved for marketing in Europe for delivery of beclomethasone, albuterol, formoterol, and budesonide. The device is similar to the pMDI in terms of its shape and operation. However, it is

TABLE 40.1 Determining Doses Left in the Dry Powder Inhaler

		Drug Container	Doses	Type Indicator	Meaning of Dose Indicator
Unit-dose DPI	Aerolizer or HandiHaler	Single capsule	1	None	Check capsule to ensure full dose was inhaled. Repeat to empty capsule
Multiple unit-dose DPI	Diskhaler	Dose blisters	4 or 8	None	Inspect visually to confirm use of all blisters
	Diskus	Blister strip	60	Red numbers	Red numbers indicate that ≤5 doses are left in DPI
Multiple-dose DPI	Flexhaler	Reservoir	60 or 120	"0"	Marked in intervals of 10 doses; "0" indicates empty
	Twisthaler	Reservoir	30	"01"	"01" indicates last dose

DPI, Dry Powder Inhaler.

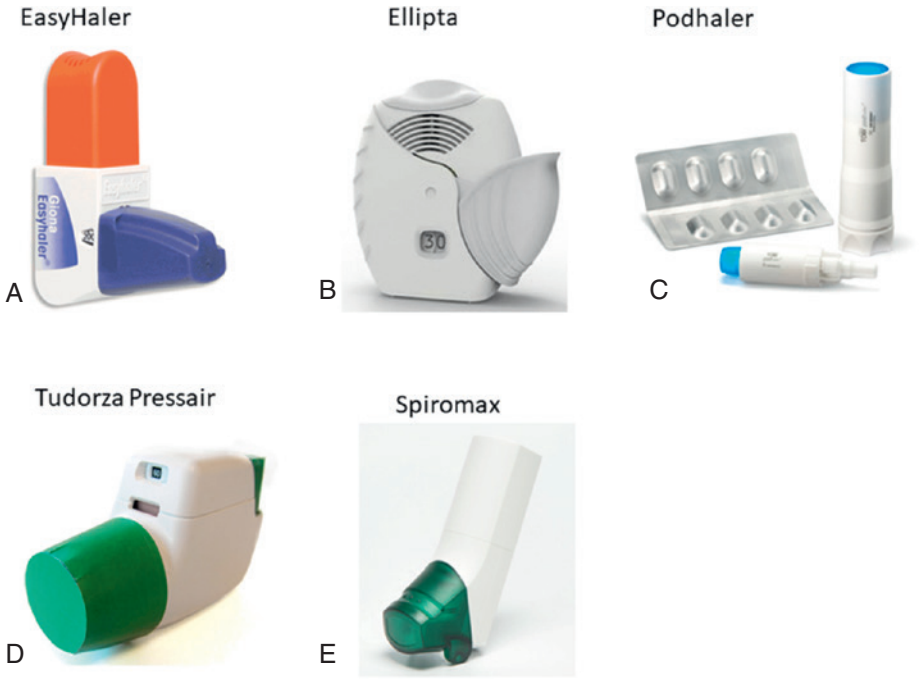


Fig. 40.12 New Dry Powder Inhalers. (A) Easyhaler (Courtesy Orion Corporation, Espoo, Finland), (B) Ellipta (Courtesy GlaxoSmithKline, Research Triangle Park, NC), (C) Podhaler (Courtesy Novartis Pharmaceutical Corporation, San Carlos, CA), (D) Tudorza Pressair (Courtesy Forest Laboratories, St Louis, MO), and (E) Spiromax (Courtesy Teva Pharmaceuticals).

a DPI and has a dose counter that gives a red signal when 20 doses are left in the device.

Ellipta. The Ellipta (GlaxoSmithKline, Research Triangle Park, NC) is a disposable multidose DPI in which the drug is stored in double-foil blister strips. The device has a three-step technique (open-inhale-close) and provides auditory feedback with the opening of the inhaler that results in loading the dose and an advancement in the dose counter. When a patient does not inhale the dose from the Ellipta, the drug is dumped internally to prevent overdosing. The Ellipta has four categories that provide different drugs or drug combinations: (1) Incruse Ellipta delivers umeclidinium, a long-acting muscarinic antagonist that is used in the treatment of COPD, (2) Breo Ellipta has a combination of fluticasone furoate and vilanterol (long-acting β2-agonist), (3) Anoro Ellipta includes a combination of umeclidinium and vilanterol, (4) Arnuity Ellipta delivers fluticasone furoate, and (5) Relvar Ellipta includes fluticasone furoate and vilanterol.

RULE OF THUMB

- Moisture in DPIs decreases aerosol delivery.
  - Do not exhale into your DPI.
- Do not store your DPI in the bathroom.
- Never submerge in water.

Podhaler. As a single-dose reusable DPI, the Podhaler (Novartis Pharmaceutical Corporation, San Carlos, CA) delivers Tobramycin (TOBI) for the treatment of chronic infection in patients with cystic fibrosis. The device produces light porous particles with improved flow and dispersion characteristics by using the PulmoSphere technology that has less interparticle cohesive forces. When using the Podhaler, a patient opens the mouthpiece, inserts the capsule in the device, and then inhales. The manufacturer suggests disposing of the device after 7 days of use.

Tudorza pressair. The Tudorza Pressair (Forest Laboratories, St Louis, MO) is a multidose DPI that delivers aclidinium bromide, a long-acting anticholinergic. The device has a dose counter that decreases by 10 doses and shows a red mark with a "0" sign when it is empty. It also has a lockout system at the end of the dose. The Tudorza Pressair provides both visual feedback and auditory feedback during therapy. The visual feedback displays red color in the control window with incorrect technique and shows green color when the patient inhales the dose completely with the correct use of the device.

Spiromax. As a multidose passive DPI, the Spiromax (Teva Pharmaceuticals, Petah Tikva, Israel) is used to deliver albuterol, fluticasone/salmeterol, and budesonide/formoterol in the treatment of pulmonary diseases in Europe. When the patient opens the cap on the mouthpiece, the dose is loaded to the DPI, and then it is ready for the patient to inhale the medication.

Nebulizers

Nebulizers generate aerosols from solutions and suspensions. The three categories of commonly used medical nebulizers include: (1) pneumatic jet nebulizers, (2) USNs, and (3) VM nebulizers. Nebulizers are also described in terms of their reservoir size. SVNs most commonly used for medical aerosol therapy hold 5 to 20 mL of medication. Large volume nebulizers hold up to 200 mL and may be used for either bland aerosol therapy (see Chapter 39) or continuous drug administration.

Pneumatic (Jet) Nebulizers

Gas-powered jet nebulizers (Fig. 40.13A) have been in clinical use for longer than 100 years. Most modern jet nebulizers are powered by high-pressure air or oxygen (O_2) provided by a portable compressor, compressed gas cylinder, or 50-psi wall outlet.

Factors affecting nebulizer performance. Nebulizer design, gas pressure, gas density, and medication characteristics affect SVN performance (Box 40.5).

Nebulizer design. As shown in Fig. 40.13B, a typical SVN is powered by a high-pressure stream of gas directed through a restricted orifice (the jet). The gas stream leaving the jet passes by the opening of a capillary tube immersed in solution. Because it produces low lateral pressure at the outlet, the high jet velocity draws the liquid up the capillary tube and into the gas stream, where it is sheared into filaments of liquid that break up into droplets. This primary spray produces a heterodisperse aerosol with droplets ranging from 0.1 to 500 µm.

This spray is directed against one or more baffles. A **baffle** is a surface on which large particles impact and fall out of suspension, whereas smaller particles remain in suspension, reducing the size of particles remaining in the aerosol. In many designs, droplets that impact baffles in the SVN return to the medication reservoir for nebulization again.

Baffles are key elements in nebulizers; well-designed baffling systems decrease both the MMAD (size) and the GSD (range of sizes) of the generated aerosol. **Atomizers** operate with the same basic principles as nebulizers without baffling and produce aerosols with larger MMAD and GSD. **Residual drug volume**,

BOX 40.5 Factors Affecting Performance of Small Volume Nebulizers

Nebulizer Design
- Baffles
- Fill volume
- Residual drug volume
- Nebulizer position
- Continuous vs. intermittent nebulization
- Reservoirs and extensions
- Vents, valves, and gas entrainment
- Tolerances in manufacturing within lots

Gas Source: Wall, Cylinder, Compressor
- Pressure
- Flow through nebulizer
- Gas density
- Humidity
- Temperature

Characteristics of Drug Formulation
- Viscosity
- Surface tension
- Homogeneity

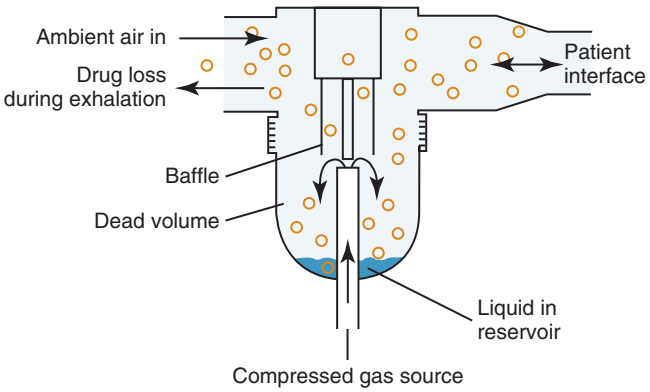


Fig. 40.13 Schematic of a small volume jet nebulizer. (From Gardenhire, D: *Rau's respiratory care pharmacology*, ed 8, St. Louis, 2012, Mosby.)

or dead volume, is the medication that remains in the SVN after the device stops generating aerosol and "runs dry."[9] The residual volume of a 3-mL dose can range from 0.5 to more than 2.2 mL, which can be more than two-thirds of the total dose. The greater the residual drug volume, the more drug that is unavailable as aerosol and the less efficient the delivery system. Residual volume also depends on the position of the SVN. Some SVNs stop producing aerosol when tilted 30 degrees from vertical. Increasing the fill volume allows a greater proportion of active medication to be nebulized. In a nebulizer with a residual volume of 1.5 mL, a fill of 3 mL would leave only 50% of the nebulizer volume (nominal dose) available for nebulization. In contrast, a fill of 5 mL would make 3.5 mL, or more than 70% of the medication, available to be inhaled. The unit-dose volumes of drugs were based on clinical response of patients using nebulizers with substantial residual drug volumes. Although increasing dose volume may increase available dose, it should be considered off-label administration, and there is no significant difference in clinical response with varying diluent volumes and flow rates.

Flow. Droplet size and nebulization time are inversely proportional to gas flow through the jet. The higher the flow of gas to the nebulizer, the smaller the particle size generated and the shorter is the time required for nebulization of the full dose. Nebulizers that produce smaller particle sizes by use of baffles, such as one-way valves, may reduce total drug output per minute compared with the same nebulizer without baffling and require more time or nominal dose to deliver a standard dose of medication to the lungs.

Gas source (hospital versus home). Gas pressure and flow through the nebulizer affect particle size distribution and output. Within operating limits, the higher the pressure or flow means the smaller the particle size and the greater the output correlates to a shorter treatment time. A nebulizer that produces an MMAD of 2.5 μm when driven by a gas source of 50 psi at 6 to 10 L/min may produce an MMAD of more than 5 μm when operated on a home compressor (or ventilator) developing 10 psi. Too low a gas pressure or flow can result in negligible nebulizer output. Consequently, nebulizers used for home care should be matched to the compressor according to data supplied by the manufacturer. Thus the combination of specific equipment improves efficient nebulization of the desired medications prescribed for the patient.

Other concerns in the use of disposable nebulizers with compressors at home involve possible degradation of performance of the plastic device over multiple uses. One study showed that repeated use of nebulizers did not alter MMAD or output as long as the nebulizer was cleaned properly. Failure to clean the nebulizer properly caused degradation of performance because of clogging of the jet orifice, reduction of the output flow, and a buildup of electrostatic charge in the device.

Density. Gas density affects both aerosol generation and delivery to the lungs. The lower the density of the carrier gas, the less aerosol impaction as gas passes through the airways, and the greater the deposition of aerosol in the lungs.[41] However, when heliox is used to drive a jet nebulizer at standard flow rates, aerosol output is substantially less than with air or O_2, and aerosol particles are considerably smaller. When driving a nebulizer with heliox, twofold to threefold greater flow is required to produce a comparable aerosol output. Heliox concentrations of 40% or greater have been shown to improve aerosol deposition.[41-43]

Humidity and temperature. Humidity and temperature can affect particle size and the concentration of drug remaining in the nebulizer. Evaporation of water and adiabatic expansion of gas can reduce the temperature of the aerosol to 10°C less than ambient temperature. This cooling may increase solution viscosity and reduce the nebulizer output while decreasing particle MMAD.[9] Aerosol particles entrained into a warm and fully saturated gas stream increase in size. These particles also can coalesce (stick together), increasing the MMAD further and, in the case of a DPI, can severely compromise the output of respirable particles. How much these particles enlarge depends primarily on the tonicity of the solution. Aerosols generated from isotonic solutions probably maintain their size as they enter the respiratory tract. Hypertonic solutions tend to enlarge, whereas evaporation can cause hypotonic droplets to evaporate and shrink.

Characteristics of drug formulation. The viscosity and density of a drug formulation affect both output and particle size. Some drugs, such as antibiotics, are so viscous that they cannot be used effectively for nebulization in some standard SVNs. In addition, in some suspensions, some aerosolized particles contain no active drug, whereas other particles, generally larger, carry the active medication.

Small Volume Nebulizers

Four categories of jet SVNs include: (1) continuous nebulizer with simple reservoir, (2) continuous nebulizer with collection reservoir bag, (3) breath-enhanced nebulizer, and (4) breath-actuated nebulizer (Fig. 40.14A, B, C, and D, respectively). The most commonly used SVN is the constant output design. Aerosol is generated continuously, with 30% to 60% of the nominal dose being trapped as residual volume in the nebulizer and more than 60% of the emitted dose wasted to the atmosphere. Continuous nebulization wastes medication because the aerosol is produced throughout the respiratory cycle and is largely lost to the atmosphere. Patients with an I:E ratio of 40:60 (or 1:1.5) lose 60% of the aerosol generated to the atmosphere. If 50% of the total dose is emitted from the nebulizer, and 50% of that aerosol is in the respiratory range and 40% of that is inhaled by the patient, less than 10% deposition is commonly measured in adults receiving continuous nebulizer therapy. In neonates and infants, given the small minute volumes and small airways with increased impaction and reduced sedimentation, deposition can be only 0.5%.

Aerosolized medication can also be conserved with reservoirs. A reservoir on the expiratory limb of the nebulizer conserves drug aerosol.

Small volume nebulizer with a reservoir. Many types of disposable SVNs are packaged with a 6-inch (15-cm) piece of aerosol tubing to be used as a reservoir (Fig. 40.14A).

Continuous small volume nebulizer with collection bag. As shown in Fig. 40.14B, bag reservoirs hold the aerosol generated during exhalation and allow the small particles to remain in suspension for inhalation with the next breath, while larger particles rain out. These additions have been attributed with a 30%

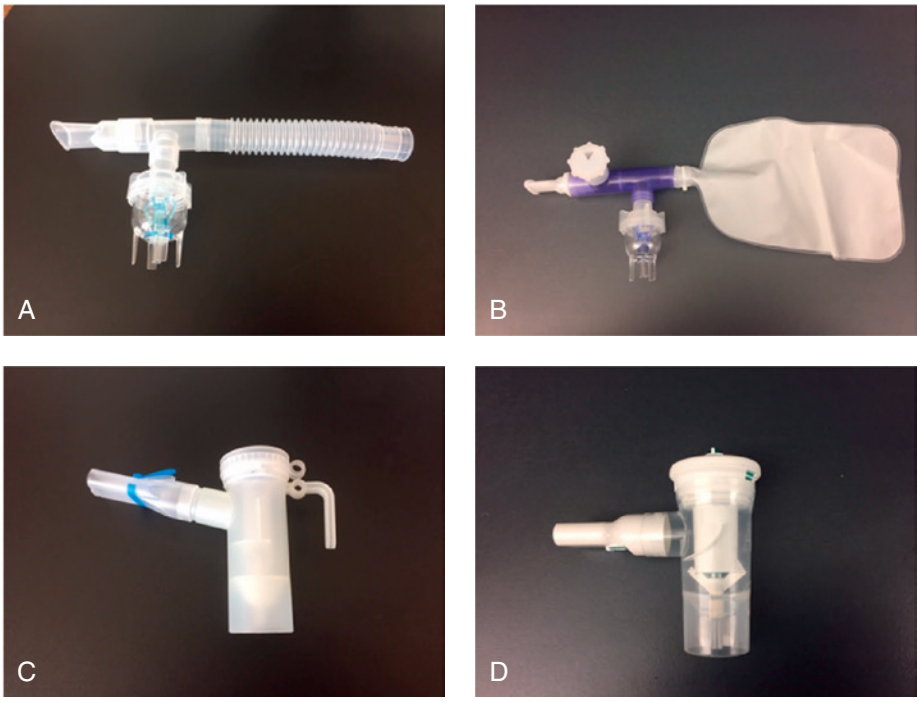


Fig. 40.14 Four categories of jet small volume nebulizers include: (A) continuous nebulizer with simple reservoir, (B) continuous nebulizer with collection reservoir bag, (C) breath-enhanced nebulizer, and (D) breath-actuated nebulizer.

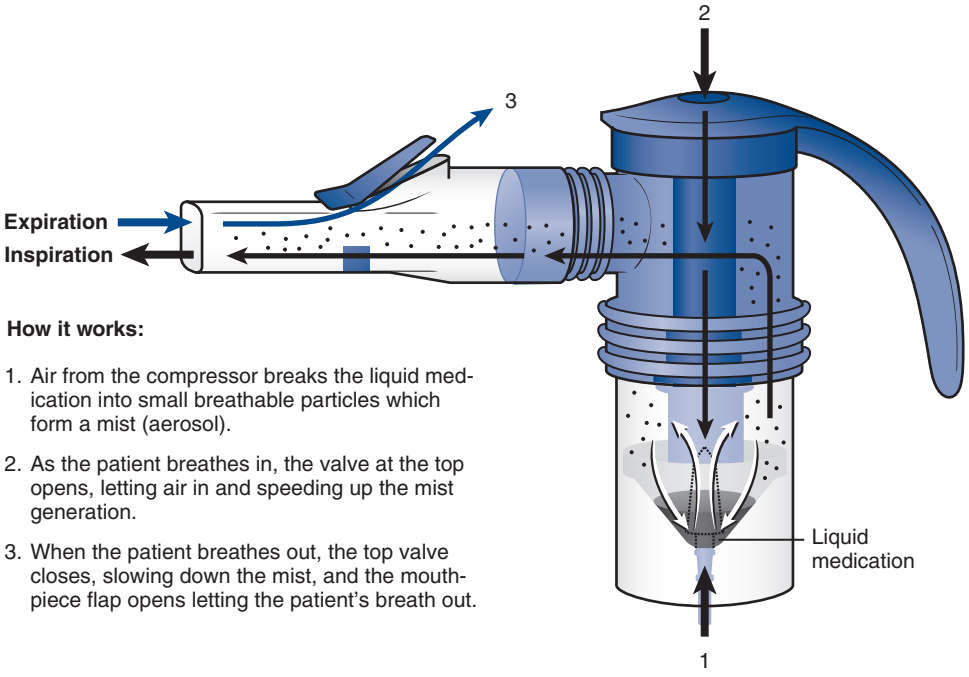


Fig. 40.15 Operating Principles of the Sprint (Pari, Midlothian, VA) Breath-Enhanced Nebulizer. (From Cairo JM, Pilbeam SP: *Mosby's respiratory care equipment*, ed 8, St. Louis, 2009, Mosby.)

to 50% increase in inhaled dose.[44] A collection bag is attached on the expiratory side of the nebulizer "T," which collects aerosol leaving the SVN when the patient is not actively inhaling. Some of the aerosol in the bag is inhaled with the next inspiration, increasing total dose efficiency.

Breath-enhanced nebulizers. **Breath-enhanced nebulizers** (Fig. 40.14C) generate aerosol continuously, using a system of vents and one-way valves to minimize aerosol waste.[44] In the Pari LC Sprint (Pari, Midlothian, VA) breath-enhanced nebulizer (Fig. 40.15), an inspiratory vent allows the patient to draw in

air through the nebulization chamber that generates and contains the aerosolized drug. On exhalation, the inlet vent closes and the aerosol exits by a one-way valve near the mouthpiece. This process can increase inhaled mass by 50% over standard continuous nebulizers and can reduce waste to the atmosphere.

MINI CLINI

Home Nebulizer Therapy

Problem

Many patients are sent home with a prescription for home nebulizer therapy prescribed with the intention of giving the patient the same quality of aerosol therapy he or she received in the hospital. However, the patient often is given the same type of nebulizer used in the hospital because it is inexpensive. These nebulizers provide an aerosol that is too large for optimal deposition in the lungs. What should be done instead?

Discussion

Home nebulizers designed for use with compressors should be matched to ensure an MMAD of 1 to 5 μm with the medication being administered. Nebulizer manufacturers such as Pari and Medic-Aid offer matched nebulizer–compressor systems for home use. Although these devices cost a little more, they are more likely to meet therapeutic objectives.

Breath-actuated nebulizers. Breath-actuated nebulizers (Fig. 40.14D) synchronize aerosol generation with inspiration, reducing waste of aerosol during exhalation and increasing inhaled dose up to threefold more than continuous and breath-enhanced nebulizers. Dosimeters, used in pulmonary function laboratories, sense inspiration and pulse airflow to the jet orifice and transform a conventional nebulizer into a breath-actuated system. Manual systems allow the user to cover a thumb port directing, compressed gas to the jet nebulizer.

AeroEclipse (Trudell Medical International, London, ON, Canada) is a breath-actuated SVN. A unique, spring-loaded, one-way valve design draws the jet to the capillary tube during inspiration and causes nebulization to cease when the patient's inspiratory flow decreases below the threshold or the patient exhales into the device (Fig. 40.16). Expiratory pressure on the valve at the initiation of exhalation moves the nebulizer baffle away from its position directly above the jet orifice, reduces the pressure, and stops aerosolization. Because aerosol is generated only during inhalation, exhaled aerosol and contamination of the environment during the expiratory phase of the breathing cycle are largely reduced.

It can be difficult to determine when a nebulizer treatment is complete. Aerosol delivery from a jet nebulizer ceased after the onset of inconsistent nebulization (sputtering).[45] Aerosol output declined by one-half within 20 seconds of the onset of sputtering. The concentration of albuterol in the nebulizer cup increased significantly when the aerosol output declined, and further weight loss in the nebulizer was caused primarily by evaporation. Most consider aerosolization past the point of initial nebulizer sputter ineffective.

Table 40.2 summarizes some of these key factors for many commercially available SVNs.[9] Numerous SVNs are on the market, and they vary widely in design and performance. SVNs of the same design and lot number can exhibit variable performance, even to the point that some nebulizers of the same model number do not work at all.[46] Managers and clinicians always must evaluate SVNs carefully before purchasing or using them. Manufacturers should provide data on the performance of their nebulizers under common use conditions.

Technique. Box 40.6 outlines the optimal technique for using an SVN for aerosol drug delivery. Use of an SVN is less technique-dependent and device-dependent than use of a pMDI or DPI

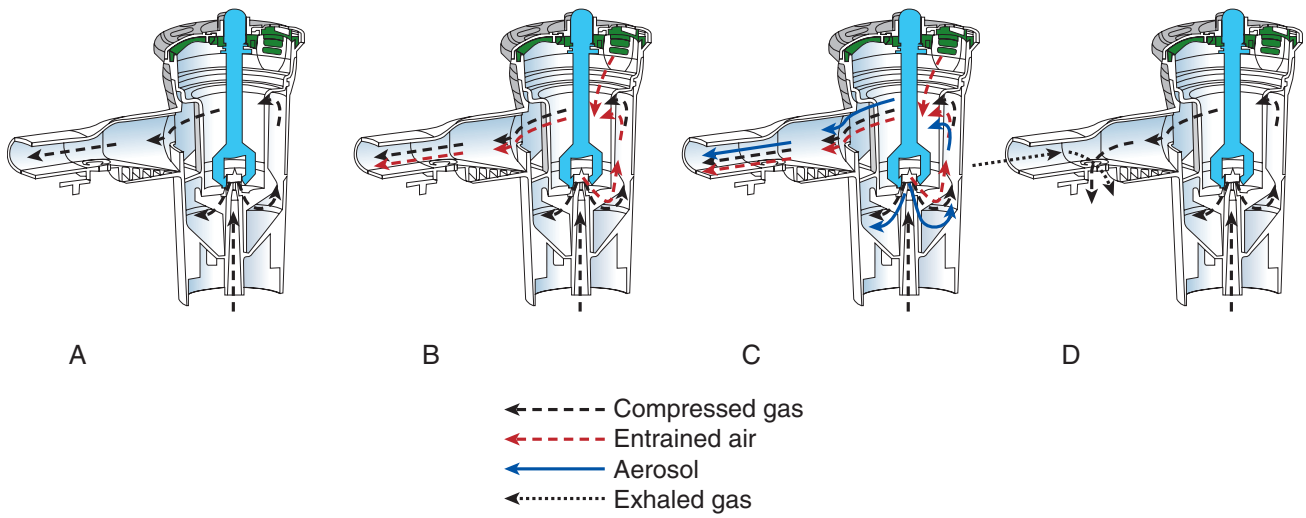


Fig. 40.16 Breath-Actuated Pneumatic Nebulizer (AeroEclipse BANII) Flow Path Diagram. (A) Before inhalation, actuator is up and compressed gas freely circulates with no aerosol produced. (B) Patient inhales, and actuator starts to move down. (C) Negative pressure pulls the diaphragm down (with actuator moved down sealing around the nozzle cover), producing aerosol. (D) Patient exhales through valve in mouthpiece; as pressure increases, the diaphragm and actuator move up, stopping aerosol production. (Courtesy Trudell Medical International, London, ON, Canada.)

TABLE 40.2 Comparison of Different Nebulizers

	Jet Nebulizer	Ultrasonic Nebulizer	Mesh Nebulizer	Smart Nebulizer
Power source	Compressed gas or electrical mains	Electrical mains	Batteries or electrical mains	Batteries or electrical mains
Portability	Restricted	Restricted	Portable	Portable
Treatment time	Long	Intermediate	Short	Short
Output rate	Low	Higher	Highest	Highest
Residual volume	0.8–2.0 mL	0.8–2 mL	≤0.2 mL	≤0.2 mL
Performance variability	High	Intermediate	Low	Low
Temperature	Decreases[a]	Increases[b]	Minimum change	Minimum change
Concentration	Increases	Variable	Minimum change	Minimum change
Cleaning	Required after single use	Required after multiple use	Required after single use	Required after single use
Cost	Very low	High	High	High

[a]For jet nebulizers, the temperature of the reservoir fluid decreases approximately 15°C during nebulization because of evaporation.
[b]For ultrasonic nebulizers, vibration of the reservoir fluid causes a temperature increase during aerosol generation, which can be 10°C to 15°C.

BOX 40.6 Optimal Technique for Using a Small Volume Nebulizer

1. Assess the patient for need (clinical signs and symptoms, breath sounds, peak flow, $\%FEV_1$).
2. Select mask or mouthpiece delivery (nose clips may be needed with mouthpiece).
3. Use conserving system (thumb port, breath actuator, or reservoir) if indicated.
4. Place drug in the nebulizer. If using a multidose vial, add saline to approved dose volume (per drug label).
5. Set gas flow to nebulizer at 6 to 10 L/min (per manufacturer label).
6. Coach patient to breathe slowly through the mouth at normal V_T.
7. Continue treatment until nebulizer begins to sputter.
8. Rinse the nebulizer with sterile water and air dry, or discard, between treatments.
9. Monitor patient for adverse response.
10. Assess outcome (change in peak flow, $\%FEV_1$).

$\%FEV_1$, Percentage forced expiratory volume in 1 s; *V_T*, tidal volume.

delivery system. Slow inspiratory flow optimizes SVN aerosol deposition. However, deep breathing and breath holding during SVN therapy do little to enhance deposition over normal tidal breathing.[47] Because the nose is an efficient filter of particles larger than 5 µm, many clinicians prefer not to use a mask for SVN therapy. As long as the patient is mouth breathing, there is little difference in clinical response between therapy given by mouthpiece and therapy given by mask. The selection of delivery method (mask or mouthpiece) should be based on patient ability, preference, and comfort.

Infection control issues. The CDC recommends that nebulizers be cleaned and disinfected, rinsed with sterile water, or air dried between uses. Jet SVNs have reservoirs that are open to and positioned below the mouthpiece or mask. This allows secretions from the patient to enter the medication cup, contaminating medication.

Multidose drug containers have been associated with contamination. After 7 days of nebulizer use, five of six multidose containers of medication solutions were found to be contaminated.[11,48] Refrigerating solutions and discarding syringes every 24 hours eliminated bacterial contamination.

RULE OF THUMB Multidose drug bottles have been associated with contamination. Therefore, single-dose amp should be preferred for aerosol drug delivery to patients with pulmonary diseases. When a multidose drug bottle is used, the solution should be refrigerated, and syringes should be discarded every 24 h to eliminate bacterial contamination.

Large Volume Jet Nebulizers

Large volume jet nebulizers are also used to deliver aerosolized drugs to the lung and are particularly useful when traditional dosing strategies are ineffective in the management of severe bronchospasm. When a patient with airway obstruction does not respond to a standard dosage of bronchodilator, it is common to repeat the treatment every 15 minutes. An alternative approach is to provide continuous nebulization with a specialized large volume nebulizer.

The high-output extended aerosol respiratory therapy nebulizers HEART (Cardinal Health, Dublin, OH) and HOPE (B & B Medical Technologies, Carlsbad, CA) are examples of devices designed for this purpose. These nebulizers have a reservoir greater than 200 mL that produces an aerosol with an MMAD of 2.2 to 3.5 µm. Actual output and particle size vary with the pressure and flow at which the nebulizer operates. A concern with continuous bronchodilator therapy (CBT) is increased drug concentration. Patients receiving CBT need close monitoring for signs of drug toxicity (e.g., tachycardia and tremor). An additional strategy is to use an intravenous (IV) infusion pump to drip premixed bronchodilator solution into a standard SVN. Although this is an equipment-intensive approach, this technique can provide dosing equivalent to intermittent nebulization for the treatments of adults with acute asthma.[49]

Another special-purpose large volume nebulizer is a *small particle aerosol generator (SPAG)* (Fig. 40.17). The SPAG was developed in the 1940s to study pathogen aerosols and subsequently manufactured by ICN Pharmaceuticals specifically for administration of ribavirin (Virazole) to infants with respiratory syncytial virus infection. The device is unique in clinical respiratory care practice. It incorporates a drying chamber with its own flow control to produce a stable aerosol. The SPAG reduces medical gas source from the normal 50 *pounds per square inch*

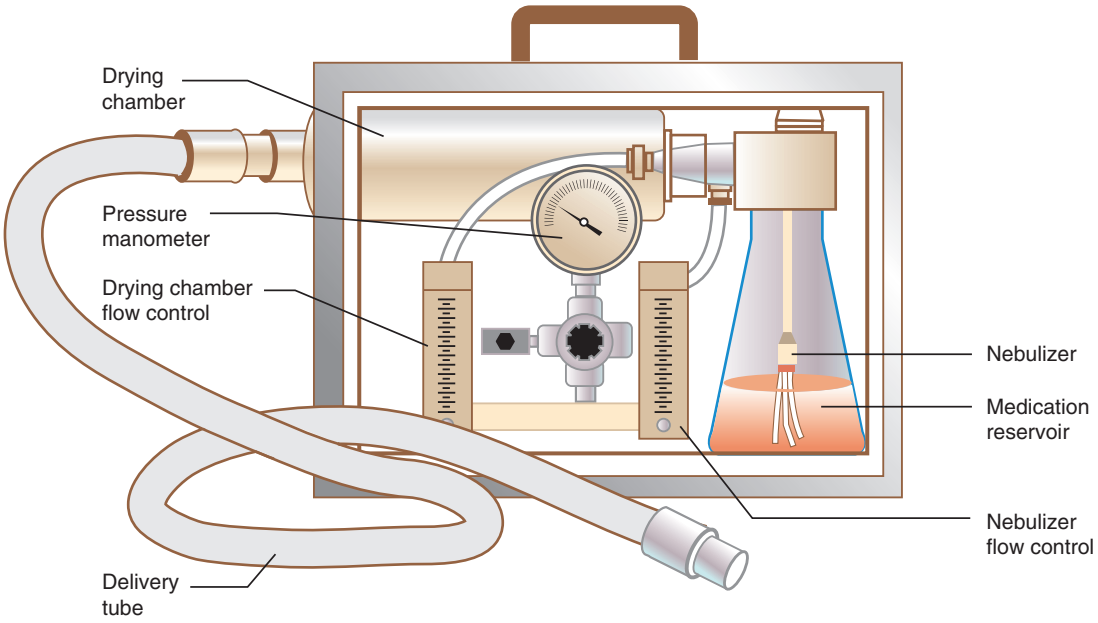


Fig. 40.17 Small-Particle Aerosol Generator.

gauge (psig) line pressure to 26 psig with an adjustable regulator. The regulator is connected to two flowmeters that separately control flow to the nebulizer and flow through the drying chamber. The nebulizer is located within the glass medication reservoir, the fluid surface and wall of which serve as primary baffles. As it leaves the medication reservoir, the aerosol enters a long, cylindrical drying chamber. Here the second (separate) flow of dry gas is added, reducing particle size by evaporation, creating a monodisperse aerosol with an MMAD of 1.2 to 1.4 µm. Nebulizer flow should be maintained at approximately 7 L/min with total flow from both flowmeters not less than 15 L/min. The latest model operates consistently even with back pressure and can be used with masks, hoods, tents, or ventilator circuits.

Two specific problems are associated in the delivery of ribavirin with SPAG. The first is caregiver exposure to the drug aerosol. Approaches to limit caregiver exposure are discussed later (see the section on Controlling Environmental Contamination). The other problem occurs only when the SPAG is used to deliver ribavirin through a mechanical ventilator circuit. Drug precipitation can jam breathing valves or occlude the ventilator circuit. This problem can be overcome by: (1) placing a one-way valve between the SPAG and the circuit, (2) filtering out the excess aerosol particles before they reach the exhalation valve, and (3) changing filters frequently to avoid increasing expiratory resistance.[47]

Hand-Bulb Atomizers and Spray Pumps

Hand-bulb atomizers and nasal spray pumps are used to administer sympathomimetic, anticholinergic, antiinflammatory, and anesthetic aerosols to the upper airway, including nasal passages, pharynx, and larynx (see also Chapter 36). These agents are used to manage upper airway inflammation and rhinitis, to provide local anesthesia, and to achieve systemic effects.

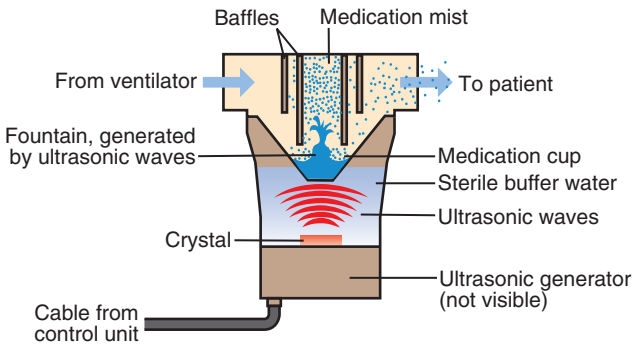


Fig. 40.18 Small volume ultrasonic nebulizers designed for use with mechanical ventilation. A vibrating piezoceramic crystal generates ultrasonic waves that pass through couplant (sterile buffer water) and the medication cup to generate a fountain (or *standing wave*) of medication that produces aerosol particles.

Because the spray pump generates relatively low pressure and does not have baffles, it produces an aerosol with large particle size (high MMAD and GSD), ideal for upper airway deposition. (Nasopharyngeal deposition is greatest for particles 5 to 40 µm.) Deposition with the hand-bulb atomizer applied to the nose occurs mostly in the anterior nasal passages with clearance to the nasopharynx. The 100-mcL puffs appear to deposit more medication than 50-mcL puffs, and deposition to a greater surface area occurs with a 35-degree spray angle than with a 60-degree angle.

Ultrasonic Nebulizers

The USN uses a piezoelectric crystal to generate an aerosol. The crystal transducer converts an electrical signal into high-frequency (1.2- to 2.4-MHz) acoustic vibrations. These vibrations are focused in the liquid above the transducer, where they disrupt the surface and create oscillation waves (Fig. 40.18). If the frequency of the

signal is high enough and its amplitude strong enough, the oscillation waves form a standing wave that generates a geyser of droplets that break free as fine aerosol particles.

USNs are capable of higher aerosol outputs (0.2 to >1.0 mL/min) and higher aerosol densities than conventional jet nebulizers. Output is determined by the amplitude setting (sometimes user selected). The greater the signal amplitude, the greater the nebulizer output. Particle size is inversely proportional to the frequency of vibrations. Frequency is device specific and is not user adjustable. For example, the DeVilbiss (Somerset, PA) Portasonic nebulizer operating at a frequency of 2.25 MHz produces particles with an MMAD of 2.5 μm, whereas the DeVilbiss Pulmosonic nebulizer operating at 1.25 MHz produces particles in the 4- to 6-μm range. Particle size and aerosol density also depend on the source and flow of gas conducting the aerosol to the patient.

Large volume ultrasonic nebulizers. Large volume USNs (used mainly for bland aerosol therapy or sputum induction) incorporate air blowers to carry the mist to the patient (see Chapter 39). Low flow through the USN is associated with higher mist density. In contrast to jet nebulizers, the temperature of the solution placed in a USN increases during use. As the temperature increases, the drug concentration increases, and proteins can be denatured.

Small volume ultrasonic nebulizers. Many small volume USNs have been marketed for aerosol drug delivery (see Fig. 40.18). In contrast to the larger units, some of these systems do not use a couplant compartment; the medication is placed directly into the manifold on top of the transducer. The transducer is connected by a cable to a power source, often battery-powered to increase portability. These devices have no blower; the patient's inspiratory flow draws the aerosol from the nebulizer into the lung.

Small volume USNs administer a wide variety of formulations ranging from bronchodilators to antiinflammatory agents and antibiotics.[9] Suspensions such as budesonide may not nebulize well with USNs, because large suspension aerosol particles that are larger than the aerosol particles remain in the medication cup. Use of a small volume USN may increase available respirable mass for designs with less residual drug volume than SVNs; this may reduce the need for a large quantity of diluent to ensure delivery of the drugs. The contained portable power source adds a great deal of convenience in mobility. However, sometimes the theoretical advantages of the ultrasonic devices are outweighed by relatively high purchase costs and poor reliability.

Small volume USNs have been used to administer undiluted bronchodilators to patients with severe bronchospasm.[50] Because the nebulizers have minimal residual drug volume, the treatment time is reduced with smaller volumes; however, it may be increased with standard dosing volumes. Some ventilator manufacturers (e.g., Maquet, Rastatt, Germany) have promoted the use of USNs for administration of aerosols during mechanical ventilation. In contrast to SVNs, USNs do not add extra gas flow to the ventilator circuit during use. This feature reduces the need to change and reset ventilator and alarm settings during aerosol administration.

Vibrating Mesh Nebulizers

The two types of commercially available VM nebulizers are active and passive.[9,51] Active VM nebulizers use a dome-shaped aperture plate, containing more than 1000 funnel-shaped apertures. The dome is attached to a plate that is also connected to a piezoceramic element surrounding the aperture plate. Electrical energy applied to the piezoceramic element vibrates the aperture plate at a frequency of approximately 130 kHz (or one-tenth that of a USN), moving the aperture plate up and down by approximately 1 to 2 μm and acting as an electronic micropump. The plate actively pumps the liquid through the apertures, where it is broken into fine droplets. The exit velocity of the aerosol is low (<4 m/s), and the particle size can range from 3 to 4 μm (MMAD), varying with the exit diameter of the apertures. Examples of an active VM nebulizer (Fig. 40.19A to C) include the Aeroneb Solo nebulizers (Aerogen, Ltd, Galway, Ireland) and the eFlow nebulizers (Pari) and Innospire Go (Phillips Respironics, Murraysville, PA, USA). An active VM nebulizer can nebulize single drops of 15 mcL of formulations containing small and large molecules, suspensions, microsuspensions, and liposomes.

Passive VM nebulizers (see Fig. 40.19D) use a mesh separated from an ultrasonic horn by the liquid solution for nebulization. A piezoelectric transducer vibrates the ultrasonic horn, which pushes fluid through the mesh. Passive VM nebulizers include the MicroAir U100, the NEU-22 (Omron, Kyoto, Japan), and the I-Neb (Philips Respironics, Murrysville, PA).

The residual drug volumes with either type of VM nebulizer range from 0.1 to 0.4 mL, in contrast to other types of liquid aerosol generators with residual drug volumes of 0.8 to 1.5 mL. Because a greater percentage of standard unit doses is emitted as aerosol, care should be exercised when transitioning to these devices to ensure that the higher dose does not create adverse effects.

Smart Nebulizers

Low-velocity (soft mist) aerosol, smaller particle size distribution, and systems that minimize residual volume of medication left in the nebulizer substantially improve aerosol device efficiency. Along with improved performance, some "smart" nebulizers have the capability to monitor patient compliance and aid in managing the patient's treatment schedule.

With pulmonary deposition increased from the old standard of approximately 10% to more than 60% of the nominal dose, these recent device improvements may be accompanied by greater systemic side effects, unless the delivered dose is reduced. The key is to be able to target an effective delivered dose to the lungs.

The I-Neb (Philips Respironics) is a breath-actuated passive VM nebulizer with *adaptive aerosol delivery* that monitors pressure changes and inspiratory time for the patient's first three consecutive breaths (Fig. 40.20).[52,53] Drug is then aerosolized over 50% of the inspiratory maneuver during the fourth and all subsequent breaths. *Targeted inhalation mode* guides the patient to take serially longer inspirations to achieve optimal inhalation duration, reducing the time for administration. When the prescribed emitted dose has been aerosolized, the system provides an audible signal indicating the treatment should be stopped and the remaining medication discarded. Built-in electronics monitor patient treatment schedules and delivered doses with the goal to improve compliance with therapy. The I-Neb has been released for delivery of prostacyclin.

Fig. 40.19 Variety of Available Mesh Nebulizers. (A) Aerogen Solo (Courtesy Aerogen, Galway, Ireland), (B) PARI e-Flow (Courtesy Pari, Midlothian, VA), (C) Innospire Go (Courtesy Philips Healthcare, Murrysville, PA), and (D) iNeb (Courtesy Phillips Healthcare, Murrysville, PA). A and B are active mesh nebulizers, while C and D are examples of passive mesh nebulizers. Active vibrating mesh (VM) nebulizer has an aperture plate with funnel-shaped holes vibrated by a piezoelectric transducer surrounding the aperture plate found in the nebulizer. Passive VM nebulizer uses an ultrasonic horn to push fluid through a stationary mesh found in the nebulizer.

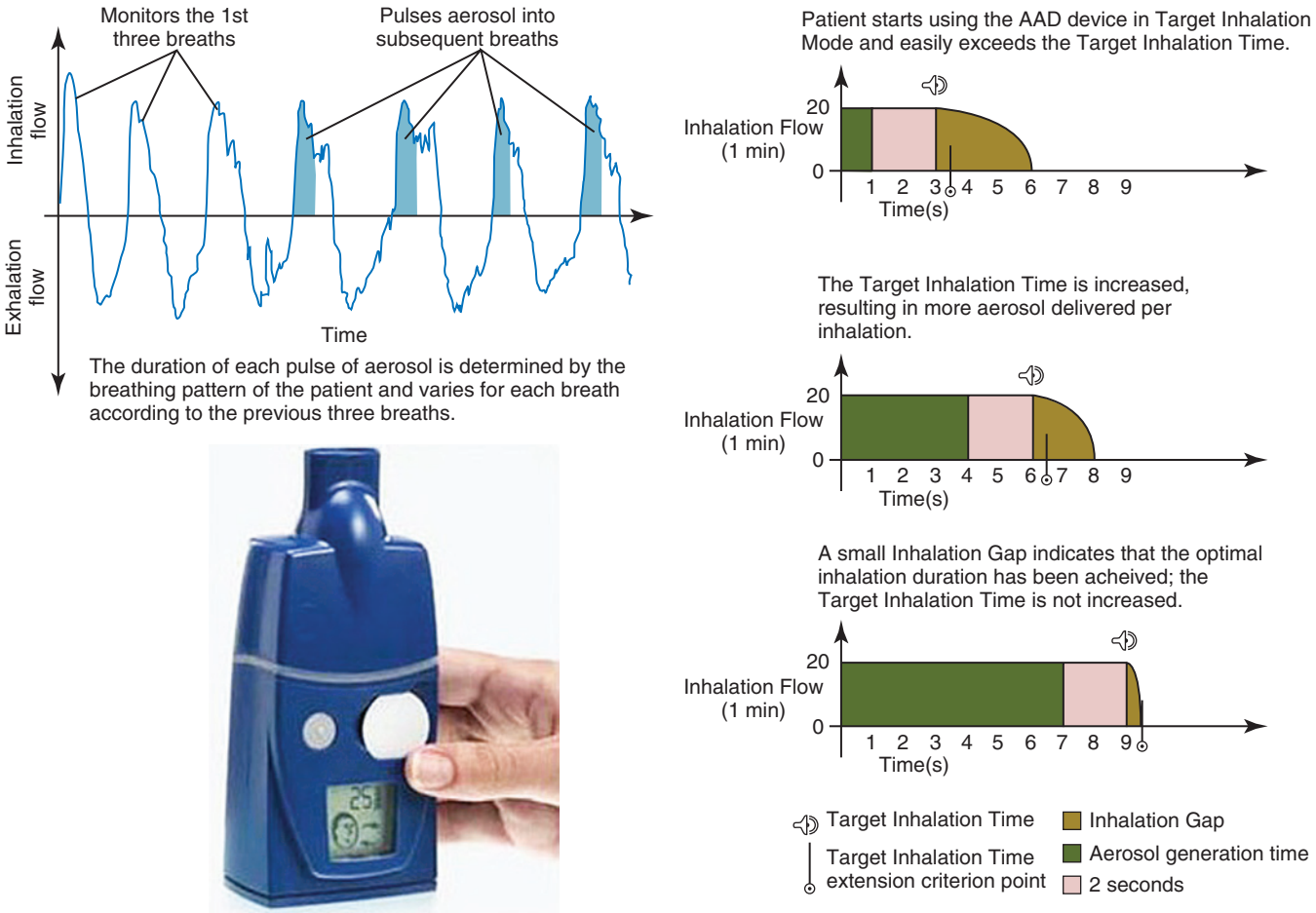


Fig. 40.20 The iNeb *(bottom left)* is a smart nebulizer with adaptive aerosol delivery (AAD) and targeted inhalation mode (TIM). AAD delivers a precise preset dose with variation between patients. A microprocessor tracks the patient's breathing pattern on a running average of the previous three breaths, generating aerosol for 50% of the predicted inspiration *(upper left)*. TIM progressively guides the patient to take longer inspirations, increasing to achieve optimal inhalation duration *(right)*.

The Akita (Activaero, Gemuenden/Wohra, Germany) allows controlled inhalation of aerosol produced by either a jet or VM nebulizer (Fig. 40.21). The Akita controls inspiratory flow to keep it slow (12 to 15 L/min), reducing impaction loss of aerosols in the upper airways. Patient pulmonary function is stored on a smart card programmed to tell the device when to generate aerosol during inspiration. Aerosol generated early targets distal airways, whereas aerosol generated later in the breath targets larger, more central airways.[54] Smart nebulizers can track the actual time, duration, and dose administered for each treatment and provide logs of use that can be downloaded for the medical or research record.

Fox. The Fox inhalation system (Vectura Group, Wiltshire, UK) is an active VM nebulizer with a flow- and volume-controlled inhalation system that increases intrapulmonary deposition. The device targets aerosol deposition in the peripheral and central airways by controlling the time of aerosol release during therapy. Although releasing the aerosol at the beginning of inspiration leads to peripheral deposition, the release of aerosols in the middle of inhalation results in aerosol deposition in central airways. The Fox inhalation system is approved for delivery of different medications in Europe but not available in the United States.

Fig. 40.21 The AKITA Smart Nebulizer.

Dance 501. The Dance 501 (Dance Biopharm, San Francisco, CA) is a VM nebulizer (Aerogen Ltd, Galway, Ireland) that is designed for the treatment of patients with diabetes. Because it generates aerosol only when inspiratory flow is between 7 and 14 L/min, it reduces impaction losses and provides optimal lung deposition.[55] Dance 501 is a small, silent, hand-held smart nebulizer that is portable and easy to use. The nebulizer has a mouthpiece with reservoir that needs to be cleaned between doses.

New nebulizer designs for liquid medications.

InnoSpire Go. The InnoSpire Go (Philips Healthcare, Newark, NY) is a hand-held mesh nebulizer that is small, silent portable, and easy to use and clean with two parts assembly. The treatment time of the InnoSpire Go is 4 minutes with salbutamol of 2.5 mL. It is battery operated with a built-in rechargeable battery that operates for up to 30 treatments. The InnoSpire Go provides audible and visual signals to patients when the treatment is complete.

Examples of nebulizers with drug device combinations.

Lonhana magnair. The Lonhana Magnair (Sunovion Pharmaceuticals Inc) delivers glycopyrrolate, which is a long-acting muscarinic antagonist (anticholinergic) used for maintenance treatment of COPD twice daily (Fig. 40.22A). It is a drug/device combination that is portable, battery powered and silent. The Lonhana Magnair is combined with a mesh nebulizer that does not require any specific breathing technique and complete dosing in 2 to 3 minutes. The device also provides two audio beeps and visual feedback with a green LED light that indicates the nebulization is complete.

Tyvaso. The Tyvaso Inhalation System (United Therapeutic Corperation, Research Triangle Park, NC) is a pulsed USN that is used for delivery of treprostinil. Device preparation requires assembly of different parts of the device including dome, inhalation piece, filters, and mouthpiece (see Fig. 40.22B). A couplant chamber is filled with water between the piezo and the medication

Fig. 40.22 New Nebulizer Technologies. Tyvaso Inhalation System. (Courtesy Tyvaso® Inhalation Device (TD-300/A) and supplier, United Therapeutics Corporation.)

cup. A daily dose is placed in the medication cup, and patients are instructed to take a set number of breaths per treatment, at set intervals during the day, with the device cleaned at the end of the day. The Tyvaso Inhalation System provides auditory and visual feedback on the patient's inhalation technique. In addition, if a patient stops inhalations during therapy, the device shows the remaining breaths in the numerical display that are needed to complete the treatment.

Cayston Altera eFlow

The Cayston Altera eFlow (Gilead Pharmaceuticals, Foster City, CA) is a mesh nebulizer with a piezoelectric element that is used to deliver aztreonam lysine (AZLI) to patients with cystic fibrosis. It is battery powered and does not require a compressor to operate.

Staccato. The Staccato (Alexza Pharmaceuticals, Mountain View, California) uses a thermal aerosol technology that has three components, including a heating substrate, a thin film of pure drug, and a channel where aerosol forms. It is a small, portable, breath-actuated device that does not require any type of special breathing technique. Therefore, unlike other DPIs, the Staccato is insensitive to patient inhalation rates. The device generates aerosols by heating a thin film of drug to form pure drug vapor. When the patient inhales, the vapor cools and condenses into 1- to 3-μm-diameter particles. Thus pure drug can be delivered to the alveoli without extensive thermal degradation and with the optimal range of particle diameter, promoting very fast systemic drug absorption. The Staccato has been approved in the United States for delivery of loxapine.

Soft Mist Inhalers

Respimat. The Respimat soft mist inhaler (Boehringer Ingelheim) is a small hand-held inhaler that uses mechanical energy to create an aerosol from liquid solutions to produce a low-velocity spray (10 mm/s) that delivers a unit dose of drug in a single actuation. To operate the device, patients twist the body of the device to load an internal spring, place the mouthpiece of the Respimat between the lips, and press a button to release the drug through a uniblock to create the aerosol, which is released over 1.1 to 1.4 seconds, depending on the formulation configuration.[56,57] The Respimat requires hand–breath coordination on the part of the patient, as does a pMDI, but because of the longer aerosolization time, it seems more likely that the patient will get a greater percentage of emitted dose despite coordination issues. Because of the small particle size and low-velocity spray, pulmonary deposition of 40% is independent of inspiratory flows with oral deposition (40%) half the oral deposition with most pMDIs and DPIs (80%). The Stiolto Respimat (tiotropium bromide and olodaterol) and the Spiriva Respimat are currently available in the United States and have been prescribed for patients with COPD.

Aqueous droplet inhaler liquid inhaler device. The Aqueous Droplet Inhaler (ADI) liquid inhaler device (Pharmaero, Copenhagen, Denmark) is a soft mist inhaler that delivers small or large volumes of liquid medications in a low-velocity aerosol mist. The ADI liquid inhaler device does not require any source of power to operate and has a five-step operation system including insert the syringe, wind up, push button, inhale, and repeat. The treatment time with the IDA liquid inhaler is 2 minutes. In addition, cleaning after treatment is not needed with the ADI liquid inhaler device because the mouthpiece used with the device is disposable.

Advantages and Disadvantages of Aerosol Systems

Knowledge of the advantages and disadvantages of various aerosol drug delivery systems is crucial for proper selection and application. Table 40.3 compares pMDI, DPI, SVN, and USN delivery systems.

Special Medication Delivery Issues for Infants and Children

Children and infants have a smaller airway diameter than adults. In addition, their breathing rate is faster, and nose breathing

TABLE 40.3 Advantages and Disadvantages of Aerosol Drug Delivery Systems

	Advantages	Disadvantages
pMDI	Convenient	Patient coordination required
	Inexpensive	Patient activation required
	Portable	High percentage of oropharyngeal deposition
	No drug preparation required	Not all medications are available
	Difficult to contaminate	Expensive
pMDI with accessory device	Less patient coordination required	More expensive than pMDI alone
	Less oropharyngeal deposition	More complex than pMDI alone
	No drug preparation needed	Less portable than pMDI alone
DPI	Less patient coordination required	Required high inspiratory flow
	Breath activated	Most units are single dose
	Breath hold not required	Risk of oropharyngeal deposition
	Built-in dose counters	Expensive
SVN	Inexpensive	Large residual volume
	Less patient coordination required	Drug preparation required
	High doses possible (even continuous)	Compressed gas or compressor required
		Long treatment time
		Contamination possible if device is not cleaned carefully
USN	Quiet	Expensive
		Drug preparation required
		Prone to electrical or mechanical breakdown
		Large residual volume
VM nebulizer	Quiet	Expensive
	Small residual volume	Drug preparation required

DPI, Dry powder inhaler, *pMDI*, pressurized metered dose inhaler; *SVN*, small volume nebulizer; *USN*, ultrasonic nebulizer; *VM*, vibrating mesh.

filters out large particles and deposits more medication in the upper airway. Furthermore, mouthpiece administration often cannot be used before 3 years of age.[58] Patient cooperation and ability vary with age and developmental level. Finally, infants and small children have lower minute volumes than adults and so inhale a smaller proportion of the output of continuous nebulizers than adults.[59]

Normal tidal breathing is the most effective method for administering aerosols to an infant. Mouth breathing enhances medication delivery to the airways of adults, but there is little evidence to show that this is true for infants, who are preferential nose breathers up to 1 year of age. Crying greatly reduces lower airway deposition of aerosol medication; therefore aerosols should not be administered to a crying child (Fig. 40.23).

MINI CLINI

Aerosol Drug Delivery and Crying Infants

Problem

Child cries during aerosol therapy.

Discussion

Crying greatly reduces inhaled dose, making aerosol ineffective. Many infants and toddlers (up to 49%) do not tolerate aerosol masks without crying and fussing. Aerosol delivery should be avoided when the infant or toddler is crying, because it just wastes the medication. Efforts can be made to turn the aerosol mask into a "toy" and treatments into playtime so the child is entertained rather than scared. Alternatively, interfaces such as tents, hoods, or nasal cannula may be better tolerated by the infant. Caution: Blow-by may be tolerated but is associated with very poor deposition and should be avoided.

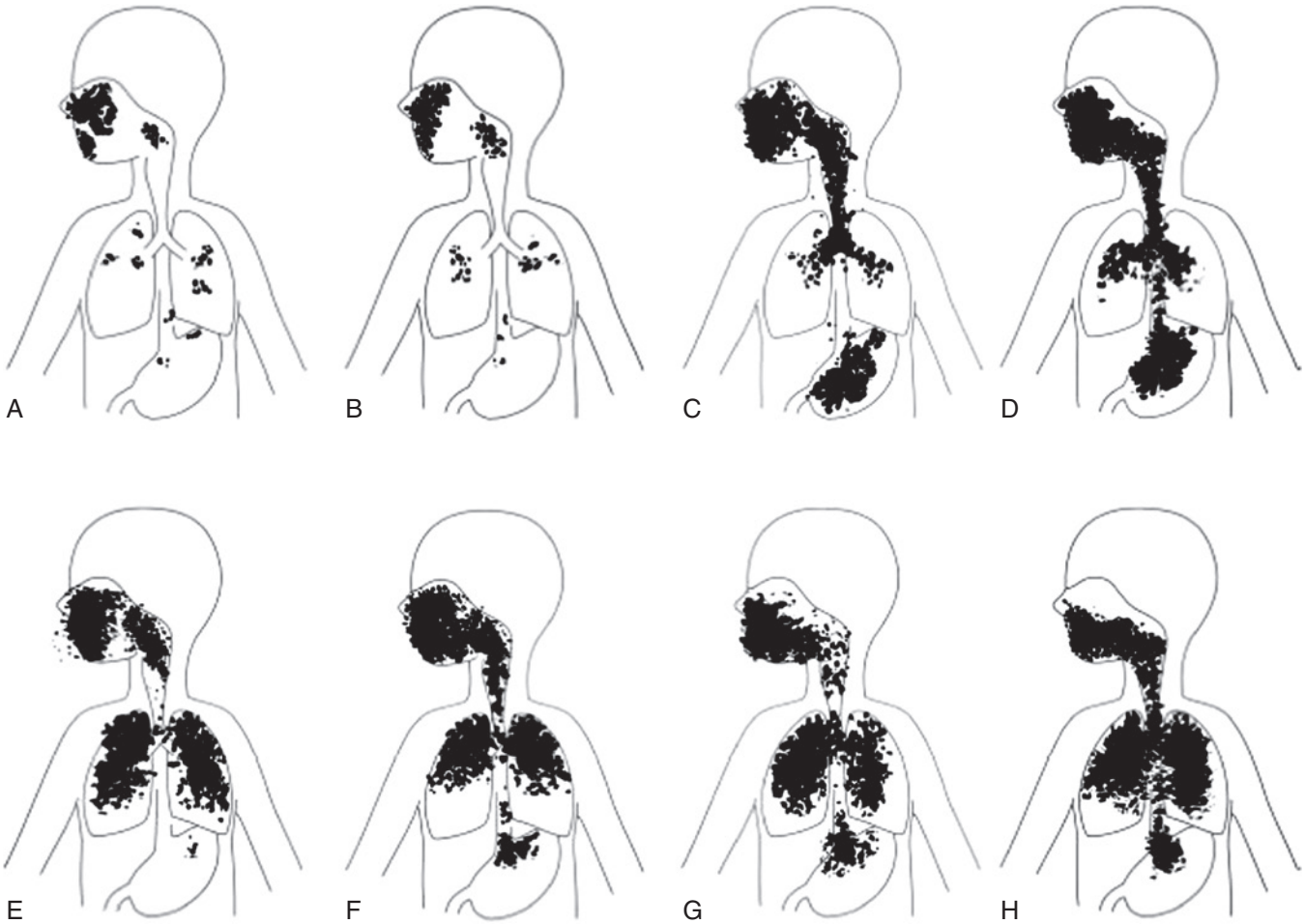


Fig. 40.23 Drug deposition of radiolabeled albuterol in a young child (A) inhaling with a pressurized metered dose inhaler (pMDI)/space through a non–tightly fitted facemask; (B) inhaling with a nebulizer through a non–tightly fitted facemask; (C and D) inhaling with a pMDI/spacer through a tightly fitted facemask, screaming during inhalation; (E and F) inhaling with a pMDI/spacer through a tightly fitted facemask, quietly inhaling; and (G and H) inhaling from a nebulizer through a tightly fitted facemask, quietly inhaling. (Redrawn from Erzinger, S, Schueepp, KG, Brooks-Wildhaber, J, et al: Facemasks and aerosol delivery in vivo, *J Aerosol Med* 20(Suppl 1.):S78–S84, 2007.)

For infants and children who can tolerate a mask, a medication nebulizer can be fitted to an appropriately sized aerosol mask. There is no difference in clinical response between mouthpiece and close-fitting mask treatment, so patient tolerance, compliance, and preference should guide selection of the device. There is evidence that the aerosol available to the patient is substantially less when a loosely fitting mask (>1 cm leak) is used rather than a snug mask or mouthpiece with either a nebulizer or a pMDI with a holding chamber.[54,58,60] If a patient cannot tolerate mask treatment (e.g., will not wear a close-fitting mask without agitation), a commonly used strategy is the "blow-by" technique, in which the practitioner directs the aerosol from the nebulizer toward the patient's nose and mouth from a distance of several inches from the face. Studies suggest a greatly reduced inhaled dose with blow-by. Rather than "blow-by," it may be more efficient to take the time to condition the infant or child to tolerate the mask without crying or to deliver medication with a close-fitting mask when the patient is asleep.[61]

As shown in Fig. 40.24, a pediatric mask with an integrated pacifier uses the infant's pull on the pacifier to hold the mask in place with improved face-mask seal which may reduce agitation and crying associated with standard masks (Soother Mask, InspiRx Inc, Somerset, NJ). Given the cognitive and functional limitations of very young patients, not all delivery devices are suitable for these patients. To help guide clinicians, the accompanying Rule of Thumb outlines age-specific guidelines for using aerosol devices in pediatric and neonatal patients.

RULE OF THUMB: Guidelines for Use of Aerosol Devices in the Care of Infants and Children

Device	Age Group
Small volume nebulizer	Neonate to all ages
Valved chamber with mask	Neonate/infant/toddler
Valved chamber with mouthpiece	>3 years
Pressurized metered dose inhaler alone	>4 years
Breath-actuated nebulizer	>4 years
Dry powder inhaler	≥4 years

Fig. 40.24 The SootherMask. (Courtesy of InspiRx, Somerset, NJ).

Spontaneous breathing in all patient populations results in greater deposition of aerosol from an SVN than occurs with positive pressure breaths (e.g., intermittent positive pressure ventilation [IPPB]). IPPB reduces aerosol deposition more than 30% compared with spontaneously inhaled aerosols.[62]

Selecting an Aerosol Drug Delivery System

pMDIs, DPIs, and nebulizers all work with comparable clinical results, as long as they are prescribed for the appropriate patients and are used properly.[1,38,63] Consequently, clinicians need to know the strengths and limitations of each type of device, match the device to each patient, and ensure that the patient or caregiver is trained to use the device properly.[30] Fig. 40.25 is an algorithm that provides guidance regarding device selection.

Regardless of the device used, the clinician must be aware of the limitations of aerosol drug therapy. Depending on the device and the patient, 10% or less of drug emitted from an aerosol device may be deposited in the lungs (Fig. 40.26). As indicated in Box 40.7, additional reductions in lung deposition can occur in many clinical situations that sometimes necessitate the use of higher dosages. Clinical efficacy varies according to both patient technique and device design. For these reasons, the best approach to aerosol drug therapy is to use an assessment-based protocol that emphasizes individually tailored therapy modified according to patient response.

MINI CLINI

Device Selection in Aerosol Therapy

Problem

The variety of aerosolized medications continues to expand, but many are limited to a specific pMDI, DPI or nebulizer. Even when we have an effective medication with excellent molecular structure, we may not be able to administer the medication because clinicians did not make the right device selection for their patient or they do not know how to use aerosol delivery devices properly.

Discussion

It is essential for clinicians to understand the characteristics of the available device, select the best device/interface combination, and know how to use them effectively. When selecting an aerosol delivery device, clinicians should use a patient-focused approach and individualize device and interface selection based on patients' age, physical and cognitive abilities, as well as patient preference and acceptance. As clinicians become familiar with the characteristics of aerosol delivery devices and know how to overcome challenges associated with aerosol therapy, they will be able to optimize aerosol drug delivery to patients.

BOX 40.7 Factors Associated With Reduced Aerosol Drug Deposition in the Lung

- Mechanical ventilation
- Artificial airways
- Reduced airway caliber (e.g., infants and children)
- Severe airway obstruction
- High gas flows
- Low minute volumes
- Poor patient compliance or technique
- Limitation of specific delivery device

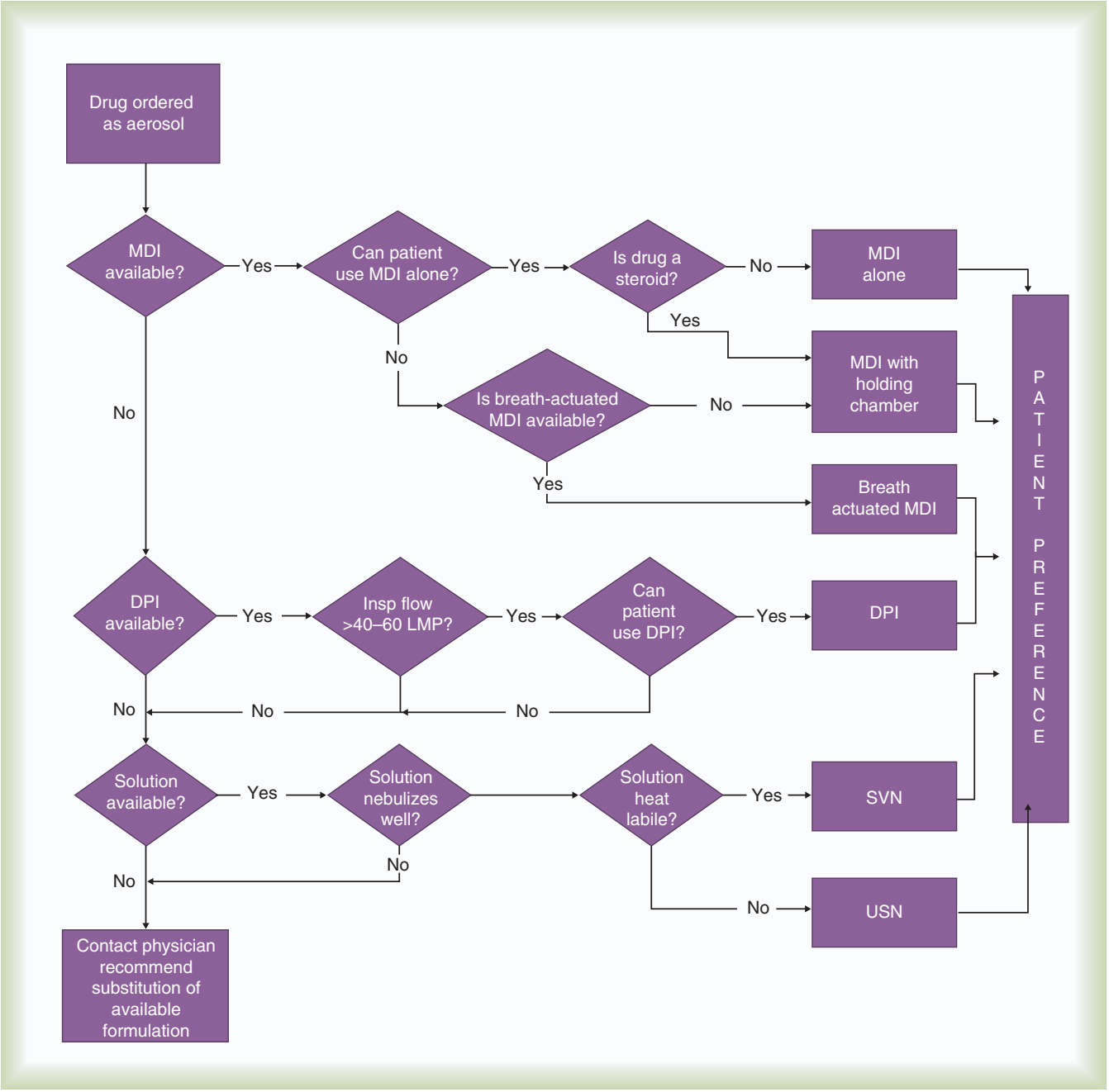


Fig. 40.25 Selecting an Aerosol Drug Delivery System. When the need is established for aerosol drug delivery, the formulations available for the prescribed medication should be determined. If a pressurized metered dose inhaler is available, it is the first choice for cost and convenience. The patient's ability to coordinate actuation with inspiration and the need to reduce oropharyngeal deposition (e.g., steroids) determine need for a holding chamber or a breath-actuated unit. Nebulizers are the first choice when the formulation is available only as a solution. When the ordered medication is unavailable for inhalation use, the respiratory therapist should recommend a substitution to the ordering physician.

ASSESSMENT-BASED BRONCHODILATOR THERAPY PROTOCOLS

Although the choice of delivery system affects how well an aerosolized drug works, it is ultimately the patient's response that determines the therapeutic outcome. Because patients vary markedly in response to the dose and route of drug administration, it makes sense to tailor aerosol drug therapy to each patient. This approach is best determined with an assessment-based protocol.

Sample Protocol

Fig. 40.27 illustrates the setup that can be used for continuous nebulization for acutely ill adults or children admitted to an emergency department. Continuous nebulization relies heavily on bedside assessment of the severity of airway obstruction based on the patient's response to varying drug dosages.

According to the algorithm, a patient with acute airway obstruction (wheezing, cough, dyspnea, and peak expiratory flow rate [PEFR] <60% of predicted value) would receive up to three SVN treatments with a standard dose of albuterol, repeated at 20-minute intervals, or four puffs of pMDI albuterol with a holding chamber (up to 12 puffs). Each treatment is followed by a dose-response assessment to determine the "best" dose. Once determined, this best dose, with the pMDI or SVN, is repeated 1 hour later, then every 4 hours as needed, supplemented with patient education. If use of the SVN or pMDI with holding chamber fails to relieve the symptoms, CBT with 15 mg/h albuterol is generally started.

Assessing Patient Response

Careful, ongoing patient assessment is key to an effective bronchodilator therapy protocol.

Use and Limitations of Peak Flow Monitoring

Because the peak flow measurement is effort dependent and volume dependent, evaluation of patient performance is subjective, and there are no good acceptability criteria. In addition, agreement between conventional spirometry values, such as forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV_1), and bedside PEFR values are poor for individual patients. Although peak flow measurement can be used at the bedside to assess treatment effectiveness and to monitor trends, conventional spirometry remains the standard for determining bronchodilator response.

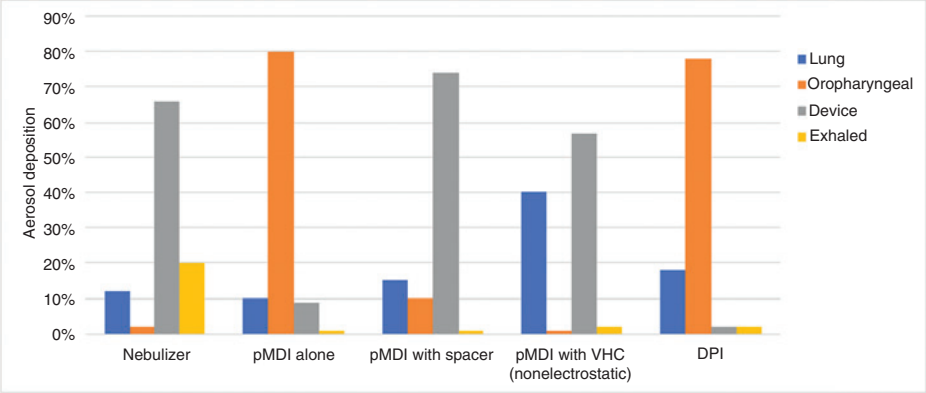


Fig. 40.26 Distribution of albuterol via nebulizer, pressurized metered dose inhaler (pMDI), pMDI with a holding chamber, and dry powder inhaler.

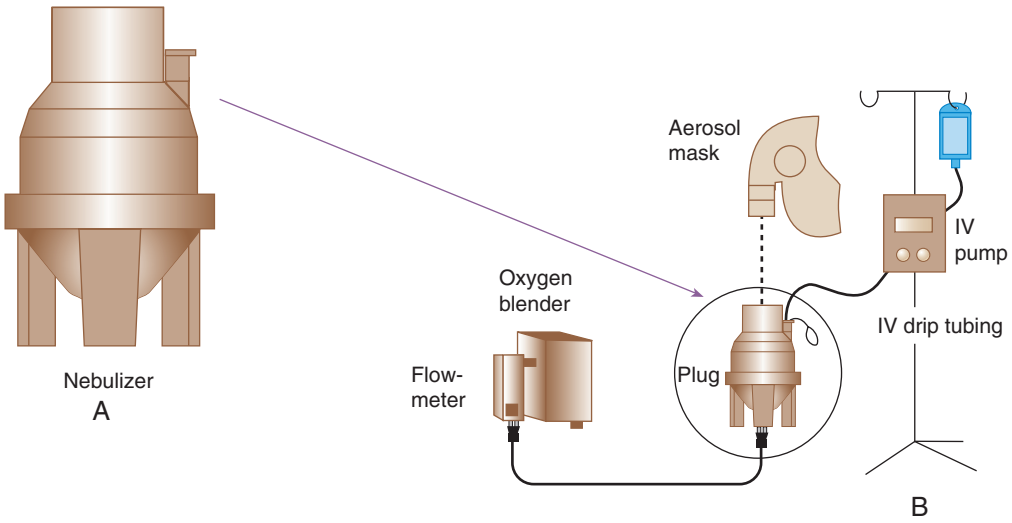


Fig. 40.27 The Setup That Can Be Used for Continuous Nebulization.

Some peak flowmeters are more accurate and reliable than others. Even different units of the same model may give variable results. For this reason, when monitoring trends, the same unit should be used for a given patient, and the patient's range should be reestablished if a different flowmeter is used.

RULE OF THUMB

- It is important to use the same flowmeter when monitoring the patient's flow rates due to variation in results among different peak flowmeters.

MINI CLINI

Spirometry and Peak Flows During Exacerbation

Problem

A patient in the emergency department presents with asthma and is having difficulty breathing. A peak flow measurement is attempted before administration of aerosol bronchodilator, but patient does not appear to be able to complete the maneuver. Do you repeat or treat?

Discussion

Definitely proceed to treat. When patients with asthma or COPD are short of breath, use of spirometry and peak flow may not be possible or reliable. Rather than repeating the test, which may further irritate or tire the patient, it is better to proceed with the bronchodilator therapy, and document that patient was unable to perform the peak flow.

Other Components of Patient Assessment

Tests of expiratory airflow for assessing patient response to therapy are commonly used, but not all patients can perform these maneuvers. Other components of patient assessment useful in evaluating bronchodilator therapy include patient interviewing and observation, measurement of vital signs, auscultation, blood gas analysis, and oximetry.

When possible, the patient should be interviewed to determine the pertinent respiratory history and current level of dyspnea. A validated dyspnea rating scale may be useful for this purpose. Initial determination of patient age and level of consciousness is helpful in selecting both delivery device and starting drug dosage. Observing the patient for signs of increased work of breathing (e.g., tachypnea, accessory muscle use) provides a baseline for assessing status as therapy progresses. Restlessness, diaphoresis, and tachycardia also may indicate severity of airway obstruction but must not be confused with bronchodilator overdose.

Increased cough has been associated with the onset of asthma. The frequency, severity, and effectiveness of cough should be assessed before and after therapy.

In terms of breath sounds, a decrease in wheezing accompanied by an overall decrease in the intensity of breath sounds indicates worsening airway obstruction or patient fatigue. Improvement is indicated when wheezing decreases and the overall intensity of breath sounds increases.

All patients with acute airway obstruction should be monitored for oxygenation status with pulse oximetry. This value can be used in conjunction with observational assessment to titrate the level of inspired O_2 given to the patient (see Chapter 42). Arterial blood gases are not essential for determining patient response to bronchodilator therapy but may be needed for patients in severe distress to assess for hypercapnic respiratory failure.

Dose-Response Assessment

Poor patient response to bronchodilator therapy often occurs because an inadequate amount of drug reaches the airway. To determine the "best" dose for patients with moderate obstruction, the respiratory therapist (RT) should conduct a dose-response titration.

A simple albuterol dose-response titration involves giving an initial four puffs (90 mcg/puff) at 1-minute intervals through a pMDI with a holding chamber. After 5 minutes, if airway obstruction is not relieved, the RT gives one puff per minute until symptoms are relieved, heart rate increases by more than 20 beats/min, tremors increase, or 12 puffs are delivered. The best dose is the dose that provides maximum relief of symptoms and the highest PEFR without side effects.

Frequency of Patient Assessment

How frequently patients should undergo assessment for bronchodilator therapy depends primarily on the acuity of the condition. An unstable patient in acute distress should undergo closer and more frequent scrutiny than a patient in stable condition. Box 40.8 provides guidance regarding the frequency of assessment according to acuity.

BOX 40.8 Frequency of Assessment of Bronchodilator Therapy

For Patient With an Acute Disorder Who Is in Unstable Condition

- Whenever possible, perform a full assessment and obtain a pretreatment baseline.
- Assess and document all appropriate variables before and after each treatment (breath sounds, vital signs, side effects during therapy, and PEFR or FEV_1).
- The frequency with which physical examination and PEFR or FEV_1 are repeated should be based on the acuteness of the disorder and the severity of the patient's condition.
- SpO_2 should be monitored continuously, if possible.
- Assessment should continue as dosages are changed to optimize patient response (e.g., if an asthmatic patient achieves 70%–90% of predicted or "personal best" or becomes symptomfree).

For Stable Patient

- In the hospital, PEFR should be measured initially before and after each bronchodilator administration. Thereafter, twice-daily determinations may be adequate.
- In the home, PEFR ideally should be measured three or four times a day: on rising, at noon, between 4 PM and 7 PM, and at bedtime.
- For a stable COPD patient at home, measuring PEFR twice a day may be adequate.
- Patients with asthma should adjust the frequency of PEFR measurement according to the severity of symptoms.
- PEFR levels before and after bronchodilator use, medication dose, date and time, and dyspnea score should be documented.
- The patient should be reevaluated periodically for response to therapy.

COPD, Chronic obstructive pulmonary disease; *FEV_1*, forced expiratory volume in 1 s; *PEFR*, peak expiratory flow rate; *SpO_2*, oxygen saturation by pulse oximeter.

Patient Education

The desired outcome of all bronchodilator protocols is restoration of normal airflow and cessation of therapy. For patients who need ongoing maintenance therapy after the acute phase of illness, the goal should be effective self-administration. An effective program of aerosol drug self-administration depends on thorough patient education. Patient education on aerosol therapy should be individualized by providing one-on-one training, using a device preferred by the patient, keeping the device consistent, and developing psychomotor skills of patients with teaching devices.

Through one-on-one training sessions, clinicians can individualize the education session to a specific patient and increase adherence to therapy and improve clinical outcomes.[64,65] The patient's ability to understand the therapy and its goals significantly affects the therapeutic efficacy of any treatment. Whenever possible, patients should be taught to understand the basic administration techniques, to keep track of dosing requirements, to recognize undesirable side effects, and to understand the options and actions required to reduce or eliminate these effects. Previous research showed a relationship between proper inhalation technique and a greater degree of satisfaction with therapy.[66,67] Therefore it is important to choose an aerosol device based on patient preference and use the same type of device for different medications to eliminate patient confusion and increase patient adherence to aerosol therapy.[63] In addition, patients should be able to demonstrate good technique regarding the use of each aerosol device that they are expected to use in self-care. Patient technique with aerosol devices can be assessed and improved through teaching devices such as the 2 Tone, Mag-Flo, or InCheckDial (Fig. 40.28). Although these teaching devices provide an objective evaluation of the patient's inhalation technique, they cannot assess the patient's preparation and handling of the device at home.[68] Practitioner demonstration followed by repeated patient return demonstration is a must and should be done frequently, with each office or clinic visit.

MINI CLINI

Patient Education Continuum—Home to Hospital to Home

Problem

A patient uses inhalers at home and presents to the ED with severe symptoms of shortness of breath and bronchospasm. The ED staff begins aerosol therapy with a jet nebulizer, which is continued in the ICU and the hospital floor until discharge, where the patient goes back to use his inhaler. He may feel better, but when he goes home, he might not be effectively self-administering his inhalers, which brings him back to the ED and hospital more frequently.

Discussion

Does the patient effectively use his inhalers at home? Up to 60% of patients do not use their inhalers well enough to benefit from the medication. When the patient goes to the hospital and receives a nebulizer that is not used at home, we have not addressed a common and obvious problem. Does the patient use their inhaler properly?

It is difficult to learn and retain education when you are fighting for breath, but once the crisis is resolved, there is a "teachable moment" in which the clinician can transfer patients to the medications they use at home, observe how they self-administer, and provide teaching to improve their self-administration skill. A little teaching time can greatly reduce costs of frequent readmissions.

It is also important to monitor patient adherence, because there is a strong association between poor adherence and hospital admission due to exacerbations.[69] In addition, nonadherence to aerosol therapy results in poor disease management, an increase in school and work absenteeism, unscheduled healthcare use, morbidity, and mortality.[69-72] Patient adherence to aerosol therapy can be monitored through patient diaries, clinical judgment, pharmacy data, biochemical measures, and electronic monitoring.[73] Monitoring adherence with patient self-reports and clinical judgment is fast and inexpensive but overestimates patient adherence to prescribed medications.[74,75] Although pharmacy data are

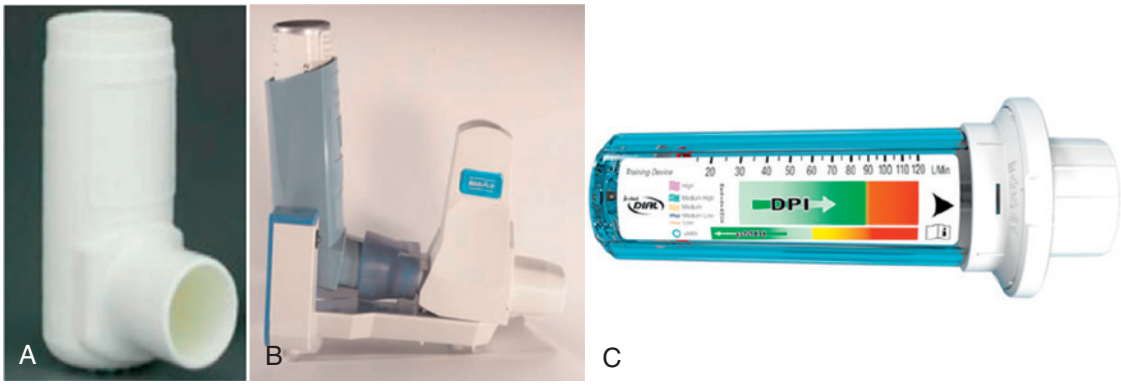


Fig. 40.28 Teaching Devices That Can Be Used for Patient Training and Assessment of Inhalation Technique. (A) 2Tone (Courtesy of Canday Med Ltd, London, UK), (B) MagFlo (Courtesy Dr Mark Levy www.animalswild.com), and (C) InCheckDial (Courtesy of ClementClark International Ltd, San Francisco, CA).

objective, valid, and inexpensive, they provide only the dates of medication dispensing and do not guarantee that the medication was taken as prescribed. Biologic measures confirm the presence of the medication in blood, urine, or saliva with a limited number of medications, and repeated analysis may be needed because it is hard to detect the presence of inhaled drugs. Electronic device monitoring provides accurate data about patient's adherence to therapy, but it is expensive.[76,77]

SPECIAL CONSIDERATIONS

Aerosol Therapy for Treatment of Pulmonary Arterial Hypertension

Iloprost (Ventavis, Actelion Pharmaceuticals US, Inc, South San Francisco, CA) and treprostinil (Tyvaso) are inhaled prostacyclins approved for treatment of pulmonary arterial hypertension. They are administered with specific nebulizers in discrete doses that are repeated throughout the day. Iloprost and treprostinil have a half-life of 60 to 90 minutes, allowing more convenient dosing to ambulatory patients.

Other formulations of epoprostenol (Veletri, Actelion Pharmaceuticals US, Inc) and epoprostenol sodium (Flolan, GlaxoSmithKline) have been administered as aerosol in the acute care setting for more than 20 years but they are only approved for IV use, not inhalation. Epoprostenol administration is associated with positive effects on symptoms, hemodynamics, exercise capacity, disease progression, and survival.[78-80] Due to their short half-life of 30 to 90 seconds, continuous nebulization is used. It is important to select an appropriate nebulizer and delivery method to improve the effectiveness of aerosol therapy in pulmonary hypertension. In the past, a variety of jet and USNs were used to administer prostaglandin I_2 (PGI_2). The particle size ranged from 2.1 μm to 5.2 μm at 6 L/min, and it was between 2.5 μm and 4 μm with the USN.[81] Jet and USNs gradually concentrate the drug solution due to the evaporation of solvent. In addition, USNs increase the temperature of the medication up to 55°C, resulting in higher evaporation and concentration effects. In contrast, mesh nebulizers generate a constant aerosol output of small particles without generating significant heat or evaporation, reducing issues with dose variability and solvent evaporation. One other advantage of mesh nebulizers is that they consistently nebulize small volumes of drug, as small as single drops and do not interfere with ventilator functions during mechanical ventilation. During drug delivery to ventilator dependent patients, filters should be placed on the expiratory limb of the ventilator circuit and changed frequently.

Acute Care and Off-Label Use

Every drug approved for inhalation to date has been designed for and tested in populations of ambulatory patients with moderate disease. As patients with lung disease become acutely and critically ill, the approved label doses, frequency of administration, and devices may not be practical or effective, especially for treatment of patients requiring ventilatory support. In such cases, clinicians may explore and consider nonstandard methods (doses, frequency, and devices) for administration of approved inhaled drugs to patients in the acute care environment, known as *off-label use*. For example, epoprosterenol and iloprost are approved for treatment of ambulatory patients with pulmonary hypertension; physicians may use them in ventilator-dependent patients, right heart failure, or hypoxemic respiratory failure because they improve right heart function, increase oxygenation, and decrease pulmonary artery pressure. Another type of off-label use involves drugs that have not been approved for inhalation, ranging from heparin to certain antibiotics. Although physicians may order such drugs via inhalation, the risk to the patient and institution is greater when the administration of such drugs via inhalation has not been thoroughly studied. All forms of off-label use should be avoided when approved, effective, and viable alternatives exist. Likewise, off-label administration should always be backed by appropriate departmental or institutional policies and procedures.

Continuous Nebulization for Refractory Bronchospasm

Patients in the emergency department with severe exacerbation of asthma or acute bronchospasm often have been taking standard doses of their bronchodilators for 24 to 36 hours before admission without response. Giving nebulizer treatments with standard bronchodilator doses and repeating the treatments until the symptoms are relieved can require hours of staff time. Administering higher doses of albuterol in short time frames can be accomplished by nebulization of undiluted albuterol or by protocol titration with a pMDI and holding chamber (up to 12 puffs). If these strategies fail to provide relief, CBT with albuterol nebulization doses ranging from 5 to 20 mg/h have proven safe and effective for adult and pediatric patients (Fig. 40.29. Recently, CBT has been used for the treatment of ventilator-dependent patients.

Fig. 40.30 shows a treatment algorithm used for high-dose therapy and CBT for pediatric patients with status asthmaticus who are unable to perform peak flow maneuvers.[82] Candidates for this protocol are children who, despite frequent β-agonist treatments, remain in extremis with bronchospasm, dyspnea, cough, chest tightness, and diminished breath sounds.

According to this protocol, children older than 6 years with tachypnea, hypoxemia, increased work of breathing, and

Fig. 40.29 Continuous Drug Delivery Line From a Syringe Pump Attached to a Nebulizer.

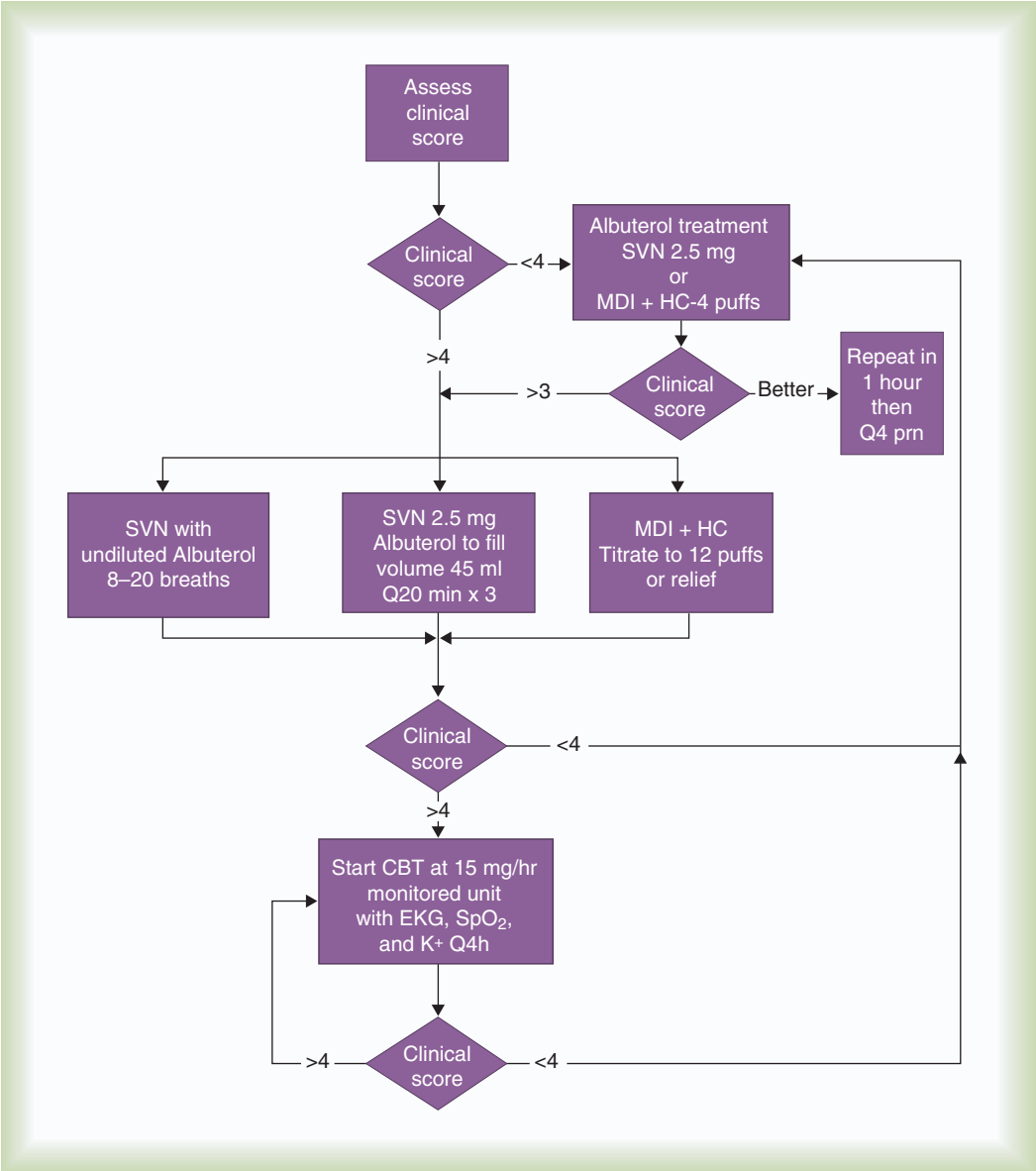


Fig. 40.30 Algorithm for continuous bronchodilator therapy (CBT) for patients younger than 5 years with pediatric asthma in extremis.

restlessness who do not respond to standard therapy are given CBT with a large volume nebulizer or SVN at a dose rate of 15 mg/h (see the accompanying Mini Clini "CBT Dosage Computations" for dosage computations). A standardized asthma score is used to evaluate children younger than 6 years for the severity of the condition (Table 40.4). Patients with an asthma score of 4 or higher are given CBT.

After CBT is started, the patient is carefully assessed every 30 minutes for the first 2 hours and thereafter every hour. A positive response is indicated by an increase in PEFR of at least 10% after the first hour of therapy. The goal is at least 50% of the predicted value. For small children, improved oxygenation (oxygen saturation by pulse oximeter [SpO_2] >92% on room air) with evidence of decreased work of breathing indicates a favorable response. Once the patient "opens up," intermittent SVN administration is resumed, or a pMDI dose-response assessment is conducted.

The patient has responded poorly to CBT if any of the indicators listed in Table 40.4 worsen. The patient must be observed for adverse drug responses, including worsening tachycardia, palpitations, and vomiting. In these situations, the attending physician must be contacted immediately.

As an alternative to large volume drug nebulizers, some protocols are based on high-dose pMDI therapy (12 to 24 puffs per hour).[83] To provide an extra margin of safety, some clinicians recommend that patients receiving CBT undergo continuous electrocardiogram monitoring and measurement of serum potassium level every 4 hours.

TABLE 40.4 Pediatric Asthma Score

	ASTHMA SCORE		
Variable	**1 Point**	**2 Points**	**3 Points**
Respiratory Rate			
2–3 years	≤34	35–39	≥40
4–5 years	≤30	31–35	≥36
6–12 years	≤26	27–30	≥31
>12 years	≤23	24–27	≥28
Oxygen saturation (%)	>95 with room air	90–95 with room air	<90 with room air or supplemental oxygen
Auscultation	Normal breathing or end-expiratory wheezing	Expiratory wheezing	Inspiratory and expiratory wheezing, diminished breath sounds, or both
Retractions	None or intercostal	Intercostal and substernal	Intercostal, substernal and supraclavicular
Dyspnea	Speaks in sentences or coos and babbles	Speaks in partial sentences or utters short cries	Speaks in single words or short phrases or grunts

From Alherbish M, Mobaireek KF, Alangari A: Admission predictability of children with asthma, *Ann Throrac Med* 13(1):39–41, 2018.

MINI CLINI

Continuous Bronchodilator Therapy Dosage Computations

Problem

Dosages for CBT are ordered in milligrams per hour, and delivery depends on both drug concentration and nebulizer output. Compute the volume of 1:200 (0.5%) albuterol and the volume of diluent (normal saline solution) needed to provide 4 hours of CBT with 15 mg/h of albuterol in a nebulizer with an output of 25 mL/h.

Discussion

Step 1: Compute the volume of albuterol given per hour (mg/h × mL/mg).

$$15.0\ \text{mg/h} \times 0.2\ \text{mL/mg} = 3.0\ \text{mL/h albuterol}$$

Step 2: Compute the volume of albuterol for the treatment period (hours × mL/h).

$$4\ \text{hours} \times 3.0\ \text{mL/h} = 12\ \text{mL/4 h albuterol}$$

Step 3: Compute the volume of nebulization solution (mL/h nebulizer output × hours).

$$25\ \text{mL/h} \times 4\ \text{hours} = 100\ \text{mL}$$

Step 4: Compute the volume of diluent required.

$$100\ \text{mL} - 12\ \text{mL} = 88\ \text{mL normal saline solution}$$

To prepare this dosage, mix 12 mL of 0.5% albuterol with 88 mL of normal saline solution, for a total nebulizer solution volume of 100 mL. In this example, residual volume of the nebulizer decreases total treatment time and dose.

Transnasal Pulmonary Aerosol Delivery

Transnasal pulmonary aerosol delivery through nasal cannula has gained increasing popularity.[84] Pediatric patients with bronchiolitis or asthma were found to become less anxious and more comfortable when inhaling bronchodilator via nasal cannula.[85-87] This route makes the long duration of aerosol inhalation feasible, as the traditional nebulizer and interface (mask or mouthpiece) are unlikely to be tolerated for extended periods of time. Aerosol delivery via high-flow nasal cannula (HFNC) has been clinically described and used for administration of bronchodilators for asthma or COPD[88] and inhaled epoprostenol for pulmonary hypertension or hypoxemia.[89]

Radiolabeled in vivo studies report aerosol lung deposition via HFNC is less than 1% in models of pediatric population[90] and less than 4% in adult population.[91,92] In vitro reports investigated influential factors, such as delivery gas type and flow, nebulizer type and placement, breathing pattern, size of nasal cannula, and role of heated humidification with a consensus that flow plays a key role in aerosol delivery via HFNC.[42,43,91-98] Previous studies report aerosol deposition to be inversely related to the HFNC flow in quite breathing.[42,43,91,95] However, distressed breathing with higher inspiratory flows (required for sicker patients) increased lung deposition at higher HFNC gas flow (≥30 L/min) but not at low flow (10 L/min). Lower gas flows result in greater lung deposition making transnasal pulmonary aerosol delivery attractive for continuous nebulization over multiple hours.

Aerosol Administration During Ventilator Support

Since the advent of modern mechanical ventilation, clinicians have administered aerosols to critically ill mechanically ventilated patients. Four primary forms of aerosol generator are used to deliver aerosols during mechanical ventilation: SVN, USN, VM nebulizer, and pMDI with third-party adapter. Table 40.5 summarizes the factors affecting aerosol drug delivery to mechanically ventilated patients. Techniques to optimize delivery to patients receiving ventilatory support are described.[99]

Regarding doses, the amount of drug required to achieve the same therapeutic end point is substantially similar for medications delivered by pMDI to intubated patients (8%) and patients who are not intubated (8% to 10%). In stable patients with COPD receiving ventilatory support, four puffs of albuterol via pMDI with chamber and 2.5 mg via SVN were shown to produce maximum bronchodilation with effects lasting for 4 hours. However, some differences in response were noted that may have been due to the level of airway obstruction and the techniques used for assessing response.

Techniques for assessing the response to a bronchodilator in intubated patients undergoing mechanical ventilation differ from techniques used in the care of spontaneously breathing patients because expiration is passive during mechanical ventilation, and forced expiratory values (PEFR, FVC, FEV_1) cannot normally be obtained. Additional techniques can be used for mechanically ventilated patients because: (1) a change in the differences between peak and plateau pressures (volume ventilation with constant flow, the most reliable indicator of a change in airway resistance during continuous mechanical ventilation) can be measured, (2) automatic positive end expiratory pressure levels may decrease in response to bronchodilators, and (3) breath-to-breath variations make measurements more reliable when the patient is not actively breathing with the ventilator.[100]

TABLE 40.5 Factors Affecting Aerosol Drug Delivery During Mechanical Ventilation

Category	Factor
Ventilator related	Mode of ventilation
	V_T
	Respiratory rate
	Duty cycle
	Inspiratory waveform
	Breath-triggering mechanism
Circuit related	Size of endotracheal tube
	Type of humidifier
	Relative humidity
	Density and viscosity of inhaled gas
Device-related MDI	Type of spacer or adapter used
	Position of spacer in circuit
	Timing of MDI actuation
SVN	Type of nebulizer used
	Fill volume
	Gas flow
	Cycling: inspiration vs. continuous
	Duration of nebulization
	Position in circuit
Patient related	Severity of airway obstruction
	Mechanism of airway obstruction
	Presence of dynamic hyperinflation
	Spontaneous ventilation
	Disease process
Drug related	Dose
	Aerosol particle size
	Targeted site for delivery
	Duration of action

MDI, Metered dose inhalers; *SVN*, small volume nebulizers; *V_T*, tidal volume.

Techniques for aerosol administration vary by type of aerosol generator and device used. The optimal technique for drug delivery to mechanically ventilated patients with each type of aerosol generator is described in Box 40.9.

MINI CLINI

Use of Heat Moisture Exhchangers During Aerosol Administration

Problem

Guidelines recommend removing heat moisture exchangers (HMEs) from between the aerosol generator and the patient airway. However, not all HMEs work the same, and some nonfiltering may be left in line.

Discussion

Filter HMEs are known to filter out the majority of aerosol passing through them. However, studies have shown that nonfilter HMEs may pass up to 60% of aerosol on to the patient.[101] If you use a nonfilter HME that is known to work with aerosol delivery, then it can remain in line, reducing the need to disconnect that patient from the ventilator before and after aerosol therapy. Because HMEs can allow aerosol to pass, they are not a substitute for high-efficiency particulate air (HEPA) filters placed in the expiratory line of the ventilator circuit. Over time, aerosol can build up an HME, increasing resistance to expiratory flow, causing increased expiratory time, air trapping, and increased work of breathing. Assess HMEs periodically, and change as appropriate.

BOX 40.9 Optimal Technique for Aerosolized Drug Delivery to Mechanically Ventilated Patients

1. Review order, identify the patient, gather equipment, and assess the need for bronchodilators.
2. Clear the airways as needed by suctioning the patient as needed.
3. If using a circuit with HME, remove HME from between the aerosol generator and the patient.
4. If using heated humidifier, do not turn off or disconnect before or during treatment.
5. Assemble equipment (tubing, nebulizer, circuit adapter).
6. Fill the nebulizer with recommended volume and medication per physician order and label.
7. Place adapter in the inspiratory limb, 6 inches from the "wye," and connect aerosol generator.
8. Turn off or minimize bias flow during treatment.
9. Connect the nebulizer to a gas or power source, as appropriate.

10a. For jet nebulizer (including SVN): Use gas source on ventilator to synchronize nebulization with inspiration, if available; otherwise, set gas flow 6 to 10 L/min as recommended on nebulizer label, and adjust ventilator volume or pressure limit and alarms to compensate for added flow and volume.

10b. For USN and VM nebulizer: Attach power source and cable from controller.

10c. For pMDI: Shake canister and connect to spacer or adapter; actuate at beginning of inspiration.

11. Observe aerosol cloud for adequate aerosol generation during nebulization.
12. After appropriate dose is administered, remove aerosol generator from the ventilator circuit.
13. Reconnect HME, as appropriate.
14. Return ventilator settings and alarms to previous values.
15. Ensure there is no leak in the ventilator circuit.
16. Rinse the nebulizer with sterile or distilled water, shake off excess water, and allow to air dry.
17. Store aerosol device in a clean, dry place.
18. Monitor heart rate, SpO_2, blood pressure, and patient-ventilator synchronization.
19. Monitor the patient for adverse response.
20. Assess the airway, and suction as needed; document findings.

HME, heat and moisture exchanger; *MDI*, pressurized metered dose inhaler; *SpO_2*, oxygen saturation by pulse oximeter; *SVN*, small volume nebulizer; *USN*, ultrasonic nebulizer; *VM*, vibrating mesh.

Use of a Small Volume Nebulizer During Mechanical Ventilation

The aerosol administered by SVN to intubated patients receiving mechanical ventilation tends to be deposited mainly in the tubing of the ventilator circuit and expiratory filter. Under normal conditions with heated humidification and standard jet nebulizers, pulmonary deposition ranges from 1.5% to 3.0%.[102] When nebulizer output, humidity level, V_T, flow, and I:E ratio are optimized, deposition can increase to 15%.

There are several disadvantages with SVN use during mechanical ventilation. Although in vitro models showed 40% higher aerosol delivery with an unheated, nonhumidified circuit compared with heated humidity, these effects have not been shown in patients. The risks associated with administering cold and

dry gas through an endotracheal tube include drying of secretions, bronchospasm, and airway obstruction. A heat and moisture exchanger should be considered a barrier to aerosol administration and should always be removed if placed between the nebulizer and the patient airway. When available with the specific ventilator being used, breath actuation can increase aerosol delivery by 30%, but it may extend administration time by more than threefold. Introducing additional flow into the ventilator circuit may change parameters of flow and delivered volumes and require changes to V_T and alarm settings during and after nebulization. The smaller the patient, the greater the impact of added flow into the ventilator circuit, where 6 L/min of additional gas flow can more than double V_T and inspiratory pressure, placing the patient at risk. Risk is high for not changing ventilator parameters and not returning parameters to pretreatment levels after administration. There is also a tendency for condensate and secretions to drain into the nebulizer reservoir, contaminating medication being delivered to the lungs.

MINI CLINI

Never Emptying Nebulizer

Problem

Jet nebulizers and ultrasonic nebulizers are frequently used to administer aerosol to patients during mechanical ventilation. Commonly, a nebulizer is filled with a standard unit dose of 3 mL of medication at the beginning of the aerosol treatment, and the RT finds as much or more fluid in the medication reservoir 20 to 30 min later. The additional fluid is usually condensate (often contaminated from patient secretions), which drains from the inspiratory limb into the gravity-dependent reservoir of the nebulizer. Even heated wire circuits may have condensate. Although pathogens in a dry circuit have minimal chance of contaminating the patient's airway, aerosolizing the pathogens provides a vehicle for infectious material to enter the airway and the lung parenchyma.

Solution

The nebulizer should be positioned so that the upper end of the reservoir is superior to (higher than) the ventilator tubing attached to both ends of the nebulizer. This position allows the condensate and secretions to drain away from the nebulizer. Alternatively, nebulizers with physical barriers between the ventilator circuit tubing and the medication reservoir can be used. These options include use of a pMDI with spacer or a VM nebulizer.

Use of a Vibrating Mesh Nebulizer During Mechanical Ventilation

Aerosol administration by a VM nebulizer has been estimated to deliver greater than 10% deposition in adults and infants without the addition of gas into the ventilator circuit. The low residual drug volume and small particle size are associated with higher efficiency. Similar to the USN, the VM nebulizer does not add gas flow into the ventilator circuit, so ventilator parameters and alarms do not need to be adjusted before, during, or after nebulization. In contrast to jet SVNs and USNs, the medication reservoir of the VM nebulizer is above the circuit and separated from the ventilator tubing by the mesh, reducing the risk of retrograde contamination of medication in the reservoir from the ventilator circuit. Because of the nature of the mesh, the reservoir can be opened and medication can be added to the nebulizer without creating a perceptible leak during ventilation. When using VM nebulizers in ventilator-dependent patients, HMEs should be removed before treatment.

Use of a Pressurized Metered Dose Inhaler During Mechanical Ventilation

Results of in vitro studies show that effective aerosol delivery by pMDIs during mechanical ventilation can range from 2% to 30%. Direct pMDI actuation by simple elbow adapters typically results in the least pulmonary deposition, with most of the aerosol impacting in either the ventilator circuit or the tracheal airway. Higher aerosol delivery percentages occur only when an actuator or spacer is placed in-line in the ventilator circuit. These spacers allow an aerosol "plume" to develop before the bulk of the particles impact on the surface of the circuit or endotracheal tube. The result is a more stable aerosol mass that can penetrate beyond the artificial airway and be deposited mainly in the lung. This situation leads to a better clinical response at lower doses.[26,39]

Aerosol Generator Placement

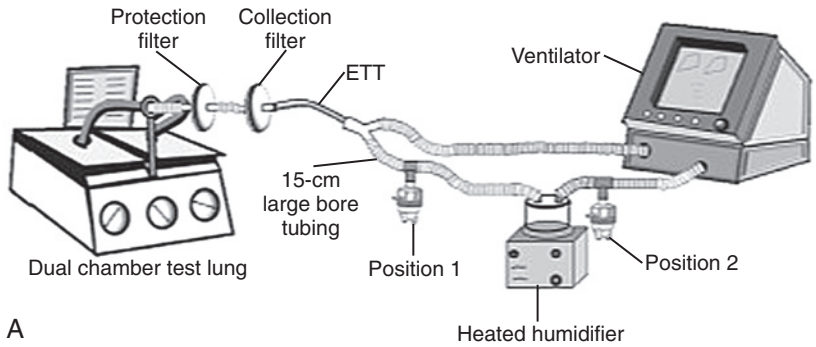
Placement of aerosol generators in the ventilator circuit can have a substantial impact on the available lung dose of drug. During adult ventilation without bias flow, placement of aerosol generators 18 to 24 inches from the patient in the inspiratory limb increases inhaled dose for jet nebulizers, where continuous gas flow acts to clear the inspiratory limb of the ventilator circuit of aerosol. In contrast, pMDI, USN, and VM nebulizer devices are more efficient when placed close to the patient at the circuit wye.[103,104] With continuous or bias flow through the adult and pediatric ventilator circuit, the delivery is reduced as flow increases, whereas placement of a VM or USN nebulizer near the ventilator increases delivery (Fig. 40.31).[104,105] For PCV with and without bias flow, as well as airway pressure release ventilation (APRV), with and without spontaneous ventilation, delivered dose was greatest with VM at the humidifier inlet. In contrast, with infant circuits, placement in the inspiratory limb closer to the patient was most efficient.

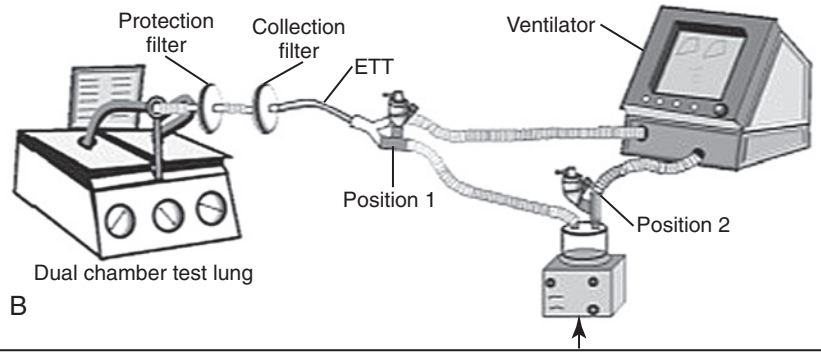
Placement During Noninvasive Ventilation

Noninvasive ventilation may be administered with standard and bilevel ventilators. Bilevel ventilators often use a flow turbine, with a fixed leak in the circuit that permits excess flow to vent to atmosphere. Placement of the aerosol generator between the leak and the patient's airway seems to provide the highest aerosol delivery efficiency.[106-108] A VM nebulizer delivers a greater inhaled dose than an SVN during noninvasive ventilation, presumably because of the lower residual drug volume and lower total flow in the circuit.[107,109,110] Delivery efficiency of aerosol devices during noninvasive ventilation ranges from 2% to 29% depending on patient population, the ventilator parameters, aerosol devices, and interfaces used in patients receiving noninvasive ventilation.[106,107,109-111] It is important to note that high flows and leakage of gas decrease aerosol delivery to patients receiving noninvasive ventilation.

Placement During Transnasal Pulmonary Delivery of Aerosol With High-Flow and Low-Flow Nasal Cannula

Transnasal delivery of aerosol to the lung via a nasal cannula with infant, pediatric, and adult models has been quantified





	Percent of nominal or emitted dose (mean ± SD %)							
	Adult lung model				Pediatric lung model			
	Position 1		Position 2		Position 1		Position 2	
	Bias flow 2 L/min	Bias flow 5 L/min	Bias flow 2 L/min	Bias flow 5 L/min	Bias flow 2 L/min	Bias flow 5 L/min	Bias flow 2 L/min	Bias flow 5 L/min
Jet nebulizer	4.7 ± 0.1*	4.0 ± 0.1*	5.2 ± 0.2*	4.7 ± 0.4*	4.2 ± 0.2*	3.8 ± 0.3*	5.2 ± 0.3*	4.1 ± 0.4*
Vibrating-mesh nubulizer	13.4 ± 1.1	9.7 ± 0.6	23.8 ± 1.0	21.4 ± 0.4	11.4 ± 0.7	8.4 ± 0.2	13.6 ± 1.3	10.6 ± 0.3

*Significant difference between jet nebulizer and vibrating-mesh nebulizer ($p < 05$).

Fig. 40.31 Placement of small volume nebulizer and vibrating mesh nebulizer aerosol generators in two positions in the ventilator circuit with 2 L/min and 5 L/min of bias flow results in different deposition efficiency.

with aerosol delivery efficiency negatively correlated with the flow of gas administered.[42,43,84,98] Use of SVN has been described, with lower delivery efficiency than VMN and greater flow in the circuit for nebulizer operation, presenting a problem with infants and children. Fig. 40.32 shows the setup with HFNC, including the location of the VM nebulizer. Placement of the VM nebulizer prior to the humidifier increases aerosol deposition with HFNC.[93] In addition to the location of the nebulizer with HFNC, the inhaled dose varies with cannula size, respiratory pattern, gas flow, and gas density. Heliox (80:20) appears to improve aerosol delivery at higher flow rates.[93] The administration of aerosolized medications via HFNC is marginally less efficient than removing the HFNC cannula during administration.[97] Administering aerosol via mouth during HFNC results in virtually no drug reaching the lungs. When delivering aerosolized medications by mask, the benefit of increased aerosol delivery must be weighed against the risk of desaturation when nasal prongs are removed. According to previous in vitro studies, aerosol drug delivery with HFNC ranged from 0.2% to 32% depending on nebulizer type, position, and flow rate used with pediatric and adult lung models.[42,43,84,93,98,112]

MINI CLINI

Aerosol by Mouth or Mask During High Flow Nasal Cannula

Problem

HFNC is prescribed to maintain FiO_2, help clear CO_2, and incrementally increase positive airway pressure with flows that exceed a patient's inspiratory flow. What happens when you administer aerosol via mouthpiece or mask during HFNC?

Discussion

Nothing good! In vitro models of infants and adults show only trace inhaled doses when aerosol is administered while HFNC is in place. It appears that the high flow from the cannula acts to blow the aerosol away from the patient, so only a small proportion of gas containing aerosol is inhaled. Transnasal pulmonary delivery or aerosol via nasal cannula has proven more efficient and more readily tolerated by patients.

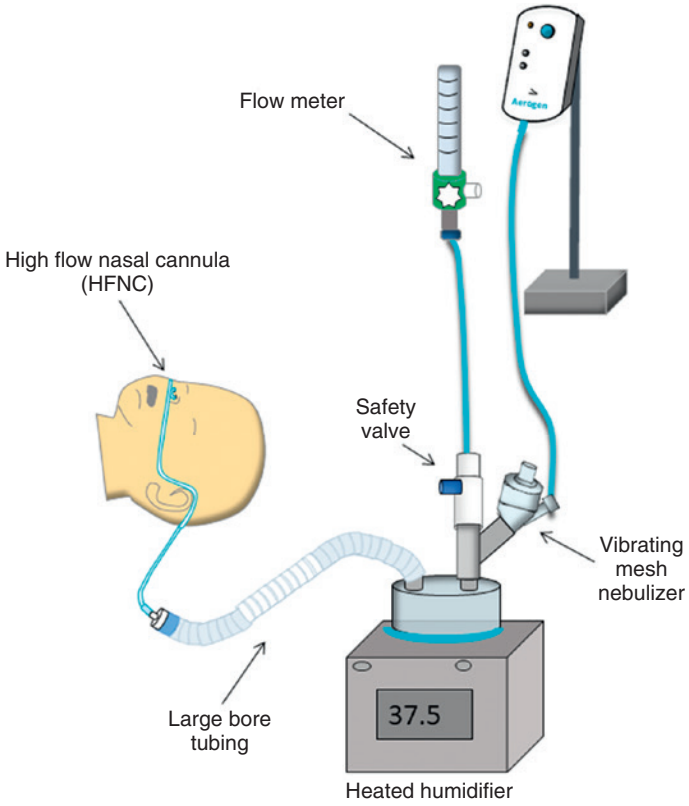


Fig. 40.32 The Setup That Will Be Used to Deliver Aerosolized Medications Through High Flow Nasal Cannula. (From *Current Pharmaceutical Biotechnology* 2017; 18(11): 877–882.)

Placement During Intrapulmonary Percussive Ventilation

Intrapulmonary percussive ventilation provides high-frequency oscillation of the airway while administering aerosol particles. During intrapulmonary percussive ventilation, the aerosol generator should be placed in the circuit as close to the patient's airway as practical. A comparison study found the MMAD was smaller with intrapulmonary percussive ventilation than with the jet (0.2 μm vs. 1.89 μm), and the fine-particle fraction was lower (16.2% vs. 67.5%). However, lung dose was similar (2.49% with intrapulmonary percussive ventilation vs. 4.2% with the jet nebulizer). It was concluded that intrapulmonary percussive ventilation was too variable and too unpredictable to recommend for drug delivery to the lung.[113]

Placement During High-Frequency Oscillatory Ventilation

When used in conjunction with high-frequency oscillatory ventilation, administration of albuterol sulfate via a VM nebulizer placed between the ventilator circuit and the patient airway has been reported to deliver greater than 10% of dose to both infants and adults.[114,115] A pMDI with adapter placed immediately proximal to the endotracheal tube achieved similar results in adult patients ventilated via high-frequency oscillatory ventilation.[116]

CONTROLLING ENVIRONMENTAL CONTAMINATION

Drugs for nebulization that escape from the nebulizer into the atmosphere or are exhaled by the patient can be inhaled by anyone in the vicinity of the treatment. The risk imposed by this environmental exposure is clear and is associated with a range of drugs and patients with infectious disease. Pentamidine and ribavirin were associated with health risks to healthcare providers even when used in conjunction with filters on exhalation ports of nebulizers, containment and scavenger systems, and *HEPA* filter hoods and ventilation systems. In addition, the aerosolization of any antibiotic should be treated in a similar manner.

Continuous pneumatic nebulizers produce the greatest amount of secondhand aerosol, with most (60%) of the aerosol produced passing directly into the environment. The Respirgard II (Vital Signs, Totowa, NJ) nebulizer was developed for administration of pentamidine, adding one-way valves and an expiratory filter to contain aerosol that is exhaled and not inhaled. Breath-actuated nebulizers, DPIs, and pMDIs tend to generate less secondhand aerosol.

A survey found that RTs were more than twice as likely as physical therapists to develop asthma-like symptoms during the course of their careers. The authors associated this with administration of ribavirin and exposure to gluteraldehyde.[16] There have been anecdotal reports of respiratory care clinicians who have developed a sensitivity to secondhand aerosol from bronchodilators. Further research is required to understand more thoroughly the hazards of secondhand exposure to aerosols in the clinical setting. Most nebulizer therapy currently delivered does not include filtering systems.

There is a requirement for caregiver protection and patient respiratory isolation when they are exposed with infectious and resistant organisms, such as tuberculosis, severe acute respiratory syndrome (SARS), and H1N1 virus. RTs have a duty to take appropriate steps to protect themselves and their patients. In these cases, the aerosols generated by the patient from coughing, speaking, or laughing can transmit disease. These aerosols can travel substantial distances between rooms and floors in institutions. Although exposure to secondhand aerosol generated by a nebulizer is undesirable, it poses less risk than the infected aerosols produced by mucosa of patients.[117] In essence, it is unlikely that any medical aerosol that is inhaled by the patient would be contaminated. Nonetheless, during the SARS outbreak, some centers outlawed use of medical aerosols to reduce exposure. Efforts should be taken to reduce transmission of both nebulizer aerosols and patient-generated aerosols to the environment.

Various techniques are available for protecting patients and caregivers from environmental exposure during aerosol drug therapy. The greatest occupational risk for RTs has been associated with the administration of ribavirin and pentamidine. Conjunctivitis, headaches, bronchospasm, shortness of breath, and rashes have been reported among individuals administering these drugs.[17,118] Patients given aerosolized ribavirin or pentamidine must be treated in a private negative room, booth, or tent or at a special station designed to minimize environmental

contamination with the caregiver wearing an N95 mask during all periods in the room during administration and for at least 10 minutes after completion of administration of the aerosol.

MINI CLINI

When to Change Expiratory Filter During Aerosol Therapy

Problem

Filters in the expiratory limb of ventilator circuits should be periodically replaced during aerosol therapy. How do you determine that period?

Discussion

Filters are often placed in the expiratory limb to protect the expiratory valves and sensors of the ventilator and reduce fugitive emissions. Over time, aerosol can build up on the filter, increasing resistance to expiratory flow, causing increased expiratory time, air trapping, and increase work of breathing. However, changing filters can be expensive, and breaking circuits can cause derecruitment of the lung.

Fig. 40.33 Emerson Treatment Booth Provides Containment of Aerosol During Therapy.

To determine filter change times during use: A test setup consisting of a high-flow flow meter running a known flow of gas (30 L/min) with a manometer positioned between flow source and filter. Measure a new filter, then place into the expiratory limb. After four treatments (or 4 hours continuous nebulization), remove the filter and retest. You can then return the filter to the circuit and repeat at regulator intervals. Plotting the increasing pressures can identify buildup drug on the filter. Substantial increase means time to change the filter. Repeating this experiment on a few patients for the different way you administer aerosol can help you to establish a filter change policy that is safe and cost efficient.

Negative-Pressure Rooms

When any antibiotic, ribavirin, or pentamidine is given, the treatment is provided in a private room. The room should be equipped for negative-pressure ventilation with adequate air exchanges (at least six per hour) to clear the room of residual aerosols before the next treatment. HEPA filters should be used to filter room or tent exhaust, or the aerosol should be scavenged to the outside.

Booths and Stations

Booths or stations should be used for sputum induction and aerosolized medication treatments given in any area where more than one patient is treated. The area should be designed to provide adequate airflow to draw aerosol and droplet nuclei from the patient into an appropriate filtration system or an exhaust system directly to the outside. Booths and stations should be adequately cleaned between patients.

A variety of booths and specially designed stations are available for delivery of pentamidine or ribavirin. The Emerson containment booth (Fig. 40.33) is an example of a system that completely isolates the patient during aerosol administration. The AeroStar aerosol protection cart (Respiratory Safety Systems, San Diego, CA) is a portable patient isolation station for administration of hazardous aerosolized medication. It has been used during sputum induction and for pentamidine treatment. The patient compartment is collapsible with a swing-out counter and three polycarbonate walls. Captured aerosols are removed with a HEPA filter. A prefilter is used to retain larger dust particles and to prevent early loading of the more expensive HEPA filter.

Filters and nebulizers used in treatments with antibiotics, pentamidine, and ribavirin should be treated as hazardous wastes and disposed of accordingly. Goggles, gloves, and gowns should be used as splatter shields to reduce exposure to medication residues and body substances. Staff members should be screened for adverse effects of exposure to the aerosol medication. The risks and safety procedures should be reviewed regularly.

In addition to the risks associated with administration of aerosol medication, risk of tuberculosis transmission has become a great concern because of an increase in case numbers and the development of multidrug-resistant strains of the organism. Tuberculosis is transmitted in the form of droplet nuclei (0.3 to 0.6 μm) that carry tuberculosis bacilli. Patients with known or suspected tuberculosis need private rooms with negative pressure ventilation that exhausts to the outside. If environmental isolation is impossible or the healthcare worker must enter the patient's room, personal protective equipment should be used.

Personal Protective Equipment

Personal protective equipment is recommended when caring for any patient with a disease that can be spread by the airborne route.[119] The greatest risk is communication of tuberculosis or chickenpox. Although environmental controls should be instituted in the care of these patients, standard and airborne precautions should also be implemented. Various masks and respirators have been recommended for use when caring for a patient with tuberculosis or other respiration-transmitted diseases. Traditional surgical masks, particulate respirators, disposable and reusable HEPA filters, and powered air-purifying respirators (PAPRs) have been used. No data are available for determining the most effective and most clinically useful device to protect healthcare workers and others, although the U.S. Occupational Safety and

Health Administration requires specific levels of protection (HEPA filters and PAPRs). Guidelines from the World Health Organization recommend surgical masks for all patient care with the exception of N95 masks for aerosol-generating procedures such as sputum induction. Evidence from laboratory studies of potential airborne spread of influenza from contagious patients indicates that guidelines related to the current 1-m respiratory zone may need to be extended to a larger respiratory zone and include eye protection.[120]

SUMMARY CHECKLIST

- An aerosol is a suspension of solid or liquid particles in gas. In the clinical setting, therapeutic aerosols are made with atomizers or nebulizers.
- The general aim of aerosol drug therapy is delivery of a therapeutic dose of the selected agent to the desired site of action.
- Where aerosol particles are deposited in the respiratory tract depends on their size, shape, and motion and on the physical characteristics of the airways. Key mechanisms causing aerosol deposition include inertial impaction, sedimentation, and brownian diffusion.
- For targeting aerosols for delivery to the upper airway (nose, larynx, trachea), particles in the 5- to 20-μm MMAD range are used; for the lower airways, 2- to 5-μm particles are used; and for the lung parenchyma (alveolar region), 1- to 3-μm particles are used.
- The primary hazard of aerosol drug therapy is an adverse reaction to the medication being administered. Other hazards include infection, airway reactivity, systemic effects of bland aerosols, and drug reconcentration.
- Drug aerosol delivery systems include pMDIs, DPIs, SVNs, large volume jet nebulizers, hand-bulb atomizers (nasal spray pumps), USNs, and VM nebulizers.
- MDIs are the preferred method for maintenance delivery of bronchodilators and steroids to spontaneously breathing patients. The effectiveness of this therapy is highly technique dependent.
- Accessory devices, spacers, and holding chambers are used with pMDIs to reduce oropharyngeal deposition of a drug and to overcome problems with poor hand–breath coordination.
- Effective use of DPIs does not require hand–breath coordination, but it does require high inspiratory flows. Some patients in stable condition prefer DPI delivery systems.
- Compared with pMDI and DPI delivery systems, use of an SVN is less technique-dependent and is more commonly used in acute care.
- Large volume drug nebulizers can be used to provide continuous aerosol delivery when traditional dosing strategies are ineffective in controlling severe bronchospasm.
- Small volume USNs can be used to administer bronchodilators, antiinflammatory agents, and antibiotics.
- Because patients vary in their response to a particular drug dose and route of administration, aerosol drug therapy should be tailored to each patient with an assessment-based protocol.
- Careful, ongoing patient assessment is the key to an effective bronchodilator therapy protocol. Components of the assessment include a patient interview, observation, expiratory airflow tests, vital sign measurements, auscultation, blood gas analysis, and oximetry.
- Protocols for CBT have proven safe and effective in the management of refractory bronchospasm in both adults and children.
- Many factors affect the efficiency of aerosol drug delivery during mechanical ventilation. Proper selection of aerosol generator type, position in the circuit, dose, and accessory equipment is needed to optimize deposition and achieve the desired clinical outcome.
- Various techniques are available to protect patients and caregivers from environmental exposure during aerosol drug therapy.

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41

Storage and Delivery of Medical Gases

David L. Vines

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Describe how medical gases and gas mixtures are produced.
- Discuss the clinical applications for medical gases and gas mixtures.
- Distinguish between gaseous and liquid storage methods.
- Calculate the duration of gas flow remaining in a compressed oxygen cylinder.
- Calculate the duration of gas flow remaining in a liquid oxygen cylinder.
- Describe how to store, transport, and use compressed gas cylinders properly.
- Distinguish between gas supply systems.
- Describe what to do if a bulk oxygen supply system fails.
- Differentiate among safety systems that apply to various equipment connections.
- Select the appropriate devices to regulate gas pressure or control flow in various clinical settings.
- Regarding gas delivery equipment, describe how to assemble it, check it for proper function, and identify malfunctions.
- Identify and correct common malfunctions of gas delivery equipment.

CHAPTER OUTLINE

KEY TERMS

American standard safety system
Bourdon gauge
cryogenic
diameter-index safety system
downstream
filling density
flammable
flow meter
fractional distillation
heliox
manifold
nonflammable
oxidizing
pin-index safety system
psig
reducing valve
regulator
Thorpe tube
upstream
zone valves

The current field of respiratory care evolved from the hospital "oxygen service." Although respiratory therapists (RTs) have assumed many more challenging roles, ensuring the safe and uninterrupted supply of medical gases remains an important responsibility.

Medical gases (Table 41.1) are classified as laboratory gases, therapeutic gases, or anesthetic gases. *Laboratory gases* are used for equipment calibration and diagnostic testing. *Therapeutic gases* are used to relieve symptoms and improve the oxygenation of patients with hypoxemia. *Anesthetic gases* are combined with oxygen (O_2) to provide anesthesia during surgery. It is important for RTs to be familiar with all aspects of gases used in the clinical setting, especially their chemical symbols, physical characteristics, ability to support life, and fire risk. In regard to fire risk, medical compressed gases are classified as either **nonflammable** (do not burn), nonflammable but supportive of combustion (also termed **oxidizing**), or **flammable** (burns readily, potentially explosive).[1] This chapter focuses on the therapeutic gases.

TABLE 41.1 Physical Characteristics of Medical Gases

Gas	Chemical Symbol	Color	Taste	Odor	Can Support Life	Flammability
Laboratory Gases						
Nitrogen	N	Colorless	Tasteless	Odorless	No	Nonflammable
Helium	He	Colorless	Tasteless	Odorless	No	Nonflammable
Carbon dioxide	CO_2	Colorless	Slightly acidic	Odorless	No	Nonflammable
Therapeutic Gases						
Air	AIR	Colorless	Tasteless	Odorless	Yes	Supports combustion
Oxygen	O_2	Colorless	Tasteless	Odorless	Yes	Supports combustion
Helium/oxygen (heliox)	He/O_2	Colorless	Tasteless	Odorless	Yes	Supports combustion
Carbon dioxide/oxygen	CO_2/O_2	Colorless	Slightly acidic	Odorless	No	Supports combustion
Nitric oxide	NO	Colorless	Tasteless	Metallic	No	Supports combustion
Anesthetic Gas						
Nitrous oxide	N_2O	Colorless	Slightly sweet	Slightly sweet	No	Supports combustion

CHARACTERISTICS OF MEDICAL GASES

Oxygen

Characteristics

O_2 is a colorless, odorless, transparent, and tasteless gas.[1] It exists naturally as free molecular O_2 and as a component of a host of chemical compounds. At *standard temperature, pressure, and dry (STPD)*, O_2 has a density of 1.429 g/L, being slightly heavier than air (1.29 g/L). O_2 is not very soluble in water. At room temperature and 1 atm pressure, only 3.3 mL of O_2 dissolves in 100 mL of water.

O_2 is nonflammable, but it greatly accelerates combustion. Burning speed increases with either (1) an increase in O_2 percentage at a fixed total pressure or (2) an increase in total pressure of O_2 at a constant gas concentration. Both O_2 concentration and partial pressure influence the rate of burning.[1,2]

Production

O_2 is produced by one of several methods. Chemical methods for producing small quantities of O_2 include *electrolysis of water* and *decomposition of sodium chlorate* ($NaClO_3$). Most large quantities of medical O_2 are produced by fractional distillation of atmospheric air.[1] Small quantities of concentrated O_2 are produced by physical separation of O_2 from air.

Fractional distillation. **Fractional distillation** is the most common and least expensive method for producing O_2. The process involves several related steps. First, atmospheric air is filtered to remove pollutants, water, and carbon dioxide (CO_2). The purified air is liquefied by compression and cooled by rapid expansion *(Joule-Thompson effect)*.

The resulting mixture of liquid O_2 and nitrogen (N, N_2) is heated slowly in a distillation tower. N_2, with its boiling point of 195.8°C (320.5°F), escapes first, followed by the trace gases of argon, krypton, and xenon. The remaining liquid O_2 is transferred to specially insulated **cryogenic** (low-temperature) storage cylinders. An alternative procedure is to convert O_2 directly to gas for storage in high-pressure metal cylinders. These methods produce O_2 that is approximately 99.5% pure. The remaining 0.5% is mostly N_2 and trace argon. US Food and Drug Administration (FDA) standards require an O_2 purity of at least 99.0%.[3]

Physical separation. Two methods are used to separate O_2 from air.[4] The first entails the use of molecular "sieves" composed of inorganic sodium aluminum silicate pellets. These absorb N_2, "trace" gases and water vapor from the air, providing a concentrated mixture of more than 90% O_2 for patient use. The second method entails use of a vacuum to pull ambient air through a semipermeable plastic membrane that allows O_2 and water vapor to pass through at a faster rate than N_2 from ambient air. This system can produce an O_2 mixture of approximately 40%. These devices, called *oxygen concentrators*, are used primarily for supplying low-flow O_2 in the home care setting. Details about their principles of operation and appropriate use are discussed in Chapter 57.

RULE OF THUMB O_2 from a liquid source or cylinder is over 99% pure, whereas O_2 from a concentrator will be 90% to 96% pure. Changing from a cylinder to a concentrator may require an increase in liter flow to maintain the patient's arterial O_2 saturation.

Air

Atmospheric air is a colorless, odorless, naturally occurring gas mixture that consists of 20.95% O_2, 78.1% N_2, and approximately 1% "trace" gases, mainly argon. At STPD, the density of air is 1.29 g/L; this is used as the standard for measuring the specific gravity of other gases. O_2 and N_2 can be mixed to produce a gas with an O_2 concentration equivalent to that of air. Medical-grade air is usually produced by filtering and compressing atmospheric air.[1,5]

Fig. 41.1 shows a typical large medical *air compressor system*. In these systems, an electric motor is used to power a piston in a compression cylinder. On its downstroke, the piston draws air through a filter system with an inlet valve. On its upstroke, the piston compresses the air in the cylinder (closing the inlet valve) and delivers it through an outlet valve to a reservoir tank. Air from the reservoir tank is reduced to the desired working

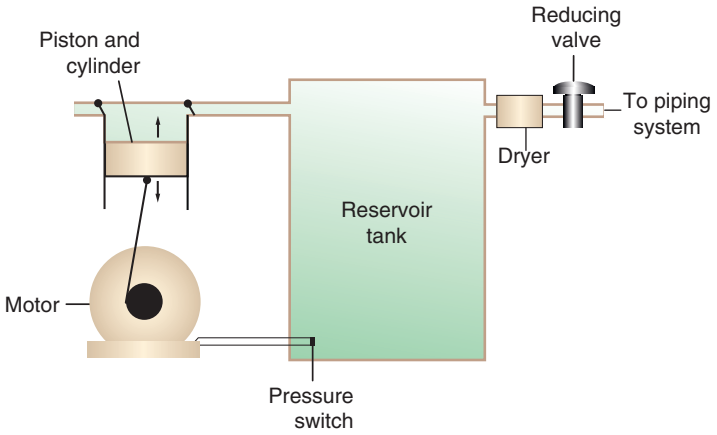

Fig. 41.1 Large Medical Air Compressor. The compressor sends gas to the reservoir at higher than line pressure. When the preset pressure level is reached, the pressure switch shuts off the compressor. Gas leaves the reservoir and passes through the dryer to remove moisture, and the reducing valve reduces gas to the desired line pressure. When reservoir pressure has decreased to near line pressure, the pressure switch turns the compressor back on. (Modified from McPherson SP, Spearman CB: *Respiratory Therapy Equipment*, ed 5, St Louis, 1995, Mosby.)

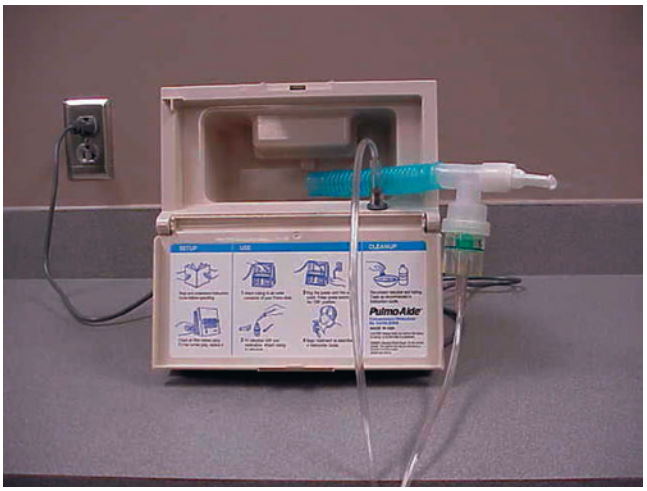

Fig. 41.2 Small portable compressor used with a handheld nebulizer to aerosolize medication.

pressure by a pressure-reducing valve before being delivered to the piping system.

For medical gas use, air must be dry and free of oil or particulate contamination.[5] The most common method used for drying air is cooling to produce condensation. For avoidance of oil or particulate contamination, medical air compressors have air inlet filters and polytetrafluoroethylene (Teflon) piston rings as opposed to oil lubrication. Large medical air compressors must provide high flow (at least 100 L/min) at the standard working pressure of 50 *pounds per square inch gauge* (**psig**) for all equipment in use. The psig is the pressure read on the gauge, which reads the pressure above atmosphere pressure. See Chapter 6 for more information on this concept.

Smaller compressors (Fig. 41.2) are available for bedside or home use. These have a diaphragm or turbine that compresses the air and generally do not have a reservoir. This design limits the pressure and flow capabilities of these devices. For this reason, small compressors must never be used to power equipment that needs unrestricted flow at 50 psig, such as pneumatically powered ventilators (see Chapter 46). However, small-diaphragm or turbine compressors are ideal for powering devices such as small-volume medication nebulizers (see Chapter 40).

RULE OF THUMB Medical air compressors must produce 50 psig of a dry gas at 100 L/min to power pneumatically driven equipment such as mechanical ventilators.

Carbon Dioxide

At STPD, CO_2 is a colorless and odorless gas with a specific gravity of 1.52 (approximately 1.5 times heavier than air).[1] CO_2 does not support combustion or life. For medical use, CO_2 is usually produced by heating limestone in contact with water. The gas is recovered from this process and liquefied by compression and cooling. The FDA purity standard for CO_2 is 99%.[6]

Mixtures of O_2 and 5% to 10% CO_2 are occasionally used for therapeutic purposes. Therapeutic uses include the management of singultus (hiccups), prevention of the complete washout of CO_2 during cardiopulmonary bypass, and regulation of pulmonary vascular pressures in some congenital heart disorders. However, CO_2 mixtures are more commonly used for the calibration of blood gas analyzers (see Chapter 19) and for diagnostic purposes in the clinical laboratory.

Helium

Helium (He) is second only to hydrogen as the lightest of all gases; it has a density at STPD of 0.1785 g/L. It is odorless, tasteless, nonflammable, and chemically and physiologically inert. Although He is present in small quantities in the atmosphere, it is commercially produced from natural gas through liquefaction to purity standards of at least 99%.[1,7]

Breathing 100% He would cause suffocation and death. For therapeutic use, He must always be mixed with at least 20% O_2. **Heliox** (a gas mixture of O_2 and He) may be used clinically to

manage severe cases of airway obstruction. Its low density decreases the work of breathing by making gas flow more laminar. It is discussed in more detail in Chapter 42.

RULE OF THUMB He lium must always be combined with at least 20% O_2. The higher the concentration of O_2 used in a heliox mixture, the less likely it is that heliox will be beneficial. Heliox mixtures of less than 60% He are rarely used clinically.

Nitric Oxide

Nitric oxide (NO) is a colorless, nonflammable, toxic gas that supports combustion. It is produced by oxidation of ammonia at high temperatures in the presence of a catalyst. In combination with air, NO forms brown fumes of nitrogen dioxide (NO_2). Together, NO and NO_2 are strong respiratory irritants that can cause chemical pneumonitis and a fatal form of pulmonary edema. Exposure to high concentrations of NO alone can cause methemoglobinemia (see Chapter 42). High levels of methemoglobin can cause tissue hypoxia.

NO is approved by the FDA for use in the treatment of term and near-term infants for hypoxemic respiratory failure. A systematic review supports the recommendation that inhaled NO at 20 ppm is beneficial in term and near-term infants with severe hypoxemia who do not have a diaphragmatic hernia (see Chapter 35).[8] Inhaled NO has not been shown to be beneficial in improving outcomes in preterm infants or adult patients with hypoxemia, and it is expensive to use clinically.

RULE OF THUMB Inhaled NO is a pulmonary vasodilator that has been shown beneficial in treating term or near-term infants with severe hypoxia who do not have a diaphragmatic hernia. Inhaled NO has not been shown to be beneficial in improving outcomes in preterm infants or adult patients with severe hypoxemia. NO is also costly.

Nitrous Oxide

Nitrous oxide (N_2O) is a colorless gas with a slightly sweet odor and taste; it is used clinically as an anesthetic agent. Similar to O_2, N_2O can support combustion. However, N_2O cannot support life and must always be mixed with at least 20% O_2. N_2O is produced by thermal decomposition of ammonium nitrate.[1]

The use of N_2O as an anesthetic agent is based on its central nervous system depressant effect. However, only dangerously high levels of N_2O provide true anesthesia. N_2O/O_2 mixtures are almost always used in combination with other anesthetic agents.

Long-term human exposure to N_2O has been associated with a form of neuropathy. In addition, epidemiologic studies have linked chronic N_2O exposure with an increased risk for fetal disorders and spontaneous abortion.[1] Based on these findings, the National Institute for Occupational Safety and Health set an upper exposure limit for hospital operating rooms of 25 ppm N_2O.[1]

STORAGE OF MEDICAL GASES

Medical gases are stored either in portable high-pressure cylinders or in large bulk reservoirs. Bulk reservoirs require a separate distribution system to deliver the gas to the patient.

Gas Cylinders

The containers used to store and ship compressed or liquid medical gases are high-pressure cylinders. The design, manufacture, transport, and use of these cylinders are carefully controlled by both industrial standards and federal regulations. Gas cylinders are made of seamless steel and are classified by the US Department of Transportation (DOT) according to their fabrication method. DOT type 3A cylinders are made from carbon steel, and DOT type 3AA containers are manufactured with a steel alloy tempered for higher strength.[1]

Markings and Identification

Medical gas cylinders are marked with metal stamping on the shoulders—stamps that supply specific information (Fig. 41.3).[1,9] Although the exact location and order of these markings vary, the practitioner should be able to identify several key items of information.

The letters *DOT* or *ICC* (Interstate Commerce Commission) are followed by the cylinder classification (*3A* or *3AA*) and the normal filling pressure in pounds per square inch (psi). Below this information there is usually the letter size of the cylinder (*E*, *G*, *H*, and so on). followed by the cylinder serial number. A third line provides a mark of ownership, often followed by the manufacturer's stamp or a mark identifying the inspecting authority. An abbreviation indicating the method of cylinder manufacturer is usually on the opposite side of the cylinder. Also in this area is information about the original safety test as well as the dates of all subsequent tests.

Safety tests are conducted on each cylinder every 5 or 10 years, as specified in DOT regulations.[1,9] During these tests, cylinders are pressurized to five-thirds of their service pressure. While the cylinder is under pressure, technicians measure cylinder leakage, expansion, and wall stress. The notation *EE* followed by a number indicates the elastic expansion of the cylinder in cubic centimeters under the test conditions. An asterisk (*) next to the test date indicates DOT approval for 10-year testing. A plus sign (+) means that the cylinder is approved for filling to 10% greater than its service pressure. An approved cylinder with a service pressure of 2015 psi can be filled to approximately 2200 psi. After hydrostatic testing, cylinders are subjected to internal inspection and cleaning.

In addition to these permanent marks, all cylinders are color-coded and labeled for identification of their contents.[1,10] Table 41.2 lists the color codes for medical gases as adopted by the Bureau of Standards of the US Department of Commerce.[10,11] For comparison, the color codes adopted by the Canadian Standards Association are also included. Color codes are not standardized internationally. For this reason, cylinder color should be used only as a guide. As with any drug agent, the cylinder's contents must always be identified by careful inspection of the label. It has been reported that gas mixtures such as heliox can become unmixed.[12] To be absolutely sure about the O_2 concentration provided by a cylinder, the user must analyze the gas before administering it (see Chapter 19).

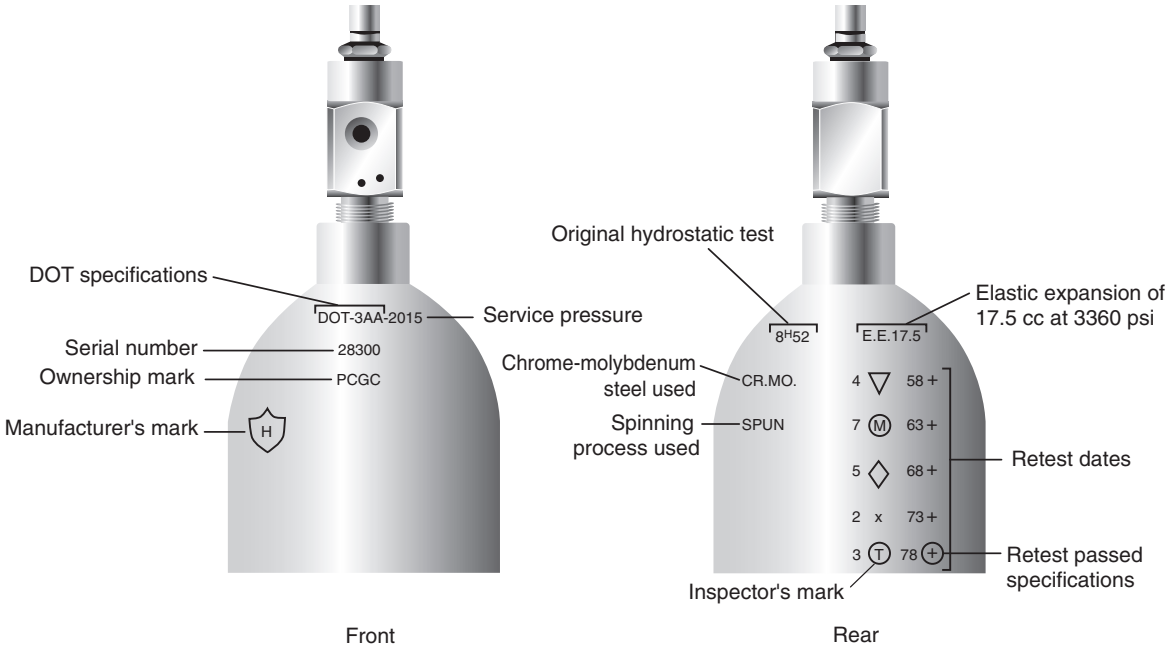

Fig. 41.3 **Typical Markings of Cylinders Containing Medical Gases.** Front and back views are for illustration purposes only; exact location and order of markings will vary. *DOT,* Department of Transportation.

TABLE 41.2 Color Codes for Medical Gas Cylinders

Gas	United States	Canada
O_2	Green	White[a]
CO_2	Gray	Gray
N_2O	Blue	Blue
Cyclopropane	Orange	Orange
He	Brown	Brown
C_2H_4	Red	Red
CO_2–O_2	Gray/green	Gray/white
He–O_2	Brown/green	Brown/white
N_2	Black	Black
Air	Yellow[a]	Black/white
N_2–O_2	Black/green	Pink

[a]Vacuum systems historically are identified as white in the United States and yellow in Canada. for this reason, the Compressed Gas Association (CGA) recommends that white not be used for any cylinders in the United States and that yellow not be used in Canada. C_2H_4, Ethylene.

RULE OF THUMB Cylinders with a service pressure of 2015 psi are usually filled to approximately 2200 psi.

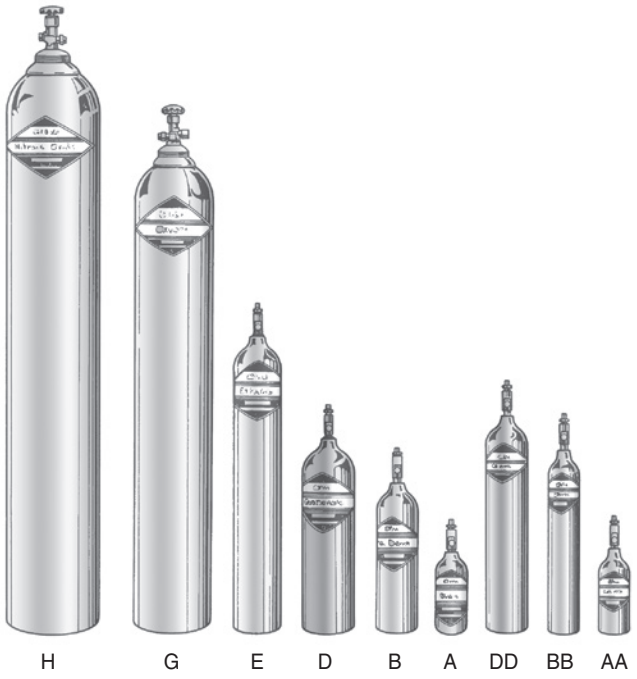

Fig. 41.4 Cylinder sizes are identified by letter designations.

Cylinder Sizes and Contents

Letter designations are used for different sizes of cylinders (Fig. 41.4). Sizes E through AA are referred to as "small cylinders" and are used most often for transporting patients and anesthetic gases. These small cylinders are easily identified because of their unique valves and connecting mechanisms. Small cylinders have a post valve and yoke connector. Large cylinders (F through H and K) have a threaded valve outlet (Fig. 41.5).

Cylinder Safety Relief Valves

In a closed cylinder, any increase in gas temperature increases gas pressure. Should the temperature increase too much (as in a fire), the high gas pressure could rupture and explode the cylinder. To prevent this type of accident, all cylinders have high-pressure relief valves of three basic designs: frangible disk, fusible plug, and spring-loaded. The *frangible metal disk* ruptures at a specific pressure. The *fusible plug* melts at a specific temperature. The *spring-loaded valve* opens and vents gas at a set high

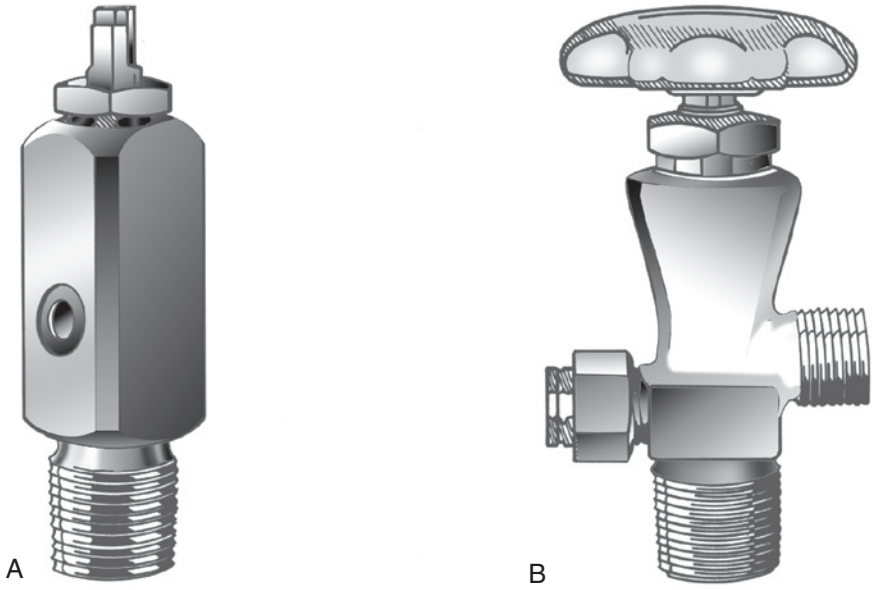

Fig. 41.5 (A) Post valve for yoke connector used with small cylinders (E through AA). (B) Large, threaded valve outlet used with large cylinders (H/K, G, and M).

pressure. In each case, the activated valve vents gas from the cylinder and prevents pressure from becoming too high.

Most small cylinders have a fusible plug relief valve. Most large cylinders have a spring-loaded relief valve. These safety relief valves are always located in the cylinder's valve stems.

Filling (Charging) Cylinders

How a cylinder is filled depends on whether its contents will be gaseous or liquid. Some gases stored in liquid form can remain at room temperature, but others must be maintained in a cryogenic (low-temperature) state.

Compressed gases. A gas cylinder is normally filled to its service pressure (the pressure stamped on the shoulder) at 21.1°C (70°F). However, approved cylinders can be filled to 10% greater than the service pressure.

Liquefied gases. Gases with critical temperatures greater than room temperature—including CO_2 and N_2O—can be stored as liquids at room temperature (see Chapter 6). Rather than being filled to filling pressure, cylinders of these gases are filled according to a specified filling density. The **filling density** is the ratio between the weight of liquid gas put into the cylinder and the weight of water the cylinder could contain if full. The filling density for CO_2 is 68%. This system allows the manufacturer to fill a cylinder with liquid CO_2 up to 68% of the weight of water that a full cylinder could hold. The filling density of N_2O is 55%.

Cylinder pressures for gases stored in the liquid phase are much lower than those for gases stored in the gas phase. Because the liquid does not fill the entire volume of a cylinder, the space above the liquid surface contains gas in equilibrium with the liquid. The pressure in a liquid-filled cylinder equals the pressure of the vapor at any given temperature.

Pressure in a cylinder depends on the state of its contents. In a gas-filled cylinder, the pressure represents the force required to compress the gas into its smaller volume. In contrast, the pressure in a liquid-filled cylinder is the vapor pressure needed to keep the gas liquefied at the current temperature.

Measuring Cylinder Contents

Because of the previously described differences in the physical state of matter of compressed and liquid gases, different methods are needed to measure the contents of the cylinder.

Compressed gas cylinders. For gas-filled cylinders, the volume of gas in the cylinder is directly proportional to its pressure at a constant temperature. If a cylinder is full at 2200 psig, it will be half full when the pressure decreases to 1100 psig. To know how much gas is contained in a compressed gas cylinder, one needs only to measure its pressure.

Liquid gas cylinders. In a liquid gas cylinder or container, the measured pressure is the vapor pressure above the liquid. This pressure bears no relationship to the amount of liquid remaining. As long as some liquid remains (and the temperature remains constant), the vapor pressure and gauge pressure remain constant. When all the liquid is gone and the cylinder contains only gas, the pressure decreases in proportion to a reduction in volume. Weighing a liquid-filled cylinder is the only accurate method for determining the contents.

> **RULE OF THUMB** Monitoring the gauge pressure is useful in determining the contents of a gas-filled cylinder. Weighing a liquid-filled cylinder is the only accurate method for determining the remaining amount of gas, since gauge pressure will decrease only after all of the liquid has converted to a gas.

Fig. 41.6 compares the behavior of compressed-gas and liquid-gas cylinders during use. The vapor pressure of liquid gas cylinders varies with the temperature of the contents. The pressure in an N_2O cylinder at 21.1°C (70°F) is 745 psig; at 15.6°C (60°F), the pressure decreases to 660 psig. As the temperature increases toward the critical point, more liquid vaporizes, and the cylinder

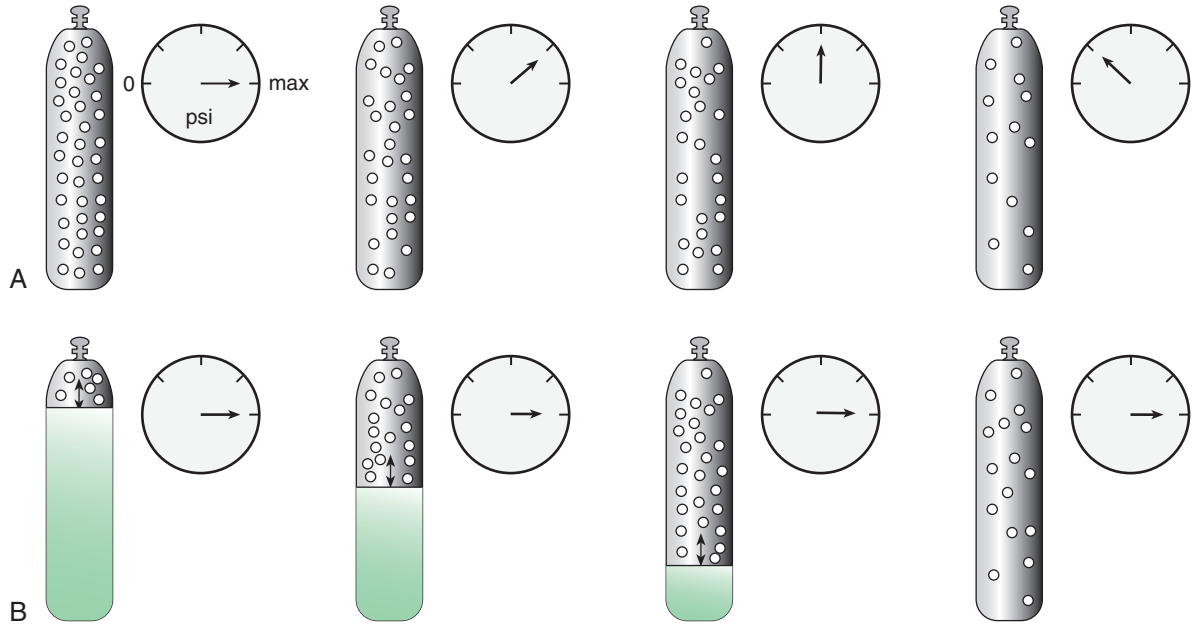

Fig. 41.6 The content of a gas-filled cylinder (A) is directly proportional to the gas pressure. A pressure decrease of 50% indicates a loss of 50% of the contained gas. In a liquid-gas cylinder (B), gauge pressure is a measure of only the vapor pressure of gas in equilibrium with the liquid phase. This value remains constant at a given temperature as long as liquid is present. Only when all the liquid has vaporized, as the cylinder nears depletion, does the gauge pressure decrease proportionately to the terminal volume of remaining gas.

pressure increases. If a cylinder of N_2O warms to 36.4°C (97.5°F) (its critical temperature), all the contents convert to gas. Only at this temperature and higher does the cylinder gauge pressure accurately reflect the cylinder's contents.

Estimating Duration of Cylinder Gas Flow

When a cylinder of therapeutic gas is used, it often is necessary to predict how long the contents will last at a given flow. The duration of flow of a cylinder can be estimated if the following are known: (1) the gas flow, (2) the cylinder's size, and (3) the cylinder's pressure at the start of therapy. For a given flow, the more gas a cylinder holds, the longer it lasts. The higher the gas flow, the quicker the cylinder empties. The duration of flow from a cylinder is directly proportional to the contents and inversely proportional to flow, as expressed in the following formula:

$$\text{Duration of flow} = \frac{\text{Contents}}{\text{Flow}}$$

Cylinder contents are generally specified in cubic feet or gallons, whereas gas flow is normally measured in liters. Table 41.3 provides the factors needed to convert these units. Rather than memorizing various cylinder contents and constantly converting metric and English units, the user can quickly calculate duration of flow by using *cylinder factors*, which are derived for each common gas and cylinder size with the following formula:

$$\text{Cylinder factor (L/psig)} = \frac{\text{Cubic feet (full cylinder)} \times 28.3}{\text{Pressure (full cylinder) in psig}}$$

TABLE 41.3 Gas Volume Conversion Factors

Liters	Cubic Feet	Gallons
28.316	1	7.481
1	0.03531	0.2642
3.785	0.1337	1

In the numerator of this equation, the English-metric conversion constant (28.3) is used to convert cubic feet to liters. Dividing the resulting volume by the pressure in a full cylinder yields the cylinder factor. The derived factor represents the volume of gas leaving a given cylinder for every 1-psig decrease in pressure. Table 41.4 provides cylinder factors for the therapeutic medical gases and common cylinder sizes.

When the factor for a given gas and cylinder is known, calculating the duration of flow is a simple matter of applying the following equation:

$$\text{Duration of flow (min)} = \frac{\text{Pressure (psig)} \times \text{Cylinder factor}}{\text{Flow (L/min)}}$$

A margin of safety must be allowed in estimation of cylinder duration of flow. Some clinicians return 30 to 40 minutes before the calculated time; others compute duration of flow to a level of 300 to 500 psig rather than 0 psig (empty). Assuming the calculations are correct and there is no change in flow, both methods ensure an uninterrupted supply. The accompanying rule of thumb presents a shortcut for estimating a cylinder's duration of flow.

TABLE 41.4 Factors for Calculation of Cylinder Duration of Flow (Minutes)

	CYLINDER SIZE			
Gas	**D**	**E**	**G**	**H and K**
O_2, O_2/N_2, air	0.16	0.28	2.41	3.14
O_2/CO_2	0.20	0.35	2.94	3.84
He/O_2	0.14	0.23	1.93	2.50

RULE OF THUMB A full E O_2 cylinder running at 10 L/min lasts approximately 60 min (1 h). A full H/K cylinder lasts at least 10 times longer (>10 h). Use these two simple rules to estimate flow duration. For example, a half-full E O_2 cylinder running at 10 L/min lasts approximately 30 min, whereas a full H cylinder running at 5 L/min lasts more than 20 h.

MINI CLINI

Computing a Cylinder's Duration of Flow

Problem

The RT needs to determine how long a G cylinder of O_2 with a gauge pressure of 800 psi set to deliver 8 L/min will last until empty.

Solution

Step 1: Determine the cylinder's factor for an O_2 G cylinder (see Table 41.4), which in this case is 2.41.

Step 2: Apply the duration of flow equation:

$$\text{Duration of flow (min)} = \frac{\text{Pressure (psig)} \times \text{Cylinder factor}}{\text{Flow (L/min)}}$$

$$\text{Duration of flow (min)} = \frac{800 \times 2.41}{8} = 241 \text{ minutes}$$

(approximately 4 hours)

Estimating Duration of Liquid Oxygen Cylinder Gas Flow

The only accurate method for determining the volume of gas in a liquid-filled cylinder is by weight. Because 1 L of liquid O_2 weighs 2.5 lb and produces 860 L of O_2 in its gaseous state, the amount of gas in a liquid O_2 cylinder can be calculated with the following formula:

$$\text{Amount of gas in cylinder} = \frac{\text{Liquid weight (lb)} \times 860}{2.5 \text{ lb/L}}$$

After the amount of O_2 remaining in the cylinder has been determined, the duration of the gas in minutes can be calculated with the following formula:

$$\text{Duration of gas (min)} = \frac{\text{Amount of gas in cylinder (L)}}{\text{Flow (L/min)}}$$

As with gaseous O_2 cylinders, a wide margin of safety is needed for estimation of cylinder duration. This margin of safety varies with the size of the portable O_2 unit or large storage container.

MINI CLINI

Computing the Duration of a Liquid Oxygen Container

Problem

The RT must estimate how long a portable liquid O_2 container will last if it contains 3 lb of liquid O_2 that supplies an O_2 delivery device running at 2 L/min.

Solution

Step 1: Determine the amount of O_2 in the cylinder.

$$\text{Amount of gas in cylinder} = \frac{\text{Liquid } O_2 \text{ weight (lb)} \times 860}{2.5 \text{ lb/L}}$$

$$= \frac{3 \times 860}{2.5}$$

$$= 1032 \text{ L}$$

Step 2: Calculate the duration of the gas in the container.

$$\text{Duration of gas} = \frac{\text{Amount of gas in the cylinder (L)}}{\text{Flow (L/min)}}$$

$$= \frac{1032 \text{ L}}{2} = \frac{516 \text{ minutes}}{60 \text{ (min/h)}}$$

$$= 8 \text{ hours } 36 \text{ minutes}$$

Gas Cylinder Safety

The following guidelines for cylinder safety are from the recommendations of the National Fire Protection Agency (NFPA)[2] and the Compressed Gas Association (CGA).[1,11] For ease of use, these safety guidelines are divided into cylinder storage, transport, and use.

Cylinder storage. The following guidelines apply to cylinder storage:

- Store gas cylinders in racks or chain cylinders to the wall to prevent them from falling or becoming damaged.
- Store cylinders away from any combustible material.
- Store gas cylinders away from sources of heat. Keep the cylinder temperature at less than 125°F (<52°C).
- Store flammable gases separately from gases that support combustion, such as air, O_2, and N_2O.
- If a cylinder is not in use, keep the protective cylinder cap in place.
- Do not store air compressors and gas cylinders together. A fire involving one or the other can damage both gas delivery systems.
- Contain and store cylinder supply systems in an enclosure that is well ventilated and drained constructed of a material with at least a 1-hour fire-resistive rating.
- Segregate full and empty cylinders; store them separately if possible.
- Place on each door or gate of the enclosure a sign indication the presence of an oxidizing gas suggesting caution in particular against smoking. This sign must be readable from a distance of at least 5 ft (1.5 m).
- Store liquid O_2 containers in a cool, well-ventilated area because of the venting of small amounts of O_2 from these low-pressure

containers. The venting of O_2 prevents these containers from overpressurizing because liquid O_2 is continuously converting to gaseous O_2.

Cylinder transport. The following guidelines apply to cylinder transport:

- Use cylinder carts with a securing mechanism for transportation of cylinders.
- Keep the protective cylinder caps in place during transportation of cylinders.
- Protect gas cylinders from striking other cylinders or objects to avoid damaging the safety devices, valve stems, or the cylinder itself.
- Avoid dropping, dragging, or rolling cylinders in transport.
- Do not transport cylinders for use that are not appropriately labeled.

Cylinder use. The following guidelines apply to cylinder use:

- Secure gas cylinders at the patient's bedside in a way that prevents them from falling. Secure cylinders to the wall with a chain, bind or chain them to a suitable cart, or support the cylinder with a stand.
- Do not use flammable materials, especially oil or grease, on regulators, cylinders, fittings, or valves. This restriction includes oily hands, rags, and gloves.
- Open the cylinder valve slightly to remove dust and dirt before attaching the regulator. When the valve is being slightly opened, make sure that no one is in front of it. "Crack" the cylinder before bringing it to the patient's bedside.
- Never use cylinder valves or regulators that need repair.
- Do not alter or deface cylinder markings or color.
- Never place cylinders near sources of heat.
- Never secure cylinders to movable objects unless the object has an apparatus that can contain the cylinder safely.
- Make sure that the connection between the regulator and the cylinder valve is an **American standard safety system** (ASSS) for H and G cylinders and a **pin-index safety system** (PISS) for E cylinders.
- When O_2 is in use, post a "No Smoking" sign unless signs at the entrances are posted that prohibit smoking in the facility.

Bulk Oxygen

Large acute care facilities use large volumes of O_2 every day. To meet these needs, a centralized bulk storage and delivery system is required. By definition, bulk O_2 storage systems hold at least 20,000 ft^3 of gas, including the onsite unconnected reserves.[2] Bulk O_2 may be stored in either gaseous or liquid form; liquid storage is most common. When needed, the O_2 flows from this central source throughout the facility by a piping system with conveniently located outlets.

A bulk O_2 system has several advantages over portable cylinders. Although initially expensive to construct, bulk O_2 systems are far less expensive over the long term. Bulk O_2 systems are less prone to interruption. These systems eliminate the inconvenience and hazard of transporting and storing numerous cylinders. Bulk O_2 systems regulate delivery pressures centrally, eliminating the need for separate pressure-reducing valves at each outlet. These systems also operate at low pressures, making them much safer than high-pressure cylinders.

Safety standards for bulk O_2 systems are set by the NFPA and are subject to further control by local fire and building codes.[2]

Gas Supply Systems

The three types of centrally located gas supply systems are an alternating supply system or cylinder **manifold** system, a cylinder supply system with reserve supply, and a bulk gas system with a reserve.[2] The *alternating supply* or *cylinder manifold system* consists of large (normally H or K size) cylinders of compressed O_2 banked together in series (Fig. 41.7). This alternating supply system has two sides: a primary bank and a reserve bank. When the pressure in the primary bank decreases to a set level, a control valve automatically switches over to the reserve bank. When this occurs, the primary bank is taken off line and the empty cylinders are replaced with full ones. The replenished primary

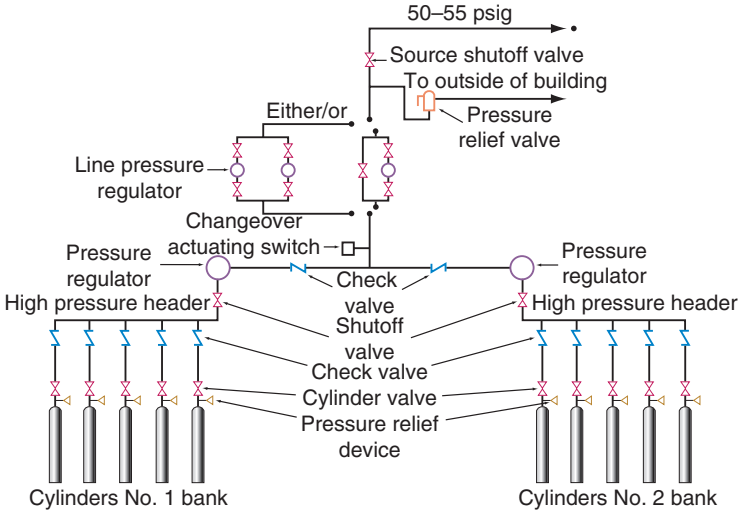

Fig. 41.7 Gas Cylinder Manifold System. The alternating supply system is composed of primary and reserve banks, which alternate to charge the piping system. (Modified from Standard for nonflammable medical gas systems, NFPA No. 56F. Copyright 1973, National Fire Protection Association, Boston, MA.)

Fig. 41.8 Alternating supply system of N_2O.

Fig. 41.9 Large stand tank and reserve tank of liquid O_2 represents a typical bulk gas system with a reserve.

bank becomes the reserve bank. These cylinder manifold systems have pressure-reducing valves for regulation of delivered pressure and normally have low-pressure alarms that sound when reserve switchover occurs; they also warn of impending depletion or malfunction. Cylinder manifolds or alternating supply systems are used to supply O_2 from a central location in small facilities or to supply specialty gases, such as N_2O, to operating rooms (Fig. 41.8).

A *cylinder supply system with a reserve* consists of a primary supply, a secondary supply, and a reserve supply. When the primary gas supply is depleted by the demand, it automatically switches to the secondary supply. Master signal panels indicate that the changeover has occurred. Such a supply system operates in a manner similar to the alternating system except that this system has a reserve supply if primary and secondary supplies become depleted. Liquid containers may be used as the primary and secondary gas sources, but the reserve supply is usually provided by high-pressure gas cylinders. Gas cylinders are used as the reserve supply because low-pressure liquid containers lose approximately 3% of their contents per day.[2]

For the sake of economy, safety, and convenience, most large health care facilities use a *liquid bulk O_2 system*. A small volume of liquid O_2 provides a very large amount of gaseous O_2 and minimizes space requirements. However, along with this advantage comes a major problem. O_2 has a critical temperature well below room temperature (−118.6°C [−181.4°F]).[1] Liquid O_2 must continually be stored below this temperature or it will revert to its gaseous state.

To stay in liquid form, O_2 is stored in large stand tanks (Fig. 41.9) at relatively low pressure (<250 psig). These tanks are similar to giant thermos bottles, consisting of inner and outer steel shells separated by an insulated vacuum chamber (Fig. 41.10). Because it eliminates heat conduction, the vacuum keeps the liquid O_2 below its critical temperature without refrigeration. When it flows through vaporizer coils exposed to ambient temperature, the liquid O_2 quickly converts back to a gas. With the O_2 in its gaseous form, the pressure is decreased to the standard working pressure of 50 psi by a pressure-reducing valve. A safety vent allows vaporized liquid O_2 to escape if warming causes cylinder pressure to increase above a set limit.

Smaller liquid cylinders are used for home O_2 supply. These cylinders come in several sizes and hold between ⅔ and 1½ ft^3 of liquid O_2. Small liquid O_2 cylinders are refilled onsite by means of transfer of liquid O_2 from a large cylinder. Chapter 57 describes the use of these small liquid O_2 cylinders in the home.

Bulk Oxygen Safety Precautions

The NFPA sets standards for the design, construction, placement, and use of bulk O_2 systems.[2] A key provision in these standards is the requirement for a reserve or backup gas supply to equal the average daily gas usage of the hospital. To meet this requirement, most large facilities have a second, smaller liquid tank. Smaller facilities may use a cylinder gas manifold as the backup.

Failure of bulk O_2 supply systems has been reported, with resultant major problems.[13–16] Failure of a bulk O_2 supply can be life-threatening to any patient receiving O_2 or gas-powered ventilatory support. For this reason, the RT team must be prepared. Adherence to an established protocol is a quick way to identify and prioritize all affected patients. When affected patients are identified, staff members move appropriate backup equipment to the bedside (e.g., portable cylinders, bag-valve-mask resuscitators). Trained personnel bypass the failed system and provide needed patient support while engineers determine the cause of the failure and correct it.

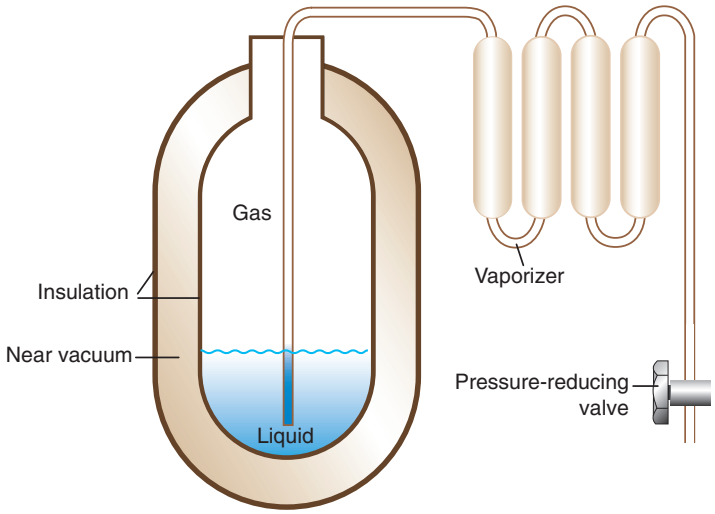

Fig. 41.10 Liquid O_2 stand tank (fixed station). (Modified from Cairo JM, Pilbeam SP: *Mosby's Respiratory Care Equipment*, ed 8, St Louis, 2010, Mosby.)

MINI CLINI

Failure of the Oxygen Supply

Problem

A delivery truck accidentally hit the hospital supply line, resulting in an O_2 leak. The O_2 supply to the hospital had to be turned off for approximately 12 h to repair the damaged pipe and allow associated testing.

Solution

Before the repair could occur, the RT team obtained H cylinders, reducing valves, O_2 hoses and quick connects and quickly moved these items to all areas of the hospital were patients required O_2. The reducing valve was connected to the H cylinder following the procedure described in this chapter and the O_2 supply line with the quick connect on one end was connected to the reducing valve. The reducing valve was set to deliver 50 psig. The zone valve was closed to the patient care area and the O_2 quick connect was connected to the O_2 outlet in an empty patient room. This setup back-feed all O_2 outlets in the patient care area. Having the zone vale closed prevents O_2 from traveling to other areas and allows the rupture gas supply line to be repaired. The RT team had to remain observant and change tanks as they neared empty. A backup tank, reducing valve, and O_2 supply line with a quick connect should always available when a patient care area is being back fed.

DISTRIBUTION AND REGULATION OF MEDICAL GASES

Before it can be administered to a patient, a medical gas must be delivered to the bedside and the pressure reduced to a workable level. This is the primary function of gas distribution and regulation systems. Modern hospital gas distribution systems deliver bulk O_2 and compressed air to patients' rooms and special care areas through an elaborate piping network. This network may include a vacuum source and, for surgical areas, N_2O. Patient transport still requires the use of portable cylinders. Whether delivery occurs by central bulk supply or cylinder, patient safety is always the primary aim. For this reason, RTs must be proficient in the use of both types of delivery systems.

Central Piping Systems

Structural standards for piping systems are established by the NFPA and are described in more detail elsewhere.[2] Fig. 41.11 shows a simple central piping gas system. The gas pressure in a central piping system is normally reduced to the standard working pressure of 50 psi at the bulk storage location. A main alarm warns of decreases in pressure or interruptions in flow from the source. **Zone valves** (Fig. 41.12) throughout the system can be closed for system maintenance or in case of fire. Wall or station outlets at the delivery sites allow for the connection of various types of equipment to the gas distribution system. Because most delivery outlets include O_2, air, vacuum, and possibly N_2O, special safety connectors are used to help prevent accidental misconnections.

Safety Indexed Connector Systems

One of the greatest risks in medical gas therapy is giving a patient the wrong gas. Carefully reading the cylinder or outlet labels is the best way to avoid these accidents. However, human error does occur. For this reason, industry has developed indexed safety systems for gas delivery. These safety systems make misconnection between pieces of equipment nearly impossible. Three basic indexed safety systems are used in the delivery and regulation of medical gases: (1) the American National Standard/Compressed Gas Association Standard for Compressed Gas Cylinder Valve Outlet and Inlet Connections, or the ASSS; (2) the **diameter-index safety system** (DISS); and (3) the PISS.[17,18]

American Standard Safety System

Adopted in the United States and Canada, the ASSS provides standards for threaded high-pressure connections between large compressed gas cylinders (sizes F through H/K) and their attachments.[17] Specifications exist for more than 60 gases and gas mixtures. Fig. 41.13 shows a typical ASSS connection between a threaded cylinder outlet and a pressure-reducing valve nipple. Use of the ASSS standards makes misconnections difficult because

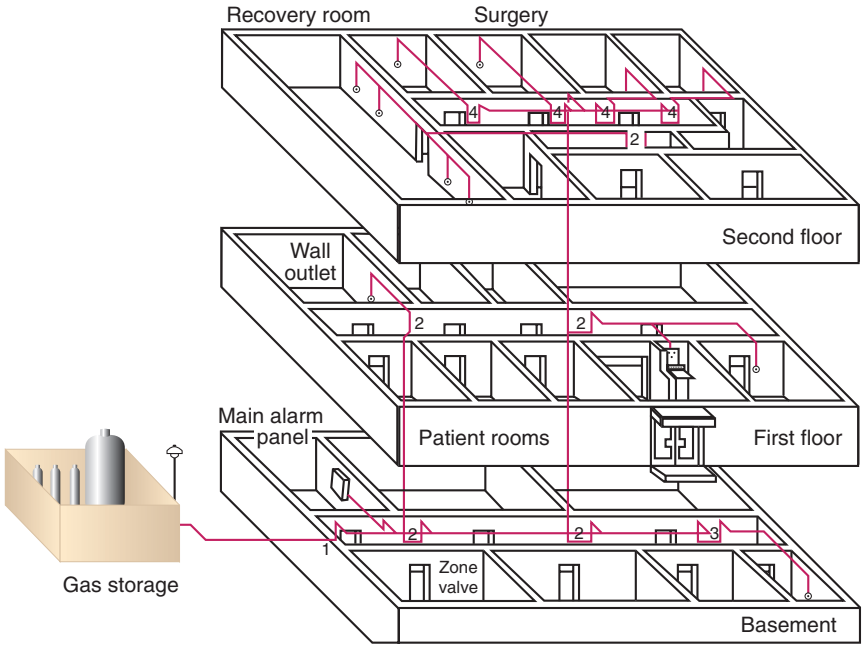

Fig. 41.11 A Hospital Piping System. Numbers indicate zone valves.

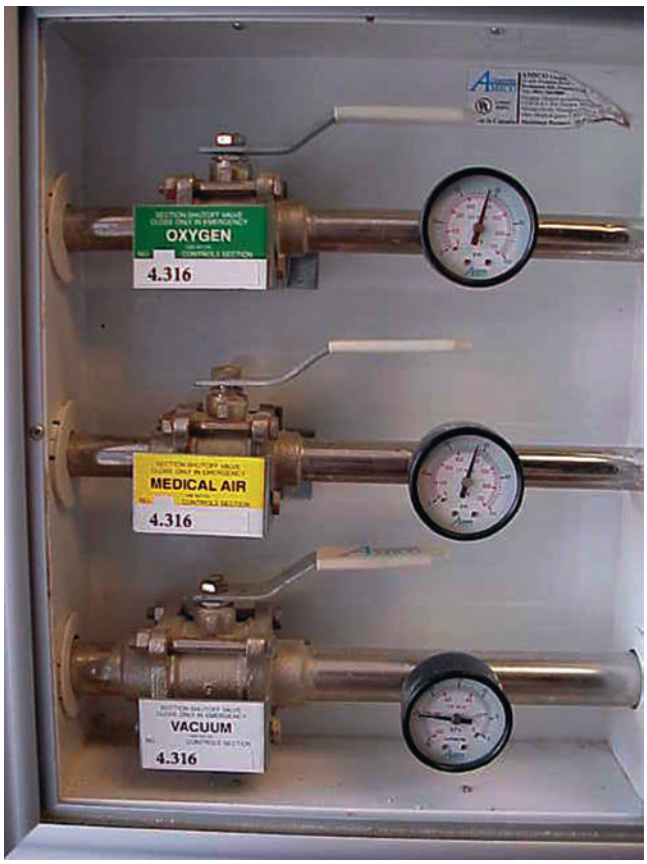

Fig. 41.12 O_2, air, and vacuum zone valves.

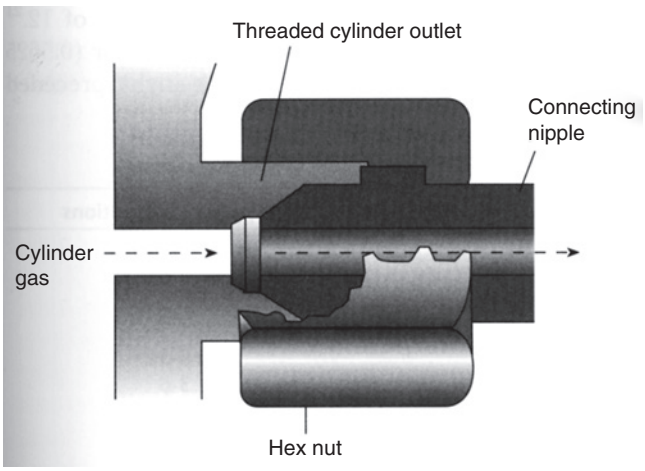

Fig. 41.13 Typical American standard supply system connection used to attach a reducing valve to a large high-pressure cylinder. A hexagonal nut is held on the nipple of the reducing valve by a circular collar. The connection is made by (1) aligning the reducing valve nipple with the conical cylinder valve outlet and (2) tightening the reducing valve hex nut onto the threaded cylinder outlet. Different threading and cylinder outlet sizes make accidental misconnections unlikely.

the size (bore) of the cylinder outlet and its threading differ based on the type of gas in the cylinder.

Because there are only 26 connections for the 62 listed gases and mixtures, each gas may not have a unique connection. Some gases have identical connections. Catalogues of cylinder equipment show the connection specifications for each type of cylinder and gas. A typical description for a large cylinder of O_2 is as follows: CGA-540 0.903-14NGO-RH-Ext. The connection for the threaded outlet of this cylinder is listed by the CGA as connection number 540. The outlet has a thread diameter (bore) of 0.903 in, there are 14 threads per inch, and the threads are right-handed (RH) and external (Ext). It is generally necessary to use only one or two outlet connections because most of the gases used by RTs are grouped within a few connector sizes. However, practitioners should be familiar with the classification scheme in general because expanding instrumentation and scope

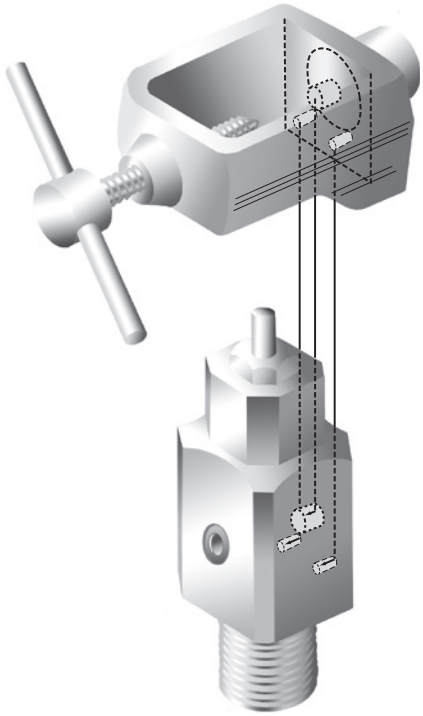

Fig. 41.14 Yoke connector showing regulator inlet and pin-indexed safety system (for cylinders size AA to E).

of services may bring RTs in contact with other gases and gas systems.

Pin-Index Safety System

Pin indexing is part of the ASSS but applies only to the valve outlets of small cylinders up to and including size E. These cylinders have a yoke type of connection. Fig. 41.14 illustrates the general structure of the pin-indexed yoke connection. The upper yoke fits over the lower valve stem. Two pins projecting from the inner surface of the yoke connector mate with two pinholes bored into the valve stem. Proper pin position aligns the small receiving nipple of the yoke with the recessed cylinder valve outlet. Tightening the hand screw on the yoke firmly seats the receiving nipple into the valve outlet. A nylon washer or bushing is typically used to ensure a leak-free connection.

Similar to the ASSS, the PISS helps prevent accidental misconnections between pieces of equipment. The exact positions of pins and pinholes vary for each gas. Unless the pins and holes align perfectly, the yoke nipple cannot seat in the recessed valve outlet. Six holes and pin positions constitute the total system. Because overlapping holes cannot be used, there are 10 possible pin combinations. Fig. 41.15 is a diagram of the location of all six possible holes and their index numbers. Table 41.5 lists the gases included in the PISS system, including their index positions.

Diameter-Index Safety System

The ASSS and the PISS provide standards for high-pressure connections between cylinders and equipment; the DISS was established to prevent accidental interchange of low-pressure (<200 psig) medical gas connectors.[18] RTs typically find DISS connections (1) at the outlets of pressure-reducing valves attached to

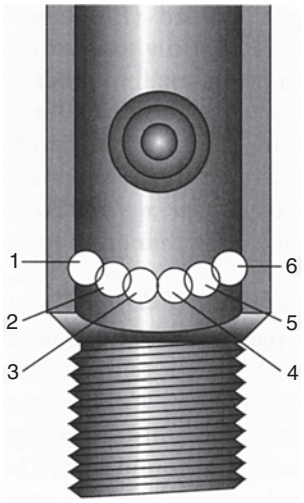

Fig. 41.15 Location of the pin-index holes in the cylinder valve face for different gases. See Table 41.5 for pin-index hole locations for various gases.

TABLE 41.5 Pin-Index Hole Positions

Gas	Pin Positions
O_2	2–5
O_2/CO_2 (CO_2 not >7%)	2–6
He/O_2 (He not >80%)	2–4
C_2H_4	1–3
N_2O	3–5
C_3H_6	3–6
He/O_2 (He > 80%)	4–6
O_2/CO_2 (CO_2 > 7%)	1–6
Air	1–5

See Fig. 41.15.
C_2H_4, ethylene; *C_3H_6*, cyclopropane

cylinders; (2) at the station outlets of central piping systems; and (3) at the inlets of blenders, flow meters, ventilators, and other pneumatic equipment.

As shown in Fig. 41.16, the DISS connection consists of an externally threaded body and a mated nipple with a nut. As the two parts are joined, the shoulders of the nipple and the bores of the body mate, with the union held together by a hand-tightened hex nut. Indexing is achieved by varying the dimensions of the borings and shoulders. There are 11 indexed DISS connections and 1 connection for O_2 for a total of 12.[18] The standard threaded O_2 connector (0.5625 inch in diameter and 18 threads per inch) preceded adoption of this safety system. Nonetheless it has been assigned a DISS number of 1240.

Although O_2 and air are generally used from a central outlet, it may be necessary to administer other gases that have different DISS connections. To avoid stocking a large variety of pressure regulators, flow meters, and connectors for special gas use, adapters can be used to convert various DISS connections. The use of adapters to bypass a safety system carries an increased risk. For this reason, RTs should exercise extreme caution when adapting equipment connections. Misconnections can occur, with negative patient consequences.[13]

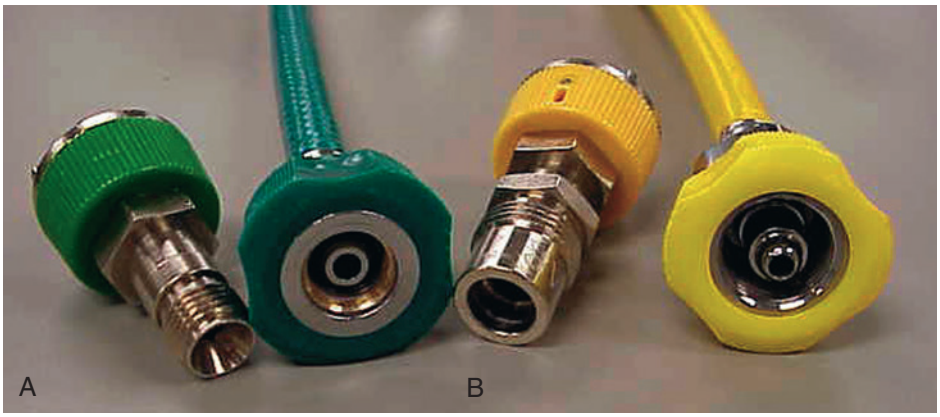

Fig. 41.16 O_2 (A) and air (B) diameter index safety system (DISS) connections. The two shoulders of the nipple allow the nipple to unite only with a body that has corresponding borings. If the match is incorrect, the nut does not engage the body threads. The difference in the shoulders and bore between the O_2 (A) and air (B) DISS connections is evident.

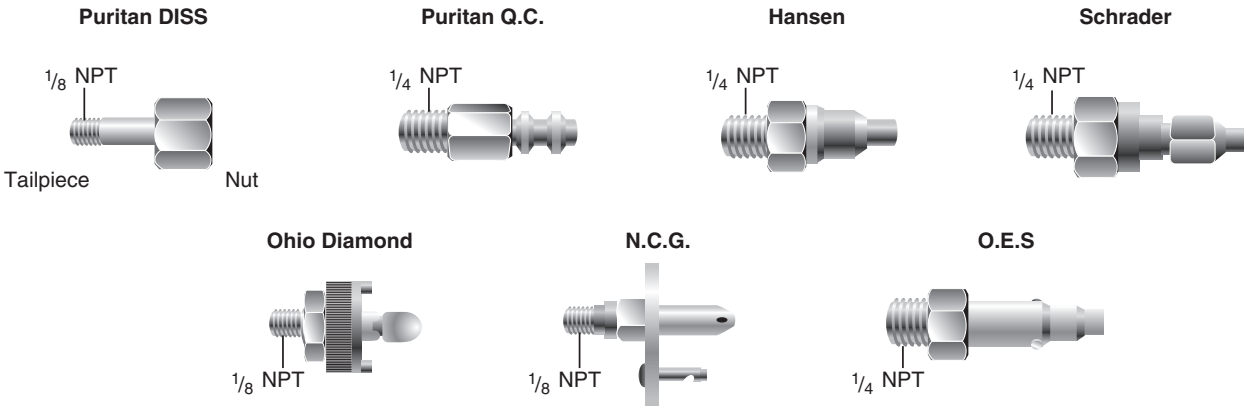

Fig. 41.17 Common brands of quick connects. *DISS,* diameter-index safety system; *NPT,* National pipe thread taper. (Courtesy Nellcor Puritan Bennett, Pleasanton, CA.)

Quick-Connect Systems

Station outlets at the patient's bedside allow quick access to a bulk supply of O_2, air, or vacuum sources. Station outlets have DISS connections or quick-connect systems that are gas specific or vacuum specific. Manufacturers have designed specially shaped connectors for each gas (Fig. 41.17). Because each connector has a distinct shape, it does not fit into an outlet for another gas and each manufacturer has its own unique design. Therefore connectors from different manufacturers are not interchangeable. As long as a facility is standardized for a single quick-connect system, this incompatibility is seldom a problem.

A variety of safety systems help prevent inadvertent misconnections between medical delivery systems and equipment. Fig. 41.18 summarizes the use of and relationships between the ASSS, PISS, and DISS systems as applied to cylinder gases. Proficiency in the proper use of these systems is a basic skill of RTs.

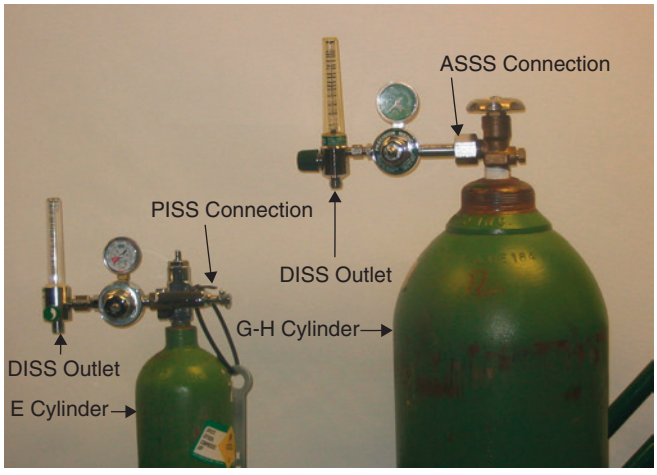

Fig. 41.18 Comparison of Safety Systems Used for Compressed Gases. The diameter-index safety system *(DISS)* connections are for low-pressure outlets (<200 psig). The American standard safety system *(ASSS)* provides for high-pressure connections with large cylinders. A variation of the ASSS entails a yoke-and-pin system *(PISS)* for connecting to small cylinders (AA through E).

Regulating Gas Pressure and Flow

Whatever the source of medical gas, the pressure and flow must be regulated or reduced to a safe level. If the goal is solely a reduction in gas pressure, a **reducing valve** is used. For control

of gas flow to a patient, a **flow meter** is used. If control of both pressure and flow is needed, a regulator is used.

Cylinder gases such as O_2 and air exert a pressure that is much too high for use with respiratory care equipment. These high pressures must be reduced to a lower "working" level. In the United States, this working pressure is 50 psig. For bulk delivery systems with individual station outlets, built-in reducing valves decrease the delivered pressure to 50 psig. This standard pressure can be directly applied to power devices such as ventilators (see Chapter 46). However, if the goal is to control gas delivery to a patient for O_2 therapy or nebulized medication (see Chapters 40 and 42), a flow meter must also be used.

High-Pressure Reducing Valves

The two basic types of high-pressure reducing valves are single stage and multiple stage. Reducing valves are available as preset or adjustable. Although all of these valves function on the same principle, the design, features, and use are different. This section differentiates preset reducing valves and adjustable reducing valves and discusses multiple-stage reducing valves.

Preset reducing valve. Fig. 41.19 shows the basic design of a high-pressure preset reducing valve. High-pressure gas (2200 psig for O_2) enters through the valve *(A)*, with the inlet pressure displayed on the pressure gauge *(B)*. The body of the valve is divided into a high-pressure chamber *(C)* and an ambient-pressure chamber *(D)* by a flexible diaphragm *(E)*. Attached to the diaphragm in the ambient-pressure chamber is a spring *(F)*, which is fixed to the other side of the chamber. Also attached to the diaphragm but in the high-pressure chamber is a valve stem *(G)* that sits on the high-pressure inlet *(H)*. Gas flows through the valve inlet *(H)* into the high-pressure chamber and on to the gas outlet *(I)*. The pressure chamber is supplied with a safety vent *(L)* preset to 200 psig to release pressure in the event of malfunction.

The spring tension is calibrated to give when the pressure on the diaphragm exceeds 50 psig. When this happens, the valve stem is pushed forward and closes the high-pressure inlet, preventing further entry of gas into the reducing valve. However, as long as gas is allowed to escape from the pressure chamber through the outlet *(I)*, the inlet valve remains open and allows gas flow. The regulator maintains a balance between outlet flow and inlet pressure. Automatic adjustment of the diaphragm–spring combination keeps the pressure in the high-pressure chamber at a near-constant 50 psig—hence the name *preset*. Preset reducing valves are normally used in conjunction with high-pressure gas cylinders to decrease the pressure to the standard 50 psig used with most respiratory care equipment.

Adjustable reducing valve. Although most respiratory care equipment works at the standard 50 psig, some devices need variable pressures. To provide variable outlet pressures from a high-pressure gas source, an adjustable reducing valve is needed. Fig. 41.20 shows the basic design of a high-pressure adjustable reducing valve. As with the preset design, the inlet valve *(H)* remains open until the gas pressure exceeds the spring tension, displacing the diaphragm and blocking further gas entry. However, whereas the preset reducing valve provides a fixed pressure, the adjustable reducing valve allows a change in outlet pressure. Outlet pressure can be changed with a threaded hand control *(K)* attached to the end of the diaphragm spring. Changing the tension on the valve spring varies pressure over a wide range, usually between 0 and 100 psig.

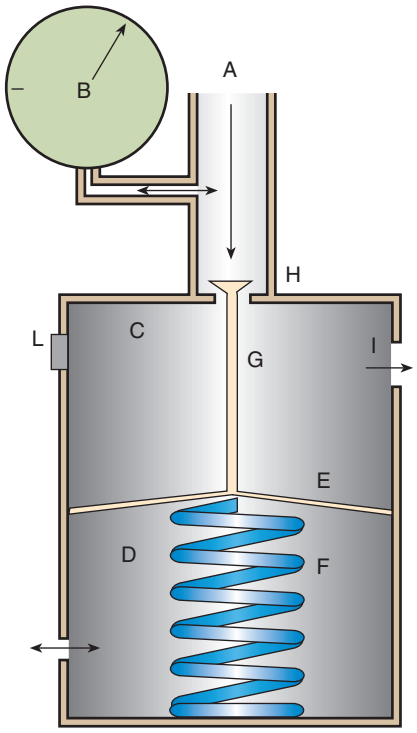

Fig. 41.19 Preset high-pressure reducing valve.

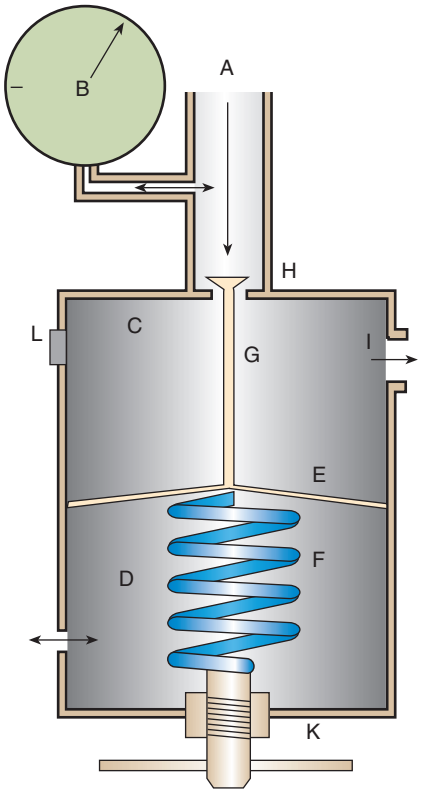

Fig. 41.20 Adjustable high-pressure reducing valve.

The adjustable reducing valve commonly is used in combination with a Bourdon-type flow gauge (discussed later). The combination of a flow meter with a reducing valve is called a **regulator**.

Multiple-stage reducing valve. As the name suggests, a *multiple-stage reducing valve* reduces pressure in two or more steps. Multiple-stage reducing valves can be either preset or adjustable and can be combined with a flow meter device as a true regulator. Two-stage reducing valves are used occasionally; three-stage units are rarely needed. A two-stage reducing valve functions as two single-stage reducing valves working in series. Gas enters the first stage, where the pressure is reduced to an intermediate level (usually 200 to 700 psig). Gas then enters the second stage, where the pressure is decreased to working level (usually 50 psig). Because each pressure chamber has one safety relief vent, the user can usually determine the number of stages in a reducing valve by noting the number of relief vents present. Because they reduce pressure in multiple steps, these valves provide more precise and smooth flow control. However, they are larger and more expensive than single-stage reducing valves. For this reason, a multiple-stage reducing valve should be considered only if minimal fluctuations in pressure or flow are critical factors, as in research activities. For routine hospital work, single-stage reducing valves are satisfactory.

Proper use of high-pressure reducing valves. When a cylinder attached to a high-pressure reducing valve is open, gas undergoes rapid decompression, followed by rapid recompression. These rapid pressure and temperature changes may cause failure of the reducing valve. Rapid temperature changes can ignite combustible materials; this risk is increased in the presence of 100% O_2. Box 41.1 provides guidelines for minimizing the risk associated with setting up O_2 cylinders with a high-pressure reducing valve or regulator.[1]

MINI CLINI

Leaky Connections

Problem

Following standard procedure, the RT attaches a pressure-reducing valve to an O_2 cylinder. When the RT opens the cylinder valve, she can hear gas leaking at or near the connection.

Solution

A leak usually indicates that the connection between the pressure-reducing valve and the cylinder outlet is not tight. If the cylinder outlet is a standard ASSS threaded connector, the connection is either cross-threaded or not properly seated and tightened. To solve this problem, the RT closes the cylinder valve and removes and reattaches the pressure-reducing valve, taking care to thread the connection properly and to tighten with a wrench. If the cylinder outlet is a pin-indexed connector, the RT closes the cylinder valve and removes the pressure-reducing valve. The RT checks to ensure that the nylon washer is present, in good condition, and properly fitted. She then reattaches the pressure-reducing valve, taking care to seat the connection properly and to tighten it by hand. If the leak continues after these corrective actions, it is likely that the pressure-reducing valve is malfunctioning and should be replaced.

BOX 41.1 Safe Procedure for Setup of an Oxygen Cylinder and Reducing Valve or Regulator

1. Secure the cylinder according to the CGA guidelines. Verify the contents from the label that matches the color code and valve indexing.
2. Remove the protective cap or wrap and inspect the cylinder valve to ensure that it is free of dirt, debris, and oil.
3. Warn any persons present that the cylinder valve is about to be "cracked" and that it will make some noise. Turn the cylinder valve away from persons present, stand to the side, and quickly open and close the valve. This removes any dust or small debris from the cylinder valve outlet.
4. Inspect the valve or regulator inlet for debris, dirt, and oil. Check the device label, and confirm that it is intended for high-pressure service and for use with the gas to be administered. O_2-reducing valves and regulators should have a label stating: *Oxygen: Use No Oil.*
5. After the valve or regulator inlet is confirmed to be free of contaminants, securely tighten (but do not force) the device onto the cylinder outlet. When connections to the cylinder are being made, use appropriate wrenches that are free of oil and grease. Never use pipe wrenches. Use only cylinder valve connections that conform to the ASSS and the PISS. Low-pressure connections must comply with the DISS or be noninterchangeable, low-pressure quick connects. Never connect fixed or adjustable orifices or metering devices directly to a cylinder without a pressure-reducing valve.
6. Confirm that the regulator or reducing valve is in the *off* or *closed* position and slowly open the cylinder valve to pressurize the attached reducing valve or regulator. After pressurization has occurred, open the cylinder valve completely and turn it back one-fourth to one-half turn (this maneuver prevents a condition known as "valve freeze," in which the valve cannot be turned).

ASSS, American Standard Safety System; *CGA,* Compressed Gas Association; *DISS,* diameter-index safety system; *PISS,* pin-index safety system.

Low-Pressure Gas Flow Meters

As with drugs, giving a medical gas to a patient requires knowledge of the dosage being delivered. Physicians often prescribe O_2 dosage as a flow in liters per minute. In addition, certain gas-mixing equipment requires accurate knowledge of input flows, sometimes involving two or more gases. Flow meters allow the rate of gas flow to a patient to be set and controlled. When the gas source is a high-pressure gas cylinder, a regulator (reducing valve plus flow meter) is required. However, when the source is a bulk central supply system, the pressure has already been reduced to 50 psig by the time it reaches the outlet stations and only a flow meter is required.

Three categories of flow meters are used in respiratory care: the flow restrictor, the **Bourdon gauge**, and the **Thorpe tube**. The Thorpe tube has two different designs: pressure compensated or not pressure compensated (uncompensated). Although uncompensated Thorpe tubes are rare, they may still be used at some institutions. For this reason, the principles underlying each of the four types of flow metering devices are compared and contrasted in the following text.

Flow restrictor. The flow restrictor is the simplest and least expensive flow meter device. As shown in Fig. 41.21, a flow restrictor consists solely of a fixed orifice calibrated to deliver a specific flow at a constant pressure (50 psig). The operation of

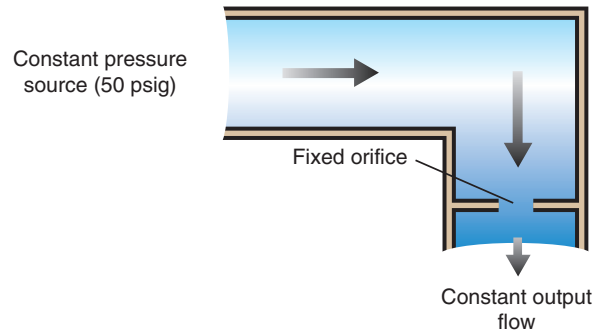

Fig. 41.21 Flow restrictor.

TABLE 41.6 Advantages and Disadvantages of Flow Restrictors

Advantages	Disadvantages
Low-cost, simple, reliable (no moving parts)	Different versions required for different flows
Cannot be set to incorrect flow	Accuracy varies with changes in source and downstream pressures
Can be used in any position (gravity-independent)	Cannot be used with high-resistance equipment

the flow restrictor is based on the principle of flow resistance. Specifically, the flow of gas through a tube can be quantified with the following equation:

$$R = \frac{P_1 - P_2}{V}$$

Rearranging the equation to solve for flow *(V)* yields the following:

$$V = \frac{P_1 - P_2}{R}$$

where V is the volumetric flow per unit time, P_1 is the pressure at the **upstream** point (point 1), P_2 is the pressure at the **downstream** point (point 2), and R is the total resistance to gas flow.

By design, a flow restrictor requires a source of constant pressure (usually 50 psig). As long as the source pressure remains fixed, $P_1 - P_2$ should stay constant. With a fixed-size orifice, the flow resistance *(R)* also remains constant. The rate of gas flow through a flow restrictor can be increased by increasing P_1 (upstream pressure) or by selecting a larger orifice size. Both fixed and adjustable orifice flow restrictors are used clinically. Commercially produced flow restrictors are calibrated at 50 psig. Table 41.6 summarizes the advantages and disadvantages of flow restrictors.

RULE OF THUMB A flow restrictor is typically used to deliver a nonadjustable flow of air or O_2 to a medication nebulizer. An adjustable flow restrictor combined with an E cylinder of O_2 is used to adjust flow to an O_2 delivery device, medication nebulizer, or resuscitation bag. It is important to remember that narrowing or pinching of the O_2 tubing going to these devices will reduce gas flow.

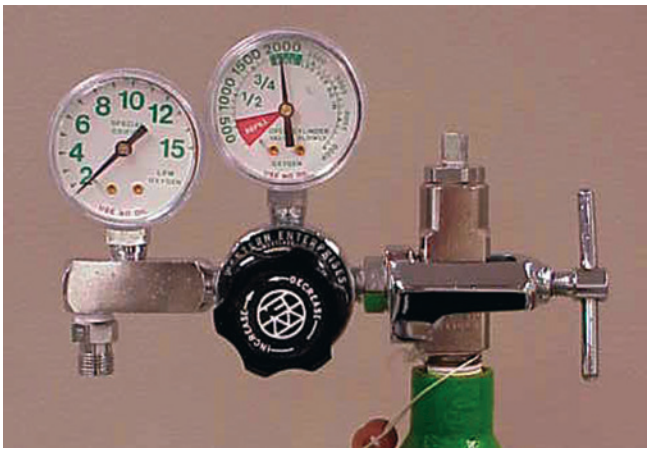

Fig. 41.22 Bourdon gauge regulator.

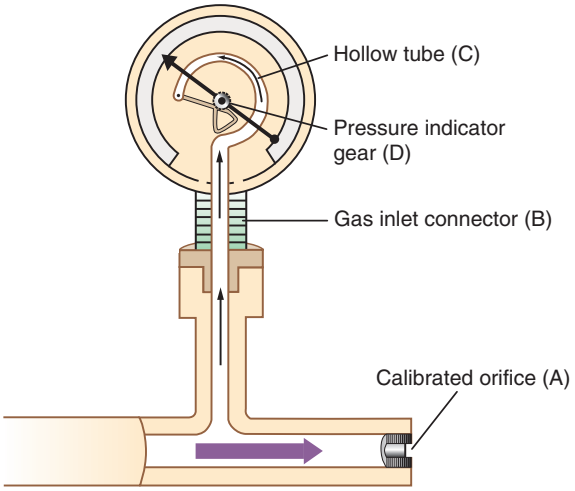

Fig. 41.23 Components of a Bourdon Pressure Gauge. See text for more information.

Bourdon gauge. A Bourdon gauge (Fig. 41.22) is a flow meter device that is always used in combination with an adjustable pressure-reducing valve. Similar to the flow restrictor, the Bourdon gauge uses a fixed orifice. In contrast to the flow restrictor, the Bourdon gauge operates under variable pressures as adjusted with the pressure-reducing valve. The Bourdon gauge is a fixed-orifice, variable-pressure flow meter, so increasing the upstream pressure increases gas flow out of the device unless downstream pressure also increases.

As shown in Fig. 41.23, a Bourdon gauge has a calibrated fixed orifice *(A)*, which creates outflow resistance. The gauge itself is attached with a connector *(B)* located proximal to the orifice. Inside the gauge is a curved hollow closed tube *(C)* that responds to pressure changes by changing shape. The force of gas pressure tends to straighten the tube, causing its distal end to move. This motion is transmitted to a gear assembly and indicator needle *(D)*. Although its reading changes based on pressure, the numbered scale is calibrated to read the needle movement in units of flow (liters per minute).

As with the flow restrictor with a fixed orifice, the output flow of the Bourdon gauge is proportional to the driving

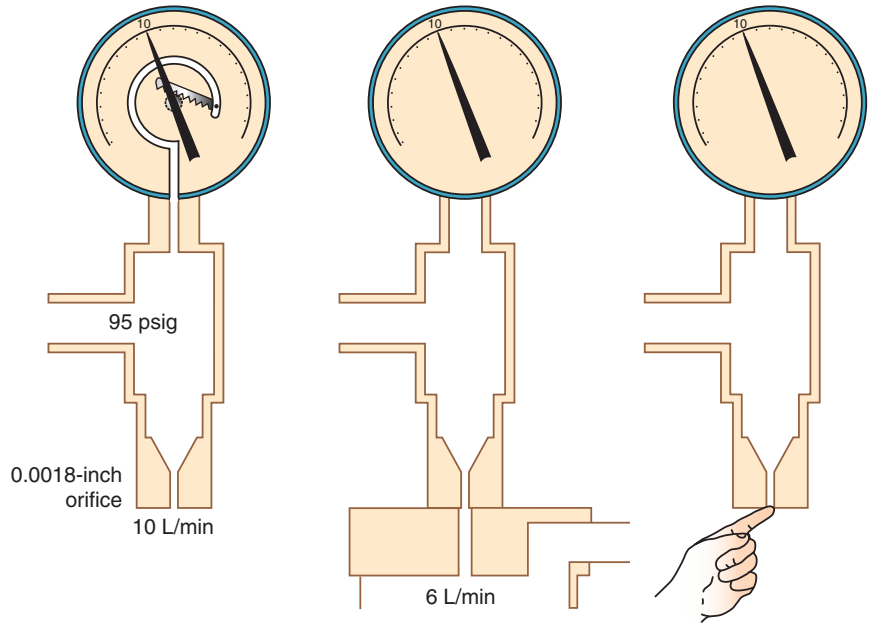

Fig. 41.24 Bourdon performance when downstream pressures increase as a result of high-resistance equipment or blockage. *Left,* Normal state with fixed orifice and no downstream resistance results in an accurate flow reading. *Center,* High-resistance nebulizer increases downstream pressure or back pressure. The result is a falsely high reading (10 L/min vs actual flow of 6 L/min). *Right,* Complete blockage (zero flow) results in flow reading on gauge.

pressure. However, the Bourdon gauge provides a continuous range of flow that the user adjusts by altering the driving pressure. Although the gauge actually measures pressure changes, it displays the corresponding flow.

As with a flow restrictor, gravity does not affect a Bourdon gauge. The Bourdon gauge is the best choice when a flow meter cannot be maintained in an upright position. This situation is common when a patient is being transported with a portable O_2 source. In these instances, keeping the E cylinder upright is seldom easy, and movement of both the O_2 supply and the patient is common. Combined with its continuous range of flows, this feature makes the Bourdon gauge the metering device of choice for patient transport.

The main disadvantage of the Bourdon gauge is its inaccuracy when pressure distal to the orifice (downstream pressure) changes. Specifically, if downstream pressure increases (as when high-resistance equipment is used), the pressure difference across the orifice and actual output flow decrease. However, the Bourdon gauge's flow reading depends on upstream pressure, which stays constant. In this situation, the gauge reading is falsely higher than the actual delivered flow. Because it measures upstream pressure, the gauge registers flow even when the outlet is completely blocked (Fig. 41.24). A user who needs accurate flow when using a device that creates high resistance should not select a Bourdon gauge. A compensated Thorpe tube should be used instead.

Integrated O_2 cylinders (Fig. 41.25), including the Grab 'n Go System (Praxair, Danbury, CT), have combined the O_2 cylinder with a pressure regulator and an adjustable flow restrictor to meter O_2 flow. These portable O_2 systems eliminate the need for separate O_2 tanks, Bourdon gauge regulators, and O_2 keys or wrenches (needed to turn on standard E-cylinders). These integrated systems virtually eliminate problems and delays associated with incorrectly mounted regulators. The practitioner simply selects the flow on the flow-adjusting knob and connects the O_2 tubing to the system connection and the patient.

Fig. 41.25 Grab 'n Go System (Praxair, Danbury, CT).

These integrated O_2 cylinders are available with a digital gauge (INTELLI-OX+TM, Airgas Healthcare) (Fig. 41.26) which displays the remaining gas volume and calculates cylinder duration. This system also incorporates visual and audible alerts. These alerts are activated when cylinder duration falls below 15 minutes or one fourth of the content is remaining. Besides the benefits stated above these systems may increase patient safety by alerting clinicians when the cylinder is nearing empty.

Fig. 41.26 INTELLI-OX+TM integrated O_2 cylinder. (Airgas Healthcare, Radnor, PA).

RULE OF THUMB The Bourdon gauge is the better choice when a flow meter cannot be maintained in an upright position, as in transporting a patient with an O_2 E cylinder. It is important to remember that narrowing or pinching of the O_2 tubing will reduce gas flow while the Bourdon gauge flow reading remains the same.

Thorpe tube. The Thorpe tube flow meter (Fig. 41.27) is always attached to a 50-psig source, either a preset pressure-reducing valve or a bedside station outlet. Compared with the flow restrictor and the Bourdon gauge, the Thorpe tube functions as a variable-orifice, constant-pressure flow meter; thus increasing the size of the orifice increases the flow of gas. Fig. 41.28 shows how a Thorpe tube works. The key component in this device is a tapered transparent tube that contains a float. The diameter of the tube increases from bottom to top. Gas flow suspends the float against the force of gravity. To read the flow, one simply compares the float position with an adjacent calibrated scale, normally calibrated in liters per minute.

Although the Bourdon gauge measures pressure, the Thorpe tube is used to measure true flow. Flow measurement involves the complex interaction of gravity and fluid dynamics. When gas begins to flow into a Thorpe tube, the initial pressure difference lifts the float. As the needle valve is opened, the float rises in the widening tube, the space available for flow around it increases, and resistance to flow decreases. The float ultimately stabilizes when the pressure difference across the float (an upward force) equals the opposing downward force of gravity.

Fig. 41.27 Thorpe tube flow meter.

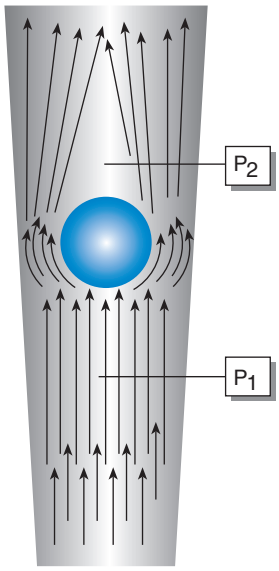

Fig. 41.28 The position of the float in a Thorpe tube flow meter is based on a balance between the force of gravity and the pressure difference ($P_2 - P_1$) across it as determined by the variable-sized orifice between the float and the tube wall.

As the needle valve of the flow meter is opened, the increase in flow initially disrupts this balance, causing an increase in the pressure difference across the float. With the upward pressure difference greater than the downward force of gravity, the float rises. However, as the float rises, the available "orifice" increases in diameter. Flow resistance around the float decreases, and the pressure difference again equilibrates with gravity. The float position stabilizes at a higher level, proportionate to the greater flow around it.

Thorpe tubes come in two basic designs: back pressure-compensated and back pressure-uncompensated. The term *pressure compensation* refers to a design that prevents changes in

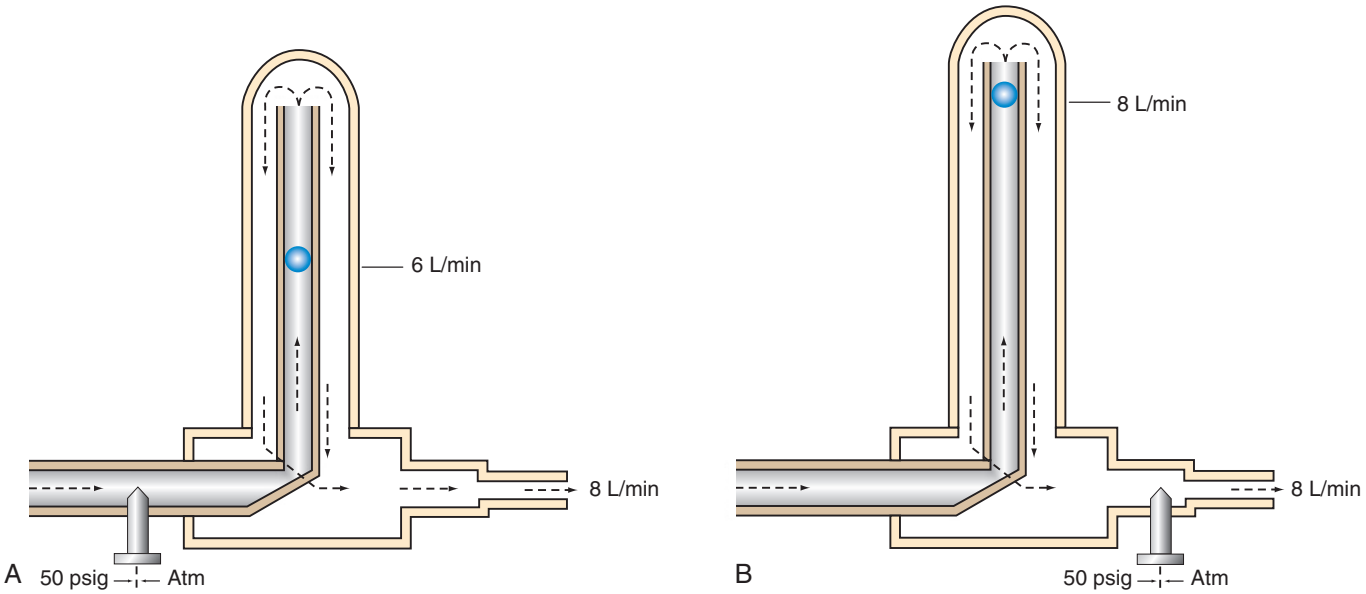

Fig. 41.29 Comparison of back pressure-uncompensated (A) and back pressure-compensated (B) Thorpe tube flow meters. In the pressure-uncompensated flow meter, the flow-control valve is proximal to the meter and the gauge records less than the actual output. In the pressure-compensated flow meter, location of the valve distal to the meter correlates the gauge reading with the output.

downstream resistance, or back pressure, from affecting meter accuracy. All manufacturers now supply only back pressure-compensated Thorpe tubes for the administration of medical gases. However, some ventilators and anesthesia machines still use back pressure-uncompensated Thorpe tubes. For this reason, clinicians using these devices must understand the effect of back pressure on their accuracy. Downstream resistance increases when the user connects a flow meter to certain types of equipment. Almost all therapy gas equipment produces some flow restriction. Devices such as jet nebulizers produce very high downstream resistance. Depending on their design, Thorpe tube flow meters respond to resistance in one of two ways.

The *uncompensated* Thorpe tube flow meter is calibrated in liters per minute but at atmospheric pressure (without restriction). Gas from a 50-psig source flows into the meter at a rate controlled by a needle valve located before the flow tube (Fig. 41.29A). When the user attaches flow-restricting equipment to the meter, downstream resistance increases, which increases pressure in the flow tube. As long as this pressure does not exceed 50 psig, gas continues to flow through the tube. However, the added downstream resistance increases the pressure in the flow tube above atmospheric pressure. At this higher pressure, a greater amount of gas flows through a given restriction than at atmospheric pressure so that the float at a given height on the scale indicates more gas flow through the tube than is actually occurring. Under these conditions, an *uncompensated Thorpe tube falsely shows a flow lower than that actually delivered to the patient.*[4]

In contrast, the scale of the compensated Thorpe tube flow meter is calibrated at 50 psig instead of at atmospheric pressure. Its flow-control needle valve is placed after (distal to) the flow tube (see Fig. 41.29B). The entire meter operates at constant 50-psig pressure. Knowing that the compensated Thorpe tube operates at 50 psig helps identify it. When a compensated Thorpe tube is connected to a 50-psig gas source with the needle valve closed, the float "jumps" and then returns to zero as the Thorpe tube is pressurized. Because the entire meter operates at constant pressure, an increase in downstream resistance increases pressure distal to the needle valve only. As long as the downstream pressure does not exceed 50 psig (in which case flow ceases), *the position of the float accurately reflects actual outlet flow*. For this reason, the pressure-compensated Thorpe tube is the preferred instrument in most clinical situations.

The only factor limiting the use of a pressure-compensated Thorpe tube is gravity. Because it is accurate only in an upright position, a Thorpe tube is not the ideal choice for patient transport. In these cases, the gravity-independent Bourdon gauge is a satisfactory alternative. Fig. 41.30 summarizes the effects of downstream resistance, or back pressure, on the Bourdon gauge and pressure-compensated and pressure-uncompensated Thorpe tube flow metering devices.

RULE OF THUMB When an accurate gas flow is needed with a device that creates a high resistance, a compensated Thorpe tube should be used instead of a Bourdon gauge. Thus a flow meter with a quick connect is attached to most O_2 and air outlets in patient care areas.

SUMMARY CHECKLIST

- All therapy gases must contain at least 20% O_2; all such gases support combustion.
- O_2 from a liquid source or cylinder is over 99% pure, whereas O_2 from a concentrator will be 90 to 96% pure. Changing from a cylinder to a concentrator may require an increase in liter flow to maintain the patient's arterial O_2 saturation.

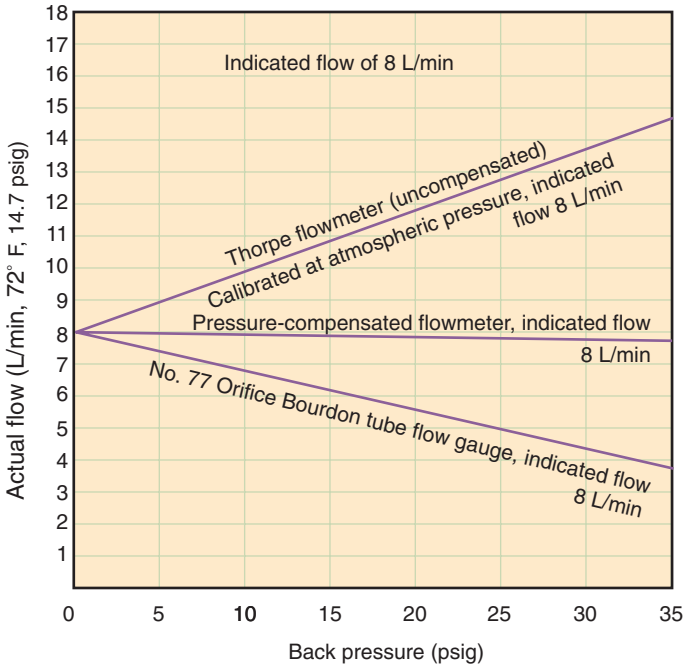

Fig. 41.30 Comparative accuracy of flow meter devices against increasing downstream pressure (back pressure). With the pressure-compensated Thorpe tube, indicated flow equals actual flow regardless of downstream pressure. With the uncompensated Thorpe tube, indicated flow is progressively lower than actual flow as downstream pressure increases. With the Bourdon gauge, indicated flow is progressively higher than actual flow as downstream pressure increases. (Modified from McPherson SP, Spearman CB: *Respiratory Therapy Equipment*, ed 5, St Louis, 1995, Mosby. Modified from Puritan-Bennett Corp, Los Angeles, California.)

MINI CLINI

Selection of Devices to Regulate Gas Pressure or Control Flow

Problem

Three staff RTs are given three separate requests to set up O_2. (1) Mark has an order to transport Ms. Patel to radiology with O_2. (2) Carmen needs to set up a pneumatically powered ventilator with O_2 in the ambulatory clinic (where there are no O_2 outlets). (3) Monica has to set up O_2 therapy with a jet nebulizer for a patient in the intensive care unit (ICU). What equipment should each RT select?

Solutions

1. Because he has to transport a patient using O_2, Mark should select an E cylinder with an adjustable regulator that includes a Bourdon gauge (unaffected by gravity) or an integrated O_2 cylinder that includes an adjustable flow restrictor.
2. Because pneumatically powered ventilators require 50 psig and no central outlets are available, Carmen needs a preset (50 psig) reducing valve and a large G or H size O_2 cylinder.
3. Because all modern ICUs have central wall outlets for O_2, Monica need only select a flow meter with the appropriate quick connect. A compensated Thorpe tube is required for metering flow through high-resistance equipment such as jet nebulizers.

- Inhaled NO is a pulmonary vasodilator; it is beneficial in treating term or near-term infants with severe hypoxia who do not have a diaphragmatic hernia.
- Inhaled NO has not been shown to be beneficial in improving pulmonary hypertension in adult patients; it is also costly.
- Medical gases are stored either in portable high-pressure cylinders or in large centralized bulk reservoirs.
- For positive identification of the contents of a medical gas cylinder, the label must be read carefully.
- The pressure in a gas-filled cylinder indicates its contents; the pressure in a liquid-filled cylinder does not.
- To compute duration of flow (minutes) of a medical gas cylinder, multiply the cylinder pressure (pounds per square inch) by the cylinder factor and divide the result by the set flow (liters per minute).
- Gas supply systems provide gas at 50 psig to outlets throughout a facility through a network of pipes. Such a system must include both zone valves for repairs or fire and alarms to warn of failure.
- Medical gas cylinders must be secured to the wall with a chain, bound or chained to a suitable cart, or placed in a specifically designed cylinder carrier.
- The protective cylinder caps must be kept in place during transportation or storage of cylinders.
- Cylinders for use that are not appropriately labeled should not be transported.
- Flammable materials, especially oil or grease, should not be used on regulators, cylinders, fittings, or valves.
- The cylinder valve should be opened slightly to remove dust and dirt before attaching the regulator.
- Cylinders should never be placed near sources of heat.
- When O_2 is in use, a "No Smoking" sign should be posted unless signs that prohibit smoking in the facility are posted in the entrances.
- Failure of a bulk gas supply system can threaten the lives of patients receiving O_2 therapy or being supported with pneumatically powered devices. A protocol must exist to deal with this emergency.
- Indexed safety systems help prevent misconnections between equipment. The ASSS provides high-pressure connections with large cylinders; the PISS does the same for small cylinders; and DISS connections are for low-pressure outlets, typically 50 psig.
- A reducing valve is used for reduction of gas pressure. A flow meter is used for control of gas flow. A regulator is used for control of both pressure and flow.
- A flow restrictor is used to provide fixed flows of O_2 or air to a medication nebulizer.
- An adjustable flow restrictor combined with an E cylinder of O_2 is used to adjust the flow to an O_2 delivery device, medication nebulizer, or resuscitation bag. It is important to remember narrowing or pinching of the O_2 tubing going to these devices will reduce this gas flow. The Bourdon gauge is the better choice when a flow meter cannot be maintained in an upright position during a patient transported with an O_2 E cylinder. Narrowing or pinching of the O_2 tubing will

reduce gas flow while the Bourdon gauge flow reading remains the same.

- When an accurate gas flow is needed with a device that creates high resistance, a compensated Thorpe tube should be used, especially with high-resistance equipment.

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42

Medical Gas Therapy

Albert J. Heuer and Anne Marie Hilse

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Describe when oxygen (O_2) therapy is needed.
- Assess the need for O_2 therapy.
- Describe what precautions and complications are associated with O_2 therapy.
- Select an O_2 delivery system appropriate for the respiratory care plan.
- Describe how to administer O_2 to adults, children, and infants.
- Describe how to identify and correct malfunctions of O_2 delivery systems.
- Assess and monitor a patient's response to O_2 therapy.
- Describe how and when to modify or recommend modification of O_2 therapy.
- Describe how to implement protocol-based O_2 therapy.
- Identify the indications, complications, and hazards of hyperbaric O_2 therapy.
- Identify when and how to administer specialty therapeutic gases.

CHAPTER OUTLINE

KEY TERMS

atmospheric pressure absolute (ATA)
bronchopneumonia
bronchopulmonary dysplasia
croup
exudative
heliox therapy
high-flow system
high-flow nasal cannula (HFNC)
hyperbaric oxygen (HBO) therapy
hyperoxemia
hyperoxic acute lung injury
hypoxemia
low-flow system
neovascularization
nitric oxide (NO)
protocol-based oxygen therapy
rebound effect
reservoir system
retinopathy of prematurity (ROP)
retrolental fibroplasia

Gas therapy is the most common mode of respiratory care. Most medical gases are drugs. As with any drug, in consultation with the physician, respiratory therapists (RTs) recommend a dosage and delivery method for medical gases, initiate therapy, monitor the response, and alter therapy in relation to the patient care plan.

OXYGEN THERAPY

There is general agreement among clinicians about the proper use of O_2 therapy.[1-4] However, as the primary member of the healthcare team responsible for O_2 administration, the RT must be well versed in all aspects of its use in clinical practice.

General Goals and Clinical Objectives

The overall goal of O_2 therapy is to maintain adequate tissue oxygenation while minimizing cardiopulmonary work. Clinical objectives for O_2 therapy are the following:

- Correct documented or suspected acute hypoxemia
- Decrease symptoms associated with chronic hypoxemia
- Decrease the workload hypoxemia imposes on the cardiopulmonary system

Correcting Hypoxemia

O_2 therapy corrects **hypoxemia** by increasing alveolar and blood levels of O_2. Correction of hypoxemia is the most tangible objective of O_2 therapy and the easiest to measure and document.

Decreasing Symptoms of Hypoxemia

In addition to relieving hypoxemia, O_2 therapy can help relieve the symptoms associated with certain lung disorders, including dyspnea.[5] O_2 therapy also may improve mental function among patients with chronic hypoxemia.[6]

Minimizing Cardiopulmonary Workload

The cardiopulmonary system compensates for hypoxemia by increasing ventilation and cardiac output. In cases of acute hypoxemia, supplemental O_2 can decrease demands on both the heart and the lungs. Patients with hypoxemia breathing room air can achieve acceptable arterial oxygenation only by increasing ventilation. Increased ventilatory demand increases the work of breathing. In these cases, O_2 therapy can reduce both the high ventilatory demand and the work of breathing.

Patients with arterial hypoxemia can maintain acceptable tissue oxygenation only by increasing cardiac output or, if the hypoxemia is chronic, by increasing the red blood cell mass (i.e., polycythemia). Because O_2 therapy acutely increases blood O_2 content, the heart does not have to pump as much blood per minute to meet tissue demands. This reduced workload is particularly important when the heart is already stressed by disease or injury, as in myocardial infarction, sepsis, or trauma.

Hypoxemia causes pulmonary vasoconstriction and pulmonary hypertension. Pulmonary vasoconstriction and hypertension increase workload of the right side of the heart. For patients with chronic hypoxemia, this increased workload over the long term can lead to right ventricular failure (cor pulmonale). O_2 therapy can reverse pulmonary vasoconstriction and decrease right ventricular workload.[7]

Assessing the Need for Oxygen Therapy

There are three basic ways to determine whether a patient needs O_2 therapy. The first is the use of laboratory measures such as arterial blood gas testing to document hypoxemia. Second, a patient's need for O_2 therapy can be based on the specific clinical problem or condition. Third, hypoxemia may cause tachypnea, tachycardia, cyanosis, and distressed overall appearance, and therefore bedside assessment can help identify such a need.

Laboratory measures for documenting hypoxemia include hemoglobin saturation and partial pressure of oxygen (PaO_2), as determined by either invasive or noninvasive means (see Chapter 19). Threshold criteria defining hypoxemia with these measures vary depending on the source, but clinicians and studies predominantly agree that strategies must be balanced to prevent hypoxemia and the emerging dangers of **hyperoxemia**. However, commonly a used threshold for hypoxemia is a PaO_2 less than 55 to 60 mm Hg or O_2 saturation (SaO_2) less than 87% to 90% in subjects breathing room air.[2]

O_2 therapy is also needed for patients with disorders associated with hypoxemia. Examples are postoperative patients or patients with carbon monoxide or cyanide poisoning, shock, pulmonary embolus, trauma, and acute myocardial infarction or during cardiopulmonary resuscitation.[1,2,8]

TABLE 42.1 Clinical Signs of Hypoxia

Finding	Mild to Moderate	Severe
Respiratory	Tachypnea	Tachypnea
	Dyspnea	Dyspnea
	Paleness	Cyanosis
Cardiovascular	Tachycardia	Tachycardia, eventual bradycardia, arrhythmia
	Mild hypertension, peripheral vasoconstriction	Hypertension and eventual hypotension
Neurologic	Restlessness	Somnolence
	Disorientation	Confusion
	Headaches	Distressed appearance
	Lassitude	Blurred vision
		Tunnel vision
		Loss of coordination
		Impaired judgment
		Slow reaction time
		Manic-depressive activity
		Coma

Careful bedside physical assessment can help determine a patient's need for O_2 therapy. Table 42.1 summarizes the common respiratory, cardiovascular, and neurologic signs used in the detection of hypoxemia. This information can be combined with more quantitative measures such as arterial blood gas results to confirm the need for supplemental O_2.

RULE OF THUMB The three basic ways to determine the need for oxygen therapy include laboratory measurements such as arterial blood gas testing, the presence of a specific clinical problem such as during cardiopulmonary resuscitation, and a result of a clinical assessment which reveals the presence of tachypnea, cyanosis, or other physical manifestation.

Precautions and Hazards of Supplemental Oxygen

There is no doubt that oxygen saves lives. It is also a potent drug, carrying with it many precautions and potential hazards. The following are five such hazards which are common and potentially severe enough to warrant additional discussion.[2]

Oxygen Toxicity/Hyperoxic Acute Lung Injury

The condition formerly known as oxygen toxicity is currently termed **hyperoxic acute lung injury**. Hyperoxia has been defined by several studies as a PaO_2 greater than 300 mm Hg. These studies demonstrate hyperoxia induced vasoconstriction, decreased cardiac output, and decreased perfusion to the brain, heart, and skeletal muscles. The threshold appears clinically important at a PaO_2 of greater than 150 mm Hg.[9]

Two factors determine the extent of harmful effects of O_2: PaO_2 and exposure time (Fig. 42.1). The higher the PaO_2 and the longer the exposure, the greater the likelihood of damage. Historically, O_2 toxicity was thought to primarily affect the lungs and the central nervous system (CNS).[9-11] However, it appears

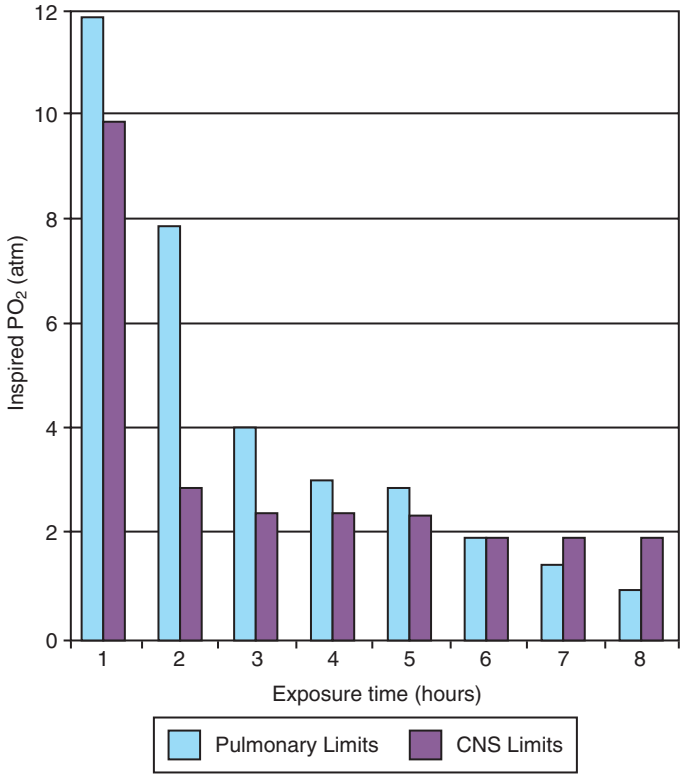

Fig. 42.1 Relationship between partial pressure of oxygen (PO_2) and exposure time causing O_2 toxicity. *CNS*, Central nervous system.

TABLE 42.2 Physiologic Responses of Healthy Individuals to Exposure to 100% Inspired Oxygen

Exposure Time (h)	Physiologic Response
0–12	Normal pulmonary function
	Tracheobronchitis
	Substernal chest pain
12–24	Decreasing vital capacity
25–30	Decreasing lung compliance
	Increasing $P(A\text{-}a)O_2$ (A-a Gradient)
	Decreasing exercise PO_2
30–72	Decreasing diffusing capacity

that CNS effects such as tremors, twitching, and convulsions occur mainly in patients breathing 100% O_2 at pressures greater than 1 atm (hyperbaric pressure). In addition, recent research suggests that high PaO_2 levels may be counterproductive in selected conditions involving ischemia and reperfusion, including myocardial infarction and stroke.[9]

Table 42.2 summarizes the physiologic response to breathing 100% O_2 at sea level. A patient exposed to a high PaO_2 for a prolonged period has signs similar to **bronchopneumonia**. Patchy infiltrates appear on chest x-rays and usually are most prominent in the lower lung fields.

Exposure to high PO_2 first damages the capillary endothelium. Interstitial edema follows and thickens the alveolar-capillary membrane. If the process continues, type I alveolar cells are destroyed, and type II cells proliferate. An **exudative** phase follows, characterized by alveolar fluid buildup, which leads to a low

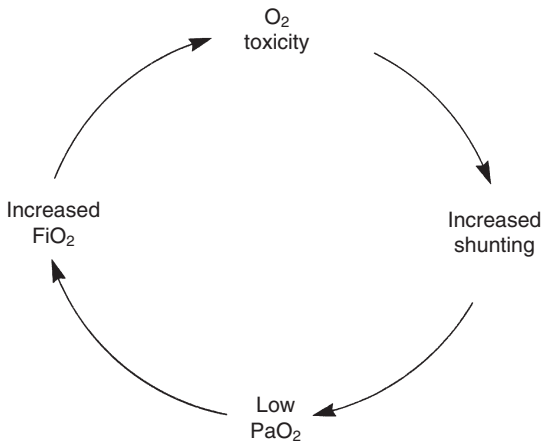

Fig. 42.2 The vicious circle that can occur in managing hypoxemia with high fractional inspired oxygen (FiO_2). High FiO_2 can be toxic to the lung parenchyma and cause further physiologic shunting. Increased shunting worsens the hypoxemia, necessitating higher FiO_2. *PaO_2*, Partial pressure of oxygen. (Modified from Flenley DC: Long-term oxygen therapy—state of the art, *Respir Care* 28:876, 1983.)

ventilation/perfusion ratio, physiologic shunting, and hypoxemia. In the end stages, hyaline membranes form in the alveolar region and pulmonary fibrosis and hypertension develop.

As the lung injury worsens, blood oxygenation deteriorates. If this progressive hypoxemia is managed with additional O_2, the toxic effects worsen (Fig. 42.2). However, if the patient can be kept alive while fractional inspired oxygen (FiO_2) is decreased, the pulmonary damage sometimes resolves.

The toxicity of O_2 is caused by overproduction of O_2 free radicals. O_2 free radicals are by-products of cellular metabolism. If unchecked, these radicals can severely damage or kill cells.[9,10]

In the presence of high PaO_2, free radicals can overwhelm the body's normal antioxidant system and cause cell damage. Cell damage provokes an immune response and causes tissue infiltration by neutrophils and macrophages. These scavenger cells release inflammatory mediators that worsen the initial injury. At the same time, local neutrophils and platelets may release more free radicals, which continue the process.

Exactly how much O_2 is safe is the subject of debate (see the following Rule of Thumb). Results of most studies indicate that adults can breathe up to 50% for extended periods without major lung damage.[11] In the past, a commonly used threshold for hypoxemia in patients breathing room air was a PaO_2 less than 55 to 60 mm Hg or SaO_2 less than 87% to 90%.[2] Rather than applying strict cutoffs, the goal always should be to use the lowest possible FiO_2 to achieve adequate tissue oxygenation. In addition, recent research indicates that excessively high SpO_2 levels in mechanically ventilated adult patients are associated with an increase in mortality. Currently, an oxygenation goal of a PaO_2 of 55 to 80 torr or an SpO_2 of 88% to 95% is recommended.[12]

RULE OF THUMB: Avoiding Oxygen Toxicity Limit patient exposure to 100% O_2 to less than 24 hours whenever possible. High FiO_2 is acceptable if the concentration can be decreased to 70% within 2 days and 50% or less in 5 days.

Because the growing lung may be more sensitive to O_2, extra caution is needed with infants. High PO_2 also is associated with **retinopathy of prematurity (ROP)** and **bronchopulmonary dysplasia** in infants.

Regardless of approach, supplemental O_2 never should be withheld from hypoxemic patients. Although the toxic effects of high O_2 concentrations can be serious, it is not FiO_2 but rather PO_2 that results in such harmful effects. If a patient needs a high FiO_2 to maintain adequate tissue oxygenation, the patient should receive it.

Depression of Ventilation

When breathing moderate to high O_2 concentrations, a very small percentage of patients with chronic obstructive pulmonary disease (COPD) and chronic hypercapnia may hypoventilate.[13,14] Decreases in ventilation of nearly 20% have been observed in these patients with accompanying elevations in arterial partial pressure of carbon dioxide ($PaCO_2$) of 20 to 23 mm Hg.[15] However, this hypoventilation is not typical of patients with COPD, and appropriate use of oxygen to avoid hypoxemia should **always** be the priority in clinical management.

One theory on why this small group of COPD patients hypoventilate is that O_2 administration and the resulting increase in arterial oxygen levels cause suppression of the hypoxic drive. In this subset of COPD patients, the normal response to increase ventilation in the presence of high partial pressure of carbon dioxide ($PaCO_2$) is blunted and the primary stimulus to breathe becomes lack of O_2 as sensed by the peripheral chemoreceptors. The increase in the blood O_2 level in these patients suppresses peripheral chemoreceptors, depresses ventilatory drive, and elevates the $PaCO_2$.[16,17] It is further suspected that high blood O_2 levels in such patients may also disrupt the normal ventilation/perfusion balance and cause an increase in dead space–to–tidal volume ratio (V_D/V_T) and in $PaCO_2$.[18]

Retinopathy of Prematurity

Retinopathy of prematurity (ROP), also called **retrolental fibroplasia**, is an abnormal eye condition that occurs in some premature or low-birth-weight infants who receive supplemental O_2. An excessive blood O_2 level causes retinal vasoconstriction, which leads to necrosis of the blood vessels. In response, new vessels form and increase in number. Hemorrhage of these delicate new vessels causes scarring behind the retina. Scarring often leads to retinal detachment and blindness.[19] ROP most often affects neonates up to approximately 1 month of age, by which time the retinal arteries have sufficiently matured. Excessive O_2 is not the only factor associated with ROP; other factors associated with ROP include hypercapnia, hypocapnia, intraventricular hemorrhage, infection, lactic acidosis, anemia, hypocalcemia, and hypothermia.

Because premature infants often need supplemental O_2, the risk of ROP poses a serious management problem. The American Academy of Pediatrics recommends keeping arterial PO_2 in an infant less than 80 mm Hg as the best way to minimize the risk of ROP.[8]

RULE OF THUMB The risk of ROP in infants can be minimized by keeping the PO_2 less than 80 mm Hg.

Absorption Atelectasis

FiO_2 values greater than 0.50 present a significant risk of absorption atelectasis.[20] Nitrogen normally is the most plentiful gas in both the alveoli and the blood. Breathing high levels of O_2 quickly depletes body nitrogen levels. As blood nitrogen levels decrease, the total pressure of venous gases rapidly decreases. Under these conditions, gases that exist at atmospheric pressure within any body cavity rapidly diffuse into the venous blood. This principle is used for removing trapped air from body cavities. Giving patients high levels of O_2 can help clear trapped air from the abdominal, cerebral, or pleural spaces.

This same phenomenon can cause lung collapse, especially if the alveolar region becomes obstructed (Fig. 42.3). Under these conditions, O_2 rapidly diffuses into the blood (see Fig. 42.3A). With no source for repletion, the total gas pressure in the alveolus progressively decreases until the alveolus collapses. Because collapsed alveoli are perfused but not ventilated, absorption atelectasis increases the physiologic shunt and worsens blood oxygenation.[20]

The likelihood of absorption atelectasis is greatest when present with other risk factors associated with low tidal volumes such as sedation, surgical pain, or CNS dysfunction. In these cases, poorly ventilated alveoli may become unstable when they lose O_2 faster than it can be replaced. The result is a more gradual shrinking of the alveoli that may lead to complete collapse, even when the patient is not breathing supplemental O_2 (see Fig. 42.3B).

Fire Hazard

Despite numerous preventive measures, fires involving enriched O_2 environments continue to occur in healthcare facilities. Fires seem to pose the greatest risk in operating rooms and in association with selected respiratory procedures. During surgery and procedures such as tracheotomies, electronic scalpels and similar devices are often used while the patient is receiving supplemental O_2. To complicate matters, even higher O_2 concentrations may exist under surgical drapes.[21] Other situations associated with increased fire risk involve home care patients smoking while receiving low-flow O_2 and the use of aluminum O_2 regulators. In addition, **hyperbaric oxygen (HBO) therapy** or therapy at increased atmospheric pressures (discussed later in this chapter) often involves the administration of supplemental O_2 and greatly increases fire risk.

Some simple strategies can be used to reduce the fire risk in healthcare facilities. Effectively managing the "fire triangle" of O_2, heat, and fuel is key. An essential component is always using the lowest effective FiO_2 for a given clinical situation. In addition, using scavenging systems to minimize O_2 buildup beneath sterile drapes during surgery or while performing tracheostomies can help reduce fire risk. Educating clinicians, patients, and caregivers about safe O_2 use is also important. In addition, fire prevention protocols for HBO therapy should be strictly followed.[21]

If a fire does occur in a healthcare facility, it is important to respond by following organizational protocol which includes applying the R.A.C.E. acronym. RACE stands for *Rescue* at-risk

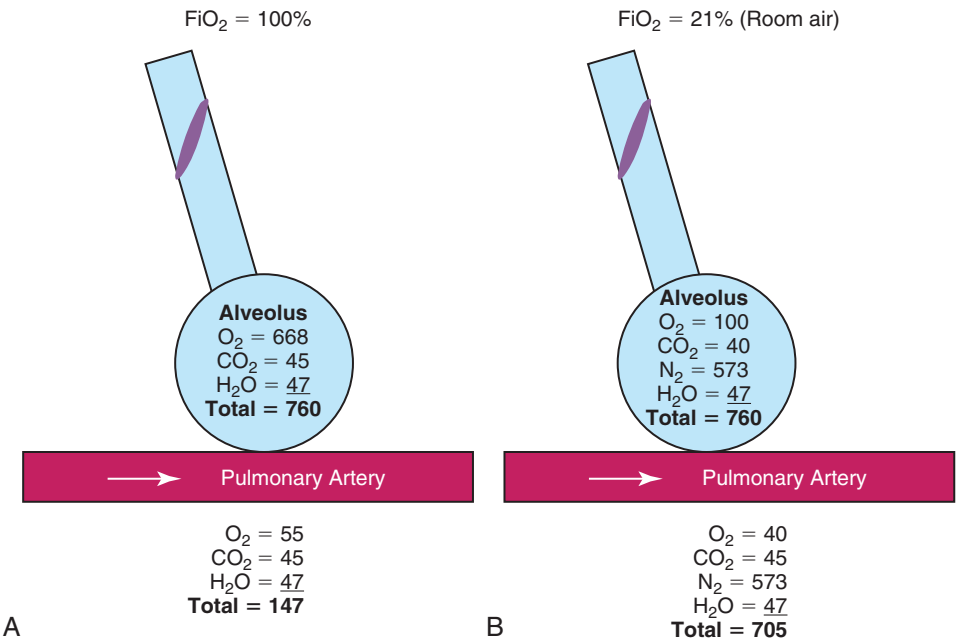

Fig. 42.3 The development of atelectasis beyond blocked airways when breathing of 100% O_2 (A) and room air (B). In each case, the sum of the gas pressures in mixed venous blood (pulmonary artery) is less than in the alveoli. The pressure gradient is much greater when breathing 100% O_2 (A), causing more rapid diffusion from the alveoli. *Note:* The gas pressures in the room air alveolus will change slightly over time, but the total will remain close to 760 mm Hg. *FiO_2*, Fractional inspired oxygen.

patients and personnel, initiate a fire *Alarm*; *Contain* to fire by closing doors, and *Extinguish* flames in a safe manner through the use of fire extinguishers. Another acronym, P.A.S.S., associated with a fire extinguisher which stands for *pull* the pin in the handle, *aim* the nozzle at the base of the fire, *squeeze* the handle, and *sweep* side to side while aiming at the base of the fire.[21]

RULE OF THUMB One of the best ways to maximize fire safety is to effectively manage the "fire triangle" by using the lowest effective O_2 concentration, eliminating potential sources of ignition and using noncombustible linens, medical supplies and equipment. However, if a fire occurs in a healthcare facility, the clinicians' response is guided by the RACE acronym. This stands for *Rescue* patients, initiate a fire *Alarm*, *Contain* the fire by closing doors and *Extinguish* the flames in a safe manner.

Oxygen Delivery Systems: Design and Performance

Proper device selection requires in-depth knowledge of both the general performance characteristics of these systems and the individual capabilities.[22] O_2 delivery devices are traditionally categorized by their design. Three basic designs exist: **low-flow systems**, **reservoir systems**, and **high-flow systems**. Enclosures are commonly identified as a fourth category. The design categories share functional characteristics, capabilities, and limitations.

The FiO_2 range of O_2 systems can be broadly divided into those designed to deliver a low (<35%), moderate (35% to 60%), or high (>60%) O_2 concentration. Some designs can deliver O_2 across the full range of concentrations (21% to 100%).

Although design plays an important role in the selection of these devices, clinical performance ultimately determines how the device is used. The user judges the performance of an O_2 delivery system by answering two key questions: (1) How much O_2 can the system deliver (FiO_2 or FiO_2 range)? (2) Does the delivered FiO_2 remain fixed or vary under changing patient demands?[22]

Regarding the FiO_2 range, O_2 systems can be broadly divided into systems designed to deliver a low (<35%), moderate (35% to 60%), or high (>60%) O_2 concentration. Some designs can deliver O_2 across the full range of concentrations (21% to 100%).

Whether a device delivers a **fixed** or **variable** FiO_2 depends on how much of the patient's inspired gas it supplies. If the system provides all of the patient's inspired gas, FiO_2 remains stable and **fixed**. If the device provides only some of the inspired gas and the patient must draw (or "entrain") the remainder from the surrounding air, it is classified as **variable**. In this case the more the patient breathes, the more air dilutes the delivered O_2, and the FiO_2 decreases. If the patient breathes less with this type of device, less air dilutes the O_2, and the FiO_2 increases. A system that supplies only a portion of the inspired gas always provides a variable FiO_2.[23] FiO_2 supplied with such systems can fluctuate widely from minute to minute and even from breath to breath.

Fig. 42.4 shows these concepts as applied to low-flow, reservoir, and high-flow systems. With the low-flow system (see Fig. 42.4A) the patient's inspiratory flow often exceeds the flow delivered by the device; the result is air dilution *(shaded areas)*. The greater the patient's inspiratory flow, the more air is breathed, and the FiO_2 varies. The high-flow system (see Fig. 42.4B) always exceeds the patient's flow and provides a fixed FiO_2. A fixed FiO_2 can be achieved with a reservoir system (see Fig. 42.4C), which stores a reserve volume (flow × time) that equals or exceeds the patient's tidal volume. For a reservoir system to provide a fixed FiO_2, the

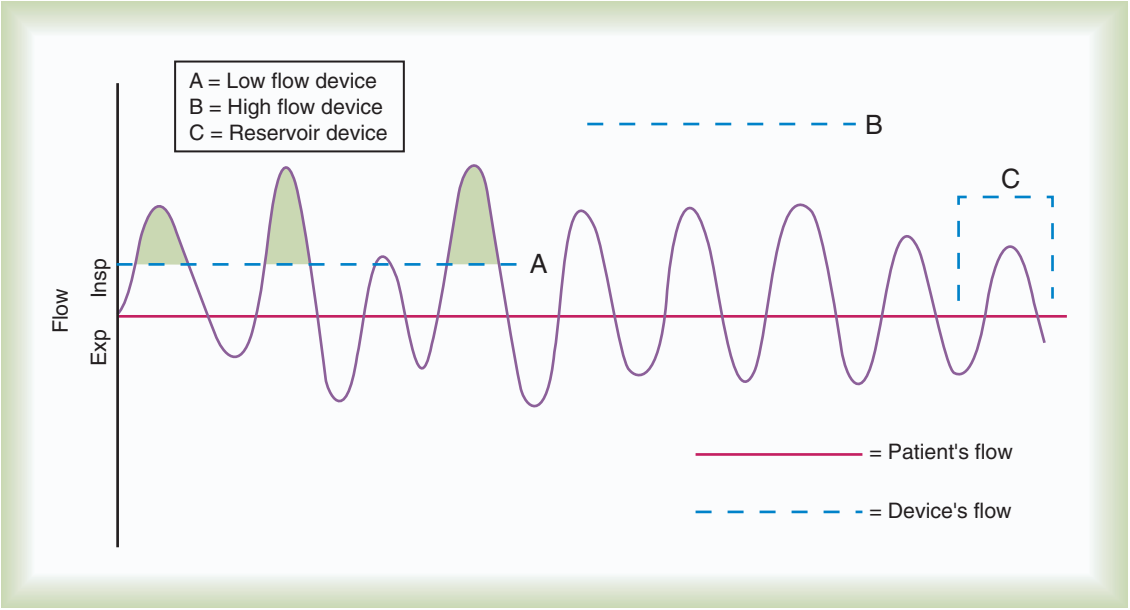

Fig. 42.4 Differences Between O_2 Delivery Systems. (A) Low-flow device. (B) High-flow device. (C) Reservoir device.

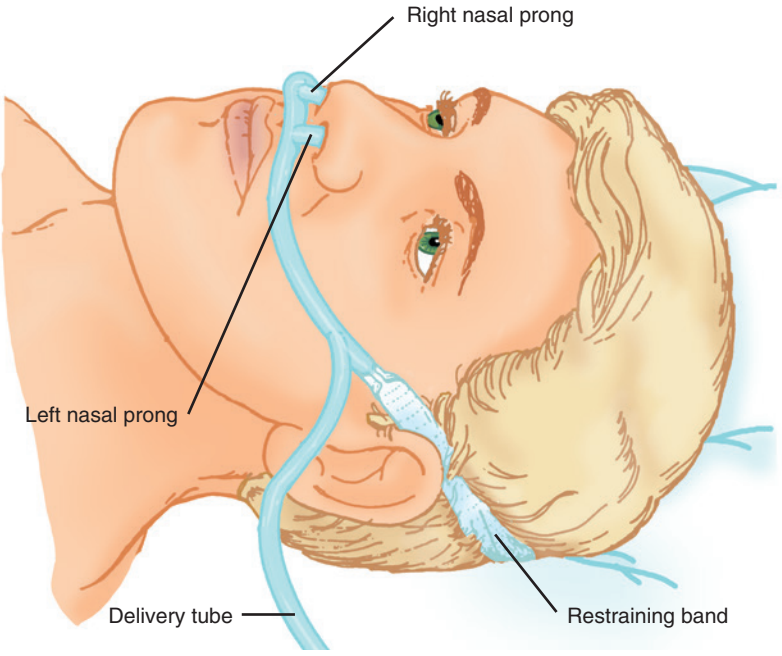

Fig. 42.5 Nasal cannula.

reservoir volume must always exceed the patient's tidal volume, and there cannot be any air leaks in the system. Table 42.3 outlines the general specifications for the common O_2 therapy systems in current use.

Low-Flow Systems

Typical low-flow systems provide supplemental O_2 directly to the airway at a flow of 8 L/min or less. Because the inspiratory flow of a healthy adult exceeds 8 L/min, the O_2 provided by a low-flow device is always diluted with air; the result is a low and variable FiO_2. Low-flow O_2 delivery systems include nasal cannula, nasal catheter, and transtracheal catheter.

Nasal cannula (low flow). A (low-flow) nasal cannula is by far the most commonly used oxygen delivery device. It consists of disposable plastic tips or prongs, approximately 1 cm long that are connected to several feet of small-bore O_2 supply tubing (Fig. 42.5). Prongs are inserted into the vestibule of the nose while supply tubing is attached directly to a flowmeter or bubble humidifier. In most cases a humidifier is used only when the input flow is greater than 4 L/min.[2] However, flows greater than

TABLE 42.3 Overview of Oxygen Therapy Systems

Category	Device	Flow	FiO_2 Range	FiO_2 Stability	Advantages	Disadvantages	Best Use
Low flow	Nasal cannula	¼–6 L/min (adults) ≤2 L/min (infants)	22%–40%	Variable	Use on adults, children, infants; easy to use; disposable; low cost; well tolerated	Unstable, easily dislodged; high flow uncomfortable; can cause dryness, bleeding; polyps; deviated septum and mouth breathing may reduce FiO_2	Patient in stable condition who needs low FiO_2; home care patient who needs long-term therapy, low to moderate FiO_2 while eating
	Nasal catheter	¼–5 L/min	22%–45%	Variable	Use on adults, children, infants; good stability; disposable; low cost	Difficult to insert; high flow increases back pressure; needs regular changing; polyps, deviated septum may block insertion; may provoke gagging, air swallowing, aspiration	Procedures in which cannula is difficult to use (bronchoscopy); long-term care of infants
	Transtracheal catheter	¼–4 L/min	22%–35%	Variable	Lower O_2 use and cost; eliminates nasal and skin irritation; improved compliance; increased exercise tolerance; increased mobility; enhanced image	High cost; surgical complications; infection; mucous plugging; lost tract	Home care or ambulatory patients who need increased mobility or do not accept nasal O_2
Resevior Systems	Reservoir cannula	¼–4 L/min	22%–35%	Variable	Lower O_2 use and cost; increased mobility; less discomfort because of lower flow	Unattractive, cumbersome; poor compliance; must be regularly replaced; breathing pattern affects performance	Home care or ambulatory patients who need increased mobility
	Simple mask	5–10 L/min	35%–50%	Variable	Use on adults, children, infants; quick, easy to apply; disposable; inexpensive	Uncomfortable; must be removed for eating; prevents radiant heat loss; blocks vomitus in unconscious patients	Emergencies; short-term therapy requiring moderate FiO_2; mouth breathing patients requiring moderate FiO_2
	Partial rebreathing mask	Minimum of 10 L/min (prevent bag collapse on inspiration)	40%–70%	Variable	Same as simple mask; moderate to high FiO_2	Same as simple mask; potential suffocation hazard	Emergencies; short-term therapy requiring moderate to high FiO_2
	Nonrebreathing mask	Minimum of 10 L/min (prevent bag collapse on inspiration)	60%–80%	Variable	Same as simple mask; high FiO_2	Same as simple mask; potential suffocation hazard	Emergencies; short-term therapy requiring high FiO_2

High flow	AEM	Varies; should provide output flow >60 L/min	24%–50%	Fixed	Easy to apply; disposable, inexpensive; stable, precise FiO_2	Limited to adult use; uncomfortable, noisy; must be removed for eating; FiO_2 >0.40 not ensured; FiO_2 varies with back pressure	Patients in unstable condition who need precise low FiO_2
	Air-entrainment nebulizer	10–15 L/min input; should provide output flow of at least 60 L/min	28%–100%	Fixed	Provides temperature control and extra humidification	FiO_2 <0.28 or >0.40 not ensured; FiO_2 varies with back pressure; high infection risk	Patients with artificial airways who need low to moderate FiO_2
	Blending system (open)	Should provide output flow of at least 60 L/min	21%–100%	Fixed	Full range of FiO_2	Requires 50 psi air/O_2; blender failure or inaccuracy common	Patients with high VE who need high FiO_2
	High-flow nasal cannula system	Up to 50 L/min, or more (depending on system)	35%–100%	Generally fixed, depending on system, input flow, and patient breathing pattern	Wide range of FiO_2 and relative/absolute humidity; use on adults, children, infants	FiO_2 is often ensured but depends on system, input flow, and patient breathing pattern; infection risk	Patients of all ages with high or variable VE who need supplemental O_2, positive pressure and humidity
Enclosure	Oxyhood	≥7 L/min	21%–100%	Fixed	Full range of FiO_2	Difficult to clean, disinfect	Infants who need supplemental O_2
	Isolette	8–15 L/min	40%–50%	Variable	Provides temperature control	Expensive, cumbersome, unstable FiO_2 (leaks); difficult to clean, disinfect; limits patient mobility; fire hazard	Infants who need supplemental O_2 and precise thermal regulation
	Tent	12–15 L/min	40%–50%	Variable	Provides concurrent aerosol therapy	Expensive, cumbersome, unstable FiO_2 (leaks); requires cooling; difficult to clean, disinfect; limits patient mobility; fire hazard	Toddlers or small children who need low to moderate FiO_2 and aerosol

AEM, Air-entrainment mask; *FiO_2,* fractional inspired oxygen; *VE,* minute volume.

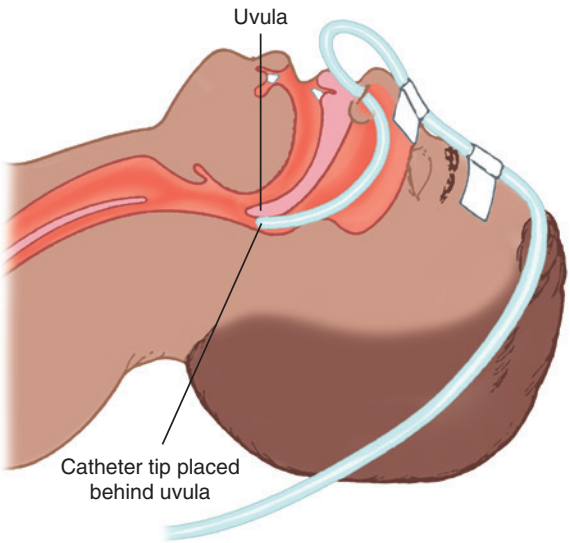

Fig. 42.6 Placement of nasal catheter in the nasopharynx.

6 to 8 L/min can cause patient discomfort.[22] Cannulas should not be used in newborns and infants if their nasal passages are obstructed, and flows generally should be limited to 2 L/min unless a specialized high-flow cannula system, discussed later in this chapter, is being used.[23] Table 42.3 lists the FiO_2 range, FiO_2 stability, advantages, disadvantages, and best use of a nasal cannula.

Nasal catheter. Nasal catheters are almost exclusively used for limited, short-term O_2 administration during specialized procedures such as a bronchoscopy. A nasal catheter is a soft plastic tube with several small holes at the tip that is inserted by gently advancing it along the floor of either nasal passage and visualizing it just behind and above the uvula (Fig. 42.6). Once in position, the catheter is taped to the bridge of the nose. If direct visualization is impossible, the catheter may be blindly inserted to a depth equal to the distance from the nose to the earlobe.

When placed too deep, the catheter can provoke gagging or swallowing of gas, which increases the likelihood of aspiration. In general, a nasal catheter should be replaced with a new one (placed in the opposite naris) at least every 8 hours. Nasal catheters are inappropriate for neonatal patients. As a result of these notable limitations, nasal catheters are rarely used currently.[4]

Transtracheal catheter. A transtracheal O_2 catheter is a thin polytetrafluoroethylene (Teflon) catheter inserted into the trachea between the second and third tracheal rings (Fig. 42.7), secured by a chain necklace. Standard tubing connected directly to a flowmeter provides the O_2 source flow.[24,25] Because flow is so low, no humidification is needed.

Because the transtracheal catheter resides directly in the trachea, O_2 builds up both there and in the upper airway during expiration. This process effectively expands the anatomic reservoir and increases the FiO_2 at any given flow. Compared with a nasal cannula, a transtracheal catheter needs approximately half of the O_2 flow to achieve a given PaO_2.[25] This reduced flow can be of great economic and practical benefit to patients needing continuous long-term O_2 therapy because it can greatly increase the duration of flow from portable O_2 systems. However, transtracheal

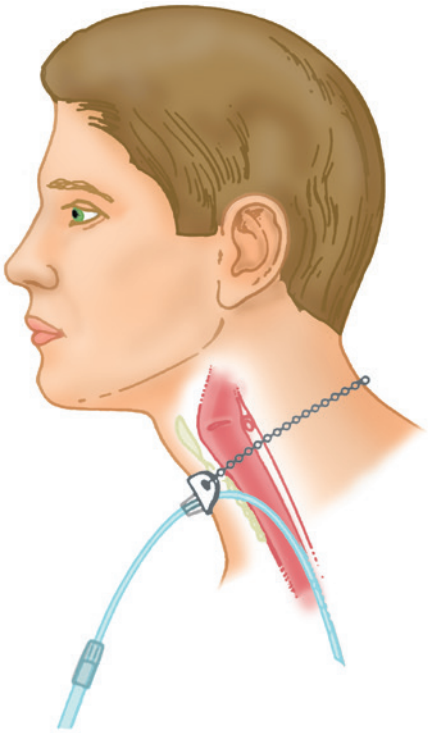

Fig. 42.7 Transtracheal O_2 catheter.

TABLE 42.4 Variables Affecting FiO_2 of Low-Flow Oxygen Systems

Increases FiO_2	Decreases FiO_2
Higher O_2 input	Lower O_2 input
Mouth-closed breathing[a]	Mouth-open breathing[a]
Low inspiratory flow	High inspiratory flow
Low tidal volume	High tidal volume
Slow rate of breathing	Fast rate of breathing
Small minute ventilation	Large minute ventilation
Long inspiratory time	Short inspiratory time
High I:E ratio	Low I:E ratio

[a]Cannula only.
FiO_2, Fractional inspired oxygen; *I:E,* inspiratory/expiratory.

O_2 therapy can pose serious problems and risks (e.g., collection of mucus which can obstruct the airway), and these devices are not currently in widespread use. Chapter 57 provides additional details on maintaining transtracheal O_2 setups. Table 42.3 lists the FiO_2 range, FiO_2 stability, advantages, disadvantages, and best use of a transtracheal catheter.

Performance Characteristics of Low-Flow Systems

Low-flow nasal systems provide O_2 concentrations ranging from 22% to 45%.[2,3,22] The range of 22%45% cited in Table 42.3 is based on 8 L/min as the upper limit of tolerable flow. These wide FiO_2 ranges occur because the O_2 concentration delivered by a low-flow system varies with the amount of air dilution. The amount of air dilution depends on several patient and equipment variables. Table 42.4 summarizes these key variables and how they affect FiO_2 provided by low-flow systems.

Simple formulas exist for estimating FiO_2 provided by low-flow systems (see the accompanying Rule of Thumb). However, given the large number of variables affecting FiO_2, the RT can never know precisely how much O_2 a patient is receiving with these systems. Without knowing the patient's exact FiO_2, the RT must rely on assessing the patient's response to O_2 therapy.

RULE OF THUMB: Estimating FiO_2 Provided by Low-Flow Systems For patients with a normal rate and depth of breathing, each 1 L/min of nasal O_2 increases FiO_2 approximately 4%. For example, a patient using a nasal cannula at 4 L/min has an estimated FiO_2 of approximately 37% (21 + 16).

Troubleshooting Low-Flow Systems

Common problems with low-flow O_2 delivery systems include inaccurate flow, system leaks and obstructions, device displacement, and skin irritation. Given the trend toward assessment of outcome of O_2 therapy (with either blood gases or pulse oximetry), ensuring the absolute accuracy of O_2 input flow generally is not essential. Nonetheless, similar to all respiratory care equipment, flowmeters should be subjected to regular preventive maintenance and testing for accuracy. Equipment that fails preventive maintenance standards should be removed from service and repaired or replaced. Table 42.5 provides guidance on troubleshooting the most common clinical problems with nasal cannulas.

Reservoir Systems

Reservoir systems incorporate a mechanism for gathering and storing O_2 between patient breaths. Patients draw on this reserve supply whenever inspiratory flow exceeds O_2 flow into the device. Because air dilution is reduced, reservoir devices generally provide higher FiO_2 than low-flow systems. Reservoir devices can decrease O_2 use by providing FiO_2 comparable with nonreservoir systems but at lower flow. Reservoir systems currently in use include reservoir cannulas, masks, and nonrebreathing circuits. In principle, enclosure systems, such as tents and hoods, operate as reservoirs surrounding the head or body.

TABLE 42.5 Troubleshooting Common Problems With a Nasal Oxygen Cannula

Problem or Clue	Cause	Solution
No gas flow can be felt coming from the cannula	Flowmeter not on	Adjust flowmeter
	System leak	Check connections
Humidifier pop-off is sounding	Obstruction distal to humidifier	Find and correct the obstruction
	Flow is set too high	Use alternative device
	Obstructed naris	Use alternative device
Patient reports soreness over lip or ears	Irritation or inflammation caused by appliance straps	Loosen straps
		Place cotton balls at pressure points
		Use a different device
Mouth breathing	Habitual mouth breathing, blocked nasal passages	Switch to simple mask or venturi mask

Reservoir cannula. Reservoir cannulas are designed to conserve O_2 and are an alternative to the pulse-dose or demand-flow O_2 systems described in Chapter 57. There are two types of reservoir cannula: nasal reservoir and pendant reservoir. Table 42.3 lists the FiO_2 range, FiO_2 stability, advantages, disadvantages, and best use of a reservoir cannula.

A nasal reservoir cannula operates by storing approximately 20 mL of O_2 in a small membrane reservoir during exhalation (Fig. 42.8). The patient draws on this stored O_2 during early inspiration. The amount of O_2 available increases with each breath and decreases the flow needed for a given FiO_2. Although the device is comfortable to wear, many patients object to its appearance and may not always comply with prescribed therapy.

The pendant reservoir system helps overcome esthetic concerns by hiding the reservoir under the patient's clothing on the anterior chest wall (Fig. 42.9). Although the device is less

Fig. 42.8 Reservoir cannula.

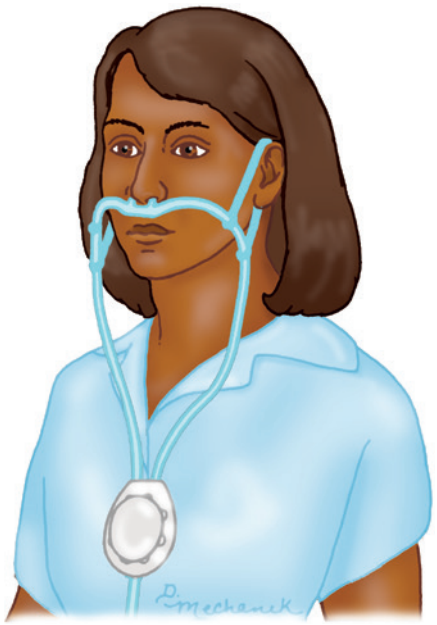

Fig. 42.9 Pendant reservoir cannula.

visible, the extra weight of the pendant can cause ear and facial discomfort.

At low flow, reservoir cannulas can reduce O_2 use 50% to 75%. A patient at rest who needs 2 L/min through a standard cannula to achieve an arterial SaO_2 greater than 90% may need only 0.5 L/min through a reservoir cannula to achieve the same blood oxygenation.[26] Although flow savings is predictable, factors such as nasal anatomy and breathing pattern can affect the performance of the device. For these devices to function properly at low flow, patients must exhale through the nose (this reopens or resets the reservoir membrane). In addition, exhalation through pursed lips may impair performance, especially during exercise. For these reasons, prescribed flow settings should be individually determined by clinical assessment, including SaO_2 monitoring.[26]

The low flow at which the reservoir cannula operates makes humidification unnecessary. Excess moisture can hinder proper action of the reservoir membrane.[26] Even regular use can cause membrane wear. For this reason, patients should replace the reservoir cannula approximately every 3 weeks.

Reservoir masks. Masks are the most commonly used reservoir systems. There are three types of reservoir masks: (1) simple mask, (2) partial rebreathing mask, and (3) nonrebreathing mask. Table 42.3 lists the FiO_2 range, FiO_2 stability, advantages, disadvantages, and best use of each of these devices.

A simple mask is a disposable plastic unit designed to cover both the mouth and the nose (Fig. 42.10). The body of the mask itself gathers and stores O_2 between patient breaths. The patient exhales directly through open holes or ports in the mask body. If O_2 input flow ceases, the patient can draw in air through these holes and around the mask edge.

The input flow range for an adult simple mask is 5 to 10 L/min. In general, if flow greater than 10 L/min is needed for satisfactory oxygenation, use of a device capable of a higher FiO_2 should be considered. At a flow less than 5 L/min in the adult population, the mask volume acts as dead space and causes carbon dioxide rebreathing.[27]

Because air dilution easily occurs during inspiration through its ports and around its body, a simple mask provides a variable FiO_2. How much FiO_2 varies depends on the O_2 input flow, the mask volume, the extent of air leakage, and the patient's breathing pattern.[28]

As shown in Fig. 42.11, a partial rebreathing mask and a nonrebreathing mask have a similar design. Each has a 1-L flexible reservoir bag attached to the O_2 inlet. Because the bag increases the reservoir volume, both masks provide higher FiO_2

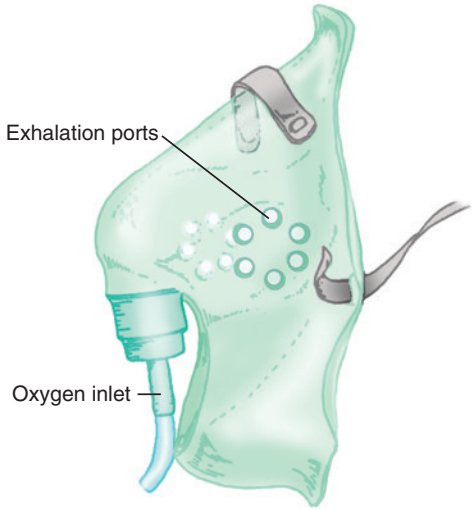

Fig. 42.10 Simple O_2 mask.

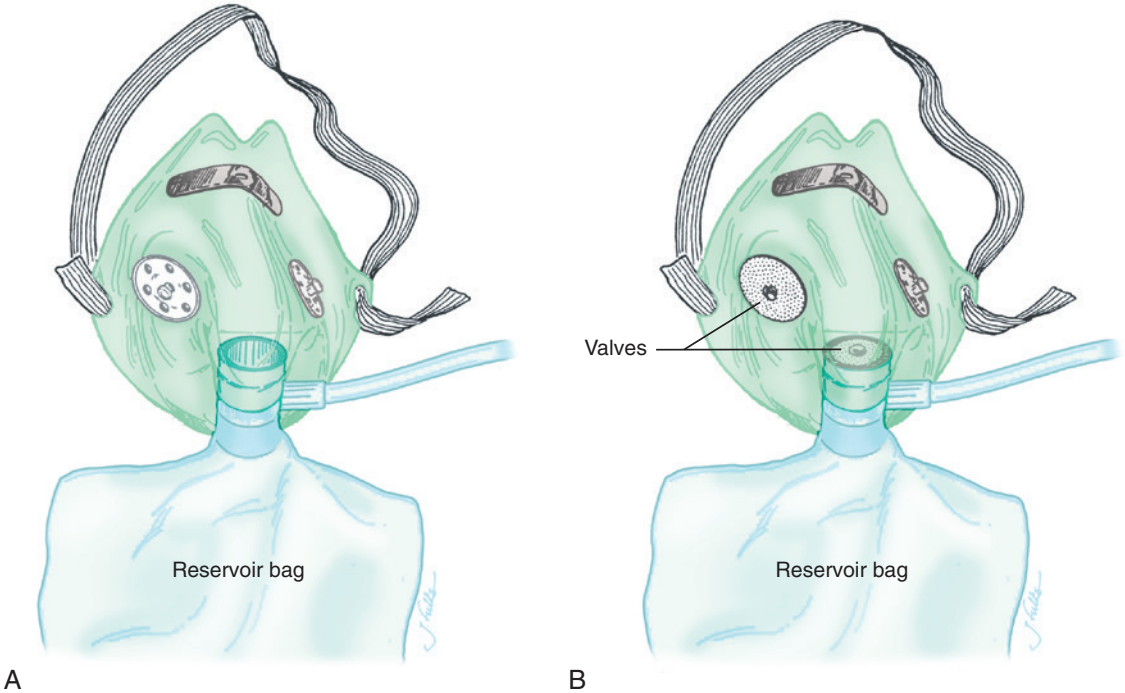

Fig. 42.11 (A) Partial rebreathing mask. (B) Nonrebreathing mask.

capabilities than a simple mask. The key difference between these designs is the use of valves. A partial rebreathing mask has no valves (see Fig. 42.11A). During inspiration, source O_2 flows into the mask and passes directly to the patient. During exhalation, source O_2 enters the bag. However, because no valves separate the mask and the bag, some of the patient's exhaled gas also enters the bag (approximately the first third). Because it comes from the anatomic dead space, the early portion of exhaled gas contains mostly O_2 and little CO_2. As the bag fills with both O_2 and dead space gas, the last two-thirds of exhalation (high in CO_2) escapes out the exhalation ports of the mask. As long as the O_2 input flow keeps the bag from collapsing more than approximately one-third during inhalation, CO_2 rebreathing is negligible.

Although it can provide a higher FiO_2 than a simple mask (see Table 42.3), a standard disposable partial rebreathing mask is subject to considerable air dilution. The result is delivery of a moderate but variable FiO_2 dependent on the same factors as with a simple mask.

A nonrebreathing mask, which is much more commonly used than a partial rebreathing mask, prevents rebreathing with one-way valves (see Fig. 42.11B). An inspiratory valve sits on top of the bag, and expiratory valves cover the exhalation ports on the mask body. During inspiration, slight negative mask pressure closes the expiratory valves, preventing air dilution. At the same time, the inspiratory valve on top of the bag opens, providing O_2 to the patient. During exhalation, valve action reverses the direction of flow. Slight positive pressure closes the inspiratory valve, which prevents exhaled gas from entering the bag. Concurrently, the one-way expiratory valves open and divert exhaled gas out to the atmosphere. Although nonrebreathing masks are often referred to as "100% oxygen devices," as indicated in Table 42.3, modern disposable nonrebreathing masks normally do not provide much more than approximately 70% O_2.[22] This is because large air leaks occur both around the mask body and through the open (nonvalved) exhalation port. This open exhalation port is a common safety feature designed to allow air breathing if the O_2 source fails but can result in air dilution (leakage) and a variable FiO_2 whenever inspiratory flow or volume are high.

Troubleshooting reservoir systems. Common problems with reservoir masks include device displacement, system leaks and obstructions, improper flow adjustment, and skin irritation. Table 42.6 provides guidance on troubleshooting the most common clinical problems with reservoir masks.

High-Flow Systems

High-flow systems use air-entrainment or gas blending, and supply a given O_2 concentration at a flow equaling or exceeding the patient's peak inspiratory flow. An air-entrainment or a blending system is used. As long as the delivered flow always exceeds the patient's demand, both systems can ensure a fixed FiO_2. The accompanying Rule of Thumb can help determine which devices truly qualify as high-flow systems.

RULE OF THUMB: High-Flow Devices To qualify as a high-flow device, a system should provide at least 60 L/min total flow. This flow criterion is based on the fact that the average adult peak inspiratory flow during tidal ventilation is approximately three times the minute volume. Because 20 L/min is close to the upper limit of sustainable minute volume for an ill person, a flow of 3 × 20, or 60 L/min, should suffice in most situations. In a few rare circumstances, flow must reach or exceed 100 L/min.

Principles of gas mixing. All high-flow systems mix air and O_2 to achieve a given FiO_2. These gases are mixed with air-entrainment devices or blending systems. Computations involving mixtures of air and O_2 are based on a modified form of the dilution equation for solutions:

$$V_F C_F = V_1 C_1 + V_2 C_2$$

In this equation, V_1 and V_2 are the volumes of the two gases being mixed; C_1 and C_2, the O_2 concentration in these two volumes; and V_F and C_F, the final volume and concentration of the resulting mixture.

Box 42.1 shows how to apply variations of this equation to compute: (1) the final concentration of a mixture of air and O_2, (2) the air-to-O_2 ratio needed to obtain a given FiO_2, (3) the total output flow from an air-entrainment device, and (4) the amount of O_2 that must be added to a volume of air to obtain a given FiO_2.

TABLE 42.6 Troubleshooting Common Problems With Reservoir Masks

Problem or Clue	Cause	Solution
Patient constantly removes mask	Claustrophobia	Use alternative device
	Confusion	Restrain patient
No gas flow can be detected	Flowmeter not on	Adjust flowmeter
	System leak	Check connections
Humidifier pop-off is sounding	Obstruction distal to humidifier	Find and correct obstruction
	High input flow	Omit humidifier if therapy is short term
	Jammed inspiratory valve	Fix or replace valve
Reservoir bag collapses when the patient inhales	Flow is inadequate	Increase flow
Reservoir bag remains inflated throughout inhalation	Large mask leak	Correct leak
	Inspiratory valve jammed or reversed	Repair or replace mask
Erythema develops over face or ears	Irritation or inflammation owing to appliance or straps	Reposition mask or straps
		Place cotton balls over ear pressure points
		Provide skin care

BOX 42.1 Equations for Computing Oxygen Percentage, Ratio, and Flow

To compute the O_2 percentage of a mixture of air and O_2:

$$\%O_2 = \frac{(\text{Airflow} \times 21) + (O_2\ \text{flow} \times 100)}{\text{Totalflow}} \quad \textbf{(Eq. 42.1)}$$

1. To compute the air-to-O_2 ratio needed to obtain a given O_2 percentage:

$$\frac{\text{Litersair}}{\text{Liters } O_2} = \frac{(100 - \%O_2)}{(\%O_2 - 21)} \quad \textbf{(Eq. 42.2)}$$

2. To compute the total output flow from an air-entrainment device (given the O_2 input):
   a. Compute the air-to-O_2 ratio (see Eq. 42.2).
   b. Add the air-to-O_2 ratio parts.
   c. Multiply the sum of the ratio parts by the O_2 input flow.
3. To compute the flow of O_2 and air needed to obtain a given O_2 percentage at a given total flow:
   a. Compute the O_2 flow:

$$O_2\ \text{flow} = \frac{\text{Totalflow} \times (O_2\% - 21)}{79} \quad \textbf{(Eq. 42.3)}$$

   b. Compute the airflow:

$$\text{Airflow} = \text{Totalflow} - O_2\ \text{flow}$$

MINI CLINI

Conflicting Assessment Information

Problem

A disoriented postoperative male patient breathing room air exhibits tachypnea, tachycardia, and mild cyanosis of the mucous membranes. Using a pulse oximeter, the respiratory therapist (RT) measures the patient's oxyhemoglobin saturation as 90%. What should the RT recommend to the patient's surgeon?

Discussion

This is a classic example of how monitoring data and results of bedside assessment can conflict. Both the patient's condition and the observed clinical signs indicate hypoxemia, but the pulse oximeter indicates adequate oxygenation. In situations such as this, it is always better to err on the side of the patient and recommend O_2 therapy—treat the patient, not the monitor. This concept is particularly important in the use of monitoring technologies known to have limited accuracy, such as pulse oximetry (see Chapter 19).

MINI CLINI

Determining FiO_2 of an Air-Oxygen Mixture

Problem

An air-entrainment device mixes at a fixed ratio of three volumes of air to each volume of O_2 (3:1 ratio). What is the resulting FiO_2?

Solution

Substituting air, O_2, and total (air + O_2) volumes into Eq. 42.1:

$$\%O_2 = \frac{(\text{Airflow} \times 21) + (O_2\ \text{flow} \times 100)}{\text{Total flow}}$$

$$\%O_2 = \frac{(3 \times 21) + (1 \times 100)}{3 + 1}$$

$$\%O_2 = 41$$

An air-entrainment device that mixes three volumes of air with one volume of O_2 provides a gas mixture with FiO_2 of approximately 0.40.

MINI CLINI

Computing Total Flow Output of an Air-Entrainment Device

Problem

A patient is receiving O_2 through an air-entrainment device set to deliver 50% O_2. The input O_2 flow is set to 15 L/min. What is the total output flow of this system?

Solution

Step 1: Compute the air-to-O_2 ratio by substituting 50 for the $\%O_2$ in Eq. 42.2:

$$\frac{\text{Liters air}}{\text{Liters } O_2} = \frac{(100 - \%O_2)}{(\%O_2 - 21)}$$

$$\frac{\text{Liters air}}{\text{Liters } O_2} = \frac{(100 - 50)}{(50 - 21)}$$

$$\frac{\text{Liters air}}{\text{Liters } O_2} = \frac{50}{29}$$

$$\frac{\text{Litersair}}{\text{Liters } O_2} = \frac{1.7}{1}$$

Step 2: Add the air-to-O_2 ratio parts:

$$1.7 + 1 = 2.7$$

Step 3: Multiply the sum of the ratio parts times the O_2 input flow:

$$2.7 \times 15\ \text{L/min} = 41\ \text{L/min}$$

An air-entrainment device set to deliver 50% O_2 that has an input flow of 15 L/min provides a total output flow of approximately 41 L/min.

Air-entrainment systems. Air-entrainment systems direct a high-pressure O_2 source through a small nozzle or jet surrounded by air-entrainment ports (Fig. 42.12). The amount of air entrained at these ports varies directly with the size of the port and the velocity of O_2 at the jet. The larger the intake ports and the higher the gas velocity at the jet, the more air is entrained.

Because they dilute source O_2 with air, entrainment devices always provide less than 100% O_2. More air entrainment increases total output flow, but lowers delivered FiO_2. For these reasons, air-entrainment devices function as true high-flow systems only at lower FiO_2. If the flow output from an air-entrainment device decreases to less than a patient's inspiratory flow, air dilution occurs, and FiO_2 becomes variable.

FiO_2 provided by air-entrainment devices depends on two key variables: the air-to-O_2 ratio and the amount of flow

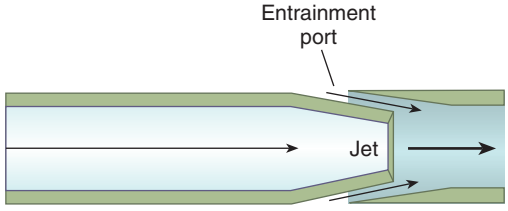

Fig. 42.12 Basic components of an air-entrainment system. Pressurized gas passes through a nozzle or jet, beyond which are air-entrainment ports. Shear forces at the jet orifice entrain air into the primary gas stream, diluting the O_2 and increasing the total flow output of the device.

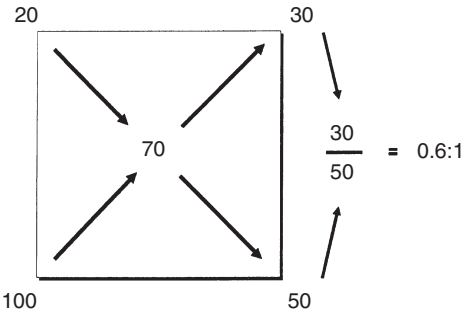

Fig. 42.13 The magic box used to estimate air-to-O_2 ratio.

resistance downstream from the mixing site. Changing the input flow of an air-entrainment device alters the total output flow but has little effect on delivered FiO_2. In general, FiO_2 remains within 1% to 2% of that specified by the manufacturer, regardless of input flow.[29]

The size of the jet and entrainment ports of a device determines the air-to-O_2 ratio and the delivered FiO_2. The accompanying Mini Clini entitled "Determining FiO_2 of an Air-Oxygen Mixture" shows how to compute the FiO_2 provided by an air-entrainment system if the air-to-O_2 ratio is known.

A more common clinical problem arises when the total output flow from an air-entrainment system must be determined. As described in the previous Rule of Thumb, the total flow output of a system determines whether it truly performs as a high-flow device. The accompanying Mini Clini entitled "Computing Total Flow Output of an Air-Entrainment Device" shows how to determine the total output flow of an air-entrainment system.

Rather than using Eq. 42.2 in Box 42.1 to compute air-to-O_2 ratio, many RTs derive quick estimates by using a simple mathematical aid called the *magic box* (Fig. 42.13). To use the magic box, one draws a square and places 20 in the top left corner and 100 in the bottom left corner. One places the desired O_2 percentage in the center of the box (as in the case illustrated in Fig. 42.13, 70%). One subtracts diagonally from lower left to the upper right (disregard the sign). One subtracts diagonally again from upper left to lower right (disregard the sign). The resulting numerator (30) is the value for air, and the denominator (50) is the value for O_2.

By convention, the air-to-O_2 ratio is expressed with the denominator (liters of O_2) set to 1. To reduce any ratio to a ratio of x:1, divide both the numerator and the denominator by the denominator. In the magic box example (also see Fig. 42.13):

$$\frac{30}{50} = \frac{30/50}{50/50} = \frac{0.61}{1}$$

The magic box can be used only for estimating the air-to-O_2 ratio. For absolute accuracy, Eq. 42.2 in Box 42.1 always should be used. Based on Eq. 42.2, Table 42.7 lists the approximate air-to-O_2 ratios for several common O_2 percentages.

The other major factor determining the O_2 concentration provided by an air-entrainment device is downstream flow resistance. In the presence of flow resistance distal to the jet, the volume of air entrained always decreases. With less air being entrained, total flow output decreases and the delivered O_2 concentration increases. More detail on this phenomenon is provided later in this chapter.[29]

TABLE 42.7 Approximate Air-to-Oxygen Ratios for Common Oxygen Concentrations

Percentage O_2	Approximate Air-to-O_2 Ratio	Total Ratio Parts
100	0:1	1
80	0.3:1	1.3
70	0.6:1	1.6
60	1:1	2
50	1.7:1	2.7
45	2:1	3
40	3:1	4
35	5:1	6
30	8:1	9
29	10:1	11
24	25:1	26

Total output flow (air + O_2) in L/min can be calculated by multiplying the total ratio parts by the O_2 input flow (L/min).

The two most common O_2 delivery systems in which air entrainment is used are the air-entrainment mask (AEM) and the air-entrainment nebulizer.

Air-entrainment (venturi) mask. The use of an O_2 mask with controlled FiO_2 by means of air entrainment was first reported in 1941 by Barach and Eckman.[30] The system provided relatively high FiO_2 (>40%) through the use of adjustable air-entrainment ports that controlled the amount of air mixed with O_2. Almost 20 years later, Campbell[31] developed an entrainment mask that provided controlled, low FiO_2 and called the device a *venturi mask* or *venti-mask*.

As the name *venti-mask* suggests, the operating principle behind these devices has often been attributed to the Venturi principle (see Chapter 6). This assumption is incorrect.[32] Rather than having an actual Venturi tube that entrains air, these devices have a simple restricted orifice or jet through which O_2 flows at high velocity. Air is entrained by shear forces at the boundary of jet flow, not by low lateral pressures. The smaller the orifice, the greater the velocity of O_2, and more air is entrained.

Fig. 42.14 depicts a typical AEM, designed to deliver a range of low to moderate FiO_2 (0.24 to 0.40). The mask consists of a jet orifice or nozzle around which is an air-entrainment port *(top drawing)*. The body of the mask has several large ports, which allow escape of both excess flow from the device and exhaled gas from the patient. In this design, FiO_2 is regulated by selection and changing of the jet adapter. The smallest jet provides the highest O_2 velocity, the most air entrainment, and the lowest FiO_2 (0.24). The largest jet provides the lowest O_2 velocity, the least air entrainment, and the highest FiO_2 (0.40). Other AEM designs may vary both jet and entrainment port size to provide an even broader range up to 50% FiO_2. The aerosol entrainment collar fits over the air-entrainment ports (see later).

For controlled FiO_2 at flow high enough to prevent air dilution, the total output flow of an AEM must exceed the patient's

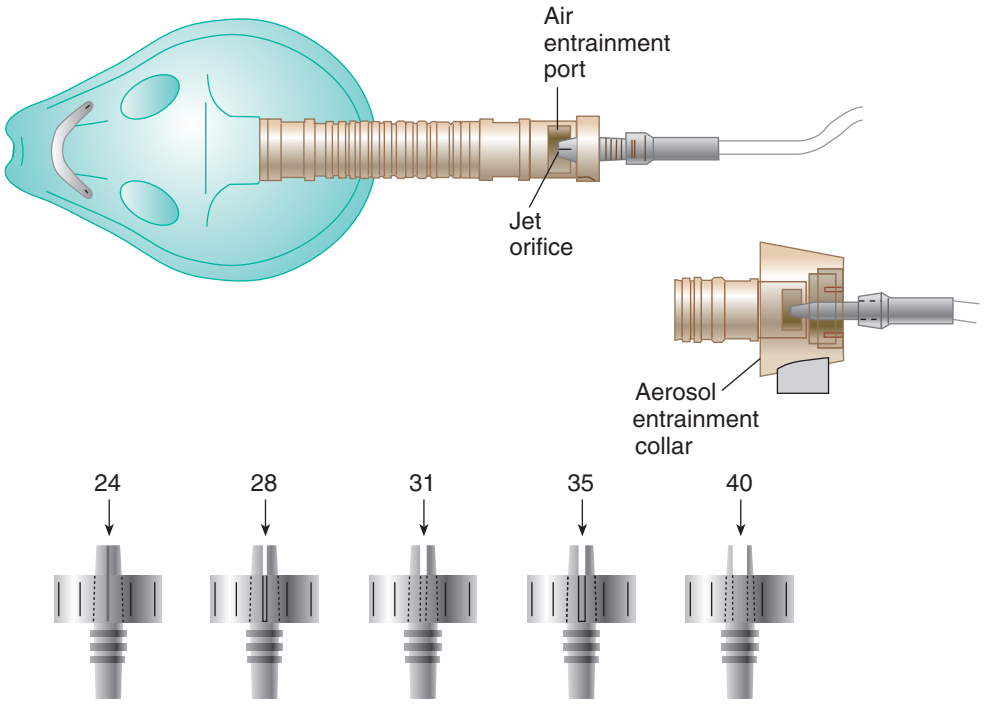

Fig. 42.14 Typical Air-Entrainment Mask. Fractional inspired oxygen (FiO_2) is regulated by changing a jet adapter. The aerosol collar allows high humidity or aerosol entrainment from an air source. (Modified from Kacmarek RM: In-hospital O_2 therapy. In Kacmarek RM, Stoller J, editors: *Current respiratory care*, Toronto, 1988, BC Decker.)

peak inspiratory flow.[29] With an entrainment ratio exceeding 5:1, an AEM set to deliver less than 35% O_2 has little trouble meeting or exceeding the 60 L/min high-flow criterion (see previous Rule of Thumb). At settings greater than 35%, total AEM flow decreases significantly, and FiO_2 becomes variable. For example, when set to deliver 50% O_2, some AEMs provide 0.39 FiO_2.[32-34]

Air-entrainment nebulizer. Pneumatically powered air-entrainment nebulizers have most of the features of air-entrainment nebulizers (AEMs) but have added capabilities, including additional humidification and temperature control. Humidification is achieved through production of aerosol at the nebulizer jet. Temperature control is provided by an optional heating element. In combination, these added features allow delivery of particulate water (in excess of needs for body temperature and pressure) to the airways. These devices are also widely known as *jet nebulizers* or *large volume nebulizers*.

Because of added humidification and heat control, air-entrainment nebulizers have been the traditional device of choice for delivering O_2 to patients with artificial tracheal airways. O_2 typically is delivered with a T tube or a tracheostomy mask. An alternative is to use an aerosol mask or a face tent to deliver an O_2 mixture to patients with intact upper airways (Fig. 42.15).[35]

AEMs can vary both jet and entrainment port size to obtain a given FiO_2; however, gas-powered nebulizers have a fixed orifice. Air-to-O_2 ratios can be altered only by varying entrainment port size. Disposable nebulizers usually have a continuous range of settings from 28% to 100%.[22]

Similar to AEMs, air-entrainment nebulizers perform as fixed-performance devices only when output flow meets or exceeds the patient's inspiratory demand. In contrast to AEMs, air-entrainment nebulizers do not allow easy increases in nebulizer output flow by means of an increase in O_2 input. With most nebulizer systems, the extremely small size of the jet needed for aerosol production limits the maximum O_2 input flow to 12 to 15 L/min at 50 psig. For example, the total output flow of an air-entrainment nebulizer set to deliver 40% O_2 ranges from 48 to 60 L/min. Although this amount may be adequate for most patients, it is insufficient for patients with very high inspiratory flow or minute volume,[35] and air entrainment nebulizers should be treated as fixed-performance devices only when set to deliver low O_2 concentration (≤35%).[33] The actual FiO_2 received by patients may be affected by the choice of airway appliance. For example, due to the open characteristics of a face tent, the FiO_2 delivered by this device is consistently less than the set FiO_2. Therefore such devices may not be appropriate for severely hypoxemic patients.[35]

There are two ways to assess whether the flow of an air-entrainment nebulizer meets the patient's needs. The first method is simple visual inspection. With this approach (generally used only with a T tube), the RT sets up the device to deliver the highest possible flow at the prescribed FiO_2 and observes the mist output at the expiratory side of the T tube. As long as mist can be seen escaping throughout inspiration, flow is adequate and the delivered FiO_2 is ensured.

The second way to assess the adequacy of nebulizer flow is to compare it with the patient's peak inspiratory flow. A patient's peak inspiratory flow during tidal breathing is at least three times minute volume. As long as the nebulizer flow exceeds this value, the delivered FiO_2 is ensured. If the patient's peak flow

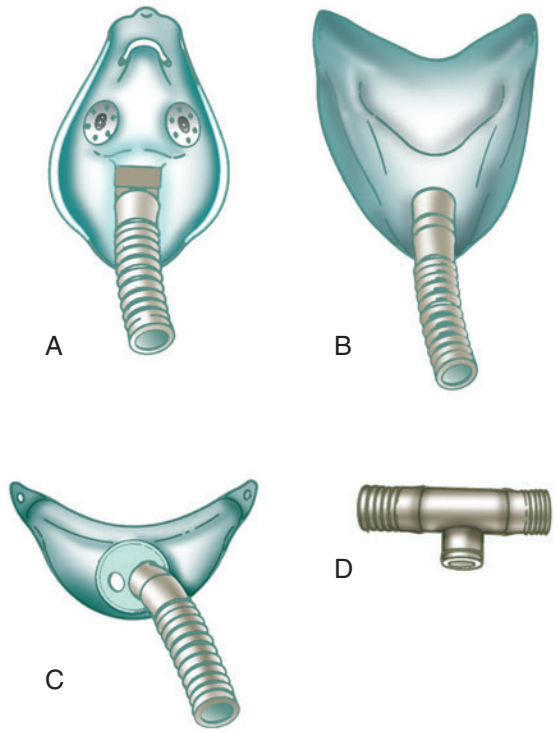

Fig. 42.15 Devices for Delivery of O_2 Mixtures With Aerosol. (A) Aerosol mask. (B) Face tent. (C) Tracheostomy collar. (D) T tube. (Modified from Kacmarek RM: In-hospital O_2 therapy. In Kacmarek RM, Stoller J, editors: *Current respiratory care*, Toronto, 1988, BC Decker.)

exceeds that provided by the nebulizer, the device functions as a low-flow system with variable FiO_2 (see the accompanying Mini Clini for an example).[35]

MINI CLINI

Computing Minimum Flow Needs

Problem

A physician orders 40% O_2 through an air-entrainment nebulizer to a patient with a tidal volume of 0.6 L and a respiratory rate of 33 breaths/min. If maximum nebulizer input flow is 12 L/min, will the patient receive 40% O_2? If not, what total flow is needed to meet this patient's needs?

Solution

1. Estimate the patient's inspiratory flow:

$$\text{Peak inspiratory flow} = VE \times 3 = (0.6 \times 33) \times 3 = 59.4 \text{ L/min}$$

2. Compute the total flow of the nebulizer:

$$\text{Sum of ratio parts}(3:1) \times \text{In put flow}(12 \text{ L/min}) = 48 \text{ L/min}$$

3. Compare value 1 with value 2 (patient with nebulizer):

$$59.4 \text{ L/min (patient)} > 48 \text{ L/min (nebulizer)}$$

Under these conditions, the patient does not receive 40% O_2. To deliver a stable 40% O_2 concentration, the total flow would have to be at least 59.4 L/min.

Troubleshooting air-entrainment systems. There are two major problems encountered with air-entrainment systems. The first is ensuring adequate flow at moderate to high FiO_2s. Another problem is that the performance of all air-entrainment devices is affected by downstream resistance, which can result in the delivery of inaccurate FiO_2s. These problems and their solutions are discussed as follows.

BOX 42.2 Increasing FiO_2 Capabilities of Air-Entrainment Nebulizers

- Add open reservoir to expiratory side of T tube
- Provide inspiratory reservoir with one-way expiratory valve
- Connect two or more nebulizers together in parallel
- Set nebulizer to low concentration; bleed-in O_2; analyze and adjust
- Use a commercial dual-flow system

FiO_2, fractional inspired oxygen.

Providing moderate to high FiO_2 at high flow. When set according to the manufacturer's specifications to provide much more than 45% to 50% O_2, AEMs simply do not generate enough flow to ensure the set FiO_2. The solution is to boost the total output flow. With AEMs, total output flow can be boosted with a simple increase in input flow. For a 35% AEM (5:1 ratio) with an input flow of 8 L/min, the total output flow is 48 L/min. This flow is insufficient to ensure 35% O_2 delivery to all patients. Simply increasing the input flow to 12 L/min boosts the output flow of the AEM by 50%, to 72 L/min. The new high flow ensures delivery of the set O_2 concentration to essentially all patients.

This solution is difficult with most air-entrainment nebulizers because the small jets in many of these devices limit O_2 flow to 12 to 15 L/min and input flow cannot be increased beyond these levels. A few nebulizer models, such as the Thera-Mist Barrel Nebulizer (Smiths Medical, London, England) and similar devices, can provide moderately high output flows of 54 L/min at FiO_2 80%. However, most air-entrainment nebulizers cannot because of the total flow-to-FiO_2 tradeoff. As a result, several alternatives for boosting the FiO_2 capabilities in these situations are presented in Box 42.2.

The simplest approach to achieving higher FiO_2 with these devices is to add a 50- to 150-mL aerosol tubing reservoir to the expiratory side of the T tube (Fig. 42.16). Given its simplicity, adding an open volume reservoir to the expiratory side of T tubes is standard procedure in most clinical settings. This approach can be used only in the treatment of intubated patients. Even then, the small reservoir size limits the ability of this system to ensure stable FiO_2, especially greater than 40%, and larger reservoirs can cause rebreathing.

Another approach to higher FiO_2 with air-entrainment nebulizers is to connect two or more devices together with a "wye" adapter (Fig. 42.17).[22] Although a single air-entrainment nebulizer set at 60% (1:1 ratio) with a maximum input flow of 15 L/min has a total output flow of only 30 L/min, connecting two of these devices together doubles the total output flow to 60 L/min (the minimum needed for a high-flow device). This approach works well only for delivery of a concentration of 60% or less to patients with a minute volume less than 20 L/min.[35]

An additional method for boosting FiO_2 provided by air-entrainment nebulizers is to set the device to a lower concentration than that prescribed (to generate high flow) while bleeding supplemental O_2 into the delivery tubing. This method increases

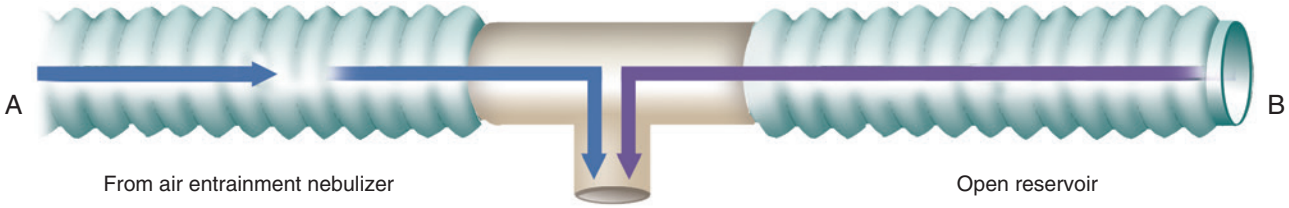

Fig. 42.16 Use of an open volume reservoir to enhance delivered O_2 concentration with a T tube. From 50 to 150 mL of aerosol tubing is connected to the expiratory side of the T tube. A, When the patient inhales, gas at the set fractional inspired oxygen (FiO_2) is drawn first through the inspiratory side of the circuit. B, If the patient's flow exceeds nebulizer flow, gas is drawn from the reservoir side. After the reservoir volume is fully tapped, room air is entrained, and FiO_2 decreases.

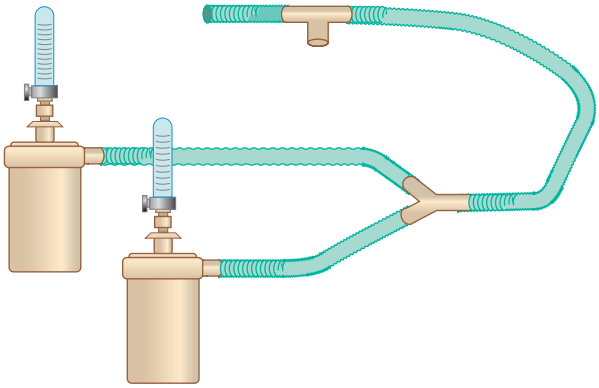

Fig. 42.17 Use of two nebulizers in parallel to provide high fractional inspired oxygen (FiO_2) at high flow.

both FiO_2 and total output flow. To achieve a specific FiO_2, the delivered concentration should be analyzed and the supplemental O_2 input flow adjusted until the desired concentration is achieved.

Commercial dual-flow systems entail a similar approach. One flow source powers the jet, while another flow source provides supplemental O_2. The Misty Ox (Vital Signs, Totowa, New Jersey) gas injection nebulizer is an example. This system is not an air-entrainment system because it does not depend on entrainment ports to increase total flow or O_2 concentration to the patient. Rather, it uses two flowmeters: one that operates the jet and one that feeds into the side of the jet manifold. The Misty Ox system can provide FiO_2 of 0.96 at a flow of 42 L/min and offers O_2 concentrations ranging from 0.21 to nearly 1.00.[35]

Problems with downstream flow resistance. Any increase in flow resistance downstream from (distal to) the point of air entrainment alters the performance of all air-entrainment systems. Increased downstream flow resistance causes back pressure. The back pressure decreases both the volume of entrained air and the total flow output of these devices. With less air entrained, the delivered O_2 concentration increases but, because total flow output also decreases, the effect on FiO_2 varies. High downstream flow resistance usually turns air-entrainment systems from high-flow (fixed) O_2 delivery systems into low-flow (variable) O_2 delivery systems incapable of delivering a precise and constant FiO_2.[29,36]

This problem explains why it is extremely difficult to deliver less than 28% to 30% O_2 with an air-entrainment nebulizer. The 5 to 6 ft (1.5 to 1.8 m) of aerosol tubing normally used with these devices produces enough flow resistance to decrease air entrainment and prevent a lower FiO_2.

A similar situation can occur when the entrainment ports of an air-entrainment device become obstructed (most common with AEMs). Delivered O_2 concentration increases, but total output flow decreases. The net effect usually is a variable FiO_2. The accompanying Mini Clini is an example of the effect of increased downstream flow resistance on the performance of an air-entrainment device.

MINI CLINI

Effect of Downstream Flow Resistance on Performance of an Air-Entrainment Device

Problem

A tracheostomy patient is receiving O_2 therapy through a T tube attached to an air-entrainment nebulizer set at 35% O_2 with an input flow of 10 L/min. Over the past 30 minutes, the patient's SpO_2 has decreased from 93% to 88%. When assessing the patient, the respiratory therapist (RT) finds that the large-bore delivery tubing of the nebulizer is partially obstructed with condensate and that aerosol mist at the T tube is not visible throughout inspiration. What is the likely problem, and what is the best solution?

Solution

The likely problem is a decrease in FiO_2 owing to the increased downstream resistance caused by the condensate. At 10 L/min input flow, the device was probably delivering approximately 60 L/min of 35% O_2 before the tubing became obstructed. Because aerosol mist is not visible at the T tube throughout inspiration, it is clear that the total output flow is no longer sufficient and that the patient is now diluting the delivered O_2 with room air. Draining the tubing solves this problem. Any other blockage of the large-bore tubing, such as tenacious secretions or being kinked in a bed rail, will cause a similar effect.

High-flow nasal cannula. A variation of the standard nasal cannula discussed earlier in this chapter is a **high-flow nasal cannula (HFNC)**. This form of oxygen delivery has been popular for pediatric and neonatal patients (see Chapter 35) with disorders including bronchiolitis and bronchopulmonary dysplasia. Currently, various systems have become available for adults, including the Vapotherm Precision Flow System (Vapotherm, Exeter, New Hampshire), which can deliver both FiO_2 and relative humidity greater than 90% by using heated, humidified O_2 flows up to 40 L/min. HFNC units offered by other manufacturers such as Fisher and Paykel's Optiflow (Irvine, California) featured

Fig. 42.18 High-flow nasal cannula setup (Courtesy Fisher & Paykel Healthcare, Inc., Irvine, California.)

in Fig. 42.18 have been shown to provide even higher flows of 60 L/min, as well as a maximum FiO_2 of more than 90%.

All HFNC systems require three components: (1) a patient interface, such as nasal prongs, (2) a gas delivery device that regulates FiO_2, and (3) a humidifier. The Vapotherm and Optiflow devices mentioned previously, feature a variety of proprietary designs that facilitate the separate control of flow and humidified supplemental oxygen. The ability to maintain a consistent FiO_2 under varying breathing patterns makes these devices suitable alternatives for early intervention in critically ill patients, as well as the preintubation and postextubation phases of care. These systems have been shown to successfully treat moderate hypoxemia through a combination of the four main features: (1) delivery of a high FiO_2, (2) meeting or exceeding the patient's minute ventilation and therefore acting as a fixed oxygen delivery device, (3) generating a distending, positive end-expiratory airway pressure (PEEP) of approximately 1 cm H_2O for each 10 L/min. of flow, and (4) washout of carbon dioxide from anatomic dead space.[37] Furthermore, the heated-humidity feature enables these systems to deliver highly humidified oxygen, thus preventing the drying effects that some high-flow devices have on the mucosa and enhancing mucociliary clearance. This advantage, along with the less confining design of these devices, makes them more comfortable and better tolerated by many patients than alternative oxygen delivery devices. As a result, such devices have become a popular substitute for both traditional high-flow oxygen devices and continuous positive airway pressure setups. Emerging research suggests additional benefits in reducing $PaCO_2$ for patients with acute hypercapneic respiratory failure.

Although definitive indications for HFNC are still evolving, patients with certain conditions seem to benefit from this modality. Table 42.8 summarizes the emerging indications for HFNC and the corresponding features which justify their use.

As a result of their features and advantages, HFNC devices are rapidly gaining popularity for being better tolerated than alternative therapies and enhancing clinical outcomes in selected patient populations. Despite the fact that some infection control concerns associated with older HFNC designs appear to have been largely overcome, several limitations persist. These include contraindications for use on patients with blocked nasal passages,

TABLE 42.8 Emerging Indications for HFNC and the Corresponding Features

Indication	HFNC Features
Hypoxemic respiratory failure *Example*: Pneumonia	High FiO_2, high-flow, PEEP, enhanced mucocilary clearance
Hypercapneic respiratory failure *Example*: COPD exacerbation	CO_2 washout, enhanced mucocilary clearance
Reduce reintubation risk. *Example:* Postextubation of a patient with significant comorbidities such as COPD.	High FiO_2, high-flow, PEEP, enhanced mucocilary clearance, CO_2 washout.
Do-not-intubate or hospice patient with respiratory failure. *Example:* End-stage lung cancer patient.	Multiple features which combat respiratory failure (see above) but more comfortable; less confining and drying than alternative therapies.
Inability to tolerate other oxygen delivery devices. *Example:* Claustrophobic COPD patient.	Multiple features which combat respiratory failure (see above) but more comfortable; less confining and drying than alternative therapies.

COPD, Chronic obstructive pulmonary disease; *HFNC*, high-flow nasal cannula; *PEEP*, positive end-expiratory airway pressure.

problems from the inability to precisely determine and monitor the level of positive pressure actually applied to the airway, and in rare instances, nasal skin erosions, mainly in neonates and infants, from an improperly fitting cannula.[38] In addition, care should also be taken not to delay escalation of treatment or emergent intubation if assessment reveals that the patient is not responding to, or simply not tolerating HFNC. Last, although HFNC may be part of the care plan for patients with a "Do Not Resuscitate" order, it should not substitute the need for formal transition to palliative care in terminally ill patients (see Chapter 58).

MINI CLINI

Indications for High-Flow Nasal Oxygen

Problem

A recently extubated patient experiencing moderate hypoxemia is having trouble tolerating a 50% venturi mask due to claustrophobia and airway dryness. When switched to a nasal cannula, his SpO_2 drops to 88%. The physician wants the patient SpO_2 to remain at 92% or higher and asks the respiratory therapist (RT) what options are available for delivering moderate oxygen concentrations to this patient while maximizing patient comfort.

Solution

A high-flow nasal oxygen setup is able to provide a moderate to high and consistent FiO_2 through varying patient breathing patterns. In addition, features including a less-confining design and delivery of a highly humidified gas tend to make them better tolerated than many other oxygen delivery systems. Hence in this instance, the RT should recommend a high-flow nasal oxygen setup.

Blending systems. When air-entrainment devices cannot provide a high enough O_2 concentration or flow, use of a gas blending system should be considered. With a blending system, separate pressurized air and O_2 sources are input, and the gases are mixed either manually or with a precision valve (blender).

This system allows precise control over both FiO_2 and total flow output. Most blending systems can provide flow much greater than 60 L/min, qualifying them as true fixed-performance delivery devices. For adults, gas is delivered from the blender either through an open system, such as an aerosol mask or T tube, or with a closed nonrebreathing system. For many patients requiring high FiO_2 and breathing spontaneously, this is the ideal setup, provided that the gas is humidified. The use of high-flow blended systems with heated humidity, as opposed to a heated aerosol, are very well tolerated by most patients, including patients with tracheostomies. In addition, because they do not produce an aerosol, they are better tolerated by tracheostomy patients than aerosol systems which can cause bronchospasm.

Mixing gases manually. When gases are mixed manually, separate air and O_2 flowmeters must be adjusted for the desired FiO_2 and flow (see the accompanying Mini Clini). For adults, this approach requires calibrated high-flow flowmeters (at least 60 L/min) and monitoring of delivered FiO_2.

MINI CLINI

Manually Mixing Air and Oxygen to Achieve Specified Concentration at a Given Flow

Problem

To mix air and O_2 manually to provide a patient with 50% O_2 at a total flow of 60 L/min, what O_2 and airflow would the respiratory therapist (RT) set?

Solution

1. Use Eq. 42.3 to compute the O_2 flow:

$$O_2 \text{ flow} = \frac{\text{Total flow} \times (O_2\% - 21)}{79}$$

$$O_2 \text{ flow} = \frac{60 \times (50 - 21)}{79}$$

$$O_2 \text{ flow} = 22 \text{ L/min}$$

2. Compute the airflow:

$$\text{Airflow} = \text{Total flow} - O_2 \text{ flow}$$

$$\text{Airflow} = 60 - 22$$

$$\text{Airflow} = 38 \text{ L/min}$$

To provide a patient with 50% O_2 at a total flow of 60 L/min, blend 22 L of O_2 with 38 L of air.

Oxygen blenders. Rather than manually mixing air and O_2, the RT more often uses an O_2 blender. Fig. 42.19 shows the major components of a typical O_2 blender. Air and O_2 enter the blender and pass through dual pressure regulators that exactly match the two pressures. Gas flows to a precision proportioning valve. Because the two gas pressures at this point are equal, varying the size of the air and O_2 inlets provides precise control over the relative concentration.

An alarm system gives an audible warning when either source gas fails or the pressure decreases below a specified value. The alarm system usually has a crossover or bypass feature whereby failure of one gas source causes the blender system to switch to the other. If the air source fails when delivering 60% O_2, the alarm sounds, and the blender switches over to delivery of 100% O_2.

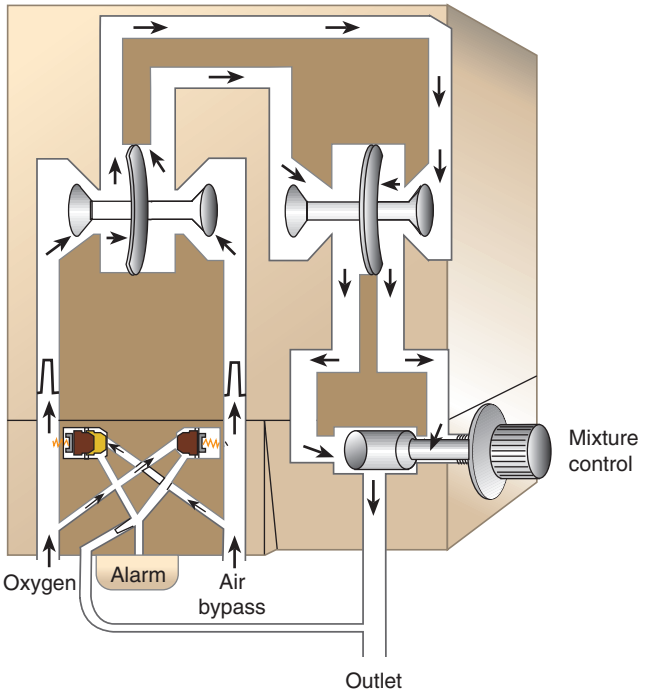

Fig. 42.19 O_2 blending device. (Modified from McPherson SP: *Respiratory therapy equipment*, ed 3, St. Louis, 1985, Mosby.)

BOX 42.3 Procedure for Confirming Operation of an Oxygen Blender

1. Confirm that inlet pressures of air and O_2 are within manufacturer's specifications.
2. Test low air and O_2 alarms by disconnecting each source; also confirm safety bypass or crossover system.
3. Analyze O_2 concentration at 100%, 21%, and specified FiO_2.

Although they allow ideal control over both FiO_2 and flow, blenders are especially prone to inaccuracy and failure.[36] Hence an operational check of any blender should be conducted before using it on a patient (Box 42.3). FiO_2 should be checked and confirmed with a calibrated O_2 analyzer at least once per shift. When a blender is used in the care of a neonate, an O_2 analyzer should be kept in-line at all times. In the use of a nonrebreathing or closed delivery system, (1) all breathing valves should be inspected and tested before application to a patient, and (2) a fail-safe inspiratory valve should be included in the delivery system.

Enclosures. The concept of enclosing a patient in a controlled-O_2 atmosphere is among the oldest approaches to O_2 therapy. Entire rooms once were used for this purpose. With current simpler airway devices, enclosures are generally used only in the care of infants and children. The primary types of O_2 enclosures used for infants and children are isolettes and hoods, both of which are discussed in Chapter 54 of this textbook.

BOX 42.4 Patient Factors in Selecting Oxygen Therapy Equipment

- Severity and cause of hypoxemia
- Patient age group (infant, child, adult)
- Degree of consciousness and alertness
- Presence or absence of tracheal airway
- Stability of minute ventilation
- Mouth breathing versus nose breathing patient

Other Oxygen Delivery Devices

Bag-mask devices. Bag-mask devices use a self-inflating bag and nonrebreathing valve features to provide up to 100% O_2. Bag-mask devices are often used in emergency life support and in critical care and are more completely discussed in Chapter 38.

Demand-flow and pulse-dose systems. Demand-flow or pulse-dose systems use a flow sensor and valve to synchronize gas delivery with inspiration. These devices can substantially extend duration of flow of a liquid or gaseous O_2 tank and are popular in alternative settings, as described in Chapter 57.

Selecting a Delivery Approach

The RT is often involved in the initial selection of an appropriate delivery system. This generally involves making recommendations based on sound patient assessment—to initiate, change, or discontinue the treatment regimen (see later section on **Protocol-Based Oxygen Therapy**).

The three *P*s—*purpose, patient,* and *performance*—are used in the initial selection or recommendation of a change in O_2 delivery system. The goal is to match the performance characteristics of the equipment to both the objectives of therapy (purpose) and the patient's special needs.

Purpose

The general purpose or objective of all O_2 therapy is to increase FiO_2 sufficiently to correct arterial hypoxemia. Other objectives, including decreasing hypoxic symptoms and minimizing increased cardiopulmonary work, follow from this primary purpose.

Patient

Key patient considerations in selecting O_2 therapy equipment for use in acute care are summarized in Box 42.4. Knowledge of these factors helps guide the RT in selecting the appropriate delivery device. For example, a simple mask at 5 to 6 L/min is probably more suitable than a nasal cannula at 4 L/min for a mouth breathing, mildly hypoxemic patient. An infant with moderate hypoxia and a normal airway usually needs an O_2 enclosure (hood or enclosed incubator).

Performance

O_2 systems vary according to actual FiO_2 delivered and stability of FiO_2 under changing patient demands. In general, the more critically ill the patient, the greater the need for a stable, high FiO_2. Less acutely ill patients generally need a lower, less exact FiO_2. Table 42.9 lists guidelines for selecting an O_2 delivery system based on the level and stability of the FiO_2 needed.

TABLE 42.9 Selection of an Oxygen Delivery System Based on Desired FiO_2 Level and Stability

Desired FiO_2 Level	DESIRED FIO_2 STABILITY	
	Fixed	**Variable**
Low (<35%)	AEM	Nasal cannula
	Air-entrainment nebulizer	Nasal catheter
	Blending system	Transtracheal catheter
	Isolette, incubator (infant)	
Moderate (35%–60%)	Air-entrainment nebulizer	Simple mask
	Blending system	Air-entrainment nebulizer
	Oxyhood (infant)	Tent (child)
High (>60%)	Blending system	Partial rebreather
	Oxyhood (infant)	Nonrebreather
	High-flow nasal cannula	

AEM, Air-entrainment mask; *FiO_2,* fractional inspired oxygen.

General Goals and Patient Categories

On the basis of overall consideration of the three *P*s, general goals can be set for several patient categories. In emergencies in which tissue hypoxia is suspected, patients should be given the highest FiO_2 possible—ideally 100%. This level can be achieved with a true high-flow or a closed reservoir system. The goal is the highest possible blood O_2 content. Clinical examples include respiratory or cardiac arrest, severe trauma, shock, carbon monoxide poisoning, and cyanide poisoning. Carbon monoxide and cyanide poisoning may necessitate HBO therapy (see later).

A critically ill adult patient with moderate to severe hypoxemia needs either a reservoir or a high-flow system capable of at least 60% O_2. Thereafter, changes in FiO_2 (and device) should be based on results of assessment of physiologic values. The goal is a PaO_2 greater than 60 mm Hg or oxyhemoglobin saturation greater than 90%.

In the care of adult patients in more stable condition but who are acutely ill with mild to moderate hypoxemia, a system capable of low to moderate O_2 concentration can be used. In these cases, stability of FiO_2 is not critical. Applicable devices include a nasal cannula at moderate flow or a simple mask. Common examples include patients in the immediate postoperative phase and patients recovering from acute myocardial infarction.

Adult patients with chronic lung disease and accompanying acute-on-chronic hypoxemia present a special case. In the care of these patients, the goal is to ensure adequate arterial oxygenation without depressing ventilation. Adequate oxygenation of these patients generally means an SaO_2 of 85% to 92% with PaO_2 of 50 to 70 mm Hg.[31,39,40] These values usually are achieved with either low-flow nasal O_2 or a low-concentration (24% to 28%) AEM. The less stable the patient's condition, the greater the need for a high-flow AEM.[22]

Because of size, discomfort, and appearance, AEMs are less well tolerated than nasal cannulas for long-term therapy. In

contrast to a cannula, an AEM must be removed for eating and drinking. Because even a short break in O_2 therapy can cause a rapid decrease in PaO_2 in some patients, these patients should be taught to switch to a nasal cannula whenever they must remove the mask.[22]

Lastly, it is sometimes necessary to modify O_2 delivery systems to facilitate patient transport. An example is a spontaneously breathing patient with a tracheostomy tube receiving a moderate FiO_2 via a blended system or an air-entrainment nebulizer connected to a tracheostomy mask. Given the impracticalities of transporting a patient on an air-entrainment nebulizer, it may be more suitable to connect a venturi adapter temporarily to provide the appropriate FiO_2 to the tracheostomy mask during the transport and then reconnect them back to the original aerosol setup immediately after the transport.

Protocol-Based Oxygen Therapy

O_2 therapy is ideally suited for protocol-based management. Bedside assessment of oxygenation by RTs and other clinicians has progressed to where it is more cost-effective and clinically appropriate to use a protocol rather than obtaining a new physician order for each change in FiO_2. An order for "O_2 therapy via protocol" permits O_2 therapy to be initiated, modified, or discontinued by the RT, provided an assessment reveals that the patient meets previously approved clinical criteria. A well-designed O_2 protocol ensures that the patient: (1) undergoes initial assessment, (2) is evaluated for protocol criteria, (3) receives a treatment plan that is modified to the need, and (4) stops receiving therapy as soon as it is no longer needed.

Fig. 42.20 shows the decision algorithm underlying an O_2 therapy titration protocol developed at the Cleveland Clinic Foundation. In the algorithm, a pulse oximetry saturation (SpO_2) of 92% is the point at which therapy is to be initiated. The patient is assessed each shift for the need of supplemental O_2, which is adjusted depending on need. When the SpO_2 is consistently 92% or greater on room air, therapy is discontinued.

HYPERBARIC OXYGEN THERAPY

HBO therapy is the therapeutic use of O_2 at pressures greater than 1 atm.[41-44] Pressures during HBO therapy usually are expressed in multiples of **atmospheric pressure absolute (ATA)**: 1 ATA equals 760 mm Hg (101.32 kPa). Most HBO therapy is conducted at pressures between 2 and 3 ATA, although other pressures may be used, often based on U.S. Navy diving treatment tables.[43-45]

Physiologic Effects

The known physiologic effects of HBO therapy are summarized in Box 42.5.[42] These effects are mainly due to either high pressure or high O_2 tension in body fluids and tissues. In conditions such as air embolism and decompression sickness, Boyle's law dictates that high pressure exerts a physical effect on air or nitrogen bubbles trapped in the blood or tissues, reducing their size, and minimizing potential harm. Because pressure is crucial in these cases, HBO treatments may be conducted at 6 ATA or more.[43,45]

BOX 42.5 Physiologic Effects of Hyperbaric Oxygen Therapy

- Bubble reduction (Boyle's law)
- Hyperoxygenation of blood and tissue (Henry's law)
- Vasoconstriction
- Enhanced host immune function
- Neovascularization

The second beneficial effect of HBO is hyperoxia. When a patient is breathing room air, only a small amount of O_2 dissolves in the plasma (approximately 0.3 mL/dl). At 3 ATA, plasma contains nearly 7 mL/dl dissolved O_2, a level exceeding average resting tissue uptake.[43]

O_2 supply to the tissues affects the immune system, wound healing, and vascular tone. A tissue PO_2 of at least 30 mm Hg is necessary for normal cellular function. Damaged and infected tissues often have a lower PO_2. Increasing O_2 supply to these tissues can help restore both white blood cell function and antimicrobial activity.

Hyperoxia affects the cardiovascular system. HBO therapy causes generalized vasoconstriction and a small decrease in cardiac output. Although these changes may decrease blood flow to a region, this effect is more than offset by the increase in O_2 content. In conditions such as burns, cerebral edema, and crush injuries, vasoconstriction may be helpful because it reduces edema and tissue swelling while maintaining tissue oxygenation.

Hyperoxia also helps form new capillary beds, a process called **neovascularization**. Although the exact mechanism is unknown, neovascularization is an essential component of tissue repair, especially in radiation-induced injuries.[43,44]

Study results suggest that HBO may be useful in many other conditions, including the management of stroke, wound healing, and treating stubborn soft tissue infections. Because HBO has emerged as a highly effective therapy for various conditions, its use in recent years has expanded.[46,47]

Methods of Administration

HBO is administered in either a multiplace or a monoplace chamber. A multiplace chamber is a large tank capable of holding a dozen or more people (Fig. 42.21A). Because patients are directly cared for by medical staff inside the tank, multiplace chambers have air locks that allow entry and exit without altering the pressure. The multiplace chamber is generally filled with air. If indicated, only the patient breathes supplemental O_2 (through a mask or another device). Because they can achieve pressures of 6 ATA or more, multiplace chambers are ideal for the management of decompression sickness and air embolism.[43-45]

A typical monoplace chamber consists of a transparent Plexiglas cylinder large enough only for a single patient (see Fig. 42.21B). During therapy, the cylinder O_2 concentration is kept at 100%. The patient need not wear a mask. Because of the high O_2 concentration, most electronic equipment cannot be used in a monoplace chamber. In addition, many ventilators do not function properly under the high atmospheric pressures. However, monitoring systems and ventilators can be adapted to allow

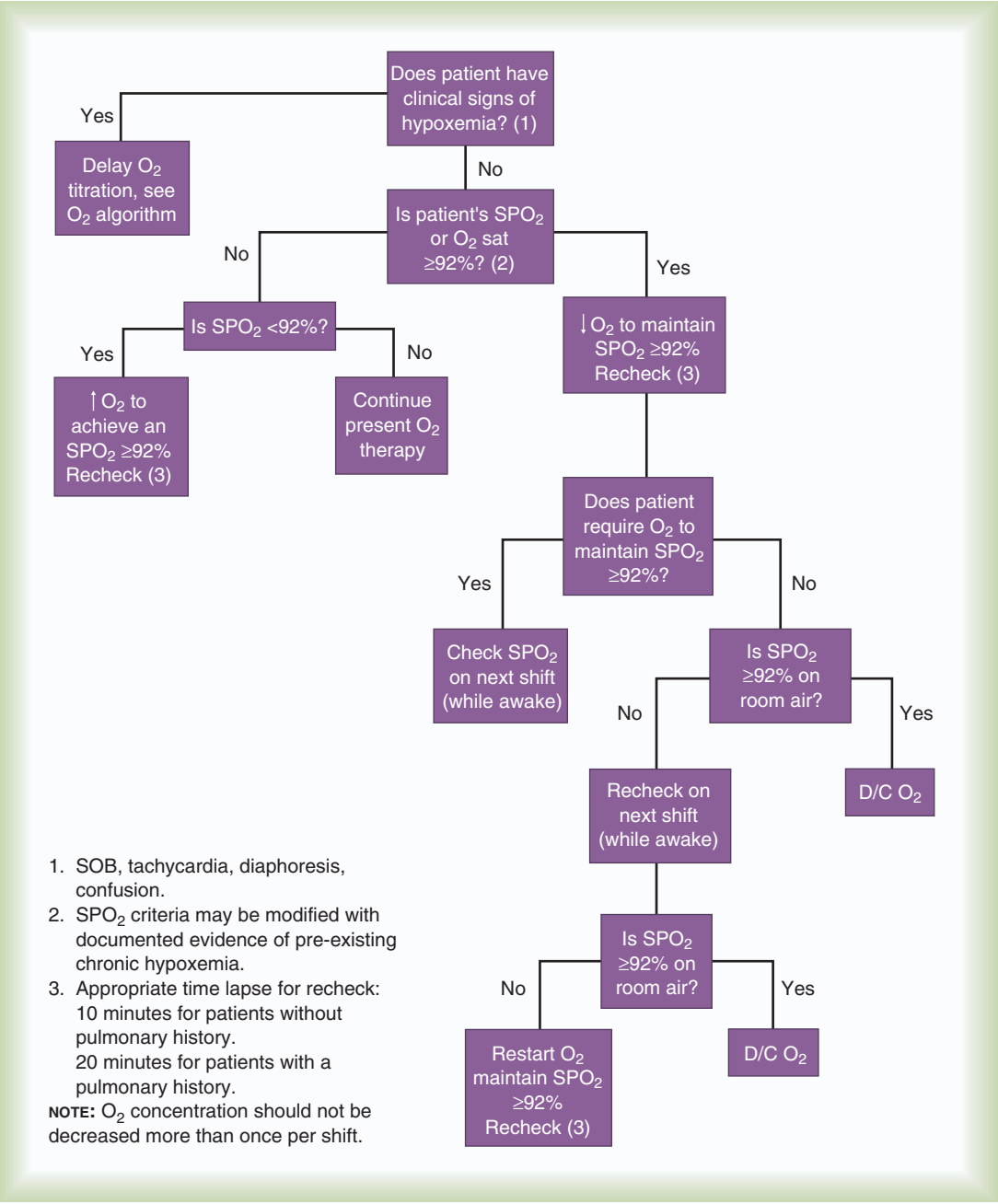

Fig. 42.20 Protocol for titration of O_2 therapy. (Courtesy the Respiratory Therapy Section, Cleveland Clinic Foundation, Cleveland, Ohio.)

treatment of a critically ill patient with hyperbaric pressure. In addition, artificial airways suited to function properly under hyperbaric conditions should be used.[42]

Indications

HBO has long been accepted as the primary treatment of divers with decompression sickness. Several other of the most common indications for HBO therapy are listed in Box 42.6. The two most common acute indications are air embolism and carbon monoxide poisoning.[42,45,47]

Air Embolism

Air embolism is a complication that can occur with certain cardiovascular procedures, lung biopsy, hemodialysis, and central line placement. HBO can decrease the size of air bubbles which may otherwise reach the cerebral or cardiac circulation and can cause symptoms or sudden death. Typical therapy for air embolism involves immediate pressurization in air to 6 ATA for 15 to 30 minutes. This step is followed by decompression to 2.8 ATA with prolonged O_2 treatment.[43-45]

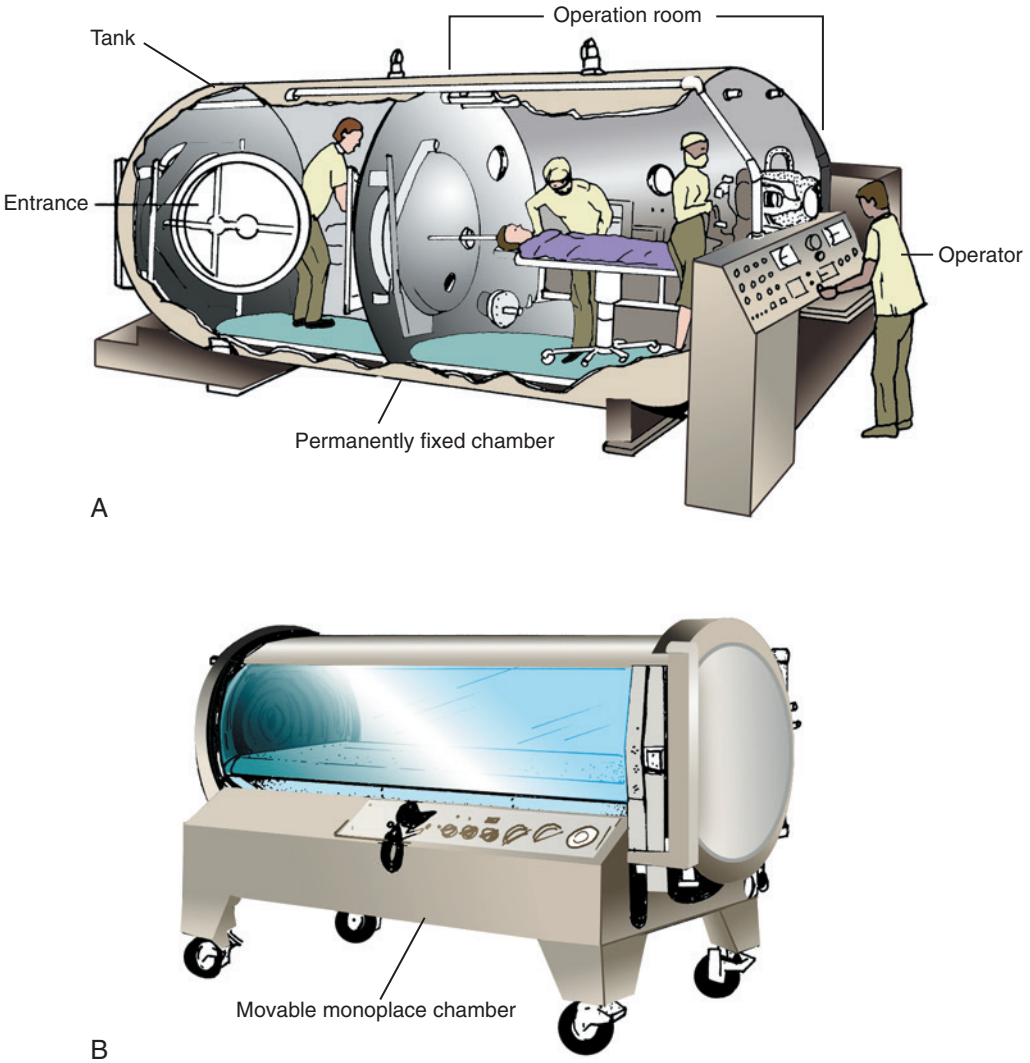

Fig. 42.21 (A) Fixed hyperbaric chamber. (B) Monoplace chamber.

BOX 42.6 Indications for Hyperbaric Oxygen Therapy

Acute Conditions

- Decompression sickness
- Air or gas embolism
- Carbon monoxide and cyanide poisoning
- Acute traumatic ischemia (compartment syndrome, crush injury)
- Acute peripheral arterial insufficiency
- Intracranial abscesses
- Crush injuries and suturing of severed limbs
- Clostridial gangrene
- Necrotizing soft tissue infection
- Ischemic skin graft or flap

Chronic Conditions

- Diabetic wounds of the lower extremities and other nonhealing wounds
- Refractory osteomyelitis
- Actinomycosis (chronic systemic abscesses)
- Radiation necrosis (hyperbaric oxygen as an adjunct to conventional treatment)

Carbon Monoxide Poisoning

Carbon monoxide poisoning accounts for approximately half of all poisoning deaths in the United States. The condition of a patient with carbon monoxide poisoning improves quickly with HBO treatment because this treatment is the fastest way to remove carbon monoxide from the blood.[47] If a patient breathes air, it takes more than 5 hours to remove only one-half of the carboxyhemoglobin in the blood. Breathing 100% O_2 reduces this "half-life" to 80 minutes. The half-life of carboxyhemoglobin under HBO at 3 ATA is only 23 minutes. Box 42.7 lists the major criteria for selecting patients with acute carbon monoxide poisoning for treatment with HBO.[47]

Complications and Hazards

Although the benefits of HBO are significant, this type of therapy also has significant risks. As a result, the benefits should be compared with the hazards before therapy is initiated. Common complications of HBO are listed in Box 42.8.[43] These complications are generally caused by high pressure, O_2 toxicity, fire, or

BOX 42.7 Criteria for Hyperbaric Oxygen Therapy for Acute Carbon Monoxide Poisoning

- History of unconsciousness
- Presence of neuropsychiatric abnormality
- Presence of cardiac instability or cardiac ischemia
- Carboxyhemoglobin level 25% (lower levels for children and pregnant women)

BOX 42.8 Major Complications of Hyperbaric Oxygen Therapy

Barotrauma
- Ear or sinus trauma
- Tympanic membrane rupture
- Alveolar overdistention and pneumothorax
- Gas embolism

Oxygen Toxicity
- Central nervous system toxic reaction
- Pulmonary toxic reaction

Other
- Fire
- Sudden decompression
- Reversible visual changes
- Claustrophobia
- Decreased cardiac output

worsening of certain existing conditions. The most frequent problems involve barotrauma to closed body cavities, such as the middle ear or sinuses. Pneumothorax and air embolism also are possible during HBO treatment but are rare in patients with normal lungs.

O_2 at high pressure can rarely be neurotoxic. Early signs of impending CNS toxicity include twitching, sweating, pallor, and restlessness and later seizures and convulsions.[44]

In terms of pulmonary O_2 toxicity, HBO treatments do not normally expose patients to high PO_2 long enough to cause damage. However, HBO may have an additive effect on critically ill patients who receive high FiO_2 between HBO treatments.[43,44]

Avoiding fire and sudden decompression are primary safety concerns. Only 100% cotton fabric should be used to avoid fire from a static electrical discharge. Other ignition sources such as matches or lighters should never be brought into HBO chambers, and alcohol- or petroleum-based products, including makeup or deodorant, should never be used. Other potential hazards of HBO involve the aggravation of existing conditions, including diabetes, epilepsy, and hypertension. These concerns can be addressed by an appropriate history and chart review, close patient monitoring, and appropriate adjustment of therapy.

There are numerous relative contraindications for HBO, many of which relate to the potential complications and hazards noted earlier. Relative contraindications include inner ear infections and seizure disorders. Absolute contradictions include an untreated pneumothorax and congenital heart defects resulting in dependency on a patent ductus arteriosus for survival.[44]

Troubleshooting

Although fire hazards restrict the use of certain electronic equipment, some state-of-the-art monitors and ventilators with solid-state circuitry can be used within the chamber. This equipment allows intensive care of critically ill patients.[42]

In regard to ventilator use, reductions in delivered tidal volume should be expected and corrected. In addition, tracheostomy or endotracheal tubes with foam or fluid-filled cuffs should generally be used to preserve cuff integrity under pressure. If not accounted for, reduced tidal volumes and leaks can lead to respiratory hypercapnia and acidosis. Hypercapnia can result in respiratory acidosis and can worsen CNS toxicity owing to cerebral vasodilation.[44] In general, pressure-regulating and flow-regulating equipment used in a hyperbaric chamber must be specifically designed for operation or equipment appropriately modified to function properly in such conditions.

OTHER MEDICAL GAS THERAPIES

O_2 is not the only medical gas administered by RTs. The potent pulmonary vasodilator **nitric oxide (NO)**, and helium-O_2 mixtures are also among other medical gases administered by RTs.

Nitric Oxide Therapy

Mode of Action

NO gas is a colorless, odorless, highly diffusible, and lipid-soluble free radical that oxidizes quickly to nitrogen dioxide (NO_2) in the presence of O_2. NO is normally produced in small amounts within the human body and activates guanylate cyclase, which catalyzes the production of cyclic guanosine 3′,5′-monophosphate (cGMP). The end result is increased cGMP levels that cause vascular smooth muscle relaxation.[48,49] The therapeutic benefit of inhaled NO (iNO) stems from improved blood flow to ventilated alveoli. The result is a reduction in intrapulmonary shunting, improvement in arterial oxygenation, and a decrease in pulmonary vascular resistance and pulmonary arterial pressure.

Indications

INOmax is indicated to improve oxygenation and reduce the need for extracorporeal membrane oxygenation in term and near-term (>34 weeks gestation) neonates with hypoxic respiratory failure associated with clinical or echocardiographic evidence of pulmonary hypertension in conjunction with ventilatory support and other appropriate agents (INOmax.com Product Information)

As approved by the U.S. Food and Drug Administration (FDA) in December 1999, INOmax (iNO) is a selective pulmonary vasodilator and is effective in term and near-term infants with hypoxemic respiratory failure (HRF) and persistent pulmonary hypertension of the newborn (PPHN).[50]

In adults, studies have shown that iNO has been effective in treating pulmonary hypertension associated with acute respiratory distress syndrome (ARDS). However, these benefits seem to be short-lived, and no significant improvement in clinical outcomes, including ventilator-days and mortality, have been shown to date. However, iNO is frequently used for the management

BOX 42.9 Potential Uses for Inhaled Nitric Oxide

- ARDS
- Persistent pulmonary hypertension of the newborn
- Primary pulmonary hypertension
- Pulmonary hypertension after cardiac surgery
- Cardiac transplantation
- Acute pulmonary embolism
- chronic obstructive pulmonary disease
- Congenital diaphragmatic hernia
- Sickle cell disease
- Testing pulmonary vascular responsiveness

of patients with acute or chronic pulmonary hypertension as a result of pulmonary or cardiac disease and as a diagnostic tool for assessing pulmonary vascular responsiveness prior to heart transplantation or other cardiac surgical procedures. But because of the high cost of NO, and the lower cost of alternative drug therapies, including inhaled epoprostenol sodium (Flolan) and similar medications (discussed in Chapter 36), most try to avoid the use of NO. iNO in adults has not been approved by the FDA. Irrespective, the potential indications for iNO are listed in Box 42.9.[50,51]

Dosing

For term and near-term neonates with hypoxic respiratory failure, the recommended dose of INOmax is 20 ppm. Treatment should be continued until underlying oxygenation desaturation has resolved. For many patients, dosages often can be reduced to less than 20 ppm at the end of 4 hours of initial treatment, as tolerated. At these levels, NO has minimal toxicity.[49-51]

Toxicity and Adverse Effects

Most of the toxic effects of NO are caused by its chemical by-products, especially NO_2. NO_2 is produced spontaneously whenever NO is exposed to O_2. NO_2 is more toxic than NO. Levels greater than 10 ppm can cause cell damage, hemorrhage, pulmonary edema, and death. The U.S. Occupational Safety and Health Administration has set the safety limit for NO_2 exposure at 5 ppm. Properly set up NO delivery systems safely and easily achieve this limit.[52]

Other harmful chemical by-products produced in reaction with NO include methemoglobin and peroxynitrite (produced when NO reacts with superoxide). Although it can occur with NO administration, methemoglobinemia is not common considering the doses commonly used and the required monitoring systems discussed later in this section. Peroxynitrite can cause severe cell damage; however, there is no hard evidence supporting its toxic effects during NO administration.

Potential adverse effects associated with NO therapy are listed in Box 42.10.[53] A poor or paradoxical response to NO has been observed in some patients. Of patients with ARDS, 40% do not have initial improvement in oxygenation with NO therapy, and some patients have experienced more severe hypoxemia (probably because of a worsening ventilation/perfusion imbalance when no shunt was present). NO inhibits platelet agglutination; however, no significant increase in bleeding time has been reported in NO trials with human subjects. Because it can quickly reduce right ventricular afterload, NO may increase left ventricular filling pressure in some patients. In the presence of congestive heart failure, this effect could cause or worsen pulmonary edema. Concerns involving increased left heart pressures also account for iNO being contraindicated for neonates with certain cardiac and vascular anomalies such as coarctation of the aorta.[50] In certain patients, the withdrawal of NO has resulted in development of hypoxemia and pulmonary hypertension, perhaps worse than they were before therapy was started. This phenomenon is known as a **rebound effect**. This rebound effect occurs because the administration of NO depresses the body's normal production of NO. When NO is finally discontinued, FiO_2 frequently needs to be initially increased then slowly reduced to baseline.[49]

Although NO has been used safely with other drugs and treatments such as dopamine, steroids, surfactant, and high-frequency ventilation, the interaction of NO with other medications is still being studied. One investigational area may involve the study of patients receiving both iNO and other NO-related compounds such as nitroglycerin and the possible development of methemoglobinemia or systemic hypotension.[51]

BOX 42.10 Adverse Effects Associated With Nitric Oxide Therapy

- Poor or paradoxical response
- Methemoglobinemia
- Increased left ventricular filling pressure
- Complications of certain cardiac anomalies (coarctation of the aorta)
- Rebound hypoxemia, pulmonary hypertension

BOX 42.11 Features of Ideal Nitric Oxide Delivery System

- Dependability and safety
- Delivery of a precise and stable dose of NO
- Limited production of nitrogen dioxide
- Accurate monitoring of NO and nitrogen dioxide levels
- Maintenance of adequate patient ventilation

NO, Nitric oxide.

Methods of Administration

NO is administered to mechanically ventilated patients through a system with the capability for operator-determined concentration of NO in the breathing gas, a constant concentration throughout the breathing cycle, and a concentration that does not cause generation of excessive iNO_2. Features of an ideal NO delivery system are listed in Box 42.11.

The INOmax DS_{IR} Plus (Delivery System-Infrared) (Mallinckrodt Pharmaceuticals, Bedminster, New Jersey) shown in Fig. 42.22 provides these features.[51,53] The INOmax DS_{IR} Plus delivers INOmax (NO) for inhalation into the inspiratory limb of the patient's breathing circuit in a manner that provides a constant dose of NO, as preset by the clinician, throughout inspiration.

Fig. 42.22 INOmax DS Plus (Delivery System-Plus) delivery system for administration of nitric oxide (NO) to mechanically ventilated patients. (Courtesy Mallinckrodt Pharmaceuticals, Bedminster, New Jersey)

This configuration tracks the ventilator flow waveforms and delivers a synchronized and proportional dose of NO through the injector module into the ventilator circuit. An integrated monitoring system continuously displays inspired FiO_2, NO_2, and NO. The INOmax DS_{IR} Plus uses several alarm systems to alert clinicians, including alarms for high and low NO and FiO_2 and high NO_2. Delivery alarms notify clinicians when the source gas (INOmax) pressure is low or if there is a monitoring failure. The device also informs clinicians when high calibrations for the monitoring system are due; low calibrations are performed automatically by the device without requiring user intervention.[53]

The delivery system requires the use of cylinder mixtures of NO containing 800 ppm of NO with the balance being nitrogen. This high concentration of NO is diluted by gases in the ventilator circuit before delivery to the patient. Because adding NO to the circuit decreases the FiO_2 (up to 10% at 80 ppm), O_2 concentration must be continuously monitored downstream from the titration site.

The INOmax DS_{IR} Plus is proven to be compatible with over seventy different ventilators including high-frequency oscillators, jet ventilators, anesthesia machines, and noninvasive breathing circuits. Other special considerations apply, and resources such as ventilator procedure manuals and department policy and procedures should be reviewed to help ensure proper setup and patient safety.[53]

The administration of iNO to spontaneously breathing patients is also possible. The INOmax DS_{IR} Plus has been interfaced with high- and low-flow nasal cannula systems and some nasal continuous positive airway pressure (CPAP) systems.[53]

Withdrawing Therapy

Care must be taken when NO therapy is withdrawn to prevent rebound effects. First, the NO level should be reduced to the lowest effective dose (ideally ≤5 ppm). Second, the patient's condition should be hemodynamically stable, and the patient should be able to maintain adequate oxygenation while breathing a moderate FiO_2 (≤0.4) on low levels of positive end expiratory pressure. Third, the patient should be hyperoxygenated (FiO_2 0.6 to 0.7) just before discontinuation of NO inhalation. Close monitoring of patients and use of these measures usually avoid an increase in pulmonary artery pressure and hypoxemia with withdrawal of NO.[50]

Helium-Oxygen Therapy

Indications

The value of helium as a therapeutic gas is based solely on its low density. As detailed in Chapter 6, when flow is turbulent, driving pressure varies with the square of the flow. Because flow in the large airways is mainly turbulent, breathing a low-density gas mixture can decrease the driving pressure needed to move gas in and out of this area. With less pressure needed to move gas through the large airways, the patient's work of breathing decreases. However, this effect is limited to large airway obstruction (flow in the small airways is not turbulent).

Helium-O_2 has been used for more than 70 years as an adjunct tool in the management of large airway obstruction.[54] **Heliox therapy** has been shown to be effective in treating acute obstructive disorders.[55,56] Either alone or combined with other therapies such as bronchodilators, helium-O_2 therapy has been shown to decrease the respiratory rate, the level of dyspnea, and the need for intubation and mechanical ventilation in patients with reversible obstructive disorders.[57] Specifically, heliox therapy has yielded promising results in the management of acute upper airway obstruction of varying origin, postextubation stridor in pediatric trauma patients, acute severe asthma, and **croup**.[57]

Guidelines for Use

Because it is inert and unable to support life, helium always must be mixed with at least 20% O_2. The most common combination is 80% helium and 20% O_2. From the standpoint of its ability to oxygenate, this mixture is comparable to air, but helium is used in place of nitrogen. Although air has a density of 1.293 g/L, the

density of an 80% helium mixture is 0.429 g/L. For a comparable flow through constricted large airways, this low-density mixture can dramatically decrease the work of breathing.

Most commonly, premixed, commercial heliox cylinders are used at the bedside. These premixed cylinders are commonly available in an 80:20 or a 70:30 combination. The 70% helium and 30% O_2 mixture has a density of 0.554 g/L and can provide additional O_2 for the management of the hypoxemia that can occur with large airway obstruction. Other combinations such as 60:40 mixtures show promising results.[57]

The low-density benefit of heliox is the same physical property that presents challenges in selecting a delivery device. Because helium is highly diffusible, administration through low-flow systems such as a nasal cannula tend not to deliver sufficient concentrations to treat obstructive disorders in adults. However, heliox administered via cannulas with an adequate seal at the nares has shown to be effective in some infants.[57] Nonetheless, heliox should generally be delivered to most spontaneously breathing patients via a tight-fitting nonrebreathing mask with a fully functional valved exhalation port. The delivery system should be high flow and sufficient to meet or exceed the patient's minute ventilation requirements. Closed systems with demand valves and reservoirs or the use of demand regulators has proven to be suitable for delivering heliox to patients with artificial airways. Ideally, an O_2 analyzer should be used to confirm the FiO_2 of the heliox mixture output flowing to the patient and all such patients should be closely monitored, including with a pulse oximetry.[57] Helium mixtures can be given through a cuffed tracheal airway with a positive pressure ventilator. However, the performance of ventilators in delivering heliox tends to vary significantly by model, and only some of them have received FDA clearance for such use. Consequently, RTs should ensure that an appropriate ventilator is being used to administer heliox, determine if a conversion factor is needed to adjust settings, and ensure that the patient is monitored closely while such an approach is being used.[57] Pressure measurements on mechanical ventilators are always accurate during the use of heliox but volume measurements can be grossly inaccurate if the ventilator is not calibrated to a heliox mixture.

Blenders have also been used to administer heliox. When a blender is used, the 80:20 heliox is generally attached to the air inlet, and an O_2 analyzer is placed downstream. However, because the accuracy of blenders tends to vary, the system's FiO_2 readings should first be tested, and the difference between the set and actual FiO_2 should be known.

Heliox has also been combined with bronchodilator therapy to treat acute obstructive disorders such as status asthmaticus. Heliox improves aerosol deposition mainly because of a reduction in turbulence and less impaction and medication loss. Because of the low density of heliox, when a nebulizer is driven by heliox, the liter flow must be increased from the customary 6 L/min to 10 to 12 L/min to achieve the same volume of aerosol generated per unit of time.

When heliox is given alone or as part of nebulization, the RT should realize that a typical hospital O_2 flowmeter is inaccurate because of the lower density of helium. Flowmeters calibrated for helium should be used to ensure accurate delivery. However, correction factors are available for O_2 flowmeters. The correction for an 80:20 helium-O_2 mixture is 1.8; this means that for every 10 L/min indicated flow, 10 × 1.8, or 18 L/min, of the 80:20 mixture actually leaves the flowmeter. For delivery of a specific flow from an 80:20 helium-O_2 source, the RT sets the flowmeter to the desired flow divided by 1.8. If a flow of 9 L/min of an 80:20 helium-O_2 mixture is needed, the RT sets the flowmeter to 9/1.8, or 5 L/min. Factors for any other mixture can be calculated if needed. The factor for a 70:30 helium-O_2 mixture is 1.6.

In addition to special flow considerations, the RT should use an O_2 analyzer to monitor heliox (actually O_2) concentrations continuously between the source of the mixture and the patient. The basis for this recommendation is that the gas is either helium or O_2, and if the FiO_2 is known, assuming there are no leaks, the remaining gas is helium. This monitoring helps ensure that the patient is receiving the therapeutic benefits of a less dense gas while maintaining the appropriate FiO_2.

MINI CLINI

Heliox for Severe Asthma

Problem

Bronchodilators and systemic steroids have just been initiated for a patient in the emergency room with a severe asthmatic attack. The physician would like your recommendation on reducing this patient's work-of-breathing until the asthma medications can take effect and possibly avoid the need for intubation and mechanical ventilation.

Solution

Breathing a low-density gas mixture such as heliox reduces the driving pressure needed to move gas in and out of the lungs. As a result, a heliox mixture of 80:20 or 70:30 should be recommended to reduce this patient's work-of-breathing until other elements of the care plan can address the underlying problems of airway obstruction due to bronchoconstriction and airway inflammation.

Troubleshooting and Hazards

The low density of helium mixtures makes them poor vehicles for aerosol transport. High-density bland water aerosols are difficult to deliver with helium mixtures. The low density of helium mixtures also makes coughing less effective. If the patient can develop an effective cough, this problem can be rectified by means of washing out the helium before coughing.

The most common side effect of helium is a benign one. When a patient is breathing a helium mixture, the spoken word is badly distorted at a pitch so high as to make it almost unintelligible. This effect is caused by the passage of a low-density gas through the vocal cords on exhalation.

A more serious problem is hypoxemia associated with breathing helium mixtures.[57] Although this problem may have been caused by using too low an O_2 concentration (20%), there is another possibility. Very rarely, some commercial helium-O_2 cylinders stored for long periods of time have been found to contain these gases in an unmixed, or separated, state. The only way to avoid this potential hazard is to analyze the O_2

concentration coming from the cylinder before administering the gas.

As clinical applications for heliox have expanded, other hazards have emerged. One potential problem is volume-induced lung injury when heliox is administered via a mechanical ventilator. This risk can be addressed by using only ventilators approved by the FDA for heliox administration. In addition, the lower density of helium-O_2 mixtures may result in greater variability in medication delivery to the airways. Careful patient monitoring during such therapy can help minimize this concern. Another rare but possible problem is hypothermia to infants receiving heliox via an oxyhood. This risk results from the high thermal conductivity of helium and can be avoided by warming and humidifying the heliox gas.[57]

Carbon Dioxide–Oxygen (Carbogen) Therapy

Although rarely used, CO_2-O_2 mixtures (carbogen) have been employed to treat hiccups, carbon monoxide poisoning, and some neonates with congenital cardiac anomalies and to prevent complete washout of CO_2 during cardiopulmonary bypass and extracorporeal gas exchange. More recently, it has been investigated as a treatment for hearing loss and seizures. However, the application of carbogen in clinical settings has been quite limited given the potential adverse effects of hypoxemia, premature ventricular contractions, hypertension, and muscle twitching.[58]

Carbogen is supplied in compressed gas cylinders as either 5%:95% or 7%:93% CO_2-O_2 mixtures. It can be administered to patients with a snug-fitting nonrebreathing mask, with a flow sufficient to prevent the reservoir from collapsing during inhalation. Because of the potential adverse effects, patients receiving carbogen should be monitored closely, especially at 7%:93% mixtures. If any significant adverse effects are noted, the therapy should be stopped.[58]

SUMMARY CHECKLIST

- O_2 therapy is used to: (1) correct acute hypoxemia, (2) decrease the symptoms of chronic hypoxemia, and (3) decrease cardiopulmonary workload.
- The need for supplemental O_2 can be assessed with laboratory measures, clinical history, and bedside patient evaluation.
- In the care of adults, children, and infants older than 28 days, O_2 therapy is indicated if PaO_2 is less than 60 mm Hg or SaO_2 is less than 90%.
- Exposure to 100% O_2 for more than 24 hours should be avoided whenever possible; high FiO_2 is acceptable if the concentration can be decreased to 0.70 within 2 days and to 0.50 or less in 5 days.
- Concern that O_2 therapy can cause hypoventilation should never preclude administration of O_2 to a patient in need. Prevention of hypoxia always is the first priority.
- The three components of the "fire triangle" are oxygen, heat, and fuel.
- If an O_2 delivery system provides all of a patient's inspired gas, FiO_2 remains stable. If the device provides only part of the inspired gas, air dilutes the O_2, and FiO_2 can vary.
- O_2 provided with low-flow devices such as a nasal cannula always is diluted with air; the result is a low and variable FiO_2.
- Reservoir devices can provide higher FiO_2 than low-flow systems or can be used to conserve O_2.
- To avoid rebreathing, a flow of at least 5 L/min should be used with O_2 masks; for reservoir masks with bags, the flow must be sufficient to prevent bag collapse.
- A nonrebreathing reservoir circuit can provide a full range of FiO_2 (21% to 100%) at any needed flow to both intubated and non-intubated patients.
- High-flow systems supply a given O_2 concentration at a flow of at least 60 L/min.
- Because entrainment devices dilute source O_2 with air, they always provide less than 100% O_2. The more air entrained, the higher the total flow, but the delivered FiO_2 is lower.
- Air-entrainment nebulizers should be treated as fixed-performance devices only when set to deliver low O_2 concentration (≤35%).
- One way to achieve high FiO_2 with air-entrainment nebulizers is to connect two or more devices together in parallel.
- Back pressure decreases both the volume of entrained air and the total flow output of air-entrainment devices.
- A HFNC can be useful in treating moderate hypoxemia, especially for patients who do not tolerate oxygen masks and need supplemental humidity.
- A blending system allows precise control over FiO_2 and total flow output; most blending systems qualify as true fixed-performance delivery devices.
- An operational check of an O_2 blender should always be conducted before the device is used.
- O_2 therapy enclosures are used mainly in the care of children and infants. Problems include limited and highly variable FiO_2 and temperature control.
- The three Ps—purpose, patient, and performance of the device—should be considered in the selection or recommendation of an O_2 delivery system.
- Protocol-based oxygen therapy ensures the patient: (1) undergoes initial assessment, (2) is evaluated for protocol criteria, (3) receives a treatment plan that is modified to the need, and (4) stops receiving therapy as soon as it is no longer needed.
- In HBO therapy, O_2 is administered at a pressure greater than 1 atm for management of conditions such as air embolism and carbon monoxide poisoning.
- iNO improves blood flow to ventilated alveoli, reduces intrapulmonary shunting, improves arterial oxygenation, and decreases pulmonary vascular resistance and pulmonary arterial pressure.
- Heliox mixtures are used to reduce the work of breathing in large airways obstruction. The low density of heliox makes standard O_2 flowmeters inaccurate and provides inaccurate volume and flow measurement on ventilators not calibrated for its use.
- Carbogen is used in the management of some neonates with congenital heart disease, to treat hiccups and to prevent complete washout of CO_2 during cardiopulmonary bypass or extracorporeal gas exchange.

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43

Lung Expansion Therapy

Daniel F. Fisher

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Understand the causes of atelectasis
- Identify which patients are at the greatest risk for developing atelectasis and needing lung expansion therapy.
- Define the clinical findings seen in atelectasis.
- Describe how lung expansion therapy is able to reverse atelectasis.
- List the indications, hazards, and complications associated with the various modes of lung expansion therapy.
- Describe the primary responsibilities of the respiratory therapist in planning, implementing, and evaluating lung expansion therapy.

CHAPTER OUTLINE

KEY TERMS

atelectasis
compression atelectasis
continuous positive airway pressure (CPAP)
deep breathing/directed cough
egophony
gas absorption atelectasis
incentive spirometry (IS)
intermittent positive airway pressure breathing (IPPB)
lobar atelectasis
noninvasive ventilation (NIV)
high-flow nasal cannula (HFNC)
positive expiratory pressure (PEP)

Pulmonary complications are common serious problems seen in patients who have undergone thoracic or abdominal surgery.[1,2] Such complications include **atelectasis** (alveolar collapse), pneumonia, and acute respiratory failure. These respiratory problems can be minimized or avoided if proper respiratory care is implemented during the perioperative period. The most common form of therapy used in high-risk patients is lung expansion therapy.

Lung expansion therapy encompasses a variety of respiratory care procedures designed to prevent or correct atelectasis. The most common modalities include **early patient mobilization, deep breathing/directed cough, incentive spirometry (IS), continuous positive airway pressure (CPAP), positive expiratory pressure (PEP), intermittent positive airway pressure breathing (IPPB), and high-flow nasal cannula (HFNC)**. The common purpose that all of these techniques share is improving pulmonary function by maximizing alveolar recruitment and optimizing airway clearance.

Various lung expansion therapies can be effective in preventing or correcting atelectasis in selected patients.[1] There is no one specific method to apply in a given situation because no advantage of any one method has been established. In fact, evidence suggests that patient preference is as important as the chosen therapy.[3] The most efficient use of resources is a primary concern with any plan to apply lung expansion therapy.

All of the following therapies share a common goal, to increase functional residual capacity (FRC). In other words, all of these supplemental techniques are designed to simulate a deep breath or sigh. In consultation with the prescribing physician, the respiratory therapist (RT) should assist in identifying patients most likely to benefit from lung expansion therapy, recommend and

initiate the appropriate and most efficient therapeutic approach, monitor the patient's response, and alter the treatment regimen as needed.

CAUSES AND TYPES OF ATELECTASIS

Although atelectasis can occur from a large variety of problems, this chapter focuses on the two primary types associated with postoperative or bedridden patients who are breathing spontaneously without mechanical assistance: (1) gas absorption atelectasis and (2) compression atelectasis. **Gas absorption atelectasis** can occur either when there is a complete interruption of ventilation to a section of the lung or when there is a significant shift in ventilation/perfusion ($\dot{V}/\dot{Q}$). Gas distal to an obstruction is absorbed by blood passing through the pulmonary capillaries, which eventually causes partial collapse of the nonventilated alveoli. When ventilation is compromised in a larger airway or bronchus, **lobar atelectasis** can develop.

Compression atelectasis occurs when the transthoracic pressure (the pressure difference between the body surface and the alveoli) exceeds the transalveolar pressure (P_{AL}) (the pressure difference between the alveoli and pleural space).[2,4,5] Compression atelectasis is primarily caused by mechanisms that increase this pressure gradient. This situation is common with general anesthesia, with the use of sedatives and bed rest, when deep breathing is painful, as when broken ribs are present or surgery has been performed on the upper abdominal region, and in morbidly obese patients. Weakening or impairment of the diaphragm can also contribute to compression atelectasis. Compression atelectasis also results from fluid overload. It is a common cause of atelectasis in hospitalized patients. It may occur in combination with gas absorption atelectasis in a patient with excessive airway secretions who breathes with small tidal volumes for a prolonged period and in the presence of expiratory flow limitation.

Factors Associated With Causing Atelectasis

Patients who have difficulty taking deep breaths without assistance include those with significant obesity, patients with neuromuscular disorders, patients under heavy sedation, and patients who have undergone upper abdominal or thoracic surgery. Diaphragmatic position and function are major contributors to atelectasis. In an anesthetized patient, there is a cephalad (toward the head) shift of the diaphragm. For patients who are supine and breathing spontaneously, the lower, dependent portion of the diaphragm performs the most movement. The opposite occurs in patients who are paralyzed—the upper portion of the diaphragm is primarily involved in movement.[4,5] Patients undergoing lower abdominal surgery are at relatively less risk for developing atelectasis than patients undergoing upper abdominal or thoracic surgery. Neuromuscular injury patients are prone to respiratory complications, the most common of which is atelectasis. Atelectasis can occur in any patient who cannot or does not take deep breaths periodically and in patients who are restricted to bed rest for any reason.[6] Atelectasis is one of the leading causes of hypoxemia after abdominal surgery and may account for 24% of deaths within 6 days of surgery.[7] It is good clinical practice to consider atelectasis during assessment of postoperative patients.

Impairment of the function of pulmonary surfactant can also have an impact on the development of atelectasis. Surfactants decrease the surface tension of the walls of the alveoli. When there is deterioration of surfactant function or amount of this vital protein, the resulting increase in surface tension can cause alveoli to collapse.[5]

Most postoperative patients also have problems coughing effectively because of their reduced ability to take deep breaths. An ineffective cough impairs normal clearance mechanisms and increases the likelihood of retained secretions, which could lead to the development of absorption atelectasis and pneumonia in a patient with excessive mucus production. Patients with a history of lung disease that causes increased mucus production (e.g., chronic bronchitis) are most prone to develop complications in the postoperative period. Similarly, a significant history of cigarette smoking should alert the RT to the high risk for respiratory complications after surgery. Such patients must be identified in the preoperative period and considered strong candidates for airway clearance and lung expansion therapy. Elective surgery for these patients may need to be postponed in some cases until such therapies can be included in the treatment plan. Lung expansion therapy in the postoperative period may help to improve clearance of secretions by improving the effectiveness of coughing and secretion removal.

RULE OF THUMB

The closer the incision is to the diaphragm, the greater the risk for postoperative atelectasis. Patients with a history of inadequate nutritional intake, as shown by an albumin level less than 3.2 mg/dL, have an increased risk for pulmonary complications in the postoperative period. This increased risk is most likely due to inadequate strength of the inspiratory muscles to maintain a normal vital capacity (VC).

Laparoscopic surgery uses a scope inserted through small incisions to perform the procedure. Use of this technique has gained widespread acceptance in gastrointestinal procedures because of shortened recovery time, less pain for the patient, and smaller incisions. All of these factors also lessen the opportunities for developing postoperative pulmonary complications.[8,9]

MINI CLINI

Risk Factors for Atelectasis

Problem

The RT is called to evaluate a 47-year-old obese man admitted to the hospital for upper abdominal surgery. He has a 60 pack-year smoking history and is scheduled for surgery tomorrow morning. Examination reveals bilateral inspiratory and expiratory coarse crackles and expiratory wheezes. He is alert and oriented with normal vital signs. His past medical history is positive for diabetes and kidney stones. What factors are present that predispose this patient to postoperative atelectasis? What treatment plan should the RT recommend?

Discussion

Several important risk factors are present in this patient. The three most important are the patient's history of smoking, obesity, and the upper abdominal site of surgery. The findings of adventitious lung sounds and positive smoking history are very suggestive of a current pulmonary problem that would probably require bronchial hygiene and bronchodilators before surgery. Postoperatively, this high-risk patient would need careful monitoring for risks of atelectasis.

CLINICAL SIGNS OF ATELECTASIS

RTs must be able to recognize the clinical signs of atelectasis in patients so that appropriate therapy can be implemented in a timely fashion. The patient's medical history often provides the first clue in identifying atelectasis. Recent upper abdominal or thoracic surgery in any patient should suggest possible atelectasis. A history of chronic lung disease or cigarette smoking or both provides additional evidence that the patient is prone to respiratory complications after major surgery or prolonged bed rest.

MINI CLINI

Physical Signs of Atelectasis

Problem

How does a patient with atelectasis present during a physical assessment?

Discussion

Depending on the severity of atelectasis, the patient could be lying in bed and start to have a requirement for supplemental oxygen. On auscultation, the breath sounds can range from shallow and distant. When asking the patient to take a deep breath, you may hear faint crackles and see an improvement in oxygen saturation.

Moderate atelectasis can present itself with an increase in respiratory rate and a consistently lower SpO_2. Breath sounds may have definite crackles and you may also hear occasional bronchial breath sounds.

Severe atelectasis can present by having the patient complain of dyspnea, requiring an increasing amount of oxygen and absent breath sounds over the affected area with distinct bronchial breath sounds in the surrounding margins.

The physical signs of atelectasis may be absent or very subtle if the patient has minimal atelectasis. When the atelectasis involves a more significant portion of the lungs, the patient's respiratory rate increases proportionally. Fine, late-inspiratory crackles may be heard over the affected lung region. These crackles are produced by the sudden opening of distal airways with deep breathing. Bronchial-type breath sounds may be present as the lung becomes more consolidated with atelectasis. Diminished breath sounds are common when excessive secretions block the airways and prevent transmission of breath sounds. Another lung sound that may be present with consolidation is **egophony**. The consolidated tissue will decrease transmission of the higher-frequency lung sounds. Egophony has also been considered to be present if, when asked to say the letter "E," the patient sounds to the practitioner as if he or she were saying "Aaay." Tachycardia may be present if atelectasis leads to significant hypoxemia.

RULE OF THUMB

There is a direct relationship between the spontaneous respiratory rate and the degree of atelectasis present. Typically, as atelectasis progresses, respiratory rate increases proportionally.

The chest x-ray is often used to confirm the presence of atelectasis. The atelectatic region of the lung has increased opacity. Evidence of volume loss is present in patients with significant atelectasis. Direct signs of volume loss on the chest film include displacement of the interlobar fissures, crowding of the pulmonary vessels, and air bronchograms. Indirect signs include: elevation of the diaphragm; shift of the trachea, heart, or mediastinum; pulmonary opacification; narrowing of the space between the ribs; and compensatory hyperexpansion of the surrounding lung.

LUNG EXPANSION THERAPY

All modes of lung expansion therapy increase lung volume by increasing the P_{AL} gradient. As detailed elsewhere in this text (Chapters 47 and 52), P_{AL} gradient represents the difference between the alveolar pressure (P_{alv}) and the pleural pressure (P_{pl}):

$$P_{AL} = P_{alv} - P_{pl}$$

With all else being constant, the greater the P_{AL} gradient, the more the alveoli expand.

As depicted in Fig. 43.1, the P_{AL} gradient can be increased by either: (1) decreasing the surrounding P_{pl} (see Fig. 43.1A) or (2) increasing the P_{alv} (see Fig. 43.1B). A spontaneous deep inspiration increases the P_{AL} gradient by decreasing the P_{pl}. Applying positive pressure to the lungs increases the P_{AL} gradient by increasing the pressure inside the lung (P_{alv}).

All lung expansion therapies use one of these two approaches. IS enhances lung expansion through a spontaneous and sustained decrease in P_{pl}. Positive airway pressure techniques increase P_{alv} in an effort to expand the lung. Positive pressure lung expansion therapies may apply pressure during inspiration only, during expiration only (as in HFNC, PEP, and flutter valves), or during both inspiration and expiration (CPAP). IS and other patient-directed therapies require an alert, cooperative patient who is capable of taking a deep breath.

The goal of any lung expansion therapy should be to implement a plan that provides an effective strategy in the most efficient manner. Staff time and equipment are the two major issues related to efficiency. For a patient with minimal risk of postoperative atelectasis, deep breathing exercises, frequent repositioning, and early ambulation are usually effective and can be done with minimal coaching and time from clinicians and without equipment.[5] For a patient at high risk for atelectasis (e.g., a patient undergoing upper abdominal surgery), IS is usually instituted. The additional staff time and equipment are justified in this high-risk group. Positive pressure therapy requires significantly more staff time and equipment and is reserved for high-risk patients who cannot perform IS techniques.

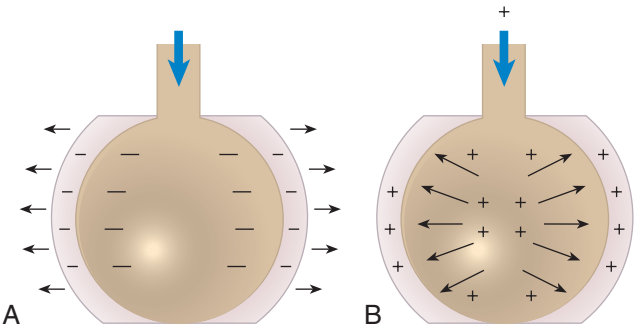

Fig. 43.1 Transalveolar pressure gradients with spontaneous inspiration (A) and positive pressure inspiration (B).

Baseline Assessment

Before beginning therapy, a baseline patient assessment should be conducted. This information helps to individualize the treatment and allows objective evaluation of the patient's subsequent response to therapy. Together with the patient's medical history, this baseline assessment also alerts the RT to possible problems or hazards associated with administering any therapy to the patient. The baseline assessment includes a general evaluation of the patient's clinical status and a specific assessment related to the chosen therapeutic goals. The general assessment, common to all patients for whom respiratory care is ordered, includes: (1) measuring vital signs, (2) assessing the patient's appearance and sensorium, (3) assessing the breathing pattern through chest auscultation, and (4) the patient's level of motivation and their ability to follow instructions.

Early Mobilization of the Patient

Intensive Care Unit Patient

Evidence supports that it is better for the overall recovery of patients to get them out of bed and provide early ambulation.[10-13] The complications of prolonged bed rest include cardiovascular, pulmonary, gastrointestinal, and skin integrity issues. Pulmonary complications of immobility include: development of atelectasis, pneumonia, and pulmonary emboli (PE).[11-13] Rates of early mobilization for intensive care unit (ICU) patients have been increasing in both Europe and the United States, along with an emphasis on decreasing morbidity in the ICU. Mobilization includes not only walking but also sitting, standing, and getting out of bed into a chair. As the patient changes body position, his or her breathing changes, as does the gas distribution within the lung. Improvements in ventilation results in less alveolar collapse.

Because of the beneficial pulmonary effects of early mobilization of the post–abdominal surgery patient, it has been suggested that mobilization should be considered as early as the day of surgery.[14] With the increasing knowledge of the benefits of early mobilization, the paradigm must change from thinking that a patient is too sick to get out of bed to one in which we must think that a patient is too sick to stay in bed.[13]

To move patients from the bed, it is important that they are not completely sedated. Along with early mobilization, there are other benefits of lighter sedation and even "sedation vacations" when all sedation for the patient is temporarily discontinued in order to reassess the need for sedation. Having a patient who is able to respond to the caregiver allows for better pain control with decreased risk of sedation-related complications.[15,16]

Non–Intensive Care Unit Patient

Having a non-ICU patient mobilize frequently may not have the technical roadblocks that are seen in the ICU such as multiple intravenous (IV) pumps, cardiovascular support devices (intra-aortic balloon pumps, ventricular assist devices, impella, or even extracorporeal membrane oxygenate [ECMO]),[17] but there is a personnel cost to moving the patient. The patient-nurse ratio is typically larger on the general medicine/surgery floors than in the ICU. The availability of support staff will also need to be coordinated.

Although early mobilization does not classify as a procedure, it does have distinct benefits in decreasing morbidity and mortality.[12,14,18,19] Early mobilization is a true multidisciplinary approach that requires the various members of the healthcare team (RT, nurse, physical therapist) to be present at the same time. Having the patient get out of bed and walk will improve ventilation and perfusion, which will prevent or lessen the occurrence of developing atelectasis, making the need for the following therapies less likely.

RULE OF THUMB—EARLY MOBILIZATION

Many of the techniques described in this chapter—IS, CPAP, IPPB, and PEP—simulate normal function if the patient were to be standing and walking. All are strong arguments for early mobilization. So get your patients out of bed and help them walk!

Incentive Spirometry

The purpose of IS is to coach the patient to take a sustained maximal inspiratory (SMI) effort resulting in a decrease in P_{AL} and maintaining the patency of airways at risk for closure. Because of its simplicity, IS has been the mainstay of lung expansion therapy for many years. IS devices are designed to mimic natural sighing by encouraging patients to take slow, deep breaths simulating a yawn or sigh. IS can be performed using devices that provide visual cues to patients when the desired inspiratory flow or volume has been achieved. IS was first described in 1972, which led to the development of a visual feedback device in 1973.[20]

The desired volume and number of repetitions to be performed are initially set by the RT or other qualified caregiver. The inspired volume goal is set on the basis of predicted values or observation of initial performance. The true benefit from IS is best achieved by repeated use and proper technique.[21]

Physiologic Basis

A sustained maximal inspiration is functionally equivalent to performing an FRC to inspiratory capacity (IC) maneuver, followed by a breath hold. Fig. 43.2 compares the alveolar and P_{pl} changes occurring during a normal spontaneous breath and an SMI during IS.

During the inspiratory phase of spontaneous breathing, the decrease in P_{pl} caused by expansion of the thorax is transmitted to the alveoli. With P_{alv} now negative, a pressure gradient is created between the airway opening and the alveoli. This transrespiratory pressure gradient causes gas to flow from the airway into the alveoli. Within certain limits, the greater the transrespiratory pressure gradient, the more lung expansion occurs.

RULE OF THUMB—INCENTIVE SPIROMETRY

IS was first developed as a simulated yawn. It was noted that as the patient yawns (sighs), oxygenation improves.

Indications

Indications for IS are listed in Box 43.1. The primary indication for IS is to treat existing atelectasis. IS may also be used as a

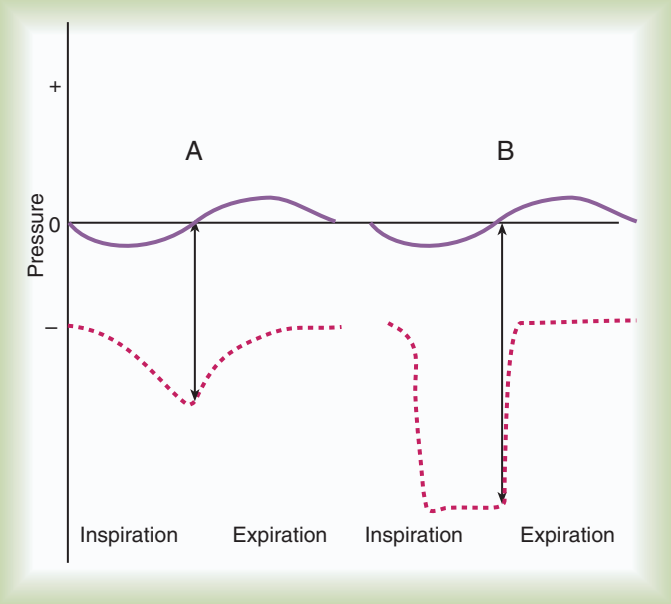

Fig. 43.2 Alveolar *(solid lines)* and pleural *(dotted lines)* pressure changes during spontaneous breathing *(A)* and sustained maximal inspiration *(B)*. Note the difference in transalveolar pressure (P_{AL}) gradients *(double arrows)*.

BOX 43.1 Indications for Incentive Spirometry

- Presence of pulmonary atelectasis
- Presence of conditions predisposing to atelectasis
  - Upper abdominal surgery
  - Thoracic surgery
  - Surgery in patients with COPD
- Presence of a restrictive lung defect associated with quadriplegia or dysfunctional diaphragm

COPD, Chronic obstructive pulmonary disease.

BOX 43.2 Contraindications to Incentive Spirometry

- Patient cannot be instructed or supervised to ensure appropriate use of device
- Patient cooperation is absent, or patient is unable to understand or demonstrate proper use of device
- Patient is unable to deep breathe effectively (VC < 10 mL/kg *or* IC < ⅓ of predicted)

IC, Inspiratory capacity.

preventive measure when conditions exist that make the development of atelectasis likely.[7]

Contraindications

IS is a simple and relatively safe modality. For this reason, contraindications are few (Box 43.2).

Hazards and Complications

Given its normal physiologic basis, IS presents few major hazards and complications; those that can occur are listed in Box 43.3.

BOX 43.3 Hazards and Complications of Incentive Spirometry

- Hyperventilation and respiratory alkalosis
- Discomfort secondary to inadequate pain control
- Pulmonary barotrauma
- Exacerbation of bronchospasm
- Fatigue

Acute respiratory alkalosis is the most common problem and occurs when the patient performs IS too rapidly or if the prescribed frequency of therapy is mismatched.[22] Dizziness and numbness around the mouth are the most frequently reported symptoms associated with respiratory alkalosis. This can be easily corrected with careful instruction and monitoring of the patient. Discomfort with deep inspiratory efforts due to pain is usually the result of inadequate pain control in a postoperative patient. Appropriate pain control before and during therapy is important.

Equipment

The original IS devices were electronic and provided the user with visual feedback even though the equipment needed for SMI is typically simple, portable, and inexpensive. Although advances in technology have produced more complex devices, there is no evidence that these devices produce any better outcomes than their lower-cost, disposable counterparts.

IS devices can generally be categorized as volume oriented or flow oriented. True volume-oriented devices measure and visually indicate the volume achieved during an SMI. The most popular true volume-oriented IS devices use a bellows that rises according to the inhaled volume. When the patient reaches a target inspiratory volume, a controlled leak in the device allows the patient to sustain the inspiratory effort for a short period (usually 5 to 10 seconds). Because the bellows types of IS devices are bulky and large, smaller devices that indirectly indicate volume based on flow through a fixed orifice have been developed. These devices sacrifice accurate measurement of the inhaled volume for portability and smaller size (Fig. 43.3).

Flow-oriented devices measure and visually indicate the degree of inspiratory flow (Fig. 43.4). This flow can be equated with volume by assessing the duration of inspiration or time (flow × time = volume). Both flow-oriented and volume-oriented devices attempt to encourage the same goal for the patient: an SMI effort to prevent or correct atelectasis. There is no benefit of one type of IS over the other.

Administration

The successful application of IS involves three phases: planning, implementation, and follow-up. Because many of the components of this process are similar to those previously described, we highlight only the key points and differences in approach.

Preliminary planning. During preliminary planning, the need for IS should be determined by careful patient assessment. Once the need is established, planning should focus on selecting specific therapeutic outcomes. Box 43.4 lists potential outcomes that can be considered for patients receiving IS.

Fig. 43.3 Volumetric Incentive Spirometer. (Courtesy DHE Healthcare, Canastoga, NY.)

Fig. 43.4 Flow-Oriented Incentive Spirometer. (From DeWit S: *Fundamental concepts and skills for nursing*, ed 2, St Louis, 2004, Saunders.)

BOX 43.4 Potential Outcomes of Incentive Spirometry

- Decrease or elimination of atelectasis
- Improved breath sounds
- Normal or improved chest x-ray
- Increased SpO_2
- Increased VC
- Improved inspiratory muscle performance and cough

SpO_2, Oxygen saturation.

Patients scheduled for upper abdominal or thoracic surgery should be screened before undergoing the surgical procedure. Assessment conducted at this point helps to identify patients at high risk for complications and allows determination of their baseline lung volumes and capacities. This approach provides an opportunity to orient high-risk patients to the procedure before undergoing surgery, increasing the likelihood of success when IS is provided after surgery.

Implementation. Successful IS requires effective patient teaching. The RT should set an initial goal that is attainable by the patient yet requires a moderate effort. Setting an initial goal that is too low for the patient results in little incentive and an ineffective maneuver, at least initially. The patient should be instructed to inspire slowly and deeply to maximize the distribution of ventilation.

The RT should watch the patient perform the initial inspiratory maneuvers and ensure the patient uses correct technique. Correct technique calls for diaphragmatic breathing at slow to moderate inspiratory flows. Demonstration is probably the most effective way to assist patient understanding and cooperation. Both the operation of the device and the proper breathing technique can be explained easily when the RT uses himself or herself as an example, and much trial and error can be avoided.

Many patients have difficulty with the slow inspiration followed by the breath hold. Nonetheless, patients should be encouraged to try not to breathe in too fast or slowly and to attempt a brief breath hold.

A normal exhalation should follow the breath hold, and the patient should be given the opportunity to rest as long as needed before the next SMI maneuver. Some patients in the early postoperative stage may need to rest for 30 seconds to 1 minute between maneuvers. This rest period helps to avoid a common tendency by some patients to repeat the maneuver at rapid rates, causing respiratory alkalosis. The goal is not rapid, partial lung inflation but intermittent, maximal inspiration.

The exact number of sustained maximal inspirations needed to reverse or prevent atelectasis is not known and probably varies according to the patient's clinical status. In fact, numerous studies have failed to report a standard frequency for either number of breaths per session or even how often to repeat the exercise during the day.[23] However, because healthy individuals average approximately six sighs per hour, an IS regimen should focus on ensuring a minimum of 5 to 10 SMI maneuvers each hour.[22]

Follow-up. Assessing the patient's performance is vital to ensuring achievement of goals. To do so, the RT should make return visits to monitor treatment sessions until the correct technique and appropriate effort are achieved. Suggested monitoring activities for IS are outlined in Box 43.5.

After the patient has demonstrated mastery of technique, IS may be performed with minimal supervision. For patients with a neuromuscular disease or spinal injury, the use of a mechanical cough device (insufflator-exsufflator) (see Chapter 44) may provide a similar therapeutic objective. There is a lack of supporting data that IS has an effect of preventing or reversing pulmonary complications in post-cardiac surgical patients or in those patients who have recently had upper abdominal surgery.[20,24]

BOX 43.5 Monitoring Patients Receiving Incentive Spirometry

Observe patient performance and use:

- Frequency of sessions
- Number of breaths per session
- Volume and flow goals achieved
- Breath hold maintained
- Effort and motivation
- Periodic observation of patient compliance, with additional instruction as needed
- Device within reach of patient and patient encouraged to perform independently
- Vital signs and breath sounds

BOX 43.6 Clinical Situations Contraindicating Intermittent Positive Airway Pressure Breathing Therapy

- Tension pneumothorax
- ICP >15 mm Hg
- Hemodynamic instability
- Active hemoptysis
- Tracheoesophageal fistula
- Recent esophageal surgery
- Radiographic evidence of blebs
- Recent facial, oral, or skull surgery
- Singultus (hiccups)
- Nausea

ICP, Intracranial pressure.

Noninvasive Ventilation

Noninvasive ventilation (NIV) provides breathing support to patients with inadequate ability to ventilate. NIV has been documented to have beneficial effects for patients who may need periodic, short-term support or patients who are experiencing exacerbations of pulmonary disease. NIV offers some benefits over traditional, invasive ventilation due to lower infection risk and reduced need for sedation because of the absence of an artificial airway. NIV is discussed in detail elsewhere (Chapter 50). In addition, variations of NIV, including IPPB, CPAP, HFNC, and PEP therapy, can be potentially valuable lung expansion tools and are discussed in the following sections.

Intermittent Positive Airway Pressure Breathing

Physiologic Basis

IPPB is a specialized form of NIV used for relatively short treatment periods (approximately 15 minutes per treatment). The intent of IPPB, unlike NIV, is not to provide full ventilatory support but to provide machine-assisted deep breaths assisting the patient to deep breathe and stimulate a cough. This section discusses the use of IPPB as a modality for the treatment of atelectasis.

IPPB has historically consisted of providing an aerosol under positive pressure, augmenting the patient's own inspiratory efforts and thus resulting in a larger tidal volume (V_T) than could be spontaneously generated. The effectiveness of IPPB as an enhancement for aerosol delivery has been shown to be incorrect. In fact, IPPB does not improve aerosol deposition at all.[3] The American Association for Respiratory Care (AARC) clinical practice guidelines (CPG) for IPPB even recommends a 10-fold increase in medication dosage when compared with other aerosol delivery methods.[14] Lung volumes are increased in IPPB because $P_{alv} > P_{pl}$. Depending on the mechanical properties of the lung, P_{pl} may exceed atmospheric pressure during a portion of inspiration. As with spontaneous breathing, the recoil force of the lung, stored as potential energy during the positive pressure breath, causes a passive exhalation. As gas flows from the alveoli out to the airway opening, P_{alv} decreases to atmospheric level, while P_{pl} is restored to its normal subatmospheric range (Fig. 43.5).

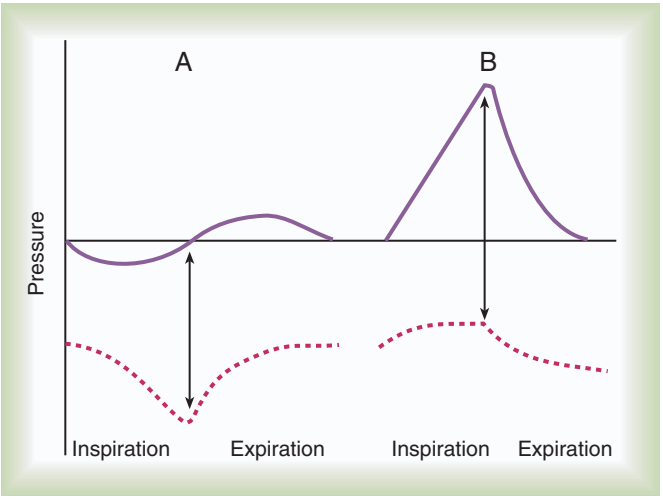

Fig. 43.5 Alveolar *(solid lines)* and pleural *(dotted lines)* pressure changes during spontaneous breathing *(A)* and intermittent positive airway pressure breathing *(B)*. Note the difference in transalveolar pressure (P_{AL}) gradients *(double arrows)*.

Indications

Although IPPB is not an effective aerosol delivery system, periodic sessions of positive pressure ventilation provided noninvasively can be useful in the treatment of pulmonary complications or exacerbations of lung disease.[12,15-17] IPPB should not be used as a single treatment modality for a patient with absorption atelectasis because of excessive airway secretions. Appropriate systemic hydration and airway clearance techniques should be used to assist in removal of excessive secretions.

In concept, IPPB treatment should provide the patient with augmented tidal volumes, achieved with minimal effort. *There are no data to support the use of IPPB as a method of preventing or expanding atelectasis.* The techniques listed later are more effective.

Contraindications

There are several clinical situations in which IPPB should not be used (Box 43.6). With the exception of untreated tension pneumothorax, most of these contraindications are relative. A patient with any of the conditions listed in Box 43.6 should be carefully evaluated before IPPB therapy is begun.

Hazards and Complications

As with any clinical intervention, certain hazards and complications are associated with IPPB. These potential problems should

BOX 43.7 Hazards and Complications of Intermittent Positive Airway Pressure Breathing

- Hyperventilation and respiratory alkalosis
- Discomfort secondary to inadequate pain control
- Pulmonary barotrauma
- Exacerbation of bronchospasm
- Fatigue

be addressed in the initial stages of planning for IPPB. The most common complication associated with IPPB is inducing respiratory alkalosis. This problem is easily avoided through proper coaching of the patient before and during treatment.

Another potential complication of IPPB is gastric distention; this occurs when gas from the IPPB device passes directly into the esophagus. Gastric distention is uncommon in an alert patient but is a significant risk for an obtunded patient. Normally, the esophagus does not open until a pressure of approximately 20 to 25 cm H_2O has been reached. Gastric distension represents the greatest risk in patients receiving IPPB at high pressures. The major hazards and complications of IPPB are listed in Box 43.7.

Administration

Effective IPPB requires careful preliminary planning, individualized patient assessment and implementation, and thoughtful follow-up.

Preliminary planning. During preliminary planning, the need for IPPB is determined and desired therapeutic outcomes are established. Box 43.8 lists potential accepted and desired outcomes of IPPB therapy. Not all the outcomes listed in Box 43.8 apply to every patient.

RULE OF THUMB

IPPB was once a mainstay therapy for respiratory care. Its nearest cousin, noninvasive ventilation, uses a mask. IPPB was generally given via a mouthpiece and nose clips.

MINI CLINI

Problem

While covering a surgical step-down floor, you are called to provide IPPB with a bland aerosol to help a patient with postoperative atelectasis.

Discussion

Because you are on the floor, you go to the patient's room, introduce yourself, and assess their pulmonary status. After you have completed your evaluation, you speak with the physician who ordered IPPB to find out what his therapeutic goals would be and you relay your evaluation of the patient. The physician states that the patient has severe atelectasis and he is concerned about developing pneumonia and wanted to try IPPB to help with lung recruitment and secretion clearance. You make the suggestion to try CPAP and give a flutter valve to the patient to use when not wearing the CPAP mask. The distending pressure from the CPAP will help to re-recruit the lung, while using PEP may aid secretion clearance by keeping the airways from collapsing on exhalation.

BOX 43.8 Potential Outcomes of Intermittent Positive Airway Pressure Breathing Therapy

- Decrease or elimination of atelectasis
- Improved breath sounds
- Normal or improved chest x-ray
- Increased SpO_2
- Increased VC
- Improved inspiratory muscle performance and cough

SpO_2, Oxygen saturation.

BOX 43.9 Monitoring Intermittent Positive Airway Pressure Breathing Therapy

Machine Performance

- Sensitivity
- Peak pressure
- Flow setting
- FiO_2

Patient Response[a]

- Breathing rate and expired volume
- Peak flow or FEV_1/FVC%
- Pulse rate and rhythm (from electrocardiogram if available)
- Sputum quantity, color, consistency, and odor
- Mental function
- Skin color
- Breath sounds
- Blood pressure
- SpO_2 (if hypoxemia is suspected)
- ICP (in patients for whom ICP is important)
- Chest x-ray (when appropriate)
- Subjective response to therapy

[a]Items should be chosen as appropriate for the specific patient.
FEV_1, Forced expiratory volume in 1 s; *FVC*, forced vital capacity; *ICP*, intracranial pressure; *SpO_2*, oxygen saturation.

Evaluating alternatives. Before starting IPPB, the RT and prescribing physician must determine therapeutic objectives for the treatment and whether simpler and less costly methods might be as effective in achieving the desired outcomes.

Discontinuation and Follow-Up

Depending on the goals of therapy and condition of the patient, IPPB treatments typically last 10 to 15 minutes. Follow-up activities include posttreatment assessment of the patient, recordkeeping, and equipment maintenance.

Posttreatment assessment. At the end of a treatment session, the patient assessment is repeated. As with the baseline assessment, this follow-up evaluation has two components. A follow-up evaluation should focus on determining any pertinent changes in vital signs, sensorium, and breath sounds, with emphasis on identifying possible untoward effects.

Treatment frequency should be determined by assessing patient response to therapy (Box 43.9). For acute care patients, orders should be reevaluated based on patient response to therapy at least every 72 hours or with any change of patient status.

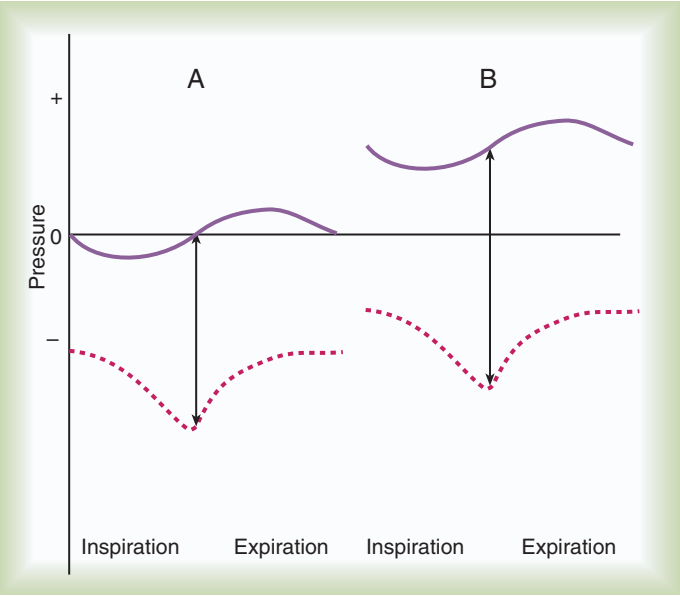

Fig. 43.6 Alveolar *(solid lines)* and pleural *(dotted lines)* pressures during spontaneous breathing (A) and continuous positive airway pressure (B). Note the difference in transalveolar pressure (P_{AL}) gradients *(double arrows)*.

BOX 43.10 Clinical Situations Contraindicating Continuous Positive Airway Pressure Therapy

- Tension pneumothorax/untreated pneumothorax
- ICP >15 mm Hg
- Hemodynamic instability
- Active hemoptysis
- Tracheoesophageal fistula
- Radiographic evidence of blebs
- Recent facial, oral, or skull surgery
- Nausea
- Hypoventilation

ICP, Intracranial pressure.

RULE OF THUMB

Many different types of interfaces can be used for CPAP therapy. They range from nasal prongs (common in neonates, Chapter 54), nasal masks, oronasal masks, and helmets. The ideal interface is that which is comfortable for the patient, does not produce excessive pressure on the face, and minimizes dead space (V_D).

Continuous Positive Airway Pressure

Physiologic Basis

Atelectasis causes a pulmonary shunt and contributes to impaired gas exchange. For areas with a low ventilation and perfusion ($\dot{V}/Q$) and an elevated FiO_2, the patient is at risk for developing gas absorption atelectasis, further complicating the situation.[25] CPAP provides a distending pressure to reinflate the collapsed airways thus improving $\dot{V}/Q$.

As can be seen in Fig. 43.6, CPAP elevates and maintains high alveolar and airway pressures throughout the full breathing cycle; this increases P_{AL} gradient throughout both inspiration and expiration. Typically, a patient on CPAP breathes through a pressurized circuit against a threshold resistor, with pressures maintained between 5 cm H_2O and 20 cm H_2O. To maintain system pressure throughout the breathing cycle, CPAP requires a source of pressurized gas.

Indications

Although evidence supports the use of CPAP therapy in the treating postoperative atelectasis, as with all mechanical techniques, the duration of beneficial effects appears limited. The corresponding increase in FRC may be lost within 10 minutes after the end of the treatment. For this reason, it has been suggested that CPAP should be used on a continuous basis until the patient recovers.

CPAP by mask also has been used to treat cardiogenic pulmonary edema. In such patients, CPAP reduces venous return and cardiac filling pressures, which is helpful in reducing pulmonary vascular congestion. Lung compliance is improved, and the work of breathing is decreased. The improvement in lung compliance and the removal of the edema from the alveoli will result in improved ventilation (decreased dead space V_D/V_T) and thus a decrease in hypercapnia.

Contraindications

Intermittent use of CPAP for correcting atelectasis is contraindicated when certain clinical situations exist. A patient who is hemodynamically unstable is unlikely to tolerate CPAP for even a short period. For those patients who are suspected to have hypoventilation, NIV is usually a better option than CPAP. CPAP is also inappropriate when the patient has nausea, facial trauma, untreated pneumothorax, or elevated intracranial pressure (ICP).

Hazards and Complications

Most hazards and complications associated with CPAP are caused by either the increased pressure or the apparatus (Box 43.10). The increased work of breathing caused by the apparatus can lead to hypoventilation and hypercapnia. An improperly fitted mask can also have detrimental effects on the success of CPAP. Too large a mask will increase the V_D.[26] A mask that is too small would require being tightly strapped onto the patient's face. This would increase their chances of developing a pressure-related wound. In addition, because CPAP does not augment spontaneous ventilation, patients with an accompanying ventilatory insufficiency may hypoventilate when CPAP is applied. Barotrauma is a potential hazard of CPAP and is more likely to occur in a patient with emphysema and blebs. Gastric distension may occur, especially if CPAP pressures greater than 25 cm H_2O are needed. This condition may lead to vomiting and aspiration in a patient with an inadequate gag reflex. A special case is the obese patient who may actually require high levels of CPAP to counteract the weight of their abdomen on the diaphragm.

Monitoring and Troubleshooting

CPAP poses a risk of hypoventilation. Experience with long-term CPAP shows that patients must be able to maintain adequate elimination of carbon dioxide on their own if the therapy is to

be successful. For these reasons, patients receiving CPAP must be closely and continuously monitored for untoward effects. In addition, it is vital that the CPAP device be equipped with a means to monitor the pressure delivered to the airways and alarms to indicate the loss of pressure owing to system disconnect or mechanical failure. There should also be a device allowing for excessive pressure to be released (pop-off). These are essential components of any CPAP device (Box 43.11).

The development of new CPAP units and improvement on the interface itself have addressed some of the comfort issues and correction of leakage associated with CPAP. The RT must also ensure that the flow is adequate to meet the patient's needs with the use of CPAP systems. Flow adjustments are made by carefully observing the airway pressure. Flow generally can be considered adequate when the system pressure decreases no more than 1 to 2 cm H_2O during inspiration.

BOX 43.11 Hazards and Complications of Continuous Positive Airway Pressure Therapy

- Barotrauma, pneumothorax
- Nosocomial infection
- Hypercarbia
- Hemoptysis
- Pressure ulcers from mask
- Gastric distension
- Impaction of secretions (associated with inadequately humidified gas mixture)
- Impedance of venous return
- Hypoventilation
- Increased V_D
- Vomiting and aspiration

V_D, Dead space.

Administration

Early administration of CPAP has been found to be beneficial for both reversing atelectasis and improving $\dot{V}/Q$.

Equipment. CPAP is most commonly delivered using either specialized CPAP machines (Fig. 43.7) or ventilators. These devices allow for a more consistent level of positive pressure and provide the benefit of some level of patient monitoring. In the case where ICU-level ventilators are used, this includes monitoring of respiratory rate, airway pressures, and alarms. In the event of a disconnect or if the patient becomes apneic, the ventilator alarms can provide a measure of safety not realized with a high-flow system and resistor valve.

Procedures. Whether used on an intermittent or continuous basis, CPAP is a complex and potentially hazardous approach to patient management. As with all therapies, the appropriate CPAP level for a patient must be determined on an individual basis. Initial application and monitoring require a broader range of knowledge and skill than is required for simpler modes of lung expansion therapy (Box 43.12).

Preliminary planning. As with all respiratory care, effective CPAP therapy requires careful planning, individualized patient

Fig. 43.7 Various continuous positive airway pressure systems. See text for description.

BOX 43.12 Potential Outcomes of Continuous Positive Airway Pressure Therapy

- Improved VC
- Increased FEV_1 or peak flow
- Enhanced cough and secretion clearance
- Improved chest x-ray
- Improved breath sounds
- Improved oxygenation
- Improved patient comfort

FEV_1, Forced expiratory volume in 1 s.

BOX 43.13 Monitoring Continuous Positive Airway Pressure Therapy

Device Performance

- Mask fit
- Set pressure
- Flow rate
- FiO_2

Patient Response[a]

- Breathing rate and expired volume
- Pulse rate and rhythm (from electrocardiogram if available)
- Mental function
- Skin color
- Breath sounds
- Blood pressure
- SpO_2 (if hypoxemia is suspected)
- Ventilation
- ICP (in patients for whom ICP is important)
- Chest x-ray (when appropriate)
- Subjective response to therapy

[a]Items should be chosen as appropriate for the specific patient.
ICP, Intracranial pressure; *SpO_2*, oxygen saturation.

assessment and implementation, and thoughtful follow-up (Box 43.13).

Evaluating alternatives. The use of CPAP, NIV, or HFNC has shown promise in decreasing the development of postoperative respiratory complications.[27]

Discontinuing and Follow-Up

Depending on the indications for CPAP (e.g., chronic heart failure [CHF]), once the underlying cause that indicated the need for CPAP has been addressed, it is possible to start to discontinue therapy. In the case of CHF, once the patient has been diuresed, they will most likely not need the positive pressure. Care for other patients may result in periods of time off therapy followed by periods back on until the patient shows signs of continued improvement.

Posttreatment assessment. Auscultation of breath sounds and monitoring oxygen saturation (SpO_2) in addition to patient assessment will help to guide the clinician.

High-flow nasal cannula. Providing supplemental oxygen via a nasal cannula has been a common practice in respiratory

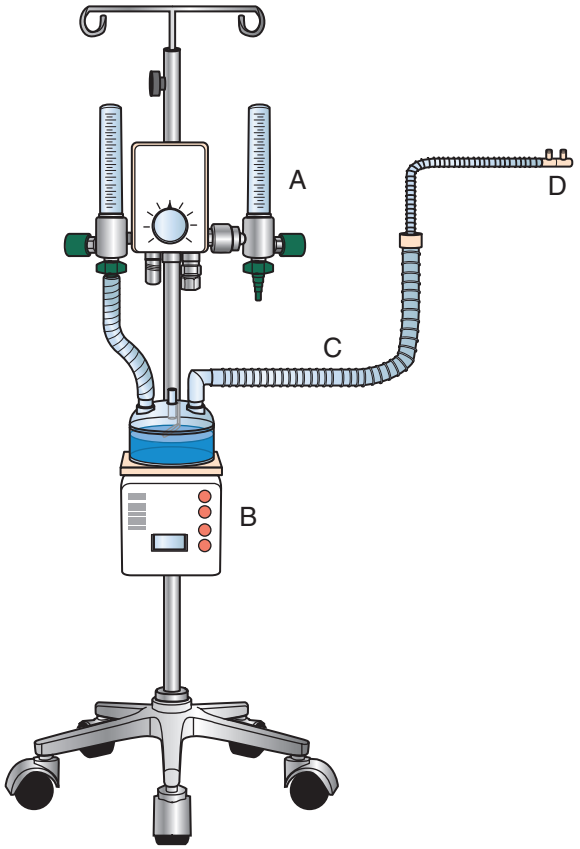

Fig. 43.8 Schematic of a high-flow nasal cannula system *(A)* air-oxygen blender, *(B)* humidifier, *(C)* circuit, *(D)* high-flow cannula.

BOX 43.14 Clinical Situations Contraindicating High-Flow Nasal Cannula Therapy

- Hypercarbic respiratory failure
- Inability to protect the airway
- Unable to tolerate high flow

care. The typical flow limit for these devices is approximately 6 L/min, which is a result of the upper airway to warm and humidify the inspired gas. Common patient complaints when standard nasal cannulas are used at high flows are headache, drying of nasal mucosa, and nosebleeds (Fig. 43.8).[26,28,29]

The small inner diameter of the standard nasal cannula also does not allow for higher flows. HFNC is specially designed with larger prongs allowing higher oxygen flow rates. In addition to the larger-bore cannula, the gas is also heated and humidified before being delivered to the patient providing a higher level of comfort. These two factors allow for the flow rate to be significantly higher, ranging from 40 to 50 L/min (Boxes 43.14 and 43.15).[28-30]

Physiologic Basis

HFNC at elevated inspiratory flows provides a more stable FiO_2. Another benefit from the enhanced flow is *washing out* the CO_2

BOX 43.15 Hazards and Complications of High-Flow Nasal Cannula Therapy

- Nosocomial infection
- Hypercarbia
- Headache
- Drying of mouth/upper airway
- Impaction of secretions (associated with inadequately humidified gas mixture)

BOX 43.16 Potential Outcomes of High-Flow Nasal Cannula Therapy

- Improved chest x-ray
- Improved breath sounds
- Improved oxygenation
- Improved patient comfort

from the anatomic dead space. This helps with ventilation because the CO_2 contained in the nasal pharynx has been eliminated and is not the first gas that enters the lowers respiratory tract with each breath. Essentially, gas flow in the upper airway is unidirectional, in through the nose and out through the mouth. This reduces anatomic dead space by approximately one-third, reducing PCO_2 by 3 to 5 mm Hg and decreasing the work of breathing.[30]

In addition to the washout, a small level of positive pressure is delivered as a result of resistance generated as with the patient breathing out against the high inspiratory flow. Most estimate that approximately 1 cm H_2O positive end-expiratory pressure (PEEP) is established for every 10 L/min flow through the HFNC. This low positive pressure will first help to recruit collapsed alveoli by increasing the P_{AL} and maintaining their inflation once reopened.[28,29] $\dot{V}/Q$ will improve as a result of the improved ventilation to previously perfused areas of the lung (Box 43.16).

Other Therapies

There are other therapies available to the RT with the aim of secretion clearance and possible treatment of postoperative pulmonary complications: intrapulmonary percussive ventilation (IPV) and high-frequency chest wall compression (HFCWC). There is a lack of supporting evidence for the effectiveness of either of these therapies, although each is similar to techniques previously discussed within this chapter. IPV is similar to IPPB with a high respiratory rate, and HFCWC is similar to chest physical therapy (CPT) using a pneumatic vest that the patient wears. These modalities are mentioned for completeness, although the evidence supporting them is low-level or anectdotal.[3,19]

Positive Airway Pressure

First introduced in Denmark during the 1970s as an airway clearance device, and similar to CPAP, PEP adjuncts use positive pressure to increase the P_{AL} gradient and enhance lung expansion.[31] In contrast to CPAP or HFNC, PAP therapy requires no complex machinery. Some methods do not even need a source of pressurized gas.

BOX 43.17 Monitoring Continuous Positive Airway Pressure Therapy

Device Performance

- Mask fit
- Flow rate
- FiO_2

Patient Response[a]

- Breathing rate
- Pulse rate and rhythm (from electrocardiogram if available)
- Mental function
- Skin color
- Breath sounds
- Blood pressure
- SpO_2 (if hypoxemia is suspected)
- Ventilation
- ICP (in patients for whom ICP is important)
- Chest x-ray (when appropriate)
- Subjective response to therapy

[a]Items should be chosen as appropriate for the specific patient.
ICP, Intracranial pressure; *SpO_2*, oxygen saturation.

Physiologic Basis

There are three current approaches to PAP therapy: PEP, flutter, and CPAP. All three techniques are effective in treating atelectasis in most postsurgical patients.[32,33] Using either PEP or flutter as part of airway clearance is described in detail in Chapter 44. This chapter focuses on the uses of PAP for treating atelectasis.

PEP threshold, resistor, and flutter valves create expiratory positive pressure only without need for continuous flow or complex machinery,[28] whereas CPAP maintains a positive airway pressure throughout both inspiration and expiration. Fig. 43.6 compares the alveolar and P_{pl} changes occurring during a normal spontaneous breath (see Fig. 43.6A) and CPAP (see Fig. 43.6B).

The following factors involving PAP, flutter, and CPAP therapy contribute to the beneficial effects: (1) recruitment of collapsed alveoli through an increase in FRC, (2) decreased work of breathing due to increased compliance or elimination of intrinsic positive end-expiratory pressure ($PEEP_i$), (3) improved distribution of ventilation through collateral channels (e.g., pores of Kohn), and (4) increase in the efficiency of secretion removal (Box 43.17).

Indications

The evidence for PEP therapy suggests that patients with expiratory airflow limitation will best respond to this therapy.[31,34] PEP mimics the maneuver of pursed-lip breathing by presenting expiratory resistance either through a flow or threshold resistor, and an elongated expiratory phase. Those patients who are good candidates for PEP therapy are those who can follow instructions and repeat the demonstration back to the RT.

Similar to IS, there is no set duration for therapy nor a set number of repetitions during each session. Currently this therapy is given for patients who may either have atelectasis or have breathlessness.

Contraindications

Similar to the contraindications for the other lung expansion therapies, an untreated pneumothorax should be considered before starting therapy. A good baseline assessment of the patient is helpful to identify any predisposing issues.

Hazards and Complications

Regardless if it is flow limited, a threshold device, or oscillating PEP, care should be taken that the patient does not hyperventilate during therapy. Signs can include dizziness, tingling in the extremities, and light-headedness. In those cases, have the patient stop therapy until they feel better and then suggest a slower regimen of breaths.

Equipment

PEP valve and mouthpiece. The device is designed to fit into a pocket and taken apart for cleaning.

Procedures. Show the device to the patient and have them take a tidal, or slightly larger than tidal, breath. Have the patient exhale through the PEP device and set the resistor to the desired strength. Repeat the instructions if they are breathing out too quickly or slowly.[31,35]

Monitoring and Troubleshooting

Check the valve for obstructions if the patient cannot breathe out from the device. Some PEP devices include a 30-day diary that can be used to track progress.

MINI CLINI—PROBLEM WITH POSITIVE EXPIRATORY PRESSURE

Problem

During a follow-up visit with a patient that you instructed in the use of PEP therapy, it is observed that the patient is struggling on exhalation through the device and does not want to use it.

Discussion

Looking at the device, you see that the resistance is set to maximum. The patient had visitors who were looking at the device and may have moved the setting. You take the time to provide some education and reassurance to the patient and show how to set the resistance and enter it into the diary. With the correct settings, the patient is more willing to continue therapy.

INITIATION OF THERAPY

The best approach for achieving a given clinical goal is always the safest, simplest, and most effective method for an individual patient. Selecting an approach for lung expansion therapy requires in-depth knowledge of both the methods available and the specific condition and needs of the patient being considered for therapy.

Preliminary Planning

Patient education and motivation are key to the success for this therapy. The PEP devices are made to be portable and allow the patient to carry them while outside of the hospital or home. Many devices are now dishwasher safe for easier cleaning.

Evaluating Alternatives

If the patient cannot tolerate PEP, then alternative therapies could be either CPAP or HFNC. Both will aid in lung recruitment using a similar mechanism, with less patient coordination.

Discontinuing and Follow-Up

PEP therapy has been shown to have a positive effect on patient self-reported breathlessness for those patients who have non-cystic fibrosis bronchiectasis or severe chronic obstructive pulmonary disease (COPD).[35] PEP can be continued at home as part of a daily regimen for pulmonary hygiene and dyspnea.

Posttreatment Assessment

Auscultation of breath sounds and reviewing the patient diary for shortness of breath can help to guide the RT in determining if the therapy should be discontinued.

SELECTING AN APPROACH

Selecting an approach for lung expansion therapy requires in-depth knowledge of both the methods available and the specific condition and needs of the patient being considered for therapy.

Fig. 43.9 presents a sample protocol for selecting an approach to lung expansion therapy. As indicated in the algorithm, the patient first must meet the criteria for therapy by having one or more of the indications previously specified. For patients meeting the inclusion criteria, the RT first determines the degree of alertness. Because an obtunded patient cannot be expected to cooperate with IS or PEP or expiratory positive airway pressure (EPAP) therapy, HFNC or CPAP is initiated with appropriate monitoring.

For a patient having no difficulty with secretions, if the VC exceeds 15 mL/kg of lean body weight or the IC is greater than 33% of predicted, IS is given. If either the VC or the IC is less than these threshold levels, IPPB is initiated, with the pressure gradually manipulated from the initial setting to deliver at least 15 mL/kg. If excessive sputum production is a compounding factor, a trial of PEP therapy is substituted for IS. Based on patient response, bronchodilator therapy and bronchial hygiene measures may be added to this regimen. If monitoring fails to reveal improvement and atelectasis persists, a trial of CPAP should be considered. Because evidence of the effectiveness of CPAP is still contradictory, its use should be limited to treating atelectasis after alternative approaches have been tried without success.

Whether or not to keep critically ill patients on complete bed rest is being critically examined in the literature.[22-27,36,37] The complications of prolonged bed rest include cardiovascular, pulmonary, gastrointestinal, and skin integrity issues. Pulmonary complications of immobility include those that have been the focus of this chapter: development of atelectasis, pneumonia, and PE.[23-27,36] Rates of early mobilization for ICU patients have been increasing in both Europe and the United States, along

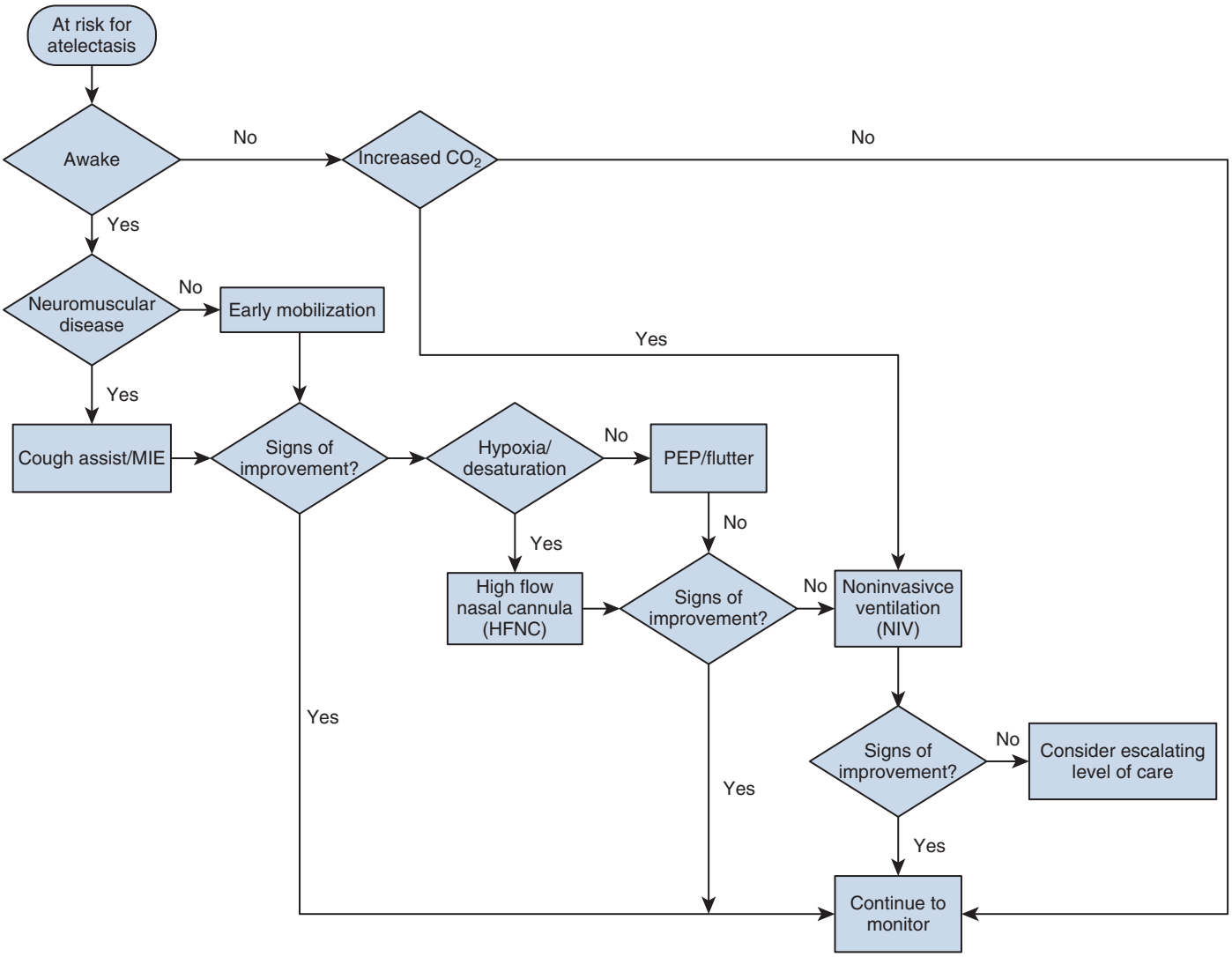

Fig. 43.9 Protocol for selecting an approach for lung expansion therapy. See text for details. *PEP*, Positive expiratory pressure. *MIE*, Mechanical insufflation exhalation.

with the an emphasis on decreasing morbidity in the ICU. Mobilization does not only include walking, but also sitting, standing, and getting out of bed into a chair. As the patient changes body position, his or her breathing changes, as does the gas distribution within the lung. Improvements in ventilation result in less alveolar collapse.

SUMMARY CHECKLIST

- Atelectasis is caused by persistent ventilation with small tidal volumes or by resorption of gas distal to obstructed airways.
- Patients who have undergone upper abdominal or thoracic surgery are at greatest risk for atelectasis.
- A history of lung disease or significant cigarette smoking increases the risk for atelectasis.
- Patients with atelectasis usually have rapid, shallow breathing; fine, late-inspiratory crackles; and abnormalities on chest radiograph.
- Lung expansion therapy corrects atelectasis by increasing the P_{AL} gradient; this can be accomplished by deep spontaneous breaths or by the application of positive pressure.
- The most common problem associated with lung expansion therapy is the onset of respiratory alkalosis, which occurs when the patient breathes too quickly.
- RTs are responsible for implementing, monitoring, and documenting results of lung expansion therapy.

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44

Airway Clearance Therapy

David L. Vines and Donna D. Gardner

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Compare the normal airway clearance mechanisms to the factors that impair their function.
- Identify pulmonary diseases associated with abnormal secretion clearance.
- State the clinical indications for airway clearance therapy.
- Describe the proper technique that would result in potential benefits of each of the following:
  - Chest physical therapy
  - Directed coughing and related expulsion techniques
  - Vibratory positive expiratory pressure therapy
  - Mechanical insufflation-exsufflation (MIE)
  - High-frequency oscillation devices
    - Vibratory positive expiratory pressure
    - High-frequency airway pressure devices
    - High-frequency oscillation compression devices
  - Mobilization and exercise
- Evaluate a patient's response to airway clearance therapy to determine changes in the treatment plan.

CHAPTER OUTLINE

KEY TERMS

active cycle of breathing technique (ACBT)
autogenic drainage (AD)
bronchiectasis
chest physical therapy (CPT)
ciliary dyskinetic syndromes
forced expiratory technique (FET)
Hertz (Hz)
High-frequency chest wall compression (HFCWC)
huff coughing
inspissation
intrapulmonary percussive ventilation (IPV)
mechanical insufflation-exsufflation (MIE)
mucous plugging
oscillation
positive expiratory pressure (PEP)
splinting

Airway clearance therapy (ACT) uses noninvasive techniques designed to assist in mobilizing and removing secretions to improve gas exchange.[1] Historically, the term **chest physical therapy (CPT)** described the primary techniques used to assist with clearing secretions from the airways. Today, there are numerous options related to airway clearance including CPT, breathing retraining techniques, positive expiratory therapy (PEP), vibratory PEP, high-frequency oscillation devices, high-frequency chest wall compression (HFCWC) devices, **mechanical insufflation-exsufflation (MIE)**, and various exercise protocols.[1–3]

This chapter focuses on ACTs or techniques used to mobilize secretions and noninvasively assist in their removal. The primary *invasive* method for removing airway secretions is suctioning and is discussed in Chapter 37. Successful outcomes in airway clearance techniques require knowledge of normal and abnormal physiology, understanding of how clearance devices work, careful patient evaluation, rigorous application of evidence-based methods, and ongoing assessment targeted at achieving therapeutic goals.[1–4]

PHYSIOLOGY OF AIRWAY CLEARANCE THERAPIES

To apply ACTs properly, one must understand how normal airway clearance mechanisms work and what can impair their function.

Normal Clearance

Normal airway clearance requires patent airways, a functional mucociliary escalator, adequate hydration, and effective cough.[5] Mucociliary clearance normally occurs from the larynx down to the respiratory bronchioles. Mucus is produced by secretory (Clara, goblet, and serous) cells and submucosal glands.[5] Ciliated epithelial cells move this mucus via a coordinated wave of ciliary motion toward the trachea and larynx, where secretions can be swallowed or expectorated. Healthy individuals produce 10 to 100 mL of secretions in the airway on a daily basis that are cleared by this mucociliary escalator.[3,5]

The cough is one of the most important protective reflexes. Coughing clears the larger airways of excessive mucus and foreign matter, assists normal mucociliary clearance, and helps ensure airway patency. As shown in Fig. 44.1, there are four distinct phases to a normal cough: *irritation, inspiration, compression,* and *expulsion*. In the initial irritation phase, an abnormal stimulus provokes sensory fibers in the airways to send impulses to the medullary cough center in the brain. This stimulus normally is inflammatory, mechanical, chemical, or thermal. Infection is a good example of an *inflammatory* process that can stimulate a cough. Foreign bodies can provoke a cough through *mechanical* stimulation. Inhaling irritating gases (e.g., cigarette smoke) can result in coughing through *chemical* stimulation. Finally, cold air may cause *thermal* stimulation of sensory nerves, producing a cough. When these impulses are received, the cough center generates a reflex stimulation of the respiratory muscles to initiate a deep inspiration (the second phase). In normal adults, this inspiration averages 1 to 2 L.

During the third or compression phase, reflex nerve impulses cause glottic closure and a forceful contraction of the expiratory muscles. This compression phase is normally about 0.2 seconds and results in a rapid increase in pleural and alveolar pressures, often greater than 100 mm Hg. At this point, the glottis opens, initiating the expulsion phase. With the glottis open, a large pressure gradient between the lungs and the atmospheric pressure exists. Together with the continued contraction of the expiratory muscles, this pressure gradient causes a violent, expulsive high velocity of airflow from the lungs. This high-velocity gas flow, combined with dynamic airway compression, creates huge shear forces that displace mucus from the airway walls into the air stream. Mucus and foreign material are expelled from the lower airways to the upper airway, where they can be expectorated or swallowed.

Abnormal Clearance

Any abnormality that alters airway patency, mucociliary function, strength of the inspiratory or expiratory muscles, thickness of secretions, or effectiveness of the cough reflex can impair airway clearance leading to retention of secretions.[3,5] In addition, some therapeutic interventions, especially interventions used in critical care, such as an endotracheal tube, can result in abnormal clearance.

Retention of secretions can result in full or partial airway obstruction. Full obstruction, or **mucous plugging**, can result in atelectasis which causes hypoxemia due to shunting. A partial obstruction restricts airflow, increasing work of breathing and possibly leading to air trapping, lung overdistension, and ventilation/perfusion ($\dot{V}/\dot{Q}$) imbalances. In the presence of pathogenic organisms, retention of secretions can also lead to infections.

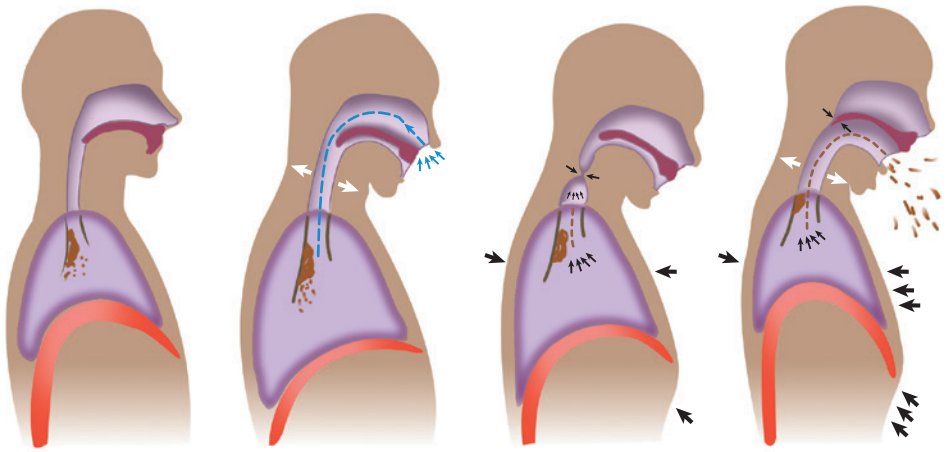

Fig. 44.1 The cough reflex. (Modified from Cherniack RM, Cherniack L. *Respiration in Health and Disease,* ed 3, Philadelphia, 1983, WB Saunders.)

TABLE 44.1 Mechanisms Impairing Cough Reflex

Phase	Examples of Impairments
Irritation	Anesthesia
	Central nervous system depression
	Narcotic analgesics
Inspiration	Pain
	Neuromuscular dysfunction
	Pulmonary restriction
	Abdominal restriction
Compression	Laryngeal nerve damage
	Artificial airway
	Abdominal muscle weakness
	Abdominal surgery
Expulsion	Airway compression
	Airway obstruction
	Abdominal muscle weakness
	Inadequate lung recoil (e.g., emphysema)

BOX 44.1 Causes of Impaired Mucociliary Clearance in Intubated Patients

- Endotracheal or tracheostomy tube
- Tracheobronchial suction
- Inadequate humidification
- High FiO_2 values
- Drugs
- General anesthetics
- Opiates
- Narcotics
- Underlying pulmonary disease

Infectious processes provoke an inflammatory response and the release of chemical mediators. These chemical mediators, including leukotrienes, proteases, and elastases, can damage the airway epithelium and increase mucus production, resulting in a vicious cycle of worsening airway clearance.[5]

In patients with retained secretions, interference with one of the four phases of cough can result in ineffective airway clearance. This occurs in patients following thoracic or upper abdominal surgery, in the intensive care unit, or with neuromuscular diseases (NMDs) such as amyotrophic lateral sclerosis (ALS), myasthenia gravis (MG), or cervical or thoracic spinal cord injuries. Table 44.1 provides examples of factors that can impair the normal cough reflex.

As indicated in Box 44.1, additional factors can impair airway clearance in critically ill patients with artificial airways, the most important of which is the airway itself.[6] The presence of an artificial airway in the trachea increases mucus secretion, and the cuff of the tube mechanically blocks the mucociliary escalator. In addition, movement of the tube tip and cuff can cause erosion of the tracheal mucosa, leading to further impairment of the mucociliary escalator. The endotracheal tube also impairs the compression phase of the cough reflex by preventing closure of the glottis (see Table 44.1). Although suctioning is used to aid secretion clearance, it too can cause damage to the airway mucosa and impair mucociliary transport. Inadequate humidification can cause thickening or **inspissation** of secretions, mucous plugging, and airway obstruction.[7] High fractional inspired oxygen (FiO_2) concentrations can impair ciliary function, resulting in retained secretions. Retained secretions can lead to acute tracheobronchitis. Several common drugs, including some general anesthetics and narcotic analgesics, may also depress mucociliary transport.[5]

RULE OF THUMB Several factors impair the mucociliary escalator resulting in increased mucus production: the presence of an artificial airway, suctioning beyond the end of an artificial airway, inadequate humidification, high concentrations of oxygen, and drugs (anesthetics and narcotic—analgesics).

Diseases Associated With Abnormal Clearance

Several diseases are associated with abnormal airway clearance, including diseases affecting airway patency, composition and production of mucus, ciliary structure and function, and normal cough reflex.[5] Internal obstruction or external compression of the airway lumen can impair airway clearance. Examples include foreign bodies, tumors, and congenital or acquired thoracic anomalies such as kyphoscoliosis. Internal obstruction also can occur with mucus hypersecretion, inflammatory changes, or bronchospasm that narrows the lumen. Examples include asthma, chronic bronchitis, and/or acute infections.

Diseases that alter normal mucociliary clearance also can cause retention of secretions. In cystic fibrosis (CF), the solute concentration of the mucus is altered because of abnormal sodium and chloride transport.[5] This alteration increases the viscosity of mucus and impairs its movement up the respiratory tract. Although less common, there are several conditions in which the respiratory tract cilia do not function properly.[5] The **ciliary dyskinetic syndromes** contribute to ineffective airway clearance. **Bronchiectasis** permanently damages and dilates airways that are prone to obstruction due to retained secretions.[5,8] Bronchiectasis is a common finding in CF and ciliary dyskinetic syndromes.[8–10]

Mucociliary function may be normal, but lack of an effective cough alters airway clearance leading to retained secretions, mucous plugs, obstructions, and atelectasis. The most common conditions affecting the cough reflex are musculoskeletal and NMD, including muscular dystrophy, ALS, spinal muscular atrophy, MG, poliomyelitis, and cerebral palsy (see Chapter 33).[11]

GENERAL GOALS AND INDICATIONS

The primary goal of ACT is to assist the patient to mobilize and remove retained secretions. Removal of these retained secretions may improve gas exchange, promote alveolar expansion, and reduce the work of breathing. Box 44.2 lists general indications for ACT.[1,3]

Airway Clearance Therapy for Acute Conditions

Patients with acute conditions in whom ACT may be indicated include: (1) acutely or chronically ill patients with copious

BOX 44.2 Indications for Airway Clearance Therapy

Acute Conditions
- Copious secretions
- Inability to mobilize secretions
- Ineffective cough

Chronic Conditions
- Cystic fibrosis
- Bronchiectasis
- Ciliary dyskinetic syndromes
- Chronic obstructive pulmonary disease patients with retained secretions.

secretions; (2) patients with retained secretions or ineffective cough (coarse crackles, worsening oxygenation and/or ventilation, volume loss on chest radiograph); (3) possibly patients with acute lobar atelectasis; or (4) patients with $\dot{V}/\dot{Q}$ abnormalities.[1] In treating *chronic* respiratory conditions, inhaled bronchodilator therapy before ACT may improve the overall effectiveness of the treatment both by opening the airways and by increasing the mucociliary activity.[12] For acute pulmonary infections and those with CF, inhaled antibiotics taken after ACT can lead to improved deposition of the antibiotic.[4] Acute conditions for which ACT is probably not indicated include: (1) routine care of chronic obstructive pulmonary disorder (COPD), (2) pneumonia without clinically significant sputum production, (3) routine postoperative care, and (4) uncomplicated asthma.[1,3]

RULE OF THUMB Bronchodilator therapy is not indicated in the acute care setting for airway clearance therapy unless the patient is wheezing due to a bronchospasm or has a chronic pulmonary condition with retained secretions.

Airway Clearance Therapy for Chronic Conditions

ACT has proved effective in secretion clearance and improving pulmonary function in chronic conditions associated with copious sputum production, including CF, bronchiectasis, and ciliary dyskinetic syndromes, and COPD patients with retained secretions.[1,3,4] Generally, sputum production must exceed 20 to 30 mL/day for ACT to improve secretion removal significantly.[3]

RULE OF THUMB Patients with copious secretions (20–30 mL/day) or inability to mobilize and expectorate secretions may benefit from airway clearance therapy.

Airway Clearance Therapy to Prevent Retention of Secretions

ACT has been used as preventive therapy in various disorders and current evidence is not supportive of this approach.[1,2] The best-documented preventive uses of ACT include: (1) body positioning and patient mobilization to prevent retained secretions in acutely ill patients, and (2) ACT combined with physical activity to maintain lung function in patients with CF.[1,2,4]

MINI CLINI

Assessing a Patient's Cough Clearance

Problem

The respiratory therapist (RT) is called by a nurse to determine a care plan to assist a patient who is having difficulty clearing secretions. The patient is an alert, obese, 45-year-old man who underwent general anesthesia and surgery for a cholestectomy 3 h earlier. Physical signs indicate retention of secretions, but there is no history of lung disease. Auscultation reveals coarse expiratory crackles. The patient is breathing spontaneously; however, his breathing is shallow and he has a very weak cough. Visual clues indicate the patient has severe pain in the epigastric area. The patient was given an injection of morphine to assist with the pain 1 h earlier.

Discussion

There is no surprise that this patient is having difficulty clearing secretions considering the recent anesthesia and receiving a narcotic analgesic, which may impair his cough. In addition, obesity (abdominal restriction), weakness, and pain are impairing the inspiration, compression, and expulsion phases of his cough effort.

The patient should immediately be started on ACT and hyperinflation or lung expansion therapies. Judicious use of pain medication, coinciding with therapies, should continue. Cough instruction including incisional splinting should be part of the plan. Early mobilization should be encouraged. Although the most common postoperative complication is atelectasis, pneumonia may also occur. The head of the patient's bed should be elevated at least to 30–45 degrees to minimize the risk of aspiration.

DETERMINING THE NEED FOR AIRWAY CLEARANCE THERAPY

Effective ACT requires proper initial and ongoing patient assessment (Chapter 16). Formulation of the respiratory care plan depends on review of the patient's medical history and interview for current symptoms, physical assessment, assessment of cough and sputum, laboratory testing (including pulmonary function tests), and radiologic evaluation. Box 44.3 lists the key factors that must be considered when assessing a patient's need for ACT.[1,3,4] Physical findings, such as a loose, ineffective cough; labored breathing pattern; decreased or bronchial breath sounds; coarse inspiratory and expiratory crackles; tachypnea; tachycardia; or fever may indicate a potential problem with retained secretions.

AIRWAY CLEARANCE METHODS

Five general approaches to ACT, which can be used alone or in combination, include: (1) CPT; (2) coughing and related expulsion techniques (including **mechanical insufflation-exsufflation [MIE]**); (3) positive airway pressure (PAP) adjuncts (**positive expiratory pressure [PEP]**, vibratory PEP, high-frequency PAP devices); (4) high-frequency oscillation devices; and (5) mobilization and physical activity. Table 44.2 provides a brief description and limitations associated with these ACTs. Appropriate use of these techniques requires an understanding of their underlying principles, relative usefulness, and methods of application.

BOX 44.3 Initial Assessment of Need for Airway Clearance Therapy

Medical Record

History of pulmonary problems causing increased secretions
Admission for upper abdominal or thoracic surgery; consider:
- Age (elderly)
- History of chronic obstructive pulmonary disease
- Obesity
- Nature of procedure
- Type of anesthesia
- Duration of procedure

Presence of artificial tracheal airway
Chest radiograph indicating atelectasis or infiltrates
Results of pulmonary function testing
Arterial blood gas values or O_2 saturation

Patient

Posture, muscle tone
Effectiveness of cough
Sputum production
Breathing pattern
General physical fitness
Breath sounds
Vital signs, heart rate and rhythm

Chest Physical Therapy Also Known as Postural Drainage and Percussion

CPT has long been considered a standard of care in patients with CF. Evidence suggests that these therapies benefit mucus transport and assist in the expectoration of secretions.[1,3,4] This therapy includes postural drainage (PD) and percussion or vibration.

CPT involves the use of positioning, gravity, and mechanical energy to help mobilize secretions. PD places the body in various positions that are intended to drain secretions from each of the patient's lung segments into the central airways, where they can be removed by cough or suctioning.[4] This drainage is accomplished by simply placing the segmental bronchus to be drained in a more vertical position, permitting gravity to assist in the process. Positions generally are held for 3 to 15 minutes (longer in special situations such as CF) and modified as the patient's condition and tolerance warrant. Specifically, with CF patients and all pediatric patients in general, head-down positioning should be avoided to prevent marked increases in intracranial pressure (ICP), especially during coughing.[2–4,13] Cough methods are used with CPT and are discussed separately.

The indications for CPT (and other ACTs) in a patient are the presence of copious secretions, the inability to mobilize and expectorate the secretions, and pulmonary disorders associated with retained secretions (CF, bronchiectasis, and ciliary dyskinetic syndromes).[1,3,4] This therapy does require a trained caregiver's assistance in order for it to be performed correctly. CPT may be most effective in conditions characterized by excessive sputum production (greater than 25 to 30 mL/day) that is not cleared by deep breathing and coughing. For maximum effect with PD, head-down positions should exceed 25 degrees below horizontal.[2–4,13] In patients with CF and pediatric patients in general head-down positioning should be avoided as discussed above.[2–4,13] If the patient cannot be placed in appropriate positions for the areas affected, another ACT should be considered. In spontaneously breathing patients, treatment frequency should be determined by assessing the patient's response to therapy. Critically ill patients, especially patients being mechanically ventilated, should be moved and rotated every 2 hours.[14]

RULE OF THUMB To achieve the maximum secretion drainage with postural drainage and percussion the head-down positions should exceed 25 degrees below horizontal. In patients with CF and pediatric patients in general head down positioning should be avoided because of increased ICP, especially of concern during coughing. If the patient cannot be placed in appropriate drainage positions for the areas affected, another ACT should be considered.

Technique

Based on a preliminary assessment of the patient and review of the physician's order, the RT should identify the appropriate lobes and segments for drainage. The RT may need to choose a different ACT method in patients with unstable cardiovascular status, hypertension, cerebrovascular disorders, or dyspnea. To avoid gastroesophageal reflux and the possibility of aspiration, treatment times should be scheduled before or at least 2 hours after meals or tube feedings to decrease the chance of vomiting or aspiration. If the patient assessment indicates that pain may hinder treatment implementation, the RT should consider coordinating the treatment regimen with prescribed pain medication. Contraindications for CPT are listed in Box 44.4.

Before positioning, the procedure (including adjunctive techniques) should be explained to the patient. The RT should inspect for incisions, monitoring leads, intravenous tubing, and oxygen (O_2) therapy equipment connected to the patient and, if necessary, make adjustments to ensure continued function during the procedure or choose a different ACT method. Before starting, during, and after the procedure, the RT should measure the patient's vital signs, auscultate the chest, and measure SpO_2 to assess the presence of hypoxemia. These simple assessments serve as baseline measurements for monitoring the patient's response during the ACT and can assist in determining outcomes. The following items also should be monitored before, during, and after CPT: subjective responses (pain, discomfort, dyspnea, response to therapy), arrhythmias, breathing pattern, sputum production (quantity, color, consistency, odor), skin color, and ICP if monitored.

Fig. 44.2 depicts the primary positions used to drain the various lung lobes and segments. Generally, to obtain the proper head-down position, the RT must lower the head of the bed by at least 16 to 18 inches to achieve the desired 25-degree angle. In the ambulatory care setting, a tilt table can be used in lieu of a hospital bed. A tilt table allows precise positioning at head-down angles up to 45 degrees. When angles this large are used, shoulder supports must be provided to prevent the patient from sliding off the tilt table.

After the patient is positioned, the RT confirms the patient's comfort and ensures proper support of all joints and bony areas with pillows or towels. The indicated position is maintained for

TABLE 44.2 Airway Clearance Therapies, Techniques, and Devices

ACT	Techniques and Devices	Limitations Associated With ACT
Chest physiotherapy (CPT) includes percussion and postural drainage	Manual percussion of the chest using cupped hands or mechanical device creates vibrations to loosen secretions and positioning uses gravity to draining secretions from the lung segments to the larger airways	• Patients who are short of breath may not tolerate being placed in Trendelenburg position. • The treatment is dependent of the patient being positioned appropriately. • Caregivers are required to perform the therapy
Active cycle of breathing	To mobilize secretions the breathing cycles includes alternating between relaxed breathing, deep breathing, and forced expiratory technique	• Patients who are unable to perform this therapy include those unable to take a deep breath or experiencing an exacerbation • This concept is difficult to perform in children less than 4 years old. • Repeated coaching may be needed in children up to the age of 10
Autogenic drainage	To loosen and move secretions into the larger airways and then expelled them, a patient can use a series of breathing patterns beginning with breaths at a low volume, then breaths at a normal tidal volume and ending with a high volume and high peak flow breath like a huff cough	• The patient's coordinated breathing is necessary making it difficult to perform when they are short of breath or unable to take a deep breath. • To perform correctly the patient needs to be an older than 10 years of age
Mechanical insufflator-exsufflator (MIE)	To expel secretions the device simulates an effective cough by using positive airway pressure on inspiration to increase tidal volume and then switching to a negative pressure to increase peak expiratory cough flows. The device may be used with a mask, mouthpiece or attached to an artificial airway. The device has an oscillatory mechanism to assist with mobilize the secretions	• In patients with bulbar ALS, the negative pressure expiratory phase may be limited by upper airway closure. • Patients with obstructive airway disorders may experience airway collapse with the negative pressure phase • Contraindicated in the presence or suspicion of untreated pneumothorax, unstable hemodynamic status, increased intracranial pressure, current maxillofacial surgery or trauma, active hemoptysis, or tympanic membrane rupture. • Caregiver is needed for this therapy
Positive expiratory pressure (PEP) or oscillatory or vibratory PEP (OPEP)	To mobilize secretions using PEP devices, an expiratory pressure of 10–20 cm H_2O is created by the patient actively exhaling against a fixed or variable orifice flow resistor. The OPEP creates flow oscillations by adding flow interruptions during the patient's active exhalation	• Patients must be able to take a deep breath and exhale with enough force to generate the PEP and oscillations. • Contraindicated in the presence or suspicion of untreated pneumothorax, unstable hemodynamic status, increased intracranial pressure, current maxillofacial surgery or trauma, active hemoptysis, or tympanic membrane rupture
High-frequency positive airway pressure devices	To loosen and move secretions into the larger airways the patient breathes in and actively exhales against short, rapid positive airway pressure pulses	• Younger patients will require a caregiver. • If the patient does not actively exhale, exhalation will depend on the patients' chest wall elastic recoil. • Contraindicated in the presence or suspicion of untreated pneumothorax, unstable hemodynamic status, increased intracranial pressure, current maxillofacial surgery or trauma, active hemoptysis, or tympanic membrane rupture
High-frequency chest wall compression	To mobilize the secretions in the larger airways the patient wears a vest that creates chest wall compression resulting in small pulses of volume at high frequencies	• Patients need to be at least 2 years of age begin using the device. • Avoid using the device in the presence of indwelling catheters or chest tubes
Mobilization and physical activity	Patients who participate in physical activity that results in increased tidal volume, heart rate, and cardiac output, and improved physical condition	• Patients may participate in physical exercise as long as their medical condition allows, or medical monitoring is available. • Caution is needed for patients at risk of developing bronchospasm in the presence of reactive airways

ACT, Airway clearance therapy; *ALS*, amyotrophic lateral sclerosis.

a minimum of 3 minutes if tolerated and longer if good sputum production results. Between positions, pauses for relaxation and breathing control are useful and can help prevent hypoxemia. Because postural drainage therapy can increase O_2 consumption, critically ill patients should be given supplemental O_2 during the procedure if SpO_2 decreases.

During the procedure, the patient is continually observed for any side effects or complications. Moderate changes in vital signs are expected during treatment. Table 44.3 lists complications and the recommended interventions. Significant problems may require immediate intervention.

Also, the RT should ensure that the patient uses appropriate coughing technique during and after positioning. When using the head-down position for non-CF and nonpediatric patients, the patient should avoid strenuous coughing because this markedly increases ICP.[1,2] Rather, the patient should use the forced expiration technique (described later in this chapter). Generally, total treatment time should not exceed 15 minutes for a routine

BOX 44.4 Contraindications to the Use of Chest Physical Therapy

The decision to use postural drainage requires assessment of potential benefits versus potential risks. Therapy should be provided for no longer than necessary to obtain the desired therapeutic results. Listed contraindications are relative unless marked as absolute *(A)*.

Positioning: All positions are contraindicated for:

- Head and neck injury until stabilized *(A)*
- Active hemorrhage with hemodynamic instability *(A)*
- Intracranial pressure (ICP) greater than 20 mm Hg
- Recent spinal surgery or acute spinal injury
- Active hemoptysis
- Empyema
- Bronchopleural fistula
- Pulmonary edema associated with congestive heart failure
- Aged, confused, or anxious patients who do not tolerate position changes
- Pulmonary embolism
- Rib fracture, with or without flail chest
- Surgical wound or healing tissue
- Large pleural effusions

Trendelenburg position contraindicated for:

- Recent gross hemoptysis related to recent lung carcinoma treated surgically or with radiation therapy
- ICP greater than 20 mm Hg
- Uncontrolled hypertension
- Distended abdomen
- Patients in whom increased ICP is to be avoided (e.g., neurosurgery, aneurysms, eye surgery)
- Uncontrolled airway at risk for aspiration (tube feeding or recent meal)
- Esophageal surgery
- External manipulation of the thorax contraindications (in addition to contraindications previously listed):
- Subcutaneous emphysema
- Recent epidural spinal infusion or spinal anesthesia
- Recently placed transvenous pacemaker or subcutaneous pacemaker
- Lung contusion
- Osteomyelitis of the ribs
- Coagulopathy
- Recent skin grafts, or flaps, on the thorax
- Burns, open wounds, and skin infections of the thorax
- Suspected pulmonary tuberculosis
- Bronchospasm
- Osteoporosis
- Complaint of chest wall pain

Excerpts from the American Association for Respiratory Care: Clinical practice guideline: postural drainage therapy. *Respir Care* 36:1418, 1991.

treatment and 30 minutes for extended treatment. Both the patient and the RT should understand that PD does not always result in the immediate production of secretions. More often, secretions are simply mobilized toward the trachea for easier removal by coughing. If the procedure causes vigorous coughing, have the patient sit up until the cough subsides.

After the procedure, the patient is repositioned to the pretreatment position, and the RT ensures the patient's stability and comfort. Immediate posttreatment assessment includes repeat vital signs, confirmation of satisfactory SpO_2, chest auscultation, and questioning the patient regarding his or her subjective response to the procedure. Because PD is coupled with other ACTs, the outcomes assessment and documentation are discussed later in the chapter.

MINI CLINI

Chest Physical Therapy (Postural Drainage, Percussion, and Vibration)

Problem

A physician's progress note indicates a potential bacterial pneumonia localized to a patient's right middle lobe. The patient has coarse breath sounds on the right midlung and a nonproductive cough. The physician orders CPT four times daily "until radiograph clears." What positions should the RT select for postural drainage, and where should the RT provide percussion?

Discussion

The correct position for draining the right middle lobe would be head down (foot of bed raised about 12 inches), with the patient rotated about 45 degrees left from supine (modified left side-lying position). Percussion should be performed on the right anterior chest wall, between the fourth and sixth ribs (see Chapter 16 for external anatomic landmarks).

RULE OF THUMB Generally, whenever you observe any patient adverse effects or complications during postural drainage, follow the "triple S rule": **stop** the therapy, return the patient to the original resting position, and **stay** with the patient until he or she is **stabilized**.

Percussion and Vibration

Percussion and vibration involve application of mechanical energy to the chest wall using either hands or various electrical or pneumatic devices. Both methods are designed to augment secretion clearance. In theory, percussion should help loosen secretions from the tracheobronchial tree, making them easier to remove by coughing or suctioning. The effectiveness of percussion as an adjunct to PD remains unclear. This controversy is due to variability in practice and the difficulty related to performing trials of percussion because percussion is only a part of the overall treatment regimen.[15]

Manual percussion. The RT performs manual percussion with his or her hands in a cupped position, with fingers and thumb closed and positioned parallel to the ribs (Fig. 44.3). This technique compresses air between the hand and chest wall. This technique should be applied against a thin layer of cloth, such as a hospital gown or bed sheet to help improve patient comfort. This technique involves the therapist's cupped hands rhythmically striking the chest wall, using both hands alternately in sequence with the elbows partially flexed and wrists loose (see Fig. 44.3). Slower, more relaxing rates are better tolerated by the patient and the therapist. This technique requires practice to determine the appropriate force and maintain a rhythmic pattern during this therapy (Fig. 44.4). Ideally, the RT should percuss back and forth in a circular pattern over the localized area for 3 to 5 minutes. Care should be taken to avoid tender areas or sites of trauma, surgery, or chest tubes, and one should never percuss directly over bony prominences, such as the clavicles, vertebrae or sternum.

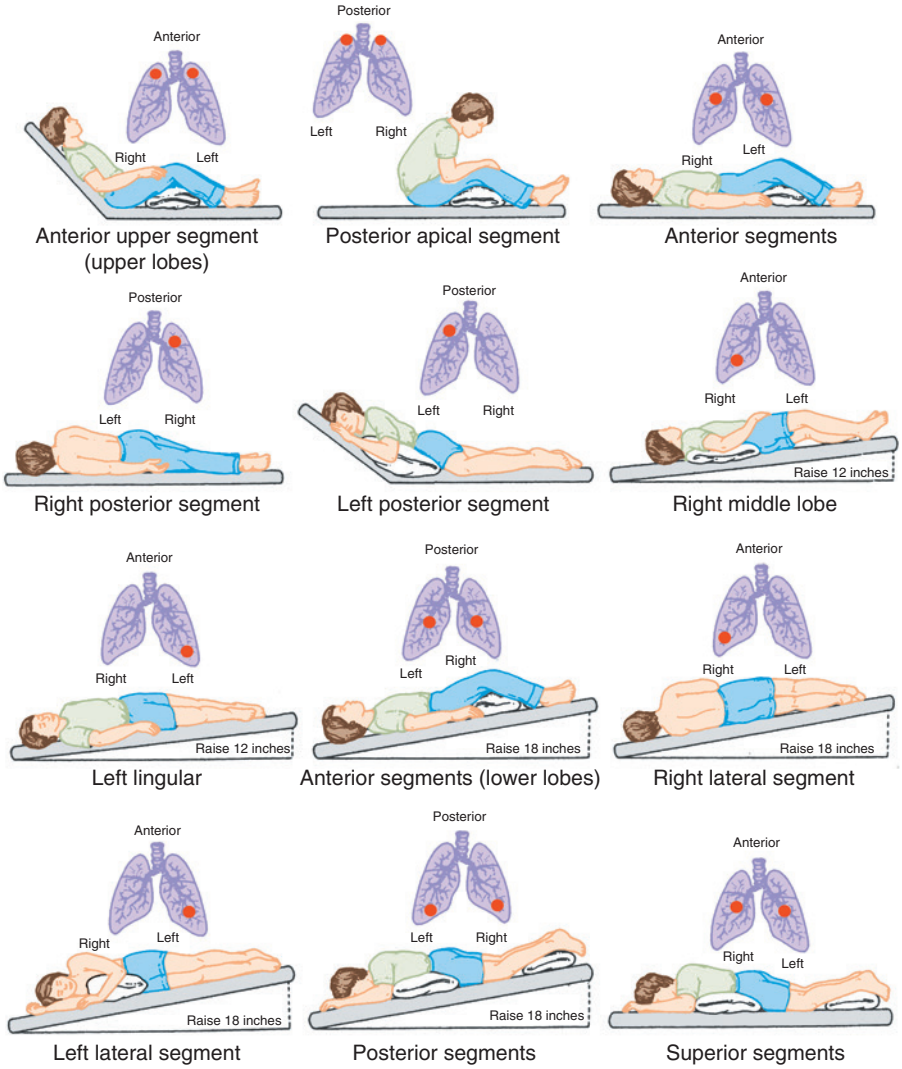

Fig. 44.2 Patient positions for postural drainage. (Modified from Potter PA, Perry AG: *Fundamentals of Nursing: Concepts, Process and Practice*, ed 4, St Louis, 1997, Mosby.)

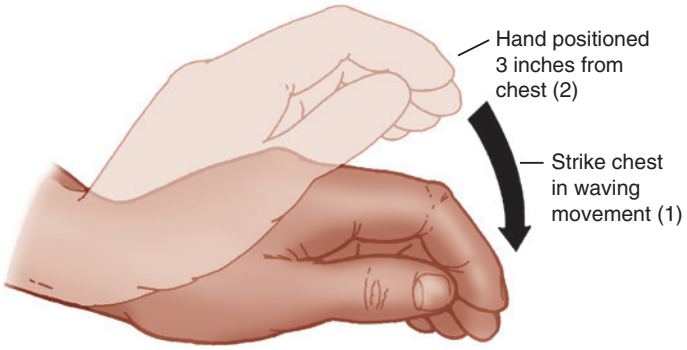

Fig. 44.3 Movement of cupped hand at wrist, to percuss chest.

Mechanical percussion and vibration. Mechanical vibration is used as an alternative to manual percussion in acutely ill patients with chest wall discomfort or injury. Various electrical and pneumatic devices have been developed to generate and apply the energy waves used during percussion and vibration. Typically, these devices have both a frequency and a percussion force control (Fig. 44.5). Most units provide frequencies between 20 and 50 cycles per second (20 to 50 **Hertz [Hz]**). Other sonic or acoustic devices may provide up to 120 Hz. Noise, excess force, and mechanical failure are all potential problems. Electrical devices also pose a potential electrical shock hazard. These devices have the advantage of reducing fatigue on the caregiver, decreasing treatment time, and delivering consistent rates, rhythms, and impact forces. These devices may improve hospitalized patients' compliance, especially when chest wall discomfort or injury is present. However, there is no firm evidence that such devices are more effective than manual techniques. For this reason, as with other ACT techniques, the selection of manual or mechanical methods should be based on individual patient factors such as age, condition, and tolerance.[2,4]

Coughing and Related Expulsion Techniques

Most ACTs only help move secretions into the central airways. Clearance of these secretions requires either coughing or suctioning. In this respect, an effective cough (or alternative expulsion measure) is an essential component of all ACT. These expulsion methods are also useful in obtaining sputum specimens for diagnostic analysis.

TABLE 44.3 Complications of Postural Drainage Therapy and Recommended Interventions

Complication	Action to Be Taken/Possible Intervention
Hypoxemia	Administer higher FiO_2 during procedure if potential for or observed hypoxemia exists. If patient becomes hypoxemic during treatment, administer 100% O_2, stop therapy immediately, return patient to original position, and consult physician
Increased intracranial pressure	Stop therapy, return patient to original resting position, and consult physician
Acute hypotension during procedure	Stop therapy, return patient to original resting position, and consult physician
Pulmonary hemorrhage	Stop therapy, return patient to original resting position, and call physician immediately. Administer O_2 and maintain an airway until physician responds
Pain or injury to muscles, ribs, or spine	Stop therapy that appears directly associated with pain or problem, exercise care in moving patient, and consult physician
Vomiting and aspiration	Stop therapy, clear airway and suction as needed, administer O_2, maintain airway, return patient to previous resting position, and contact physician immediately
Bronchospasm	Stop therapy, return patient to previous resting position, and administer or increase O_2 delivery while contacting physician. Administer physician-ordered bronchodilators
Arrhythmias	Stop therapy, return patient to previous resting position, and administer or increase O_2 delivery while contacting physician

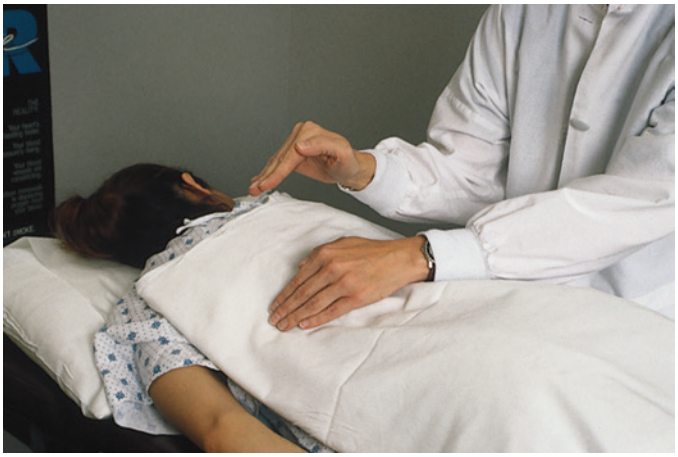

Fig. 44.4 Hand placement for chest physical therapy. (From Harkreader H, Hogan M, Thobaben M: *Fundamentals of Nursing, Caring and Clinical Judgment*, ed 3, St Louis, 2007, Saunders.)

RULE OF THUMB Clinicians should coach the patient to create an effective cough with most airway clearance techniques to fully clear secretions.

Fig. 44.5 Example of an electrically powered mechanical percussor. (Courtesy General Physiotherapy, Inc. St Louis, MO.)

Directed Cough

Directed cough is a deliberate maneuver that is taught, supervised, and monitored. It aims to assist in creating a productive cough in patients unable to clear secretions with an effective spontaneous cough. In patients with copious secretions, directed coughing is an effective clearance method clearing secretions from the central—but not peripheral—airways. In addition to aiding in the removal of retained secretions from central airways, it should be a routine part of all ACT and may be helpful in obtaining sputum specimens for diagnostic analysis.

Box 44.5 lists the relative contraindications and potential complications associated with directed cough. These patients should be monitored for pain, discomfort, dyspnea, pulse rate, cardiac rhythm (if an electrocardiogram is available), breath sounds, pulse oximetry if desaturation is suspected, breathing pattern, skin color, sputum production, and ICP if elevated. To determine the effectiveness of directed cough techniques, therapists should evaluate the patient for any of the following outcome changes: increased sputum production, decreased pulse and respiratory rate, clearing of the breath sounds, improved O_2 saturation, and possibly clearing of infiltrates on the chest x-ray.

Standard technique. After the clinical need for directed coughing has been established, the RT should assess the patient for any factors that could limit the success of directed cough and relative contraindications. An effective directed cough is impossible with unresponsive, paralyzed, or uncooperative patients. In addition, some patients with severe COPD or severe restrictive disorders (including neurologic, muscular, or skeletal abnormalities) may be unable to generate an effective spontaneous cough. Pain, systemic dehydration, tenaciously thick secretions, artificial airways, or use of central nervous system depressants can also impact efforts to implement an effective directed cough. If any of these limitations exist, the RT should recommend an alternative to directed cough such as an assisted cough, which is discussed later in this chapter.

Patient education is a critical part of developing an effective directed cough. The three most important aspects in teaching a patient to have an effective cough are: (1) instruction on proper positioning, (2) instruction on breathing control, and (3) exercises to strengthen the expiratory muscles.[16] These activities are modified according to the patient's underlying clinical problem.

RULE OF THUMB Adequate expiratory muscle strength as well as proper instruction regarding patient positioning and breathing control are essential components to an effective directed cough.

BOX 44.5 Directed Cough

Contraindications

Directed cough is rarely contraindicated. The contraindications listed must be weighed against potential benefit in deciding to eliminate cough from the care of the patient. Listed contraindications are relative:

- Inability to control possible transmission of infection from patients suspected or known to have pathogens transmittable by droplet nuclei (e.g., *Mycobacterium tuberculosis*)
- Presence of elevated intracranial pressure or known intracranial aneurysm
- Presence of reduced coronary artery perfusion, such as in acute myocardial infarction
- Acute unstable head, neck, or spine injury
- Manually assisted directed cough with pressure to the epigastrium may be contraindicated in the presence of increased potential for regurgitation or aspiration, acute abdominal pathology, abdominal aortic aneurysm, hiatal hernia, pregnancy, bleeding diathesis, or untreated pneumothorax
- Manually assisted directed cough with pressure to the thoracic cage may be contraindicated in the presence of osteoporosis or flail chest

Hazards and Complications

- Reduced coronary artery perfusion
- Reduced cerebral perfusion
- Incontinence
- Fatigue
- Rib or costochondral fracture
- Headache
- Visual disturbances, including retinal hemorrhage
- Bronchospasm
- Muscular damage or discomfort
- Incisional pain, evisceration
- Anorexia, vomiting
- Gastroesophageal reflux
- Spontaneous pneumothorax
- Pneumomediastinum
- Subcutaneous emphysema
- Cough paroxysms
- Chest pain
- Central line displacement

Excerpts from the American Association for Respiratory Care: Clinical practice guideline: directed cough. *Respir Care* 38:495, 1993.

First, patients are taught to assume a sitting position with one shoulder rotated inward and the head and spine slightly flexed to aid exhalation and allow easy thoracic compression. It is difficult to generate an effective cough in the supine position. The patient's feet should be supported to provide abdominal and thoracic support for the patient. If the patient is unable to sit up, the RT should raise the head of the bed and ensure that the patient's knees are slightly flexed with the feet braced on the mattress.

Breathing control measures help ensure that the inspiration, compression, and expulsion phases of the cough are maximally effective and coordinated. For effective inspiration, the patient should be taught to inspire slowly and deeply through the nose, using the diaphragm. In patients with copious amounts of sputum, such breaths alone may stimulate coughing by loosening secretions in the larger airways.

After confirming that the patient can take a good, deep inspiration, the RT has the patient bear down against the glottis, in much the same manner as would occur with straining when lifting weights or during a bowel movement. For patients with pain or patients subject to bronchial collapse, it is probably best that they be shown how to "stage" their expiratory effort into two or three short bursts. For these patients, this method is generally less fatiguing and more effective in producing sputum than a single violent expulsion. Effective breathing control and effective coughing are best taught by demonstration. The RT demonstrates the various phases of the cough sequence while emphasizing the correct technique. The RT explains how to avoid common errors, such as simple throat clearing and weak cough efforts.

Proper positioning and breathing control alone may not result in an effective cough and clear secretions. This limitation is usually due to weak breathing muscles. Muscle weakness is common in patients with NMD, COPD, or those needing long-term ventilatory support. The breathing muscles may atrophy due to disease progression, lack of appropriate nutrition, or lack of use during mechanical ventilation. In these cases, either suctioning or using the mechanical insufflation-exsufflation (MIE) device may be effective in helping clear these secretions.

Modifications to directed cough technique. Modifying the normal directed cough to the needs of the individual patient may lead to a productive cough effort. Good clinical examples of the need to modify directed cough are seen in surgical patients, patients with COPD, and patients with neuromuscular disorders.

In surgical patients, preoperative training in deep breathing and directed cough can help prepare the patient for the postoperative regimen. This preparation can minimize the anxiety related to pain that commonly impairs an effective cough in these patients. In addition, coordinating the coughing sessions with prescribed pain medication and **splinting** the operative site can enhance the effectiveness of these sessions. The RT can use his or her hands with a pillow or blanket to support the area of incision during the expiratory phase of the cough. Eventually, the patient can learn to use a pillow or blanket roll to splint the incision site. The **forced expiratory technique (FET)** (discussed subsequently) may also be valuable in these patients.

In some patients with COPD, the high pleural pressures during a forced cough may compress the smaller airways and limit the effectiveness of the cough. FET maybe beneficial in these patients because the technique reduces transpulmonary pressures and decreases airway compression or closure.[15] In this situation, the patient is placed in the sitting position previously described. The patient is instructed to take in a moderately deep breath slowly through the nose. To help enhance expulsion, the patient should exhale with moderate force through pursed lips, while bending forward. This forward flexion of the thorax enhances expiratory flow by upward displacement of the abdominal contents. After three or four repetitions of this maneuver, the patient is encouraged to bend forward and initiate short staccato-like bursts of air. This technique relieves the strain of a prolonged hard cough, and the staccato rhythm at a relatively low velocity minimizes airway collapse. These staccato-like bursts of air against an open glottis are referred to as *huffing*. With this technique the patient is instructed to make the sound "huff, huff, huff" rapidly with the mouth and glottis open. **Huff coughing** is also referred to as FET.[15]

RULE OF THUMB Huff coughing or FET should be used to prevent small airway compression due to high pleural pressures during a forced cough in patients with COPD, CF, or bronchiectasis.

Forced Expiratory Technique

As stated above, FET consists of one or two forced expirations of middle to low lung volume without closure of the glottis, followed by a period of diaphragmatic breathing and relaxation.[16] The goal of this method is to help clear secretions with less change in pleural pressure and less likelihood of bronchiolar collapse. To help keep the glottis open during FET, the patient is taught to phonate or "huff" during expiration. The period of diaphragmatic breathing and relaxation following the forced expiration is essential in restoring lung volume and minimizing fatigue. Comparative clinical studies on the effectiveness of FET have shown favorable results. The technique is particularly useful in patients prone to airway collapse during normal coughing, such as patients with COPD, CF, or bronchiectasis.[17,18]

Manual Assisted Cough

Patients with neuromuscular conditions present a special challenge in cough management. These patients typically are unable to generate the forceful expulsion needed to move secretions toward the trachea.[11] If this problem results in retained secretions, there are only three options: (1) placement of an artificial airway and removal of secretions by suctioning (see Chapter 37), (2) manually assisted cough, and/or (3) MIE.

Manually assisted cough (quad—cough) is an external application of pressure to the thoracic cage or epigastric region, coordinated with a forced exhalation. In this technique, the patient takes as deep an inspiration as possible, assisted as needed by the application of positive pressure using a self-inflating manual resuscitation bag or ventilator. At the end of the patient's inspiration, the RT exerts pressure under the diaphragm (lateral costal margins or epigastrium) abruptly. This pressure increases the force of compression throughout expiration; this mimics the normal cough mechanism by generating an increase in the velocity of the expired air and may be helpful in moving secretions toward the trachea, where they can be removed by suctioning. Assisted cough with pressure to the lateral costal margins is contraindicated in patients with osteoporosis or flail chest. Assisted cough using epigastric pressure is contraindicated in unconscious patients with unprotected airways, in pregnant women, and in patients with acute abdominal pathology, an abdominal aortic aneurysm, or a hiatal hernia.

Active Cycle of Breathing Technique

To emphasize that FET should include breathing exercises, the originators of this technique modified the procedure and renamed it the **active cycle of breathing technique (ACBT)**. ACBT consists of repeated cycles of breathing control, thoracic expansion, and FET (Box 44.6). *Breathing control* involves gentle diaphragmatic breathing at normal tidal volumes for 5 to 10 seconds with relaxation of the upper chest and shoulders. This phase is intended to help prevent bronchospasm. The thoracic expansion exercises involve deep inhalation, approaching vital capacity, with relaxed exhalation, which may be accompanied by percussion, vibration, or compression. The *thoracic expansion* phase is designed to help loosen secretions, improve the distribution of ventilation, and provide the volume needed for FET. The subsequent FET moves secretions into the central airways. Postoperative patients may require splinting at the thoracic or abdominal incision site. Although ACBT can be performed in the sitting position, it is most beneficial when combined with PD. When ACBT is compared with similar methods of secretion clearance, studies indicate that ACBT can provide comparable results in terms of both sputum production and distribution of ventilation.[2,19] ACBT is not useful with young children (<2 years old) or critically ill patients. Caution should be taken in patients with reactive airways during ACBT.

BOX 44.6 Active Cycle of Breathing Technique Sequence

1. Relaxation and breathing control
2. Three or four thoracic expansion exercises
3. Relaxation and breathing control
4. Repeat three to four thoracic expansion exercises
5. Repeat relaxation and breathing control
6. Perform one or two forced expiratory techniques (huffs)
7. Repeat relaxation and breathing control

MINI CLINI

Modifications to Directed Cough

Problem

A patient who has been diagnosed with ALS who has been attending your multidisciplinary clinic for the last few years returns for a follow-up visit. The patient states that she has noticed that her cough is not as powerful as it has been and that she is "winded" when walking distances. The RT assesses the patient and finds: pulse rate of 80, respiratory rate of 24, and breath sounds of scattered wet crackles in both lungs. The patient performs spirometry and maximum inspiratory pressure (MIP) and maximum expiratory pressure (MEP) maneuvers. Her forced vital capacity (FVC) is 70% of predicted; MIP is negative 50 cm H_2O and MEP is 55 cm H_2O sitting; and MIP is negative 40 cm H_2O and MEP is 40 cm H_2O supine. The therapist reviews the values from the previous visit 3 months earlier and finds FVC was 75% of predicted and MIP was a negative 65 cm H_2O and the MEP was 70 cm H_2O both sitting and supine.

Discussion

Based on this assessment, the patient's lung volumes and muscle strength have declined. She also has retained secretions and would benefit from ACT and possibly MIE to assist with secretion removal. The patient began HFCWC to mobilize these secretions and MIE to assist in expectorating the secretions. This therapy should take place at least twice a day.

Autogenic Drainage

Autogenic drainage (AD) is another modification of directed coughing, designed as an airway clearance mechanism that can be performed independently by trained patients.[18] During AD, the patient uses diaphragmatic breathing to mobilize secretions by varying lung volumes and expiratory airflow in three distinct phases (Fig. 44.6). For maximum benefit, the patient should be in the sitting position. Patients are taught to control their expiratory flows to prevent airway collapse while trying to achieve a

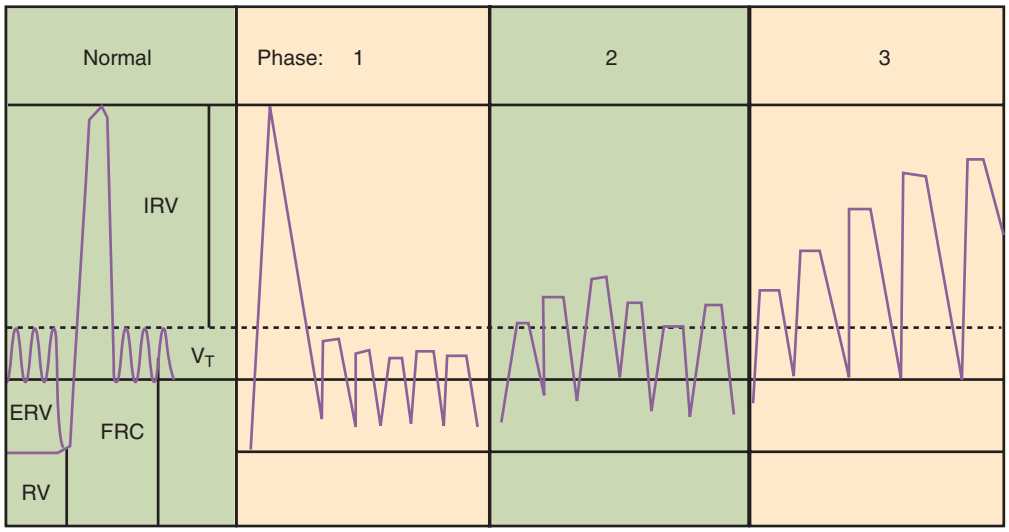

Fig. 44.6 Spirogram of lung volumes during three phases of autogenic drainage. Phase 1 involves a full inspiratory capacity maneuver, followed by breathing at low lung volumes. This phase is designed to "unstick" peripheral mucus. Phase 2 involves breathing at low-to-middle lung volumes to collect mucus in the middle airways. Phase 3 is the evacuation phase, in which mucus is readied for expulsion from the large airways. *IRV,* Inspiratory reserve volume; *ERV,* expiratory reserve volume; *FRC,* functional reserve volume; *RV,* residual volume. (Modified from Hardy KA, Anderson BD: Noninvasive clearance of airway secretions, *Respir Care Clin North Am* 2:323, 1996.)

mucous "rattle" rather than a wheeze. Coughing should be suppressed until all three breathing phases are completed.

In patients with CF, AD provides sputum clearance comparable to postural drainage percussion on a vibration (PDPV) but is less likely to produce O_2 desaturation. In addition, AD seems to be tolerated better by patients and has the advantage of being performed without assistance from a caregiver.[18]

Mechanical Insufflation-Exsufflation

The MIE device (also called *cough-assist device* or "coughlator") has gained popularity in its use to manage secretions in patients with certain neuromuscular disorders (Fig. 44.7).[11] The reason is growing evidence that MIE helps prevent respiratory complications in patients with NMD by helping them generate sufficient expiratory flow rates needed for effective secretion clearance.[1,11]

NMD patients who are not able to demonstrate a peak cough flow greater than 180 L/min or not able to generate an effective cough may benefit from MIE.[11,20] The American Association for Respiratory Care Clinical Practice Guideline for ACT recommends cough assist techniques when peak cough flows are less than 270 L/min in NMD patients.[1] The MIE devices have incorporated oscillation during inspiration or expiration to assist in mobilizing secretion The MIE delivers a positive pressure breath of 30 to 50 cm H_2O over a 1- to 3-second period via a face mask or artificial airway. The airway pressure is abruptly reversed to −30 to −50 cm H_2O and maintained for 2 to 3 seconds. Peak expiratory "cough" flows obtained with this device are in the normal range (mean 7.5 L/s); far better than can be achieved with manually assisted coughing. Expiratory flows remain high in the immediate post-exsufflation period, indicating that MIE does not promote airway collapse. Newer MIE devices have incorporated oscillation during inspiration or expiration to assist in mobilizing secretions.

Fig. 44.7 Mechanical insufflation-exsufflation device (mie, cough assist device).

A typical treatment session with the MIE consists of about five cycles (inspiration and expiration) followed by a period of normal spontaneous or assisted breathing (to avoid hyperventilation). This process is repeated five or more times until secretions are cleared from the airway and the patient is able to either suction or spit them out.

MIE delivered using an oronasal mask is effective, provided there is no fixed airway obstruction or glottic collapse during exsufflation that is present with bulbar ALS. For patients with severe restrictive disease and NMD who are not able to take deep breaths, insufflation pressures should be increased gradually based on the patient and their assessment to avoid chest wall muscle strains. Abdominal distension is infrequent and reduced by decreasing airway pressures during insufflation, not exsufflation.

Precautions should be observed using MIE with patients with known cardiac instability. It may be beneficial to monitor heart rate and O_2 saturation closely in these patients. MIE is contraindicated in patients with a history of bullous emphysema or previous barotrauma such as pneumothorax or pneumomediastinum.

Positive Airway Pressure Adjuncts

PAP adjuncts are used to help mobilize secretions and treat atelectasis. As adjuncts for airway clearance, these methods are usually paired with other airway clearance techniques such as directed cough. Indications for PAP adjuncts are like those listed early for all ACT. These devices elevate airway pressure and also may be beneficial in treating atelectasis. See Chapter 43 to review the use of these methods to treat atelectasis. Box 44.7 lists the contraindications and potential complications associated with PAP adjuncts. The following discussion will focus on the use of PAP devices for secretion clearance.

Positive Expiratory Pressure and Oscillating Positive Expiratory Pressure

PEP therapy involves active expiration against a fixed orifice flow resistor or variable orifice threshold resistor capable of developing pressures of 10 to 20 cm H_2O. Most fixed orifice devices allow adjustment of the orifice size to achieve a targeted PEP level. In theory, PEP therapy helps move secretions into the larger airways by providing a constant back-pressure that prevents airway collapse during expiration and the airway behind the mucus fills via collateral ventilation. A subsequent huff or FET maneuver may allow the patient to generate the flows needed to expel mucus from blocked airways.

PEP devices are available as PEP only or oscillating PEP (OPEP). OPEP devices (some refer to this as vibratory PEP) provide rapid fluctuations in airway pressure as the patient exhales. The frequency of the vibrations/oscillations has been reported to range from 10 to 30 Hz with amplitudes ranging from 20 to 100 torr at flows of 10 and 25 L/min.[21] Clinical studies of PEP and OPEP therapy showed that secretion clearance improved in hospitalized patients with CF,[2,22] and in COPD patients with secretion retention.[1] Generally, compared with other airway clearance methods (PDPV, AD, ACBT) in patients with CF, PEP therapy provides comparable mucociliary clearance, with the added advantages of being potentially self-administered and cost-effective.[1,15] Patients may prefer PEP over CPT.[15] PEP therapy

BOX 44.7 Positive Airway Pressure Adjuncts for Airway Clearance Therapy

Contraindications

Although no absolute contraindications to the use of positive airway pressure adjuncts have been reported, the following should be carefully evaluated before initiating therapy:

- Patients unable to tolerate increased work of breathing (acute asthma, chronic obstructive pulmonary disease)
- Intracranial pressure (ICP) greater than 20 mm Hg
- Hemodynamic instability
- Acute sinusitis
- Active hemoptysis
- Untreated pneumothorax
- Known or suspected tympanic membrane rupture or other middle ear pathology
- Recent facial, oral, or skull surgery or trauma
- Epistaxis
- Esophageal surgery
- Nausea

Hazards and Complications Include

- Pulmonary barotraumas
- Increased ICP
- Cardiovascular compromise (myocardial ischemia, decreased venous return)
- Skin breakdown and discomfort from mask
- Air swallowing, vomiting, and aspiration
- Claustrophobia
- Increased work of breathing that may lead to hypoventilation and hypercapnia

Excerpts from the American Association for Respiratory Care: Clinical practice guideline: use of PAP adjuncts to bronchial hygiene therapy. *Respir Care* 38:516, 1993.

cannot be used in young children (<3 years old). Patients also must be able to take a deep breath (>10 to 12 mL/kg) to generate adequate pressure, oscillations, and prolonged exhalations.

There are several available PEP and OPEP devices on the market, and manufacturer instructions on recommended application are included with each device (Fig. 44.8). Most of these are single-use commercial devices. A general clinical procedure for application of PEP therapy is presented in Box 44.8.[14] Regardless of the equipment used, it is important that actual intended PEP levels are reached, so monitoring and coaching of the patient for correct use is essential. There may be significant changes in the pressure amplitude and PEP with various devices as airway resistance increases, which warrants further clinical investigation regarding these findings clinical impact.[23]

RULE OF THUMB Patients must also be able to take a deep breath (>10–12 mL/kg predicted body weight [PBW]) to generate adequate pressure, oscillations, and prolonged exhalations during PEP therapy.

Common strategies for PEP therapy vary, with frequency determined by assessment of patient response. Studies provide conflicting results related to the amount of time and intervals of therapy sessions during acute exacerbations associated with CF and COPD. Two to four times daily are common frequencies used for PEP therapy. Aerosol drug therapy may be added to a PEP session using either an in-line handheld nebulizer or a metered dose inhaler attached to the one-way valve inlet of the

Fig. 44.8 Positive expiratory devices. (A) Flutter. (B) TheraPEP. (C) Acapella (Choice is used for a range of flows. Green is used for flows higher than 15 L/min. Blue is used for flows less than 15 L/min.). (D) Aerobika. (E) RC-Cornet.

BOX 44.8 Clinical Procedure for Positive Airway Pressure Therapy

1. Assess need for positive airway pressure (PAP) therapy and design a treatment program to accomplish treatment objectives.
   a. Bring equipment to bedside and provide initial therapy to patient, adjusting pressure settings to meet patient need.
   b. After initial patient treatment or training, communicate treatment plan to physician and nurse, and provide instruction to nursing staff if required.
2. Explain purpose of PAP therapy to patient; teach patient "huff" (directed cough procedure).
3. Instruct patient to:
   a. Sit comfortably.
   b. If using a mask, apply it tightly but comfortably over the nose and mouth. If mouthpiece is used, place lips firmly around it and breathe through mouth.
   c. Take in a breath that is larger than normal, but do not completely fill lungs.
   d. Exhale actively, but not forcefully, creating a PAP of 10–20 cm H_2O during exhalation (determined with manometer during initial therapy sessions). Length of inhalation should be approximately one-third of the total breathing cycle (inspiratory-to-expiratory ratio of 1 : 3 to 1 : 4).
   e. Perform 10–20 breaths.
   f. Remove the mask or mouthpiece and perform two or three "huff" coughs; rest as needed.
   g. Repeat above cycle four to eight times, not to exceed 20 min.
4. Evaluate patient for the ability to self-administer.
5. When appropriate, teach patient to self-administer. Observations on several occasions of proper technique, uncoached, should precede allowing the patient to self-administer without supervision.
6. When patients are also receiving bronchodilator aerosol, administer in conjunction with PAP therapy by placing a nebulizer in line with the PAP device.
7. When PAP device is visibly soiled, rinse it with sterile water and shake or air dry; leave within reach at patient's bedside in a clear plastic bag.
8. Send the PAP device (if single-patient use) home with the patient or discard it on discharge. If device is nondisposable, send in-house for high-level disinfection.
9. Document in the patient's medical record procedures performed (including device, settings used, pressure developed, number of breaths per treatment, and frequency), patient response to therapy, patient teaching provided, and patient ability to self-administer.

system. The combination of aerosol drug therapy with PEP seems to improve the efficacy of bronchodilator administration because of better distribution to the peripheral airways.[24] Some PEP devices can be modified to incorporate a mask for patients with ALS, toddlers, or stroke patients who are unable to use a mouthpiece.

High-frequency vibrations or **oscillations** refer to the rapid vibratory movement of small volumes of air back and forth in the respiratory tract. At frequencies of 12 to 25 Hz, these oscillations are thought to physically loosen secretions and move them toward the larger airways, which enhances airway clearance. There are two general approaches: airway application of oscillation methods such as OPEP discussed above or **high-frequency airway pressure devices (HFPAP) such as intrapulmonary percussive ventilation**, or external (chest wall) application referred to as **high-frequency chest wall compression (HFCWC)** devices.

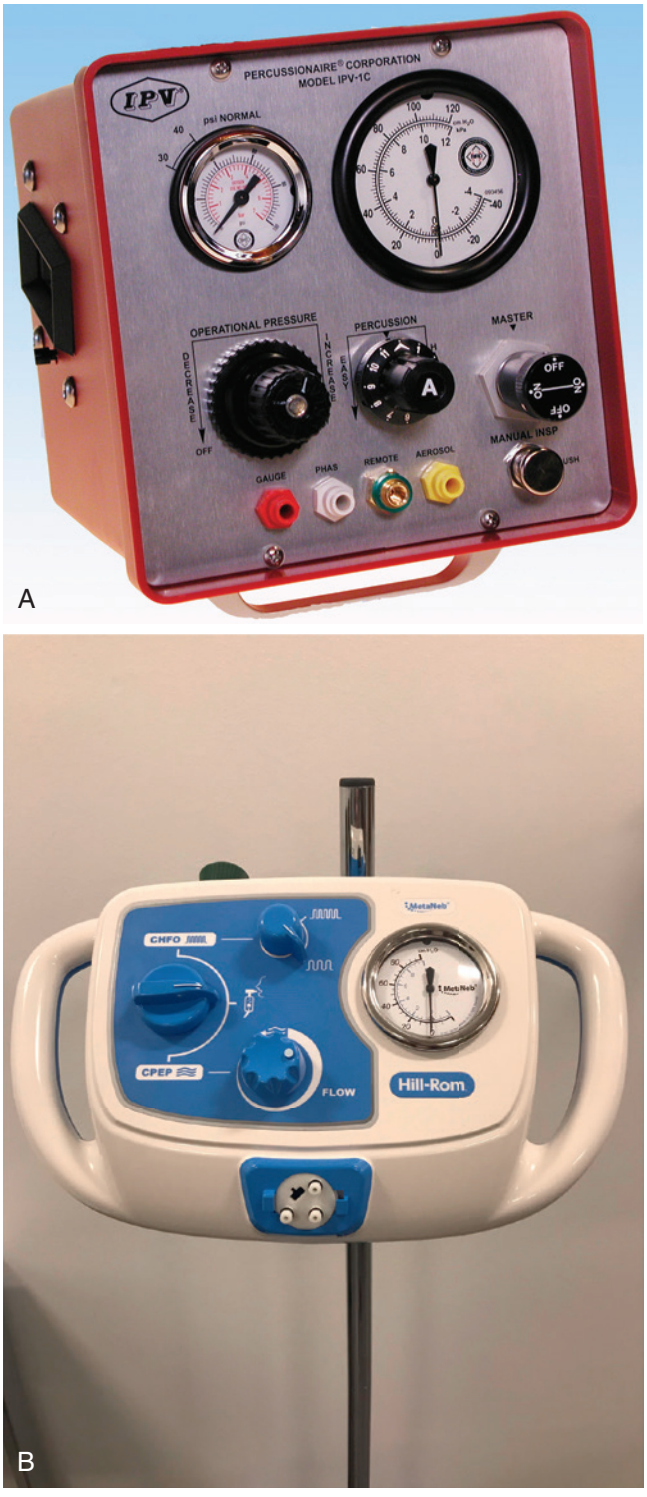

Fig. 44.9 (A) Intrapulmonary percussive ventilator, IPV. (Courtesy Percussionaire, SandPoint, Idaho.) B. MetaNeb. (Courtesy of HILL ROM.)

It is thought that the mucus moves because of the vibrations of the airways created when the oscillation frequency resembles the resonance frequency of the pulmonary system.[21,25]

High-Frequency Positive Airway Pressure Devices

HFPAP devices include the **intrapulmonary percussion ventilator (IPV)** and the **Metaneb** (Fig. 44.9). The IPV (Percussionaire

Corporation, Sandpoint, IN [some refer to this device as the Percussionator]) device (see Fig. 44.9A) was developed by Dr. Forest M. Bird in the late 1980s and it uses a pneumatic device to deliver a rapid series of pressurized gas minibursts at rates of 200 to 300 cycles per minute (1.7 to 5 Hz) to the airway.[26] During the percussive cycle, the patient can inhale and exhale through the device as this oscillating airway pressure is applied. This device also delivers aerosolized medication through its own nebulizer and relies on chest wall recoil or active patient exhalation. Previous research suggests that interpulmonary percussive ventilation is equivalent to other airway clearance strategies in enhancing sputum expectoration in patients with obstructive pulmonary diseases and pediatric patients with NMD.[4,27] The therapy is well tolerated by stable patients and may provide a more effective alternative for airway clearance in patients unable to take a deep inspiration. In a group of severe COPD patients receiving two treatments per day for 4 weeks, both IPV and HFCWC improved activities of daily living and pulmonary functions compared to the control group. IPV also significantly improved health status assessment and inflammatory cells in sputum compared to HFCWC.[28] Further studies are needed to determine the impact on healthcare utilization and hospital readmission.

Another HFPAP is the Metaneb device (Hill-Rom, Inc. Batesville, IN; Fig. 44.9B), which uses similar characteristics that provides a pneumatic form of chest physiotherapy. The Metaneb is able to deliver high-frequency rates, with oscillatory percussive breaths during inspiration and expiration, and resistance levels on exhalation. The Metaneb can deliver aerosol therapy during the lung expansion and secretion clearance cycles. The therapy lasts about 10 minutes alternating between the lung expansion and secretion clearance cycles depending on patient comfort. The percussion rate varies between 170 and 230 breaths/min.

Both Metaneb and IPV have venturi devices housed inside the device. The venturi devices create high-frequency percussions during inspiration and expiration, which result in a pressure gradient.[25] The pressure gradient creates an accelerated expiratory airflow and secretions move up into the larger airways for the patient to expel or are suctioned from an artificial airway.[25] In addition, hyperinflation occurs at the same time assisting the patient with a deeper breath, which improves cough effectiveness. These devices are used in the hospital setting. Clinical trials using both devices demonstrate they are effective at enhancing secretion removal.[1,2,22,25,27]

High-Frequency Chest Wall Compression

HFCWC devices are passive oscillatory devices. These devices use a two-part system: (1) a variable air-pulse generator, and (2) a nonstretch inflatable vest that wraps around the patient's entire torso. Examples of these devices are; Electromed—SmartVest; Hill Rom—The Vest; RespirTech—inCourage, and the AfflowVest (Fig. 44.10). Either one or two large-bore tubing(s) connect the vest to the air-pulse generator. Table 44.4 lists the devices, air-pulse waveforms, and hose configurations. The generator inflates and deflates the vest, creating pressure pulses against the thorax resulting in chest wall oscillations and moving secretions forward. The AfflowVest is battery operated, digitally programed and uses a technology that mimics hand CPT to mobilize secretions. HFCWC devices are used in hospital or home settings. The therapy is typically performed for a 30-minute session two to six times per day at oscillatory frequencies between 5 and 25 Hz. These therapy sessions depend on patient need and response. Clinical

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Using High-Frequency Positive Airway Pressure Devices

Problem

A 60-year-old postoperative patient with a 20 pack-year smoking history admits to the surgical intensive care unit following a laparoscopic procedure. The patient is currently receiving 4 L/min nasal cannula with a pulse O_2 saturation of 92%. Their breath sounds are bilateral course rales that do not clear when the patient coughs. Their inspiratory vital capacity is only 550 mL which is 7.9 mL/kg of their predicted body weight. The critical care physician asks that you recommend an effective ACT.

Discussion

Based on this assessment, the patient's lung volumes are too low to effectively perform vibratory PEP therapy. IPV would assist in moving the secretions into the larger airway and increasing the patient's lung volume. This therapy should be every 4 h with the patient sitting up in the bed or chair. Fill the nebulizer with 15 mL of normal saline. Rotate the frequency knob to the easy position by turning this knob counterclockwise until it stops. Set the operating pressure at 20 psi to start. Have the patient breathe on the device through the mouthpiece. Push the button on the manual remote switch located on the nebulizer. Encourage the patient to slowly inhale and exhale through the device as it percusses. They also may need to splint their cheeks to avoid air and pressure loss. If the chest wall of the patient is not wiggling or visibly moving the operating pressure should be slowly increased to approximately 30 psi. Every few minutes the frequency can be increased or changed from easy to hard as tolerated by the patient. Provide breaks in this therapy to instruct the patient on a directed cough. Therapy should last approximately 15 min. The patient should be observed for signs of syncope or light headedness, changes in heart rate or breath sounds, and oxygen saturation.

Fig. 44.10 The Vest Airway Clearance System for high-frequency chest wall oscillation. (Copyright 2011 Hill-Rom Services, Inc., Batesville, IN. Reprinted with permission. All rights reserved.)

TABLE 44.4 High-Frequency Chest Wall Oscillator Device Comparison

Company	Device	Air Pulse	Hose Configuration
Hill Rom	Vest	Sine waveform	Double hose
Electromed	SmartVest	Sine waveform	Single hose
RespirTech	InCourage	Triangle waveform	Double hose
AfflowVest	AfflowVest	Direct Dynamic Oscillation	None—battery operated

trials with HFCWC have reported better or equivalent secretions clearance compared to other ACTs in CF patients.[17,18,22,29] Studies in other populations have shown some improvement, as measured by patient perception, increased compliance, or outcome.[1,11,15]

The Biphasic Cuirass Ventilation (BCV) device is an alternative to the vest devices. It may be used to provide noninvasive ventilation and/or cough assist. It uses a chest cuirass or shell that encompasses the anterior chest wall. The shell is connected to the generator that controls both phases of the respiratory cycle. The chest wall will expand when the negative pressure is applied. This device is capable of a frequency range between 1 and 999 oscillations per minute, I:E ratios of 1:6 and 6:1, and inspiratory and expiratory pressures of −70 to 70 cm H_2O. The recommended application is two sets of cycles that include a few minutes at a frequency between 600 and 700 at an I:E of 1:1, followed by a higher frequency at an inverse I:E ratio.[25]

Exercise, Mobilization, and Physical Activity

Immobility is a major factor contributing to complications in chronic disease and hospitalized patients. Early mobilization is recommended to reduce complications in hospitalized patients and is recommended as adjunctive therapy along with another ACT in CF to aid airway clearance and overall health benefits.[1,30] Physical activity may also improve lung function, exercise tolerance, quality of life, and adherence to therapy. For more on the use of exercise in ambulatory patients with severe lung disease see Chapter 56.

SELECTING AIRWAY CLEARANCE TECHNIQUES

Selection Factors

Box 44.9 specifies many factors that should be considered when selecting an airway clearance strategy. The correct application and patient motivation to perform the ACT are critical components regardless of the setting. No ACT is successful if it is abandoned by the patient. Likewise, no routine strategy is likely to be followed without results. In this regard, increased sputum production, less shortness of breath, and perhaps improved physical activity are a few outcomes that can be used to motivate patients and gain their ongoing cooperation. Age, disease process, available resources, and patient preference often affect the choice of ACT. Patient and caregiver goals for treatment should be discussed jointly, with the intent of choosing the method that best fits the patient's goals and lifestyle. The RT's skill and patience in teaching the ACT is also a factor in determining the success of the therapy. The patient's learning needs and barriers to learning also should be considered. Because patients reject methods that are fatiguing, this should be considered in method selection. In addition, the patient's disease either may suggest the best approach or may impose certain limitations that preclude using a particular method. Cost is a critical factor in selecting all treatment strategies. There are multiple inexpensive options that are effective. Patient or caregiver education also plays an important role in the effectiveness of the therapy (see Chapter 55).

BOX 44.9 Key Factors in Selecting an Airway Clearance Strategy

- Patient's motivation
- Patient's goals
- Patient's ability to comprehend—literacy and cognition levels
- Patient's physical limitations
- Physician/caregiver goals
- Effectiveness of technique
- Ease of learning and teaching
- Skill of therapists
- Patient fatigue associated, or work required to use device
- Need for assistance to use the equipment
- Limitations of technique based on disease type and severity
- Costs (direct and indirect)
- Desirability of combining methods

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Recommending Airway Clearance Strategies

Problem

The RT is asked to evaluate and recommend an appropriate ACT regimen for a 7-year-old active girl with CF who is being cared for in her home by elderly grandparents.

Discussion

Generally, appropriate secretion clearance strategies for this patient include exercise, vibratory PEP, CPT, ACBT, high-frequency chest wall oscillation (HFCWO), and IPV. CPT would be difficult to implement in this patient's home setting (elderly caregivers), so emphasis should be placed on either vibratory PEP with ACBT or HFCWO and FET. An exercise plan should also be incorporated into the overall strategy. Dietary and medication considerations are also important.

Outcome Assessment

Specific outcome criteria indicating a positive response to ACT are listed in Box 44.10. Generally, achievement of one or more of these outcomes indicates that the therapy is meeting its objectives and should be continued. Not all criteria are required to justify continuing ACT. Because secretion clearance is affected by patient hydration, the RT may need to wait for at least 24 hours after optimal systemic hydration has been achieved to see any evidence of increased sputum production. In the interim, bland aerosol therapy may be useful for sputum induction and mobilizing secretions.

Breath sounds may seem to "worsen" after therapy by changing from diminished breath sounds before therapy to coarse crackles. This change is due to the loosening of secretions and their movement into the larger airways, an intended purpose of the therapy. These coarse crackles should clear after coughing

BOX 44.10 Assessment Outcomes After Airway Clearance Therapy

The following items represent individual criteria that indicate a positive response to therapy (and support continuation of therapy). Not all criteria are required to justify continuation of therapy (e.g., a ventilated patient may not have sputum production >30 mL/day but has improvement in breath sounds, chest radiograph, or increased compliance or decreased resistance).

- Change in sputum production
- Change in breath sounds of lung fields being drained
- Patient subjective response to therapy
- Change in vital signs
- Change in chest radiograph
- Change in arterial blood gas values or O_2 saturation
- Change in ventilator variables

Excerpts from the American Association for Respiratory Care: Clinical practice guideline: postural drainage therapy. *Respir Care* 36:1418, 1991.

or suctioning. In addition, the patient's chest x-ray may significantly improve after receiving a few ACTs.

In terms of the patient's subjective response to therapy, the patient should be encouraged to report any pain, discomfort, shortness of breath, dizziness, or nausea during or after therapy. Any of these adverse effects may be grounds for either modifying or stopping treatment. Patient reports of easier clearance or increased volume of secretions after therapy support continuing therapy.

Based on assessment results, ACT orders should be reevaluated for need at least every 2 to 3 days for hospitalized patients. Patients receiving home care should be reevaluated at least every 3 months or whenever their status changes.

Documentation and Follow-Up

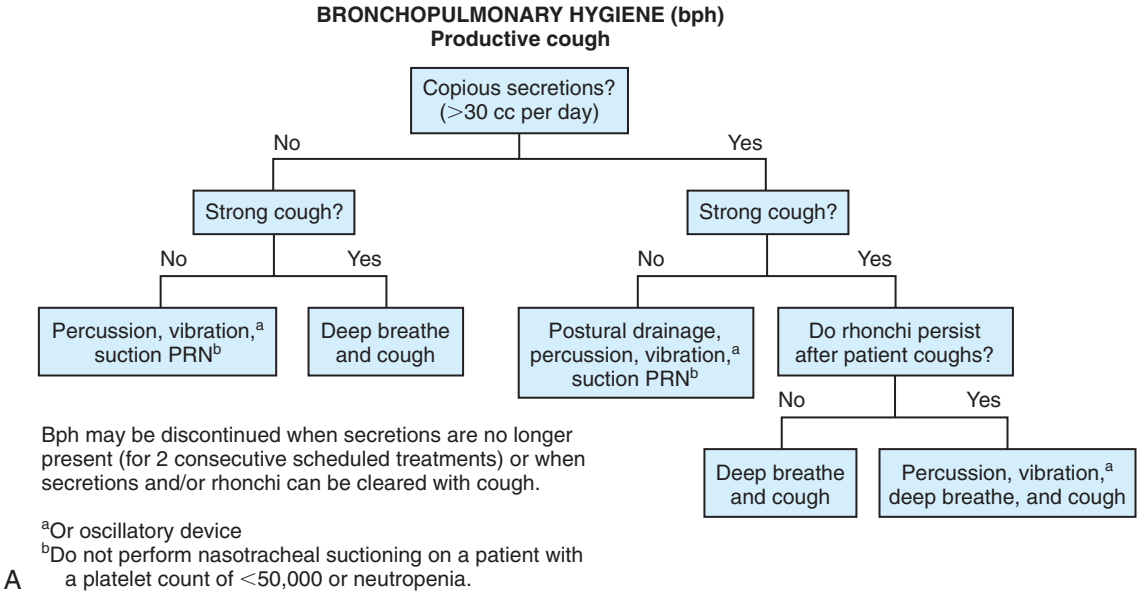
The chart entry for ACT should include the device, the therapy provided, the positions used, the time of treatment, patient tolerance, pre– and post–vital signs and breath sounds, subjective and objective indicators of treatment effectiveness (including amount, color, and consistency of sputum produced), and any adverse effects observed.

Protocol-Based Airway Clearance

Numerous RT-driven protocols have been published for ACT. All of these protocols involve rigorous assessment of the patient both to establish preliminary need and to determine continuation of or modification in therapy. Fig. 44.11 is an algorithm used in one such protocol. Changes in therapy occur throughout and are based on the patient's response and the RT's evaluation.

SUMMARY CHECKLIST

- Normal airway clearance requires a patent airway, a functional mucociliary escalator, and an effective cough.
- Patients with copious secretions (20 to 30 mL/day) or inability to mobilize and expectorate secretions may benefit from ACT.
- The primary goal of ACT is to help mobilize and remove retained secretions, improve gas exchange, and reduce the work of breathing.
- Retained secretions can increase the work of breathing, cause air trapping, worsen $\dot{V}/\dot{Q}$ imbalance, promote atelectasis and shunting, and increase the incidence of infection.
- Disorders associated with abnormal secretion clearance include foreign bodies, tumors, congenital or acquired thoracic anomalies, asthma, chronic bronchitis, CF, bronchiectasis, and acute infections.
- Musculoskeletal and neurologic disorders can impair coughing and lead to mucous plugging, airway obstruction, and atelectasis.
- Both mechanical and treatment factors impair mucociliary clearance in intubated patients.
- Clinical signs consistent with retained secretions include ineffective cough, absent or increased sputum production, a labored breathing pattern, abnormal or adventitious lung sounds (e.g., coarse crackles, decreased breath sounds), tachypnea, tachycardia, and fever.
- Turning promotes lung expansion, improves oxygenation, and prevents retention of secretions.
- Postural drainage involves placing the segmental bronchus to be drained in a vertical position relative to gravity and holding the position for 3 to 15 minutes.
- Cough methods must be modified in surgical patients, patients with COPD, and patients with neuromuscular disorders.
- FET, or huff cough, consists of one or two forced expirations of middle to low lung volume without closure of the glottis, followed by a period of diaphragmatic breathing and relaxation.
- ACBT consists of repeated cycles of breathing control, thoracic expansion, and FET.
- During AD, the patient uses diaphragmatic breathing to mobilize secretions by varying lung volumes and expiratory airflow in three distinct phases.
- MIE involves delivery of a positive pressure breath followed by the quick application of negative pressure; positive expiratory flows exceed flows developed by manually assisted coughing.
- PEP or vibratory therapy is a self-administered clearance technique involving active expiration against a variable-flow resistance, followed by FET; patients frequently prefer PEP over other methods.
- At high frequencies (12 to 25 Hz), airway oscillations enhance cough clearance of secretions.
- Airway oscillations can be created externally (HFCWC) or at the airway opening (flutter valve, Accapella, Aerobika, IPV, Metaneb).
- Adding physical activity to mobilization and coughing enhances mucus clearance, improves overall aeration and $\dot{V}/\dot{Q}$ matching, and improves pulmonary function.
- If performed correctly, no ACT has been proven better than another.
- Numerous factors must be considered in trying to select the best airway clearance strategy for a given patient.
- Outcomes of therapy should include subjective and objective measures.
- ACT protocols are beneficial to patient and practitioner.



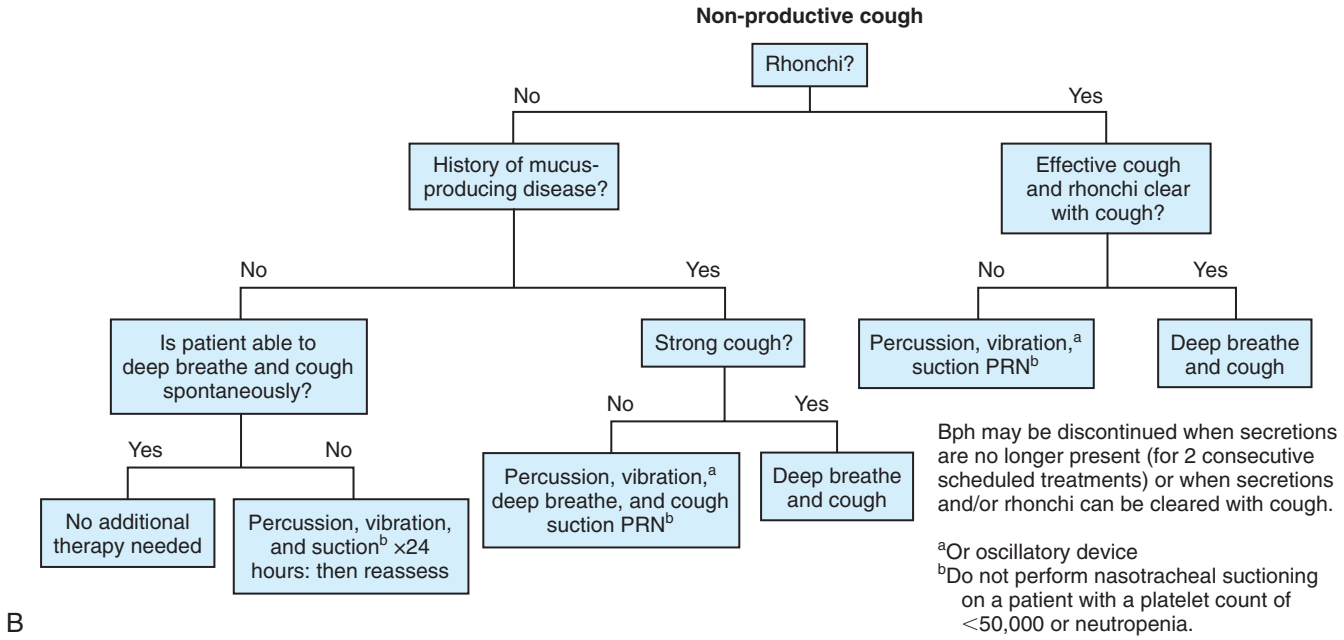


Fig. 44.11 Example of algorithm underlying an airway clearance protocol. (A) An algorithm used in patients with productive cough. (B) An algorithm used in patients with a nonproductive cough. (Bronchial Hygiene Algorithm from the Cleveland Clinic Respiratory Therapy Consult Service Handbook. Courtesy of the Cleveland Clinic.)

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45

Respiratory Failure and the Need for Ventilatory Support

Loutfi S. Aboussouan

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Define acute respiratory failure.
- Differentiate between hypoxemic respiratory failure (type I) and hypercapnic respiratory failure (type II).
- Discuss the causes of acute respiratory failure.
- Discuss the differences between chronic respiratory failure and acute-on-chronic respiratory failure.
- Identify the complications of respiratory failure.
- Discuss the indications for ventilatory support.
- Discuss general management principles of hypoxemic and hypercapnic respiratory failure.
- Discuss indications for noninvasive ventilation.

CHAPTER OUTLINE

KEY TERMS

auto-PEEP
barotrauma
dynamic hyperinflation
hypercapnic respiratory failure (type II)
hypoxemic respiratory failure (type I)
maximum expiratory pressure (MEP)
maximum inspiratory pressure (MIP)
maximum voluntary ventilation (MVV)
muscle fatigue
noninvasive ventilation (NIV)
orthodeoxia
platypnea
positive end-expiratory pressure (PEEP)
respiratory alternans
sniff nasal inspiratory pressure
pressure-time index
work of breathing

Respiratory failure is a clinical problem that all respiratory care practitioners must be skilled at identifying, assessing, and treating. The hospital mortality of patients requiring intensive care unit (ICU) admission with respiratory failure significantly decreased from 43.5% in 1993 to 32.2% in 2009.[1] The need for oxygen (O_2) delivery, mechanical ventilation, and other modalities in the management of such patients makes the respiratory therapist's (RT) role indispensable.

Respiratory failure is the "inability to maintain either the normal delivery of O_2 to the tissues or the normal removal of carbon dioxide (CO_2) from the tissues"[2] and often results from an imbalance between respiratory workload and ventilatory strength or endurance. Criteria based on arterial blood gases (ABGs) were established by Campbell who categorized respiratory failure into hypoxemia without hypercapnia, and hypoxemia with hypercapnia.[3] Generally, *failure* is defined as arterial partial pressure of oxygen (PaO_2) less than 60 mm Hg (also referred to as **hypoxemic** or **type I respiratory failure**), alveolar partial pressure of carbon dioxide ($PaCO_2$) 50 mm Hg or greater (**hypercapnic** or **type II respiratory failure**), or both, while breathing room air at sea level. Respiratory failure can be an acute or a chronic process. Hypercapnic respiratory failure is also known as *ventilatory failure* or "bellows" failure. Patients with baseline acid–base derangement (e.g., chronic obstructive pulmonary disease [COPD], neuromuscular disease, thoracic or parenchymal restrictive lung disease) may be chronically hypercapnic and in chronic ventilatory failure. Although ABG analysis is helpful in distinguishing hypoxemic (type I) and hypercapnic (type II) respiratory failure, many patients in acute respiratory failure develop both hypoxemia and hypercapnia.

HYPOXEMIC RESPIRATORY FAILURE (TYPE I)

The primary causes of hypoxemia are the following:

- Ventilation/perfusion ($\dot{V}/\dot{Q}$) mismatch
- Shunt
- Alveolar hypoventilation
- Diffusion impairment
- Perfusion/diffusion impairment
- Decreased inspired O_2
- Venous admixture or anatomic shunt

These entities are briefly discussed here and are discussed in more detail in Chapters 11 and 12.

Ventilation/Perfusion Mismatch

There are regions in healthy lungs where ventilation and perfusion are not evenly matched, so it seems logical that this is the most common cause of hypoxemia. West described a high $\dot{V}/\dot{Q}$ ratio at the apex of the lungs and a low ratio at the bases.[4] This concept can be oversimplified as there being more air than blood at the apices and more blood than air at the bases.

Pathologic $\dot{V}/\dot{Q}$ mismatch occurs when disease disrupts this balance, and hypoxemia results (Fig. 45.1A). Most commonly, areas of low $\dot{V}/\dot{Q}$ ratio are seen in which ventilation is decreased despite adequate blood flow. Obstructive lung diseases are frequent causes. The bronchospasm, mucous plugging, inflammation, and premature airway closure that signal asthmatic or emphysematous exacerbations worsen ventilation and create $\dot{V}/\dot{Q}$ mismatch. Infection, heart failure, and inhalation injury may lead to partially collapsed or fluid-filled alveoli, also resulting in decreased ventilation and reduced blood O_2 levels.

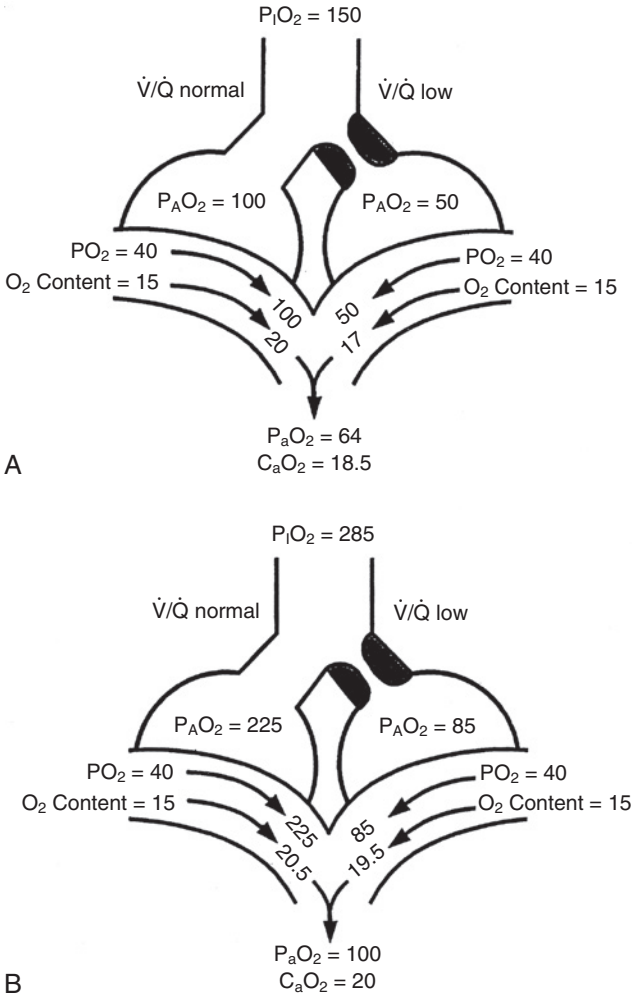

Fig. 45.1 Hypoxemia caused by $\dot{V}/\dot{Q}$ mismatch showing the effect of supplemental O_2. $\dot{V}/\dot{Q}$ is normal on the left side of each idealized lung unit and low on the right. Only O_2 exchange is shown, and P(A – a) O_2 is assumed to be zero. (A) With room air, not enough O_2 reaches the poorly ventilated alveolus to saturate its capillary blood fully. (B) With 40% O_2, PaO_2 in this alveolus is increased enough to make capillary PO_2 nearly normal. PaO_2 in the mixed blood from the two capillaries is determined by the average of the O_2 contents of the two streams of blood, not by the PaO_2 values. (Modified from Pierson DJ, Kacmarek RM: *Foundations of respiratory care*, New York, 1992, Churchill Livingstone.)

Clinical Presentation

Because patients present with hypoxemia, the initial goal is always to treat the low PaO_2 or SpO_2 (arterial O_2 saturation by pulse oximeter). $\dot{V}/\dot{Q}$ mismatch responds to supplemental O_2 (see Fig. 45.1B). Hypoxemia commonly causes dyspnea, tachycardia (rapid heart rate), and tachypnea (rapid breathing rate), but these are very nonspecific findings. However, patient observation is extremely valuable. The use of accessory muscles of respiration (scalene, pectoralis major, and sternomastoid) is an important

sign that normal diaphragmatic inspiration is inadequate. In an elderly, cachectic, or barrel-chested individual who is leaning forward on his or her arms, COPD is the likely diagnosis. Nasal flaring may be present. Lower extremity edema suggests cardiac failure as the cause of hypoxemia. Cyanosis may be peripheral and primarily due to decreased blood flow. Central cyanosis, seen most easily as a bluish tint around the lips, occurs when greater than 5 g/dL of unsaturated hemoglobin is present. This finding is more common in patients with polycythemia (an increase in red blood cells) but may be subject to wide observer variability. More severe hypoxemia can lead to significant central nervous system (CNS) dysfunction, ranging from irritability to confusion to coma.

Auscultation and percussion are very useful when added to patient observation. Bilateral wheezing, especially in a young patient in respiratory distress, often identifies the bronchospasm of asthma. Upper airway disease or fluid-filled airways may also result in wheezing. Breath sounds that are diminished bilaterally with increased resonance on percussion are common in emphysema. Unilateral abnormalities are significant. Wheezing in one lung may suggest an endobronchial lesion, whereas the absence of breath sounds and decreased resonance on one side of the chest may reflect collapse, infection, edema, or effusion as potential causes of $\dot{V}/\dot{Q}$ mismatch. Discordant exam findings with increased resonance on percussion and decreased breath sounds on the same side may suggest a pneumothorax. Unilateral crackles and decreased resonance on percussion generally indicate an alveolar filling process (mass, infection, fluid).

Radiographically, $\dot{V}/\dot{Q}$ mismatch can manifest as a "black" radiograph, with large or hyperinflated lungs as in the case of obstructive disease. A "white" chest radiograph is evident when alveoli are partially occluded. The "blackness" or "whiteness" of the lung fields on the plain chest radiograph has important diagnostic value in assessing a patient with acute respiratory failure.

Shunt

Shunt is an extreme version of $\dot{V}/\dot{Q}$ mismatch in which there is no ventilation to match perfusion ($\dot{V}/\dot{Q} = 0$). Two types of shunt can occur: anatomic and physiologic. About 2% to 3% of the blood supply is shunted via the bronchial and thebesian veins that feed the lungs and heart; this is normal anatomic shunt. Pathologic anatomic shunt occurs as a result of right-to-left blood flow through cardiac openings (e.g., atrial or ventricular septal defects) or in pulmonary arteriovenous malformations. Physiologic shunt accompanies $\dot{V}/\dot{Q}$ mismatch and leads to hypoxemia when alveoli collapse or are filled with fluid or exudate. Common etiologies of physiologic shunting include atelectasis, pulmonary edema, and pneumonia. Shunt does not respond to supplemental O_2 when the gas-exchange unit (the alveolus) is not open (Fig. 45.2A) or when the blood does not come into contact with ventilated areas of the lung (anatomic shunt).

Clinical Presentation

The clinical presentation and patient observations in shunting are very similar in many ways to the presentation of $\dot{V}/\dot{Q}$ mismatch. Bilateral or unilateral crackles are common owing to the alveolar filling process. Unilateral absence of breath sounds may indicate significant collapse, mass, or effusion; these conditions require treatment before oxygenation can improve. The parenchyma on chest radiograph may be "white" with physiologic causes of shunting as may occur in the acute respiratory distress syndrome (ARDS). Anatomic shunts may be harder to diagnose as the chest x-ray may appear normal, but can be diagnosed by using 100% O_2 breathing techniques, contrast-enhanced echocardiography, macroaggregated albumin scanning, or pulmonary angiography.[5] Shunt is differentiated from $\dot{V}/\dot{Q}$ mismatch by the lack of increase in PO_2 as fractional inspired oxygen (FiO_2) is increased (see Fig. 45.2B).

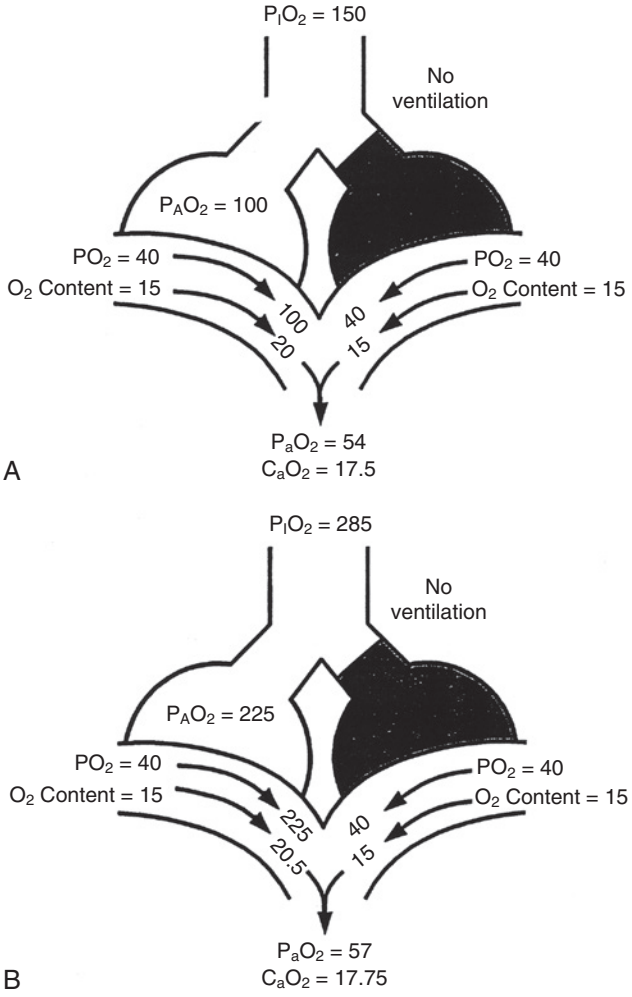

Fig. 45.2 Alveolar-capillary diagram of intrapulmonary (capillary) shunting showing why supplemental O_2 fails to correct hypoxemia. Only O_2 exchange is shown, and $P(A - a)O_2$ is assumed to be zero. (A) With room air, although blood leaving the normal alveolar-capillary unit is normally saturated, blood passing the capillary on the right "sees" no O_2 because its alveolus is unventilated, and it leaves the unit unsaturated. When the two streams of blood mix, the resulting PaO_2 is determined by the average of the O_2 contents, not by the PO_2 values. (B) Addition of 40% O_2 fails to correct the hypoxemia because O_2 content is not significantly increased in the normal unit, and capillary blood in the unventilated unit still "sees" no O_2. Even 100% O_2 could not completely reverse the oxygenation defect in this example; this is very different from the effect with low $\dot{V}/\dot{Q}$ as illustrated in Fig. 45.1. (Modified from Pierson DJ, Kacmarek RM: *Foundations of respiratory care*, New York, 1992, Churchill Livingstone.)

Alveolar Hypoventilation

Alveolar hypoventilation is discussed subsequently in the section on hypercapnic respiratory failure (type II).

Diffusion Impairment

Diffusion refers to movement of gas across the alveolar-capillary membrane along a pressure gradient. Although diffusion impairment is rarely a cause of significant hypoxemia at rest, its effects become more pronounced with exercise, which limits the time for gas exchange. Diffusion impairment in interstitial lung disease (e.g., pulmonary fibrosis, asbestosis, sarcoidosis), in which the thickening and scarring of the interstitium prevent normal gas exchange, may contribute 19% of the alveolar-arterial O_2 gradient at rest, and up to 40% during exercise).[6] Emphysema, with its alveolar destruction, also has decreased transfer of O_2 and CO_2 between the alveolus and the capillary. The reduced ventilation in both diseases implies that $\dot{V}/\dot{Q}$ mismatch also plays a role in the resulting hypoxemia.

Pulmonary vascular abnormalities also can lead to diffusion impairment. Anemia, pulmonary hypertension, and pulmonary embolus all may reduce capillary blood flow, resulting in diminished gas transfer.

Clinical Presentation

Signs and symptoms are related to the specific disease. Interstitial lung disease is a possible cause of a dyspneic patient with a dry cough and fine, basilar crackles on auscultation, and clubbing of the nail beds. Rheumatologic manifestations may be present if the underlying cause is a connective tissue disorder. Joint abnormalities, Raynaud disease, and *telangiectasia* (a vascular lesion formed by dilation of a group of small blood vessels) may be observed. The pallor of anemia can be a clue to poor gas exchange, although chronic hypoxemia may lead to polycythemia and possibly cyanosis. Pulmonary hypertension may cause signs of right-sided heart failure, such as edema, jugular venous distension, and a louder pulmonary component of the second heart sound.

Diffusion impairment can also manifest with multiple, varied radiographic forms. The hyperinflated, dark chest x-ray of emphysema was mentioned earlier. Interstitial disease may manifest with reduced lung volumes with interstitial markings. An enlarged right ventricle and pulmonary arteries may be evident in secondary pulmonary hypertension.

Perfusion/Diffusion Impairment

Perfusion/diffusion impairment is a cause of hypoxemia in individuals with liver disease complicated by the hepatopulmonary syndrome.[7] In this condition, right-to-left intracardiac shunt combines with dilated pulmonary capillaries, resulting in impaired gas exchange because the normal alveolar partial pressures of O_2 may be insufficient to drive the O_2 molecules to the center of the dilated pulmonary vasculature. Cirrhosis is the most common liver disease associated with the hepatopulmonary syndrome, and portal hypertension is usually present. Although shunt is a component of the syndrome, significant supplemental O_2 can overcome the hypoxemia, so this is commonly called a *perfusion/diffusion defect.*

Clinical Presentation

Obvious signs of liver disease (e.g., ascites, jaundice, and spider nevi) may or may not be present. Digital clubbing can occur in hepatopulmonary syndrome. ***Platypnea***, which is the sensation of dyspnea when moving to the upright position from the supine position, may be a patient complaint. **Orthodeoxia,** an actual decrease in the measured O_2 level when standing, may parallel this subjective sensation.

Decreased Inspired Oxygen

Also clinically uncommon, hypoxemia may develop when the inspired O_2 is less than usual. The most common situation in which this occurs is at high altitude, where hypoxemia occurs not because of a decrease in the fraction of O_2 in the ambient air (which remains 21%) but from barometric pressure decreases, which results in a decrease in the partial pressure of inspired O_2. Even with pressurized airplanes, air travelers with chronic hypoxemia may still need supplemental O_2 because the altitude equivalent inside a commercial airliner may be up to 8000 feet.[8] Similarly, mountain climbers sometimes require O_2 masks. Cases of patient-O_2 disconnects and delivery of an incorrect gas source are also included in this category.

Inspired O_2 less than 21% can also be used diagnostically and therapeutically. The Hypoxia Altitude Simulation Test replicates inspired partial pressure of O_2 (PiO_2) during air travel by asking the potential traveler to inhale a hypoxic mixture. Inhaling at FiO_2 of 15% replicates the PiO_2 found at an altitude of 8000 feet (108 mm Hg), and so is useful to assess whether the patient may require supplemental O_2 during commercial air travel. For a lower altitude of 5400 feet, an equivalent FiO_2 of 17% can be calculated.[8] Infants with certain cyanotic congenital heart defects (e.g., hypoplastic left ventricle) may benefit from FiO_2 below room air level. In the preoperative state, low FiO_2 helps prevent pulmonary dilation and the excessive pulmonary blood flow, which could flood the lungs.

Clinical Presentation

The signs and symptoms of hypoxemia may be present, with the cause related to the patient environment such as the altitude.

Venous Admixture

A decrease in mixed venous O_2 increases the gradient by which O_2 needs to be stepped up as it passes through the lungs and can contribute to the development of hypoxemia. Congestive heart failure with low cardiac output is the most common cause of low mixed venous O_2, owing to increased peripheral extraction of O_2. Other factors may contribute to hypoxemia, such as $\dot{V}/\dot{Q}$ mismatch and shunting.[9] Other causes include low hemoglobin concentration and increased O_2 consumption. A low mixed venous O_2 may have a significant effect on the final arterial O_2 tension when lung disease is present.

Clinical Presentation

Signs and symptoms of congestive heart failure (e.g., rales on chest auscultation, pedal edema, etc.) or underlying lung disease, or both, may be present.

Differentiating the Causes of Acute Hypoxemic Respiratory Failure

It is important to recognize the physiologic basis of each of the three main causes of hypoxemic respiratory failure (hypoventilation, $\dot{V}/\dot{Q}$ mismatch, and shunt). Hypoventilation differs from the other two causes in manifesting with a normal alveolar-to-arterial PO_2 difference [$P(A-a)O_2$] indicating normal lung parenchyma (Table 45.1). A clinical determination of this difference is made by subtracting PaO_2 from PAO_2 (partial pressure of alveolar O_2) derived from the alveolar air equation:

$$PAO_2 = FiO_2(P_B - P_{H_2O}) - PaCO_2/R$$

where P_B is barometric pressure, P_{H_2O} is water vapor tension, and R is the respiratory exchange ratio (0.8).

The $P(A-a)O_2$ ranges from 10 mm Hg in young patients to approximately 25 mm Hg in elderly patients while breathing room air (see the accompanying Rule of Thumb). In patients with hypoxemia caused by hypoventilation, treatment can be focused on improving ventilation because the hypoxemia is purely a result of alveolar displacement of O_2 by elevated CO_2.

RULE OF THUMB The mean alveolar-to-arterial difference [$P(A-a)O_2$] in PO_2 increases slightly with age and can be estimated with the following equation:

$$\text{Mean age–specific } P(A-a)O_2 = (\text{age}/4) + 4$$

Example: A 76-year-old person living at sea level:

$$P(A-a)O_2 = (76/4) + 4 = 19 + 4 = 23 \text{ mm Hg}$$

A $\dot{V}/\dot{Q}$ mismatch and shunt both result in elevated $P(A-a)O_2$ levels, indicating that the resultant hypoxemia is due to an abnormality of lung tissue, requiring treatment to address that abnormality. When the RT encounters an increased $P(A-a)O_2$, a $\dot{V}/\dot{Q}$ mismatch and anatomic shunt can be differentiated by means of O_2 administration (see Figs. 45.1 and 45.2). A significant response to applying even small amounts of O_2 identifies $\dot{V}/\dot{Q}$ mismatch as the cause of hypoxemia because altered $P(A-a)O_2$ has not been totally obliterated. True hypoxemia shows little or no improvement in oxygenation even with 100% FiO_2 (see Table 45.1). As a result, treatment of intrapulmonary shunt must be directed toward opening collapsed alveoli or clearing fluid or exudative material before O_2 can be beneficial at below toxic levels. Testing to rule out anatomic shunt should be done in the right clinical setting (e.g., clear or black parenchyma on the chest radiograph).

TABLE 45.1 Differentiating the Cause of Hypoxemia

Cause	$P(A-a)O_2$	Response to Increased FiO_2
Hypoventilation	Normal	Marked
Shunt	Increased	Minimal
$\dot{V}/\dot{Q}$ mismatch	Increased	Marked

FiO_2, Fractional inspired oxygen.

HYPERCAPNIC RESPIRATORY FAILURE (TYPE II)

Hypercapnic respiratory failure (type II), also known as *pump, bellows,* or *ventilatory failure,* is characterized by an elevated $PaCO_2$, creating an uncompensated respiratory acidosis (whether acute or acute-on-chronic). $PaCO_2$ and alveolar ventilation ($\dot{V}_A$) are inversely related, meaning that alveolar and arterial PCO_2 levels are doubled when alveolar ventilation is halved. This is illustrated by the metabolic hyperbola relationship:

$$PaCO_2 = (0.863\ \dot{V}CO_2)/\dot{V}_A$$

$$\dot{V}_A = MV\ (1 - V_D/V_T)$$

where $\dot{V}_A$ is alveolar ventilation (L/min), MV is minute ventilation (L/min), V_D/V_T is dead space–to–tidal volume ratio, and $\dot{V}CO_2$ is CO_2 production (mL/min).

This equation demonstrates a rectangular hyperbola relation between the $PaCO_2$ and ventilation (Fig. 45.3). Patients with chronic hypercapnia and low ventilation are on a steeper section of the metabolic hyperbola such that a minor drop in ventilation results in a significant increase in $PaCO_2$, making them more susceptible to developing a sudden further increase in $PaCO_2$ when even minor respiratory exacerbations occur. Also, with chronically elevated arterial $PaCO_2$, the ventilatory response to a further increase in $PaCO_2$ is more blunted.[10] This leads to an *acute ventilatory failure superimposed on chronic ventilatory failure.*

Similarly, this relationship shows that $PaCO_2$ may increase as dead space (V_D/V_T) rises or as CO_2 production ($\dot{V}CO_2$) increases. Additionally, a change in the $\dot{V}/\dot{Q}$ distribution of the lung toward lower ratios not only causes hypoxemia, as shown in Figs. 45.1 and 45.2, but also, to a lesser extent, can cause an elevation of $PaCO_2$ by reducing the CO_2 discharge from the pulmonary circulation to the alveoli. However, increased dead space, increased $\dot{V}CO_2$, and shifts in the $\dot{V}/\dot{Q}$ distribution toward lower ratios all are usually matched by a corrective increase in ventilation because respiratory control mechanisms tend to maintain the $PaCO_2$ constant. The following sections describe mechanisms of hypercarbia caused by an imbalance between

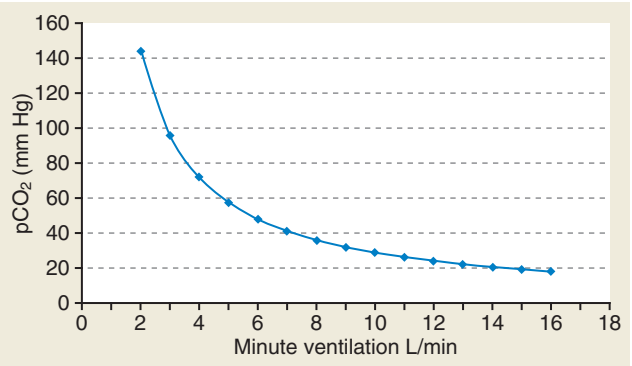

Fig. 45.3 The metabolic hyperbola. Due to the hyperbolic relationship between the pCO_2 and ventilation, a minor drop of ventilation occurring at an already low minute ventilation results in a significantly greater increase in the pCO_2 relative to an equivalent drop occurring at a higher minute ventilation.

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Differentiating Causes of Hypoxemia

Problem

Two patients present with the following ABG values at sea level:

Patient A		Patient B	
pH	7.45	pH	7.21
$PaCO_2$	33 mm Hg	$PaCO_2$	72 mm Hg
PaO_2	40 mm Hg	PaO_2	53 mm Hg
HCO_3^-	22 mEq/L	HCO_3^-	28 mEq/L
SaO_2	70%	SaO_2	81%
FiO_2	0.21	FiO_2	0.21

1. Define the respiratory condition indicated by each ABG analysis.
2. What is the $P(A-a)O_2$ for each blood gas?
3. Identify the type of respiratory failure in each case.
4. In which case would administration of 100% FiO_2 help improve oxygenation?

Discussion:

1. Patient A exhibits uncompensated respiratory alkalosis with hypoxemia. Patient B exhibits partially compensated respiratory acidosis with hypoxemia.
2. Patient A:
   $PAO_2 = 0.21\ (760 - 47) - 33/0.8 = 108$ mm Hg
   $PaO_2 = 40$ mm Hg
   $P(A-a)O_2 = 108 - 40 = 68$ mm Hg on room air
   Patient B:
   $PAO_2 = 0.21\ (760 - 47) - 72/0.8 = 60$ mm Hg
   $PaO_2 = 53$ mm Hg
   $P(A-a)O_2 = 60 - 53 = 7$ mm Hg on room air
   The normal values for $P(A-a)O_2$ range from 10 mm Hg in young people to approximately 25 mm Hg in elderly people while breathing room air.
3. Patient A has hypoxemic respiratory failure (type I) as characterized by below-normal PaO_2 (40 mm Hg). $PaCO_2$ is also below normal (33 mm Hg), indicating hyperventilation is occurring in an effort to improve the oxygenation. Patient B has hypercapnic respiratory failure (type II) as characterized by an above-normal $PaCO_2$ (72 mm Hg), indicating that hypoventilation (ventilatory failure) is occurring. There is also an elevation of HCO_3^- (28 mEq/L), indicating that the acute ventilatory failure is superimposed on chronic ventilatory failure. This patient is also hypoxemic (53 mm Hg).
4. Patient A has hypoxemic respiratory failure with $P(A-a)O_2$ of 68 mm Hg, which is well above normal, indicating an oxygenation defect. The administration of 100% O_2 in this case would help to determine the cause of the defect. Specifically, a marked rise in PO_2 in response to 100% FiO_2 would point to $\dot{V}/\dot{Q}$ mismatch as the cause, whereas shunt would be implicated if PaO_2 did not respond to the increase in delivered O_2. In the latter condition, some form of positive end-expiratory pressure (PEEP) would be necessary to improve gas exchange by improving functional residual capacity. Patient B has hypercapnic respiratory failure (ventilatory failure) with hypoxemia, but with $P(A-a)O_2$ of 7 mm Hg, which is within the normal range. A pure ventilatory defect is the cause of hypoxemia, and administration of 100% FiO_2 would not raise the PO_2 value. Depending on the full patient scenario, this patient may require noninvasive mechanical ventilation or intubation and invasive mechanical ventilation to restore normal acid–base status.

CO_2 exposure (external or internal) and CO_2 clearance (central and respiratory effector mechanisms). Hypoxemia may often accompany pump failure simply because of the displacement of alveolar PO_2 (PAO_2) by the increased $PaCO_2$ from alveolar hypoventilation. This situation is identified on a room air ABG assessment by a normal $P(A-a)O_2$, as discussed previously. The presence of an increased $P(A-a)O_2$ indicates that accompanying hypoxemia is present, most likely as a result of $\dot{V}/\dot{Q}$ mismatch or shunt. The disorders that cause hypercapnic respiratory failure (ventilatory failure) are discussed next.

Unexpected Exposure to Breathing Carbon Dioxide

Although most cases of increased $PaCO_2$ are due to hypoventilation, an unexpected exposure to breathing CO_2 can occur in certain situations.

Clinical Presentation

These unexpected exposures follow unusual clinical situations including defective CO_2 scrubbers in anesthesia machines or life-support systems in scuba units, airtight chambers, spacecrafts, or submersible crafts. Occupational exposures also occur in spelunkers in caves (from groundwater seepage), individuals who work with dry ice (dry ice is a solid form of CO_2), miners, and firefighters.

Increased Carbon Dioxide Production

Fever, agitation, exertion, shivering, hypermetabolism, and excess caloric intake all can result in an increase in $\dot{V}CO_2$, with resulting hypercapnia in patients with additional impairment in respiratory control and CO_2 exhalation mechanisms.

Clinical Presentation

The most common clinical scenario involving increases in CO_2 production probably involves mechanically ventilated patients with already compromised lung function, in whom attempts to liberate from artificial ventilation are complicated by type II respiratory failure. Recognition and correction of fever, agitation, hypermetabolic states, and excess caloric intake, particularly due to carbohydrate-rich enteral solutions, may contribute to a favorable outcome.

Impairment in Respiratory Control

Both central (medullary) and peripheral (aortic and carotid bodies) chemoreceptors responding to CO_2 tension and O_2 tension stimulate the drive to breathe.[10] This ventilatory drive can be decreased by various factors, such as drugs (overdose or sedation), bilateral carotid endarterectomy with incidental resection of the carotid bodies, brainstem lesions, diseases of the CNS (multiple sclerosis, Parkinson disease, or elevated intracranial pressure [ICP]), hypothyroidism, morbid obesity (e.g., obesity-hypoventilation), and sleep apnea.[11] Patients at risk of having a decreased ventilatory drive usually can be identified by their clinical situation (e.g., CNS insult, overdose of sedative medications), and the clinician should be attentive to reversible causes.

Clinical Presentation

The key feature of decreased ventilatory drive is bradypnea (slow breathing) and perhaps ultimately apnea. A normal respiratory rate is usually no less than 12 breaths/min in adults. Drug overdose or a brain disorder can manifest with an altered level of consciousness, ranging from being merely lethargic to being obtunded and comatose, with decreased respirations. Evidence

of drug use by history or toxicity screen confirms the diagnosis of drug overdose. Evidence of head trauma and brain computed tomography (CT) scan abnormalities are important in the diagnosis of a brain disorder. Although hypothyroidism classically manifests with fatigue, weight gain, hyporeflexia, and constipation, it can also progress to significant hypoventilation and myxedema coma. Patients with obesity-hypoventilation may have a rapid, shallow breathing pattern, which results from decreased compliance and microatelectasis. Although these patients may also have nighttime sleep apnea, daytime $PaCO_2$ is also elevated because of a decrease in the drive to breathe and metabolic factors.[12] See Fig. 45.3 for the relationship between PCO_2 and minute volume.

Impairment in Exhaling Carbon Dioxide

Neurologic Diseases

The lungs inhale and exhale under the guidance of the CNS. In some patients, the CNS signal does not reach its goal, resulting in neuromuscular dysfunction. Examples include spinal trauma, motor neuron disease in which lesions of the anterior horn cells may gradually lead to progressive ventilatory failure (e.g., amyotrophic lateral sclerosis or poliomyelitis), motor nerve disorders (including Guillain-Barré syndrome and Charcot-Marie-Tooth disease), disorders of the neuromuscular junction (e.g., myasthenia gravis and botulism), and muscular diseases (including muscular dystrophy, myositis, critical care myopathy, and metabolic disorders).[13]

Clinical presentation. Although hypercapnia may be a common end point, these diseases have varied clinical presentations. Patient observation is a key skill. Drooling, slurred speech (dysarthria), and weak cough are common bulbar signs in amyotrophic lateral sclerosis and myasthenia gravis. In progressive neuromuscular disease, as muscle wasting and weakness become more severe, diaphragmatic insufficiency develops, and supine paradoxical breathing and orthopnea are common.[14] Guillain-Barré syndrome commonly causes lower extremity weakness progressing to respiratory failure in 20% to 30% of patients.[15] Weak cough and gag may be seen, which can threaten airway patency and lead to microatelectasis, hypoxemia, and uncompensated respiratory acidosis. Myasthenia gravis does not always cause respiratory failure.[16] These diseases are quite different in clinical course, but there is much overlap in their presentations, and they commonly result in respiratory **muscle fatigue** and failure and elevated $PaCO_2$.

Increased Work of Breathing

Despite normal respiratory drive, nerve transmission, and neuromuscular response, hypercapnic respiratory failure can still occur if the imposed workload cannot be overcome.[2] Most commonly, this situation occurs when increased dead space accompanies COPD, or when elevated airway resistance accompanies asthma. Both of these obstructive airway diseases may increase respiratory work requirements excessively due to the presence of intrinsic **positive end-expiratory pressure** (**auto-PEEP**). Increased workload can also result from thoracic abnormalities such as pneumothorax, rib fractures with a flail chest, pleural effusions, and other conditions creating a restrictive burden on the lungs. Finally, requirements for increased minute ventilation can arise when increased CO_2 production accompanies hypermetabolic states, such as in extensive burns.

Clinical presentation. The RT must be alert to the possibility of respiratory failure when a heavy load is imposed on the respiratory system. Patients with asthma or COPD should present with hyperventilation during an exacerbation, but if breathing becomes more rapid but shallow, it may indicate impending failure. This increased V_D/V_T ratio leads to hypercapnia because the significant airway obstruction does not resolve with treatment. Diminished breath sounds in a young patient with asthma likewise can be a concerning sign. Irritability, confusion, and ultimately coma are possible signs in worsening hypercapnia, as they are in hypoxemic respiratory failure. More subtle findings include muscle tremor owing to catecholamine release and papilledema resulting from cerebral vasodilation in states of elevated arterial PCO_2.[17]

In summary, hypercapnic (type II) respiratory failure, also known as *ventilatory failure*, develops when ventilation is impaired due to intrinsically or extrinsically increased CO_2 exposure; impairment in respiratory control; or impairment in exhalation mechanisms, including neurologic disease or pulmonary and chest wall disorders associated with increased work of breathing (Table 45.2).

CHRONIC RESPIRATORY FAILURE (TYPE I AND TYPE II)

For some patients with pulmonary disease and respiratory failure, the condition has developed over weeks to months to years and has become a chronic state, allowing compensatory adaptive mechanisms to develop. Most commonly, chronic hypercapnic respiratory failure accompanying COPD or obesity-hypoventilation syndrome prompts a renal response, and the kidneys retain bicarbonate to elevate the abnormally low blood pH. However, this compensatory metabolic alkalosis would not be expected to restore the pH all the way to normal. Chronic hypercapnic respiratory failure is also known as *chronic ventilatory failure*.

RULE OF THUMB Chronic and acute hypercapnic respiratory failure can be differentiated by the severity of change in pH.[18]

- Acute hypercapnic failure (acute ventilatory failure): pH decreases 0.08 for every 10 mm Hg increase in $PaCO_2$
- Chronic hypercapnic failure (chronic ventilatory failure): pH decreases 0.03 for every 10 mm Hg increase in $PaCO_2$.

Similarly, polycythemia may result from prolonged hypoxemic respiratory failure (e.g., sleep apnea) when O_2 delivery to the tissues is compromised, and erythropoietin levels increase to elicit erythrocytosis. Hemoglobin also releases O_2 more easily as the O_2 dissociation curve shifts to the right in the face of acidosis. Finally, O_2 delivery to the brain is enhanced when hypercapnia results in increased cerebral blood flow.[19]

Acute-on-Chronic Respiratory Failure

Chronic respiratory failure can be complicated by acute setbacks that create acute-on-chronic respiratory failure. Patients with

TABLE 45.2 Causes of Respiratory Failure

	TYPE II (HYPERCAPNIC)			
Type I (Hypoxemic)	**Increased Exposure**	**Impaired Respiratory Control**	**Neurologic Disease**	**Increased Work of Breathing**
ARDS	Extrinsic	Drug overdose	Spinal cord trauma	Obstructive lung disease
Pulmonary embolism	Defective CO_2 scrubbers (anesthesia or life-support systems)	Bilateral endarterectomy with carotid body resection	Motor neuron	COPD
Pulmonary edema	Occupational exposure (miners, spelunkers, dry-ice workers, firemen)	Central sleep apnea	Poliomyelitis	Asthma
Septic shock	Intrinsic	Hypocapnia	Amyotrophic lateral sclerosis	Upper airway obstruction
Pulmonary infection	Fever	Cheyne-Stokes	Motor nerve	Obesity-hypoventilation
Viral	Shivering	Acromegaly	Phrenic nerve	Pneumothorax
Bacterial	Hypermetabolism	Hypothyroid	Guillain-Barré	Severe burns
Fungal	Agitation	Brainstem lesions	Charcot-Marie-Tooth	Chest wall disorders
Inhalation	Excess caloric intake	Cerebrovascular accident	Neuromuscular junction	Kyphoscoliosis
Smoke		Encephalitis	Myasthenia gravis	Ankylosing spondylitis
Chemical		Multiple sclerosis	Botulism	
Water		Parkinson disease	Muscular	
Pleural effusion		Metabolic alkalosis	Muscular dystrophy	
Interstitial lung disease		Primary alveolar hypoventilation	Myositis	
Obstructive lung disease		(Ondine's curse)	Myopathy	
Aspiration		Congenital central hypoventilation	Acid maltase	
Primary pulmonary hypertension		Carotid body resection	Metabolic	
		Obesity-hypoventilation		

ARDS, Acute respiratory distress syndrome; *CO_2*, carbon dioxide; *COPD*, chronic obstructive pulmonary disorder.

chronic hypercapnic respiratory failure are at significant risk for this condition, as indicated by the fact that COPD is now the third leading cause of death in the United States.[20] Acute-on-chronic respiratory failure can also be the presenting manifestation of neuromuscular disease that is complicated by pulmonary infection.[21] Most common precipitating factors include bacterial or viral infections, congestive heart failure, pulmonary embolus, pneumothorax, chest wall dysfunction, and noncompliance with treatment. In these patients, the presence of respiratory failure cannot be judged by the normal ABG criteria but by a significant change from the baseline $PaCO_2$ to a level having the potential to cause morbidity and mortality.

Treatment goals include normalizing pH (avoiding mechanical ventilation if possible), elevating SaO_2 to 90% (if hypoxemia is also present), improving airflow, treating infection, monitoring and maintaining fluid status, and preventing or treating complications as necessary. Deaths are less due to respiratory failure, and are more associated with older age, the underlying illness, associated complications, and whether intubation was required.[22] Episodes of acute respiratory failure in these patients seem to have a significant long-term hazard, with mortality rates reaching 59% within the year after a critical illness requiring mechanical ventilation and tracheostomy.[23]

Patients with chronic **hypoxemic respiratory failure (type I)** are at similar risk for acute deterioration of hypoxemia. Infection and heart failure can result in worsening of the marginal oxygenation status of patients with interstitial pulmonary fibrosis or primary pulmonary hypertension.

Complications of Acute Respiratory Failure

Although respiratory failure is life-threatening by itself, complications frequently arise that can add significantly to morbidity and mortality. Especially in patients with ARDS, more deaths are due to complications (e.g., sepsis, multiorgan failure) than to the primary disease.[24] Modern ICUs with sophisticated mechanical ventilation can prolong but may not preserve life. Pulmonary complications such as emboli, **barotrauma**, and infection may be due to treatment strategies such as catheters, mechanical ventilation, and endotracheal tubes. A wide array of nonpulmonary complications may develop, including bacteremia, malnutrition, psychosis due to prolonged ICU stays, cardiac disorders (e.g., arrhythmias, hypotension), gastrointestinal ailments (e.g., hemorrhage, dysmotility), and renal disturbances (e.g., acute renal failure, positive fluid balance).

Clinical Presentation

Clinically, a patient with respiratory muscle fatigue shows an initially increased respiratory rate followed by *bradypnea* (slowed respiratory rate) and apnea as fatigue ensues. **Respiratory alternans,** which is a phasic alternation between rib cage and abdominal breathing, may also occur. Opinions vary on the sensitivity and specificity of abdominal motion paradox in patients with respiratory muscle weakness, but at least some investigators suggest that respiratory muscle paradox is an early sign (see Chapter 16). When ventilatory failure is full-blown, ABG results show hypercapnia with acidosis. As mentioned earlier, the

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Acute or Chronic Hypercapnic Respiratory Failure

Problem:

A 55-year-old man presents to the emergency department complaining of increased shortness of breath and yellow-green sputum production for 1 week. He is alert and oriented. He has a 60 pack-year smoking history. Vital signs are blood pressure 165/90 mm Hg, pulse 120 beats/min, respirations 25 breaths/min, and temperature 100.5°F oral.

ABG values on room air are as follows:

pH	7.28
$PaCO_2$	70 mm Hg
PaO_2	35 mm Hg
HCO_3^-	36 mm Hg
SaO_2	66%

1. Define the respiratory condition indicated by the ABG results.
2. What is the $P(A-a)O_2$?
3. What type of respiratory failure is present?
4. What kind of therapy is indicated?

Discussion:

1. The ABG values indicate a partially compensated respiratory acidosis with hypoxemia.
2. $PAO_2 = 0.21\ (760 - 47) - 70/0.8 = 62$ mm Hg
   $PaO_2 = 35$ mm Hg
   $P(A-a)O_2 = 62 - 35 = 27$ mm Hg on room air
3. This is hypercapnic respiratory failure (type II), also known as *ventilatory failure*. However, in acute failure, the pH decreases 0.08 for every 10 mm Hg increase in $PaCO_2$. In this patient, $PaCO_2$ has increased 30 mm Hg (70 – 40), and the pH has decreased 0.12. The pH would be expected to decrease 0.24 (3×0.08) if this were acute ventilatory failure. This is a case of acute-on-chronic failure. The HCO_3^- of 36 mEq/L (normal 22 to 26 mEq/L) also indicates that renal compensation has occurred, which takes days to achieve. The $P(A-a)O_2$ is 27 mm Hg, which is above normal, indicating that hypoxemia cannot be explained fully by hypoventilation.
4. Because the patient is alert, conservative therapy to improve lung function is indicated. O_2 administration to achieve SaO_2 of at least 90% is required. If PaO_2 does not respond to O_2 administration, shunt is present, and positive airway pressure may be necessary. Antibiotics are indicated for the probable infection (fever, discolored sputum), and bronchopulmonary hygiene (bronchodilators, steroids, cough assist) is indicated to improve ventilation.

presence of hypercapnia with acidosis can also indicate that the respiratory center is not responding properly.[10]

Tachypnea is the cardinal sign of increased work of breathing. Tachypnea occurs when the respiratory center increases breathing frequency in an attempt to lessen respiratory excursion and reduce the amount of work performed by the respiratory muscles.[25] Overall workload is reflected in the minute volume needed to maintain normocapnia.

Indications for Ventilatory Support

For each type of oxygenation and ventilatory failure, the goal of mechanical ventilation is either to support the patient until the underlying problem resolves or to maintain support of the patient with chronic ventilatory problems. These goals may be achieved by improving alveolar ventilation and arterial oxygenation, increasing lung volume, or reducing work of breathing.[26]

TABLE 45.3 Physiologic Indicators for Ventilatory Support, Classified by Mechanism Underlying Respiratory Failure

Mechanism	Normal Values	Support Indicated
Inadequate Alveolar Ventilation		
$PaCO_2$ (mm Hg)	35–45	>55
pH	7.35–7.45	<7.20
Inadequate Lung Expansion		
Tidal volume (V_T) mL/kg	5–8	<5
Vital capacity (VC) mL/kg	65–75	<10
Respiratory rate	12–20	>35
Inadequate Muscle Strength		
Maximum inspiratory pressure (cm H_2O)	–80–100	–≤20
Vital capacity (VC, mL/kg)	65–75	<10
Maximum voluntary ventilation (MVV, L/min)	120–180	<2× VE
Increased Work of Breathing		
Minute ventilation ($\dot{V}_E$)	5–6	>10
V_D/V_T (%)	0.25–0.40	>0.6
Hypoxemia		
$P(A-a)O_2$ on 100% O_2 (mm Hg)	25–65	>350
PaO_2/FiO_2	350–450	<200

FiO_2, Fractional inspired oxygen; *$PaCO_2$,* partial pressure of carbon dioxide; *PaO_2,* partial pressure of oxygen; *VE,* minute ventilation.

This section discusses the indications for mechanical ventilation for hypoxemic (type I) and hypercapnic (type II) respiratory failure. Hypoxemic respiratory failure is divided into processes that require short-term and long-term ventilatory support. Hypercapnic respiratory failure is broken down into unstable ventilatory drive, muscle fatigue, excessive work of breathing, and alveolar hypoventilation.

Parameters Indicating Need for Ventilatory Support

Although various measurements have been proposed to help decide if a patient needs mechanical ventilation, the clinical status of the patient is the most important criterion. Table 45.3, and the discussion that follows, review common physiologic indicators for initiating support by the underlying cause of respiratory failure.

Hypoxemic respiratory failure. Severe, refractory hypoxemia is a common indication for intubation and ventilatory support. Table 45.3 lists different measures of hypoxemia that have been used to assess the need for ventilatory support. Most commonly, PaO_2 is compared with FiO_2 as with the PaO_2/FiO_2 ratio or the alveolar-arterial O_2 difference [$P(A-a)O_2$]. Indicators of profoundly impaired oxygenation suggesting the need for intubation, high inspired O_2 administration, and PEEP include $P(A-a)O_2$ value of 350 mm Hg on FiO_2 of 1.0 or a PaO_2/FiO_2 value of less than 200. These values are useful for all causes of hypoxemic respiratory failure (type I) but cannot help distinguish if the process is a readily reversible one, such as pulmonary edema or atelectasis, or a process that resolves more slowly, such as acute

lung injury. Frequently, patients have a combination of hypoxemic and hypercapnic respiratory failure.

Hypercapnic respiratory failure (ventilatory failure). As previously discussed, hypercapnic (type II) respiratory failure or ventilatory failure can be caused by increased ventilatory dead space, increased CO_2 production, or decreased alveolar ventilation. All of these processes cause an increase in $PaCO_2$.[9] Assessment of the pH allows a determination of whether the problem is acute or chronic. Chronic hypoventilation is compensated by the kidneys' retention of bicarbonate, although this response requires several days. The following example shows the importance of pH in interpreting the significance of elevated $PaCO_2$.

	Patient A	Patient B
$PaCO_2$	60 mm Hg	60 mm Hg
Serum HCO_3^-	25 mEq/L	36 mEq/L
pH	7.25	7.38

Although both patients in this example have the same level of hypercapnia, only patient A exhibits acute ventilatory failure with an elevated $PaCO_2$ but normal serum bicarbonate (25 mEq/L). Patient B has a compensated respiratory acidosis from chronic hypercapnic respiratory failure, as indicated by the normal pH and elevated serum bicarbonate (36 mEq/L). This condition is also known as *chronic ventilatory failure*. The distinction between acute and chronic ventilatory failure is very important in respiratory care and emphasizes the need to use both $PaCO_2$ and pH as indicators for ventilatory support. The trend in pH and $PaCO_2$ values is also useful in assessing the effects of therapies in correcting acute ventilatory failure.

Significance of elevated alveolar partial pressure of carbon dioxide. Because elevated $PaCO_2$ increases ventilatory drive in healthy subjects, the existence of hypoventilation suggests other problems with the respiratory apparatus. Specifically, the presence of acute respiratory acidosis indicates one of three major problems: (1) the respiratory center is not responding normally to elevated $PaCO_2$; (2) the respiratory center is responding normally, but the signal is not getting through to the respiratory muscles; or (3) despite normal neurologic response mechanisms, the lungs and chest bellows are incapable of providing adequate ventilation because of parenchymal lung disease or muscular weakness.[10]

ASSESSMENT OF RESPIRATORY FATIGUE, WEAKNESS, FAILURE, AND WORK OF BREATHING

Respiratory Muscle Weakness

Respiratory muscle weakness refers to the decreased capacity of a rested muscle to generate force and decreased endurance.[27] Respiratory muscle weakness occurs most commonly in patients with neuromuscular disease. Other conditions that lead to muscle weakness by increasing demand include COPD, kyphoscoliosis, and obesity.

The respiratory muscle strength is assessed by volitional tests, such as the **maximum inspiratory pressure (MIP)**, **maximum expiratory pressure (MEP)**, and **sniff nasal inspiratory pressure**; and non-volitional tests that involve stimulation of the phrenic nerve.[28] The **maximum voluntary ventilation (MVV)**, though previously thought to be a more specific test of respiratory muscle weakness, is generally proportionally reduced to the vital capacity (see Table 45.3).[28] A MIP of −30 cm H_2O or less (more negative) usually indicates adequate respiratory muscle strength to continue spontaneous breathing, but the overall trend needs to be considered. This consideration is especially important in patients with myasthenic crisis or Guillain-Barré syndrome, where values of MIP that are becoming less negative may be the only clue to impending respiratory failure.

Respiratory Muscle Fatigue

Fatigue is usually defined as a condition in which there is loss of the capacity to develop force or velocity of a muscle resulting from muscle activity under either a sustained or repetitive stimulation, which is reversible by rest.[29] It can be caused by both the specific demands placed on the muscle and the reduced supply of necessary nutrients. The demand on a muscle is raised by increased work of breathing, increased strength of muscle contraction, and decreased muscle efficiency. Hypoxemia, decreased inspiratory muscle blood flow, poor nutrition, and the inability of a muscle to extract energy from supplied nutrients can lead to fatigue as well.[27]

There are three types of respiratory **muscle fatigue**: Central fatigue, peripheral high-frequency fatigue, and peripheral low-frequency fatigue.[28] In central fatigue, the reduced respiratory muscle force is due to an impairment in central or motor-neuron drive with a preserved neuromuscular junction and muscular function. In this condition, the muscle's force response is preserved in response to direct electrical stimulation but impaired with maximal voluntary effort. One explanation is that stress-loaded breathing results in a central opioid expression that reduces the central neuronal output. In peripheral fatigue, the muscle's force response falls with direct electrical stimulation. A decline in muscle force with high frequencies of 50 to 100 Hz may be due to an impaired neuromuscular junction, reduced sarcolemmal membrane excitability, or a reduction in action potential propagation. In contrast, a decline in muscle force with low frequencies of 1 to 20 Hz may be due to a decrease in contractile protein activation despite an intact sarcolemmal action potential, and is likely due to a decrease in Ca2+ release. The recovery from low-frequency peripheral fatigue can be prolonged for hours or even days.[28]

Respiratory Failure

Respiratory failure is an unfavorable imbalance between a respiratory workload, on the one hand, and ventilatory muscle strength and endurance, on the other hand. The **pressure-time index** takes into account the fact that respiratory muscle endurance depends both on the magnitude of the respiratory load in relation to respiratory strength (P_{di}/P_{dimax}) and on the duration of the inspiratory effort in relation to total breath time (the duty cycle, or T_i/T_{tot}). This index $[(P_{di}/P_{dimax}) \times (T_i/T_{tot})]$ determines whether a respiratory load can be tolerated without development of respiratory muscle failure. Values of the pressure-time index

less than 0.15 are generally tolerated for over 1 hour without fatigue, whereas indices greater than 0.18 usually result in fatigue and respiratory failure within less than 40 minutes in a time frame that is inversely related to the index.[28] Comparing the spontaneous minute ventilation with MVV is also a helpful index because fatigue and failure are both likely to occur if the minute ventilation exceeds 60% to 80% of MVV.[28]

These closely related concepts of weakness, fatigue, and failure usually overlap and can result in acute or chronic respiratory failure. Respiratory muscle weakness can predispose to ventilatory muscle fatigue. Whether fatigue always leads to failure has been debated.[30] In one study, weaning failure was not accompanied by low-frequency fatigue of the diaphragm despite the presence of diaphragm weakness.[31]

Work of Breathing

Work of breathing (WOB) is the amount of pressure needed to move a given volume of air into the lung with a relaxed chest wall. Work of breathing is due to physiologic work and imposed work. Physiologic work involves overcoming the elastic forces of both the lung tissue and the chest wall during inspiration, and overcoming the resistance to the flow of air through the airways.[32] Normal WOB in Joules per liter of ventilation is 0.35 J/L, but it can also be expressed in power terms (Joules per minute of ventilation) with a normal value of 2.4 J/min.[32] Airway and pulmonary parenchymal abnormalities can cause auto-PEEP and active expiration, which increase the physiologic WOB. For example, auto-PEEP in a patient with COPD imposes a threshold load, as inspiratory muscles have to initiate a contraction equal to the auto-PEEP before the lung volume can increase.[32,33] Additionally, whereas expiration is normally passive and does not add to the WOB, it is more active in COPD due to the involvement of abdominal muscles to assist expiration, which adds to the WOB.[32] In intubated patients, sources of imposed work of breathing include the endotracheal tube ventilator circuit, and settings that may contribute further to **auto-PEEP.** Excessive WOB is the most common cause of respiratory muscle fatigue and can interfere with weaning. For example, 96% of patients with a physiologic work of breathing less than 0.8 J/L in one study were successfully liberated from ventilatory support and extubated.[34]

CHOOSING A VENTILATORY SUPPORT STRATEGY FOR DIFFERENT CAUSES OF RESPIRATORY FAILURE

The remainder of this chapter briefly discusses current ventilatory strategies for hypoxemic and hypercapnic respiratory failure. The clinical application of specific modes of mechanical ventilation is described in Chapters 46 and 49, and noninvasive ventilation (NIV) is reviewed in more detail in Chapter 50. When it has been determined that the patient needs ventilatory support, the initial decision is whether to intubate or to ventilate noninvasively. In the acute setting, this decision is sometimes based on the underlying process, the type of respiratory failure, and how rapidly the underlying process can be reversed.

Noninvasive Ventilation

Noninvasive ventilation (NIV) can be defined as any mode of ventilatory support that is provided without endotracheal intubation, including continuous positive airway pressure (CPAP) alone or in combination with any mode of pressure-limited or volume-limited ventilation.[35] NIV can improve hypoxemia and hypercarbia through several mechanisms including but not limited to: (1) compensating for the inspiratory threshold load imposed by intrinsic PEEP;[33] (2) supplementing a reduced tidal volume;[36] (3) partial or complete unloading of the respiratory muscles;[36] (4) reducing venous return and left ventricular afterload;[37] (5) alveolar recruitment;[38] (6) preventing intermittent narrowing and collapse in patients with obstructive sleep apnea/hypopnea syndrome by using pressure to splint the airway open during sleep;[39] and (7) improving lung function (particularly functional residual capacity) and daytime gas exchange in obstructive sleep apnea/hypopnea syndrome.[40] NIV is appropriate in both acute[41] and chronic[42] respiratory failure.

Noninvasive Ventilation in Acute Conditions

Exacerbations of Chronic Obstructive Pulmonary Disease

NIV is considered to be a standard of care in patients hospitalized with an exacerbation of COPD, hypercapnia with a $PaCO_2$ greater than 45 mm Hg and a pH less than 7.35.[43] For instance, NIV reduces mortality by 46% (the number needed to treat to avoid 1 death is 12), reduces the need to intubation by 65% (the number needed to treat to avoid 1 intubation is 5), reduces the hospital stay by 3.4 days, and reduces complications.[43]

Cardiogenic Pulmonary Edema

NIV is a recommended option in treating acute respiratory failure as part of cardiogenic pulmonary edema. Use of CPAP or NIV in these patients can significantly reduce the dyspnea score, heart rate, acidosis, and hypercapnia within the first hour after the start of treatment.[44,45] In the largest study of NIV for cardiogenic pulmonary edema, no improvement was seen in mortality, rates of intubation, rate of admission to the critical care unit, or mean length of hospital stay,[44] but smaller trials showed decreased intubation and mortality rates with NIV.[45] Selection and methodologic criteria may explain the difference (see Chapter 50).

Acute Asthma

NIV is used in about 40% of those who require some form of ventilatory support for an asthma exacerbation.[46] Less than 5% of those fail NIV, with a higher risk for failure in patients with a preceding hospitalization within the year, pneumonia, or diabetes. Those who fail end up staying in the hospital longer.[46] Otherwise, the group receiving NIV has a lower mortality and shorter length of stay.[46]

Acute Respiratory Distress Syndrome

A large international study (the LUNG-SAFE study) found that NIV was used in about 15% of patients with the ARDS, regardless of severity.[47] However, results have been generally disappointing, especially in more severe ARDS. For example, although NIV can prevent intubation in 78% of those with mild ARDS, that success rate drops to 50% to 60% in moderate and severe

ARDS.[47] More concerning, the mortality of those who fail NIV is high at 42.3%.[47] Of even greater concern, compared to invasive ventilation, NIV is associated with a worse mortality that is most apparent in those with a PaO_2/FiO_2 ratio less than 150 mm Hg.[47] Reasonable recommendations in the management of ARDS would be to start with high-flow nasal O_2 if O_2 needs exceed the 6 L per minute that can be delivered by nasal prongs. This approach does not decrease the intubation rates compared to standard O_2 therapy through a facial mask or to NIV, but it increases the ventilator-free days and reduces mortality.[48] If this fails, NIV can be tried in experienced centers, possibly with a helmet interface (shown to reduce intubation rates and mortality compared to a standard facial mask).[49] However, rapid reassessment of oxygenation is recommended, so that invasive ventilation is not unnecessarily delayed if those approaches fail.

Noninvasive Ventilation in Chronic Conditions

Obesity-Hypoventilation Syndrome

Obesity-hypoventilation syndrome refers to the presence of daytime hypercapnia ($PaCO_2$ >45 mm Hg) in obese individuals (body mass index >30 kg/m^2) when no other cause of hypoventilation is present. Factors associated with daytime hypercapnia include an increased body mass index, sleep apnea, a lower mean overnight O_2 saturation, and severity of restrictive pulmonary function.[50] In a randomized study comparing CPAP to NIV in the management of the obesity-hypoventilation syndrome, both interventions reduced the $PaCO_2$ and improved quality without a significant difference between the two interventions.[51]

Stable Chronic Obstructive Pulmonary Disease

NIV in the home setting for patients with severe COPD can prolong survival, improve quality of life, reduce hospitalization, and improve lung function, provided the patients and device setting are well chosen. For example, hypercapnic patients are most likely to benefit from NIV, and general recommendations for NIV use include those with a daytime PaCO2 ≥ 50 mm Hg or greater than 53 mm Hg more than 2 weeks after a hospital stay for an acute exacerbation.[52] The settings that have been found to be helpful include higher pressures and higher pressure support with inspiratory positive airway pressure (IPAP) of 22 to 24 cm H_2O while keeping the expiratory positive airway pressure (EPAP) low at 4 to 5 cm H_2O, and with a backup rate of 14 to 18 breaths per minutes.[52]

Neuromuscular Diseases and Thoracic Cage Abnormalities

Even in progressive neuromuscular disorders, NIV can prolong survival, improve quality of life, and reduce hospitalization rates.[53] Other NIV techniques using rocking beds, pneumobelts, and negative pressure ventilation are much less frequently used and are becoming less easily available.

Invasive Ventilatory Support

Patients with profound hypoxemia from a process that is expected to resolve slowly, such as acute lung injury, usually require intubation and mechanical ventilation. Other indications for intubation include conditions where NIV may be poorly tolerated or even possibly harmful, such as the presence of upper airway obstruction, inability to clear secretions or protect the airway, or inability to achieve a proper mask fit. Both hypoxemic and hypercapnic types of respiratory failure can be managed effectively by invasive mechanical ventilation.

Acute Respiratory Distress Syndrome

Profound hypoxemic respiratory failure is often due to severe pneumonia and ARDS. Patients with these conditions have very noncompliant lungs. Volume-cycled ventilation in patients with ARDS frequently leads to high peak airway and plateau pressures. Ventilating these patients with small tidal volumes (about 4 to 8 mL/kg) and aiming for a plateau pressure below 30 cm H_2O reduces complications associated with mechanical ventilation and improves survival.[54]

Increased Intracranial Pressure

Hyperventilation applied acutely and for short periods may be used to reduce ICP. The goal is to lower $PaCO_2$ to between 25 mm Hg and 30 mm Hg, which causes alkalosis. Alkalosis helps reduce cerebral blood flow until ICP can be controlled by other measures. Ongoing ventilatory support should maintain PCO_2 in the range of 30 to 40 mm Hg. By maintaining PCO_2 in this range, sudden increases in ICP can be quickly controlled by short-term hyperventilation. Although reducing blood flow can reduce brain swelling and ICP, cerebral ischemia can also result. Another concern in ventilating patients with elevated ICP is

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Indications for Continuous Positive Airway Pressure Versus Continuous Mechanical Ventilation With Positive End-Expiratory Pressure

Problem:

A patient in the ICU is severely tachypneic and hypoxemic. The respiratory rate is 30 breaths/min. On approximately 50% O_2 by mask at sea level, PaO_2 is 50 mm Hg, $PaCO_2$ is 30 mm Hg, pH is 7.51, and HCO_3^- is 23 mEq/L. The patient is in distress but alert and able to cooperate and follow instructions.

1. What is this patient's $P(A-a)O_2$?
2. What type of respiratory failure is this?
3. What is the appropriate initial therapy?

Discussion:

This patient does not have hypercapnic respiratory failure, as is confirmed by the low $PaCO_2$ (30 mm Hg). The patient does have a serious oxygenation defect, as confirmed by the increased $P(A-a)O_2$.

$$PAO_2 = 0.50\,(713) - 30/0.8 = 318\ \text{mm Hg}$$

$$P(A-a)O_2 = 318 - 50 = 268\ \text{mm Hg}$$

The elevated $P(A-a)O_2$ is explained by the presence of severe intrapulmonary shunt. Shunts this severe can occur only when significant airway closure and atelectasis are present. The mode of therapy should be aimed at reinflating collapsed alveoli and keeping the alveoli open throughout the breathing cycle. In this patient, alveolar ventilation is not impaired ($PaCO_2$ = 30 mm Hg). CPAP alone may be effective in reducing shunt. (CPAP does not provide ventilation.) CPAP may be applied noninvasively via face mask, as would be indicated in this alert, cooperative patient. If hypercapnia and acidemia develop, mechanical ventilation with PEEP would be indicated.

MINI CLINI

Acute Hypercapnic Respiratory Failure

Problem:
A patient with COPD presents to the emergency department in moderate respiratory distress. He is alert and cooperative. The respiratory rate is 26 breaths/min. Lung examination shows poor air entry with expiratory wheezing. Room air ABGs show pH 7.24, $PaCO_2$ 60 mm Hg, and PaO_2 60 mm Hg.
1. What type of respiratory failure is this?
2. How should the patient be managed?

Discussion:
ABGs show an acute respiratory acidosis with normal $PAO_2 - PaO_2$ gradient.

$$PAO_2 = 0.21 * (713) - 60/0.8 = 74$$

$$P(A-a)O_2 = 74 - 60 = 14\ mm\ Hg$$

This patient has hypercapnic respiratory failure related to obstructive lung disease, also known as *ventilatory failure*. In addition to bronchodilators and corticosteroids, the RT should aim to improve ventilation to reverse the respiratory acidosis. In this patient, who is alert and cooperative, NIV using a face mask may be tried. Initial mask ventilation can start in the pressure support ventilation mode with a level of support of 10 cm H_2O and 5 cm H_2O PEEP. Tidal volume should be maintained at approximately 6 to 8 mL/kg. If this patient deteriorates despite therapy, he will need to be intubated and mechanically ventilated.

using PEEP to manage hypoxemia. There is a concern that increased intrathoracic pressure due to PEEP would cause decreased cerebral venous return leading to increased ICP. Also, there is concern that PEEP can decrease cerebral perfusion by limiting cardiac output. The use of PEEP in patients with elevated ICP may require invasive monitoring of ICP because the combination of decreased cerebral perfusion and elevated ICP can (but not always) narrow cerebral perfusion pressure.[55] Elevation of the head of the bed can offset the increased ICP associated with the application of PEEP.

Obstructive Lung Disease

Patients with obstructive lung disease have markedly increased airway resistance that leads to a decrease in the rate of expiratory flow with resulting hyperinflation. These patients frequently have problems with elevated airway pressure or **dynamic hyperinflation** (auto-PEEP), which can cause barotrauma and ineffective triggering of the ventilator.[56]

The goal in managing patients with obstructive lung disease and respiratory failure is to oxygenate and ventilate the patient successfully, while avoiding dyssynchrony and dynamic hyperinflation. In these patients, lower tidal volumes (6 to 8 mL/kg), moderate respiratory rates, and high sustained (square wave) inspiratory flow rates (70 to 100 L/min) are recommended to avoid dynamic hyperinflation.[57] These maneuvers reduce inspiratory time and prolong expiratory time, which allows a patient with obstructive lung disease to have a longer time to exhale.

Another consideration in patients with obstructive lung disease is the inspiratory threshold load imposed by auto-PEEP, resulting in increased patient inspiratory work.[33] In this case, applied (or extrinsic) PEEP can compensate for this threshold load and reduce the work of breathing for patient-triggered breaths in any assisted ventilatory mode.[33]

Ventilatory Support in Chronic Hypercapnic Respiratory Failure

The goal of therapy in hypercapnic respiratory failure (acute ventilatory failure) is to guarantee a set minute ventilation. In treating patients with chronic ventilatory failure, the goal is to normalize the pH but not the $PaCO_2$. Correction of $PaCO_2$ in a patient with chronic hypoventilation from diverse causes can lead to a posthypercapnic metabolic alkalosis, which can produce hypokalemia, seizures, and arrhythmias.

SUMMARY CHECKLIST

- Acute respiratory failure is identified by PaO_2 less than 60 mm Hg or $PaCO_2$ greater than 50 mm Hg, or both, in otherwise healthy individuals at sea level.
- Hypoxemic respiratory failure is most commonly due to $\dot{V}/\dot{Q}$ mismatch, shunt, or hypoventilation.
- Hypercapnic respiratory failure, also known as *ventilatory failure*, results from decreased ventilatory drive, neurologic disease, or increased work of breathing.
- Chronic respiratory failure may manifest with hypercapnia and evidence of a compensatory metabolic alkalosis (chronic ventilatory failure) or with polycythemia reflecting chronic hypoxemia.
- The clinical condition of the patient is the most important factor in determining the need for ventilatory support.
- Excessive work of breathing is the most common cause of respiratory muscle fatigue.
- Acute exacerbations of COPD and cardiogenic edema represent two acute conditions in which NIV has benefit.
- Increased FiO_2 and PEEP are the main treatments for severe hypoxemia.
- The goal of treating hypercapnic respiratory failure (acute ventilatory failure) is to normalize the pH.

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46

Mechanical Ventilators

Robert L. Chatburn and Teresa A. Volsko

CHAPTER OBJECTIVES

After reading this chapter you will be able to

- Define a mechanical ventilator
- Describe the key design features of ventilator displays
- Discuss the importance of properly setting alarm thresholds
- Explain how the compliance of the patient circuit affects volume delivery
- Describe the 10 maxims used to develop a standardized ventilator taxonomy
- Demonstrate how to classify any mode of ventilation
- List the three main goals of mechanical ventilator support
- Discuss the differences between conventional and high-frequency ventilators

CHAPTER OUTLINE

KEY TERMS

adaptive targeting scheme
assisted breath
bio-variable targeting scheme
continuous mandatory ventilation (CMV)
continuous spontaneous ventilation (CSV)
control circuit
cycling
driving pressure
dual targeting scheme
elastance
intelligent targeting scheme
intermittent mandatory ventilation (IMV)
loaded breathing
machine cycled
machine triggered
mandatory
mode
pressure-control ventilation
resistance
servo targeting scheme
optimal targeting scheme
patient cycled
patient triggered
spontaneous breath
targeting scheme
tidal pressure
time constant
time-control
trigger
volume-control ventilation

To safely and effectively initiate and manage a mechanical ventilator, the respiratory therapist (RT) must have a basic understanding of (1) ventilator design principles related to patient-ventilator interaction; (2) appropriate clinical application of ventilatory modes (i.e., the proper matching of ventilator capability with physiologic need); and (3) the physiologic effects of mechanical ventilation, including gas exchange and pulmonary mechanics. This chapter focuses on the first of these. It explains classification terminology and outlines a framework for understanding current and future ventilatory support devices.[1]

HOW VENTILATORS WORK

Some basic knowledge of mechanics is helpful to understand how ventilators work. A ventilator is simply a machine that is designed to perform some portion of the work of breathing. These machines deliver a variety of medical gas mixtures, such as nitric oxide, helium, and oxygen. Sophisticated software and advanced monitoring systems make it possible to deliver a variety of breathing patterns to meet patient needs for safety, comfort, and, eventually, liberation (i.e., extubation).

Ventilators are used along the whole continuum of care, from intensive care units (ICUs) to patient transport to long-term and home care. They all require energy in the form of either electricity or compressed gas to function. The energy is transmitted or transformed (by the ventilator's drive mechanism) in a predetermined manner (by the **control circuit**) to augment or replace the patient's muscles in performing the work of breathing (the desired output).

RULE OF THUMB For patient transport, you must use either a pneumatically powered ventilator or one that can run solely on batteries. Always take along a manually powered bag-valve-mask resuscitator, and for long transports be sure to have backup power available (extra cylinders or batteries).

A basic schematic of an ICU ventilator is shown in Fig. 46.1. A simplified description of ventilator operation is as follows: High-pressure gas (air and oxygen, usually from a centrally located compressor and liquid oxygen source and piped into ICU rooms) enters the ventilator at 50 psi (in the United States). Inside the ventilator, the gas pressures of air and oxygen sources are usually reduced. The flow of gas to a reservoir is then controlled by two valves. The relative flows of air and oxygen to the reservoir controls the FiO_2. Output flow from the reservoir to the patient is managed by a high-flow proportional valve (i.e., flow is proportional to the voltage applied to the valve). The flow to the patient is coordinated with the exhalation valve that intermittently occludes the exhalation path. Thus, when the output flow valve is open and the exhalation valve is closed, gas flows into the lungs. When the output flow valve is closed and the exhalation valve is open, gas flows from the lungs, through the exhalation system, and to the atmosphere. Software controls the intricate interaction between the output valve and the exhalation valve to produce a variety of breathing patterns. These patterns can be dictated by the ventilator or entirely controlled by the patient's brain or ventilatory demand.

RULE OF THUMB Ventilators used near magnetic resonance imaging (MRI) equipment must be MRI compatible. Even when an MRI-compatible ventilator is used during imaging, it is important to maintain the ventilator within the designated safe distance from the MRI device.

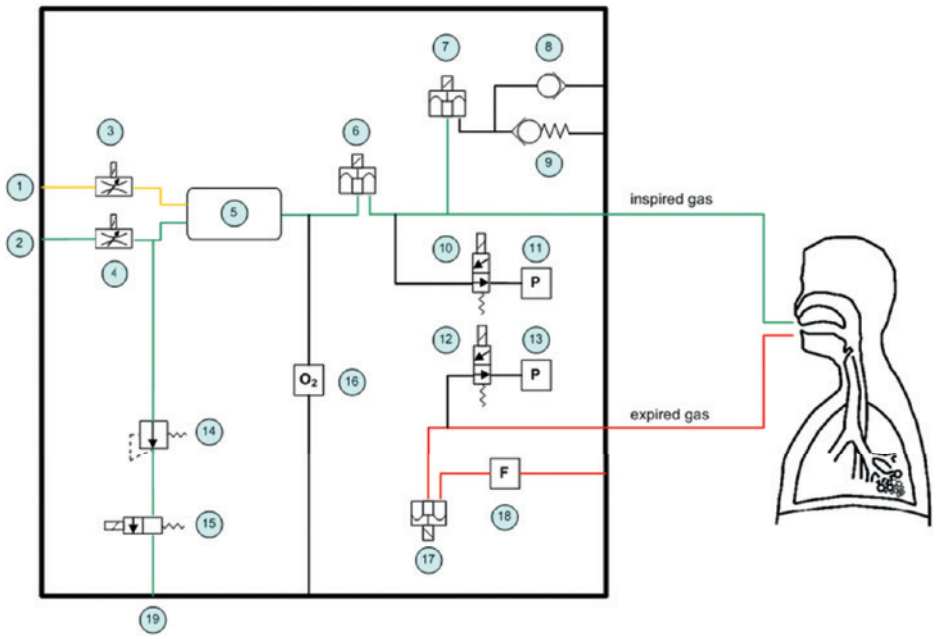

Fig. 46.1 Simplified Schematic of a Modern Intensive Care Ventilator. High-pressure gas enters the ventilator through the gas inlet connections for oxygen and air *(1,2)*. Mixing takes place in a reservoir *(5)* and is controlled by two valves *(3,4)*. Inspiratory flow from the reservoir is controlled by a separate proportional valve *(6)*. On the inspiratory circuit there is a safety valve *(7)* and two nonreturn valves *(8,9)*. In normal operation the safety valve is closed so that inspiratory flow is supplied to the patient's lungs. When the safety valve is open, spontaneous inspiration of atmospheric air is possible through the emergency breathing valve *(8)*. The emergency expiratory valve *(9)* provides a second channel for expiration when the expiratory valve *(17)* is blocked. Also on the inspiratory circuit are an inspiratory pressure (P) sensor *(11)* and a pressure sensor calibration valve *(10)*. The exhalation circuit consists of the expiratory valve *(17)*, expiratory pressure sensor *(13)* with its calibration valve *(12)*, and an expiratory flow *(F)* sensor *(18)*. The expiratory valve is a proportional valve and is used to adjust the pressure in the patient circuit. Conversion of mass flow to volume (barometric temperature and pressure saturated, BTPS) requires knowledge of ambient pressure, measured by another pressure sensor (not shown). Pressure in the patient circuit is measured with two independent pressure sensors *(11,13)*. Oxygen flow to the nebulizer port *(19)* is controlled by a pressure regulator *(14)* and a solenoid valve *(15)*. (Reproduced, with permission Mandu Press Ltd.)

The Operator Interface

The ventilator's operator interface (i.e., control panel) has evolved a lot over the last 45 years. Originally the displays on ventilators were very simple: operator inputs, or settings, were accomplished with hard-wired knobs, buttons, and dials. The ventilator outputs, such as alarm conditions and ventilating pressure, were displayed with bulbs, light-emitting diodes (LEDs), and meters. Some simple transport ventilators still use analog displays. The development of inexpensive microprocessors has led manufacturers to use digital displays almost exclusively on all types of ventilators. Today most ICU ventilators have computer touch screens for visual displays of ventilator data. They are usually designed as "virtual" instruments, meaning that knobs, buttons, dials, and meters are simulated on the screen, and may rely on only a single mechanical dial and perhaps a few buttons to set multiple parameters (Fig. 46.2).

Ventilator Displays

Ventilator displays serve three main functions: (1) to display the inputs—that is, the current state of the settings and allow changes to be made; (2) to show the outputs—meaning the measured values that characterize normal patient–ventilator interactions; and (3) to show alarm conditions. Additional functions include trends of past settings or measured values, performance of special monitoring or automated procedures such as the determination of optimal positive end-expiratory pressure (PEEP), and miscellaneous ventilator configuration settings and patient data.

Alphanumeric values. Measured or calculated data in the form of alphanumeric values are presented in numbers or text. Typically FiO_2, pressures (mean, baseline, peak, and plateau), volumes (inhaled/exhaled tidal volume, minute ventilation), peak inspiratory and expiratory flow, and frequency are represented as numeric values. A variety of calculated parameters including I:E ratio, percent leak, resistance, and compliance may also be displayed.

Trends. Trends provide clinicians with measured or calculated data related to ventilatory support over time. Gradual or sudden changes in the patient's ventilatory status can be identified by evaluating trends. Alarm logs can also be accessed and provide an additional layer of detail important for adjusting alarm limits to minimize nuisance alarms and enhance safety. Alarm logs can be invaluable in the event of a suspected ventilator failure and may be used as evidence in a legal investigation if significant patient harm has occurred.

Waveforms and loops. Graphic displays of pressure, volume, and flow convey a wealth of information. Not only is it possible to determine the mode of ventilation by examining these graphics, but the causes of patient–ventilator asynchrony can also be determined, including flow asynchrony, delayed or premature cycling, and missed triggers. Graphic representations of respiratory mechanics are helpful for identifying the ventilator parameters to be adjusted to improve the ventilator–patient interaction.[2] When pressure, volume, or flow is graphed on the vertical axis with time on the horizontal axis, a waveform or "scalar" display (Fig. 46.3) is the result. Loop displays plot one variable against another as *x-y* graphs (Fig. 46.4).

Pressure-volume (PV) loops can be used to set optimal PEEP and tidal volume levels (Fig. 46.5). PV loops are manually created by using a "super syringe" to inject discrete volumes of gas and then measuring static pressures (static pressure–volume curve). Alternatively, one can use the ventilator at very low constant inspiratory flows (<10 L/min) to minimize the pressure due to flow resistance and create what are called *quasi-static* loops. One

Fig. 46.2 Example of a modern intensive care unit ventilator display.

MINI CLINI

The Use of Trending Data to Optimize the Application of Mechanical Ventilation

Problem

A 43-year-old female in respiratory distress has a predicted body weight of 60 kg. She is intubated and receiving mechanical ventilation with the following settings:

Mode: PC-CMV
Set frequency: 20/min
Inspiratory pressure: 15 cm H_2O
PEEP: 8 cm H_2O
FiO_2: 0.60
Inspiratory time: 1 second

The following trends are available: Date	8/8	8/8	8/8	8/8	8/8	8/8
Time	0000	0200	0400	0600	0800	1000
V_T (mL)	420	415	390	385	373	362
Total frequency (breaths/min)	20	20	20	20	20	20
Minute ventilation (L/min)	5.04	4.98	4.68	4.62	4.48	4.34

V_T, tidal volume.

What value does the trend monitoring provide for the clinician? What additional data are needed for the clinician to optimize ventilation?

Answer

The data show that the patient has had no respiratory effort over the 10 recorded hours displayed on the data trend. This can be seen by comparing the set frequency with the total frequency. The trends also show that the tidal volume has decreased over time. This can be attributed to an increase in airway resistance or a reduction in lung compliance (or both) because the mode was a form of pressure ventilation. Accessing the trends for airways resistance will enable the clinician to differentiate between problems of airways resistance and lung compliance. If the airways resistance has remained relatively stable, the pulmonary compliance has decreased. Additional testing, such as chest x-ray and arterial blood gas monitoring, may be required to determine pathologic changes such as atelectasis as well as changes in acid-base balance.

very convenient approach is to automate the process using a slow-pressure ramp, which allows both identification of lung recruitability and determination of optimal PEEP.[3] The patient must be heavily sedated and/or paralyzed to avoid errors due to the patient's inspiratory efforts and to minimize patient anxiety and discomfort during the maneuver. For volume-control modes, pressure-volume loops are useful in displaying overdistention. Flow-volume loops are helpful for identifying the need to suction and/or response to bronchodilator therapy. Fig. 46.6 is an example of a composite display showing numeric values, waveforms, and loops.

RULE OF THUMB A pressure-volume curve will take the shape of a "bird's beak" when overdistention is present. This shape occurs because pressure continues to rise but there is no concomitant rise in volume during inspiration. Reducing the delivered tidal volume (by decreasing the set volume during volume-control ventilation or reducing the inspiratory pressure during pressure-control ventilation) will reduce overdistention.

Picture Graphics

An interesting development in ventilator displays involves the use of picture graphics to represent useful information about the patient–ventilator system (Fig. 46.7). Clinicians may also perceive lower subjective workloads when they are using picture graphics.

Alarm Settings

The purpose of ventilator alarms is to bring events to the attention of the clinician. Events are conditions or occurrences requiring clinician awareness or intervention. Ventilators typically announce the priority of alarms (i.e., low or high risk to patient) by means of different colors of lights and/or different sound tones and loudness. The actual setting of alarm thresholds is a complicated topic that has been studied but for which little information is available regarding mechanical ventilation. The basic goal is to maximize true alarms and minimize false alarms. A high rate of false alarms leads to what is called "alarm fatigue," meaning that clinicians get used to the warnings and eventually ignore them. False alarms can also lead to inappropriate responses. On average, ICU alarms occur six times per hour with only a small percentage (23%) indicating an actual urgent clinical situation and a high percentage (44%) being false-positive alarms.[4,5]

Although few studies have addressed mechanical ventilator alarms specifically,[6] it is not hard to imagine similar results for these devices. Ventilator alarms are usually set by the operator (or as default values by the ventilator) as either a set value or a set percentage of the current value. Examples would be low and peak airway pressure alarms set at the current value plus or minus 5 cm H_2O or low and high tidal volume ventilation per minute set at plus or minus 25% of the current value. The problem is that the parameters for which clinicians want to set alarms—and three in particular are highly variable—involve significant portions of readings at extreme values. Therefore limits set as absolute values or percentages may reduce safety for some extreme values while also increasing nuisance events for other values. Further research is needed to identify optimization algorithms (i.e., maximize safety and minimize nuisance), perhaps using artificial intelligence tools to adjust alarm thresholds automatically according to changing patient conditions.

RULE OF THUMB Setting alarms limits appropriately is an important to preventing harm. It is important to verify alarm settings when ventilator parameters are adjusted and with each patient–ventilator safety check.

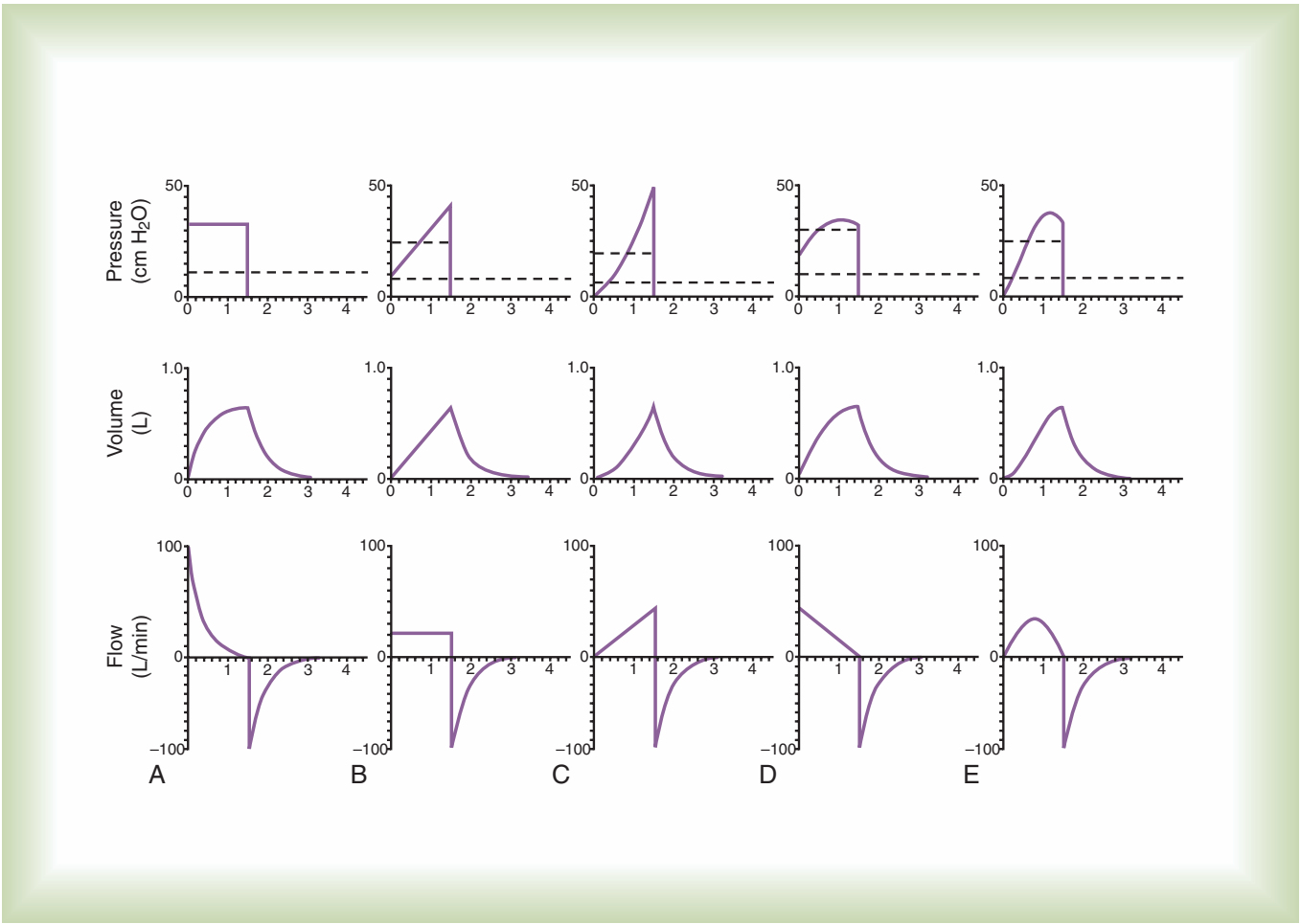

Fig. 46.3 Model Pressure, Volume, and Flow Waveforms Generated With a Computer Using the Equation of Motion. (A) Pressure-controlled inspiration with a rectangular pressure waveform (identical to flow-controlled inspiration with an exponential decay flow waveform). (B) Flow-controlled inspiration with a rectangular flow waveform (identical to volume-controlled inspiration with an ascending-ramp volume waveform). (C) Flow-controlled inspiration with an ascending ramp flow waveform. (D) Flow-controlled inspiration with a descending ramp flow waveform. (E) Flow-controlled inspiration with a sinusoidal flow waveform. The short dotted lines represent mean inspiratory pressure and the long dotted lines represent mean airway pressure (assuming zero positive end expiratory pressure). Note that for the rectangular pressure waveform in A, the mean inspiratory pressure is the same as the peak inspiratory pressure. For all waveforms, V_T = 644 mL, compliance = 20 mL/cm H_2O, and resistance = 20 cm H_2O/L per second.

The Patient Interface

The patient interface is the connection between the ventilator and the patient—typically a system of plastic hoses often called the *patient circuit*. From the perspective of understanding how ventilators work, the important thing to know about the patient circuit is that it contributes to discrepancies between the desired and actual ventilator output values. This is because the patient circuit has its own compliance and resistance. Thus, due to patient circuit resistance, the pressure measured on the inspiratory side of a ventilator will always be higher than the pressure at the airway opening. In addition, the volume and flow coming out of the ventilator will exceed that delivered to the patient because of the compliance of the patient circuit.

Using an analogy to electrical circuits, compliance of the delivery circuit can be shown to be connected in series with compliance of the respiratory system (that is, both elements sharing the same driving pressure). Consequently the total compliance of the ventilator–patient system is simply the sum of the two compliances. Similarly, the delivery circuit's resistance is connected in series with the respiratory system's resistance (that is, both elements sharing the same flow), so that the total resistance is the sum of the two. Based on these assumptions, the relationship between the volume input to the patient (at the point of connection to the patient's airway opening) and the volume output from the ventilator (at the point of connection to the patient circuit) can be described by the following equation:

$$\text{Volume input to patient} = \frac{\text{Volume output from ventilator}}{1 + C_{pc}/C_{rs}} \qquad \textbf{46.1}$$

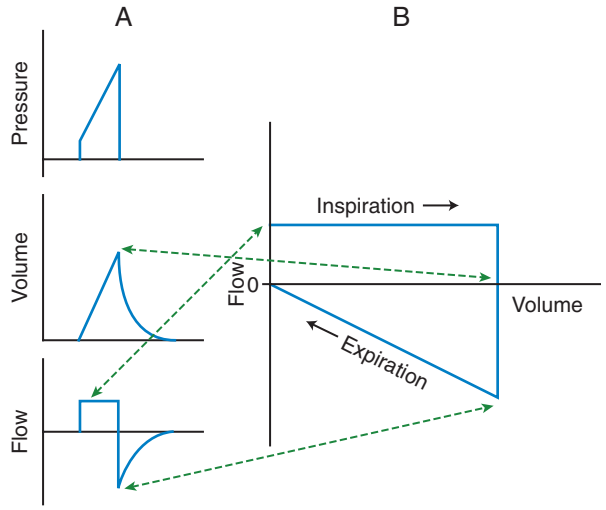

Fig. 46.4 Idealized waveforms (A) for volume-control ventilation with corresponding idealized dynamic (not static or quasi-static) pressure-volume loop (B). The dotted line arrows show the correspondence between the waveform display and the loop display for the initial pressure rise, peak pressure, and tidal volume. (Courtesy Mandu Press Ltd.)

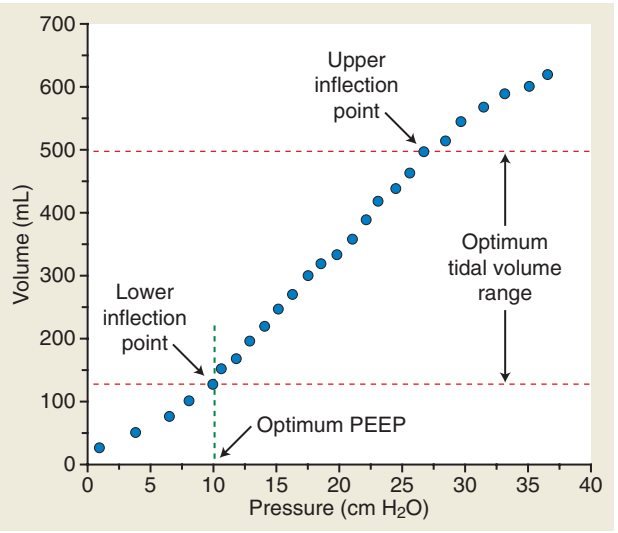

Fig. 46.5 Static pressure-volume loop. *PEEP*, Positive end expiratory pressure. (Courtesy Mandu Press Ltd.)

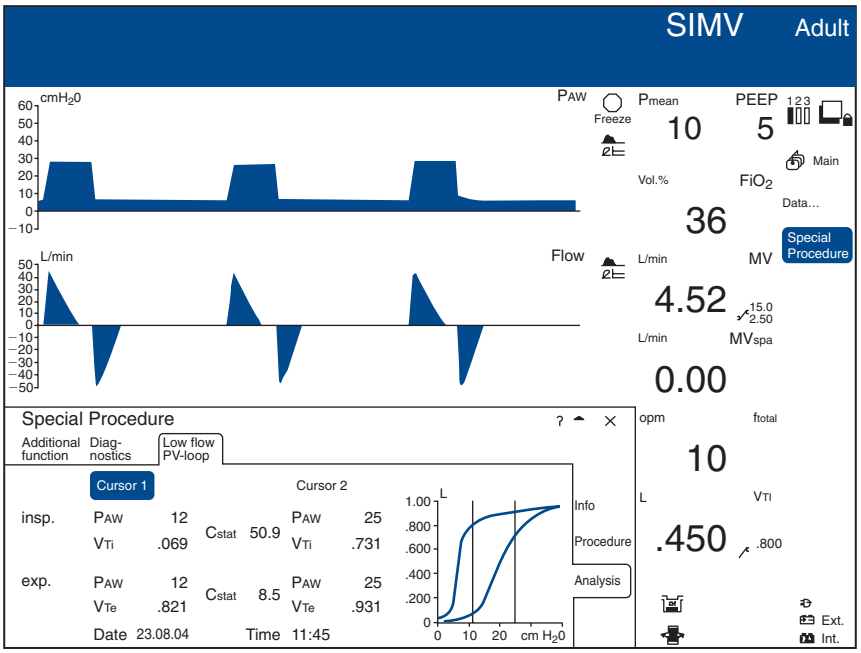

Fig. 46.6 Portion of display screen on the Dräger Evita XL ventilator. (Courtesy Dräger Medical.)

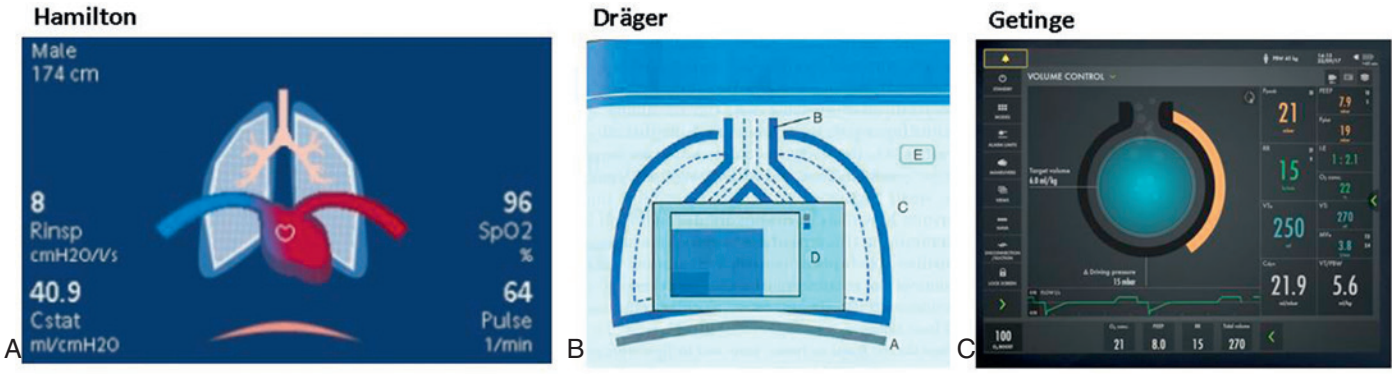

Fig. 46.7 Examples of picture graphic displays on (A) the Hamilton G5 ventilator, (B) the Dräger V500 ventilator, and (C) Genting Servo U ventilator.

where C_{pc} is the compliance of the patient circuit and C_{rs} is the total compliance of the patient's respiratory system. The equation shows that the larger the patient circuit's compliance compared with the patient's respiratory system, the larger the denominator on the right-hand side of the equation. Therefore the delivered tidal volume is smaller than the volume coming from the ventilator's drive mechanism.

Assuming that the volume exiting the ventilator is the set tidal volume, the patient circuit's compliance (C_{pc}) is calculated as follows:

$$C_{pc} = \frac{\text{Set tidal volume}}{P_{plat} - \text{PEEP}} \quad \textbf{46.2}$$

where P_{plat} is the pressure measured during an inspiratory hold maneuver with the Y-piece of the patient circuit occluded (patient not connected) and PEEP is end-expiratory pressure (that is, baseline pressure). Most authors recommend the use of peak inspiratory pressure (PIP) for P_{plat} in this equation, which is acceptable but may lead to a slight underestimation of the patient circuit's compliance. P_{plat} is lower than PIP because of the flow-resistive pressure drop of the patient circuit if pressure is not measured at the Y-piece. This difference is greatest in small-bore corrugated patient circuit tubing but is probably insignificant.

The effects of patient circuit compliance are most troublesome during volume-controlled ventilation. For example, in neonatal ventilation, the patient circuit's compliance can be as much as three times that of the respiratory system even with small-bore tubing and a small-volume humidifier. Thus, in an attempt to deliver a preset tidal volume, the volume delivered to the patient may be as little as 25% of that exiting the ventilator whereas 75% is compressed in the patient circuit.

MINI CLINI

A respiratory therapist is preparing use a portable ventilator while transporting a 10-year-old child to the computed tomography (CT) suite. The child is intubated with a 5.0 cuffed endotracheal tube (ETT) and receiving volume control (VC)-CMV on the following settings:

V_T: 250 mL
Set rate: 14/min
PEEP: 5 cm H_2O
FiO_2: 0.40

Monitored parameters are as follows:

Total rate: 14
P_{plat}: 20 cm H_2O
PIP: 22 cm H_2O
Exhaled V_T: 244 mL

Calculate the tubing compliance.

Answer

$$C_{pc} = \frac{\text{Set tidal volume}}{P_{plat} - \text{PEEP}}$$

$$C_{pc} = \frac{250\,\text{mL}}{20\,\text{cm}\,H_2O - 5\,\text{cm}\,H_2O}$$

$$C_{pc} = \frac{250\,\text{mL}}{15\,\text{cm}\,H_2O}$$

$$C_{pc} = 16.7\,\text{mL/cm}\,H_2O$$

During pressure-control ventilation, the compliance of the patient circuit has the effect of rounding the leading edge of a rectangular pressure waveform, reducing the peak flow and possibly also reducing the volume delivered to the patient. This effect is prevented if the pressure limit is maintained for at least five time constants of the respiratory system.

For both pressure- and volume-control ventilation, the patient circuit's compliance and resistance—along with the resistance of the exhalation valve (in series with the patient circuit and respiratory system resistance)—increase the expiratory time constant. Thus a large circuit compliance coupled with a short expiratory time can lead to inadvertent PEEP (or auto-PEEP).

In summary, the set values for pressure, volume, and flow may be different from the output (from ventilator) values due to calibration errors and the effects of the patient circuit. These two general sources of error cause discrepancies between the desired and actual patient values.

IDENTIFYING MODES OF MECHANICAL VENTILATION

Ventilator manufacturers coin unique names for modes available on their respective devices, primarily as marketing tools. As a result, there have been no industry standards for naming modes of ventilation. This makes it difficult for clinicians to understand how the various modes of ventilation function. In some cases, ventilator modes function in the same way but have very different names. For example, pressure-control ventilation plus adaptive pressure ventilation on the Hamilton Galileo is the same as pressure-regulated volume control on the Siemens Servo 300. Volume control continuous mandatory ventilation (VC-CMV) on the Maquet SERVO-i ventilator and the PB 840 have identical names and function very differently.[7]

The 10 Maxims for Understanding Modes

There is a formal taxonomy for classifying modes of ventilation.[1] The purpose of the taxonomy is the same as the taxonomy for drugs (i.e., to allow the clinician to identify which modes are the same among over 300 unique names coined by manufacturers). The best way to understand the taxonomy is to review 10 fundamental concepts (or maxims) that explain the basic principles of ventilator design and patient–ventilator interaction.

A Breath Is One Cycle of Positive Flow (Inspiration) and Negative Flow (Expiration) Defined in Terms of the Flow-Time Curve

Breath delivery is one of the most basic functions a mechanical ventilator performs. A breath can simply be defined as one cycle of inspiratory flow followed by a matching expiratory flow (Fig. 46.8).

Inspiratory time and expiratory time are the two most basic definitions in reference to a breath. Inspiratory time is defined as the period from the start of inspiratory flow to the start of expiratory flow. Inspiratory time is equal to inspiratory flow time plus inspiratory hold time. Inspiratory flow time is the period from the start of inspiratory flow to the end of inspiratory flow. Inspiratory hold (or pause time) is the period from

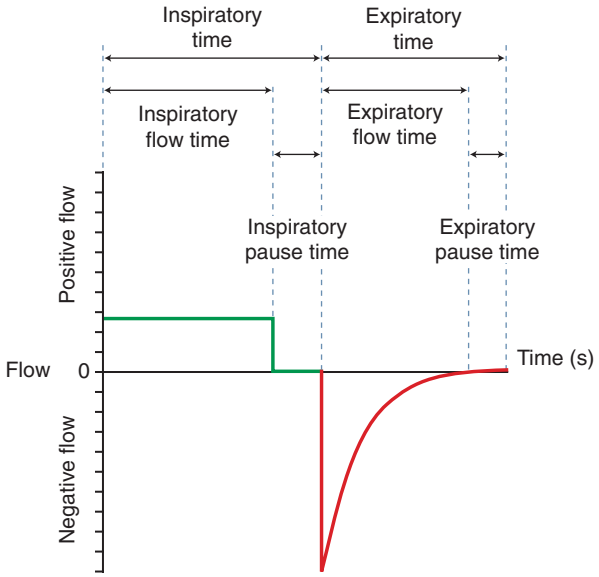

Fig. 46.8 A breath is defined in terms of the flow-time waveform. (Courtesy Mandu Press Ltd.)

the end of inspiratory flow to the start of expiratory flow. On some ventilators, the operator can set inspiratory hold time directly. On others, hold time is the difference between the preset inspiratory time and the inspiratory flow time due to the preset tidal volume at the preset inspiratory flow (i.e., inspiratory flow time = tidal volume/inspiratory flow). It may be used to create a static airway pressure also known as *plateau pressure*. During an inspiratory pause, the flow of gas to and from the patient ceases. Therefore the pressure displayed during the inspiratory pause, or plateau pressure, can be used to calculate respiratory system's resistance and compliance. The period from the start of expiratory flow to the start of inspiratory flow is known as *expiratory time*.

RULE OF THUMB A completely accurate plateau pressure cannot be obtained when the patient is actively breathing. When a patient has an active respiratory drive, sedation may be needed to temporarily suppress the drive while the plateau pressure is obtained.

A Breath Is Assisted If the Ventilator Provides Some or All of the Work of Breathing

Ventilators are designed to assist with the patient's work of breathing. *Work* is defined in terms of the pressure necessary to deliver the tidal volume to the respiratory system. In the simplest case (i.e., constant inspiratory pressure), work is the pressure change during inspiration times the volume change (i.e., tidal volume). An **assisted breath**, therefore, is one for which the ventilator does *some* work on the respiratory system whereas the patient does the rest.

On a ventilator graphic display, an assisted breath is identified as one in which airway pressure rises above baseline during inspiration (recall from maxim 1, inspiration is identified by flow above zero). A drop in airway pressure below baseline during inspiration indicates that the patient is doing work to initiate the breath and to move gas into his or her lungs. In this case, we say the breath is "loaded" rather than assisted. Some loading is unavoidable if the patient must signal to the ventilator when to start inspiratory flow by a drop in airway pressure, called *triggering* (see further on).[8] Optimization of ventilator settings minimizes **loaded breathing** by maximizing the synchrony between the ventilator output and the patient's demand.

A Ventilator Assists Breathing Using Either Pressure Control or Volume Control Based on the Equation of Motion for the Respiratory System

To understand how a ventilator assists breathing, we make use of a very important model of patient–ventilator interaction called the *equation of motion for the respiratory system*. This equation is a mathematical model describing a physical model composed of a single flow-conducting tube (representing the airways) and a single elastic compartment (representing the lungs and chest wall), as shown in Fig. 46.9. There are many versions of this equation, but the simplest version as it relates to ventilator mode classification is as follows:

$$P_{vent}(t) = EV(t) + R\dot{V}(t) \qquad \textbf{46.3}$$

where $P_{vent}(t)$ is inspiratory pressure generated by the ventilator as a function of time, E is the **elastance** of the respiratory system ($\Delta P/\Delta V$); $V(t)$ is volume as a function of time, R is respiratory-system **resistance** ($\Delta P/\Delta \dot{V}$); and $\dot{V}(t)$ is flow as a function of time. *Note that all these variables are measured relative to their end expiratory values.* Sometimes the equation is written with compliance ($C = \Delta V/\Delta P$) instead of elastance, in which case the term $EV(t)$ becomes $V(t)/C$. If the patient is spontaneously triggering the ventilator, the extra inspiratory force is accounted for by the variable representing muscle pressure, P_{mus}, and the left side of Eq. 46.3 becomes $P_{mus} + P_{vent}$, indicating that the work of breathing is shared in some way between the patient and the ventilator. However, if the patient is breathing independent of the ventilator, the left side of Eq. 46.3 is simply P_{mus} (normal spontaneous breathing).

A plot of $P_{vent}(t)$, $V(t)$, and $\dot{V}(t)$ versus time yields the waveforms seen on ventilator displays (Fig. 46.10). If the shape of the pressure waveform is determined by the ventilator settings, and is unaffected by changes in respiratory system mechanics, then the ventilator is providing *pressure control* (PC). In other words, the ventilator controls the left-hand side of Eq. 46.3, and the volume and flow waveforms will be dependent on E and R. In more practical terms, if the operator sets inspiratory pressure, or inspiratory pressure is controlled by the ventilator to be proportional to some measure of the patient's inspiratory effort, then by definition the mode of ventilation is a form of pressure control. One very confusing issue with **pressure-control ventilation** is that sometimes the operator sets the magnitude of the pressure waveform relative to atmospheric pressure (called *PIP*) and other times the magnitude is set relative to PEEP, in this case simply termed inspiratory *pressure*.[9]

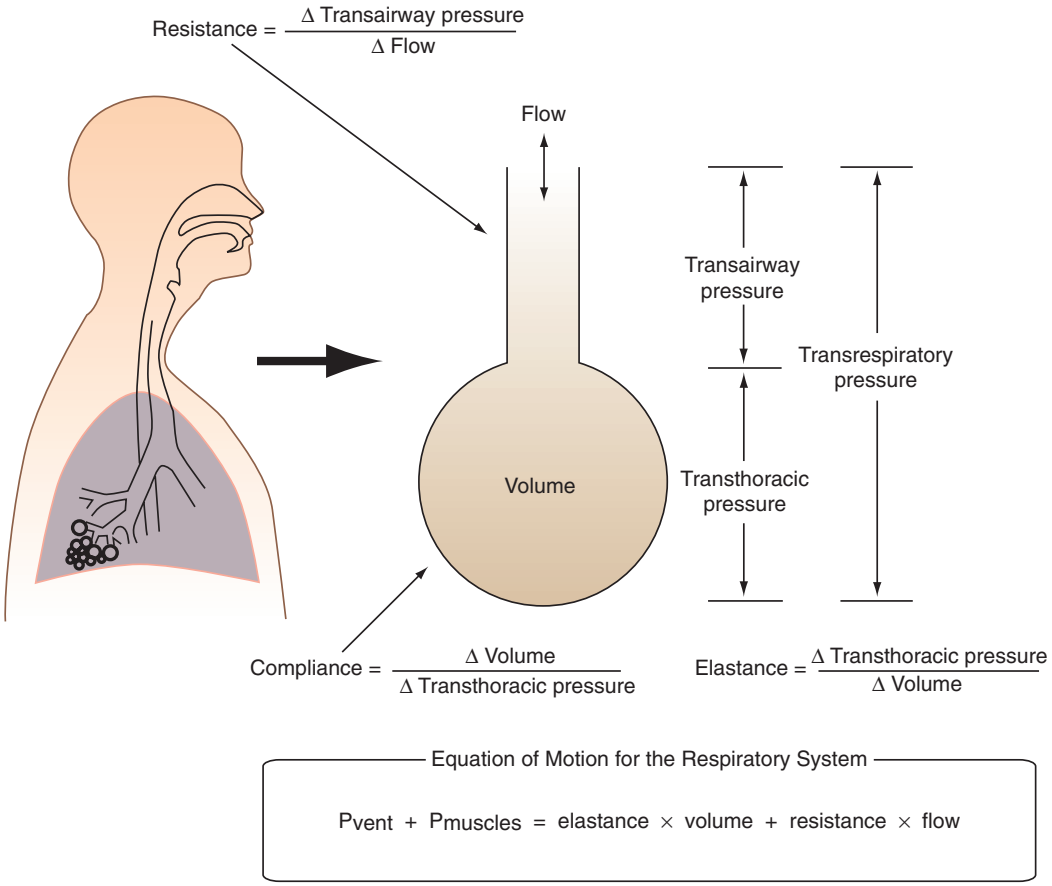

Fig. 46.9 The Respiratory System Can Be Modeled As a Single-Flow Conducting Tube Connected to a Single Elastic Compartment. This physical model can be described by a mathematical model called the *equation of motion* for the respiratory system. In this model, pressure, volume, and flow are variables (i.e., functions of time), whereas resistance and elastance (or compliance) are constants.

RULE OF THUMB In the equation of motion, the term EV (or V/C) is called **driving pressure**, ΔP. Perhaps a more accurate term is **tidal pressure**, P_T (because it is simply tidal volume scaled by elastance or compliance). If you do not know the value of E or C, ΔP can be calculated at the bedside as P_{plt} (PEEP + auto-PEEP). Note that in the literature, ΔP is sometimes defined as PIP minus PEEP during pressure-control modes. This kind of ΔP will overestimate tidal pressure if inspiratory flow has not returned to zero during the preset inspiratory time (i.e., tidal delivery is not complete). Hence we should distinguish between set and measured ΔP, or ΔP_{set} vs ΔP_{meas}, or better, simply use ΔP_{set} vs P_T.

Refer again to Fig. 46.10. If the shapes of the volume and flow waveforms are determined by the ventilator settings, and are unaffected by respiratory system mechanics, the ventilator is providing *volume control* (VC). In other words, the ventilator controls the right-hand side of Eq. 46.3, and the pressure waveform will be dependent on E and R. In more practical terms, if the tidal volume *and* inspiratory flow are preset, then by definition the mode of ventilation is volume control. The term *volume control* is used rather than *flow control* merely for historical reasons. Note that during **volume-control ventilation**, *both* volume and flow are preset prior to inspiration. We emphasize this because there are some *pressure-control modes* that allow the operator to set a target tidal volume but allow the ventilator to determine the flow. There are also pressure-control modes that allow the operator to set the maximum inspiratory flow but not the tidal volume. In this case, tidal volume delivery depends on the operator-set inspiratory pressure target and the mechanics of the patient's respiratory system.

In some rare cases of nonconventional ventilation, inspiratory flow, inspiratory volume, and inspiratory pressure are all dependent on respiratory system mechanics. As no parameters of the pressure, volume, or flow waveforms are preset, the only control of the breath is the timing (i.e., inspiratory and expiratory times). When this happens, the mode is called a form of time control. Examples of this are high-frequency oscillatory ventilation (3100 ventilator, CareFusion, San Diego, CA) and volumetric diffusive respiration (Percussionaire, Sagle, ID).

One way to compare volume- and pressure-control modes of ventilation is to first recognize that the aim is to control the patient's minute ventilation (because minute ventilation determines the $PaCO_2$ for a given rate of metabolic CO_2 production). Next, we can relate the operator-set variables that control minute ventilation for VC versus PC. A convenient way to do this is with influence diagrams, which are graphic illustrations that show how things are interrelated by using circles to represent (in this case) ventilator settings and lines to represent relationships.

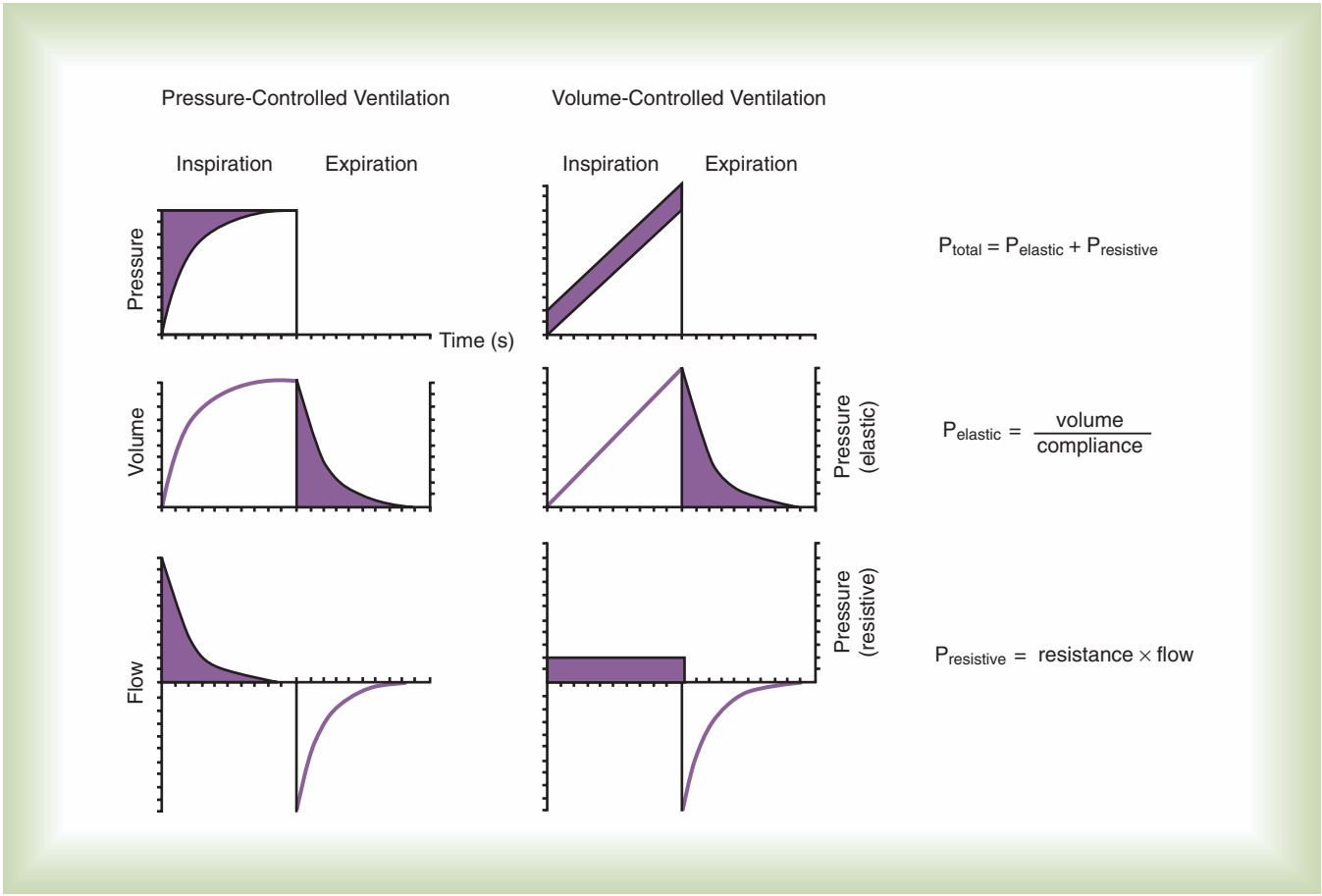

Fig. 46.10 Idealized Waveforms for Volume-Control and Pressure-Control Ventilation. Note that the volume waveform has the same shape as the transthoracic or lung pressure waveform (i.e., pressure due to elastic recoil). The flow waveform has the same shape as the pressure waveform due to airway resistance. The shaded areas represent pressures due to resistance; the open areas represent pressure due to elastic recoil. The dotted lines represent mean airway pressure. Note that the mean pressure at the airway is the same as that in the lung and that mean pressure for volume-control ventilation is less than that for pressure-control ventilation.

Fig. 46.11 shows the influence diagram for volume-control ventilation and Fig. 46.12 shows the influence diagram for pressure-control ventilation. The equations that relate the ventilator settings are given in Table 46.1.

In summary:

Volume control means that *both* volume and flow are preset prior to inspiration.

Pressure control means that inspiratory pressure is preset to some constant value or is proportional to inspiratory effort.

Time control means that pressure, volume, and flow are all dependent on changing respiratory system mechanics and nothing is predetermined except inspiratory and expiratory times.

RULE OF THUMB During volume-control modes, the operator-set flow will affect the inspiratory and expiratory times (if frequency is held constant). A flow-time waveform is helpful in evaluating whether the operator-set flow is sufficient for the patient. When flow does not return to baseline before the start of the next breath, a longer expiratory time is needed. Increasing the inspiratory flow will decrease inspiratory time and increase expiratory time, giving the patient more time to exhale.

Breaths Are Classified According to the Criteria That Trigger (Start) and Cycle (Stop) Inspiration

The definition of a breath (maxim 1) implies that the ventilator knows when to start (**trigger**) and when to stop (**cycle**) inspiratory flow. Several signals can be used to trigger inspiration, including time and changes in airway pressure, volume, or flow. An electrical signal from the diaphragm can also be used to trigger inspiration. Common cycle signals are the same as those for triggering. *Sensitivity* is a term used to describe the amount that the trigger or cycle signal must change before inspiration starts or stops. Fig. 46.13 shows an algorithm that can be used to identify trigger and cycle variables.

Trigger Variable and Cycle Events Can Be Initiated by Either the Patient or the Machine

There are instances when disease processes weaken the diaphragm or when medications, such as sedatives or paralytic agents, interfere with the patient's ability to generate trigger and cycle signals. Hence it is important to have a backup machine trigger system. However, when a patient's ability to generate trigger and cycle signals is intact, it is important to deliver inspiratory flow in

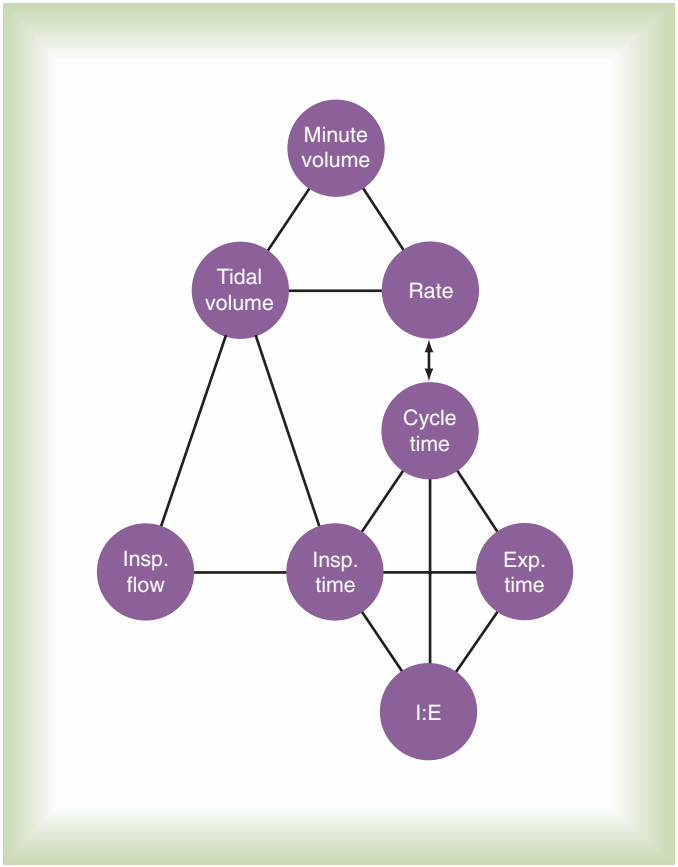

Fig. 46.11 Influence Diagram for Volume-Control Ventilation. Variables are connected by straight lines such that if any two are known, the third can be calculated (see Table 46.1).

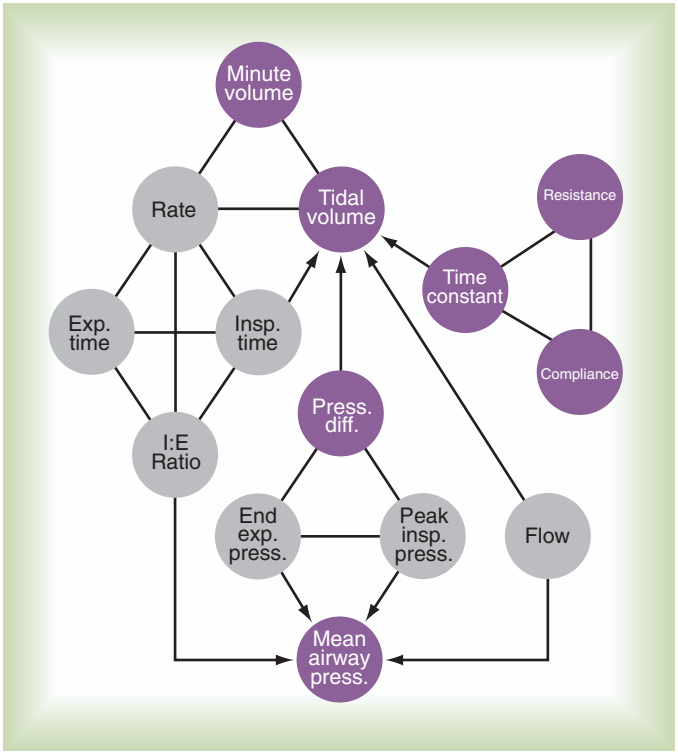

Fig. 46.12 Influence Diagram for Pressure-Control Ventilation. Variables are connected by *straight lines* such that if any two are known, the third can be calculated (see Table 46.1). *Arrows* represent relations that are more complex. *Purple circles* represent variables that are directly controlled by ventilator settings. *Gray circles* show indirectly controlled variables.

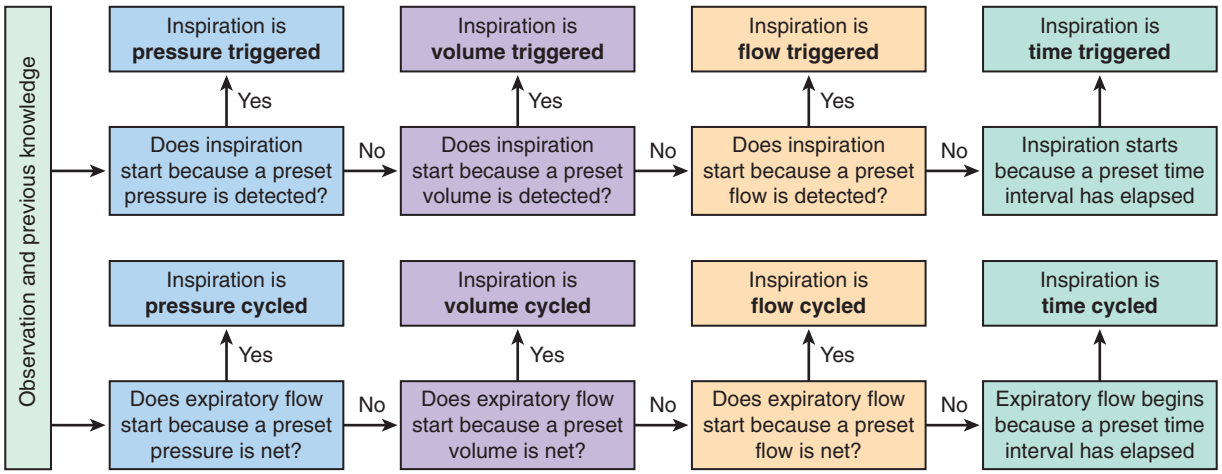

Fig. 46.13 Algorithm for determining the trigger and cycle variables during a breath on a mechanical ventilator.

synchrony with the patient's breathing efforts. Hence machine-initiated trigger and cycle capabilities are built into the mode of ventilation. The trigger variable can be either time, pressure, flow, or volume.

Machine triggering: Inspiration may be triggered by the machine after a preset time interval (e.g., because of a preset breathing frequency). In this instance, inspiration has started regardless of any inspiratory efforts made by the patient. During such a breath, therefore, we say that inspiration is machine-triggered. Minute ventilation threshold is another signal that a ventilator can use to machine-trigger inspiration. Minute ventilation is calculated by dividing the tidal volume by the time for one breath cycle (equivalent to multiplying tidal volume by frequency). Depending on the brand of ventilator used, the

TABLE 46.1 Equations Relating the Important Parameters for Volume-Controlled and Pressure-Controlled Ventilation

Mode	Parameter	Symbol	Equation
Volume-controlled	Tidal volume (L)	V_T	$V_T = \dot{V}_E \div f$ $V_T = \dot{V}_I \times T_I$
	Mean inspiratory flow (L/min)	$\bar{\dot{V}}_I$	$\bar{\dot{V}} = 60 \times V_T \div T_I$ $\bar{\dot{V}}_I = \frac{\dot{V}_E \times TCT}{T_I}$
Pressure-controlled	Tidal volume (L)	V_T	$V_T = \Delta P \times C \times (1 - e^{-t/\tau})$
	Instantaneous inspiratory flow (L/min)	$\dot{V}_I$	$\dot{V}_I = \left(\frac{\Delta P}{R}\right) e^{-t/\tau}$
	Pressure gradient (cm H_2O)	ΔP	$\Delta P = PIP - PEEP$
Both modes	Exhaled minute ventilation (L/min)	$\dot{V}_E$	$\dot{V}_E = V_T \times f$
	Total cycle time or ventilatory period (seconds)	TCT	$TCT = T_I + T_E = 60 \div f$
	I:E ratio	I:E	$I:E = T_I : T_E = \frac{T_I}{T_E}$
	Time constant (seconds)	τ	$\tau = R \times C$
	Resistance (cm H_2O/L/s)	R	$R = \frac{\Delta P}{\Delta \dot{V}}$
	Compliance (L/cm H_2O)	C	$C = \frac{\Delta V}{\Delta P}$
	Elastance	E	$E = \frac{1}{C}$
	Mean airway pressure (cm H_2O)	$\bar{P}_{aw}$	$\bar{P}_{aw} = \left(\frac{1}{TCT}\right) \int_{t=0}^{t=TCT} P_{aw} dt$
Primary variables	Pressure (cm H_2O)	P	
	Volume (L)	V	
	Flow (cm H_2O/L/s)	$\dot{V}$	
	Time (s)	τ	
	Inspiratory time (s)	T_I	
	Expiratory time (s)	T_E	
	Frequency (breaths/min)	f	
	Base of natural logarithm (≈2.72)	e	

PEEP, Positive end-expiratory pressure; *PIP*, peak inspiratory pressure.

clinician may be able to set a minimum threshold for minute ventilation. In this case, inspiration is triggered when minute ventilation drops below a preset threshold.

Machine cycling: A variety of signals may be used to implement machine-cycled inspiration. *Volume cycling* refers to inspiration that ends due to a preset tidal volume. Cycling due to a preset inspiratory time (or inspiratory pause time) is referred to as *time cycling*.

Patient triggering: This means that inspiration starts when the ventilator detects an inspiratory effort. When the patient makes an inspiratory effort, the ventilator commonly detects this by a change in airway pressure, volume, or flow. Inspiratory effort may also be detected by electrical signals derived from the movement of the diaphragm or expansion of the chest wall.

Patient cycling: This means that inspiration stops when the ventilator detects that inspiratory effort has ceased (or perhaps that the patient has made an expiratory effort). Patient cycling is most often based on the decrease in inspiratory flow in pressure-control modes. In fact, some ventilators allow the operator to set the expiratory cycle threshold in terms of a percentage of the peak inspiratory flow. For example, note in Fig. 46.11 (for pressure-control ventilation) during the inspiratory time, flow decays exponentially. Suppose that the peak inspiratory flow was 100 L/min. If the flow cycle threshold is set at 25% of peak flow, then inspiration would be cycled off when flow dropped below 25 L/min. Suppose further that this resulted in an inspiratory time of 1 second. Now, if the cycle threshold was raised to 50%, inspiration would end at 50 L/min and the inspiratory time would be shorter. This is an example of patient cycling that occurs with a mode of ventilation called *pressure support*, which delivers pressure-controlled breaths to spontaneously breathing patients.

Time Constant: In the previous example, the rate of the exponential fall in flow (for a passive breath) is determined by the resistance and compliance of the respiratory system. Indeed, exponential curves are important because they describe both volume and flow during inspiration and expiration, as shown in Fig. 46.10. The rate of the change of an exponential curve is important because it relates to ventilator settings. This rate of change is described in terms of the **time constant**. The time constant is the time required for an exponential curve to reach about 63% of its final (steady-state) value. Mathematically, the time constant for the respiratory system is calculated as the product of resistance and compliance. For example, if resistance is 10 cm H_2O/L per second and compliance is 0.040 L/cm H_2O,

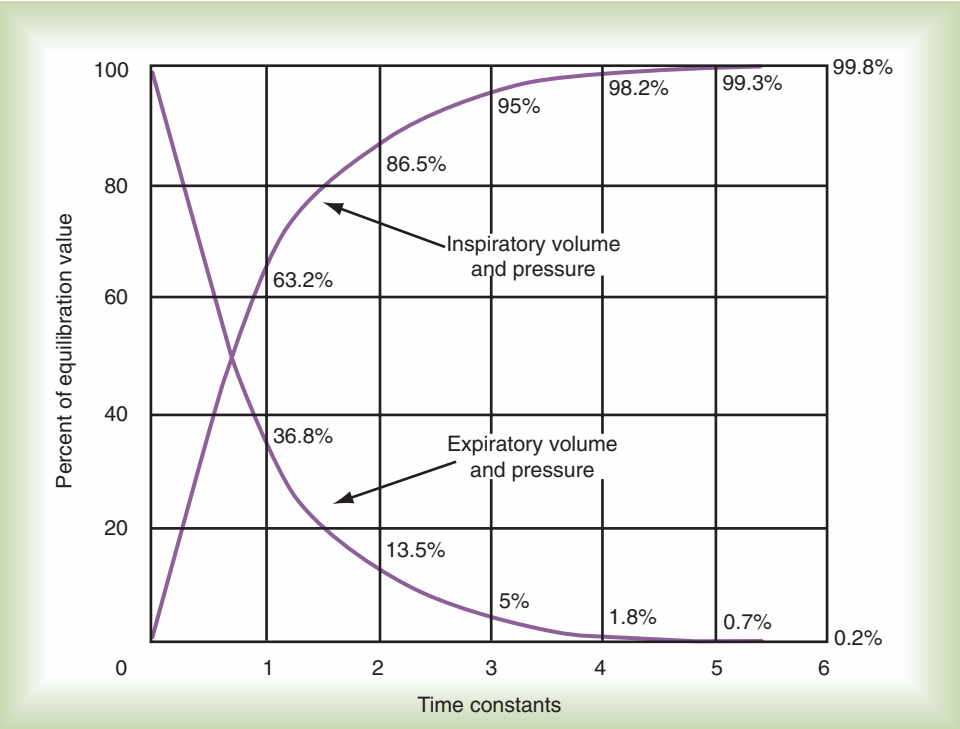

Fig. 46.14 The Time Constant Is a Measure of How Long the respiratory System Takes to Passively Inflate or Deflate in Response to a Sudden Change in Transrespiratory System Pressure. The time constant is calculated as the product of resistance times compliance and is expressed in units of time, usually seconds.

then the time constant is $10 \times 0.04 = 0.4$ seconds. It takes about five time constants for full inspiration (in pressure-control modes) or full expiration (in any mode, Fig. 46.14). Hence inspiratory time in pressure-control modes must be at least five time constants long to deliver the maximum tidal volume. For any mode, expiratory time must be at least five time constants long to prevent gas trapping (i.e., delivering the next breath while the patient is still exhaling). This is undesirable because gas trapping will decrease tidal volume delivery in pressure-control modes and cause lung overexpansion in volume-control modes.

The mechanics of the respiratory system plays a critical role in patient triggering and cycling. These factors are easiest to understand in the passive patient ($P_{mus} = 0$). Let us first consider the cycling of inspiration. If the ventilator delivers a constant inspiratory flow, then peak airway pressure is determined by the preset flow and the elastance and resistance of the patient's respiratory system. Suppose the ventilator is set to cycle inspiration off when a preset pressure threshold is met; for a given preset inspiratory flow, the elastance and resistance of the patient's respiratory system determines the time for this threshold. If these patient-determined factors change, inspiratory time will change. Cycling occurs independently of any preset machine-generated signal and inspiration is patient-cycled. Thus pressure cycling is a form of patient cycling. This can also be observed when a patient makes an expiratory effort, such as a cough, in response to airway irritation by the device's interface or by secretions. Pressure cycling most often occurs as an alarm condition (high-pressure alarm), but it is also a routine cycling mechanism used in automatic resuscitators.[10]

In summary:

Patient-triggering means starting inspiration based on a signal from the patient, which is independent of a machine-triggered signal.

Machine-triggering means starting inspiratory flow based on a signal (usually time) from the ventilator, which is independent of a patient-triggered signal.

Patient cycling means ending inspiratory time based on signals representing the patient-determined components of the equation of motion (i.e., elastance or resistance) and including effects due to inspiratory effort. Flow cycling is a form of patient cycling because the rate of flow decay to the cycle threshold, and hence the inspiratory time, is determined by patient mechanics.

Machine cycling means ending inspiratory time independent of signals representing the patient-determined components of the equation of motion.

Machine versus patient triggering and cycling variables can be identified using a simple algorithm (Fig. 46.15)

RULE OF THUMB When mechanical ventilatory support is being initiated, trigger sensitivity must be set appropriately for the patient's inspiratory efforts. Trigger thresholds set too high may cause a delay in flow delivery. In other words, the sensitivity is set too low, meaning not sensitive enough to detect the patient's inspiratory effort. On the other hand, trigger thresholds set too low may cause autotriggering. In other words, the sensitivity is set too high. Autotriggering means that inspiration is inadvertently triggered at a high rate and without trigger signals from the patient. Trigger thresholds set at either extreme (too high or too low) contribute to patient–ventilator synchrony problems, reduce patient comfort, and impair effective ventilation.

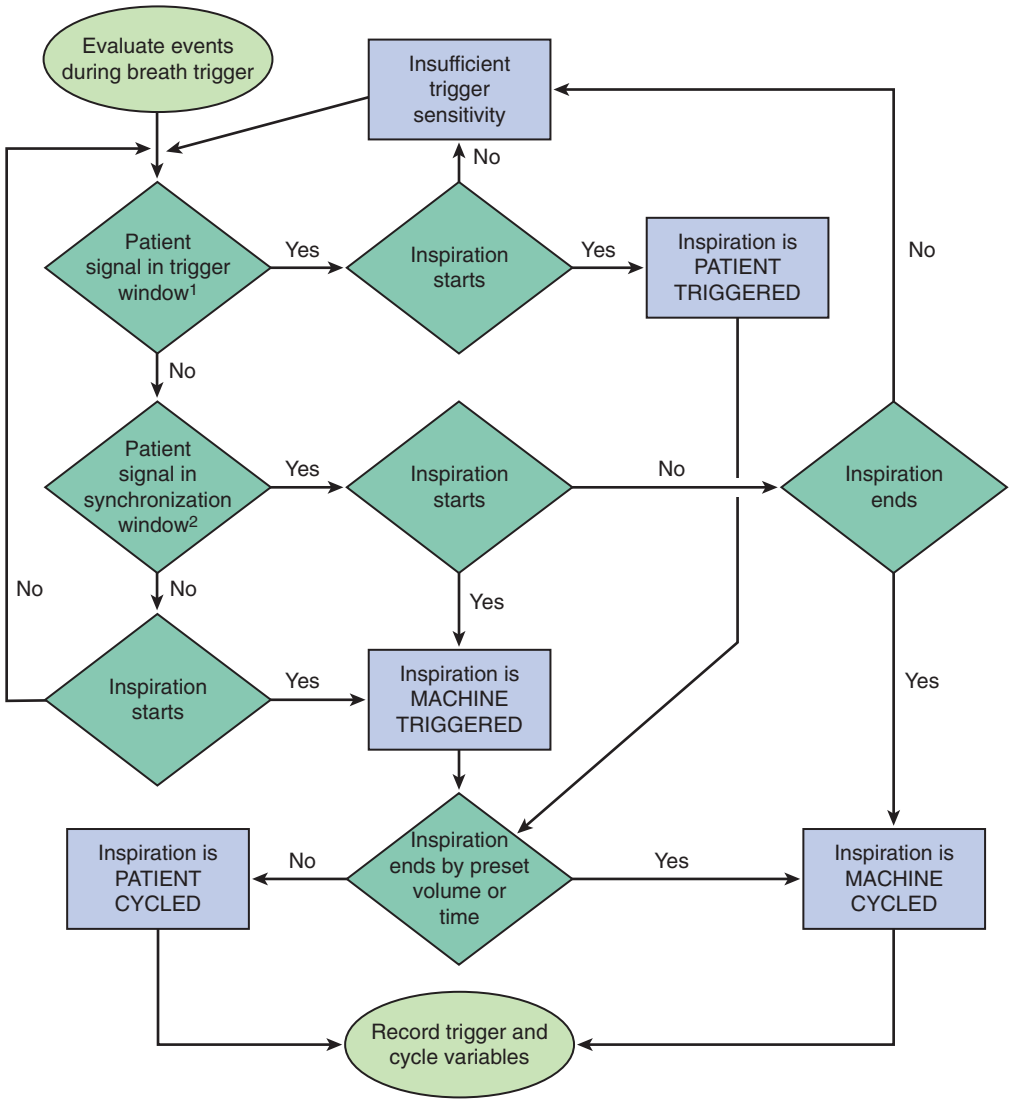

Fig. 46.15 An algorithm for distinguishing between machine versus patient events for triggering and cycling. (Courtesy Mandu Press Ltd.)

Breaths Are Classified as Spontaneous or Mandatory Based on Both the Trigger and Cycle Events

The terms *spontaneous* and ***mandatory*** describing types of breaths are fundamental concepts for the classification of modes. The dictionary definition of *spontaneous* is "without premeditation or external stimulus." If we apply this definition to breathing, it implies that the patient retains substantial control over timing. Therefore **spontaneous breaths** are those for which the patient determines the start and end of inspiration independent of any machine settings for inspiratory and expiratory times. In terms of the previous two maxims, then, a spontaneous breath is one for which inspiration is both triggered and cycled by the patient. A spontaneous breath may occur during a mandatory breath (e.g., airway pressure-release ventilation). The definition given here applies for assisted and unassisted breathing. For unassisted breathing, the brain provides the trigger and cycle signals. For assisted breathing, the signals may come from the brain or the ventilator.

A mandatory breath is a breath for which the patient has lost control over timing (i.e., frequency or inspiratory time). During a mandatory breath, the start and/or end of inspiration is determined by the ventilator, independent of the patient. Again, in terms of the previous two maxims, a mandatory breath is one for which the machine triggers or cycles inspiration (or both). A mandatory breath can occur during a spontaneous breath (e.g., high-frequency jet ventilation). A mandatory breath is, by definition, assisted.

In summary:

A *spontaneous breath* is one for which inspiration is both triggered and cycled by the patient.

A *mandatory breath* is anything else (machine triggered and patient cycled; patient triggered and machine cycled; machine triggered and machine cycled).

There Are Three Basic Breath Sequences: Continuous Mandatory Ventilation, Intermittent Mandatory Ventilation, and Continuous Spontaneous Ventilation

Spontaneous and mandatory breaths come out of a ventilator much as dots and dashes come out of a telegraph machine. Because there are only two types of breaths, it follows that there are only three possible breath sequences: all breaths are mandatory, called **continuous mandatory ventilation (CMV)**; there are both mandatory and spontaneous breaths, called **intermittent mandatory ventilation (IMV)**; and all breaths are spontaneous, called **continuous spontaneous ventilation (CSV)**.

More specifically, CMV is a breath sequence for which spontaneous breaths are not possible between mandatory breaths because every patient trigger signal in the trigger window produces a machine-cycled inspiration (i.e., a mandatory breath). CMV is commonly referred to as assist/control. Machine-triggered mandatory breaths may be delivered at a preset frequency with this breath sequence. The mandatory breath frequency for CMV is the set *minimum* value for the frequency. The total frequency may be higher than the set frequency but never below it. In some pressure-controlled modes on ventilators with an active exhalation valve, spontaneous breaths may occur during mandatory breaths, but the defining characteristic of CMV is that spontaneous breaths are not permitted between mandatory breaths.

IMV has three variations.

1. Mandatory breaths are always delivered at the set frequency (e.g., synchronized intermittent mandatory ventilation (SIMV) volume-control mode on the Servo U ventilator). When a synchronization window is used, the actual ventilatory period for a mandatory breath may be shorter than the set period. Some ventilators, such as the Dräger Evita V500, will add the difference to the next mandatory period to maintain the set mandatory breath frequency.
2. Mandatory breaths are delivered only when the spontaneous breath frequency falls below the set frequency. One example is the spontaneous/timed (S/T) mode on the Philips Bilevel positive airway pressure (BiPAP) noninvasive ventilator.
3. Mandatory breaths are delivered only when the measured minute ventilation (i.e., product of breath frequency and tidal volume) drops below a preset threshold. Examples of this variation include Dräger's mandatory minute volume ventilation mode and Hamilton's adaptive support ventilation mode.

In contrast to CMV, in IMV the mandatory breath frequency can never be higher than the set rate, but it may be lower (i.e., the set frequency is a *maximum* value).

Note that use of the definitions for mandatory and spontaneous breaths for determining the breath sequence (i.e., CMV, IMV, CSV) assumes normal ventilator operation. For example, coughing during VC-CMV may result in patient cycling for a patient-triggered breath due to the pressure alarm limit. Although inspiration for that breath is both patient triggered and patient cycled, this is not normal operation and the sequence does not turn into IMV.

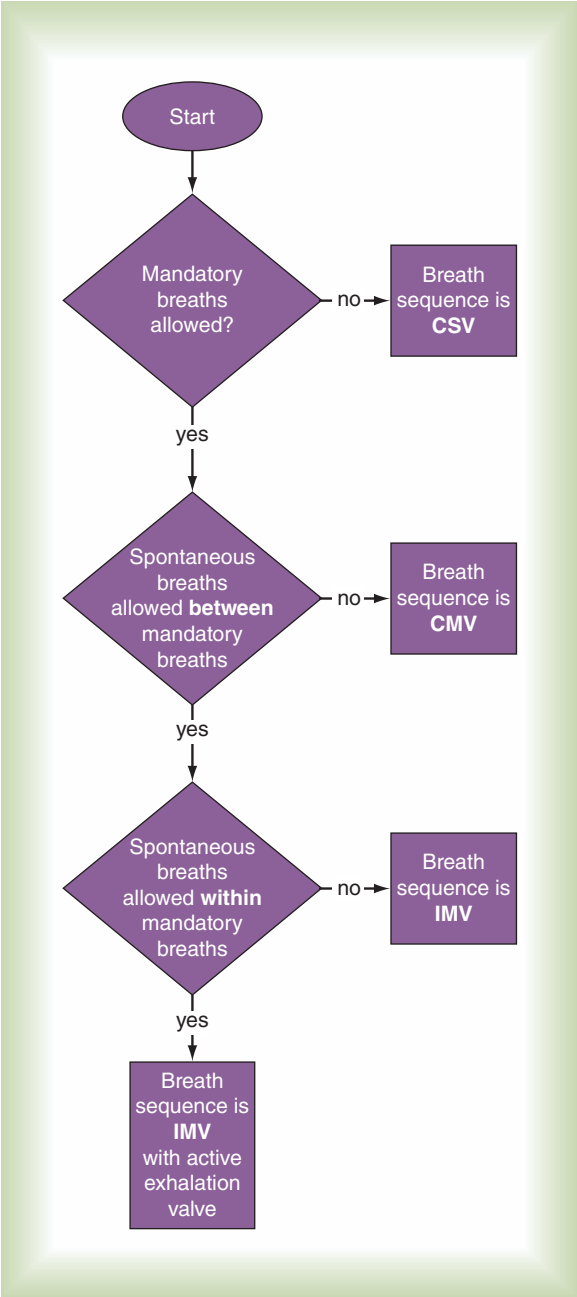

Fig. 46.16 Algorithm distinguishing between continuous spontaneous ventilation *(CSV)*, continuous mandatory ventilation *(CMV)*, and intermittent mandatory ventilation *(IMV)*.

CSV means that all breaths are spontaneous. Alternatively, you could think of it as the opposite of CMV, meaning that mandatory breaths are not permitted between spontaneous breaths.

Note that the definition of a breath sequence depends on the definition of spontaneous and mandatory breaths (maxim 6) and those definitions rely on the definitions of machine versus patient triggering and cycling (maxims 4 and 5). The distinctions between CMV, IMC, and CSV are illustrated in Fig. 46.16.

There Are Five Basic Ventilatory Patterns: VC-CMV, VC-IMV, PC-CMV, PC-IMV, and PC-CSV

A ventilatory pattern is a sequence of breaths (CMV, IMV, or CSV) with a designated control variable (volume or pressure)

for the mandatory breaths (or the spontaneous breaths for CSV). Thus, with two control variables and three breath sequences, there are five possible ventilatory patterns: VC-CMV, VC-IMV, PC-CMV, PC-IMV, and PC-CSV. The VC-CSV combination is not possible because volume control implies that inspiration ends when the preset tidal volume is delivered, which implies ventilator cycling, and ventilator cycling makes every breath mandatory, not spontaneous (maxim 6).

For completeness, we include the possibility of a time-control (TC) ventilatory pattern such as TC-IMV. Although this is uncommon and nonconventional, it is possible, as demonstrated by modes such as high-frequency oscillatory ventilation and intrapulmonary percussive ventilation. Because any mode of ventilation can be associated with one and only one ventilatory pattern, the ventilatory pattern serves as a simple mode classification system.

Ventilatory patterns are a simple mode classification system that offers practical advantages in clinical situations. We can use it to describe different modes a patient may experience without using the names for modes that vary depending on the ventilator manufacturer. For example, during surgery, there may be no need to worry about patient–ventilator synchrony; thus we might say VC-CMV was used (instead of saying volume assist/control or CMV, names that relate to specific ventilators).

RULE OF THUMB Tidal volume is an important ventilator parameter to set. During volume-control modes, the tidal volume is initially set at 4–6 mL/kg of predicted body weight. Setting the tidal volume too high can contribute to lung overdistention (volutrauma). When a tidal volume is set too low, hypoventilation can occur. Arterial blood gases and volumetric or end-tidal CO_2 monitoring can be used to evaluate the effectiveness of ventilation. Arterial blood gases and pulse oximetry can be used to evaluate the effectiveness of oxygenation.

Postoperatively, we could say we switched to PC-CMV to allow unrestricted inspiratory flow when the patient began to make some breathing effort (instead of saying pressure assist/control or pressure control; again, names of modes on specific ventilators). When the patient is evaluated for extubation, a "spontaneous breathing trial" may be attempted using PC-CSV (instead of saying pressure support or volume support). Referring to modes in terms of breathing patterns instead of specific names on particular ventilators simplifies both verbal communication and, perhaps more important, documentation in the patient's record.

RULE OF THUMB Tidal volume cannot be set directly during PCV. To prevent overdistention or hypoventilation, monitor the inhaled tidal volume during mandatory PCV breaths. Inhaled tidal volume should follow lung protective strategies. The inspiratory pressure should be set to deliver a tidal volume of 4–8 mL/kg predicted body weight. Arterial blood gases can be used to monitor the effectiveness of ventilation and oxygenation. Noninvasive monitors such as volumetric or end-tidal CO_2 monitoring may be used to evaluate ventilation and pulse oximetry to monitor oxygenation.

Ventilatory Patterns Vary According to Their Targeting Schemes (Set-Point, Dual, Bio-Variable, Servo, Adaptive, Optimal, and Intelligent)

Although the concept of ventilatory patterns may serve as a simple classification system in some cases, a more precise way to identify the differences among modes is necessary. To do this, we need a deeper understanding of the feedback control schemes used by engineers who design modes. We refer to these as **targeting schemes**.

Targeting schemes. Fig. 46.17 shows the schematic of a closed-loop or feedback control scheme. The operator sets a desired *input*—for example, inspiratory pressure. The software sends control signals to the flow-control and exhalation valves. The manipulated variable (typically flow) is delivered to the patient. The resulting inspiratory pressure (the *output*) is measured as a feedback signal and compared with the input setting. A variety of disturbances—such as patient circuit characteristics, leaks, patient ventilatory efforts, and respiratory system mechanics, to name a few—can affect the output. Any difference between the input and output generates an error signal. That signal is passed on to the control valves to bring the output closer to the input. This system is referred to as a *targeting scheme* in this chapter as it relates to modes of ventilation.

The targeting scheme is a key component of a mode description. A target is basically a predetermined goal of ventilator output. Pressure, volume, and flow waveforms are called *within-breath* targets. Inspiratory pressure, rise time, inspiratory flow, and tidal volume (set-point and dual targeting), and a constant proportionality between inspiratory pressure and patient effort (**servo targeting**) are examples of within-breath targets. Preset values within a breath that end inspiration—such as tidal volume, inspiratory time, or percent of peak flow—may also be considered cycle variables.

There may also be *between-breath targets*. These serve to modify the within-breath targets or the overall ventilatory pattern. Between-breath targets are used with more advanced targeting

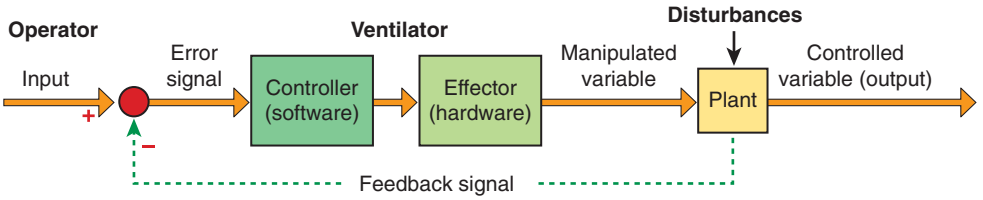

Fig. 46.17 Schematic of a closed-loop feedback-control scheme for a ventilator. (Courtesy Mandu Press Ltd.)

schemes, where targets act over multiple breaths. A simple example of a between-breath target is comparing actual exhaled volume to a preset between-breath tidal volume to automatically adjust the within-breath constant pressure or flow target for the next breath. Average tidal volume (for adaptive targeting), percent minute ventilation (for **optimal targeting**), combined PCO_2, volume, and frequency values describing a zone of comfort (for **intelligent targeting**) are examples of between-breath targets and targeting schemes.

At least seven targeting schemes are used on commercially available ventilators:[11]

1. *Set point:* This is the most common type and is found on all ventilators. The operator sets all parameters of the pressure waveform (pressure-control modes) or volume and flow waveforms (volume-control modes) and the ventilator makes no automatic adjustments to the targets. The advantage is simplicity. The disadvantage is that changing patient condition may make the settings inappropriate, so that frequent manual adjustments are necessary. Modes using set-point targeting include those named volume or pressure assist/control, volume or pressure SIMV, and pressure support.
2. *Dual:* The ventilator can automatically switch between volume-control and pressure-control during a single inspiration. The advantage is the ability to adjust to changing patient condition and assure either a preset tidal volume or PIP, whichever is deemed most important. The disadvantage is that some forms are complicated, difficult to set, and need constant readjustment. The original mode using **dual targeting** was called *volume assured pressure support*. In this mode, inspiration started off in pressure control but changed to volume control if flow decayed to the preset value before the tidal volume was delivered.[12] A much more common example of the opposite approach (switching from volume control to pressure control), is flow adaptive volume control on the Maquet SERVO-i ventilator. If the patient makes little or no inspiratory efforts, the mode looks like VC-CMV (e.g., assist/control). But if the patient makes strong enough efforts, the mode looks like PC-CSV (e.g., pressure support).[7] Many Servo I and Servo U ventilators are in use with this targeting scheme as the default (and perhaps only) option for volume control modes. The clinician must be aware of this because, with sufficient inspiratory effort, the patient can turn what was expected to be a mandatory volume-control breath into a spontaneous pressure-controlled breath (actually a pressure-support breath). Hence tidal volume can be much higher than set.
3. *Bio-variable:* This is an unusual targeting scheme. Studies have shown that varying tidal volume breath by breath to mimic normal breathing improves gas exchange.[13] Currently this **bio-variable targeting scheme** is available in only one mode, variable pressure support on the Dräger V500 ventilator. The operator sets a target inspiratory pressure and a percent variability from 0% to 100%. A setting of 0% means that the preset inspiratory pressure will be delivered for every breath. A 100% variability setting means that the actual inspiratory pressure will vary randomly from PEEP/CPAP level to double the preset pressure-support level.
4. *Servo:* The output of the ventilator (pressure/volume/flow) automatically follows a varying input. In current modes, this means that the inspiratory pressure is proportional to the patient's inspiratory effort; the more assistance the patient demands, the more the ventilator delivers. No other targeting scheme does this. The disadvantage is that it requires estimates of artificial airway and/or respiratory system mechanical properties or special equipment to monitor the respiratory effort signal. This targeting scheme is found on all ventilators that offer some form of automatic tube compensation (ATC).[14] Servo targeting makes possible the modes called proportional assist ventilation (PAV)[15] and neurally adjusted ventilatory assist (NAVA).[16]
5. *Adaptive:* The ventilator automatically sets targets between breaths in response to varying patient conditions. The advantage is that it can adjust to changing patient lung mechanics (including inspiratory effort). The disadvantage is that the automatic adjustment may be inappropriate if the algorithm assumptions are violated or they do not match the patient's actual physiology.[17] The first mode to use this was called *pressure regulated volume control*. This targeting scheme is now available on virtually all ICU ventilators and is given various names, including *volume guarantee, volume control plus, adaptive pressure ventilation,* and *autoflow.* In the literature, this is often called "volume targeting" or "volume-targeted pressure control."
6. *Optimal:* The ventilator automatically adjusts the targets of the ventilatory pattern to either minimize or maximize some overall performance characteristic. The advantage is that it can adjust to changing patient conditions. The disadvantage is that the automatic adjustment may be inappropriate if the algorithm assumptions are violated or they do not match the patient's actual physiology. The only mode currently using this is adaptive support ventilation (ASV) on Hamilton ventilators.[18]
7. *Intelligent:* This is a targeting scheme that uses artificial intelligence programs such as fuzzy logic, rule-based expert systems, and artificial neural networks. The advantage is that it can adjust to changing patient conditions. The disadvantage is that the automatic adjustment may be inappropriate if the algorithm assumptions are violated or they do not match the patient's actual physiology. The only modes currently using this scheme are Dräger's SmartCare/PS[19] and Hamilton's IntelliVent[20] (not available in the United States).

These targeting schemes, along with example modes that use them, are summarized in Table 46.2.

A Mode of Ventilation Is Classified According to Its Control Variable, Breath Sequence, and Targeting Schemes

In general terms, a mode of ventilation is a predefined pattern of interaction between the ventilator and the patient. Historically, modes have been referred to by the names coined by ventilator manufacturers, who use them as marketing devices. As a consequence, there are now so many different names that understanding and comparing all modes has become nearly impossible.

TABLE 46.2 Specifications for Some Modes Found on the Draeger Evita XL Ventilator

Name (Abbreviation)	Description	Advantage	Disadvantage	Example Mode Name	Ventilator (Manufacturer)
Set-point (s)	The operator sets all parameters of the pressure waveform (pressure-control modes) or volume and flow waveforms (volume-control modes).	Simplicity.	Changing patient conditions may make settings inappropriate.	Volume control CMV	Evita Infinity V500 (Drager)
Dual (d)	The ventilator can automatically switch between volume control and pressure control during a single inspiration.	It can adjust to changing patient conditions and ensure either a preset V_T or PIP, whichever is deemed most important.	It may be complicated to set correctly and may need constant readjustment if not automatically controlled by the ventilator.	Volume control	Servo-I (Maquet)
Servo (r)	The output of the ventilator (pressure/volume/flow) automatically follows a varying input.	Support by the ventilator is proportional to inspiratory effort.	It requires estimates of artificial airway and/or respiratory system mechanical properties.	Proportional assist ventilation	PB840 (Covidien)
Adaptive (a)	The ventilator automatically sets target(s) between breaths in response to varying patient conditions.	It can maintain stable V_T delivery with pressure control for changing lung mechanics or patient inspiratory effort.	Automatic adjustment may be inappropriate if algorithm assumptions are violated or if they do not match physiology.	Pressure-regulated volume control	Servo-I
Bio-variable (b)	The ventilator automatically adjusts the inspiratory pressure or V_T randomly.	It simulates the inspiratory time or V_T observed during normal breathing and may improve oxygenation or mechanics.	Manually set range of variability may be inappropriate to achieve goals.	Variable pressure support	Evita Infinity V500
Optimal (o)	The ventilator automatically adjusts the targets of the ventilator pattern to either minimize or maximize some overall performance characteristic (e.g., work or rate of breathing).	It can adjust to changing lung mechanics or patient inspiratory effort.	Automatic adjustment may be inappropriate if algorithm assumptions are violated or if they do not match physiology.	ASV	GS (Hamilton Medical)
Intelligent (i)	This is a targeting scheme that uses artificial intelligence programs such as fuzzy logic, rule-based expert systems, and artificial neural networks.	It can adjust to changing lung mechanics or patient inspiratory effort.	Automatic adjustment may be inappropriate if algorithm assumptions are violated or if they do not match physiology.	SmartCare/PS IrdelliVent-ASV	Evita Infinity V500 S1 (Hamilton Medical)

ASV, Adaptive support ventilation; *CMV*, continuous mandatory ventilation; *PIP*, peak inspiratory pressure; V_T, tidal volume.

The solution is to use a *taxonomy*. A taxonomy is a formal classification system.

Classification systems are important for organizing large amounts of information, as in biology (e.g., order, family, genus, species) and in large databases (e.g., Amazon.com) to facilitate searches. The use of a taxonomy for modes of ventilation makes it easier (1) to compare research reports and facilitate the development of evidence-based clinical practice; (2) for clinicians to select the most appropriate modes, making optimal ventilator management more likely; and (3) for manufacturers to communicate with clients, thus improving the effectiveness of both sales and training.

The taxonomy of modes is based on the concepts of the control variable, the breath sequence, and the targeting scheme, as described in the previous nine maxims.

A Taxonomy for Mechanical Ventilation

A taxonomy is a hierarchy (outline) of concepts starting with the most general and progressing to more specific with each successive level of the outline. The ventilator mode taxonomy has four hierarchical levels.[1]

1. Control variable (pressure, volume, or time)
   A. Breath sequence (CMV, IMV, or CSV)
      i. Primary breath targeting scheme (for CMV or CSV)
         a. Secondary breath targeting scheme (for IMV)

The "primary breath" is either the only breath there is (mandatory for CMV and spontaneous for CSV) or it is the mandatory breath in IMV. The targeting schemes can be represented by single lowercase letters: set-point = s, dual = d, servo = r, bio-variable = b, adaptive = a, optimal = o, intelligent = i. For example, on the Medtronic PB 980 ventilator there is a mode called A/C

volume control. This mode is classified as volume control continuous mandatory ventilation with set-point targeting, represented by VC-CMVs. A mode with the same functionality on the Dräger Evita V500 ventilator is called *CMV*. On that ventilator, you can alter the targeting scheme by activating a feature called *autoflow*. This changes the mode to pressure control continuous mandatory ventilation with adaptive targeting, or PC-CMVa.

Finally, some modes represent compound targeting schemes. For example, some ventilators offer tube compensation, a feature that increases inspiratory pressure in proportion to flow to support the resistive load of breathing through an artificial airway. This is a form of servo targeting. On the Dräger Evita V500, you can add tube compensation to CMV with autoflow to get a mode classified as PC-CMVar (*ar* represents the compound targeting scheme composed of servo added to set-point). A mode classified as pressure-control intermittent mandatory ventilation with set-point control for both primary (mandatory) and secondary (spontaneous) breaths would have a tag that looks like this: PC-IMVs,s. If you added tube compensation to the spontaneous breaths (e.g., Medtronic PB 980), the tag would change to PC-IMVs,sr. If you added it to both mandatory and spontaneous breaths (e.g., Dräger Evita V500), the tag would change to PC-IMVsr,sr.

The structure of this mode classification system is reminiscent of the taxonomy of biologic organisms comprising order (control variable), family (breath sequence), genus (primary targeting scheme), and species (secondary targeting scheme). Modes in the same "species" can be further differentiated by describing their "species variety" in terms of their phase variables (i.e., trigger and cycle variables plus the within- and between-breath targets and control algorithms). An example of the use of a "species variety" description is to distinguish between proportional assist ventilation and neurally adjusted ventilatory assist, both of which are forms of PC-CSVr. They can be distinguished simply by noting that PAV breaths are triggered and cycled with flow signals whereas NAVA is triggered and cycled with an electrical signal representing diaphragm activation. Of course there are a great many other distinguishing features (e.g., targeting algorithms), but these are better described in the operator's manuals than in a general classification table.

How to Classify Modes

Translating the name of a mode into a mode classification using the taxonomy we have described is a simple three-step procedure:

Step 1: Identify the control variable. Simply put, if you set inspiratory pressure, or if pressure is proportional to inspiratory effort, then the control variable is pressure. On the contrary, if you set tidal volume and inspiratory flow, then the control variable is volume. Fig. 46.18 shows the decision algorithm with a few refinements to accommodate dual targeting.

Step 2: Identify the breath sequence. Fig. 46.19 shows the decision rules.

Step 3: Identify the targeting schemes for the primary and (if applicable) secondary breaths (see Table 46.2).

Examples

To demonstrate these steps, we will classify some of the most commonly used modes in ICUs, starting with A/C volume control (Medtronic PB 980). For this mode, both inspiratory volume and flow are preset, so the control variable is volume. Every breath is volume cycled, which is a form of machine cycling. Any breath for which inspiration is machine cycled is classified as a mandatory breath. Hence the breath sequence is CMV. Finally, the operator sets all the parameters of the volume and flow waveforms, so the targeting scheme is set-point. Thus the mode is classified as volume-control continuous mandatory ventilation with set-point targeting (the tag or abbreviation is thus VC-CMVs).

Another common mode is volume control plus (Medtronic PB 980). For this mode, the operator sets a tidal-volume target but not the inspiratory flow. Because setting volume alone (like setting flow alone) is a necessary but not sufficient criterion for volume control, the control variable is pressure. Spontaneous breaths are allowed between mandatory breaths, which means that the breath sequence is IMV. The ventilator adjusts the inspiratory pressure of mandatory breaths to achieve an average preset tidal volume, making the primary targeting scheme adaptive. Spontaneous breaths between mandatory breaths are either CPAP or pressure support, so the targeting scheme is set point. The mode tag is thus PC-IMVa,s.

A very common mode for spontaneous breathing trials (or for assistance of spontaneous breaths in IMV modes) is pressure support. For this mode, the operator sets an inspiratory pressure, so the control variable is pressure. All breaths are patient triggered and patient cycled (note what was said about flow cycling earlier), so the breath sequence is CSV. Because the ventilator does not adjust any of the parameters of the breath, the targeting scheme is set point and the tag is PC-CSVs.

If carefully applied, the taxonomy has the power to clarify and unmask hidden complexity in a mode that has a cryptic name. Take, for example, the mode called CMV+ autoflow on the Dräger Evita V500 ventilator. Although CMV on this ventilator is the same as the "volume assist/control" described earlier, adding the "autoflow" feature changes it to a completely different mode. For CMV + autoflow, the operator sets a target tidal volume but not inspiratory flow. Indeed, inspiratory flow is highly variable because the ventilator actually sets the inspiratory pressure within a breath. Thus the control variable, according to the equation of motion, is pressure. Every inspiration is time cycled and hence every breath is mandatory and the breath sequence is CMV. The ventilator adjusts the inspiratory pressure between breaths to achieve an average tidal volume equal to the preset value using an **adaptive targeting scheme**. Thus the mode is classified as pressure control continuous mandatory ventilation with adaptive targeting (PC-CMVa).

On the other hand, the taxonomy can also unmask the complexity in an apparently simple mode. The mode called volume control (Getinge SERVO-U) allows setting of tidal volume and inspiratory time. Setting both volume and inspiratory time is equivalent to setting mean inspiratory flow (flow = volume/time), hence the control variable is volume. Every breath is normally time cycled and hence mandatory, so our initial thought is that the breath sequence is CMV. The tricky part is the targeting scheme. The operator's manual states that "if a pressure drop of 3 cm H_2O is detected during inspiration, the ventilator (switches) to pressure support with a resulting increase in

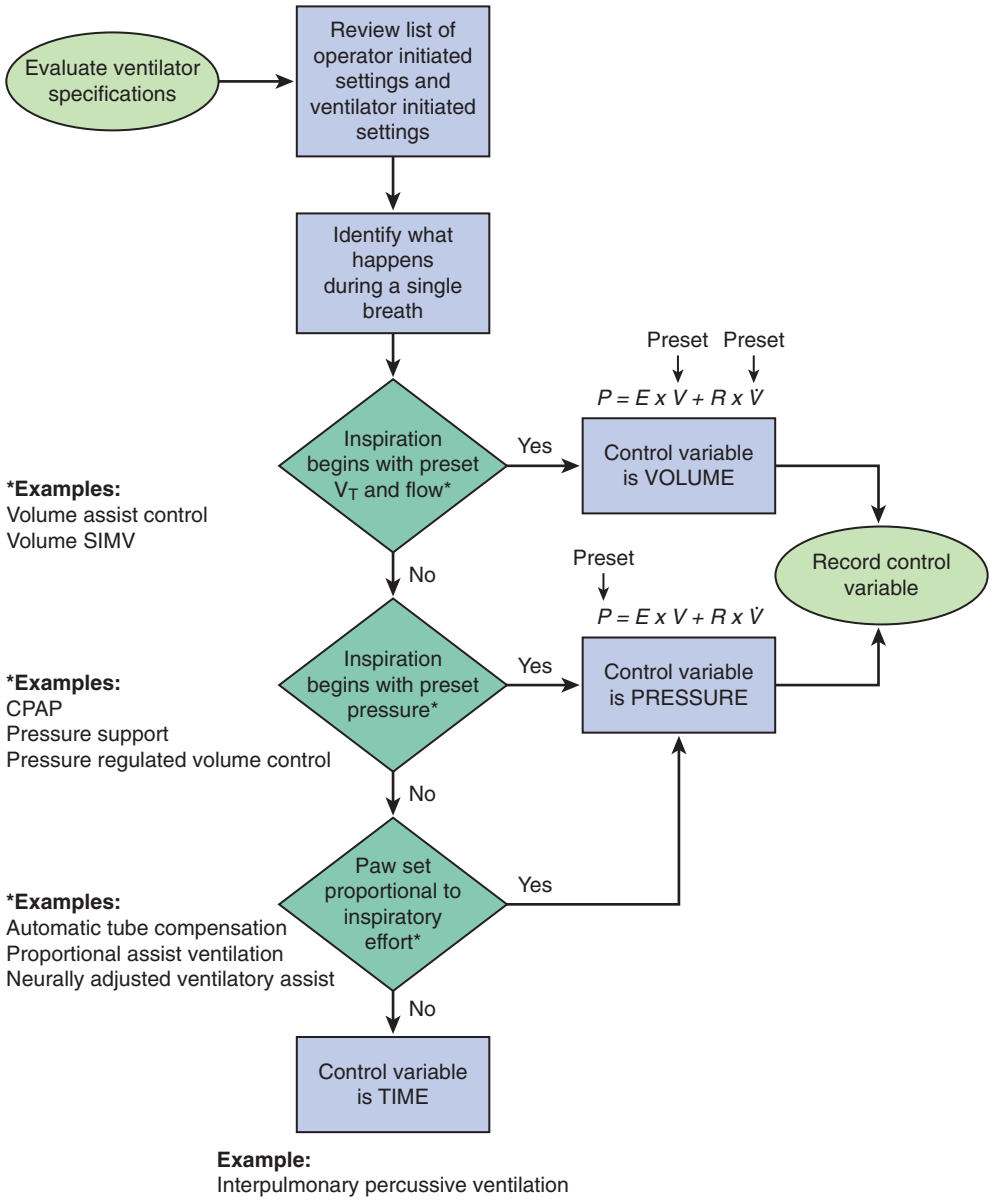

Fig. 46.18 Algorithm for determining the control variable of a mode. (Courtesy Mandu Press Ltd.)

inspiratory flow." This indicates dual targeting as described in maxim 9. Noting that the breath may switch to pressure support alerts us that the breath sequence is not what it first seemed to be. A breath may be patient triggered with a patient inspiratory effort, and if the effort is large enough and long enough, inspiration is flow cycled, not time cycled. Flow cycling (at a certain percentage of PIP) is a form of patient cycling because the time constant of the patient's respiratory system determines when the cycle threshold is met for passive exhalation. Alternatively, the patient may make an expiratory effort that cycles inspiration off. Either way, a patient-triggered and patient-cycled breath is a spontaneous breath. Thus spontaneous breaths may occur between mandatory breaths and the breath sequence is actually IMV. Finally, the tag for this mode is VC-IMVd,d. Note that with dual targeting modes, we need to identify which control variable is in effect at the start of inspiration (see Fig. 46.18) and in this case it is volume. In contrast, the mode called *pressure A/C with machine volume* (Vyaire Avea) incorporates dual targeting; it starts out in pressure control and may switch to volume control.

Finally, some modes are composed of compound targeting schemes. For example, some ventilators offer tube compensation, a feature that increases inspiratory pressure in proportion to flow to support the resistive load of breathing through an artificial airway. This is a form of servo targeting. On the Dräger Evita V500, tube compensation can be added to CMV with AutoFlow to get a mode classified as PC-CMVar (*ar* represents the compound targeting scheme composed of servo added to set-point, with no comma because there are only primary breaths). A mode classified as pressure control intermittent mandatory ventilation with set-point control for both primary (mandatory) and secondary (spontaneous) breaths would have a tag that looks

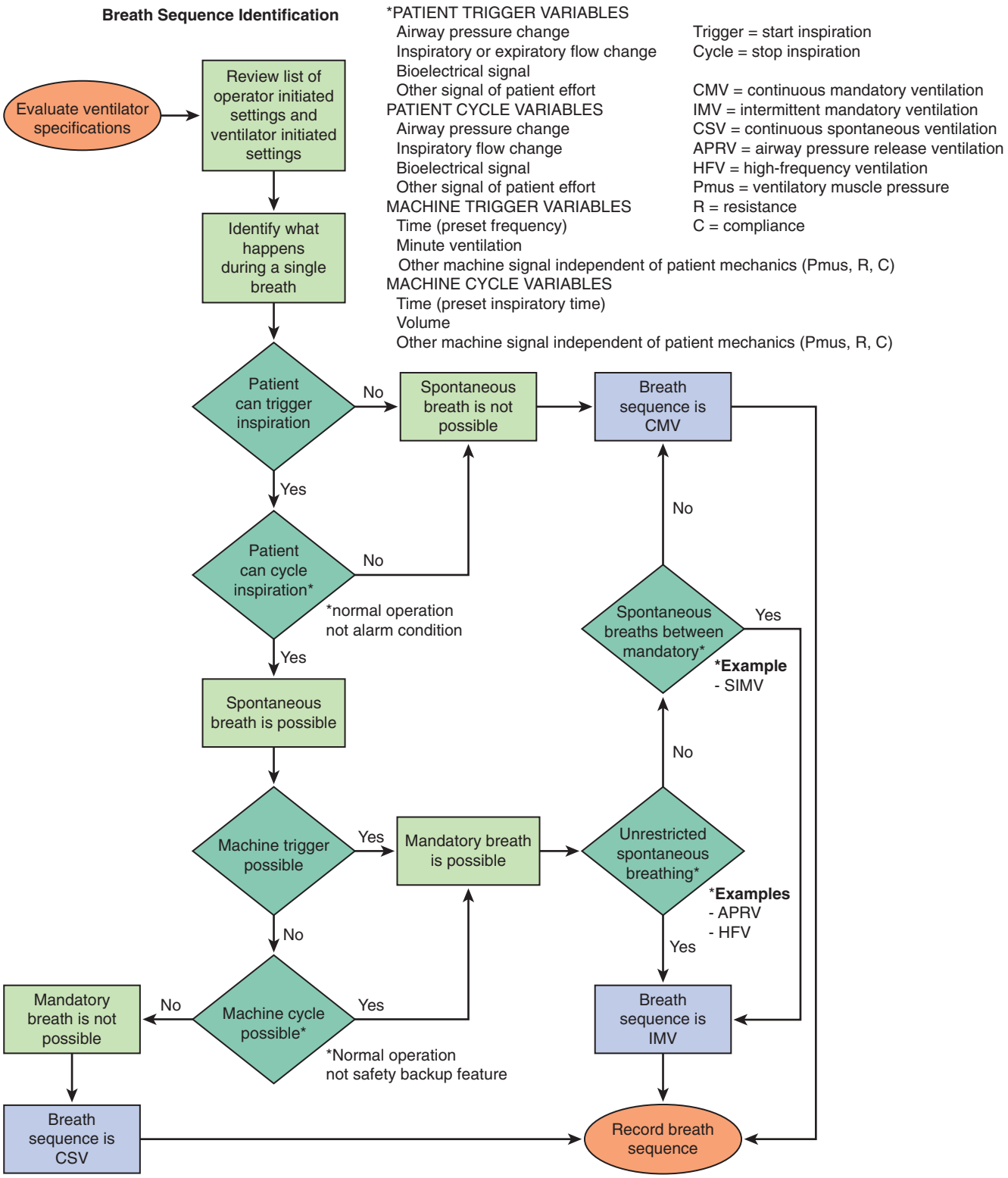

Fig. 46.19 Algorithm for determining the breath sequence of a mode. (Courtesy Mandu Press Ltd.)

like this: PC-IMVs,s (with a comma to denote primary and secondary breaths). If you added tube compensation to the spontaneous breaths (e.g., Medtronic PB 980), the tag would change to PC-IMVs,sr. If you added it to both mandatory and spontaneous breaths (e.g., Dräger Evita V500), the tag would change to PC-IMVsr,sr. Another example is IntelliVent mode (Hamilton G5 ventilator), which uses optimal targeting to minimize the work rate and intelligent targeting to establish lung protective limits and adjust PEEP and FiO_2. The tag for this mode is PC-CMVoi,oi.

TABLE 46.3 Example of Pocket Card Comparing Mode Names From Two Common ICU Ventilators

Covidien PB 840	Mode Tag
A/C volume control	VC-CMVs
SIMV volume control with pressure support	VC-IMVs, s
SIMV volume control with tube compensation	VC-IMVs, r
A/C pressure control	PC-CMVs
A/C volume control plus	PC-CMVa
SIMV pressure control with pressure support	PC-IMVs, s
SIMV pressure control with tube compensation	PC-IMVs, r
Bilevel with pressure support	PC-IMVs, s
Bilevel with tube compensation	PC-IMVs, r
SIMV volume control plus with pressure support	PC-IMVa, s
SIMV volume control plus with tube compensation	PC-IMVa, r
Spont pressure support	PC-CSVs
Spont tube compensation	PC-CSVr
Spont proportional assist	PC-CSVr
Spont volume support	PC-CSVa
Maquet Servo-1	**Mode Tag**
Volume control	VC-IMVd, d
SIMV (volume control)	VC-IMVd, d
Automode (volume control to volume support)	VC-IMVd, a
Pressure control	PC-CMVs
Pressure-regulated volume control	PC-CMVa
SIMV (pressure control)	PC-IMVs, s
Bi-Vent	PC-IMVs, s
Automode (pressure control to pressure support)	PC-IMVs, s
SIMV pressure-regulated volume control	PC-IMVa, s
Automode (pressure-regulated volume control to volume support)	PC-IMVa, a
Spontaneous/continuous positive airway pressure	PC-CSVs
Pressure support	PC-CSVs
Neurally adjusted ventilatory assist	PC-CSVr
Volume support	PC-CSVa

a, adaptive; *d,* dual; *PC-CMV,* pressure control continuous mandatory ventilation; PC-CSV, pressure control continuous spontaneous ventilation; PC-IMV, pressure control intermittent mandatory ventilation; *r,* servo; *s,* set-point; *VC-CMV,* volume control continuous mandatory ventilation; VC-IMV, volume control intermittent mandatory ventilation.

The utility of this taxonomy becomes evident when modes on different ventilators are being compared (e.g., for making a purchase decision). For example, suppose your hospital has standardized on two common ICU ventilators, the Medtronic PB 980 and the Getinge SERVO-U. An example of how modes can be compared across ventilators is shown in Table 46.3.

COMPARING MODES OF MECHANICAL VENTILATION

The use of the ventilator mode taxonomy allows clinicians to appropriately match the technology to the patients' needs. Clinicians must not only know what tool to use but also how to use it. Knowing how to use a mode involves understanding the technologic capabilities of the mode and how they serve the goals of mechanical ventilation. These goals are safety, comfort, and liberation. *Safety* means maintaining adequate gas exchange and hemodynamics while avoiding harm in the form of atelectrauma and volutrauma. *Comfort* means optimizing synchrony between the patient and the ventilator. *Liberation* means getting the patient off the ventilator in the shortest time with the fewest adverse events.

These goals can be further refined into specific objectives and clinical aims that may then be applied to individual patients. Goals, objectives, and aims are the product of a clinical assessment. After identifying the patient's need, the clinician simply matches those needs to the technological capabilities of the available modes of ventilation.[21]

MINI CLINI

Calculate the Expiratory Time Setting From the Frequency and Inspiratory Time

Problem

You are assigned to the neonatal intensive care unit (NICU) and have successfully intubated a newborn term infant diagnosed with respiratory distress syndrome. You are manually ventilating the infant with a flow-inflating bag at a frequency of 25 breaths/min. An inline manometer indicates the PIP is approximately 24 cm H_2O and the PEEP is 4 cm H_2O. The infant's vital signs (heart rate, respiratory rate, and blood pressure) are within normal limits and SpO_2 is 95%. The pressure and frequency you are using manually will serve as the initial ventilator settings on an infant ventilator. With this particular ventilator, however, setting the inspiratory and expiratory times determines the frequency. The attending physician has requested an inspiratory time (T_I) of 0.3 s. Calculate the expiratory time (T_E) necessary to give the desired frequency.

Discussion

Step 1: Compute the total cycle time (TCT) using the frequency (f):

$$TCT = \frac{1}{f} = T_I + T_E$$

$$f = \frac{25\ \text{breaths}}{\text{minute}} \times \frac{1\ \text{minute}}{60\ \text{seconds}} = \frac{25\ \text{breaths}}{60\ \text{seconds}}$$

$$TCT = \frac{1}{25\ \text{breaths}/60\ \text{seconds}} = \frac{60\ \text{seconds}}{25\ \text{breaths}} = \frac{2.4\ \text{seconds}}{\text{breath}}$$

Step 2: Compute the expiratory time:

$$T_E = TCT - T_I = 2.4 - 0.3 = 2.1\ \text{seconds}$$

Step 3: Check the digital display to verify the set frequency remains at 25/min.

TYPES OF VENTILATORS

Conventional Versus High-Frequency Ventilators

Ventilators may be divided into categories according to type and the setting in which the ventilator will be used. The two main categories are conventional and nonconventional. Conventional ventilators produce breathing patterns that are at or near physiologic normal values for the intended population (e.g., adult, pediatric, and infant). There are also manufacturing limits on

MINI CLINI

Calculate Inspiratory Hold Time Given Set Inspiratory Time, Tidal Volume, and Flow

Problem

You are performing a patient–ventilator assessment on an ICU patient with blunt chest trauma. The ventilator is set to deliver VC-IMV. The physician wants the minimum mean airway pressure for the given level of ventilation to preserve the patient's already low cardiac output. She asks you to make sure that the night shift therapist removed the inspiratory hold. Determine from the ventilator settings alone whether there is an inspiratory hold, and if so, make the appropriate changes to eliminate it.

Ventilator settings are as follows:

Tidal volume: 500 mL = 0.5 L

Inspiratory flow: 60 L/min = 1 L/s

Inspiratory time: 0.8 s

Frequency: 10 breaths/min

Discussion

Step 1: Calculate the inspiratory flow time (T_{IF}) using appropriate unit conversions:

$$T_{IF} = \frac{\text{tidal volume}}{\text{inspiratory flow}}$$

$$= \frac{500\,\text{mL}}{60\,\text{L/minute}} \times \frac{1\,\text{L}}{1{,}000\,\text{mL}} \times \frac{60\,\text{seconds}}{1\,\text{minute}} = 0.5\,\text{seconds}$$

Step 2: Compare the set inspiratory time (0.8 s) with the flow time resulting from the tidal volume and flow settings (0.5 s). Inspiratory time lasts longer than inspiratory flow. Because inspiration is time cycled, this means that there is an inspiratory hold of duration equal to 0.8 – 0.5 = 0.3 s.

Step 3: You could eliminate the inspiratory hold either by decreasing the inspiratory flow or decreasing the inspiratory time. Your goal is to minimize the mean inspiratory pressure. You choose to decrease inspiratory time for two reasons: (1) it decreases the I:E ratio and may allow more time for spontaneous breaths to occur, thus lowering mean intrathoracic pressure; (2) decreasing inspiratory flow may make tidal volume delivery slower than the patient demands, thus decreasing patient–ventilator synchrony.

the maximum breath rate a conventional ventilator may deliver. The US Food and Drug Administration places a maximum breath rate limit of 150 breaths/min for conventional ventilators. Tidal volumes that are either set by the operator or delivered to the patient as a result of a preset pressure through a conventional ventilator are sufficient or large enough to clear anatomic dead space. Conversely, high-frequency ventilators typically produce respiratory frequencies or breathing rates that are much higher than physiologically possible and tidal volumes that are less than anatomic dead space.

Conventional Ventilators

Conventional ventilators are called that mainly because they are designed to deliver ventilatory patterns (i.e., tidal volume and frequency) that are within the range of normal breathing. They may be used with a variety of interfaces in the critical care setting. Options are available on this type of ventilator for use with an artificial airway (endotracheal or tracheostomy tube) or noninvasively with a variety of interfaces (e.g., nasal, oronasal, or full face masks). The availability of the noninvasive option eliminates the need for a stand-alone noninvasive ventilator. However, stand-alone noninvasive ventilators do have applications and are also used in the critical care setting. Ventilators used in the critical care environment have the capability to assess and monitor complex ventilator–patient interactions.

High-Frequency Ventilators

High-frequency ventilators are called that because they are designed to deliver ventilatory tidal volumes well below normal while maintaining minute ventilation by using frequencies well above normal. The original idea behind the design of these machines was to minimize lung movement during open chest surgery and to minimize the risk of volutrauma when premature infants were being ventilated.

The availability of sophisticated devices such as jet ventilators and high-frequency oscillators facilitates the ventilatory management of infants, children, and adults in the PC-IMV mode who fail to maintain adequate oxygenation and acid-base balance with conventional ventilatory support. High-frequency jet ventilators, such as the Bunnell Life Pulse (Bunnell Inc., Salt Lake City, UT), deliver short bursts, or jet pulses, of mixed gas through a special adaptor for endotracheal tubes or a specially designed endotracheal tube. High-frequency jet ventilators require a high-pressure source (20 to 50 psig) to function. This type of ventilator consists of a system for regulating inlet pressure (psig), a cycling mechanism, and a device such as an air-oxygen blender for controlling FiO_2. The small volumes of gas are delivered at rapid rates (4 to 250 times the normal respiratory rate). The benefits of rescue and elective use of high-frequency jet ventilation (HFJV) as a treatment for acute lung disease and acute respiratory distress syndrome are unclear. However, the literature supports its effectiveness in maintaining alveolar ventilation and reducing morbidity during surgical repair of tracheal and airway anomalies.

High-frequency oscillation (HFO) also allows very small tidal volumes to be delivered at rapid frequencies (180 to 1200 cycles per second). High-frequency oscillators utilize a piston or diaphragm to produce the airflow oscillations. Tidal volume is dependent on the force and distance the piston moves from baseline. A special endotracheal tube is not required to implement this form of PC-IMV. The SensorMedics 3100A and 3100 B high-frequency oscillators (Vyaire, San Diego, CA) are approved and commercially available for use in neonatal/pediatric (<35 kg) and pediatric/adult populations (>35 kg), respectively.

However, the application of HFO to adults with the acute respiratory distress syndrome has been shown to be potentially deterimental.[22,23]

RULE OF THUMB High-frequency oscillators do not have an internal backup battery. In the event of a power failure, the ventilator will power down. Always plug the ventilator into a red outlet. The red outlet will provide backup generator power during an electrical outage. Portable external batteries may also be purchased. When a portable external battery is used, plug the high-frequency oscillator into the portable battery, then plug the external battery into a red power outlet.

Classification of Ventilators by Use

Ventilators may also be categorized by the setting in which they are used, specifically critical care, subacute care, home care, long-term care, and transport. Their designs match the needs of the population as well as the unique characteristics of the setting in which they are used. Ventilator manufacturers have paid particular attention to economic constraints that health care facilities are facing. Innovations in ventilator design have broadened their use across settings. An example of this is the use of ventilators for different patient ages. Although ventilators are not subcategorized as adult or pediatric in this chapter, is it crucial for the practitioner to be aware of factors such as minimal tidal volume limits, trigger sensitivity, response time, and availability of leak compensation a ventilator for use with the pediatric population is being selected.

Critical Care Ventilators

Critical care ventilators provide clinicians with sophisticated methods for breath delivery. This class of ventilators also provides advanced monitoring capabilities and tools that enable clinicians to readily assess the patient–ventilator interaction. Calculations of lung mechanics parameters including auto-PEEP, static and dynamic compliance, inspiratory/expiratory resistance, rapid shallow breathing index, time constant, and work of breathing are integrated into ventilators used in this environment. Integrated physiologic noninvasive and invasive assessment tools, such as esophageal pressure monitoring and end-tidal CO_2 monitoring, are also commercially available. The availability of these features equips bedside caregivers with the tools needed to assess patient–ventilator interaction and match ventilator capability with physiologic need.

Subacute Care Ventilators

Generally, mechanically ventilated patients in this setting have a stable cardiopulmonary status. Their condition is such that the care provided does not depend heavily on high-technology monitoring or complex diagnostic procedures. Rather, the focus is on coordinated services aimed at managing complex medical conditions, liberation from ventilatory support, and rehabilitation services. Ventilators used in this care venue have less sophisticated monitoring systems and mode options. Subacute care may be rendered in freestanding facilities or within a specialized unit within a hospital. As a result, the design of ventilators used in this environment bridge the gap between those designed specifically for critical care and those designed for home care and extended skilled care.

Home Care Ventilators

Patients with chronic respiratory failure from primary pulmonary disease, trauma, or neuromuscular disease may require ventilatory assistance to augment or replace spontaneous breathing and maintain life. Ventilators designed for use in the home or at long-term care institutions facilitate the transition of patients from the acute and subacute care environment to one focusing on enhancing the individual's quality of life and providing services to sustain or improve physical and physiologic function in a cost-efficient manner. Ventilators must be able to support the ventilatory needs of the patient and provide supplemental oxygen in a venue where compressed gas resources are limited, power supply interruptions may occur, and patient mobility needs must be met. The interface on this type of ventilator is much simpler than on ventilators used in critical or subacute care. The availability of a low-pressure input port is an essential feature that allows supplemental oxygen to be delivered by stationary and portable devices commonly used in the home, such as oxygen concentrators, small high-pressure tanks, and portable liquid oxygen reservoirs. Machine dimensions are also an important consideration, and this type of ventilator is generally compact in nature. The option to lock operator-set parameters minimizes the occurrence of inadvertent setting changes and concomitant alterations in alveolar ventilation and acid-base balance.

Ventilators used in home care and extended care facilities require not only an internal battery for brief power interruptions but also connections for an external battery when the power supply is interrupted for extended periods due to natural disasters, human-made occurrences, and participation in academic, employment, or recreational activities.

Transport Ventilators

Transport means moving a patient to different locations within the hospital (internal transport) or between a hospital and an external location (external transport). Transport ventilators share attributes common to ventilators used in the home and critical care environments. Indeed, sometimes home care ventilators and ICU ventilators are used for transport. But a dedicated transport ventilator must be lightweight, compact, durable, maintained on a reliable power supply, and consume relatively little compressed gas. The ventilator interface should be easy to navigate, allowing the clinician to set or change parameters prior to or during movement to and from a prescribed destination. Operator-set and monitored data should be visible under optimal conditions or conditions of low ambient light. These characteristics enhance patient safety and minimize the potential for complications or adverse effects to occur during air or ground transport. Monitoring is also an important consideration. Clinical practice guidelines recommend the level of monitoring during patient transport be analogous with that provided to the patient during stationary care. Modern transport ventilators provide the ability to display scalar waveforms and numerical data.

Noninvasive Ventilators

Noninvasive ventilation is used across the continuum of care—from critical care to home care—with individuals of any age. As previously mentioned, a noninvasive ventilation feature may be incorporated in critical care ventilators and home care ventilators. However, stand-alone noninvasive ventilators exist and are extensively used in a variety of settings from the hospital to home. In the acute and critical care setting, noninvasive ventilators have been used to reduce complications associated with diagnostic procedures, such as bronchoscopy, as well as in the treatment of acute respiratory insufficiency, respiratory failure, and the prevention of postextubation failure. This technology has also been associated with positive outcomes in the outpatient

setting. The literature reports the use of noninvasive ventilation to restore and maintain adequate alveolar ventilation with individuals compromised by neuromuscular disorders, congestive heart failure, chronic obstructive lung disease, and sleep-disordered breathing.

There are features common to home and hospital-grade units that enhance patient comfort and promote adherence to therapy. Ramp time allows the clinician to program a delay in the initiation of a delivered inspiratory pressure. Ramp time is usually adjustable (e.g., 0 to 45 minutes), during which the patient breathes at a preset or operator-set expiratory pressure (e.g., 4 cm H_2O). Likewise, rise time can be altered to reduce pressure overshoot and enhance breath delivery. The ability to detect and quantify interface leak, estimated tidal volume, and minute ventilation delivery are additional helpful tools. Hospital-grade units have the capability to display patient data in graphic and numeric form. Clinicians are able to view pressure, flow, and scalar waveforms. As with critical care ventilators, careful analysis of waveforms may assist clinicians in the identification and correction of patient–ventilator synchrony.

MINI CLINI

A respiratory therapist is preparing to noninvasively ventilate a 3-year-old patient with muscular dystrophy. The physician ordered the following settings:
PIP relative to atmospheric pressure: 12 cm H_2O
PEEP: 4 cm H_2O
Rate: 16/min
FiO_2: 0.35
Calculate the set driving pressure, ΔP_{set}:

$$\Delta P_{set} = PIP - PEEP = 12 - 4 = 8\ cm\ H_2O$$

If the child's ventilation is not sufficient on these settings, increasing the ΔP_{set} will improve ventilation. This can be accomplished by increasing the set inspiratory pressure. Note that we probably cannot calculate P_T because tidal volume measurement is uncertain during noninvasive ventilation (due to leaks) and hence we probably cannot even calculate compliance (or elastance).

SUMMARY CHECKLIST

- Ventilators can be described in terms of their input power requirements (e.g., electrical or pneumatic) and how the input power is transformed into desired outputs of pressure, volume, and flow.
- Ventilator displays serve three main functions: (1) to display the inputs, that is, the current state of the settings and allow changes to be made; (2) to show the outputs, meaning the measured values that characterize normal patient–ventilator interactions; and (3) to show alarm conditions.
- The patient interface is the connection between the ventilator and the patient—typically a system of plastic hoses often called the *patient circuit*.
- The important thing to know about the patient circuit is that it contributes to discrepancies between the desired and actual ventilator output values.
- A key feature of a ventilator is the variety of modes of ventilation that it offers.
- A mode of ventilation is a predetermined pattern of interaction with the patient. Modes are given many confusing names but they can be understood using a taxonomy or classification system.
- A breath is one cycle of positive flow (inspiration) and negative flow (expiration) defined in terms of the flow-time curve.
- A breath is "assisted" if the ventilator provides some or all of the work of breathing.
- A ventilator assists with the work of breathing by using either pressure control or volume control according to the equation of motion for the respiratory system. This equation relates pressure, volume, and flow as variables of time.
- Two key parameters of respiratory system mechanics are elastance (Δpressure/Δvolume) and resistance (Δpressure/Δflow). Sometimes compliance (Δvolume/Δpressure) is substituted for elastance.
- Pressure control means that pressure is preset or is proportional to patient effort. Inspiratory flow and volume are dependent on respiratory system mechanics (including inspiratory effort).
- Volume control means that inspiratory flow and volume delivery are preset. Inspiratory pressure is dependent on respiratory system mechanics (including inspiratory effort).
- Breaths are classified according to how inspiration is triggered (started) and stopped (cycled).
- Either the machine (ventilator) or the patient may initiate the trigger and cycle events.
- A spontaneous breath is one for which inspiration is **patient triggered** and **patient cycled**. A mandatory breath is one for which inspiration is **machine triggered** and/or **machine cycled**.
- Spontaneous breaths may be assisted (meaning that the ventilator provides some portion of the work of breathing) or unassisted. Mandatory breaths are generally assisted.
- The breath sequence of a mode is the pattern of mandatory versus spontaneous breaths. CSV means that all breaths delivered by the ventilator are spontaneous. IMV means that spontaneous breaths can occur between mandatory breaths. CMV means that spontaneous breaths cannot occur between mandatory breaths.
- The targeting scheme is a description of the relation between operator settings and ventilator outputs for a mode. Currently all modes can be classified as having one of six targeting schemes (set-point, dual, servo, adaptive, optimal, and intelligent).
- Mode classification is based on identifying three main components: the primary control variable, the breath sequence, and the targeting schemes used for mandatory and spontaneous breaths.
- Ventilators can themselves be classified by the environments in which they are used. Examples include: critical care, subacute care, home care, transport, and noninvasive ventilators.

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47

Physiology of Ventilatory Support

Robert M. Kacmarek

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Discuss the pressures and pressure gradients that affect gas delivery during spontaneous breathing, negative pressure ventilation (NPV), and positive pressure ventilation (PPV).
- Identify the effects of mechanical ventilation on oxygenation, ventilation, and lung mechanics.
- Describe the currently available modes of mechanical ventilation.
- Discuss the indications and physiologic effect of positive end-expiratory pressure (PEEP).
- Describe the cardiovascular effects of PPV and NPV.
- Describe the effects of PPV on intracranial pressure, renal function, liver and splanchnic perfusion, gastrointestinal function, and central nervous system.
- Identify and list the complications and hazards of providing mechanical ventilatory support.
- Discuss how to minimize adverse effects of mechanical ventilation.

CHAPTER OUTLINE

KEY TERMS

aerophagia
atelectrauma
autoregulation
barotrauma
biotrauma
driving pressure
mean airway pressure
passive
patient–ventilator asynchrony
plateau pressure
time constant
transairway pressure
transalveolar pressure
trans–chest wall pressure
transdiaphragmatic pressure
transpulmonary pressure
transrespiratory pressure
transthoracic pressure
volutrauma

Mechanical ventilation can be beneficial or detrimental depending on how it is applied and modified as the patient's condition changes. Respiratory therapists (RTs) must be able to anticipate the physiologic effects of mechanical ventilation and respond appropriately when complications arise. This chapter familiarizes the reader with (1) the physiologic effects of mechanical ventilation on lung and cardiovascular function and other body systems, (2) the basic approaches to providing mechanical ventilation, and (3) the complications and hazards of mechanical ventilation. A solid understanding of the normal physiology of breathing is essential for all RTs, especially when working with patients receiving mechanical ventilation. RTs must understand intrathoracic pressure changes associated with spontaneous, negative pressure, and positive pressure breathing. Intrathoracic pressure changes are necessary for ventilation to occur; however, large changes in these pressures may also induce physiologic changes in other systems.

PRESSURE AND PRESSURE GRADIENTS

For gas to flow through the airway, a pressure gradient must exist. The airway begins at the mouth and end at the alveoli, so mouth pressure (*pressure at the airway opening* [P_{awo}]) and *alveolar pressure* (P_{alv}) are important in describing gas flow, as are *intrapleural pressure* (P_{pl}) and *body surface pressure* or atmospheric pressure (P_{bs}). In addition, *intra-abdominal pressure* (P_{ab}) affects the impact of P_{pl} change on diaphragm movement. P_{pl} is the pressure in the pleural space, the virtual space between the visceral and parietal pleurae, and is usually negative in relation to P_{alv}. Fig. 47.1 shows a graphic model of the respiratory system with these pressures identified as points in space. The respiratory system is everything that exists between the airway opening and the body surface. The associated pressure difference is **transrespiratory pressure** (P_{TR}), defined as $P_{awo} - P_{bs}$. The components of P_{TR} correspond to the components of the graphic model. The airways are represented by **transairway pressure** (P_{TA}), defined as $P_{awo} - P_{alv}$. The lungs are represented by the **transalveolar pressure**: ($P_L = P_{alv} - P_{pl}$). However, clinically what can be measured is **transpulmonary pressure**: ($P_{TP} = P_{awo} - P_{pl}$). The chest wall is represented by **trans–chest wall pressure**: ($P_{TCW} = P_{pl} - P_{bs}$). If the lungs and chest wall are lumped together, they can be represented by **transthoracic pressure**: ($P_{TT} = P_{alv} - P_{bs}$).

Another pressure gradient not defined in Fig. 47.1 that also affects gas movement is the **transdiaphragmatic pressure** (P_{di}). This pressure gradient is the difference between P_{ab} and pleural pressure and affects diaphragmatic movement: ($P_{pl} - P_{ab}$).

Airway, Alveolar, and Intrathoracic Pressure, Volume, and Flow During Spontaneous Ventilation

Spontaneous breathing is normally an autonomic phenomenon. In other words, we do not think about breathing; it is controlled by the autonomic nervous system. Not until our breathing is stressed, do we consider the effort to breathe or the energy expended. At end-exhalation, P_{pl} is slightly negative. Alveolar, mouth, and body surface pressures are zero. The diaphragm contracts in response to stimulation of the phrenic nerve via

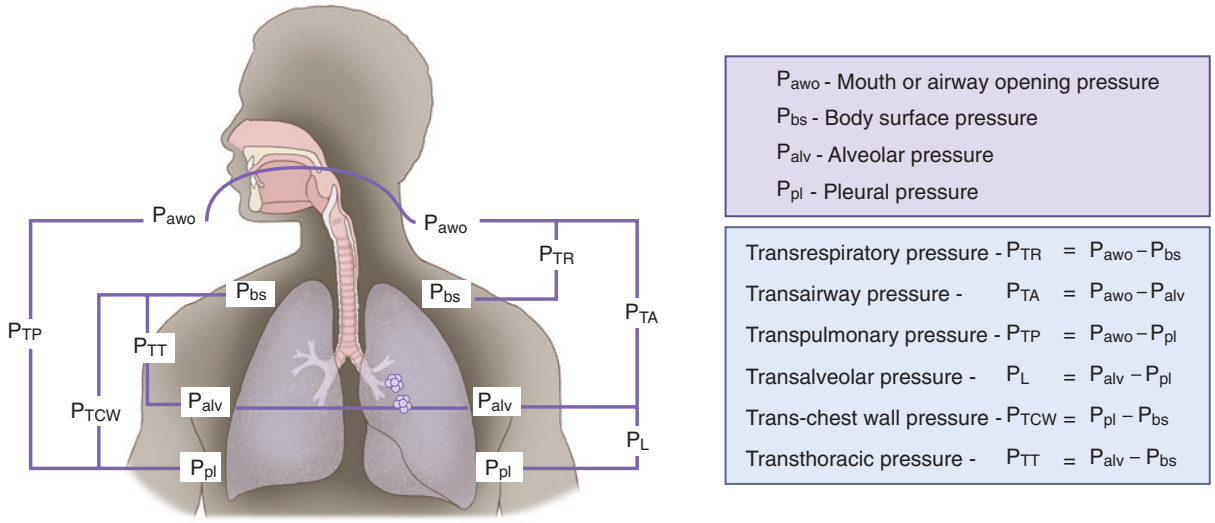

Fig. 47.1 Pressures and Pressure Gradients in the Lung. Airflow is a function of the transairway pressure *(P_{TA})*, which is the pressure gradient between the airway *(P_{awo})* and the alveoli *(P_{alv})*. Transalveolar pressure *(P_L)* maintains alveolar inflation, and transpulmonary pressure *(P_{TP})* is the pressure needed to expand the lungs and chest wall.

TABLE 47.1 Changes in Airway Pressure Gradients During Spontaneous, Negative, and Positive Pressure Ventilation

Pressure (cm H_2O) Ventilation Type	Transpulmonary Pressure	Transthoracic Pressure	Transairway Pressure	Transrespiratory Pressure
Spontaneous				
Inspiration	Small increase (+)	Increase (+)	Increase (+)	Constant (–)
Expiration	Small increase (–)	Increase (–)	Increase (–)	Constant (+)
Negative (NPV)				
Inspiration	Small increase (+)	Increase (+)	Increase (+)	Constant (–)
Expiration	Small increase (–)	Increase (–)	Increase (–)	Constant (+)
Positive (PPV)				
Inspiration	Small increase (+)	Increase (+)	Increase (+)	Increase (+)
Expiration	Decrease (–)	Decrease (–)	Decrease (–)	Decrease (–)

NPV, Negative pressure ventilation; *PPV*, positive pressure ventilation.

the respiratory center in the medulla of the brain. When the diaphragm contracts, it descends into the abdominal cavity, decreasing P_{pl}. When P_{pl} becomes more negative, P_{alv} becomes negative as well. The effects of spontaneous breathing on the pressure gradients are shown in Table 47.1. Under normal circumstances, a decrease in P_{pl} results in decreased P_{alv}, increased P_{TA}, and inspiration of a tidal volume (V_T) (Fig. 47.2).

At end-inspiration, P_{alv} returns to zero when the muscles of inspiration stop contracting. Lung recoil causes a sudden increase in P_{alv} in relation to pressure at the mouth, reversing the P_{TA} gradient, and air flows out of the lungs. However, at end-expiration the P_{TP} and P_L return to a positive value. If there were to stay negative, alveoli would collapse. Normally, there is a short end-expiratory pause before the next inspiration.

V_T and flow during spontaneous ventilation may be described by the equation of motion.[1,2] The equation of motion describes the relationship between muscle pressure (analogous to pleural pressure in spontaneous breathing), compliance, resistance, flow, and volume as follows:

$$P_{musc} = \text{Volume/Compliance} + (\text{Resistance} \times \text{Flow})$$

where P_{musc} is muscle pressure (P_{tp}), volume is V_T, compliance is lung-thorax compliance, resistance is airway resistance (R_{aw}), and flow is gas flow through the airway. When the equation is rearranged, volume inhaled during spontaneous ventilation is proportional to muscle pressure and lung-thorax compliance and inversely related to the product of R_{aw} and flow:

$$\text{Volume} = [P_{musc}/(\text{Resistance} \times \text{Flow})] + \text{Compliance}$$

Ventilation (owing to P_{TP}) is the sum of the pressure needed to move gas through the airways (P_{TA}) and the pressure needed to inflate the alveoli (P_L):

$$\text{Transpulmonary pressure} = P_{TA} + P_L$$

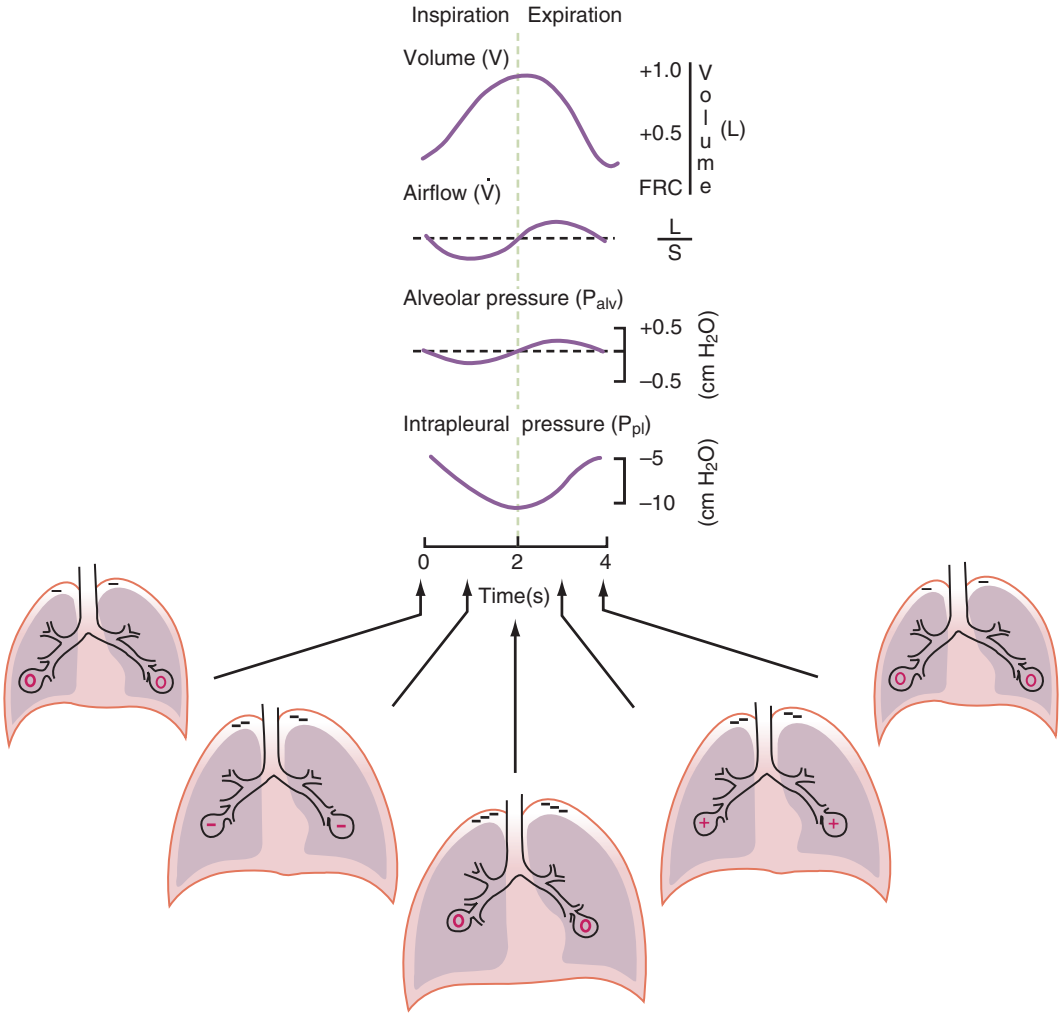

Fig. 47.2 Changes in pressure, volume, and flow during a single spontaneous breath. *FRC*, Functional residual capacity. P_{rs}, Transrespiration system pressure. (Modified from Martin L: *Pulmonary physiology in clinical practice: the essentials for patient care and evaluation*, St. Louis, 1987, Mosby.)

Airway, Alveolar, and Intrathoracic Pressure, Volume, and Flow During Negative Pressure Mechanical Ventilation

Mechanical negative pressure ventilation (NPV) is similar to spontaneous breathing. NPV decreases pleural pressure (P_{pl}) during inspiration by exposing the chest to subatmospheric pressure. Negative pressure at the body surface (P_{bs}) is transmitted first to the pleural space and then to the alveoli (P_{alv}). Because the airway opening remains exposed to atmospheric pressure during NPV, a P_{TA} gradient is created. Gas flows from the relatively high P_{awo} (zero) to the relatively low pressure in the alveoli (negative). As with spontaneous breathing, alveolar expansion during NPV is determined by the magnitude of the P_{TP} gradient. During expiration in both spontaneous breathing and NPV, the lungs and chest wall passively recoil to their resting end-expiratory levels. As this recoil occurs, pleural pressure becomes less negative, and P_{alv} increases above atmospheric pressure (Fig. 47.3). This increase in P_{alv} reverses the P_{TA} gradient. As P_{alv} becomes greater than P_{awo}, gas flows from the alveoli to the airway opening. The effects of NPV on the pressure gradients are shown in Table 47.1.

Volume and flow during NPV also are described by the equation of motion except P_{TA} developed by the ventilator fully or partially replaces the patient's respiratory muscle pressure as follows:

$$P_{musc} + P_{vent} = \text{Volume/Compliance} + (\text{Resistance} \times \text{Flow})$$

In this equation, P_{vent} is the pressure the ventilator develops to overcome the patient's lung-thorax compliance and R_{aw} to deliver the V_T. In this case, P_{vent} is negative but is the driving force behind decreasing the P_{pl} and increasing the transairway and transpulmonary pressures.

Physiologic complications associated with NPV are uncommon because NPV simulates normal spontaneous breathing. The most common problems with NPV are related to interference with caring for the patient caused by the device surrounding the chest (the iron lung or chest cuirass). Supplemental oxygen

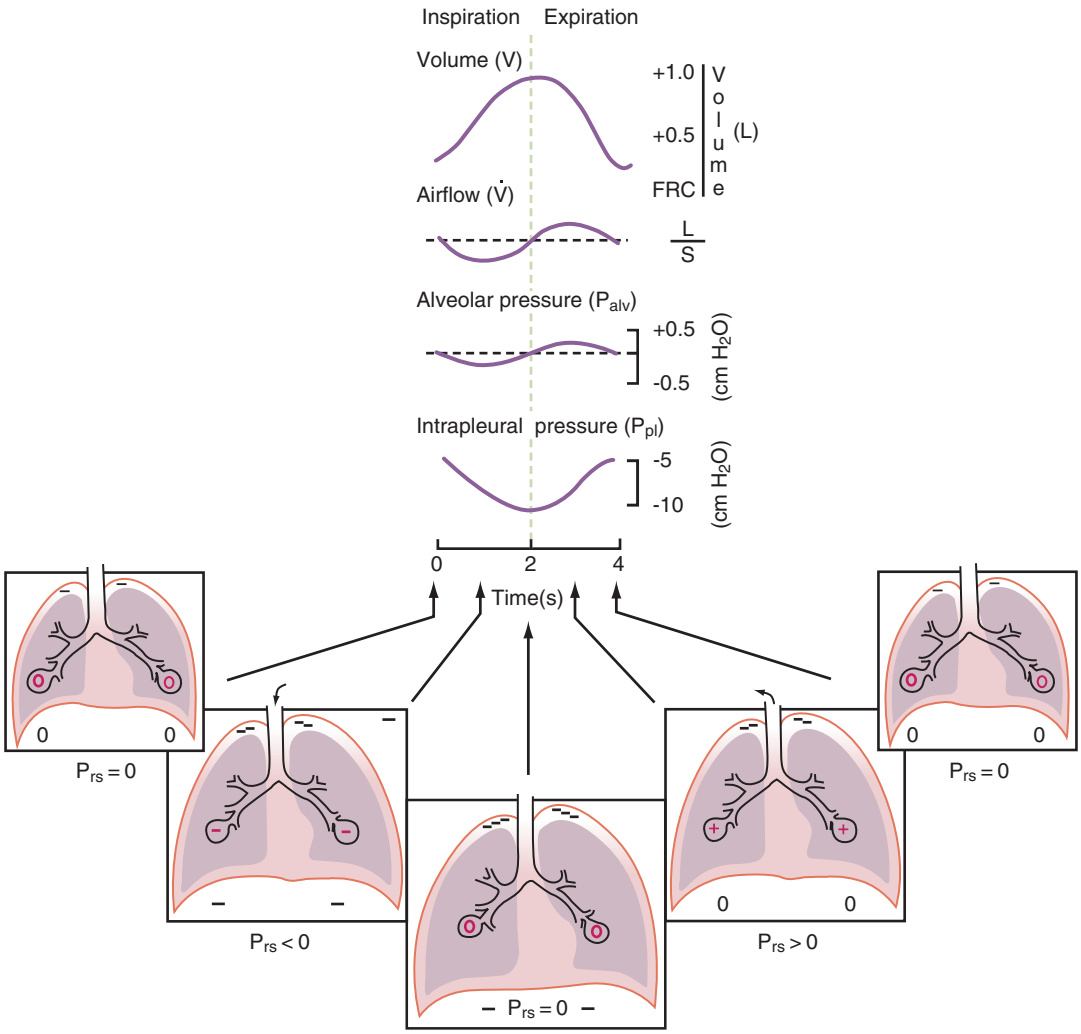

Fig. 47.3 Changes in Pressure, Volume, and Flow During a Single Mechanical Negative Pressure Breath. The box surrounding the lungs represents the enclosure formed by the negative pressure ventilator. *FRC*, Functional residual capacity. (Modified from Martin L: *Pulmonary physiology in clinical practice: the essentials for patient care and evaluation*, St. Louis, 1987, Mosby.)

(O_2) cannot be provided to the patient through the negative-pressure ventilator. Depending on patient need, low-flow or high-flow O_2 delivery devices must be used to provide O_2 therapy. Immediate access to patients requiring routine or emergent medical care may be difficult in systems that enclose the entire thorax and lower body, such as the iron lung and Porta-Lung (Respironics Inc., Murrysville, PA) (see Chapter 50). These systems may impede venous return by creating a negative pressure in the abdomen and lower half of the body, which may lead to hypotension, a phenomenon known as "tank shock." The risk of glottis closure and the development of obstructive sleep apnea have been reported in association with NPV of patients with chronic obstructive pulmonary disease (COPD) and neuromuscular dysfunction.

RULE OF THUMB A negative end-expiratory transpulmonary pressure results in collapse of alveoli, atelectasis. During mechanical ventilation PEEP is applied to maintain a positive end-expiratory transpulmonary pressure.

Airway, Alveolar, and Intrathoracic Pressure, Volume, and Flow During Positive Pressure Mechanical Ventilation

Pressure mechanical ventilation (positive pressure ventilation [PPV]) causes air to flow into the lungs because of an increase in airway pressure, not a decrease in pleural pressure as occurs during spontaneous breathing and NPV (Fig. 47.4). However, similar to spontaneous breathing and NPV, PPV causes an increase in P_{TP}, which allows gas to flow into the lungs. Gas flows into the lungs because P_{awo} is positive, and P_{alv} is initially zero or less positive. P_{alv} rapidly increases during the inspiratory phase of PPV. The increased P_{alv} expands the airways and alveoli. Because P_{alv} is greater than pleural pressure (P_{pl}) during PPV, positive pressure is transmitted from the alveoli to the pleural space, causing pleural pressure to increase during inspiration. Depending on the compliance and resistance of the lungs, pleural pressure may markedly exceed atmospheric pressure during a portion of inspiration. These changes in pleural pressure during PPV

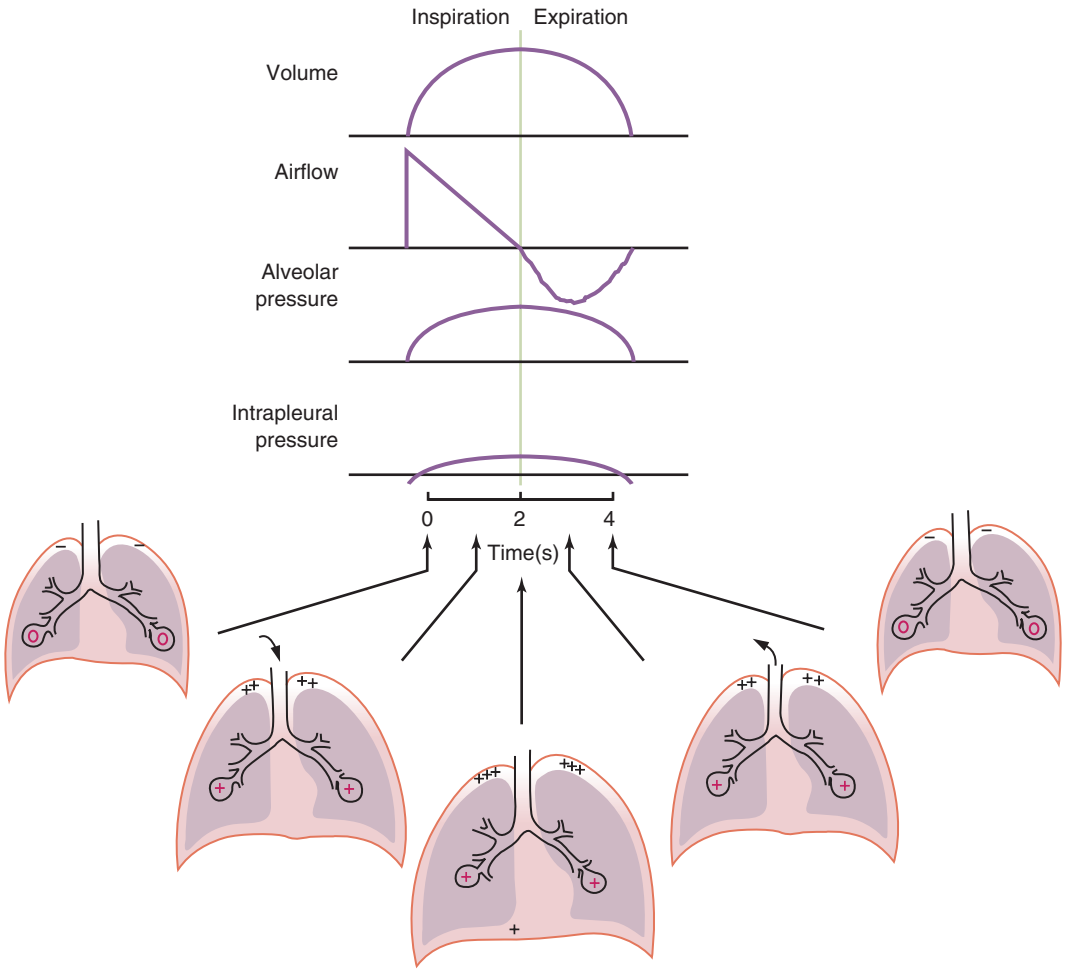

Fig. 47.4 Changes in Pressure, Volume, and Flow During a Single Decelerating Flow, Positive Pressure Breath. *Arrows* into and out of the trachea represent airflow. (Modified from Martin L: *Pulmonary physiology in clinical practice: the essentials for patient care and evaluation*, St. Louis, 1987, Mosby.)

can lead to significant physiologic changes (see later sections). Pressure gradients during PPV are similar to pressure gradients during spontaneous breathing and NPV except that they are created by a positive P_{awo} instead of a negative pressure in the pleural space (see Table 47.1). All pressure gradients change in the same direction as during NPV and spontaneous breathing except the P_{TR}, which changes in the opposite direction and becomes more positive instead of negative.

Similar to spontaneous breathing, the recoil force of the lungs and chest wall, stored as potential energy during the positive pressure breath, causes passive exhalation. As gas flows from the alveoli to the airway opening, P_{alv} decreases to atmospheric level, while pleural pressure is restored to its normal subatmospheric level (see Fig. 47.4).

Volume and flow during PPV are also described by the equation of motion. The magnitude of P_{vent} depends not only on the patient's lung mechanics but also on the P_{musc} of the patient. If the patient makes no effort, P_{vent} is responsible for all volume and flow. During volume-controlled ventilation, as muscle effort increases, P_{vent} decreases and V_T remains constant. During pressure-controlled ventilation, as P_{musc} increases, V_T increases and P_{vent} remains unchanged.

RULE OF THUMB Ideally, the transpulmonary pressure should be as low as possible during mechanical ventilation. A transpulmonary pressure less than approximately 28 cm H_2O minimizes the development of ventilator-induced lung injury. If the plateau pressure is kept less than 28 cm H_2O, the transalveolar pressure can never exceed this level during controlled ventilation.

EFFECTS OF MECHANICAL VENTILATION ON VENTILATION

Minute Ventilation

The primary indication for mechanical ventilation is *hypercapnic respiratory failure,* also known as *ventilatory failure*. For patients with acute ventilatory failure, the goal of mechanical ventilation is improving alveolar ventilation to compensate for the patient's inability to maintain a normal $PaCO_2$. $PaCO_2$ is inversely related to alveolar ventilation, which is related to minute ventilation. Minute ventilation ($\dot{V}_E$) is the product of V_T and ventilatory rate (f):

$$\dot{V} = V_T \times f$$

Use of a mechanical ventilator usually implies a change in V_T, ventilatory rate, or both from preintubation values. A normal

spontaneous V_T is approximately 5 to 7 mL/kg. The currently accepted V_T for all patients acutely requiring mechanical ventilation is 4 to 8 mL/kg predicted body weight (PBW). These volumes are always based on PBW regardless of the size of the patient. The mechanical ventilator rate depends on the patient's status. For postoperative ventilation, a rate of 12 to 20 breaths/min may be adequate. Conditions that necessitate a higher initial rate include acute respiratory distress syndrome (ARDS), pulmonary fibrosis, acutely increased intracranial pressure (ICP) (with caution; see later), and metabolic acidosis. Conditions that may necessitate a lower rate include acute asthma exacerbation, to allow an increased expiratory time to minimize air trapping. When an appropriate V_T is established, the set rate is adjusted to achieve desired $PaCO_2$. Mechanical ventilation increases minute ventilation by increasing V_T, ventilator rate, or both.

MINI CLINI

Alveolar, Transpulmonary, and Transalveolar Pressures

Problem

Mr. Jones is 58 years old, 5 feet 8 inches tall, and weighs 410 lb and is being ventilated because of ARDS. His current ventilator settings are pressure control mode, peak pressure 37 cm H_2O, PEEP 20 cm H_2O, FiO_2 0.50, respiratory rate 26 breaths/min, and V_T 400 mL. At the end of expiration gas flow returns to zero approximately 100 ms before the end of the breath. What are the end-inspiratory and end-expiratory alveolar, transpulmonary, and transalveolar pressures for Mr. Jones?

Solution

Because there is a short end-inspiratory pause, it is reasonable to assume that the peak airway pressure in pressure control is equal to the average peak P_{alv}. The term average is used here because alveolar units have different time constants and as a result different peak pressures, but when there is an end-inspiratory equilibration of pressure, the resulting value is the average pressure across all lung units. To be more confident of this value, an additional end-inspiratory pause can be added for a single breath to determine better the end-inspiratory pause pressure or plateau pressure. End-expiratory transpulmonary is determined by an end-expiratory pause. As with the end-inspiratory pause, this ensures that the pressure reading reflects the average pressure across all alveoli at end-exhalation.

To determine the end-inspiratory and end-expiratory P_{TP} ($P_{awo} - P_{pl}$) and P_L ($P_{alv} - P_{pl}$), an estimate of pleural pressure must be made. The ideal method is to measure the esophageal pressure. Although not exactly equal to the pleural pressure, it accurately reflects changes in pleural pressure. Some authors have also recommended evaluation of bladder pressure, which changes in the same manner as esophageal pressure. The reading from the esophageal catheter at the time an end-expiratory pause was applied was 23 cm H_2O. The end-expiratory P_{TP} and P_L are the same: 25 to 23 cm H_2O or 2 cm H_2O. The reading at end-inspiration is 28 cm H_2O. The end-inspiratory P_{TP} and P_L are the same: 37 to 28 cm H_2O or 9 cm H_2O. This is because Mr. Jones was ventilated in pressure control, and there was a short end-inspiratory pause, so both peak and **plateau pressures** were equal. However, if he was ventilated in volume ventilation and the peak airway pressure might be 45 cm H_2O, while the plateau pressure (P_{plat}) remained 37 cm H_2O when an end-inspiratory pause was added, the transalveolar pressure and P_{TP} would still be the same: 37 – 28 cm H_2O or 9 cm H_2O.

Mr. Jones is receiving lung protective ventilation because his transalveolar pressure is only 9 cm H_2O at end-inspiration. The high airway pressures are needed because of his large body mass, which minimizes the transmission of pressure across the lung, reducing lung stretch.

Increased Alveolar Ventilation

Alveolar ventilation ($\dot{V}_A$) is inversely related to $PaCO_2$ as defined by the following relationship:

$$\dot{V}_A = (\dot{V}CO_2 \times 0.863)/PaCO_2$$

where $\dot{V}CO_2$ is carbon dioxide (CO_2) production.[2]

As alveolar ventilation decreases, $PaCO_2$ increases. As CO_2 production increases, alveolar ventilation must increase to maintain the same $PaCO_2$. Mechanical ventilation may be needed in either case. It is more useful to look at this equation solved for $PaCO_2$ because changes in $PaCO_2$ usually correlate with the need for mechanical ventilation:

$$PaCO_2 = (\dot{V}CO_2 \times 0.863)/\dot{V}_A$$

If $\dot{V}_A$ decreases or $\dot{V}CO_2$ increases, $PaCO_2$ increases, and hypercapnic respiratory failure follows; mechanical ventilation may be indicated in this setting. Because mechanical ventilation increases ventilation, $PaCO_2$ can be decreased to the desired level depending on the total ventilatory rate.

Ventilation/Perfusion Ratio

Spontaneous ventilation results in gas distribution mainly to the dependent and peripheral zones of the lungs. Controlled PPV tends to reverse this normal pattern of gas distribution, and most of the delivered volume is directed to nondependent lung zones (Fig. 47.5). This phenomenon is caused partly by the inactivity of the diaphragm and chest wall during controlled PPV. Although these structures actively facilitate gas movement during spontaneous breathing, inactivity of these structures during controlled PPV impedes ventilation to dependent lung zones. An increase in ventilation to the nondependent zones of the lung, where there is less perfusion, increases the ventilation/perfusion ($\dot{V}/\dot{Q}$) ratio, effectively increasing physiologic dead space. The increase in $P(A - a)O_2$ often observed with PPV is caused by areas of low $\dot{V}/\dot{Q}$ ratio.

PPV decreases the $\dot{V}/\dot{Q}$ ratio in the bases and dependent lung zones mainly as a result of ventilation being primarily distributed to nondependent lung zones. The $\dot{V}/\dot{Q}$ ratio may also increase in nondependent lung zones because of the effect of PPV on perfusion. PPV can compress the pulmonary capillaries. This compression increases pulmonary vascular resistance and decreases perfusion. Minimal blood flow perfuses the areas with the greatest V_T and contributes to a further increase in dead space. Conversely, blood intended for these areas is diverted to regions with lower vascular resistance—generally more dependent lung regions. Pulmonary blood flow during PPV tends to perfuse

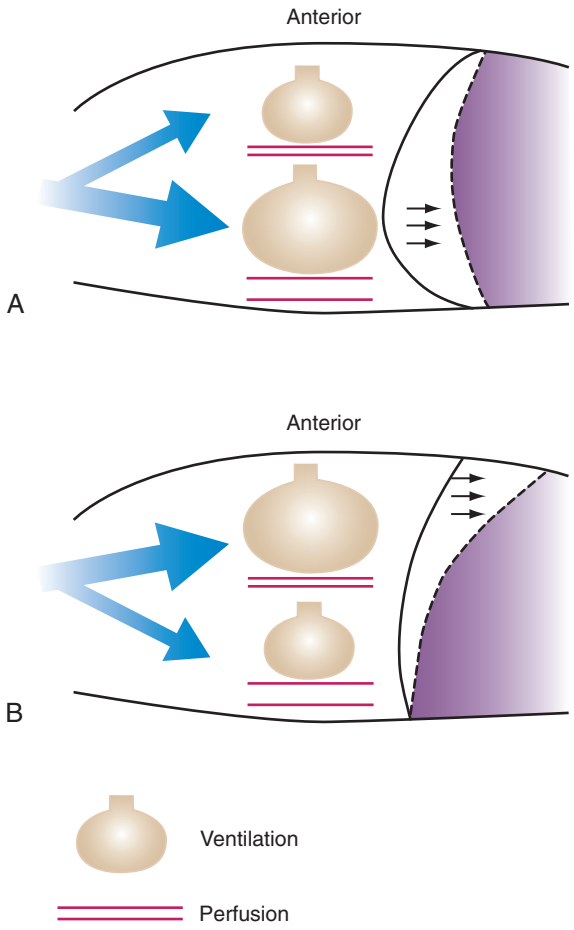

Fig. 47.5 Effect of Spontaneous Ventilation and Positive Pressure Ventilation (PPV) on Gas Distribution in a Supine Subject. (A) During spontaneous ventilation, diaphragmatic action distributes most ventilation to the dependent zones of the lungs, where perfusion is greatest. The result is a nearly normal $\dot{V}/\dot{Q}$ ratio. (B) Partly because of diaphragmatic inactivity, PPV reverses this normal pattern of gas distribution, and most delivered volume is directed to the upper lung zones. An increase in ventilation to the upper lung zones, where there is less perfusion, increases the $\dot{V}/\dot{Q}$ ratio, effectively increasing physiologic dead space. At the same time, higher alveolar pressure in the better ventilated upper lung zones diverts blood flow away from these areas to the areas receiving the least ventilation. The result is areas of low $\dot{V}/\dot{Q}$ ratio and impaired oxygenation. (Modified from Kirby RR: *Clinical application of ventilatory support*, New York, 1990, Churchill Livingstone.)

the least well-ventilated lung regions. This perfusion decreases the $\dot{V}/\dot{Q}$ ratio in those areas and increases the $P(A-a)O_2$.

Alveolar and Arterial Carbon Dioxide

Normal alveolar carbon dioxide tension ($PACO_2$) is 40 mm Hg, whereas mixed venous blood typically has a $P\bar{v}CO_2$ of 45 mm Hg. Under normal circumstances, CO_2 moves out of the blood at the pulmonary capillary interface; the result is a $PaCO_2$ of 40 mm Hg. In the event of a decrease in alveolar ventilation or an increase in CO_2 production, $PaCO_2$ increases. Mechanical ventilation can increase minute volume and alveolar ventilation and reduce $PACO_2$ and $PaCO_2$. With an increase in V_D/V_T, $PaCO_2$ increases if there is no change in minute volume; this may occur when alveolar blood flow is decreased by acute pulmonary embolism, an excessive level of positive end-expiratory pressure (PEEP), or advanced dead space–producing disease such as emphysema or pulmonary embolism.

When inappropriate PEEP is used and blood flow is diverted from ventilated alveoli to hypoventilated alveoli; the result is an increased $\dot{V}/\dot{Q}$ ratio. In emphysema, formation of bullae is coincident with the destruction of pulmonary capillaries; the result is large areas of poorly perfused but ventilated alveoli. Pulmonary emboli may completely occlude pulmonary vessels; the result is lack of perfusion to alveoli distal to the blockage.

Acid–Base Balance

Respiratory acidosis, occurs when minute ventilation and alveolar ventilation per minute ($\dot{V}_A$) are inadequate to meet the needs of the body. Volume delivery also decreases if high airway pressures develop secondary to volume loss as a result of ventilator circuit tubing compliance (compressible volume loss). Ventilator circuits may have compliance of 1 to 3 mL/cm H_2O, which effectively reduces V_T:

$$\text{Volume lost} = \text{Tubing compliance} \times (\text{Peak pressure} - \text{PEEP})$$

Tubing compliance was a concern with older ventilators; however, most intensive care unit (ICU) ventilators in use at the present time allow the user to compensate for compressible volume loss as a result of tubing compliance. When activated, the volume set is the volume delivered to the patient. This issue is discussed in more detail later in the chapter.

An increase in V_D/V_T ratio can cause a reduction in alveolar ventilation, even though minute ventilation may be normal or increased. These problems emphasize the importance of proper selection of V_T and mandatory rate. When respiratory acidosis exists, the patient may become restless and anxious, resulting in **patient–ventilator asynchrony** (see Chapter 48). A communicative patient may complain of dyspnea. If these symptoms are observed, especially when $PaCO_2$ is increased, minute ventilation generally should be increased.

Respiratory alkalosis occurs if the minute ventilation is too high. A patient who is dyspneic, anxious, or in pain may develop this condition; the usual manifestations are an increased ventilatory rate or patient–ventilator asynchrony or both. The ventilator can cause respiratory alkalosis secondary to an inappropriately high V_T or rate. Regardless, the result is excessive minute and alveolar ventilation. This condition requires that the RT adjust the ventilator appropriately and address the patient's pain or anxiety to avoid the systemic effects of a prolonged alkalosis.

With metabolic acidosis, the patient tries to compensate by increasing minute ventilation to blow off CO_2 in an effort to increase the pH. The resulting increase in work of breathing (WOB) may lead to ventilatory muscle fatigue and continued respiratory failure. The best therapy for metabolic acidosis is to manage the underlying cause while supporting the patient's ventilation as needed. Many patients cannot be liberated from mechanical ventilation until the underlying acidosis is controlled.

With metabolic alkalosis, in an effort to compensate for the increased pH, the patient tries to decrease minute ventilation. If weaning is attempted when the patient has a metabolic alkalosis, the patient may continue to hypoventilate and weaning

may fail. As with metabolic acidosis, the underlying cause should be determined and managed. Common causes of metabolic alkalosis include hypochloremia or hypokalemia secondary to gastrointestinal loss, diuretics, or steroid administration. See Chapter 14 for details on acid–base balance.

EFFECTS OF MECHANICAL VENTILATION ON OXYGENATION

Inspired Oxygen

Mechanical ventilators usually deliver an increased fractional inspired oxygen (FiO_2) ranging from room air (0.21) to 100% O_2 (1.0). As a result, the alveolar partial pressure of oxygen (PAO_2) and arterial partial pressure of oxygen (PaO_2) may be restored to normal with appropriate management. The effectiveness of increased FiO_2 in the management of hypoxemia depends on the cause of hypoxemia. Hypoxemia caused by a decrease in the $\dot{V}/\dot{Q}$ ratio or hypoventilation is more responsive to increased FiO_2 than hypoxemia caused by a diffusion defect or shunt. Hypoxemia caused by hypoventilation responds well to an increase in FiO_2, but alveolar ventilation can be restored only by improved ventilation. Hypoxemia caused by diffusion defect and shunt generally respond better to an increase in PEEP than to an increase in FiO_2. If the patient is receiving mechanical ventilation and has adequate alveolar ventilation, failure of the PaO_2 to respond to increased FiO_2 likely means that hypoxemia is due to a diffusion defect or shunt.

It should be remembered that FiO_2 in an acutely ill patients should not be applied excessively.[3] Sufficient current data indicate that hyperoxia increases mortality of critically ill patients. As a result, the FiO_2 should be adjusted to ensure that the PaO_2 is 55 to 80 mm Hg and/or the SpO_2 is 88% to 95%.

Alveolar Oxygen and Alveolar Air Equation

Increasing FiO_2 increases PAO_2, according to the alveolar air equation (see Chapter 11).[2]

When FiO_2 is increased, PAO_2 increases as well, if there is no change in $PaCO_2$ or the respiratory exchange ratio. $PaCO_2$ may change with a change in alveolar ventilation or metabolic rate. O_2 consumption and CO_2 production increase with an increase in metabolic rate, such as with fever or overfeeding. If metabolic rate and alveolar ventilation are constant, an increase in FiO_2 results in a proportional increase in PAO_2.

RULE OF THUMB It should be remembered that FiO_2 in an acutely ill patients should not be applied excessively. Sufficient current data indicate that hyperoxia increases mortality of critically ill patients. As a result, the FiO_2 should be adjusted to ensure that the PaO_2 is 55–80 mm Hg and/or the SpO_2 is 88%–95%.

Arterial Oxygenation and Oxygen Content

Mechanical ventilation at FiO_2 of 0.21 may restore arterial oxygenation if the only cause of hypoxemia was hypoventilation. Hypoventilation may be the sole cause with central nervous system depression, apnea, and neuromuscular disease. With other causes of hypoxemia, an increase in FiO_2 is needed to increase arterial O_2 content.

O_2 content (see Chapter 12) is directly related to arterial oxygenation and hemoglobin concentration. Under circumstances of normal diffusion, FiO_2, and hemoglobin concentration, the arterial content is normal at approximately 19.8 mL O_2/100 mL blood. As defined by this equation, CaO_2 decreases if hemoglobin concentration, arterial saturation, or PaO_2 decreases.

Decreased Shunt

Mechanical ventilation alone does not decrease shunt. Otherwise, it would be much easier to restore PaO_2 in patients with ARDS. Administration of PEEP with mechanical ventilation or to a spontaneously breathing patient in the form of continuous positive airway pressure (CPAP) helps to maintain open alveoli and stabilize small, collapsed, or fluid-filled alveoli. The results are an increase in alveolar surface area for diffusion and improvement in $\dot{V}/\dot{Q}$ matching and arterial oxygenation.

PEEP or CPAP should be used judiciously (see later in this chapter and Chapter 49). High pressure can overdistend alveoli and redistribute pulmonary blood flow to capillaries surrounding poorly ventilated alveoli, resulting in increased shunt.

Increased Tissue Oxygen Delivery

When a mechanical ventilator is used to improve arterial oxygenation by increasing FiO_2 or PEEP, CaO_2 increases. However, the increase in CaO_2 represents only part of tissue O_2 delivery because O_2 delivery is defined by CaO_2 and cardiac output, as follows[2]:

$$DO_2\ (\text{tissue oxygen delivery in ml/min}) = CaO_2\ (\text{ml } O_2/100\ \text{ml blood}) \times \text{Cardiac output (L/min)} \times 10$$

where 10 is a constant for converting deciliters to milliliters.

Normal tissue O_2 delivery is approximately 990 mL/min because the normal CaO_2 is approximately 20 vol%, and the normal cardiac output is approximately 5 L/min. When PaO_2, CaO_2, and cardiac output are adequate, so is tissue O_2 delivery. When PEEP is needed to improve PaO_2, it must be used cautiously because PEEP increases intrathoracic pressure. When intrathoracic pressure is increased, pleural pressure around the heart also increases, and the increase can affect the mechanical activity of the heart and impede venous return and decrease cardiac output. As discussed in Chapter 49, careful titration of PEEP must include monitoring the cardiovascular status of the patient. *Optimal PEEP* provides adequate arterial oxygenation and tissue O_2 delivery.

EFFECTS OF POSITIVE PRESSURE MECHANICAL VENTILATION ON LUNG MECHANICS

Time Constants

The time necessary for **passive** inflation and deflation of the lung or each alveolus is determined by the product of compliance and resistance. This product is the **time constant** of the lung or alveolar unit. The compliance of a "normal" lung is approximately 0.1 L/cm H_2O, and resistance of a normal lung

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Oxygen Delivery

Problem

Oxygen delivery (DO_2) depends on PaO_2, hemoglobin concentration, and cardiac output. The formula for DO_2 is:

$$DO_2 = CaO_2 \times \text{Cardiac output (L/min)} \times 10$$

where CaO_2 is the arterial oxygen content, and 10 is the conversion factor between deciliters and milliliters. Normal DO_2 is 990 mL/min. DO_2 is normal when the hemoglobin concentration is 15 g/dL, cardiac output is 5.0 L/min, and PaO_2 is 100 mm Hg:

$$DO_2 = [15\,g\,Hb \times 1.34\,ml\,O_2/g\,Hb \times 0.97\,(SaO_2)] + 0.003 \times 100\,mm\,Hg] \times (5.0\,L/min) \times 10$$
$$= 19.8\,(CaO_2) \times 5\,(L/min) \times 10 = 990\,ml/min$$

When the practitioner calculates DO_2 and determines it to be low, the component of the formula that is low denotes the problem and the therapeutic target. If CaO_2 is low because of a low hemoglobin concentration, increasing the hemoglobin concentration with blood transfusion is indicated. If CaO_2 is low because of low PaO_2 or SaO_2, increasing PaO_2 and SaO_2 with O_2 or PEEP is indicated. If cardiac output is low, the cause (decreased preload, increased afterload, decreased contractility, or bradycardia) is determined, and appropriate therapy is initiated. Frequently, a decrease in CaO_2 results in an increase in the cardiac output to compensate for decreased DO_2.

Example:

Given PaO_2 of 65 mm Hg, hemoglobin concentration of 10 g/dL, SaO_2 of 91%, and cardiac output of 4.8 L/min, what increase in cardiac output is necessary to maintain DO_2 of 900 mL/min?

DO_2 at given values is $[(1.34 \times 10 \times 0.97) + (0.003 \times 65)] \times 4.8 \times 10 = 633\,ml/min$

An increase in cardiac output to 6.8 L/min results in DO_2 that is close to normal: $[(1.34 \times 10 \times 0.97) + (0.003 \times 65)] \times 6.8 \times 10 = 897$ mL/min. However, an increase in cardiac output to 6.8 L/min increases myocardial work. Because the cause of decreased DO_2 in this patient is hypoxemia and anemia, the goal of therapy should be to increase PaO_2. This strategy allows cardiac output and work to return to normal while adequate DO_2 is maintained. Increasing the hemoglobin concentration is normally not performed by transfusion unless the hemoglobin concentration is less than 8–10 g/dL because of the adverse effects associated with transfusions.

is approximately 2.5 cm H_2O/L/s. The time constant for a normal lung is 0.25 second (1.0 L/cm H_2O × 0.25 cm H_2O/L/s). For patients with normal lungs, 95% of the alveoli are inflated within three time constants (i.e., within 0.75 second). In four time constants (1.0 second), 98% of alveoli are inflated, and in five time constants (1.25 second), 99.3% of alveoli are inflated. The same numbers apply for exhalation.

The two major factors that affect alveolar time constants are changes in compliance and changes in resistance. If compliance or resistance decreases, the time constant for a given lung unit decreases, and the lung fills and empties faster. If compliance or resistance increases, the time constant increases, and it takes more time to fill and empty the lung.

There are clinical implications for patients with disorders consistent with abnormal time constants. A longer inspiratory time may be needed for patients with asthma because R_{aw} is increased. Attempting to ventilate these patients with a normal inspiratory time may result in inadequate volume to affected lung units because the airways are obstructed, and volume is likely to travel to airways with the lowest resistance. Inspiratory time in severe asthma needs to be set between approximately 1.0 to 1.5 seconds to ensure adequate gas delivery. The primary limiting factor is that the airways are also obstructed during exhalation. The expiratory time must also be longer to allow as complete an exhalation as possible.

Asthma is very different from COPD, in which the inspiratory time constant is normal, but the expiratory time constant is long. In general, asthma requires very slow respiratory rates with longer than normal inspiratory and expiratory times to account for the altered time constants during both inspiration and expiration. Patients with COPD generally tolerate a more rapid rate because only the expiratory time constant is lengthened. In both of these situations, air trapping is very common because of the long expiratory time constants. In patients with COPD, inspiratory times are generally short (approximately 0.7 to 0.9 second). In patients with ARDS or acute lung injury (ALI), time constants are very short, and as a result inspiratory times can also be very short. Most patients with ARDS require an inspiratory time of only 0.5 to 0.8 second. Expiratory time constants are also short—hence the ability to ventilate these patients rapidly with small V_T. Respiratory rates greater than 30 breaths/min are frequently well tolerated by patients with ARDS. The major concern with patients with ARDS and their short time constants is that any disruption of the airway rapidly results in a loss of lung volume. Atelectasis occurs with disconnections from the ventilator in 1 seconds. As a result, *all* patients with ARDS should be suctioned *only* with inline suction catheters, and any circuit disconnection should be avoided. Ventilator management in the care of patients with COPD, asthma, and ARDS is described in detail in Chapter 49.

Increased Pressure

Peak inspiratory pressure (PIP) is the highest pressure produced during the inspiratory phase. It is the sum of the pressures necessary to overcome R_{aw} and lung and chest wall compliance. PIP is also known as *peak pressure* or *peak airway pressure*.

P_{plat} is the pressure observed during a period of inflation hold or end-inspiratory pause. To obtain a P_{plat}, the RT initiates an inspiratory pause time of 0.5 to 2.0 seconds. During inspiration, the peak pressure is reached and then immediately followed by the inspiratory pause. During the pause, pressure decreases to a pressure plateau. When a valid P_{plat} is obtained, the inspiratory pause time is returned to zero. P_{plat} represents the average peak P_{alv}. In volume-controlled ventilation, P_{plat} is always lower than peak pressure because the peak pressure is the sum of the P_{alv} and the pressure needed to overcome R_{aw}. When flow is delivered by a square waveform, the difference between P_{plat} and peak pressure is the pressure necessary to overcome R_{aw}. If the V_T is divided by the difference between the P_{plat} and total PEEP (applied plus auto-PEEP), the quotient is the quasistatic lung-thorax compliance[4]: The reason for this is that the baseline pressure prior to the start of inspiration is the total PEEP, not the applied PEEP.[4]

$$C_{static} = V_T/(P_{plat} - PEEP)$$

This value is referred to as the lung-thorax compliance because the compliance of the lungs and the compliance of the rib cage are being calculated as a unit. The lung compliance cannot be determined without the use of an esophageal balloon.[4] Ideally, the volume lost owing to tubing compliance should be subtracted from the V_T if the ventilator does not compensate for it, making the equation[4]:

$$C_{static} = \text{Adjusted } V_T / (P_{plat} - \text{total PEEP})$$

It may be more useful to follow trends in lung compliance, rather than making judgments on only one calculation. A downward trend in compliance means that the lungs or chest wall is stiffer, as in ARDS.

R_{aw} during volume ventilation is estimated by the difference between PIP and P_{plat} divided by the inspiratory flow ($\dot{V}_I$) in L/s, provided that the flow is constant (square waveform)[4]:

$$R_{aw} = (PIP - P_{plat}) / \dot{V}_I$$

During mechanical ventilation, the P_{plat} should be less than 28 cm H_2O.[5,6] At levels greater than 28 cm H_2O, alveolar damage from overdistention is likely. This form of *ventilator-induced lung injury (VILI)* is referred to as **volutrauma** (see later). This trauma can result in air leakage from alveoli, the release of inflammatory mediators, and multisystem organ failure (MSOF). When the P_{plat} approaches 28 cm H_2O during either volume or pressure ventilation, the pressure limit or the V_T should be decreased. This approach to ventilation is referred to as *lung protective ventilation*.[4–6] In addition the **driving pressure**, P_{plat} minus PEEP should be less than 15 cm H_2O.[7] Driving pressure greater than 15 cm H_2O increases mortality and driving pressures less than 15 cm H_2O decreases mortality. Many consider the driving pressure the most important variable in relation to ventilator induced lung injury.[7]

RULE OF THUMB When measuring lung mechanics, R_{aw} and compliance always use the same ventilator settings to make comparisons from one point in time to another much easier. In adults, typical settings are volume ventilation, V_T 500 mL, square wave flow, and peak flow set at 60 L/min.

Mean Airway Pressure

Mean airway pressure is the average pressure across the total cycle time (TCT). The mean airway pressure ($P_{\overline{AW}}$) can be calculated manually if the flow is constant, as follows[4]:

$$P_{\overline{AW}} = \tfrac{1}{2}(PIP - PEEP) \times (\text{Inspiratory time}/TCT) + PEEP$$

Mean airway pressure is computed by the ventilator as the integral of the pressure signal over the TCT (as a rolling average), so the RT can record the ventilator computed value rather than manually calculating it. Because expiratory (baseline) pressure is lower than inspiratory pressure, the mean pressure is between peak and end-expiratory pressure. The variables affecting mean pleural and mean airway pressure are summarized in Box 47.1. For a given minute volume, partial ventilatory support modes such as synchronized intermittent mandatory ventilation (SIMV) result in lower mean airway and pleural pressures than continuous mandatory ventilation (CMV) modes. For a specific mandatory breath, as peak pressure increases, so does mean pressure. Likewise, long inspiratory times increase mean pressure. Prolonging expiratory time has the opposite effect on mean airway pressure. In general, the harmful cardiovascular effects of PPV are more likely to occur when $P_{\overline{AW}}$ or inspiratory-to-expiratory (I:E) ratio increases (e.g., >1:1).

BOX 47.1 Factors That Increase Mean Airway Pressure

- Absence of spontaneous ventilation
- Increasing positive pressure
- Increasing duration of inspiration
- Decreasing duration of expiration
- Nature of inspiratory waveform
- Increasing level of positive end-expiratory pressure
- Decreasing compliance, increasing airways resistance

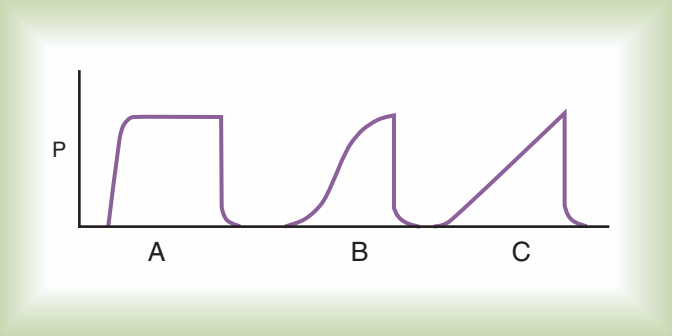

Fig. 47.6 Pressure patterns resulting from a descending ramp flow waveform *(A)*, a sine wave flow waveform *(B)*, and a constant flow waveform *(C)*. Because waveform *A* has the highest pressure for the longest inspiratory time, it also has the greatest mean airway pressure.

The pressure waveform of a mandatory breath affects mean pressure. In Fig. 47.6, for a given inspiratory time, the constant pressure pattern (curve *A*) results in the greatest area under the airway pressure curve and the highest mean airway pressure. A constant pressure pattern is normally produced by a pressure targeted breath that provides decreasing (descending ramp) flow. The effect of PEEP on mean airway pressure is simple: Every 1 cm H_2O of applied PEEP increases the mean airway pressure 1 cm H_2O.

Effect of Peak Airway Pressure on Lung Recruitment

As peak airway pressure increases, previously collapsed, small, or partially fluid-filled alveoli are recruited (i.e., reopened).[8] This reopening of alveoli increases alveolar surface area and restores functional residual capacity (FRC). At the alveolar level, the surface area available for diffusion is increased. As a result, PaO_2 increases, consistent with Fick's law. The use of extrinsic PEEP maintains the airways and recruited open alveoli. Extrinsic PEEP is controlled directly by the PEEP control on the ventilator, and the RT always knows how much extrinsic PEEP is present. Several factors, including inverse ratio ventilation (IRV), may add intrinsic

PEEP or auto-PEEP by starting the next breath before the previous exhalation has ended. The amount of intrinsic PEEP added by IRV can be estimated by an end-expiratory pause, which stops the next breath from being delivered. During this end-expiratory pause, alveolar and mouth pressures equilibrate, and the total PEEP is now presented by the ventilator. The amount of auto-PEEP present is the difference between the total PEEP and the extrinsic PEEP:

$$\text{Intrinsic PEEP (auto-PEEP)} = \text{Total PEEP} - \text{Extrinsic PEEP}$$

Increased Lung Volume: Tidal Volume

The volume delivered during pressure-controlled modes varies with changes in set pressure, patient effort, and lung mechanics. For all pressure-targeted modes, the volume delivered at a given pressure decreases as compliance decreases. An increase in resistance, active exhalation, or muscle tensing by the patient during inspiration also decreases delivered volume in pressure ventilation.

If pressure serves as the limit variable instead of the cycle variable, changes in R_{aw} during pressure-limited ventilation may or may not affect delivered volume. In this case, the key factor is the time available for pressure equilibration. Volume can remain constant even if R_{aw} increases, as long as there is sufficient time for alveolar and airway pressures to equilibrate. However, if insufficient time is available for pressure equilibration, delivered volume decreases as R_{aw} increases. The length of time needed for pressure equilibration is usually at least three times greater than the time constant for the respiratory system. In pressure modes, ventilator-delivered flow varies with patient effort and lung mechanics; this tends to avoid patient–ventilator asynchrony.[9]

Increased Functional Residual Capacity

FRC is not known to change significantly with the application of PPV alone because passive exhalation allows the end-expiratory pressure to return to atmospheric pressure with each breath. If an increase in FRC is to be achieved, PEEP or CPAP must be applied. PEEP or CPAP does not recruit collapsed lung units but prevents lung units that have been opened from collapsing at end-expiration. Peak airway pressure recruits lung volume. The magnitude of the increase in FRC sustained by PEEP or CPAP is proportional to the lung-thorax compliance. With acute restriction, as PEEP is increased, lung compliance improves. Initially, the FRC gain as PEEP is added is small. There is no practical way of measuring FRC in all patients, so other methods of determining an increase in FRC are used, such as improving PaO_2 at a constant FiO_2, increasing PaO_2/FiO_2 ratio, decreasing shunt fraction, or decreasing FiO_2 while maintaining PaO_2. The management of PEEP is described in more detail in Chapter 49.

Pressure-Volume Curve and Lung Recruitment in Acute Respiratory Distress Syndrome

Fig. 47.7 depicts the pressure-volume (P-V) relationship of the lung-thorax in an idealized patient with ARDS.[8] On the inflation P-V curve, there are two points of inflection: the lower inflection point referred to as P_{flex} or *lower corner pressure,* and an upper inflection point, also referred to as *upper corner pressure*. These

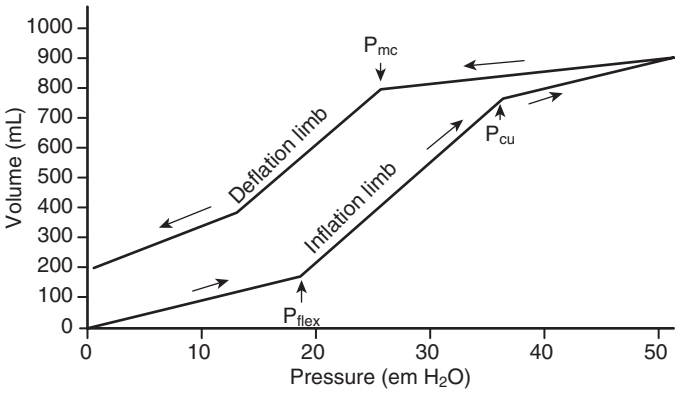

Fig. 47.7 Pressure-Volume (P-V) Curve of the Lung-Thorax Indicating the Inflation and Deflation Limbs. *Arrows* indicate direction of flow. P_{CL}, Lower corner pressure or P_{flex} or lower inflection point; P_{CU}, upper corner pressure or upper inflection point; P_{MC}, point of maximum compliance change. (Modified from Godon S, Fujino Y, Hromi JM, et al: Optimal mean airway pressure during high frequency oscillation, *Anesthesiology* 94:862–868, 2001.)

two points represent defined changes in compliance. The lower inflection point represents an abrupt increase in lung-thorax compliance as collapsed or atelectatic lung begins to be recruited.[10] The upper deflection point represents the point where the rate of lung recruitment decreases and over inflation begins.[10] It is most important to realize from this graph that the lung is recruited by pressure and that the higher the peak airway pressure, the greater the potential for lung to be recruited. The maximum pressure needed to recruit a given patient's lung is unknown; however, pressures up to 50 cm H_2O most likely are safe with most patients when applied for short (1 to 3 minutes) periods.[11–13] If these pressures were applied for longer periods, lung injury would most likely result.

The deflation limb of the P-V curve is similar in shape to the inflation limb but is separated from the inflation limb. This hysteresis (separation) is a result of surfactant and surface tension interactions. Basically, less pressure is required to keep the lung open on the deflation limb of the P-V curve than on the inflation limb; this is obvious on examination of the volume maintained in the lung at P_{flex}, or 20 cm H_2O. On the inflation limb, lung volume increases approximately 200 mL at 20 cm H_2O, but on the deflation limb, lung volume increases approximately 550 mL. The goal of an open lung approach to ventilation that has been proposed by many authors is to open the lung and then to ventilate the patient on the deflation limb of the P-V curve at the least PEEP maintaining the lung open.[11–13]

Fig. 47.7 is an idealized P-V curve; actual patient P-V curves in ARDS are not as well defined. In approximately 20% of patients with ARDS, P_{flex} cannot be identified on the inflation P-V curve. As a result, despite two positive randomized controlled trials using P_{flex} to set PEEP,[14,15] the use of P-V curves clinically has not become common practice; a second reason for this is the difficulty of measuring the P-V curve. However, many newer ICU ventilators are including algorithms that allow P-V curves to be performed by the ventilator with the ventilator identifying P_{flex}.

The approach to setting PEEP that ensures ventilation on the deflation limb of the P-V curve and the minimal PEEP to sustain the benefit of lung recruitment is a decremental PEEP trial immediately after a lung recruitment maneuver (RM).[13,14,16] Many different approaches to performing lung RMs have been published, but the approach that is considered the safest and most efficacious is the use of pressure-controlled continuous mandatory ventilation (PC-CMV).[13,14,16] To perform a lung RM with PC-CMV, high enough PEEP must be set to avoid derecruitment after each inspiration. Essentially, a minimum of 20 cm H_2O PEEP is required during the RM. Peak pressure is usually stopped at 40 cm H_2O, but if the patient tolerates the pressure hemodynamically, it may be increased to 50 cm H_2O (PEEP 35 cm H_2O), ensuring a driving pressure of no more than 15 cm H_2O (Box 47.2). Inspiratory time is increased to approximately 2.0 to 3.0 seconds, and respiratory rate is decreased to approximately 10 to 15 breaths/min. The maneuver is applied for 1 to 3 minutes. During the RM, the patient must be sedated to apnea to avoid fighting the ventilator.

Before any RM, the patient must be hemodynamically stable. RMs should not be performed in patients with existing **barotrauma** or with a high likelihood of developing barotrauma (blebs or bullae) or in patients who are hemodynamically unstable. In addition, RMs are most effective and result in the least adverse reaction if performed early during ARDS. During and after the RM, the patient must be carefully monitored for hemodynamic and oxygenation instability and the development of barotrauma.

After an RM, the best way to identify the minimum effective PEEP level that maintains the lung open is to perform a decremental PEEP trial.[13,14,16] This trial is performed by changing the mode from PC-CMV to volume-controlled continuous mandatory ventilation (VC-CMV), V_T 4 to 6 mL/kg, inspiratory time 1.0 second or less, PEEP 20 to 25 cm H_2O, and rate set at the maximum that does not cause auto-PEEP.[17] After stabilization (3 to 5 minutes), dynamic compliance is measured.[17] PEEP is then decreased 2 cm H_2O, the patient allowed to stabilize (30 to 45 seconds), and measurement of dynamic compliance is repeated; this is continued until the PEEP level at which the compliance decreases is identified. In general, compliance at 20 to 25 cm H_2O PEEP is low and increases as PEEP is decreased; compliance then decreases as PEEP is decreased further. Open lung PEEP is the PEEP associated with the highest compliance. Set PEEP is open lung PEEP plus 2 cm H_2O.

After open lung PEEP is identified, the lung is again recruited because during the decremental PEEP trial derecruitment occurred. After recruitment, PEEP is set at the identified level, ventilation is adjusted using a lung protective V_T (4 to 8 mL/kg), and rate is adjusted to normalize PCO_2. After all is set, FiO_2 is decreased to the level that maintains PaO_2 in the range of 55 to 70 mm Hg. Repeat RMs may be needed if the patient did not respond to the initial RM or if the patient is disconnected from the ventilator and derecruitment occurs. A successful RM is one that allows the FiO_2 to be reduced to less than 0.5.

The use of RM has been documented in many case series; however, no data have been published indicating that outcome is improved as a result of RMs and decremental PEEP settings. Research is ongoing.

BOX 47.2 Effects of Positive Pressure Ventilation on System Other Than the Lungs

Increased intracranial pressure
Decreased cerebral perfusion pressure
Decreased renal blood flow
Decreased urinary output
Decreased sodium and potassium excretion
Increased plasma renin activity
Increased plasma aldosterone level
Increased vasopressin level
Decreased atrial natriuretic hormone level
Decreased liver and splanchnic perfusion
Increased serum bilirubin level
Decreased gastrointestinal function
Gastric mucosal ischemia
Development of stress ulcers
Gastric distention

RULE OF THUMB A lung RM is most likely to be successful if it is performed early in the course of ARDS. Ideally a lung RM should be performed once the patient is fully stabilized after intubation and initiation of mechanical ventilation. The longer the patient is mechanically ventilated, the less likely it is that the RM would be successful.

Increased Dead Space

The dead space fraction is increased with the institution of mechanical ventilation owing to inspiratory mechanical bronchodilation and the preferential ventilation of more nondependent alveoli, the reduction of blood flow away from ventilated alveoli, and the continued perfusion of basilar or dependent alveoli (see Fig. 47.5). This increase is concurrent with a decrease in $\dot{V}/\dot{Q}$ ratio.

Decreased Work of Breathing

Although improper ventilator management can increase WOB (poor patient–ventilator interaction, see Chapter 48 for details), one of the primary objectives of mechanical ventilation is to decrease WOB. PPV can significantly reduce WOB in patients with actual or impending respiratory muscle fatigue. RTs frequently see patients relax as the ventilator assumes a major portion of their WOB. To lessen WOB, ventilation must be sufficient to meet the patient's needs. Otherwise, a spontaneously breathing patient tends to resist the ventilator, and an asynchronous breathing pattern develops. Inappropriately applied PPV can result in alveolar hypoventilation and consequently a considerable increase in the patient's WOB.

Mode, trigger setting, and inspiratory flow have an effect on WOB. WOB consists of two components: (1) ventilator work (WOB_{vent}) occurring as the ventilator forces gas into the lungs and (2) patient work (WOB_{pt}) as the inspiratory muscles draw gas into the lungs. The magnitude of WOB_{pt} depends on compliance, resistance, and ventilatory drive and on ventilator variables,

such as trigger sensitivity, peak flow, cycling coordination, and V_T.[18,19]

Regardless whether flow or pressure triggering is selected, either should always be set as sensitive as possible without causing autotriggering. The less sensitive the setting, the greater the patient effort. In older generation ventilators, flow triggering was shown to require less effort than pressure triggering.[20] However, with the newest generation of ICU ventilators, both are equally effective.[21]

As described in Chapter 46, a mode of ventilation is a ventilatory pattern that can be described by identifying the control variable, breath sequence, and targeting scheme. The breath sequence may be thought of as being on a continuum from assuming very little to assuming all WOB. As the breath sequence is changed from continuous spontaneous ventilation (CSV) to CMV, the ventilator assumes more WOB. An example of this transition would be from CPAP to pressure support to CMV. In CPAP, a continuous spontaneous mode of ventilation, the patient assumes all WOB. The ventilator merely provides constant positive pressure throughout the patient's breathing cycle. The ventilator assumes more WOB during CMV. Pressure support is also an example of CSV. During pressure support ventilation (PSV), the patient determines breath timing (length of inspiration and expiration) and frequency. Depending on the set inspiratory pressure, the clinician may program the ventilator to provide a minimal to a maximal amount of WOB. In instances where the patient has no spontaneous efforts, all breaths during CMV are time triggered and all work performed is WOB_{vent}. Although it may be advantageous for the ventilator to assume all WOB for a while, extended periods of passive ventilation may cause diaphragmatic atrophy, which may unnecessarily prolong the need for mechanical ventilation and delay weaning. At initiation of patient-triggered pressure or volume modes, WOB_{pt} resumes.

During assisted ventilation, pressure-targeted modes are generally more capable of meeting patient ventilatory demands and minimizing WOB_{pt}.[22] As pressure level is increased, ventilatory muscles are unloaded, V_T increases for a given amount of patient effort, and WOB_{pt} decreases. Most clinicians increase pressure level until the breathing pattern approaches normal—that is, until the spontaneous ventilatory rate is 15 to 25 breaths/min and the spontaneous V_T is normal (5 to 8 mL/kg).

Measuring WOB is technically difficult. It is often accomplished by esophageal balloon monitoring, in which a balloon is placed in the distal third of the esophagus, and a pneumotachometer is attached to the airway (see Chapter 52). WOB is the integral of the esophageal pressure and V_T. Normal WOB is 0.6 to 0.9 J/L.[23]

MINIMIZING ADVERSE PULMONARY EFFECTS OF POSITIVE PRESSURE MECHANICAL VENTILATION

Decreasing Pressure

The main objective of mechanical ventilation is to provide a minute ventilation appropriate to achieve adequate alveolar ventilation and supplemental O_2 and PEEP to provide adequate arterial oxygenation.

MINI CLINI

Overcoming an Increase in the Work of Breathing

Problem

A patient's WOB is minimal during mechanical ventilation with an appropriate V_T and rate. As the ventilator support is gradually discontinued and the patient is expected to take over more of WOB, R_{aw} associated with breathing through an endotracheal tube may become clinically important. The RT must be able to recognize this problem readily and know how to correct it.

A patient has received mechanical ventilation in volume-controlled continuous mandatory ventilation mode for the past week. The patient's condition is now clinically stable, and ventilation is provided by PSV. As the PSV pressure level is reduced to 8 cm H_2O, the patient begins using accessory muscles to breathe, the spontaneous respiratory rate increases to 30 breaths/min, and the patient reports shortness of breath. Blood gas values are acceptable, and no abnormal lung sounds are present. What is the problem, and what should the RT do?

Solution

The patient may be experiencing excessive WOB because of R_{aw} associated with the endotracheal tube; a small sized tube or partial obstruction of the tube with secretions may be the problem. Other possibilities that should be considered include deterioration in the patient's cardiopulmonary status, but the normal blood gas values and lung sounds suggest the problem is not the lungs. Passing a suction catheter through the tube may help to identify the problem. If the catheter does not pass easily, the tube may be partially obstructed. Two options exist: change the tube or extubate the patient. Because the tube would need to be removed regardless of the choice, a trial extubation should be considered. Because this patient is at risk immediately after extubation, noninvasive ventilation should be started. If the patient cannot tolerate extubation, an appropriate-sized endotracheal tube can be reinserted.

Peak pressure is the result of the pressure required to overcome system resistance and compliance. Although there is no absolute maximum pressure, most practitioners try to avoid peak pressures greater than 40 cm H_2O. As the peak pressure approaches 40 cm H_2O, it is important to consider the causes. Factors that increase R_{aw} include airway edema, bronchospasm, and secretions and ETT obstruction. The RT can manage or avoid these problems by ensuring adequate humidity, bronchial hygiene (suctioning, airway care), and administration of bronchodilators and antiinflammatory drugs. Factors that increase the pressure needed to inflate the lung and overcome compliance include alveolar and interstitial edema, atelectasis, fibrosis, and chest wall restriction.

P_{plat} reflects mean maximum P_{alv}. P_{plat} of 28 cm H_2O or greater has an increased likelihood of causing lung injury.[4–6] If P_{plat} approaches 28 cm H_2O during volume ventilation, the V_T should be decreased so that the P_{plat} is less than 28 cm H_2O, or with pressure ventilation, target pressure should be set less than 28 cm H_2O.[5,24] The patient population where this guideline is most likely violated is the markedly obese patient who may require more than 20 cm H_2O PEEP. (See Chapter 30.)

Driving pressure is the difference between P_{plat} and total PEEP and should not exceed 15 cm H_2O.[7] As described earlier, the lower the driving pressure the lower the risk of mortality. Even in the markedly obese patient, if the V_T and PEEP are set properly the driving pressure can be kept below 15 cm H_2O, even when the P_{plat} exceeds 28 cm H_2O.

Mean airway pressure is decreased by decreasing inspiratory time, V_T, respiratory rate, PEEP, or PIP. Increased mean airway pressure reduces venous return and may reduce cardiac output.

RULE OF THUMB Driving pressure (plateau pressure minus PEEP) should be less than 15 cm H_2O. Driving pressure greater than 15 cm H_2O increase mortality and driving pressures less than 15 cm H_2O decrease mortality. Many consider the driving pressure the most important variable in relation to ventilator induced lung injury.

Positive End-Expiratory Pressure or Continuous Positive Airway Pressure

PEEP is the application of positive pressure at end-exhalation. PEEP is used primarily to improve oxygenation in patients with refractory hypoxemia. As a rule, refractory hypoxemia exists when PaO_2 cannot be maintained at greater than 50 to 60 mm Hg with FiO_2 0.50 or greater. PEEP improves oxygenation in these patients by maintaining alveoli open, restoring FRC, and decreasing physiologic shunting. The improved alveolar volume provided by PEEP allows a lower FiO_2. Other values such as lung compliance, shunt fraction, and PaO_2/FiO_2 ratio also may improve when PEEP is appropriately applied. PEEP may be indicated in the care of patients with COPD who have dynamic hyperinflation (auto-PEEP).[25,26] (See discussion later in this chapter.)

Beneficial and harmful effects are associated with the use of PEEP (Table 47.2). Detrimental effects of inappropriately high levels of PEEP include decreased cardiac output, increased pulmonary vascular resistance, and increased dead space. When one or more of these problems occur, PEEP is decreased to the previous level or to a value between the current level and the previous level. If cardiac output decreases and an increase in PEEP is necessary to maintain oxygenation, intravenous fluid, inotropic cardiac drugs, or both are administered to restore cardiac output.

PEEP is contraindicated in the presence of a tension pneumothorax. PEEP should be applied cautiously in patients with severe unilateral lung disease because PEEP would overinflate the lung with higher compliance. The result is lung overdistention and compression of adjacent pulmonary capillaries. Independent lung ventilation can be used to apply separate inspiratory and baseline pressures to the right and the left lung when severe unilateral lung disease is present.[27] PEEP is not contraindicated in the care of patients with increased ICP, caution must be used to prevent the application of PEEP from increasing ICP further. In general, if the head of the bed can be elevated to a height equal to the amount of PEEP applied, the hydrostatic pressure increase caused by the PEEP can by offset by the elevation of the head of the bed.

TABLE 47.2 Physiologic Effects of Positive End-Expiratory Pressure

Beneficial Effects of Appropriate PEEP	Detrimental Effects of Inappropriate PEEP
Restored functional residual capacity, avoids derecruitment	Increased pulmonary vascular resistance
Decreased shunt fraction	Potential decrease in venous return and cardiac output
Increased lung compliance	Decreased renal and portal blood flow
Decreased work of breathing	Increased intracranial pressure
Increased PaO_2 for a given FiO_2	Increased dead space

PEEP, Positive end-expiratory pressure.

RULE OF THUMB Refractory hypoxemia exists when PaO_2 cannot be maintained at greater than 50–60 mm Hg with FiO_2 0.50 or greater. This situation is an indication for PPV with PEEP or CPAP because an increased end-expiratory pressure with either of these modalities improves oxygenation by stabilizing lung open decreasing physiologic shunting.

Effects of Ventilatory Pattern

The most commonly used inspiratory flow patterns are constant or square and descending ramp during volume-controlled ventilation and exponential decay during pressure-controlled ventilation. In mechanical and computer models, a descending ramp (volume-controlled ventilation and pressure control ventilation) flow pattern improves gas distribution to lung units with long-time constants. The literature often refers to the descending ramp as a decelerating flow pattern. Similar findings in humans have been reported. Compared with a square flow waveform, a descending ramp has been shown to reduce peak pressure, inspiratory work, V_D/V_T, and $P(A-a)O_2$ without affecting hemodynamic values.[28] In addition, compared with volume-controlled ventilation with a square flow waveform, pressure-controlled ventilation with an exponential decay flow waveform may result in a higher PaO_2, lower $PaCO_2$, and lower PIPs. However, mean airway pressure is higher with pressure-controlled ventilation compared with volume-controlled ventilation because pressure rapidly increases to the set inspiratory pressure and remains constant throughout inspiration. During pressure-controlled ventilation, flow is responsive to patient demand. The ventilator delivers flow to the patient in proportion to patient demand. Flow is also greater at the onset of inspiration, resulting in V_T delivery at a time when the lungs are most compliant, the beginning of the breath. As a breath ends, flow is least, and the volume delivered is small. The result is a lower peak airway pressure for any given V_T.

In most spontaneously breathing persons, lower inspiratory flows improve gas distribution. However, during PPV, low inspiratory flow may lead to lengthy inspiratory times and air trapping if expiratory time is too short. High ventilator inspiratory flow allows more time for exhalation and reduces the incidence of air trapping. Avoidance of air trapping improves gas exchange and reduces WOB in patients with high ventilatory demands.[19,29]

An inflation hold also affects gas exchange. By momentarily maintaining lung volume under conditions of no flow, an inflation hold allows additional time for gas redistribution between lung units with different time constants. In both animal and human studies, increasing the length of an inflation hold decreases the V_D/V_T, $PaCO_2$, and inert gas washout time. Adding an inflation hold effectively increases total inspiratory time, shortening the time available for exhalation and predisposes patients with airway obstruction to auto-PEEP. In practice, an inflation hold

should be used only to obtain P_{plat} values. Because the technique prevents the onset of exhalation, asynchrony occurs if the patient is actively breathing.

Trigger Site and Work of Breathing

Studies have examined the effects of sensing a patient's inspiratory effort at the tip of the endotracheal tube rather than in the ventilator circuit, as is done with all ventilators. Triggering and managing gas delivery by measurement of pressure at the tip of the endotracheal tube decreases patient effort and improves synchrony; however, no practical system has been designed.[30] In addition, the efficiency of ventilator flow and pressure triggering seems to improve with each new generation of mechanical ventilator.

PHYSIOLOGIC EFFECTS OF VENTILATORY MODES

Volume-Controlled Ventilation Versus Pressure-Controlled Ventilation

Fig. 46.5 illustrates the important variables for volume ventilation modes. The figure shows that the primary variable to be controlled is the patient's minute ventilation. A particular ventilator may allow the operator to set minute ventilation directly. More frequently, minute ventilation is adjusted by means of a set V_T and frequency. V_T is a function of the set inspiratory flow and the set inspiratory time. Inspiratory time may be affected by the set frequency and, if the I:E ratio is set. The mathematical relationships among all these variables are shown in Table 47.3.

With pressure-controlled ventilation, the goal is also to maintain adequate minute ventilation. However (as the equation of motion shows), when pressure is controlled, V_T and minute ventilation are determined not only by the ventilator's pressure settings but also by the elastance and resistance of the patient's respiratory system. Minute ventilation and hence gas exchange are less stable in pressure-controlled modes than in volume-controlled modes. Fig. 46.6 shows the important variables for pressure-controlled ventilation. V_T is not operator set. It is the result of the patient inspiratory effort, the set inspiratory pressure, the patient's lung mechanics, and the inspiratory time. On most ventilators, the speed with which inspiratory pressure is achieved (i.e., the pressure rise time) is adjustable. That adjustment affects the shape of the pressure waveform and the mean airway pressure.

TABLE 47.3 Equations Relating the Important Parameters for Volume-Controlled and Pressure-Controlled Ventilation

Mode	Parameter	Symbol	Equation
Volume-controlled	Tidal volume (L)	V_T	$V_T = \dot{V}_E \div f$ $V_T = \dot{V}_I \div T_I$
	Mean inspiratory flow (L/min)	$\bar{\dot{V}}_I$	$\bar{\dot{V}}_I = 60 \times V_T \div T_I$ $\bar{\dot{v}}_I = \frac{\dot{v}_E \times TCT}{T_I}$
Pressure-controlled	Tidal volume (L)	V_T	$V_T = \Delta P \times C \times (1 - e^{-t/\tau})$
	Instantaneous inspiratory flow (L/min)	$\dot{v}_I$	$\dot{v}_I = \left(\frac{\Delta P}{R}\right) e^{-t/\tau}$
	Pressure gradient (cm H_2O)	ΔP	$\Delta P = PIP - PEEP$
Both modes	Exhaled minute ventilation (L/min)	$\dot{V}_E$	$\dot{V}_E = V_T \times f$
	Total cycle time or ventilatory period (s)	TCT	$TCT = T_I + T_E = 60 \div f$
	I:E ratio	I:E	$I{:}E = T_I : T_E = \frac{T_I}{T_E}$
	Time constant (s)	τ	$\tau = R \times C$
	Resistance (cm H_2O/L/s)	R	$R = \frac{\Delta P}{\Delta \dot{V}}$
	Compliance (L/cm H_2O)	C	$C = \frac{\Delta V}{\Delta P}$
	Elastance	E	$E = \frac{1}{C}$
	Mean airway pressure (cm H_2O)	$\bar{P}_{aw}$	$\bar{P}_{aw} = \left(\frac{1}{TCT}\right) \int_{t=0}^{t=TCT} P_{aw} dt$
Primary variables	Pressure (cm H_2O)	P	
	Volume (L)	V	
	Flow (cm H_2O/L/s)	$\dot{V}$	
	Time (s)	τ	
	Inspiratory time (s)	T_I	
	Expiratory time (s)	T_E	
	Frequency (breaths/min)	f	
	Base of natural logarithm (≈2.72)	e	

Continuous Mandatory Ventilation

CMV (also referred to as *assist/control*) is a mode of ventilation in which total ventilatory support is provided by the mechanical ventilator. All breaths are mandatory and delivered by the ventilator at a preset volume or pressure, breath rate, and inspiratory time. If the patient has spontaneous respiratory efforts, the ventilator delivers a patient-triggered breath. If patient efforts are absent, the ventilator delivers time-triggered breaths. The clinician needs to set an appropriate trigger level and flow rate for the patient in this mode of ventilation. There is a potential for the ventilator to autotrigger when the trigger level is set too sensitive. As a result, hyperventilation, air trapping, and patient anxiety often ensue. However, if the trigger level is not sensitive enough, the ventilator does not respond to the patient's inspiratory efforts, which results in increased WOB.

Occasionally, all attempts to optimize patient comfort, reduce WOB, and achieve the goals of this mode of ventilation are futile. In cases in which this mode is poorly tolerated and spontaneous triggering is counterproductive to the goals set for a particular patient, sedation or paralysis or both may be required. These agents may be used to minimize patient effort and normalize WOB.

Volume-Controlled Continuous Mandatory Ventilation

VC-CMV is indicated when a precise minute ventilation or blood gas parameter, such as $PaCO_2$, is therapeutically essential to the care of patients.[29] Theoretically, volume control (with a constant inspiratory flow) (Fig. 47.8) results in a more even distribution of ventilation (compared with pressure control) among lung units with different time constants where the units have equal resistances but unequal compliances (e.g., ARDS).[30]

During VC-CMV, volume is guaranteed, but airway pressure varies depending on changes in the patient's lung mechanics. A reduction in lung compliance or an increase in resistance causes higher peak airway pressures. Care should also be taken when setting the inspiratory flow. Avoid setting a flow that fails to match patient needs or exceeds patient demand. An insufficient flow rate would result in an imposed increase in the patient's WOB and a concomitant increase in O_2 consumption. The inspiratory phase may be prematurely shortened if the set inspiratory flow exceeds patient demands. Meticulous patient monitoring and use of VC-CMV allow the clinician to achieve precise and predictable physiologic results. VC-CMV results in gas exchange and hemodynamic stability at the same level as PC-CMV, and either can be used effectively during controlled ventilation; the patients are passively ventilated. However, when the patient is actively triggering the ventilator, better patient ventilator synchrony and less WOB are achieved during PC-CMV than VC-CMV.

Pressure-Controlled Continuous Mandatory Ventilation

Similar to VC-CMV, PC-CMV can be used as a basic mode of ventilatory support. The primary difference between volume-controlled and pressure-controlled ventilation is the control variable with which the clinician is most concerned.[31,32] Theoretically, pressure control (with a constant inspiratory pressure) (Fig. 47.9) results in a more even distribution of ventilation (compared with volume control) among lung units with different time constants when units have equal compliances but unequal resistances.[30] The instability of V_T caused by airway leaks can be minimized by using pressure-controlled rather than volume-controlled ventilation. Increased V_T stability may lead to better gas exchange and lower risk of pulmonary volutrauma.[33]

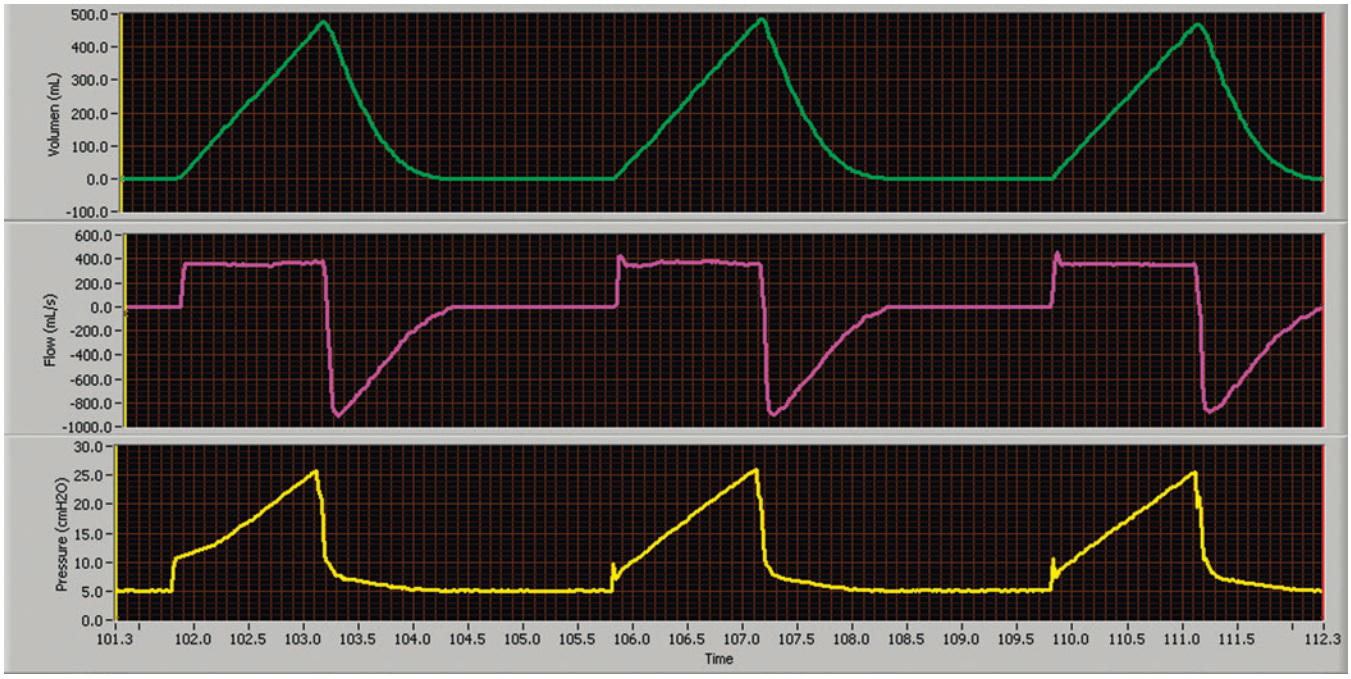

Fig. 47.8 Volume-Controlled Continuous Mandatory Ventilation. *Top,* V_T; *middle,* flow; *bottom,* airway pressure waveform. V_T, Tidal volume.

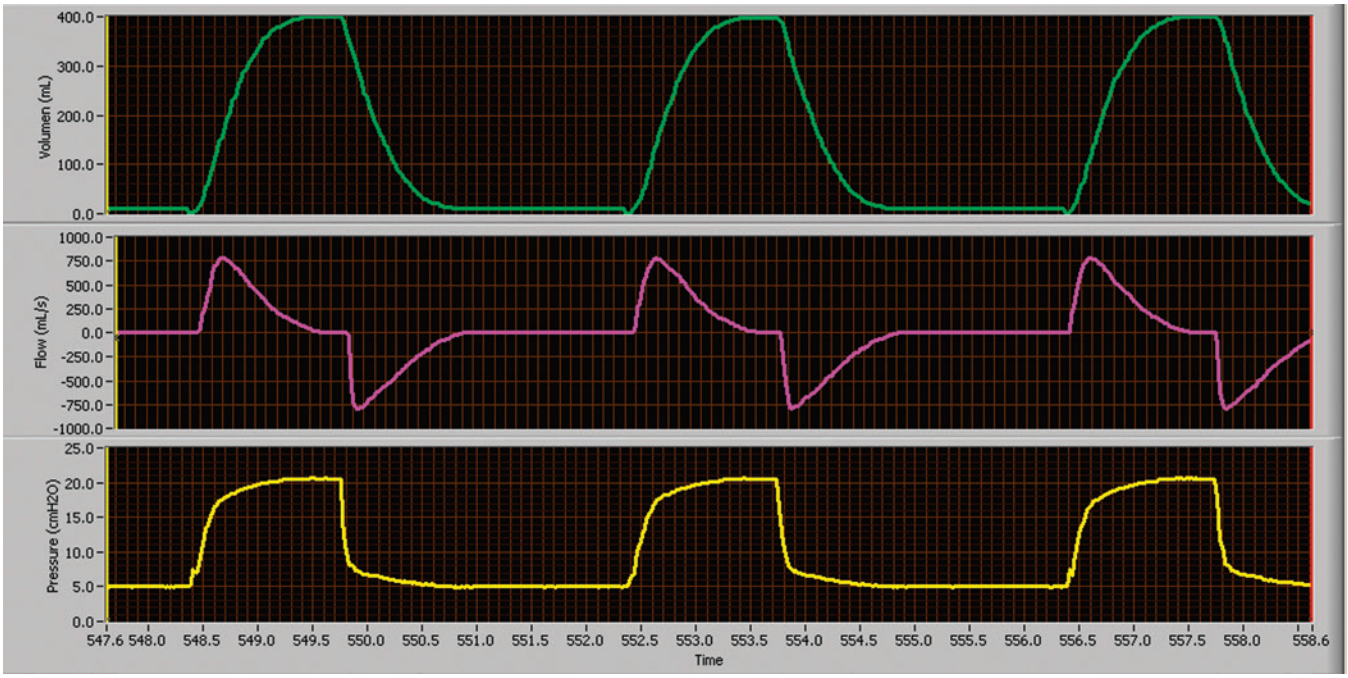

Fig. 47.9 Pressure-Controlled Continuous Mandatory Ventilation. *Top,* V_T; *middle,* flow; *bottom,* airway pressure waveform. *V_T,* Tidal volume.

Use of a rectangular pressure waveform opens alveoli earlier in the inspiratory phase during PC-CMV and results in a higher mean airway pressure than VC-CMV with a rectangular flow waveform, allowing more time for oxygenation to occur.[34] However, in PC-CMV, inspiratory flow is not a parameter set by the clinician. It is variable and dependent on patient effort and lung mechanics, improving patient comfort and patient-ventilator synchrony. However, as lung mechanics or patient effort or both change, volume delivery (V_T and minute ventilation) changes.

Because V_T is not directly controlled, the driving pressure (P_{plat} – PEEP) is the primary parameter used to alter the breath size and CO_2 tensions. Typically, PIP is adjusted to provide the patient with a V_T within the desired range.[35] As with VC-CMV, the mandatory breath rate set by the clinician depends on the presence of ventilatory muscle activity and the severity of lung disease. When higher mandatory breath rates are needed (>30 breaths/min), it is essential for the clinician to provide a sufficient expiratory time and prevent air trapping.

As long as lung mechanics and patient effort remain constant, the volume and peak flow delivered to the patient remain unchanged.[36] When patient effort decreases, or compliance decreases, or resistance increases, less volume is delivered for the preset pressure for each breath. Conversely, improvements in patient effort and mechanics can dramatically increase the volume delivery to the patient in this mode. Close V_T monitoring is required to avoid ventilator-induced hyperventilation or hypoventilation and ventilator-induced lung injury.

The patient's cardiac index and O_2 consumption should be closely monitored as well. Higher mean airway pressures may impair cardiac output. In addition, PC-CMV with IRV can lead to the development of auto-PEEP, which can impair venous return, compromise O_2 delivery to the tissues, and result in marked air trapping.[37]

Pressure-Controlled Inverse Ratio Ventilation

PC-CMV may be used to accomplish pressure-controlled inverse ratio ventilation (PC-IRV), by increasing the inspiratory time directly or by increasing the I:E ratio to the desired value. PC-IRV is defined as pressure-controlled ventilation with an I:E ratio greater than 1:1 (Fig. 47.10). Although some studies have shown improvement in oxygenation with PC-IRV versus CMV with PEEP, others have shown concurrent decreases in cardiac output.[31,38] In general, if applied PEEP in normal ratio ventilation is equal to total PEEP (applied and intrinsic PEEP) in PC-IRV, the oxygenation benefits are equivalent without the marked depression in cardiac output.

Intermittent Mandatory Ventilation

As a partial support mode, IMV allows or requires the patient to sustain significant WOB. The level of mechanical support needed depends on the specific physiologic process causing the need for mechanical ventilation, presence or degree of ventilatory muscle weakness, and presence and severity of lung disease. In this mode, mandatory breaths are delivered at a set rate. Between the mandatory breaths, the patient can breathe spontaneously at his or her own V_T and rate (Fig. 47.11). Breaths can occur separately (e.g., IMV); breaths can be superimposed on each other (e.g., spontaneous breaths superimposed on mandatory breaths, as in bilevel positive airway pressure [bilevel PAP] or airway pressure release ventilation [APRV]); or mandatory breaths can be superimposed on spontaneous breaths, as in

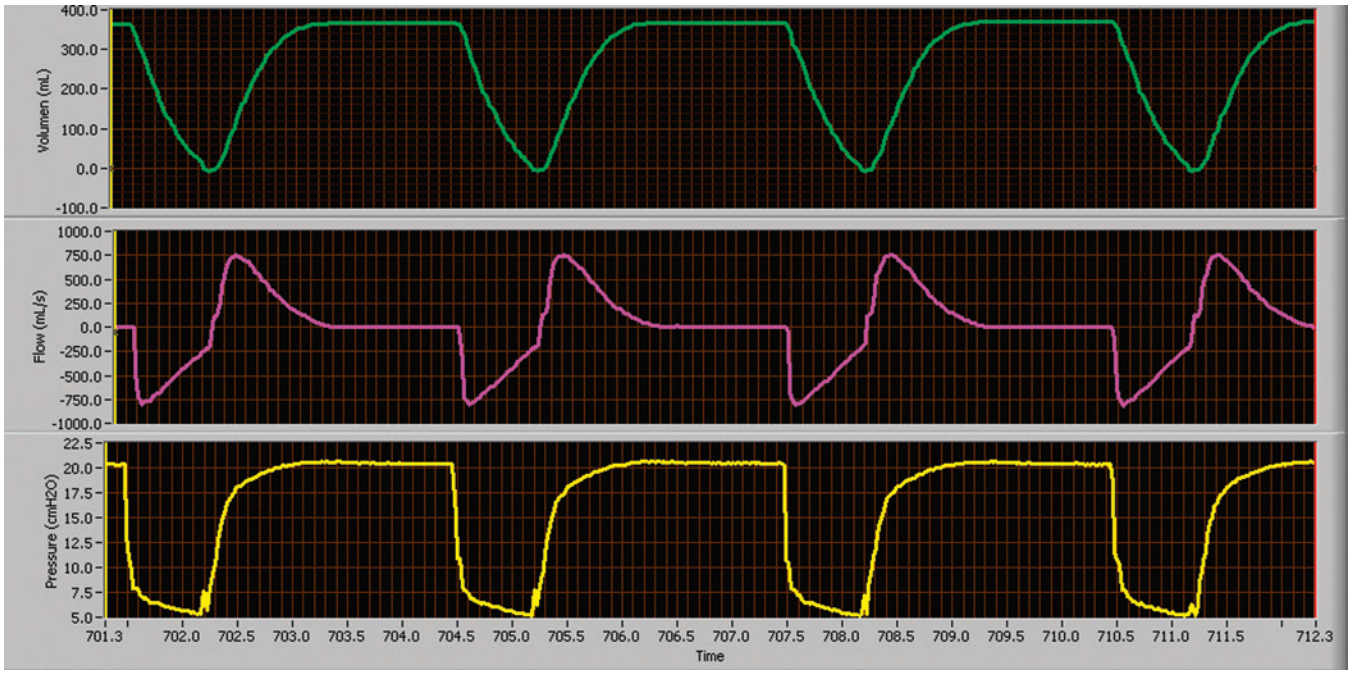

Fig. 47.10 Pressure-Controlled Inverse Ratio Ventilation. The flow waveform for any breath does not return to baseline before the next breath, resulting in auto–positive end-expiratory pressure and an increase in mean airway pressure. *Top,* V_T; *middle,* flow; *bottom,* airway pressure waveform. *V_T,* Tidal volume.

MINI CLINI

Using Pressure-Controlled Ventilation

Problem

The RT is caring for a 20-year-old patient with ARDS. The patient has no respiratory effort. Current ventilator settings are as follows:
Mode: VC-CMV
V_T: 400 mL
Frequency: 25 breaths/min
PEEP: 14 cm H_2O
FiO_2: 1
PIPs monitored on the ventilator: 35–40 cm H_2O
Mean airway pressure: 20–22 cm H_2O
Plateau pressure: 27 cm H_2O

An arterial blood gas is obtained, which reveals pH 7.28, PCO_2 41 mm Hg, and PO_2 50 mm Hg. The physician would like to employ pressure-controlled ventilation. What are the appropriate initial settings in PC-CMV mode to maintain the current minute ventilation?

Solution

Initial ventilator setting would be as follows:
Ventilator frequency, PEEP, and FiO_2: the same
Frequency: 25 breaths/min
PEEP: 14 cm H_2O
FiO_2: 1

To keep the minute ventilation constant, the RT needs to set the PIP high enough to deliver the same V_T as in volume control (400 mL).

1. Calculate the patient's respiratory system compliance:

$$\begin{aligned}\text{Compliance} &= V_T/P_{plat} - \text{total PEEP}\\ &= 400\,\text{mL}/27\,\text{cm}\,H_2O - 14\,\text{cm}\,H_2O\\ &= 31\,\text{mL/cm}\,H_2O\end{aligned}$$

2. Calculate the pressure limit in PC-CMV mode to achieve the target V_T. Because the pressure limit is measured relative to PEEP on this ventilator, the equation is:

$$\begin{aligned}\text{Ventilating pressure} &= V_T/\text{Compliance}\\ &= 400\,\text{mL}/31\,\text{mL/cm}\,H_2O\\ &= 13\,\text{cm}\,H_2O\\ \text{PIP in PC} &= \text{ventilating pressure} + \text{PEEP}\\ &\text{PC set } 13\,\text{cm}\,H_2O + \text{peep } 14\,\text{cm}\,H_2O\\ &\text{or } 27\,\text{cm}\,H_2O\end{aligned}$$

A shortcut is to realize that the required pressure limit is the P_{plat} on VC-CMV. The PIP (relative to atmospheric pressure) is 27 cm H_2O.

high-frequency ventilation administered during spontaneous breathing. Spontaneous breaths may be assisted (e.g., PSV) (Fig. 47.12) or unassisted.

When the mandatory breath is patient-triggered, modern day ventilators deliver the mandatory breath in synchrony with the patient's inspiratory effort. If no spontaneous efforts occur, the ventilator delivers a time-triggered breath. Because spontaneous breaths decrease pleural pressure, ventilatory support with IMV usually results in a lower mean intrathoracic pressure than CMV, which can result in a higher cardiac output.[39]

When used to wean a patient from mechanical ventilation, the intent of IMV is to provide respiratory muscle rest during the mandatory breaths and exercise during spontaneous breaths. However, studies have shown that IMV increases the WOB,

MINI CLINI

Determining Appropriate Ventilator Rate

Problem

A 36-year-old woman with traumatic brain injury was intubated in the emergency department with a 7-mm endotracheal tube and transferred to the RT in the neurointensive care unit. She is paralyzed and sedated. Her current ventilator settings are as follows:

Mode: VC-CMV

V_T: 405 mL

Frequency: 15 breaths/min

FiO_2: 0.5

The pulse oximeter displays 97%, and end-tidal CO_2 monitor is reading 49. The patient's weight is estimated at 45 kg. End-tidal CO_2 is stable and 4 mm Hg higher than $PaCO_2$. The clinical goal is to minimize ICP. Because intracranial blood flow is inversely proportional to $PaCO_2$, ventilation should be increased to maintain $PaCO_2$ at approximately 35–40 mm Hg. The RT needs to make appropriate ventilator changes to achieve the target $PaCO_2$.

Discussion

The current V_T is already large at 8 mL/kg. The increase in ventilation must be achieved by increasing frequency. Because the patient is paralyzed, the ventilation level is controlled by the set frequency, and $PaCO_2$ is predictable. The new frequency required is calculated using the following equation:

$$\text{Required frequency} = \text{Current frequency} \times \text{Current } PaCO_2 / \text{Desired } PaCO_2$$

$$\text{Required frequency} = 15 \text{ breaths/min} \times 49 \text{ mm Hg}/35 \text{ mm Hg} = 21 \text{ breaths/min}$$

asynchrony and weaning prolongs the duration of mechanical ventilation compared with PSV and spontaneous breathing trials.[40,41] In general at this stage in the development of ventilatory support we would recommend against the routine use of SIMV.

Volume-Controlled Intermittent Mandatory Ventilation

Volume-controlled intermittent mandatory ventilation (VC-IMV) has been advocated for patients with relatively normal lung function recovering from sedation or rapidly reversing respiratory failure.[42,43] However, the use of IMV has greatly decreased over the years in favor of VC-CMV, PC-CMV, and PSV, and there are no specific situations in adults where IMV would be the optimal mode.

Pressure-Controlled Intermittent Mandatory Ventilation

PC-IMV has been traditionally associated with mechanical ventilation of infants not only because of their oxygenation problems but also because traditionally it had been difficult to control V_T at such small values.[44,45]

Liberation from this mode involves the gradual reduction of the PIP and the mandatory breath rate. As lung compliance improves, adjustments in PIP are necessary to prevent overdistention of the lung. Adjustments in PIP and set mandatory breath rate are critical to prevent hyperventilation.

Airway Pressure Release Ventilation

A mode related to both PC-IRV and PC-IMV is APRV, in which the patient breathes spontaneously throughout periods of high and low applied CPAP (Fig. 47.13).[46] APRV intermittently

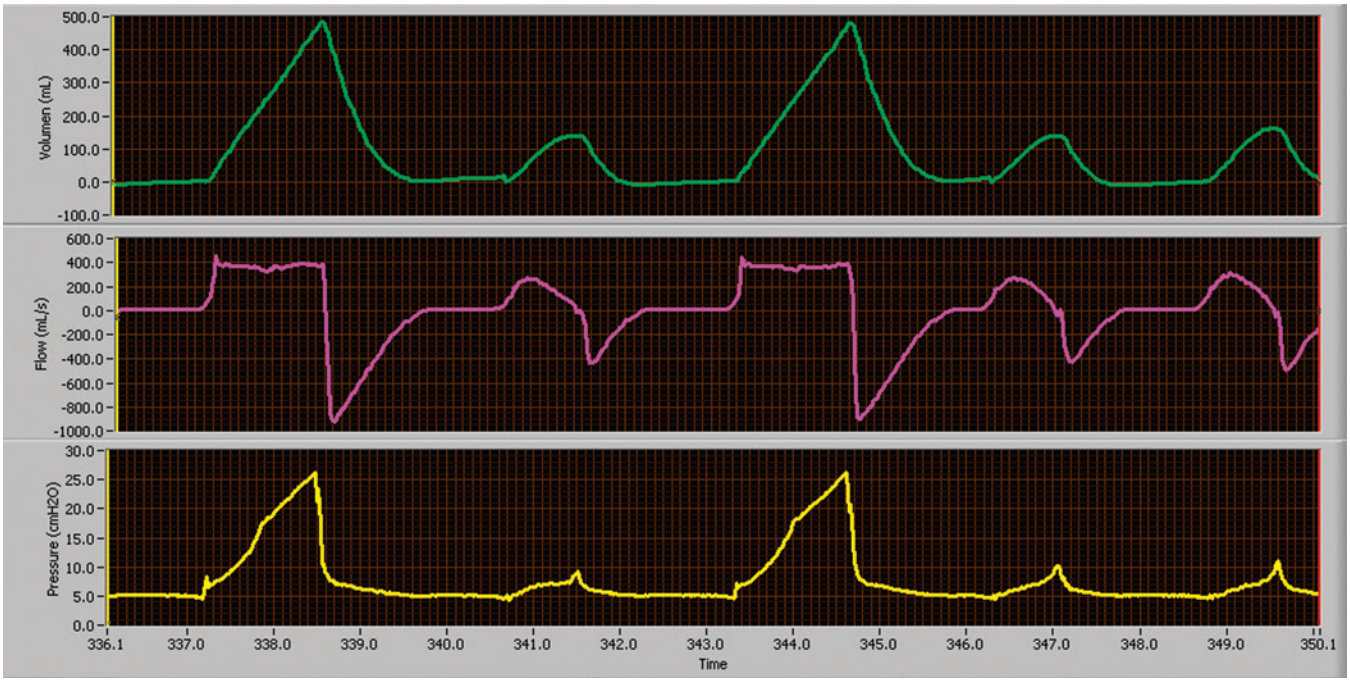

Fig. 47.11 Volume-Controlled Synchronized Intermittent Mandatory Ventilation + Continuous Positive Airway Pressure. *Top,* V_T; *middle,* flow; *bottom,* airway pressure waveform. V_T, Tidal volume.

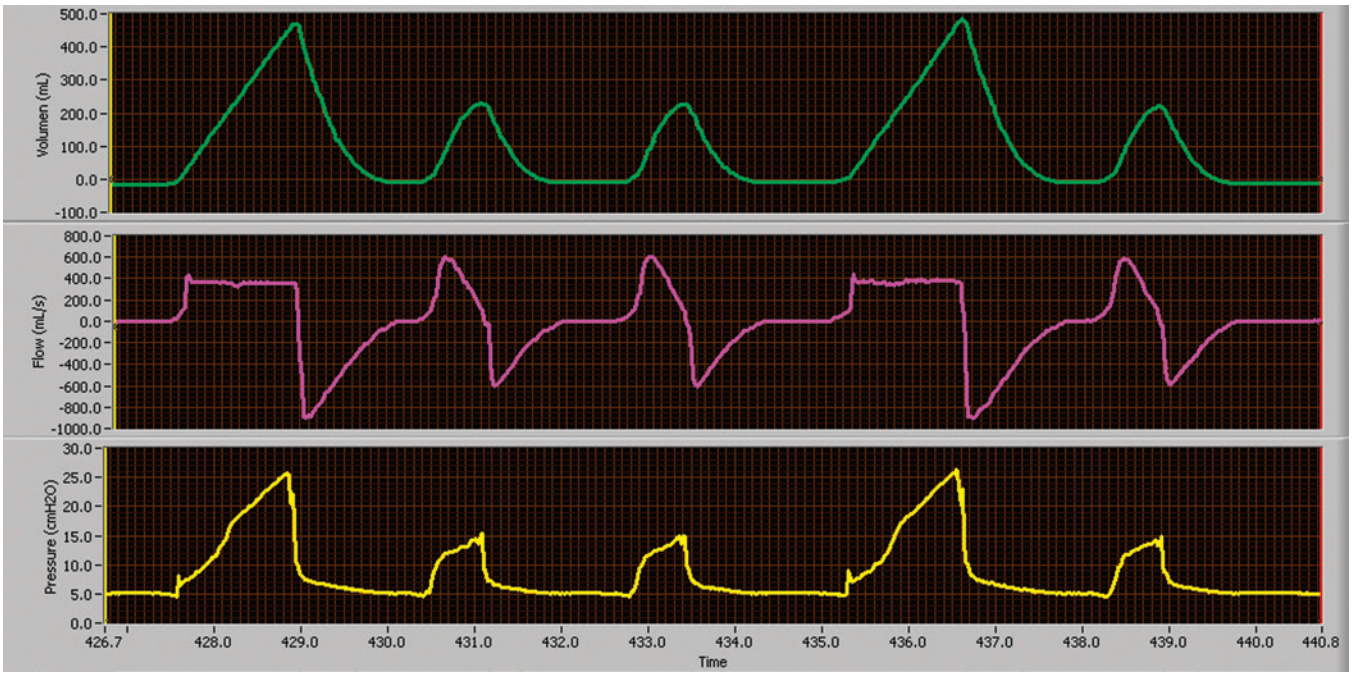

Fig. 47.12 Volume-Controlled Synchronized Intermittent Mandatory Ventilation + Pressure Support Ventilation (PSV). The addition of PSV to the spontaneous breaths increases spontaneous tidal volume. *Top,* V_T; *middle,* flow; *bottom,* airway pressure waveform. V_T, Tidal volume.

Fig. 47.13 Airway Pressure Release Ventilation (APRV). In APRV, the patient is able to breathe spontaneously throughout the total cycle time. *Top,* V_T; *middle,* flow; *bottom,* airway pressure waveform. V_T, Tidal volume.

decreases or "releases" the airway pressure from an upper pressure (P_{high}) or CPAP level to a lower pressure (P_{low}) or CPAP level. The pressure release usually lasts approximately 0.2 to 1.5 seconds depending on whether or not air trapping is desired. In Fig. 47.13, inspiratory time is longer than expiratory time, and spontaneous breaths are superimposed on this mandatory pattern of pressurization and release. Spontaneous breaths may be supplemented by PSV. This is a feature of APRV available on some ventilators, where APRV is referred to as *bilevel ventilation.* In APRV, the I:E ratio is usually greater than 1 : 1, which is similar to PC-IRV, but APRV allows spontaneous breathing throughout inspiratory and expiration.[47]

APRV also provides ventilation and oxygenation without adversely affecting hemodynamic values because of the periodic reductions in intrathoracic pressure during the spontaneous breaths. In addition, peak airway pressure during APRV may be less than with VC-IRV for comparable oxygenation and ventilation.[48] APRV compared with conventional volume-controlled or pressure-controlled SIMV showed that with APRV there was a decrease in peak airway pressures, improved hemodynamics, and a decreased need for vasopressor and inotropic support.[49] However, the cost of these potential benefits is patient effort; WOB is markedly increased and P_{TP} is excessive, potentially inducing lung injury during APRV.[47] There are no data to indicate a better outcome with APRV than with other approaches to ventilatory support when a similar approach to managing oxygenation is used. Specific indications for APRV are unclear. Recent data imply that APRV results in greater mortality in pediatric patients than conventional ventilatory modes of ventilation,

Continuous Spontaneous Ventilation

Spontaneous breath modes include modes in which all breaths are initiated and ended by the patient. The level of support these modes of ventilation provide determines the amount of WOB the patient ultimately assumes. CPAP, PSV,[50] automatic tube compensation (ATC), proportional assist ventilation (PAV), and neurally adjusted ventilatory assist (NAVA) are continuous spontaneous breath modes.[51]

Continuous Positive Airway Pressure

CPAP is spontaneous breathing at an elevated baseline pressure (Fig. 47.14). Breaths are patient-triggered and cycled.[52,53] V_T depends on patient effort and lung mechanics. CPAP increases P_{alv} and maintains alveoli open. In contrast to NPV and PPV, airway pressure with CPAP is theoretically constant (baseline pressure ±2 cm H_2O) throughout the respiratory cycle. Because airway pressure does not change, CPAP does not provide ventilation. For gas to move into the lungs during CPAP, the patient must create a spontaneous P_{TA} gradient. Although NPV and PPV produce the pressure gradients needed for gas flow into the lungs, CPAP maintains alveoli at greater inflation volume, restoring FRC. An important physiologic feature of CPAP is that as alveoli are maintained open, FiO_2 needed to maintain adequate PaO_2 may decrease. Oxygenation becomes more efficient at any given FiO_2, as measured by PaO_2/FiO_2 ratio and shunt fraction. The potential side effects associated with PPV also exist for CPAP but usually to a lesser degree.

Pressure Support Ventilation

PSV is a form of PC-CSV that assists the patient's inspiratory efforts (Fig. 47.15). At very low levels of support, this mode unloads WOB the ventilator circuitry imposes on the respiratory muscles.[54] If the level of support is maximized, the ventilator may assume all WOB.[55] The result of high levels of support is a reduction in the respiratory rate, reduction in respiratory muscle activity, reduction in O_2 consumption, and improvement or stabilization of spontaneous V_T.[56,57] However, the positive attributes of this mode of ventilation can be negated if ventilator parameters are not properly set. The ventilator must be able to detect spontaneous patient effort. It is critical for the clinician to adjust the trigger sensitivity correctly. Of equal importance is the clinician-set rise time, the time required for the ventilator to reach the inspiratory pressure limit, and termination criteria, the minimal flow resulting in cycling to exhalation (see Chapter 48). Ventilator graphics are often helpful when adjusting these parameters and optimizing patient–ventilator synchrony.

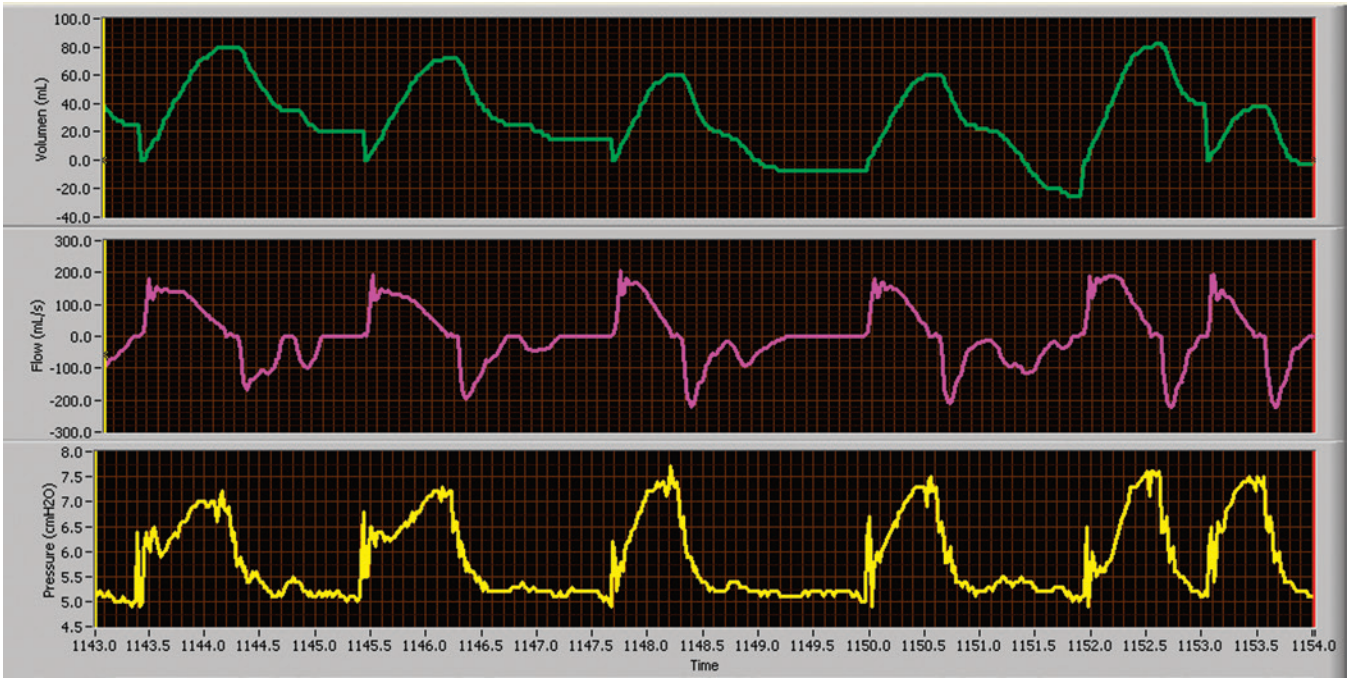

Fig. 47.14 Continuous Positive Airway Pressure. *Top,* V_T scalar; *middle,* flow scalar; *bottom,* airway pressure scalar. *V_T,* Tidal volume.

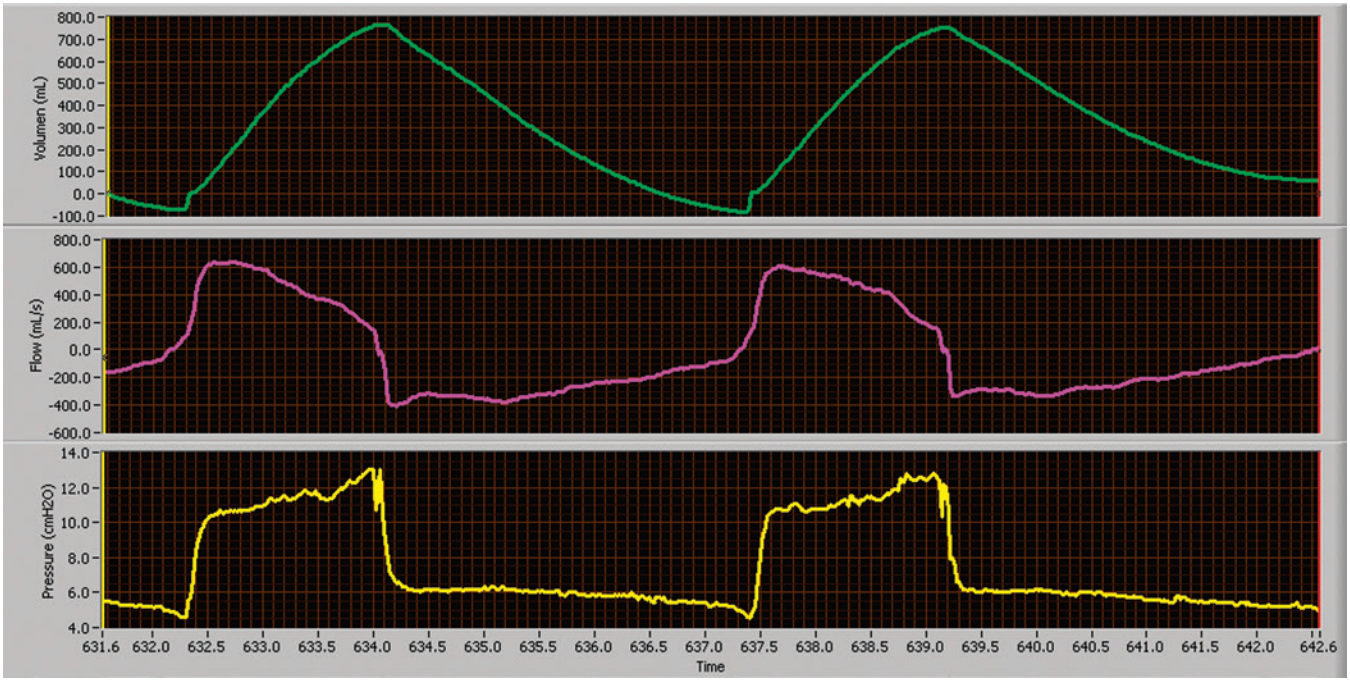

Fig. 47.15 Pressure Support Ventilation. *Top,* V_T; *middle,* flow; *bottom,* airway pressure waveform. V_T, Tidal volume.

Regardless of the level of support provided, the patient has primary control over the breath rate and inspiratory time and flow rate delivered during this mode of assisted ventilation. The V_T resulting from a PSV breath depends on the preset pressure level, patient effort, and mechanical forces opposing ventilation (lung–chest wall compliance and R_{aw}). Of all of the classic modes of ventilation, PSV exerts the least control over the patient's ventilatory pattern and as a result should improve patient-ventilator synchrony. Since the first description of PSV in 1982, it has been used either to overcome the imposed resistance associated with the artificial airway or to provide ventilatory support with minimal control.[58] PSV is useful in any patient with an intact ventilatory drive and a stable ventilatory demand.

Bilevel PAP (BiPAP; Respironics, Inc., Murrysville, PA) is simply PSV with PEEP applied noninvasively.[59] With bilevel PAP, inspiratory positive airway pressure (or PSV) and PEEP are set. The duration of inspiratory positive airway pressure and expiratory positive airway pressure can be independently adjusted to set the I:E ratio. Although it was originally developed to enhance the capabilities of home CPAP systems used for management of obstructive sleep apnea, bilevel PAP has been successfully used in the home and the hospital for noninvasive ventilatory support of patients with acute and chronic respiratory failure.[60] (See Chapter 50 for details.)

Example. An example of the use of PC-CSV is noninvasive PSV and PEEP in the management of a patient with COPD in an acute exacerbation. As described in detail in Chapter 50, noninvasive ventilation has been shown in this setting to decrease the frequency of intubation, length of mechanical ventilation, development of ventilator-associated pneumonia, and patient mortality.

Proportional Assist Ventilation

PAV is based on both the mechanics of the total respiratory system and the resistive properties of the artificial airway; that is, the ventilator delivers a pressure assist in proportion to the patient's desired V_T (volume assist) and to the patient's instantaneous inspired flow (flow assist). The response of these two aspects of ventilatory assistance is automatically adjusted to meet changes in the patient's ongoing ventilatory demand. This algorithm is based on the law of motion as it applies to the respiratory system:

$$P_{musc} + P_{appl} = (Volume \times E) + (Flow \times R)$$

where P_{musc} is pressure generated by the respiratory muscles, P_{appl} is pressure applied by the ventilator, and E and R are elastic and resistance properties of the respiratory system. Assuming that E and R are linear during inspiration, the instantaneous flow and volume to be delivered are proportional to the resistive and elastic WOB. The ventilator continuously measures the instantaneous flow and volume and periodically measures the E and R. Using this information, the ventilator software adjusts gas delivery by estimating P_{musc} and assisting P_{musc} in a proportional manner, the percentage of support set by the clinician. The patient is the determinant of the ventilatory pattern. Patients are given the freedom to select a ventilatory pattern that is rapid and shallow or slow and deep. If the patient desires a small V_T, a low level of pressure is applied, and if a large V_T is desired, a high pressure is applied. The ventilator does not force any control variable except the unloading of E and R in a proportional manner. See Chapter 46 for details on operation of PAV.

Numerous studies have evaluated the effect of PAV during noninvasive PPV.[61–65] Most of these comparisons were between

PAV and PSV,[61,65] and in almost all of these comparisons the patients evaluated had chronic respiratory failure and were in an acute exacerbation. Patients managed with PAV had a lower refusal rate, had a more rapid reduction in respiratory rate, and developed fewer complications.[63,64] In these studies, gas exchange and respiratory pattern did not differ between PSV and PAV, but the patients ventilated with PAV were more comfortable. PAV has also been shown to be essentially equivalent to PSV in stable patients with chronic ventilatory failure[62] and in patients with acute cardiogenic pulmonary edema.[65]

PAV has been most widely studied during invasive mechanical ventilation.[66–68] As with the evaluation of PAV in other settings, most of the comparisons focused on the physiologic response observed when PSV is changed to PAV. In general, during invasive ventilation, the change from PSV to PAV results in lower V_T, more rapid respiratory rate, lower peak airway pressure, and lower mean airway pressure without significant changes in gas exchange or hemodynamics.[69–71] In a randomized comparison of PAV versus PSV each for a 48-hour period in a series of critically ill patients,[68] the percentage of patients' failing the transition to PAV or PSV differed, 11% failing PAV versus 22% failing PSV. In addition, the proportion of patients developing asynchrony was greater with PSV versus PAV. The current data on PAV indicate it can sustain the same patients as PSV—patients who can breathe spontaneously and manage their ventilator drive normally.

Neurally Adjusted Ventilatory Assist

From a conceptual perspective, NAVA is essentially the same as PAV except that PAV responds to changes in airway pressure and flow, whereas NAVA responds to changes in diaphragmatic electromyograph (EMG) activity. However, for NAVA to function properly, a specially designed nasogastric catheter with a 10-cm length of EMG electrodes must be in place. Both PAV and NAVA respond to patient effort providing ventilatory support in a proportional manner. The clinician does not set pressure, volume, flow, or time in either mode. The only parameter set is the proportion of effort unloaded by the ventilator; in NAVA, this is set as the number of cm H_2O pressure applied per microvolt of inspiratory diaphragmatic EMG activity.

NAVA responds similarly to PAV; when compared with pressure support, NAVA results in low airway pressures, smaller tidal volumes, more rapid rates, and increased patient–ventilator synchrony.[72,73] PEEP titration also affects baseline diaphragmatic EMG activity. As PEEP is increased, EMG activity decreases. Minimal EMG activity seems to correspond to optimal PEEP level.[74]

NAVA application in neonates results in similar outcomes as observed in adults.[75,76] After the change to NAVA, V_T tends to decrease, respiratory rate to increase, and peak diaphragmatic EMG activity to decrease. In addition, despite the open ventilating system (uncuffed artificial airway), triggering and cycling are still primarily neurally activated.[75,76]

The most important advantage of PAV and NAVA over traditional modes of ventilation is improved synchrony. The specific indications for PAV and NAVA are not fully established; however, both can be reasonably used in any patient with an intact ventilatory drive. The primary indication would be a patient with a significant level of asynchrony.

Automatic Tube Compensation

ATC is similar to the flow assist aspect of PAV but considers only the resistance of the endotracheal tube.[77] ATC is an adjunct that automatically adjusts the airway pressure to compensate for endotracheal tube resistance to gas flow by maintaining tracheal pressure constant at the baseline level.[77] The goal is to eliminate WOB imposed by the endotracheal tube. In ATC, the RT inputs into the ventilator the type and size of artificial airway (endotracheal tube or tracheostomy tube) and the percentage compensation desired (10%–100%). The ventilator continuously measures flow and calculates the amount of pressure needed to overcome the resistance of the airway (pressure = resistance × flow). As a result, the greater the inspiratory demand, the greater the pressure applied. Pressure varies throughout the breath.

ATC may be applied during inspiration (positive airway pressure) or during both inspiration and expiration (negative airway pressure). However, expiratory ATC may result in early airway closure and increased air trapping. ATC has been referred to as *electronic extubation,* meaning that if the airway pressure is low during inspiration (5 to 7 cm H_2O), it is simply overcoming the resistance of the endotracheal tube with a normal inspiratory effort.[78] Consequently, many clinicians consider this an indication that spontaneous ventilation can be maintained without ventilatory support and the patient should be considered for extubation. Although in theory the use of ATC to wean patients appears ideal, no data to date have indicated that ATC weans patients faster than spontaneous breathing trials.

Adaptive Modes and Dual Control

The first adaptive control/dual control mode was described by Amato and colleagues.[79] Their major finding was that the ventilatory workload imposed on the inspiratory muscles during volume-assured PSV was significantly reduced using dual control. In this mode, pressure support is combined with volume control. However, this benefit was due to the fact that inspiration started out in pressure support and stayed there unless the V_T target was not met. The improvement was mostly a result of the improved synchrony between the patient and the machine. These investigators did not show a specific benefit of the actual dual nature of the mode (i.e., switching from pressure support to volume control), and no evidence has been published in the literature since then supporting this mode. Anecdotal reports indicate that it is difficult to adjust pressure, volume, and flow settings to make the mode work properly, in particular, if the mechanical properties of the patient's respiratory system are changing rapidly.

Pressure-regulated volume control (PRVC), or PC-CMV, and *volume support (VS)*, or PC-CSV, are examples of adaptive control/dual control modes. PRVC is based on pressure-controlled ventilation, and VS is based on PSV. In both modes, the ventilator attempts to maintain a target V_T by adjusting the pressure level based on the previous breath. When a clinician places a patient in PRVC, a target V_T, minimal breath rate, and maximum (i.e., alarm) pressure limit are clinician set, whereas for a patient placed

in VS, a target V_T and maximum (i.e., alarm) pressure limit are clinician set. In both modes, once the patient is connected to the ventilator, the patient–ventilator interaction that occurs in the first few breaths is critical. Initially, the ventilator calculates total system compliance. On the succeeding three or four breaths, the ventilator monitors the peak airway pressures and expiratory V_T. The ventilator determines the pressure level necessary to deliver the clinician-set "target" V_T, for the given total system compliance.

The patient–ventilator interaction is monitored on a breath-by-breath basis. If the patient's lung compliance improves (or patient effort increases), the ventilator delivers subsequent breaths at a lower pressure level to maintain the target V_T. This adjustment by the ventilator reduces the risk of alveolar overdistention and volutrauma. Conversely, the ventilator responds to worsening pulmonary compliance (or decreasing patient effort) by increasing the pressure limit until the V_T is achieved. The ventilator makes pressure level changes in small increments, 1 to 3 cm H_2O per breath, and does not exceed the maximum pressure limit set by the clinician. These automatic ventilator responses to changes in a patient's lung mechanics minimize the risk of ventilator-induced hyperventilation or hypoventilation. The desired outcome is a stable or consistent minute ventilation and enhanced patient comfort. However, the major problem with these modes is that the ventilator cannot distinguish between the patient improving and heightened levels of ventilator demand. If patient demand results in a larger V_T, the ventilator ventilates less.[80]

In most ventilators, pressure can be decreased all the way to the PEEP level. This situation can lead to ventilatory failure.[80] Both RPVC and VS should be used very cautiously in all patients with a normal or increased ventilatory demand. Randomized comparison between these modes and other, more traditional, modes failed to show any outcome benefit.[81,82]

Example. PRVC or VS has been used in infants with respiratory distress syndrome.[83] Rapidly changing pulmonary mechanics from surfactant administration are associated with complications such as pulmonary air leaks, intraventricular hemorrhage, and bronchopulmonary dysplasia. These adaptive modes respond to changes in a patient's lung mechanics and may reduce the incidence of these common complications.

Adaptive support ventilation (ASV), or PC-IMV, is an example of optimal control in adaptive ventilation. ASV is a pressure-targeted mode that optimizes the relationship between V_T and respiratory frequency based on lung mechanics as predicted by Otis.[84] ASV uses a pressure ventilation format establishing a ventilatory pattern that minimizes WOB and auto-PEEP, while limiting peak airway pressure. In this regard, ASV is similar to PC-CMV and PRVC in its gas delivery format. It differs from PC-CMV and PRVC by its additional algorithmic control of the ventilatory pattern.[85] ASV automatically determines the V_T and respiratory rate that best maintains the peak pressure below the target level.[86] The clinician inputs the patient's ideal body weight, high pressure limit, PEEP, FiO_2, inspiratory rise time, flow cycle percentage, and percentage of predicted minute volume desired. The ventilator periodically measures dynamic compliance and the respiratory time constant and determines the desired mandatory rate. Ideal body weight is used by the ventilator to calculate the minute volume, which is divided by the rate for determination of V_T.[87] The newest adaption to ASV is referred to as Intellivent. With this adaption the ventilator operates the same as with ASV but in addition has the ARDSnet PEEP/FIO_2 tables programed into the ventilator algorithm. Thus, as the patient's SpO_2 changes, PEEP and FIO_2 are adjusted as dictated by the ARDSnet protocols.

When ASV is compared with VC-IMV, ASV decreases inspiratory load and improves patient–ventilator synchrony.[88] Others have shown that ASV resulted in a shorter duration of intubation than VC-IMV in postoperative cardiac patients with no complications.[89] More recently, Belliato and colleagues[90] comparing PC-IMV (optimal) to ASV showed that the ventilator was able to differentiate between patient types and select appropriate settings.[91] Using a lung model, Sulemanji and coworkers[92] determined that ASV could provide better lung protection than a fixed V_T of 6 mL/kg ideal body weight. ASV control has been adapted to respond to end-tidal CO_2 levels.[92] This new adaptation allows specific algorithms to be selected based on patient diagnosis: ARDS, COPD, brain injury, or healthy lung. This mode is the most sophisticated of the closed loop control modes available on ICU ventilators at the present time. However, additional study is needed to determine fully the type of patient in whom ASV is most useful. Current data would indicate ASV works very well in patients under controlled approaches to ventilatory support, but additional data in spontaneously ventilated patients are needed before it can be recommended in these patients.

RULE OF THUMB Most patients requiring ventilatory support can be effectively ventilated with volume assist/control, pressure assist/control, and PSV modes.

Patient Positioning to Optimize Oxygenation and Ventilation

Patients receiving mechanical ventilation are turned frequently, usually at least every 2 hours, unless turning is contraindicated. Kinetic beds continually rotate patients and are designed to help prevent atelectasis, hypoxemia, secretion retention, and pressure ulcers. When patients are kept immobile, pooling of secretions in dependent lung zones can promote nosocomial pneumonia, and shrinking of dependent alveoli leads to decreases in ventilation and hypoxemia. However, the use of rotating kinetic beds is controversial in the prevention of nosocomial pneumonia.[93] No data are available to indicate that these very expensive beds improve patient outcome.

Patients with unilateral lung disease benefit from being placed in positions that promote matching of ventilation and perfusion. In unilateral lung disease, only one lung is affected by atelectasis, consolidation, or pneumonia. If the affected lung is placed in the dependent position, blood flow follows. The resultant poor $\dot{V}/\dot{Q}$ ratio in the affected lung contributes to venous admixture and hypoxemia. However, if the patient is rotated so that the good lung is in the dependent position, these relationships are reversed. With the good lung down, blood flows to well-ventilated

alveoli, and $\dot{V}/\dot{Q}$ matching and arterial blood gas values improve. An added benefit of this maneuver is that the affected lung is placed in a postural drainage position, which promotes gravity drainage of retained secretions so that they can be removed.

Prone Positioning

A similar phenomenon has been described in ARDS. In a supine patient with ARDS, alveoli in the bases and posterior segments become atelectatic. Shunt increases, and the patient requires a high FiO_2 and PEEP for adequate oxygenation. If the patient is rotated into the prone position, several mechanisms have been proposed to improve oxygenation.[94] Blood flow is redistributed to areas that are better ventilated. This redistribution improves $\dot{V}/\dot{Q}$ relationships. Prone positioning removes the weight of the heart from its position over the lungs while the patient is supine. Pleural pressure in the now nondependent collapsed lung becomes more negative, improving alveolar recruitment. In addition, the stomach no longer lies over the dependent basilar posterior segments of the lower lobes.

A number of studies have demonstrated some benefit of prone positioning.[95–98] However, several persons are needed to "flip" the patient while ensuring monitoring lines and catheters are not disrupted and the patient is not inadvertently extubated. Wound dehiscence, facial or upper chest wall necrosis despite extensive padding, cardiac arrest immediately after movement to the prone position, dependent edema of the face, and corneal abrasion have been reported.[96] A recent meta-analysis of existing randomized controlled trials indicated no outcome benefit from prone positioning in patients with ARDS.[97] However, this meta-analysis also found that patients with PaO_2/FiO_2 less than 100 mm Hg were the group most likely to benefit from prone positioning. A subsequent randomized controlled trial showed the same results.[98] Considering the complications associated with prone positioning, only patients with very severe hypoxemia (PaO_2/FiO_2 <100 mm Hg) should be placed prone.

RULE OF THUMB Patients who have unilateral or dependent consolidation or atelectasis and severe hypoxemia may benefit from positioning with the affected lung or segments in the nondependent position to promote improvement in $\dot{V}/\dot{Q}$ relationships. Prone positioning is indicated only if the PaO_2/FiO_2 is less than 100 mm Hg. When positioning the patient, great care should be taken to avoid the hazards associated with prone positioning.

CARDIOVASCULAR EFFECTS OF POSITIVE PRESSURE MECHANICAL VENTILATION

Thoracic Pump and Venous Return During Spontaneous and Mechanical Ventilation

The lungs and heart have a close functional relationship, and impaired performance of one affects the other. For this reason, the RT must fully understand what happens to cardiovascular function when a patient receives ventilatory support.

Early studies of the effect of PPV on the cardiovascular system showed an early, small, and transient increase in cardiac output that was followed almost immediately by a marked reduction in left ventricular outflow. In general, the reduced cardiac output in these cases was directly related to the amount of pressure applied. More specifically, the decrease in left ventricular output corresponded to the increase in pleural pressure that occurred with PPV. Fig. 47.16 compares the effects of spontaneous inspiration with the effect observed during PPV. Negative pleural pressure during spontaneous inspiration normally enhances venous return, increases right atrial filling, and improves pulmonary blood flow (see Fig. 47.16A). In combination, these factors increase left atrial and left ventricular filling and left ventricular stroke volume.

However, during PPV, pleural pressure becomes positive (see Fig. 47.16B). Positive pleural pressure compresses the intrathoracic veins and increases central venous and right atrial filling

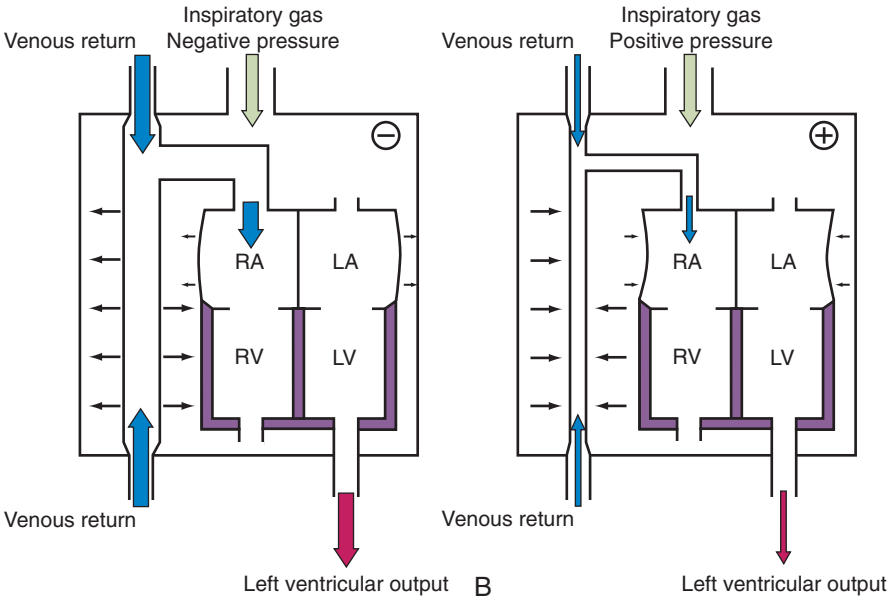

Fig. 47.16 Relationship between pleural pressure and cardiac output in spontaneous (A) and positive pressure (B) breathing. *LA,* Left atrium; *LV,* left ventricle; *RA,* right atrium; *RV,* right ventricle.

pressures. As these pressures increase, venous return to the heart is impeded, and right ventricular preload and stroke volume decrease, as does pulmonary blood flow. Blood already in the pulmonary circulation is initially displaced into the left side of the heart and causes a transient increase in filling pressure and output. This initial effect lasts for only a few heartbeats. If positive pressure is continued, flow both to and from the left side of the heart decreases.

The high impedance encountered by blood returning to the right heart causes venous pooling, mainly in the capacitance vessels of the abdominal viscera. This process effectively removes a large volume of blood from the circulation, which can further impair left ventricular output. These interactions are magnified when pleural pressure is increased further or circulating blood volume is low.[99] The venous impedance caused by PPV is not limited to blood flow coming from the abdomen. An increase in central venous pressure can restrict return flow from the brain. Impedance to venous return from the brain can increase ICP and reduce cerebral perfusion pressure (CPP). In combination with a decrease in left ventricular output, an increase in ICP during PPV can significantly impair cerebral perfusion and possibly result in cerebral ischemia and cerebral hypoxia.

In healthy individuals, the effects of PPV on cerebral blood flow (CBF) are minimized by autoregulatory mechanisms that maintain cranial perfusion pressures within a narrow range. However, patients with preexisting cerebrovascular problems and patients who already have an elevation in ICP may be at risk of decreased cerebral perfusion with PPV. Examples include neurosurgical patients and patients with head injuries, intracranial tumors, or cerebral edema from any cause. ICP monitoring may be necessary in the care of these patients.

Compensation in Healthy Persons

A decrease in cardiac output or blood pressure is rare among individuals with a normal cardiopulmonary system who are receiving mechanical ventilation. Compensatory mechanisms used to counter the decrease in stroke volume include increased heart rate, increase in systemic vascular and peripheral venous resistance, and shunting of blood away from the kidneys and lower extremities, which results in a consistent blood pressure. Because these compensatory mechanisms function by reflexes, the reflexes must be intact. Factors that block or blunt these vascular reflexes include sympathetic blockade, spinal anesthesia, spinal cord transection, and polyneuritis.

Pulmonary Vascular Pressure, Blood Flow, and Pulmonary Vascular Resistance

In patients with a normal cardiopulmonary system who are receiving mechanical ventilation, there is no significant increase in pulmonary vascular pressure or pulmonary vascular resistance and no decrease in pulmonary blood flow. However, when alveoli are distended by increased V_T or high PEEP, pulmonary blood flow is impeded because of the alveoli pressure against the pulmonary capillaries. The pressure increases right ventricular afterload and volume and decreases right ventricular output. The ventricular septum may be shifted to the left, but this effect is more consistent with a high PEEP. This condition decreases left ventricular filling and output. The magnitude of these changes is proportional to lung compliance. As lung compliance decreases, the stiffer lungs can retain the increased pressure imposed by PEEP. In other words, the increased pressure in the lung is not transmitted to the vasculature to impede right ventricular output. An increase in P_{pl} secondary to an increase in lung pressure impedes venous return and decreases cardiac output further. In general, at an optimal PEEP that sustains lung open, the increase in pulmonary vascular resistance is minimized. A decrease in lung volume and an increase in lung volume over normal FRC levels both adversely affect pulmonary vascular resistance. This maintaining lung volume by appropriate PEEP minimizes cardiovascular impairment associated with mechanical ventilation.

Right and Left Ventricular Function

Under conditions of a normal cardiovascular system with normal ventilation values, there are no significant changes in right or left ventricular function. Otherwise, mechanical ventilation would be difficult to manage, and the mortality and morbidity among patients receiving ventilation would be much higher. Right or left ventricular dysfunction appears to occur if the patient is hypovolemic, is receiving an excessive V_T, or is receiving more or less than optimum PEEP. The common factor is excessive P_{alv}, enough to overcome or impede pulmonary blood flow or venous return.

Effect on Left Ventricular Dysfunction

PPV can improve cardiac output in some patients. In patients with left ventricular failure, application of PPV can increase both the left ventricular ejection fraction and the cardiac output. These improvements occur because PPV decreases left ventricular afterload in these patients. Afterload is an important factor in determining cardiac output, as is the resistance of the systemic vasculature. When afterload increases, cardiac output decreases (heart failure). When afterload is decreased by PPV or pharmacologic therapy, cardiac output may increase. This phenomenon explains why the cardiovascular status of some patients deteriorates when PPV is discontinued or treatment is changed from full to partial ventilatory support.

Endocardial Blood Flow

Blood flow in the coronary arteries depends on the gradient between the systemic diastolic pressure and the left ventricular end-diastolic pressure (represented by the pulmonary capillary wedge pressure). Any factor that decreases systemic diastolic pressure or increases wedge pressure decreases endocardial perfusion pressure. The factors of PPV that may decrease the systemic diastolic pressure are high mean airway pressure owing to a high PEEP, large V_T, or long inspiratory time. Factors that may increase the wedge pressure include excessive PEEP and left ventricular failure.

Cardiac Output, Cardiac Index, and Systemic Blood Pressure

When the cardiovascular system is normal with normal ventilation values, there are no significant changes in cardiac output, cardiac index, or systemic blood pressure. Cardiac output can

be affected by a decrease in stroke volume with PPV, but this decrease is compensated by an increase in heart rate. Because the cardiac index is the quotient of cardiac output and body surface area (cardiac index = cardiac output in liters per minute/body surface area in square meters), a change in cardiac output would be reflected in the cardiac index. Systemic arterial pressure remains stable because of reflex compensation, which increases systemic vascular resistance. Cardiac output, cardiac index, and arterial pressure decrease only when mean airway pressure is high and P_{pl} increases precipitously. Hypotension owing to PPV alone is rare because clinicians do all that is necessary to prevent it, including adequate fluid administration, proper management of mean airway pressure and PEEP, and use of vasoconstricting drugs. Most cases of hypotension during mechanical ventilation are caused by sepsis and the accompanying vascular collapse.

RULE OF THUMB Patients most likely to experience hemodynamic effects of mechanical ventilation are patients with a normal or increased lung compliance associated with decreased chest wall compliance. In this setting, there is little lung stretch but maximum transmission of ventilating pressure to the intrathoracic space.

MINIMIZING CARDIOVASCULAR EFFECTS OF POSITIVE PRESSURE MECHANICAL VENTILATION

The effect of PPV on the circulatory system depends primarily on two major factors: mean pleural pressure and cardiovascular status.

Mean Pleural Pressure

Pleural pressure is the pressure in the virtual pleural space. At the bedside, pleural pressure usually is measured indirectly as the esophageal pressure through an esophageal balloon connected to a pressure transducer. Because the esophagus is close to the pleurae, separated by only the flexible esophageal wall, change in esophageal pressure reflects change in pleural pressure but may not equal actual pleural pressure. An alternative to measuring pleural pressure is measuring mean airway pressure. Mean airway pressure is linearly related to mean pleural pressure and can be used clinically for monitoring of pressure changes.[100]

The effect of PEEP on pleural pressure is complex and depends on the patient's lungs and thoracic mechanics. Some of the pressure generated by a ventilator reaches the alveoli, where it is transmitted across the alveolar walls to the pleural space. How much of this P_{alv} is transmitted to the pleural space depends on lung and thoracic mechanics.

In general, for a given P_{alv}, the more compliant the lung, the greater is the increase in pleural pressure. A patient with a disease causing a loss of elastic tissue, such as emphysema, is more subject to the cardiovascular effects of positive pressure than a person with normal lungs. In contrast, a lung with low compliance transmits less pressure to the pleural space; this explains, in part, why high levels of PEEP often are used with minimal cardiovascular effects on patients with low lung compliance (e.g., ARDS).

When the compliance of the chest wall is reduced, expansion of the thorax is limited, and more P_{alv} is transmitted to the pleural space. Patients who have normal lungs but have thoracic restriction, as caused by kyphoscoliosis and spondylitis, are more subject to the cardiovascular effects of positive pressure than individuals with normal chest wall compliance. A similar effect can occur in patients with normal thoracic compliance who actively oppose a mandatory breath by contracting the expiratory muscles (as might occur in patient–ventilator asynchrony). Contraction of the expiratory muscles effectively decreases thoracic compliance and causes more P_{alv} to be transmitted to the pleural space.

If resistance to airflow is high, less of the pressure generated at the airway reaches the alveoli. The high peak airway pressure common in patients with obstructive disorders is not reflected in high pleural pressure.

The effects of moderate increases in pleural pressure on cardiac output in healthy persons are minimal. In healthy persons, as left ventricular stroke volume decreases, compensatory responses increase both the cardiac rate and the tone of the venous capacitance vessels. These normal responses ensure adequate blood flow and perfusion pressure. However, if the patient already is hypovolemic or has lost peripheral venomotor tone, cardiovascular compensation may be impossible. In these cases, even a small increase in pleural pressure may result in a marked decrease in cardiac output.

Decreasing Mean Airway Pressure

Mean airway pressure is affected by respiratory rate, V_T, inspiratory time, inspiratory pause, expiratory time, I:E ratio, peak pressure, baseline pressure (PEEP or CPAP), and inspiratory flow waveform. If a decrease in mean airway pressure is necessary, altering any factor that contributes to mean airway pressure has an effect. If the PaO_2 is high, one of the most effective changes is a decrease in PEEP because it has a 1:1 relationship with mean airway pressure. If a decrease in PEEP is indicated, the RT must ensure that desaturation does not occur when the decrease has been accomplished. If the patient is being hyperventilated, a decrease in mandatory rate or V_T also decreases mean airway pressure.

The best way to determine the magnitude of the change is to use the mean airway pressure monitor on the ventilator. The peak pressure usually decreases with a decrease in V_T. In pressure-controlled modes, the peak pressure may be decreased directly. The P_{plat} is a reflection of mean peak P_{alv}. In volume-controlled ventilation, a decrease in V_T decreases P_{plat}. In pressure-controlled ventilation, the pressure setting may be reduced to limit P_{plat}. Efforts that increase lung compliance, such as PEEP or administration of diuretics to decrease interstitial edema, also may affect P_{plat}. Inspiratory time, expiratory time, and I:E ratio affect mean airway pressure. As inspiratory time lengthens or expiratory time decreases, mean airway pressure increases.

Fluid Management and Cardiac Output

The relationship between cardiac output and preload (end-diastolic volume) is described by the Frank-Starling phenomenon, which states, "in the normal heart, the diastolic volume (preload) is the principal force that governs the strength of ventricular

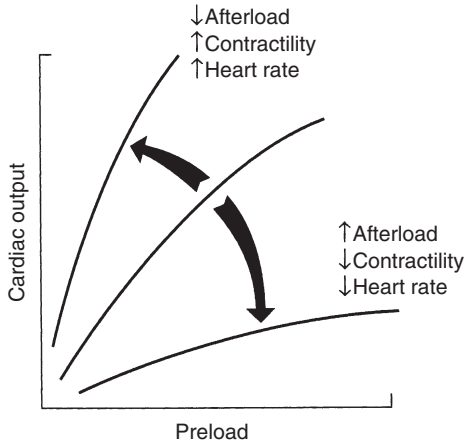

Fig. 47.17 Effects of preload, afterload, contractility, and heart rate on cardiac output function curve. (Modified from Green JF: *Fundamental cardiovascular and pulmonary physiology*, ed 2, Philadelphia, 1987, Lea & Febiger.)

contraction."[101] As preload (stretch) increases, so does force and presumably stroke volume. Stroke volume continues to increase with preload until the heart is distended by excess preload, after which stroke volume decreases. Another cause of a decrease in stroke volume is the decrease in ventricular contractility that occurs when afterload increases as the result of hypertension. With hypertension comes dilation and distention of the ventricles, which make the heart structurally abnormal. In an abnormal heart, it takes much less preload to put the heart into failure. Failure in this case is defined as decreased stroke volume despite increased preload (Fig. 47.17).

When a patient receives PPV, there is risk of a decrease in venous return (preload) because of the increase in P_{pl}. Stroke volume may decrease, but the decrease is compensated for by a reflex increase in heart rate and vasomotor tone. Because of these compensatory mechanisms, most patients with a normal cardiopulmonary status who receive mechanical ventilation do not need additional fluid to maintain cardiac output. However, certain conditions can increase the risk of relative or actual hypovolemia, and the increase can decrease stroke volume, even if normal reflex compensation is present. These conditions include hypovolemic shock (owing to trauma and blood loss), sepsis (in which the normal reflex compensation is not present), and high PEEP and high mean airway pressure. In these conditions, fluid or blood administration may be necessary to maintain cardiac output and end-organ perfusion. In some patients who receive PPV with PEEP, an increase in PEEP can decrease cardiac output as discussed earlier. In this case, the outcome of PEEP in terms of improved tissue oxygenation (oxygen delivery [DO_2] = CaO_2 × cardiac output) should be determined. If tissue O_2 delivery decreases because of a decrease in cardiac output, but CaO_2 increases, fluid administration may be indicated to restore cardiac output by increasing preload.

Pharmacologic Maintenance of Cardiac Output and Blood Pressure

First-line therapy for decreased cardiac output and blood pressure is fluid administration, unless the patient has congestive heart failure. In heart failure, inotropic therapy is indicated for decreased myocardial contractility, and vasodilators and diuretics are used to control hypertension, which decreases afterload. Diuretics are used to control fluid overload and to decrease preload to the distended heart. These factors in combination may return the heart to a more optimal portion of the Frank-Starling curve and improve stroke volume.

EFFECTS OF POSITIVE PRESSURE MECHANICAL VENTILATION ON OTHER BODY SYSTEMS (Box 47.2)

Increased Intracranial Pressure

Perfusion of the brain is quantified by the CPP. The CPP is the difference between mean arterial pressure (MAP) and ICP. CPP may decrease in any case in which MAP decreases or ICP increases. If CPP decreases, CBF decreases. The result is cerebral ischemia and a decrease in cerebral O_2 metabolism. The cerebral circulation has the ability to maintain CBF even when CPP changes, a process called *cerebral autoregulation*. Cerebral **autoregulation** is a function of cerebral vascular resistance. If CPP decreases, cerebral vascular resistance decreases to maintain CPP. Cerebral autoregulation functions as long as CPP is in the range of 60 to 150 mm Hg and is limited by the ability of the cerebral arterioles to constrict and dilate. Under normal conditions, cerebral O_2 delivery and CPP exceed the metabolic needs of the brain for O_2 and glucose.

Normal MAP is 93 mm Hg if arterial pressure is 120/80 mm Hg. Normal ICP is less than 10 mm Hg, so normal CPP is approximately 80 to 85 mm Hg. CPP decreases when MAP decreases or ICP increases. Conditions leading to a decrease in MAP are shock, high PEEP, and high mean airway pressure. Increases in ICP are caused by traumatic brain injury (TBI), cerebral hemorrhage, cerebrovascular accident (stroke), and tumors. A CPP greater than 60 mm Hg maintains CBF and cerebral O_2 metabolism.

CO_2 is a potent cerebral vasodilator and an important regulator of the cerebral arteriolar diameter. As $PaCO_2$ decreases from 40 mm Hg, systemic pH increases. CO_2 concurrently diffuses across the blood-brain barrier. The result is an increased cerebrospinal fluid (CSF) pH. Although $PaCO_2$ is monitored in patients with TBI, the CSF pH modulates cerebral vascular resistance in an effort to decrease the ICP. When mechanical hyperventilation is used, cerebral vascular resistance increases, and the result is decreased ICP; this is why hyperventilation has been used in the management of TBI and acute increased ICP. However, in the presence of an already decreased CPP, CBF may decrease to the point at which cerebral ischemia is likely; this is the problem with immediate hyperventilation of a patient with TBI. In addition, prolonged hyperventilation allows renal excretion of bicarbonate, which allows the CSF pH to return to normal and negates any positive effect of hyperventilation on ICP. The effect of hyperventilation on the reduction of ICP lasts 1 hour. If hyperventilation is withdrawn and arterial pH and $PaCO_2$ return to normal values, the CSF pH decreases. Subsequent CSF acidosis leads to cerebral vasodilation and a rebound increase in CBF and ICP that exceeds the values before hyperventilation. For

these reasons, hyperventilation must be used cautiously in the treatment of patients with TBI.[102] Normally patients with TBI are managed with a $PaCO_2$ that is relatively normal, 35 to 40 cm H_2O.

Treatment of a Patient With a Closed Head Injury

Guidelines for the management of severe TBI were developed by neurosurgeons in the Joint Section on Neurotrauma and Critical Care.[103] The recommendation is as follows: "The use of prophylactic hyperventilation ($PaCO_2$ <35 mm Hg) during the first 24 hours after TBI should be avoided because it can compromise cerebral perfusion during a time when CBF is reduced. Hyperventilation therapy may be necessary for brief periods when there is acute neurologic deterioration or for longer periods if there is intracranial hypertension refractory to sedation, paralysis, CSF drainage, and osmotic diuretics." The Joint Section further noted that "in the absence of increased ICP, chronic, prolonged hyperventilation therapy ($PaCO_2$ <35 mm Hg) should be avoided after TBI." These findings have resulted in several recommendations regarding the care of patients with TBI, as follows:

1. Patients with TBI may have transient, short periods of increased ICP, called *plateau waves*. Plateau waves may be caused by suctioning, repositioning, or other noxious stimuli. During a plateau wave, acute hyperventilation can control ICP until the pressure returns to baseline, at which time ventilation is resumed at the previous rate.
2. Hyperventilation should be avoided after TBI; other methods can be used to decrease elevated ICP. These methods include ventriculostomy for drainage of CSF, craniotomy for removal of mass lesions, osmotic diuretics, sedation, placing the patient in the semi-Fowler position, and paralysis. CPP should be maintained at greater than 70 mm Hg.
3. Intubation should be attempted only after the patient has been sedated, to prevent the associated increase in ICP. Exhaled partial pressure of end-tidal carbon dioxide ($PETCO_2$) should be monitored to maintain a constant $PaCO_2$ after arterial blood gas values are determined to find the correlation between $PaCO_2$ and $PETCO_2$.
4. ICP should be maintained at less than 20 mm Hg.[103]

Effect on Renal Function

Some patients receiving long-term PPV retain salt and water. In critically ill patients, water retention usually is evident when rapid weight gain occurs. In addition, such patients may have a reduced hematocrit, which is also consistent with hypervolemia secondary to water retention. These early observations are attributed to the direct and indirect effects of PPV on renal function.

In terms of direct effect, PPV can reduce urinary output 30% to 50%. This reduced urinary output during PPV is associated with a simultaneous reduction in renal blood flow, glomerular filtration rate, and sodium and potassium excretion.

Decreases in MAP to less than 75 mm Hg reduce renal blood flow, glomerular filtration rate, and urinary output. However, MAP this low seldom is caused by PPV alone, and kidney autoregulatory mechanisms generally can keep renal perfusion pressure within normal limits over a wide range of arterial pressures. Because restoring cardiac output to normal does not entirely restore urinary output compromised by PPV, other mechanisms must be involved. Impaired renal function during PPV is better associated with a decrease in intravascular volume.

The indirect effect of PPV on renal function may be most important. PPV has a marked effect on the water-retaining and sodium-retaining hormonal systems. Specifically, long-term PPV increases plasma renin activity, plasma aldosterone level, and level of vasopressin (urinary antidiuretic hormone). In addition, PPV decreases atrial natriuretic hormone levels (Fig. 47.18).

Decreased right atrial transmural pressure is primarily responsible for the decrease in atrial natriuretic hormone, which leads to sodium retention. Similarly, vasopressin secretion may be enhanced by stimulation of the left atrial stretch receptors, which innervate the posterior pituitary gland. Increased secretion of vasopressin (antidiuretic hormone) and activation of the renin-angiotensin-aldosterone system lead to a decrease in urine output.

Decreased Liver and Splanchnic Perfusion

The effects of PPV on the liver and intestine are related to its effects on the cardiovascular system. Hepatic dysfunction with PPV can occur in patients with otherwise normal livers and manifests as an increase in serum bilirubin level. These effects appear to be directly related to the reduction in hepatic blood flow that occurs with PPV. Regardless of cause, these effects are aggravated by PEEP but can be reversed when cardiac output is returned to pre-PEEP levels with intravascular volume infusions.

Decreased Gastrointestinal Function

An increase in splanchnic resistance can contribute to gastric mucosal ischemia and helps explain the high incidence of gastrointestinal bleeding and stress ulceration in patients receiving long-term PPV. Stress ulcers (erosions of the gastric mucosa) are common among patients with life-threatening illness. Impaired blood flow inhibits the ability of the gastric mucosa to replace itself normally every 2 or 3 days. Stress ulcers are caused by impaired blood flow, not gastric acidity. Gastroduodenal motility also is severely impaired in mechanically ventilated patients.[104] These factors may result in translocation of bacteria from the intestine to the blood and nosocomial septicemia. Mechanical ventilation for more than 48 hours and most other conditions necessitating ICU admission are considered indications for stress ulcer prophylaxis. Optimal prophylaxis for stress ulcers is restoration of mesenteric blood flow. Pharmacologic approaches include administration of a cytoprotective agent (sucralfate) and an acid suppression agent (cimetidine or ranitidine).[101]

Gastric distention can be caused by **aerophagia** secondary to an artificial airway cuff leak or by the use of mask ventilation (pressure >20 to 25 cm H_2O). The RT can prevent this complication by taking great care to ensure that the cuff is properly inflated. If patients being ventilated noninvasively are swallowing air, an artificial airway may be considered. In the case of aerophagia and gastric distention, a nasogastric tube may be inserted to evacuate the air.

Bleeding from erosion through the surface vessels of the gastric mucosa is one consequence of stress ulceration. The incidence of bleeding from stress ulcers is almost 100%, but only

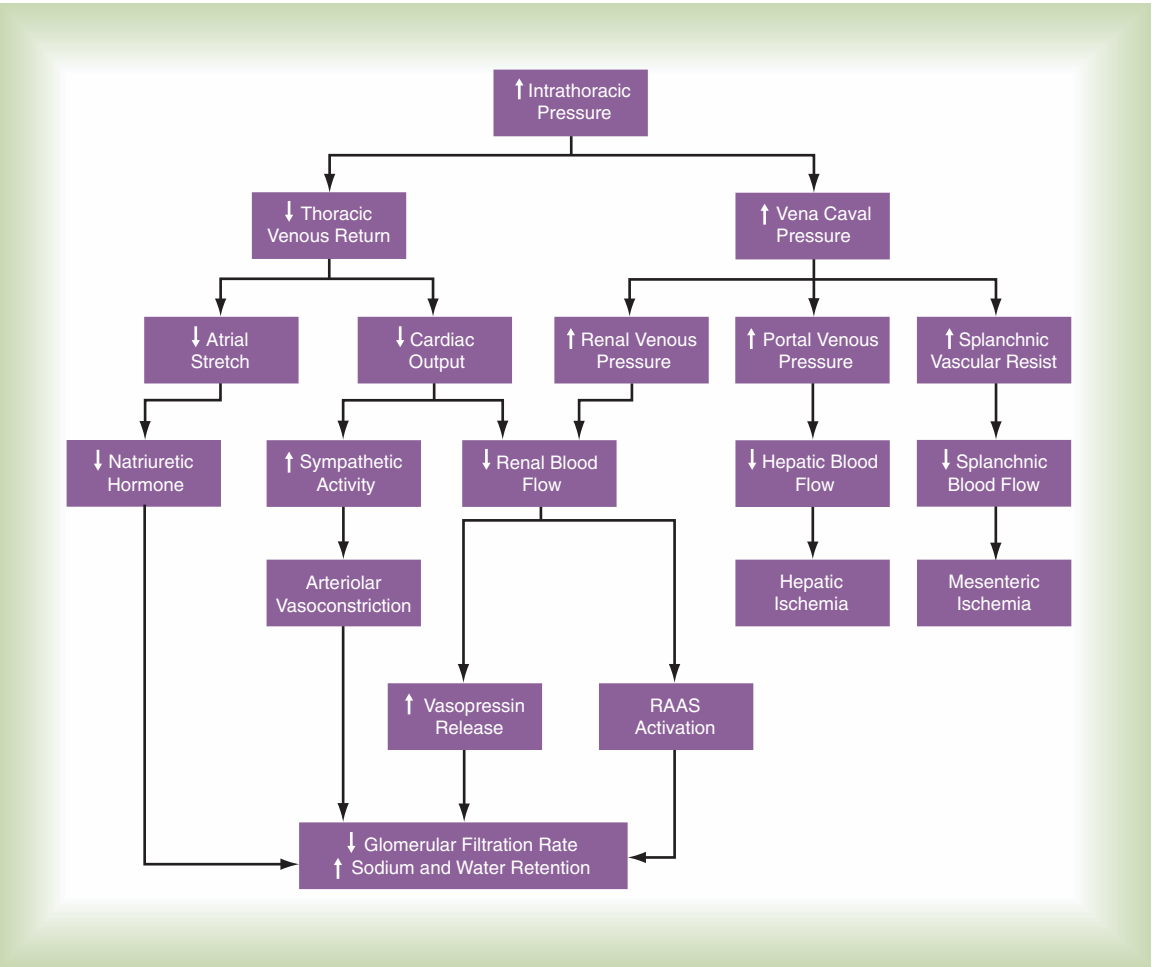

Fig. 47.18 Cardiac, renal, hepatic, and splanchnic effects associated with increased intrathoracic pressure caused by positive pressure ventilation. *RAAS,* Renin-angiotensin-aldosterone system; ↑, increased; ↓, decreased. (Modified from Florete OG, Gammage GW: Complications of ventilatory support. In Kirby RR, Banner MI, Downs JB, editors: *Clinical applications of ventilatory support*, New York, 1990, Churchill Livingstone.)

approximately 5% of bleeding is clinically apparent hemorrhage, and less than 1% to 2% necessitates blood transfusion.

Because patients receiving mechanical ventilation often have an artificial airway or are obtunded, a nutritional deficit may exist. Even in a normal metabolic state, intravenous solutions of saline and dextrose provide only a fraction of the required calories and micronutrients. Patients in the ICU often are hypermetabolic and need two to three times the normal calories. See Chapter 23 for details on nutritional support.

Effect on Central Nervous System

Patients in the ICU are placed into an artificial environment over which they have little control. From the start, the patient loses autonomy. When mechanical ventilation is introduced, the patient is sedated and possibly paralyzed and may not return to a normal, awake level of consciousness until discharged from the ICU. Instead, the patient is kept somnolent (easily aroused and aware) or is stuporous (arousable with difficulty and impaired awareness) or comatose (arousable but unaware).[101] The presence of an artificial airway makes communication difficult. Caregivers should make a paper tablet and pen, communication board, or communication cards available to patients who are aware enough to write or use them.

Sedatives, Hypnotics, and Neuromuscular Blocking Agents

Sedation is necessary but should always be the minimal level required for the management of the nearly inevitable agitation, fear, and anxiety associated with the ICU environment, pain, invasive and noninvasive procedures, and loss of normal sleep pattern. The Society of Critical Care Medicine has published guidelines for sedation and analgesia in the care of critically ill patients.[105]

The level of sedation is monitored with the Modified Ramsay Sedation Scale (Box 47.3). Sedation is titrated to achieve a level of 2 to 3 on the Ramsay scale. This way the patient is responsive yet not restless or agitated and not paralyzed or comatose.

According to the Society of Critical Care Medicine, facilitation of mechanical ventilation in severe ARDS is the most common reason for prolonged neuromuscular blockade. Neuromuscular

BOX 47.3 Modified Ramsay Sedation Scale

1. Agitated, anxious, restless
2. Calm, cooperative, oriented, tranquil
3. Responds to verbal commands
4. Brisk response to light touch
5. Unable to be assessed (paralyzed)

blocking agents are used with mechanical ventilation to improve gas exchange, to avoid ICP spikes, to avoid hemodynamic instability, and to prevent bodily injury. Because they paralyze but do not sedate, neuromuscular blocking agents always are used in conjunction with appropriate sedative or analgesic agents (see earlier). In the absence of a sedative, a patient under the influence of a neuromuscular blocking agent is paralyzed and fully aware of the surroundings. During neuromuscular blockade, patients should be assessed for the degree of blockade that is being sustained.[105] The patient is observed for ventilatory effort, and train-of-four stimulation is performed. Neuromuscular blockade should be allowed to dissipate daily so that clinical evaluation, assessment of concomitant sedation and analgesia, and evaluation of the need for continued paralysis can be conducted.

Opioids

Pain is a major issue in any patient in the ICU. An ETT is very painful, and all of the procedures performed in the ICU tend to be painful. As a result, careful attention to the of pain medication is indicated. Much of the anxiety and discomfort treated with sedatives should be treated with pain medication. Appropriate management of pain and sedation reduces the likelihood delirium developing.

COMPLICATIONS OF MECHANICAL VENTILATION

Negative Pressure Ventilation

Pulmonary

Hypoventilation during NPV can be caused by a decrease in the P_{TA} owing to inadequate negative pressure or leaks in the ventilator or patient–ventilator interface. Iron lung negative pressure ventilators rely on a tight seal at the patient's neck and at all access ports in the tank. Chest cuirass ventilators rely on a tight seal between the cuirass and thorax. Poncho-type ventilators must remain free of leaks or tears. When there is a leak at any of these points, P_{TA} decreases, and the result is a decrease in minute ventilation.

Hyperventilation can occur if the pressure is more negative than is necessary. The results are increased P_{TA}, increased V_T, and increased minute ventilation.

Cardiovascular

Abdominal blood pooling can occur in patients receiving NPV in an iron lung. The negative pressure exerted on the thorax also is exerted on the more compliant abdominal wall. When the pressure in the iron lung becomes negative, the abdominal wall is pulled outward and with it the viscera and associated blood supply. Venous return to the heart, cardiac output, and systemic blood pressure decrease; the result is a condition called "tank shock."

Positive Pressure Ventilation: Artificial Airway Complications

Chapter 37 describes complications related to artificial airways.

Complications Related to Pressure

Ventilator-associated lung injury is the term used to define lung injury in humans owing to mechanical ventilation. These are complications resulting from high pressure, infection, and patient-ventilator asynchrony. High ventilation pressure has long been associated with barotrauma. Barotrauma is categorized as pneumothorax, pneumomediastinum, pneumopericardium, and subcutaneous emphysema (Fig. 47.19). All of these complications are descriptions of extra-alveolar air. High ventilatory pressure can cause gas to escape through ruptured alveoli. The eventual location of the escaping gas defines the type of barotrauma. If gas escapes through ruptured alveoli into the pleural space, pneumothorax occurs. Gas escaping along perivascular sheaths to the mediastinum produces pneumomediastinum. Further dissection from the mediastinum to tissue planes in the neck and chest wall results in subcutaneous emphysema and potentially pneumomediastinum and pneumoperitoneum.

Pneumothorax is identified by observation of a decrease in chest movement, hyperresonance on percussion, possible deviation of the trachea away from the affected side, and decreased or absent breath sounds over the affected side. In nonintubated patients, there may also be a decrease in vocal fremitus over the affected side. A line separating lung tissue from air is observed on the chest radiograph, although the line sometimes is difficult to see in a small (<20%) pneumothorax (see Chapter 21). Respiratory distress increases with increasing pneumothorax, as does hypoxemia. Normally, in spontaneously breathing patients, intrapulmonary and pleural pressures are equal in pneumothorax. PPV can cause P_{pl} to increase (tension pneumothorax).

Tension pneumothorax is life threatening because it tends to develop very rapidly in patients who are mechanically ventilated and shifts the mediastinum, heart, and great vessels; the results are a decrease in cardiac output and hypotension. Tension pneumothorax is a medical emergency; it is relieved by insertion of a large-bore needle into the pleural space through the anterior second or third interspace above the rib. This maneuver is followed by chest tube insertion. While waiting for needle decompression, the patient may be ventilated with 100% O_2 at a low V_T and airway pressure. Pneumomediastinum and pneumoperitoneum are identified on a chest radiograph by the presence of air in these locations.

Complications Related to Volume

VILI has been defined as the application of pressure, positive or negative, to the lungs causing damage. The damage has been described as an increase in permeability of the alveolar-capillary membrane, pulmonary edema, cell wounding and necrosis, and diffuse alveolar damage as the result of using an inappropriate

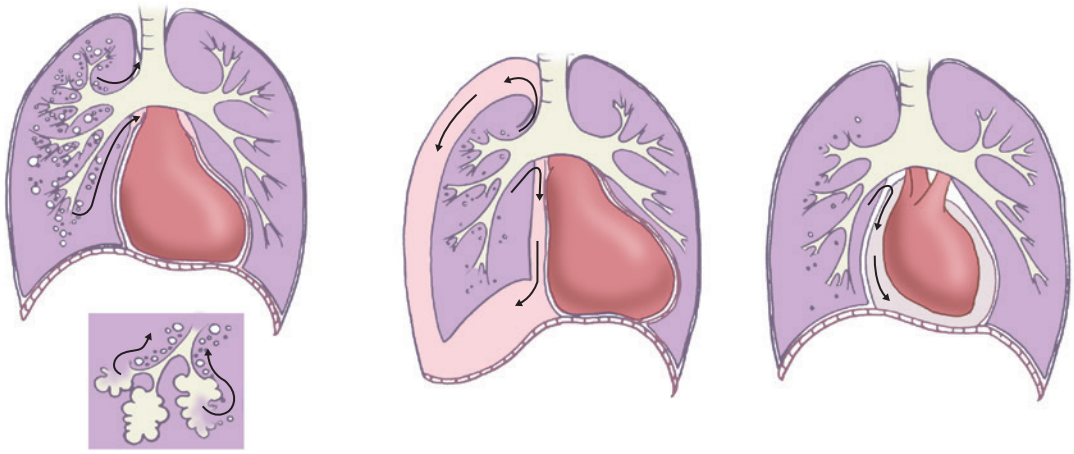

Fig. 47.19 Pulmonary Barotrauma. (A) Ruptured alveoli are indicated in framed alveoli at bottom. Air dissects from alveoli along vascular sheaths to the hilum and then to the pleural space. (B) Pneumothorax. Origin of air in lung tissue and its pathway to inflate the pleural space are indicated. The heart shifts to the left because of high pressure in the right side of the chest. (C) Course of air from the lung to pericardial space. The distended pericardial space causes cardiac tamponade. (Modified from Korones SB: *High-risk newborn infants*, ed 4, St Louis, 1986, Mosby.)

ventilation strategy. Several more recent reviews summarize the mechanisms, effects, and means to prevent VILI.[106–108]

It has been shown that overdistention, as opposed to volume or pressure per se, is an important determinant of lung damage. Animals ventilated with large V_T (>30 mL/kg) develop severe injury—hence the term **volutrauma**. The degree of alveolar distention is determined by the P_{TP} (P_{plat} minus the pleural pressure), which must be approximated by the esophageal pressure. As P_{plat} increases, so does P_{TP}, increasing the likelihood of lung damage. Lung damage may also occur when ventilating at low V_T, if alveoli are allowed to deflate and reinflate repeatedly with each breath. This injury is called **atelectrauma**. These two factors have led to the recommendation that lungs should be opened ("recruited") and kept open by an appropriate PEEP level and ventilated to a P_{plat} of no more than 28 cm H_2O by decreasing V_T and a driving pressure of no more than 15 cm H_2O. This technique is called the *open lung technique* and is described in detail in Chapter 49.

Factors that predispose a patient to VILI include underlying lung disease (injured lungs are more susceptible to VILI), systemic inflammation, surfactant dysfunction, aspiration, pulmonary edema, extremes of age, and heterogeneous lung ventilation. An important factor is the uneven distribution of ventilation, especially in ARDS. Because ARDS is a heterogeneous disorder, there are areas of both low and normal compliance. A given pressure in an area of low compliance may allow lung units to open and close with each breath, causing atelectrauma. The same pressure in an area of normal compliance may cause overdistention and stretch injury. Pulmonary edema is a prominent feature of VILI, owing to an increase in alveolar-capillary membrane permeability. Microvascular damage is characterized by separation of capillary endothelial cells, disruption of alveolar epithelium, and destruction of alveolar type I cells.

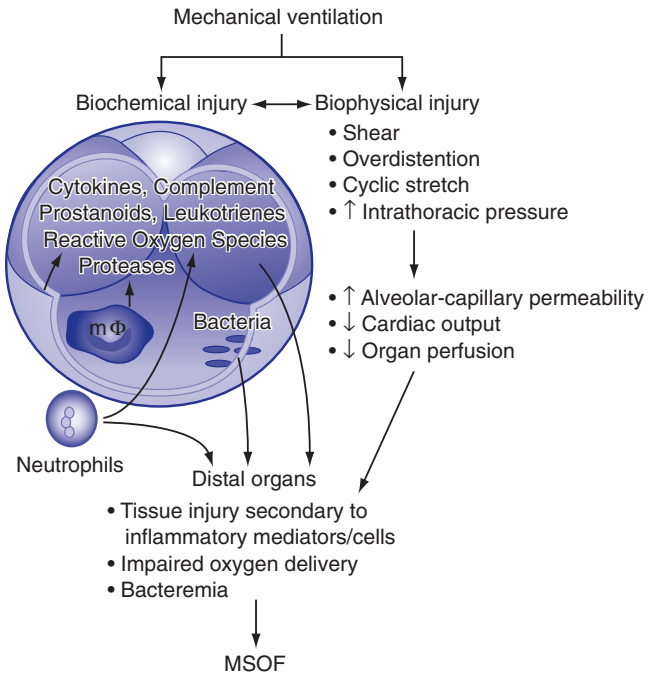

Fig. 47.20 Mechanisms by which mechanical ventilation might contribute to multisystem organ failure (MSOF). (From Mason RJ, Broaddus VC, Murray JF, et al: *Murray and Nadel's textbook of respiratory medicine*, ed 4, Philadelphia, 2005, Saunders.)

VILI occurs via two mechanisms, as shown in Fig. 47.20.[109] One mechanism is the physical disruption of tissues and cells *(biophysical injury)*. Physical disruption of the tissues occurs as air ruptures across the alveolar epithelial surface and tracks along the bronchovascular sheath. Air tracks into the interstitium causing pulmonary interstitial emphysema, into the pleural space

causing pneumothorax, and into the pericardium causing pneumopericardium. The pulmonary capillary epithelium also fails in response to high-volume ventilation, resulting in hemorrhage and edema. Another factor in biophysical injury is the interdependence of adjacent alveoli and terminal bronchi. When the lung is unevenly expanded, alveolar collapse increases the traction forces between alveoli. This recruitment-derecruitment develops pressures up to 140 cm H_2O across lung units, resulting in air-filled cavities and pseudocysts. Finally, injurious ventilation causes surfactant to become dysfunctional or deficient or both.

The second mechanism is the release of inflammatory mediators *(biochemical injury)*. When the lungs are abnormally stretched, this is detected by cells and converted into biochemical signals, a process called *mechanotransduction*. These biochemical signals cause the release of cytokines, complement, prostanoids, leukotrienes, reactive O_2 species, and proteases. The release of these substances has been called **biotrauma**. These mediators go on to the terminal organs and cause tissue inflammation, impairment of O_2 delivery, and bacteremia (see Chapter 29), leading to MSOF. As mentioned earlier in the chapter, hyperinflation during mechanical ventilation causes bacteria to "spill over" from the gut into the bloodstream, a process called *translocation*. In this manner, translocation contributes to MSOF, as bacteria migrate into the blood and then to terminal organs. Other factors contributing to MSOF are an increase in circulating cell death (apoptotic) factors, suppression of the peripheral immune response, and individual genetic variability.

Alveolar distention occurs when the lungs are stiff and the chest wall is normal or when one or both lungs are ventilated with a high P_{plat}. P_{plat} ideally should be maintained at less than 28 cm H_2O in all patients. However, in patients with a stiff chest wall (marked obesity, fluid overload, increased abdominal pressure), higher P_{plat} can be tolerated without injury because of the reduction in P_{TP} caused by the stiff chest wall. In this setting driving pressure can normally be maintained less than 15 cm H_2O.

Human studies have compared high and low V_T ventilation, using ICU mortality, ventilator-free days, and overall mortality as outcome variables. The consensus is that a low V_T strategy, with PEEP adequate to keep lungs open to avoid atelectrauma, results in a significantly better outcome. In studies in which inflammatory mediators were also measured, high V_T groups had a higher level of inflammatory mediators.[110,111] VILI is related to both mechanical and chemical factors. On one hand, overstretch directly injures the alveolar epithelium and capillary endothelium. On the other hand, through mechanotransduction, cells release many inflammatory mediators into the blood, leading to MSOF.

Auto–Positive End-Expiratory Pressure

Air trapping occurs with incomplete emptying of lung units. Lung units prone to air trapping are units with long-time constants (i.e., with high resistance or high compliance). Air trapping during PPV is often referred to as *dynamic hyperinflation, auto-PEEP, occult PEEP,* or *intrinsic PEEP*. This problem associated with air trapping cannot be determined by simple observation of airway pressure. Auto-PEEP often goes unrecognized. Refer to Chapter 48 for details on the management of auto-PEEP.

Oxygen Toxicity

O_2 toxicity causes lung tissue damage and an increase in the permeability of the alveolar-capillary membrane. As suggested in Chapter 42, factors associated with the development of O_2 toxicity include elevated FiO_2, long duration of exposure, and patient susceptibility. FiO_2 of 0.6 or more for longer than 24 to 48 hours is associated with the development of O_2 toxicity. In the presence of a high concentration of O_2, O_2 free radicals are produced. These radicals are the hydroxyl (OH^-), perhydroxyl (HO_2), and superoxide (O_2^-) radicals. Free radicals normally are rapidly detoxified by the enzyme superoxide dismutase, which is produced by alveolar type II cells. With higher FiO_2, the presence of free radicals is greater, and type II cells are less likely to produce superoxide dismutase. The presence of free radicals increases the permeability of the alveolar-capillary membrane. The combination of direct injury by free radicals and decreased surfactant production leads to exudation of fluid into the alveoli and a subsequent decrease in compliance. Every effort should be made to decrease FiO_2 whenever it exceeds 0.6. The decrease usually is accomplished with application of PEEP or CPAP. However, the evidence supporting the development of O_2 toxicity in critically ill patients is poor, and appropriate oxygenation should never be sacrificed for the purpose of avoiding O_2 toxicity.

Current recommendations are that FiO_2 should be adjusted to maintain the PaO_2 55 to 80 mm Hg or the SpO_2 88% to 95% to decrease mortality risk. It has been clearly demonstrated that maintaining hyperoxia increases the risk of death in ICU patients.

Ventilator-Associated (Nosocomial) Pneumonia

Pneumonia is the second most common nosocomial infection, primarily affecting infants and young children, adults older than 65 years, patients with severe underlying disease, immunosuppressed patients, patients who have depressed sensorium, patients with cardiopulmonary disease, and patients who have had thoracoabdominal surgery. RTs should be prepared to prevent this threat to respiratory patients, who are 6 to 21 times more susceptible to the development of nosocomial pneumonia than the general population. A review by Craven[112] stated that healthcare costs related to each case of nosocomial pneumonia are approximately $40,000. Most of these cases of pneumonia are caused by aspiration of bacteria that have colonized the upper gastrointestinal tract or oropharynx. Intubation greatly increases the risk of nosocomial pneumonia because the lower airway is left exposed, and normal protective mechanisms are bypassed. This type of pneumonia has been known for years as *ventilator-associated pneumonia*. This name has been challenged because it is not the ventilator but rather the microaspiration of microorganisms in oral or gastrointestinal secretions that causes the infection. Secretions that sit on the top of the endotracheal or tracheostomy tube cuff are aspirated via the small folds in the cuff. Most cases of pneumonia are polymicrobial, consisting of gram-negative organisms. However, methicillin-resistant *Staphylococcus aureus* has been common in the past 10 years. The endotracheal or tracheostomy tube is a site of bacterial growth, and these bacteria become encased in what is referred to as a

biofilm. The use of a silver-coated endotracheal tube,[113] use of endotracheal tubes with alternative cuff designs,[114] use of subglottic suction airways,[115] proper cuff care,[116] the use of devices to remove biofilm from the inside of the ETT,[117] and avoidance of lavaging when suctioning all reduce the risk of aspiration. See Chapter 37 for details.

Prevention of Ventilator-Associated Pneumonia

In addition to standard precautions, specific infection control procedures apply to the use of endotracheal tubes and ventilators. These ventilator bundles for prevention of ventilator-associated pneumonia include the following[116]:

- Perform appropriate hand hygiene. Hands should be disinfected with a sanitizer (e.g., Cal-Stat hand sanitizer) before entering any patient's room regardless of the reason and when leaving the patient's room regardless of the activities that occurred in the room.
- Perform gentle suctioning (to help prevent coughing, aspiration, and sloughing of biofilm).
- Place the patient in a semirecumbent position (30- to 45-degree head elevation).
- Do not routinely change ventilator circuits.
- Drain and discard inspiratory tube condensate away from the patient, or prevent its formation by using heated wire circuits or heat and moisture exchangers.
- Use a metered dose inhaler rather than a nebulizer for medication administration. If a small volume nebulizer is used, it should be replaced after each treatment (i.e., one nebulizer = one treatment). However, the new vibrating disc nebulizers are as protective as meter dose inhalers.
- Interrupt sedatives daily to evaluate patient readiness to wean from the ventilator—this is effective in decreasing the length of intubation and mechanical ventilation.
- Assess daily the ability of the patient to perform a spontaneous breathing trial.
- Use noninvasive ventilation whenever possible to avoid intubation.
- Perform regular oral hygiene at least every 4 hours.

Early tracheostomy has been evaluated as a possible preventive measure, but several studies and meta-analyses showed no advantage of tracheostomy in preventing ventilator-associated pneumonia.[112] Other measures that may decrease the likelihood of nosocomial infection include the use of closed suction systems; use of disposable resuscitation bags; and high-level disinfection of ventilators, O_2 analyzers, and other equipment between patients.

Ventilator Malfunction

Ventilator malfunction can be categorized as a failure in the patient circuit or a failure in the ventilator. Failures in the patient circuit include failures related to the endotracheal tube: cuff rupture, main stem intubation, laryngeal intubation, esophageal intubation, soft tissue erosion because the cuff pressure is too high, and disconnection from the circuit. Failures in the tubing circuit include leaks anywhere there is a tubing connection; a leak at the site of a nebulizer or metered dose inhaler (Fig. 47.21); humidifier malfunctions that include failure to fill the reservoir, overheating, or mechanical failure; and exhalation valve failure.

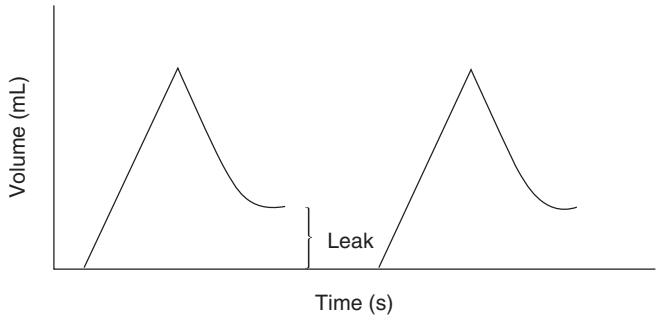

Fig. 47.21 Volume-Time Waveform Illustrating a Leak in the Ventilator Circuit. Note the abrupt end of expiration before the tracing reaches the baseline.

These failures are recognized by the ventilator as changes in respiratory rate, airway pressure, or V_T outside the limits set on the alarms.

Airway and ventilator malfunctions can be avoided with proper care of the endotracheal tube (taping the tube snugly), ensuring equal breath sounds, checking to ensure the tubing is patent and free of leaks, and ensuring that all connections are firmly made. If patient activity is the cause of ventilator disconnection, patient teaching to refrain from attempting to disconnect the ventilator or pulling on or biting the tube or sedation or restraint may be necessary. Failures related to the ventilator include electrical failure, microprocessor failure, exhalation valve failure, internal volume leakage, gas supply failure, and any failure that could result in an increase or decrease in minute ventilation or FiO_2. Ventilators have alarms that alert the RT to these dysfunctions.

Patient safety is always the primary concern when a malfunction is detected. For this reason, a manual resuscitator always should be placed near the bedside. If the reason for the patient's distress is clear, such as disconnection at the endotracheal tube, the connection is reestablished, and patient comfort and ventilation are ensured. If the reason is not obvious, the patient is ventilated with a manual ventilator while the cause of the malfunction is investigated. The steps for managing sudden distress in a patient receiving ventilatory support are listed in Table 47.4.

RULE OF THUMB Always have a manual ventilator (bag-valve-mask device [Ambu bag]) at the bedside of a patient receiving mechanical ventilation. Ensure that the manual ventilator is connected to an O_2 source. If the patient is receiving PEEP, ensure that the manual ventilator is equipped with a PEEP valve that provides PEEP equivalent of that being administered to the patient with the ventilator. Keep the patient connection of the manual ventilator clean and covered and the valve free of secretions.

Operator Error

The provision of mechanical ventilation is highly complex, the equipment used is very sophisticated, and the potential options to be applied to a given patient increase each year. As a result, clinician error is an ongoing concern. To minimize the possibility of error, a clinician should never make an adjustment to a

TABLE 47.4 Causes of Sudden Respiratory Distress and Remedies in a Patient Receiving Ventilatory Support

Cause	Remedy
Patient Related	
Artificial airway problems	Assessment of cuff, airway position (see Chapter 37)
Pneumothorax	Chest tube insertion
Bronchospasm	Bronchodilator therapy
Secretions	Suctioning, tracheobronchial hygiene
Pulmonary edema	Therapy directed at cause of pulmonary edema
Auto-PEEP	Decreased minute volume, tracheobronchial hygiene, decrease in I:E
Abnormal respiratory drive	Therapy directed at cause, possible sedation or paralysis
Alteration in body posture	Repositioning of patient
Abdominal distention	Therapy directed at cause, insertion of nasogastric tube
Anxiety	Reassurance, anxiolytics, assessment of minute ventilation
Patient–ventilator asynchrony	Assessment of flow and sensitivity, auto-PEEP, change of mode to accommodate patient's pattern of ventilation
Ventilator Related	
System leak	Assessment of connections in the ventilator circuit
Circuit malfunction	Assessment of circuit with test lung, replace if necessary
Inadequate FiO_2	Assessment of SpO_2, assessment of FiO_2 with analyzer, increase in FiO_2, or replacement of blender or ventilator if malfunction is found
Inadequate ventilatory support	Review of therapeutic strategy for the patient (see Chapter 49)
Improper flow-trigger setting	Adjust trigger and flow to patient demand

PEEP, Positive end-expiratory pressure.

mechanical ventilator unless he or she has been properly trained to operate the ventilator and the clinician's skills at using the machine have been assessed by an independent evaluator. It is essential for the operator to document ventilator settings in a consistent manner and to understand the terminology used when documenting the ventilator–patient interaction charted in medical record. Appropriate operation of the mechanical ventilator should be assessed on a regular basis based on the severity and criticality of the patient's clinical presentation. To minimize errors, any adjustment should be checked to ensure that the appropriate change was actually made and that the patient responded as expected. A clinician should never leave the bedside of a patient until the clinician is assured that the patient is being ventilated as ordered and that the ventilator is responding as expected. Patient safety should always be the primary concern of all RTs.

SUMMARY CHECKLIST

- Response to an increase in FiO_2 helps to determine the cause of hypoxemia.
- Hypoxemia responsive to an increase in FiO_2 is likely caused by a low $\dot{V}/\dot{Q}$ ratio.
- Hypoxemia unresponsive to increased FiO_2 is likely caused by a diffusion defect or shunt.
- Alveolar ventilation and CO_2 production determine $PaCO_2$.
- Mechanical ventilation should increase alveolar ventilation and may decrease CO_2 production when WOB is relieved. These factors decrease $PaCO_2$.
- Mechanical ventilation with positive pressure increases dead space and increases $\dot{V}/\dot{Q}$ ratio.
- Inspiratory or expiratory time can be manipulated to improve oxygenation and alveolar emptying in disorders that affect alveolar time constants.
- Physiologic benefits of PPV include improved oxygenation and ventilation, alveolar expansion, decreased WOB and cardiac work, and improved O_2 delivery.
- No outcome differences have been identified among the various modes of ventilation except that SIMV prolongs the weaning process. However, modes of ventilation that allow the patient control over the process of gas delivery have been shown to improve patient–ventilator synchrony.
- No single flow pattern has been shown to be the most physiologically beneficial. However, research results indicate better oxygenation, ventilation, and patient–ventilator synchrony with the decelerating flow compared with the square wave flow pattern.
- A decelerating flow waveform tends to have a lower peak and a higher mean airway pressure, whereas a square wave tends to have a higher peak and a lower mean airway pressure.
- Flow triggering appears to decrease WOB compared with pressure triggering on older generation ventilators.
- PEEP is used to restore FRC in acute restrictive disease and to splint the airways in obstructive disease.
- WOB is decreased by the appropriate application of mode, trigger variable, and flow.
- PPV is detrimental to the $\dot{V}/\dot{Q}$ ratio primarily by shifting ventilation to areas that are less perfused. PPV can cause hyperventilation, tissue damage, and barotraumas if not carefully managed.
- PPV can decrease venous return and cardiac output, especially when it increases intrapleural and mean airway pressures.

- PPV can cause renal, hepatic, and gastrointestinal malfunction primarily owing to decreased perfusion of the capillary tissue beds.
- Elevation of the head, osmotic diuretics, and CSF drainage are effective means of decreasing ICP in TBI. Acute hyperventilation should be used only temporarily until other, more effective means can be used.
- Ventilator bundles should always be adhered to during mechanical ventilation to minimize the development of ventilator-associated pneumonia.
- Patient safety and error-free patient care are the first priority when caring for any patient.

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48

Patient–Ventilator Interactions

Robert M. Kacmarek

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Discuss the reasons why appropriate patient–ventilator interactions are critical to ensuring safe and effective mechanical ventilation
- Discuss those clinical issues that can result in poor patient–ventilator interaction
- Discuss and define the different types of asynchronies commonly observed during mechanical ventilation
- Discuss the control variables that affect appropriate patient–ventilator interaction and identify the modes of ventilation that are most likely to result in asynchrony
- Discuss the steps that should be taken to determine the cause and correction of asynchrony before sedation is considered
- Discuss what should be done to modify or eliminate flow asynchrony
- Discuss the setting of rise time during pressure-targeted ventilation
- Discuss what should be done to modify double triggering/reverse triggering
- Discuss what should be done to modify missed triggering
- Discuss what should be done to modify delayed triggering
- Discuss what should done to modify autotriggering
- Discuss the setting of expiratory cycling criteria during pressure support ventilation
- Discuss the reasons why proportional assist ventilation and neurally adjusted ventilatory assist modes are most likely to result in the least asynchrony
- Discuss the measurement of P_{100} during the patient–ventilator assessment to identify excessive ventilatory drive and modify approaches to ventilatory support

CHAPTER OUTLINE

KEY TERMS

atrophy
autotriggering
cycle asynchrony
diaphragmatic dysfunction
double triggering
fatigue
endobronchial intubation
expiratory cycling criteria
innominate artery rupture
missed triggering
mode asynchrony
neurally adjusted ventilatory assist (NAVA)
P_{100} or $P_{0.1}$
patient–ventilator asynchrony
proportional assist ventilation (PAV)
reverse triggering
rise time
tension pneumothorax
tracheal malasia
tracheal stenosis
tracheoesophageal fistula
trigger asynchrony
trigger delay

In general it is relatively easy to set and adjust the ventilator during controlled mechanical ventilation because the patient does not actively interact with the mechanical ventilator. Though rarely used, controlled mechanical ventilation is provided entirely as a result of the adjustments made by the managing clinician. This is not true during assisted patient-triggered ventilation or partial ventilatory support. In this setting the patient and the ventilator must interact intimately, the ventilator must be set to meet the patient's ventilatory demand, and the patient must be capable of adjusting to the settings of the ventilator. In many modes of mechanical ventilation the patient must follow the lead of the ventilator—that is, adjust to the way the ventilator is set and breathe with a ventilatory pattern that is consistent with the parameters defined by the mode of ventilation applied and the specific settings.[1,2] When this interaction is not good, **patient–ventilator asynchrony** occurs or the patient is characterized as "fighting the ventilator."[3] However, it must be noted that there are many other clinical/technical issues that can result in poor patient–ventilator interaction. In this chapter all aspects of patient–ventilator interaction are discussed with a focus on what should be done to improve the interaction. It is important to remember that sedation of the patient is **ALWAYS** the last intervention to be considered to improve patient–ventilator interaction. When sedation is used, it should be administered sparingly. The patient, airway, and ventilator should all be carefully assessed and necessary adjustments made before deciding whether sedation will be needed to improve patient–ventilator interaction.[3]

RULE OF THUMB Appropriate patient–ventilator interaction during patient-triggered assisted ventilation requires intimate coordination between the demands of the patient's respiratory center and the settings of the mechanical ventilator.

Patient–ventilator interaction refers to patient comfort, work of breathing (WOB), and synchrony during patient-triggered breaths. Generally, ventilatory support should be initially adjusted to minimize the WOB and to allow the ventilatory muscles to rest.[3,4] **Diaphragmatic dysfunction** often accompanies ventilatory failure, and a sustained increase in workload can lead to structural injury to the ventilatory muscles.[5] When the ventilatory muscles become fatigued, at least 24 hours is required for recovery.[6] At the other extreme, complete rest of the diaphragm, as in controlled ventilation, may lead to diaphragmatic deconditioning, weakness, and atrophy in 48 hours.[6] In the presence of spontaneous breathing, inappropriate ventilator settings may further increase patient work and **fatigue**.[2] However, careful selection of ventilator settings can reduce the workload to a normal range without resulting in deconditioning and **atrophy** of the respiratory muscles.[2]

EFFECTS OF POOR PATIENT–VENTILATOR INTERACTION ON OUTCOME

Regardless of the cause of the poor patient–ventilator interaction, the result is negative for the patient. At a minimum, hemodynamics, ventilatory pattern, and gas exchange are adversely affected. Patients may become hypotensive, hypertensive, tachycardic, or bradycardic. Their ventilatory pattern may markedly change to a rapid shallow pattern or they may attempt to inhale large tidal volumes (V_T) at a slow rate when their ventilatory drive is affected by pharmacologic agents. Normally, poor patient–ventilator interaction results in hypoxemia due to poor matching of ventilation and perfusion or increased true shunt. Both hypercarbia and hypocarbia may result, based on the stimulus. Those who experience hypoxemia will frequently respond with hyperventilation. However, if hemodynamic compromise is present, hypercarbia is normally the result.[3] The reason for this is an alteration in dead space. Any decrease in cardiac output will result in an increase in dead space, which promotes hypercarbia unless the patient has the ability to increase the minute ventilation.

Most causes of poor patient–ventilator interaction are of rather short duration because the continuation of the cause frequently has significant negative short-term effects. For example, a tension pneumothorax during mechanical ventilation must be corrected quickly or it will lead to cardiac arrest. Obstruction of the airway, even if only partial, normally results in marked changes in airway pressure or V_T, which should rapidly alert clinicians to the problem. Bronchospasm or pulmonary edema are usually rapidly recognized by the changes in clinical presentation and alterations in patient response to the ventilator. Patient–ventilator asynchrony is a more subtle problem that can be difficult to identify and can persist for the entire time that the patient is mechanically ventilated. Identification of asynchrony calls for a careful assessment of patient and ventilator waveforms and sometimes also a lengthy observation of waveforms. Although asynchrony is more subtle than other causes of poor patient–ventilator interaction, its effects in the long term can be very serious. Recent data indicate that asynchrony occurs in all patients receiving assisted patient-triggered ventilation, is most significant during the morning when clinician–patient interaction is greatest, is present even during periods of sedation, and varies from mild to very severe.[7] It is most important to remember that asynchrony has been associated with increased length of mechanical ventilation, length of stay in the intensive care unit (ICU), and length of hospitalization. The need for tracheostomy and ICU and hospital mortality are also increased.[7-10] At this time it cannot be said that asynchrony causes an increase in mortality, but patients who have high levels of asynchrony have greater ICU and hospital mortality than those who have lower levels of asynchrony. Therefore, a careful review of ventilator waveforms and ventilator settings should occur during every patient–ventilator assessment, and adjustments should be made to minimize the level of asynchrony every time the clinician assess a patient.

RULE OF THUMB Asynchrony has been associated with increased length of mechanical ventilation, ICU and hospital length of stay, the need for tracheostomy, and ICU and hospital mortality.

CAUSES OF POOR PATIENT–VENTILATOR INTERACTIONS

The primary causes of poor patient–ventilator interaction are listed in Table 48.1. It is important to note that most of these

TABLE 48.1 Causes of Poor Patient–Ventilator Interaction

Patient-Related Causes
Abnormal respiratory drive
Abdominal distension
Alteration in body posture
Artificial airway problems
Agitation
Bronchospasm
Drug-induced problems
Dynamic hyperinflation
Fever
Hemodynamic compromise
Hypoxemia
Pneumothorax
Pulmonary edema
Pulmonary embolism
Secretions
Ventilator-Related Causes
Circuit malfunction
Inadequate F_iO_2
Inadequate ventilator support
System leak
Patient–ventilator asynchrony

issues also result in sudden respiratory distress. Except for some forms of asynchrony, the causes listed in Table 48.1 can arise in patients under both controlled and assisted ventilated.

Change in Clinical Status

One of the primary causes of poor patient interaction with the mechanical ventilator is a change in the patient's clinical status.[3] Excessive secretions, bronchospasm, and agitation are the most common and regularly seen causes of poor patient-ventilator interaction, and these issues should be assessed at every patient–ventilator assessment. In addition, fever, hypoxemia, and hemodynamic compromise are also regular causes of poor patient–ventilator interaction (see Table 48.1). When these issues are present, the cause should be identified and rapidly corrected. In addition, artificial airway problems, pneumothorax, pulmonary edema, pulmonary embolism, dynamic hyperinflation, alterations of body position, drug administration, and abdominal distention can all cause poor patient–ventilator interaction.[3]

Artificial Airways

Artificial airway problems are a common cause of sudden respiratory distress. As outlined in Chapter 37, a number of problems can suddenly occur with artificial airways. Of primary concern is the development of biofilm on the internal surface of the endotracheal tube, as illustrated in Fig. 48.1. Biofilm develops on all endotracheal tubes. Extensive biofilm development on the inner surface of the endotracheal tube can markedly alter a patient's clinical presentation and also place him or her at higher risk for pulmonary infection.[11] Patients who are aspirating oral secretions around the endotracheal tube or who produce excessive secretions in the lower airway can easily develop obstructions

Fig. 48.1 An endotracheal tube with biofilm/secretions partially occluding greater than half of the airway. (From Mietto C, Foley K, Salerno L, et al: Removal of endotracheal tube obstruction with a secretion clearance device, *Respir Care* 59:e122–e126, 2014.)

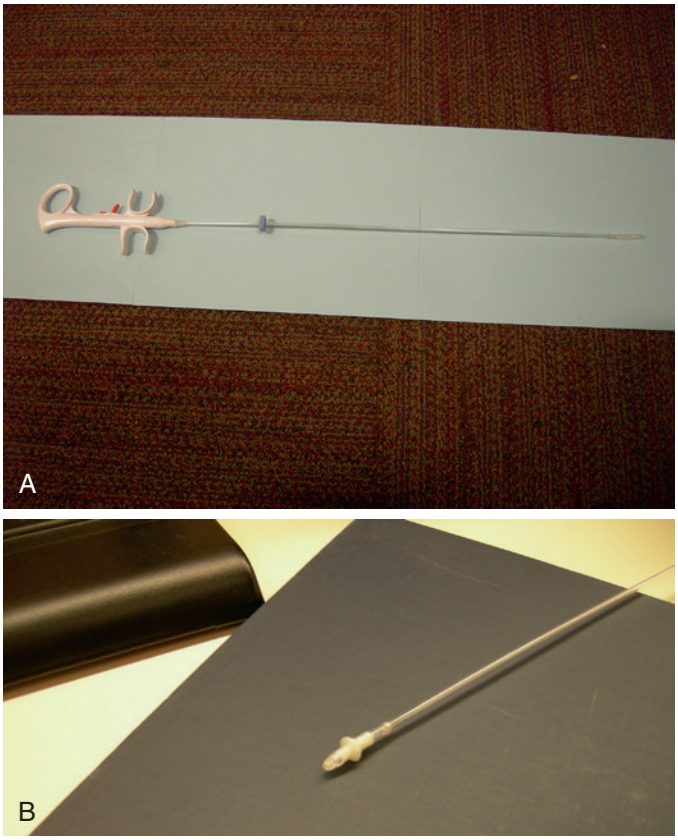


Fig. 48.2 (A) Picture of a mucus shaver device. This device is designed to remove biofilm/secretions from the inside of an artificial airway. (B) The dilated tip of the mucus shaver inflated to remove secretions.

that occupy more than 50% of the lumen of the endotracheal tube. This can rapidly progress to complete occlusion if proper humidification is not provided.[12] If the lumen of the endotracheal tube is almost totally obstructed, airway resistance markedly increases, resulting in an increase in peak airway pressure during volume ventilation and a decrease in V_T in pressure ventilation. This is an airway emergency requiring immediate action. Either the endotracheal tube must be changed or the secretions must be removed. A number of devices designed to remove secretions from the lumen of the artificial airway are currently on the market (Fig. 48.2). These "mucus shavers" can help to avoid the need to change the airway and can also dramatically improve ventilation.[13,14]

Another common problem with endotracheal tubes is movement of the airway into the oral pharynx or movement into the right mainstem bronchus. Thus it is important to determine the location of the endotracheal tube at each patient–ventilator assessment. Depending the patient's height, the tube should be positioned about 22 to 25 cm from the teeth (incisors) in men and about 19 to 23 cm from the teeth in women (see Chapter 37). In addition, following intubation, the location of the tip of the tube in relation to the carina must be evaluated. In adults, the tip of the tube should be 3 to 5 cm above the carina; its length at the teeth should also be noted and regularly reassessed to ensure proper placement.

A right mainstem intubation presents with sudden increases in airway pressure and absent breath sound on the left side of the chest. Depending on the patient's status, hypoxemia, hypercarbia, and hemodynamic compromise may be present. Careful movement of the tube to the proper position at the teeth corrects this problem. Following adjustment, however, a chest x-ray should always be taken to ensure proper positioning. Flexion and extension of the head and neck always results in movement of the tip of the endotracheal tube. Extension of the head and neck moves the tip closer to the carina and flexion moves the tip closer to the pharynx. This movement on average is 1 to 3 cm in either direction and can be as much as 7 cm.

Kinking of the endotracheal tube is also a potential problem. This usually occurs in a patient with a well-secured endotracheal tube that the patient is actively trying to move out of the airway by biting and "tonguing" the tube. This causes the tube to move toward the oral pharynx, but because it is well secured, it kinks. The result is increased airway resistance. Inability to pass a suction catheter more than a short distance into the airway and visualization of the tube in the mouth and pharynx identifies this problem. Repositioning of the tube is indicated. Differentiation of tube kinking from tube obstruction can be difficult, but biofilm and secretion obstruction usually occurs in the lower third of the airway and kinking the middle to the first third of the airway.

Long-term artificial airway placement can also result in the development of **tracheal stenosis**, **tracheal malasia**, **tracheoesophageal fistula**, and **innominate artery rupture**. Of these, innominate artery rupture is the most devastating. It requires surgical intervention and can be fatal. It is difficult to identify the problem until the rupture actually occurs. However, in some patients the tracheostomy tube will start to pulsate with eroding of the tracheal wall toward the innominate artery, allowing the pulse to be counted from the pulsation.

Pneumothorax

Another life-threatening situation during mechanical ventilation is the development of a pneumothorax, which in most circumstances is a tension pneumothorax. That is, with every positive-pressure breath, more gas moves into the pleural space but is unable to exit it. As a result, the pressure in the pleural space continues to increase, causing lung collapse and eventually complete cardiovascular collapse and cardiac arrest. Treatment is decompression of the pleural space and the placement of a chest tube, as described earlier.

A tension pneumothorax typically develops very rapidly. Airway pressure increases with each breath in volume ventilation, whereas V_T decreases with each breath in pressure ventilation. The change is more dramatic in volume ventilation than in pressure ventilation because, in pressure ventilation, the pressure in the pleural space can increase only to the peak pressure set by the clinician, whereas in volume ventilation pressure can increase to the pressure limit setting, which may be very high. As pressure increases, the affected side's lung collapses and begins to compress the unaffected side. In severe cases, the mediastinum and trachea are shifted away from the side with the pneumothorax. Patients rapidly become hemodynamically unstable. Breath sounds are absent on the side of the pneumothorax, the percussion note is hyperresonnant on the affected side, and palpation of the chest generally shows a rise and fall only of the side of the chest opposite the pneumothorax.

RULE OF THUMB A tension pneumothorax causes increasing airway pressure with each breath in volume ventilation and decreasing V_T with each breath in pressure ventilation. As pressure in the pleural space increases, lung collapse occurs.

Airway Emergencies

A rapid deterioration in the patient's clinical status associated with increased airway pressure and decreased V_T associated with progressive hemodynamic compromise and deteriorating gas exchange should always alert clinicians to the possibility of three problems: tension pneumothorax, airway obstruction, and right mainstem intubation. Box 48.1 lists the steps that should be taken to identify the cause of the problem. Removing the patient from the ventilator and manually ventilating (using an AMBU bag) with rapid shallow breaths will eliminate the ventilator as the cause of the concern. Rapid suctioning of the airway will determine if airway obstruction is the problem. If obstruction is not the problem, then **endobronchial intubation** or a **tension pneumothorax** is the cause. If assessment of the patient is consistent with a tension pneumothorax and the tube is at the correct length at the teeth, the problem is almost always a tension pneumothorax. Severe hemodynamic compromise and continued increasing of airway pressure are not normally seen in a right mainstem intubation.

BOX 48.1 Management of Sudden Respiratory Distress

1. Remove the patient from the ventilator.
2. Initiate manual ventilation using a self-inflating bag delivering 100% oxygen. If unable to ventilate, remove airway and bag-mask ventilate.
3. Perform a rapid physical examination and assess monitored indices.
4. Check patency of the airway (pass a suction catheter). If airway is completely obstructed, remove airway and bag-mask ventilate.
5. If death is imminent, consider and treat the most likely causes (e.g., pneumothorax, airway obstruction).
6. After the patient is stabilized, undertake more detailed assessment and management.

MINI CLINI

Management of Emergency Airway Issues

Problem

Mr. Smith is a 36-year-old victim of a motor vehicle accident presenting with massive head and chest trauma. He is immediately intubated in the emergency department and mechanically ventilated in the volume control mode. He has received sedation and paralysis and is ventilated with the following settings: V_T 500 mL (6 mL/kg predicted body weight [PBW]), rate 22/min, peak flow 40 L/min, inspiratory time 0.66 seconds, 10 cm H_2O positive end-expiratory pressure (PEEP), and an F_iO_2 of 60%. At these settings his SpO_2 is 95%, pulse is 78/min, and arterial blood pressure is 110/70. His peak airway pressure is 24 cm H_2O, and his plateau pressure is 18 cm H_2O. He has received a total of 4 L of fluid.

The respiratory therapist (RT) standing at the bedside observes a breath-by-breath increase in the patient's peak airway pressure, and the high-pressure alarm sounds at 50 cm H_2O. His SpO_2 has decreased to 88% and appears to be decreasing breath by breath. His pulse is 140/min and blood pressure is 80/50. The RT observes that the patient's trachea is deviated to the left, and on auscultation there are no breath sounds on the left. The percussion note is hyperresonant on the left side and on palpitation the RT notes a rise only of the right chest. What should be done?

Solution

Clearly some dramatic change in the ability to ventilate the patient has rapidly occurred. This presentation is most likely the result of an airway obstruction, a mainstem intubation, or a tension pneumothorax. Therefore the patient should immediately be disconnected from the ventilator and the endotracheal tube suctioned. This will eliminate obstruction of the airway and the ventilator as the problem. It is most likely not a mainstem intubation because most such intubations are into the right mainstem bronchus and the fact that breath sounds are absent on the right eliminates this. In addition, the patient's presentation is more consistent with a tension pneumothorax; rapid deterioration, hyperresonant on the affected side, deviated trachea way from the affected side, and an increase in peak airway pressure with each breath (see Chapter 16).

Immediate decompression of the chest with a 19-gauge needle is indicated, followed by insertion of a chest tube. Decompression is done by sliding the needle over the third rib at the mid-nipple line. Blood vessels and nerves run along the lower border of the ribs, not the upper border. During these procedures, very gentle ventilation with a manual ventilator should occur with 100% oxygen and a rapid shallow pattern minimizing pressure to avoid extending the pneumothorax.

The Mechanical Ventilator

A potential but infrequent cause of poor patient–ventilator interaction is malfunction of the mechanical ventilator. Poor responsiveness and ventilator circuit issues can be a problem, but with the newest generation of mechanical ventilators these technical malfunctions are rarely the cause of poor patient–ventilator interaction. However, the ventilator settings should be checked to ensure that an appropriate V_T, respiratory rate, and F_iO_2 are being delivered.

RULE OF THUMB The percentage of breaths on average that are asynchronous is about 3%, but at some periods of time in some patients over 50% of the breaths may be asynchronous![7]

VARIABLES CONTROLLED DURING MECHANICAL VENTILATION

During spontaneous ventilation the individual has complete control over the process of gas movement into and out of the lungs. In health, normal breathing is a process that generally goes unnoticed; we breathe without conscious thought of breathing and without any effort. As we know from the equation of motion (discussed in detail in Chapter 47), all of the WOB is provided by the individual during spontaneous breathing. During controlled ventilation the patient has absolutely no control over the process of ventilation. The ventilator moves gas into and out of the lungs based on how the clinician decides to set the mechanical ventilator. Thus, from the patient's perspective, no active work is performed and no concern exists for coordination between what the respiratory center desires versus how the clinician sets the ventilator. Of course, to achieve controlled ventilation, the patient must be pharmacologically medicated to apnea. Assisted mechanical ventilation is very different from either spontaneous breathing or controlled ventilation. In this case the patient and the ventilator must intimately interact. Ideally the ventilator is set to meet the neurologic output from the respiratory center and there is no competition between the respiratory center and the ventilator. However, this is rarely achieved in critically ill patients. The percentage of breaths on average that are asynchronous is about 3%, but during select time periods in some patients over 50% of the breaths are asynchronous.[7]

TABLE 48.2 Variables Controlled During Different Modes of Mechanical Ventilation Possible Variables Controlled: Pressure, Flow, Volume, and Time

Volume A/C	Volume
	Flow
	Time
Pressure A/C	Pressure
	Time
Pressure support	Pressure
PAV and NAVA	None

A/C, Assist/control; *NAVA*, neurally adjusted ventilatory assist; *PAV*, proportional assist ventilation.

Generally, the more control exerted by the ventilator, the greater the likelihood that the patient will be asynchronous.[15-17] With the classic modes of ventilation, the ventilator leads and the patient must follow. Specifically, if the clinician sets the inspiratory time at 1.0 second or the V_T at 400 mL, this is what the patient must accommodate to. This accommodation is difficult, and as a result, asynchrony occurs. Depending on the mode of ventilation, the ventilator can control one or more of the following gas delivery variables: pressure, flow, volume, or time (Table 48.2). The more variables controlled, the greater the likelihood of asynchrony. Volume ventilation is the most controlling mode of ventilation because the ventilator in some way controls volume, flow, and time. The only variable the patient can control is pressure. As a result, the likelihood of asynchrony is greater with volume assist/control (A/C) than with any other mode of ventilation. With pressure A/C, the ventilator controls only pressure and time; less control means less likelihood of asynchrony. In pressure support, only the pressure is controlled; thus, of all the classic modes of ventilation, the mode that is least likely (if set properly) to cause asynchrony is pressure support. However,

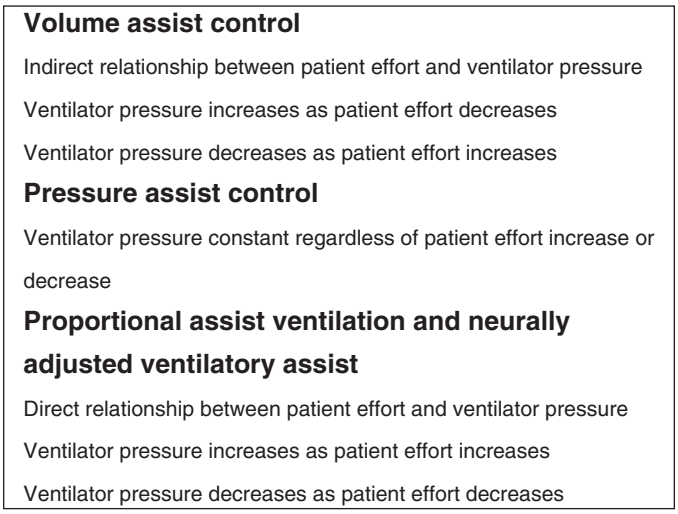


Fig. 48.3 Ventilator Modes: Relationship Between Ventilator Pressure and Patient Effort During Various Forms of Ventilatory Support. Proportional assist ventilation and neurally adjusted ventilatory assist present the ideal relationship between patient effort and ventilator pressure. As patient effort increases, ventilator pressure increase, and as patient effort decreases, ventilator pressure decreases. With pressure ventilation, ventilator pressure is constant regardless of change in patient effort. Volume ventilation establishes an inverse relationship between patient effort and ventilator pressure. As patient effort increases, ventilator pressure decreases, and as patient effort decreases, ventilator pressure increases.

as is well documented in the literature,[18-23] **proportional assist ventilation (PAV)** and **neurally adjusted ventilatory assist (NAVA)** are the modes of ventilation that are least likely to cause asynchrony because they do not exert any control over the patient. These modes do not control pressure, flow, volume or time. What they do is provide a proportional assist based on patient demand (see Chapters 46 and 47). They do not require the patient to conform to the settings of the clinician, but instead they require the ventilator to follow the output of the respiratory center, and as a result the patient's respiratory center controls the ventilatory pattern—thus, less asynchrony.[18-23]

Fig. 48.3 discusses the response of different modes of ventilation to patient demand.[24] As noted, when patient demand (effort) increases in volume ventilation, the ventilator provides less support; that is, an inverse relationship between patient effort and ventilator pressure is established. In pressure ventilation, when patient demand increases, the ventilator support remains unchanged. However, in PAV and NAVA, as patient effort increases, ventilatory support increases, and as patient effort decreases, ventilatory support decreases.[22,24] Control is by the patient's respiratory center, creating greater synchrony than any other approaches to ventilatory support.

RULE OF THUMB The ventilator can control one or more of the following gas delivery variables: pressure, flow, volume, or time. The more of these variables controlled by the ventilator, the greater the likelihood of asynchrony.

TYPES OF ASYNCHRONY

Table 48.3 lists the types of asynchrony. **Flow asynchrony** occurs when the flow from the ventilator does not match the flow demand of the patient.[25-29] This can occur in any mode of ventilation but most commonly occurs in volume ventilation because the clinician sets the V_T, peak flow, flow waveform, and inspiratory time. Thus, the patient's respiratory center must demand exactly the same gas delivery each and every breath that equals that set on the ventilator, or there will be flow asynchrony.

TABLE 48.3 Types of Asynchrony

Flow asynchrony	Inadequate flow at onset and during inspiration to meet patient demand, can induce lung injury if not corrected.	
Trigger asynchrony	Poor coordination of patient's initiation of inspiration and ventilator response. Double triggering can induce lung injury.	Trigger delay Double trigger Missed trigger Autotrigger Reverse triggering
Cycling asynchrony	Poor coordination of patient's desire to exhale and ventilator response.	Inappropriately short inspiratory time, Inappropriately long inspiratory time
Mode asynchrony	Inappropriate mode	

There are several forms of **trigger asynchrony**, and each can occur in any mode of ventilation. The most common form of trigger asynchrony is **trigger delay**, in which the length of time between the beginning of neuro-inspiration and activation of the ventilator is excessive.[29] Under normal circumstances, trigger delay should not exceed 100 ms to avoid patient perception of the delay and an increase in ventilatory drive.[29-31] Another common form of trigger asynchrony is **missed triggering**, in which the patient is unable to trigger the ventilator with each inspiratory effort. Frequently a pattern of missed triggering and triggering is established.[32-34] That is, for every two or three inspiratory efforts, the ventilator is triggered only once.[31-34] **Double triggering** is usually a result of the patient's ventilatory center desiring a larger breath or a longer inspiratory time than is set on the ventilator.[35] This causes the patient to continue inspiration when the ventilator transitions into the expiratory phase, resulting in the ventilator triggering a second time. The biggest problem with double triggering is that there may be no exhalation after the first breath, so that the actual delivered V_T may be up to double what is set on the ventilator. Double triggering is most common with volume A/C because of the precise setting of the V_T. **Autotriggering** is a much less frequent form of trigger asynchrony. It is the seemingly automatic triggering of the ventilator without any patient inspiratory effort.[36]

The most recently described from of trigger asynchrony is **reverse triggering**. With reverse triggering a controlled mechanical breath results in stimulation of the respiratory center, which then triggers the subsequent breath.[37,38] This form of asynchrony occurs only during controlled ventilation. Most of the other forms of asynchrony occur only during assisted ventilation.

Cycle asynchrony occurs when the ventilator ends the breath at a time different from when the patient's respiratory center wants to end the breath.[39-42] It is more common in pressure-targeted than in volume-targeted ventilation, but it can occur

TABLE 48.4 Causes of Asynchrony

Inappropriately Set Sensitivity	
Inappropriately set PEEP	If inadequate, atelectasis inducing greater patient effort
Auto-PEEP	Causes missed triggering
Volume A/C	Inadequate peak flow
	Inappropriate inspiratory time
	Inadequate or excessive V_T
Pressure A/C or pressure support	Inappropriate rise time
	Inappropriate inspiratory time or inappropriate inspiratory termination criterion
	Inadequate or excessive driving pressure
Inappropriate mode of ventilation	Patient unable to tolerate mode of ventilation without excessive ventilation asynchrony

A/C, Assist/control; PEEP, positive end-expiratory pressure; V_T, tidal volume.

in all modes of ventilation. Cycle asynchrony is described in two forms: asynchrony that results in an inappropriately long inspiratory time, and asynchrony that results in an inappropriately short inspiratory time.

Mode asynchrony is the selection of a mode of ventilation that is highly unlikely to meet a patient's inspiratory demand. As should be obvious from Table 48.2, during assisted ventilation it is most likely that mode asynchrony will occur with volume A/C, followed by pressure A/C, and then pressure support. It is least likely to occur with PAV and NAVA.[18-22,43]

CAUSES OF ASYNCHRONY

Table 48.4 summarizes the major causes of asynchrony. Across all modes of ventilation, inappropriately set sensitivity, inappropriate selection of PEEP, and the presence of auto-PEEP result in asynchrony. The one exception to this is NAVA; because NAVA is controlled by the diaphragmatic electromyographic (EMG) signal, the presence of auto-PEEP does not affect the function of this mode.[34] All other modes are triggered by airway pressure, flow, or volume and are dramatically affected by auto-PEEP. In volume ventilation, poor matching of the ventilator settings to the patient's ventilatory drive results in asynchrony. Specifically, inadequate peak flow and inadequate or excessive inspiratory time result in asynchrony. In pressure A/C or pressure support ventilation, asynchrony is caused by inappropriately set rise time, inappropriately set inspiratory time (pressure A/C) or termination criteria (pressure support), and inadequate or excessive V_T. Finally, selection of an inappropriate mode can cause asynchrony (see Chapters 47 and 49).

RULE OF THUMB Asynchrony is a result of inappropriate matching of the ventilator's settings and the patient's ventilatory demand or the presence of auto-PEEP.

FLOW ASYNCHRONY

Volume Ventilation

Flow asynchrony can occur in any mode of ventilation but is more common in volume A/C because a precise flow pattern

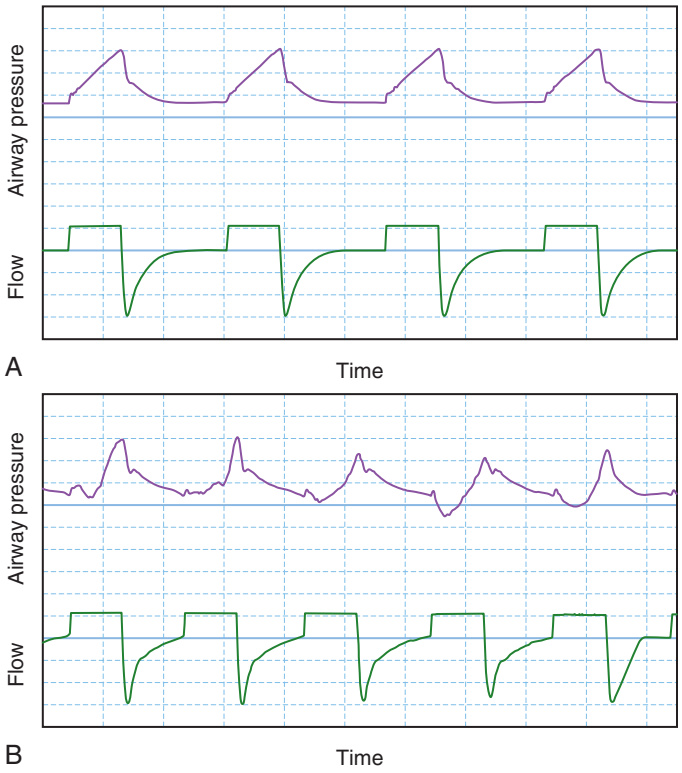


Fig. 48.4 Flow Asynchrony During Volume Assist/Control. (A) Airway pressure and flow waveforms during controlled volume ventilation. Note the linear increase in airway pressure over time. (B) Same patient with severe flow asynchrony during patient-triggered ventilation. The ventilator is not able to meet patient demand, resulting in a markedly altered airway pressure waveform. The difference between the area under the airway pressure-versus-time waveforms (A and B) is equal to the work of breathing preformed by the patient during patient-triggered ventilation.

and peak flow is set, resulting in the selected V_T being delivered in a precise inspiratory time. This is not physiologic; with normal spontaneous breathing, there is a large variability in the ventilatory pattern from breath to breath.

If a patient is spontaneously triggering the ventilator, peak flow delivery during volume ventilation should match the patient's inspiratory flow demand.[25,26] Most adult patients with moderate to strong ventilatory demands require a peak flow of 60 L/min or greater. As shown by Marini and colleagues,[25,26] if the peak flow does not meet the patient's inspiratory demand, the WOB performed by the patient increases (Fig. 48.4). In this setting, the efficiency of the work may be greater than during spontaneous breathing, but the overall patient work may be similar.[25,26] In volume ventilation, there is always an indirect relationship between the work provided by the ventilator and the patient's WOB (see Fig. 48.3). The more work the patient does, the less work the ventilator performs for the patient. If the patient is triggering the positive pressure breaths, the WOB is shared between the patient and the ventilator. For this reason, patients initially receiving assisted ventilation show altered gas delivery patterns after they are sedated to apnea. With the transition to controlled ventilation, the peak airway pressure usually increases during volume ventilation.[44] Because the patient no longer performs a portion of the WOB, the work performed by the ventilator

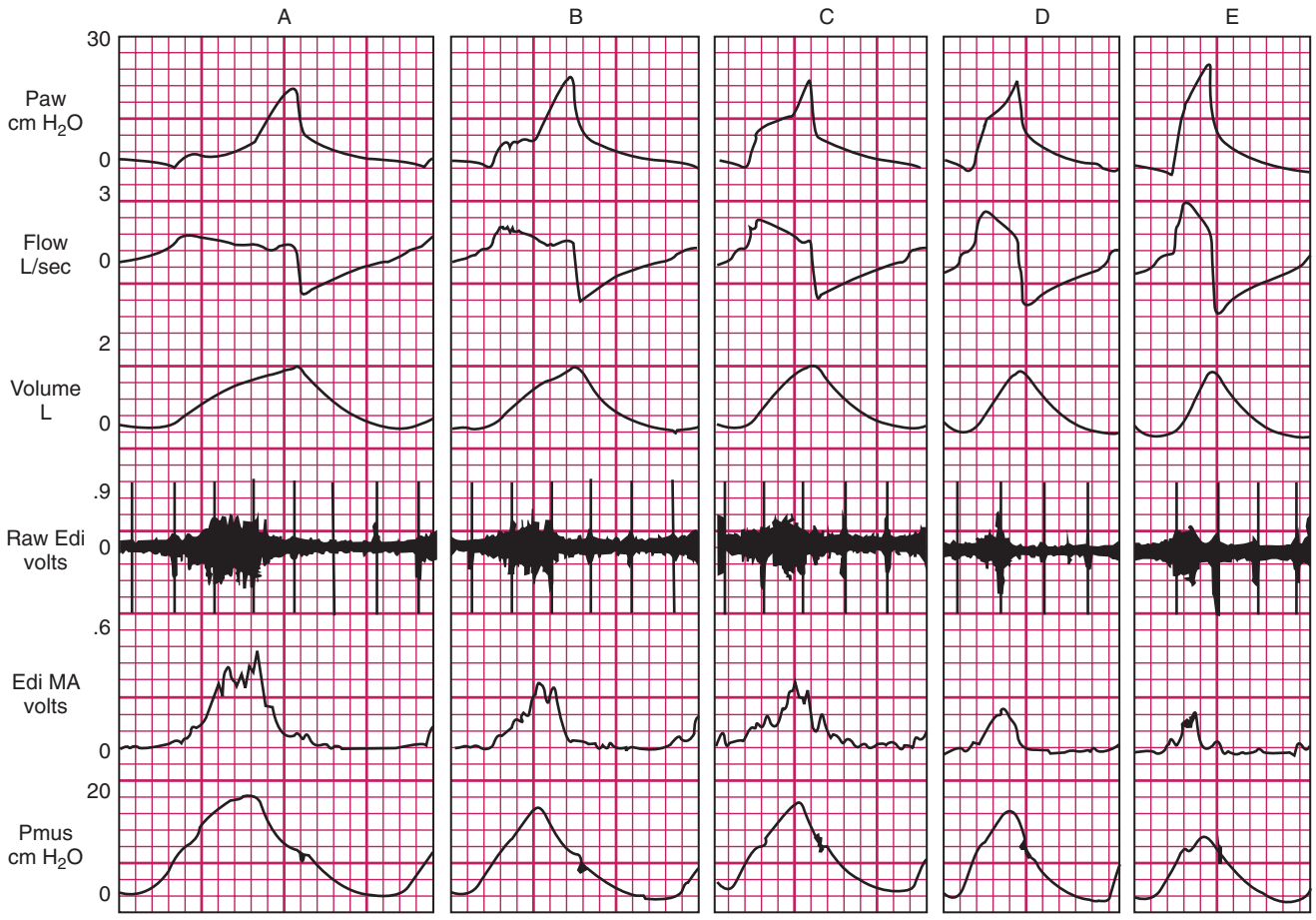


Fig. 48.5 Airway pressure *(P_{aw})*, flow, volume, raw *(R_{aw})* electromyographic activity of the diaphragm *(E_{di})*, integrated E_{di}, and muscular work of the diaphragm *(P_{mus})* in volume ventilation during varying inspiratory flow and inspiratory time settings (columns *A, B, C, D, E*). As peak flow is increased and inspiratory time is decreased (left to right), indices of patient effort and work are decreased. Ideal settings of flow and inspiratory time generally can be identified by observing the airway pressure curve during volume ventilation. The closer the airway pressure curve is to the ideal curve (*D* and *E*), the less the patient's work. (From Fernandez R, Mendez M, Younes M: Effect of ventilator flow rate on respiratory timing in normal humans, *Am J Respir Crit Care Med* 159:710–719, 1999.)

must increase. The opposite is also true in volume ventilation when the patient's ventilatory demand is high—the patient can be doing a disproportionate amount of work if the ventilator is not set to meet the patient's inspiratory demand.

Most ventilators during volume A/C can deliver gas flow in a decelerating or square-wave flow pattern. If the patient is triggering inspiration, we recommend a decelerating flow pattern, especially when a small V_T is being delivered.[44,45] A decelerating flow pattern allows a high peak flow to be delivered but also ensures that the inspiratory time can be adequately set. In patients who are sedated and who are not triggering the ventilator, the choice of flow waveform is unimportant, and the setting of peak flow depends on the inspiratory time and V_T desired by the clinician.

If a patient is triggering every breath, the set inspiratory time should equal the patient's neuro-inspiratory time.[46] As illustrated in Fig. 48.5, when the ventilator's inspiratory time is decreased to equal the patient's desired inspiratory time and peak flow is increased to match the patient's demand, the patient's WOB and effort correspondingly decrease (Box 48.2). This improvement in asynchrony can be performed without changing the V_T, as illustrated in Fig. 48.5. A patient with a moderate to high ventilatory demand rarely desires an inspiratory time greater than 1 second.[44] Many adults with moderate or high ventilatory demands desire an inspiratory time between 0.6 and 0.9 second.[45] Carefully matching the ventilator's inspiratory time with the patient's inspiratory time generally markedly improves patient–ventilator synchrony.

BOX 48.2 Flow Asynchrony: Volume Ventilation

To correct flow asynchrony:

- Change to decelerating flow
- Increase peak flow (>60 L/min)
- Match ventilator's inspiratory time to patient's inspiratory time
- Ensure that the airway pressure waveform is as similar as possible to the ideal airway pressure waveform during controlled volume ventilation
- Change to a pressure-targeted mode of ventilation

In general, the airway pressure waveform during volume A/C ventilation should be similar to the airway pressure waveform during controlled ventilation except for a slight dip in pressure at the start of the breath indicating patient triggering (see Fig. 48.4). The more the actual waveform differs from the ideal, the greater the patient WOB and the greater the asynchrony.[25,26] If the ventilator cannot be set to meet patient demand and all other potential causes of asynchrony have been ruled out, the patient will require sedation or a change in the mode of ventilation. In general, the mode should be changed before the patient is sedated.

RULE OF THUMB Flow asynchrony can occur in any mode of ventilation but is more common in volume A/C; since a precise flow pattern and peak flow are set, the selected V_T are delivered in a precise inspiratory time.

Pressure Ventilation

Flow asynchrony occurs in pressure ventilation but it is less likely than in volume ventilation if the ventilator is set properly. All newer-generation critical care ventilators include an inspiratory pressure **rise time** or pressure slope control. This control functions only with pressure-limited breaths (pressure support ventilation [PSV], pressure control ventilation [PCV], pressure regulated volume control [PRVC], volume support, airway pressure release ventilation, pressure synchronized intermittent mandatory ventilation [SIMV]). The purpose of this control is to adjust the rate at which flow increases from baseline to peak (Fig. 48.6).[46-48] Generally, rise time should be set at a value that ensures adequate inspiratory gas flow (meeting or exceeding patient demand) without an excessive "overshoot" of the pressure at the beginning of inspiration. A slow or low rise time increases the patient's WOB (Fig. 48.7).[46-48] If the rise time is inadequate to meet the patient's demand, a concavity during the initial part of inspiration is noted, similar to what occurs in volume A/C with inadequate flow.[49] As in volume ventilation, the rise time should be set to ensure that the actual airway pressure waveform matches the ideal airway pressure waveform (Box 48.3).

RULE OF THUMB Flow asynchrony can be greatly improved in volume ventilation by increasing peak flow and decreasing inspiratory time. In pressure ventilation, flow asynchrony can be corrected by adjusting rise time.

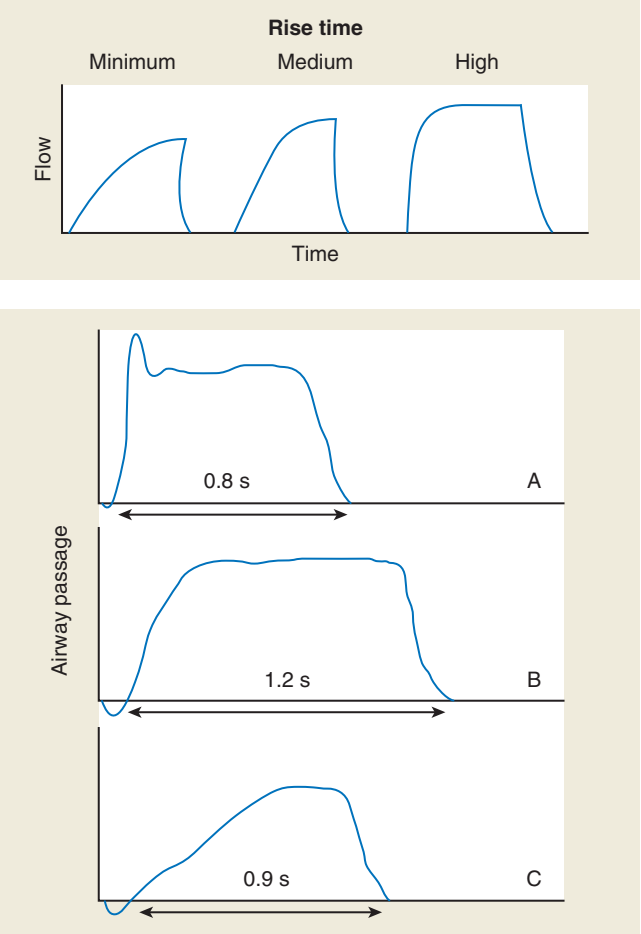


Fig. 48.6 The Effect of Different Rise Time Settings. When rise time is adjusted, the slope of the flow acceleration from zero to peak flow is altered. A slow rise time indicates that peak flow will not be achieved until some time after the midpoint of the breath. A high rise time indicates that peak flow will be obtained early in the breath. A medium rise time is somewhere in between. The actual setting variation depends on the ventilator's manufacturer.

BOX 48.3 Flow Asynchrony: Pressure Ventilation

To correct flow asynchrony:

- Adjust rise time until the initial airway pressure rises rapidly without any concavity but does not exceed the set pressure at the beginning of inspiration.
- If inadequate flow: initial concavity in airway pressure, increase rise time.
- If excessive flow: initial airway pressure exceeds the set level, decrease rise time.

TRIGGER ASYNCHRONY

As noted in Table 48.3, there are numerous types of trigger asynchrony; of these, missed triggering is a common cause of asynchrony. However, the single most important variable affecting trigger asynchrony is the presence of auto-PEEP.

Auto–Positive End-Expiratory Pressure/Missed Triggering

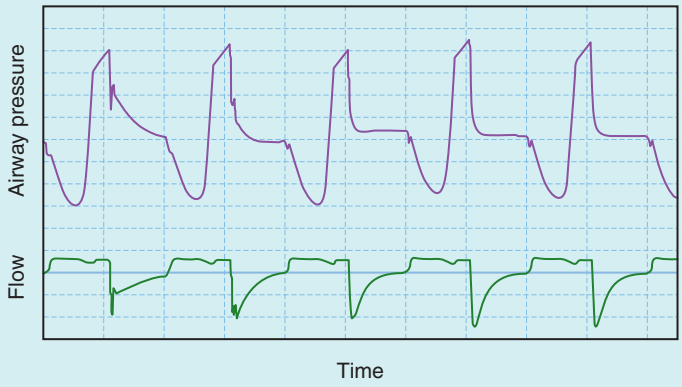
As illustrated in Fig. 48.8, auto-PEEP is a result of air trapped in the lung at the end of exhalation.[50] It can be measured in most ventilators by performing an expiratory pause. Auto-PEEP is most commonly caused by dynamic airway obstruction,[51] but it is also caused by an expiratory time that is too short (and inspiratory time that is too long) or the delivery of excessive minute ventilation/V_T.[52] In dynamic airway obstruction, because of airway disease, the structural integrity of the airways is compromised. A loss of smooth muscle causes the airway diameter to change from inspiration to expiration. During expiration the elastic recoil of the lung and thorax causes these damaged airways to at least partially collapse and in some cases totally collapse, trapping gas behind the obstruction or limiting flow to the point that at end-exhalation there is gas in the lung periphery under pressure or the presence of auto-PEEP.[50,51] The presence of auto-PEEP is not uniform. In some lung units no auto-PEEP is present, and in

MINI CLINI

Assist/Control Volume Ventilation, Square Wave

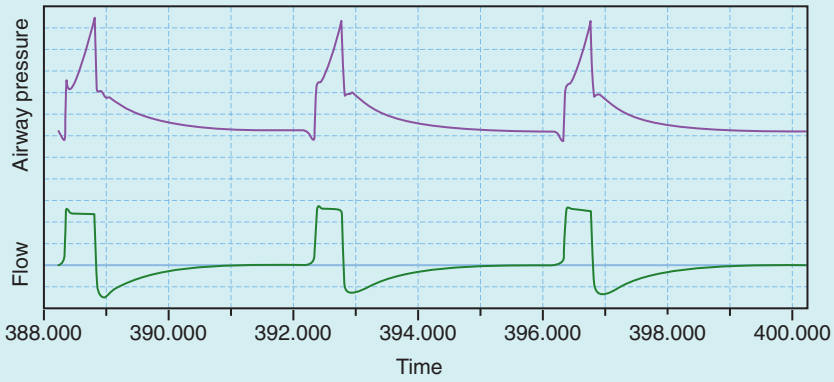
Problem

Mrs. Jones, who is 68 years old, has chronic obstructive pulmonary disease (COPD). She presented in the emergency department with an acute exacerbation and was initially managed with noninvasive pressure support at 8 cm H_2O PEEP. However, after 24 hours she was intubated and mechanically ventilated in volume A/C. She was started at a V_T of 300 mL (5 mL/kg PBW) with an inspiratory time of about 1.0 s and a peak square-wave flow of 20 L/min. Her PEEP level is set at 8 cm H_2O and F_iO_2 at 50%. Her SpO_2 is 90%, pulse 120/min, blood pressure 150/100, and respiratory rate 30/min. You study her airway pressure and flow waveforms and observe the following:



Solution

The shape of the airway pressure-versus-time curve would indicate that there is marked flow asynchrony. The airway pressure during triggering is below baseline for a considerable period of time and the rise in the airway pressure curve is concave and does not reach peak pressure until more than halfway through the inspiratory time. To try to correct this, peak flow should be increased to 50 L/min and the inspiratory time decreased to 0.6 s. When this is done, the following airway pressure and flow waveforms are obtained. These much more closely resemble the ideal waveforms during controlled ventilation.



others there are varying levels of auto-PEEP. When auto-PEEP is measured, the average level of auto-PEEP is determined.

Auto-PEEP can develop in any patient who is mechanically ventilated if the minute ventilation/V_T is excessive and cannot be passively exhaled in the expiratory time defined by the respiratory center.[52] Auto-PEEP essentially has the same effect as applied PEEP but only in the lung units where auto-PEEP develops. In reference to asynchrony, auto-PEEP is the primary reason why missed triggering occurs. Essentially the patient cannot decompress the auto-PEEP with every inspiratory effort, and missed triggering occurs. In patients with COPD, auto-PEEP can be greater than 15 cm H_2O and frequently shows a pattern of one triggered breath to one, two, or three missed triggered breaths (Fig. 48.9).[53]

RULE OF THUMB The primary cause of missed triggering is auto-PEEP. This is normally corrected by decreasing minute ventilation and/or increasing expiratory time. But in the patient with chronic airway obstruction, PEEP is applied to minimize the effort needed to trigger the ventilator.

Applied PEEP has been advocated in the presence of auto-PEEP when the cause of the auto-PEEP is dynamic airway obstruction.[51] In this setting, applied PEEP in the presence of auto-PEEP is indicated only if the patient has difficulty triggering the ventilator. Because the patient is breathing spontaneously, the measurement of auto-PEEP (end-expiratory pause) is very difficult; the patient frequently forces exhalation, negating the measurement. The presence of auto-PEEP is generally indicated by the

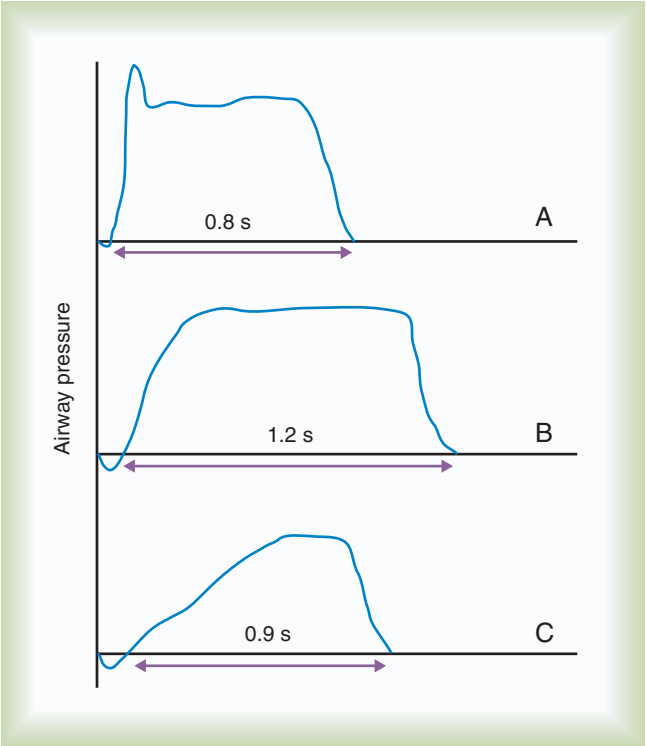


Fig. 48.7 Effect of Changing Rise Time During Pressure-Targeted Breaths for a Patient Who Prefers a Moderate Flow. (A) Flow exceeds patient demand; a pressure spike and short inspiratory time result. (B) As flow decreases, inspiratory time lengthens and the pressure spike disappears. Machine output matches patient demand. (C) When flow is reduced further, patient demand exceeds machine flow; the result is deformation of the pressure waveform and a decrease in inspiratory time. (Modified from Branson RD, Campbell RS, Davis K, et al: Altering flow rate during maximum pressure support ventilation [PSV_{max}]: effect on cardiorespiratory function, *Respir Care* 35:1056–1069, 1990.)

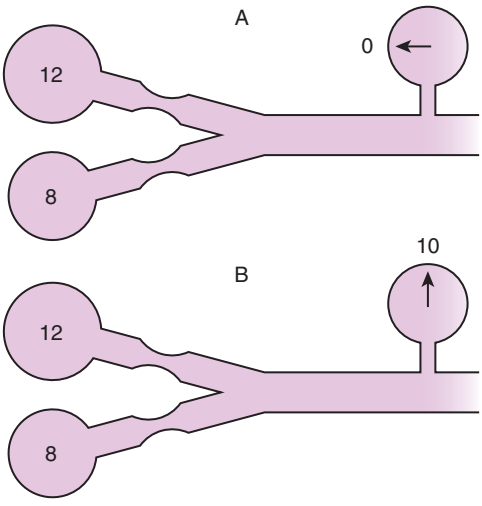


Fig. 48.8 (A) Two alveoli with different auto-PEEP levels and no end-expiratory pause. (B) The same alveoli with an end-expiratory pause. Note that in (A) the end-expiratory pressure is zero, since the system is open at end exhalation, whereas in B the average auto-PEEP level (10 cm H_2O) is indicated on the manometer because of the end-expiratory pause.

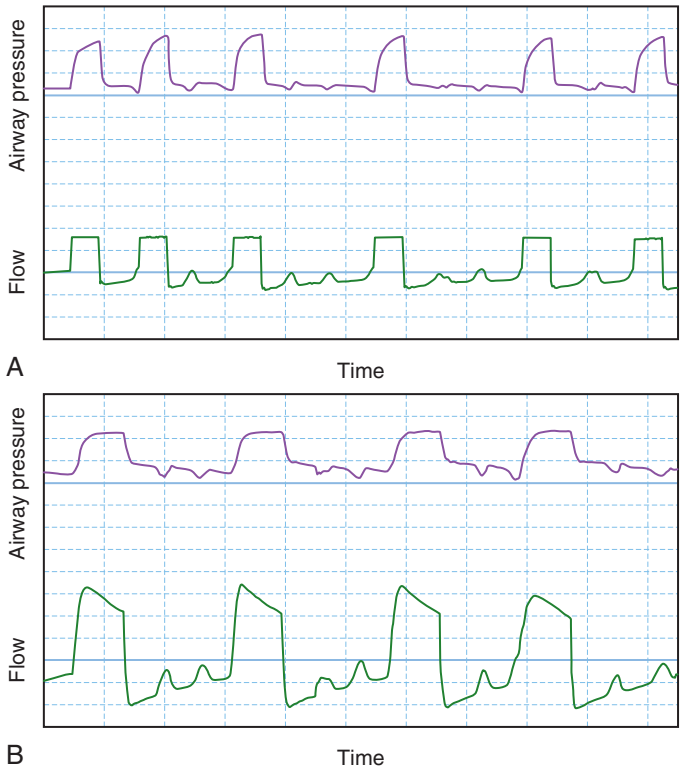


Fig. 48.9 Missed triggering during volume assist/control (A) and pressure-support ventilation (B). Arrows indicate missed triggered breaths.

expiratory flow waveform (Fig. 48.10) and the fact that there are missed triggered breaths. That is, the patient inspires but is unable to trigger the ventilator. In this case, PEEP is slowly applied in increments of 1 to 2 cm H_2O, rechecking the patient and ventilator response with each adjustment. When the patient is able to trigger the ventilator with each inspiratory effort, the PEEP level is set properly.[51] The exact auto-PEEP level may never be known in these patients; however, this is unimportant. What is important is that each patient effort triggers the ventilator. Research indicates that if the amount of PEEP applied does not exceed approximately 80% of the measured auto-PEEP, the patient's lung mechanics are not affected by the application of PEEP.[53,54] Airway pressures and V_T should be monitored during the application of PEEP to ensure that intrinsic PEEP does not increase as PEEP is applied. With the application of PEEP, airway pressure (volume ventilation) should not increase and V_T (pressure ventilation) should not decrease unless intrinsic PEEP is increased. Box 48.4 summarizes methods for minimizing the effects of auto-PEEP. An absolute contraindication to applied PEEP is an uncontrolled tension pneumothorax. However, PEEP should be cautiously applied in any patient with severe intrinsic lung disease, hypotension, and/or elevated intracranial pressure. During controlled ventilation, increasing PEEP simply because of the presence of auto-PEEP is not indicated.

RULE OF THUMB In the presence of dynamic airway obstruction, the application of PEEP offsets the effect of auto-PEEP on missed triggering.

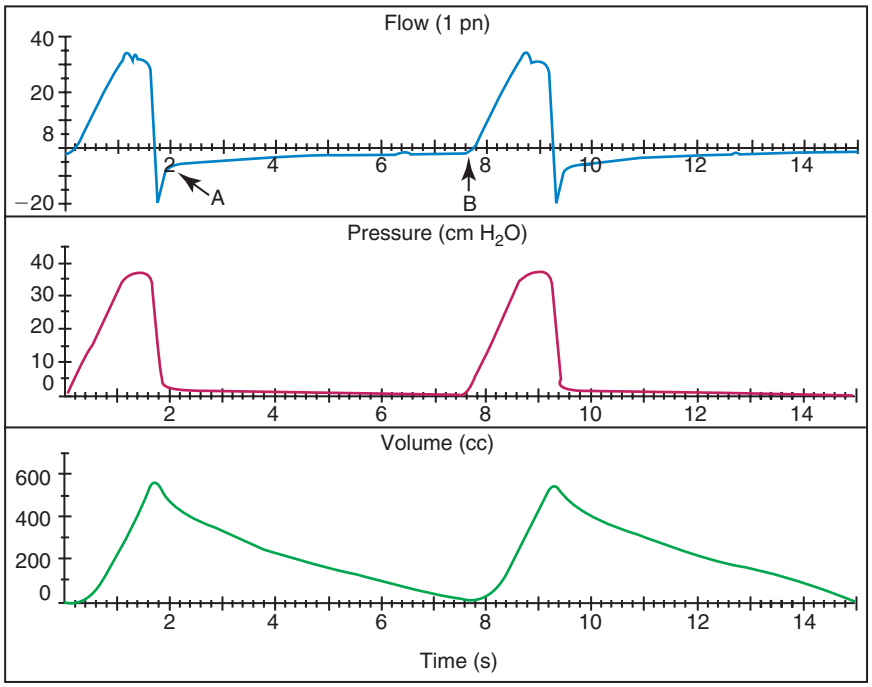


Fig. 48.10 Airway flow, pressure, and volume in a patient with severe airflow obstruction and auto-positive end-expiratory pressure (PEEP). There is a rapid decrease in expiratory flow at the onset of exhalation because of the obstruction *(arrow A)*, and there is a lack of return of flow to baseline at the end of the breath *(arrow B)*. This type of expiratory flow pattern, regardless of the expiratory time, indicates auto-PEEP. The amount of auto-PEEP cannot be determined from this example, but whenever end expiratory flow is greater than zero, auto-PEEP is present.

BOX 48.4 Techniques for Minimizing Effects of Auto-Positive End-Expiratory Pressure

- Decrease airflow obstruction
- Manage secretions
- Implement aggressive bronchodilation
- Use larger endotracheal tubes
- Modify ventilatory pattern, decrease minute ventilation/V_T /respiratory rate, and increase expiratory time
- Decrease inspiratory time
- Increase inspiratory flow (on ventilators with inspiratory peak flow control)
- Decrease percentage inspiratory time (on ventilators with % inspiratory time [T_i control)
- Decrease V_T
- Increase expiratory time
- Decrease rate
- Use low-compressible volume circuit
- Apply PEEP or CPAP to balance auto-PEEP in patients actively triggering ventilation

CPAP, Continuous positive airway pressure; *PEEP*, positive end-expiratory pressure; *V_T*, tidal volume.

In patients without intrinsic lung disease who develop auto-PEEP, dynamic airway obstruction is not present. Auto-PEEP is a result of excessive minute ventilation/V_T. Usually returning the V_T to the recommended 4 to 8 mL/kg PBW level eliminates the auto-PEEP and as a result the missed triggering.[52]

Outside of auto-PEEP the only other factor that can result in missed triggering is inappropriately set sensitivity. In general, sensitivity should be set as sensitive as possible without causing autotriggering. Should flow or pressure sensitivity be used? With older-generation ICU ventilators, pressure sensitivity was less effective than flow sensitivity.[55,56] But in today's generation of ICU ventilators, both function equivalently.[30] When both are set appropriately, neither should be the cause of missed triggering.

RULE OF THUMB Excessive minute ventilation/V_T in patients without dynamic airways obstruction results in auto-PEEP. Decreasing V_T to the range of 4 to 6 mL/kg PBW generally eliminates the auto-PEEP.

Trigger Delay

Trigger delay is caused by an inappropriately set sensitivity or when auto-PEEP is insufficient to cause mistriggering.[30,47] Normally the trigger delay should be minimal, less than 100 ms. When it exceeds 150 ms, the cause should be determined. Adjusting the sensitivity, setting the V_T appropriately, and/or applying PEEP should correct delayed triggering unless there is a true ventilator malfunction (Box 48.5).

Autotriggering

Setting the sensitivity control to be overly sensitive will cause autotriggering. In addition, autotriggering can be caused by the movement of water accumulated in the ventilator circuit. The back-and-forth movement of fluid in the circuit can cause triggering of the ventilator. Leaks in the ventilator circuit are the most likely cause of autotriggering. The most easily missed cause of autotriggering is in the patient who has undergone cardiac surgery and is in a hyperdynamic state.[36] Forceful contraction

MINI CLINI

Assist/Control Volume-Targeted Ventilation and Auto–Positive End-Expiratory Pressure

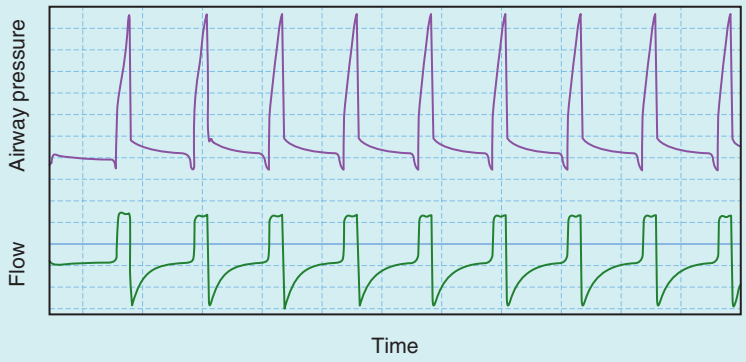
Problem

Mr. Garcia, 72 years old, has severe COPD. He has been intubated and mechanically ventilated for the last 3 days. The ventilator is set with a PEEP of 5 cm H_2O, F_iO_2 of 0.4 and an A/C V_T of 480 mL (6.5 mL/kg PBW). The ventilator's respiratory rate is 18/min. The patient's pulse is 105/min, blood pressure 130/90, and SpO_2 92%. When you look at the ventilator you notice the following airway pressure and flow waveforms:

In addition, when you palpate Mr. Garcia's diaphragm, you note that it is contracting at a rate of 36/min with the ventilator responding at a rate of only 18/min.

Solution

The expiratory flow does not return to baseline before the patient attempts to inspire. As a result, Mr. Garcia has auto-PEEP. To correct this, either Mr. Garcia's V_T should be decreased or applied PEEP should be increased. Since his V_T is at 6.5 mL/kg PBW it is unlikely that a further change will affect the level of auto-PEEP. Because he has dynamic airway obstruction from his severe COPD, adding PEEP to balance the auto-PEEP across the dynamic airway obstruction should decrease the pressure gradient to trigger the ventilator. PEEP should be increased in 1 to 2 cm H_2O steps until Mr. Garcia can trigger the ventilator with every inspiratory effort. At an applied PEEP level of 12 cm H_2O the mistriggering disappeared.



BOX 48.5 Correcting Trigger Delay

Trigger delay is caused by
- Auto-PEEP
- Poor sensitivity setting
- Ventilator malfunction

Corrected by
- Minimizing auto-PEEP
- Apply PEEP
- Decrease minute volume/V_T
- Appropriately set sensitivity
- Replace ventilator

PEEP, positive end-expiratory pressure; *V_T*, tidal volume.

of the heart can trigger the ventilator. Careful assessment of diaphragmatic contraction and readjustment of the sensitivity setting are indicated (Box 48.6).

Double Triggering

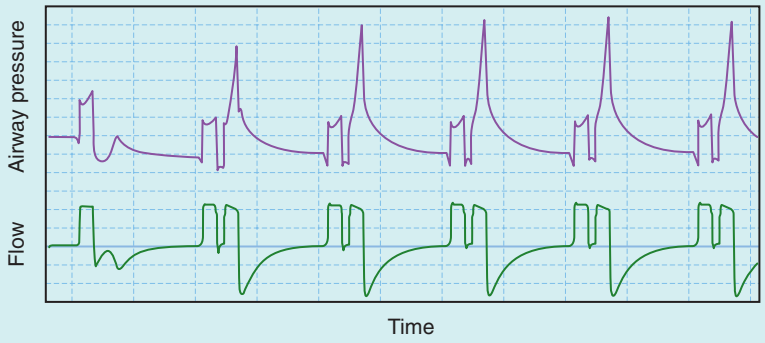
Double triggering most commonly occurs in volume A/C when the V_T delivered is less than the patient demands or the inspiratory time set on the ventilator is less than the neuro-inspiratory time.[37] Double triggering is a problem because, as demonstrated in Fig. 48.11, in most cases of double triggering there is no exhalation between the two breaths. Thus, the V_T during the double-triggered breath is twice the set V_T. A patient with a lung-protective V_T of 6 mL/kg PBW would periodically be receiving a V_T of 12 mL/kg PBW, which is clearly not a lung-protective V_T.[57,58] Double triggering can usually be corrected by increasing the V_T (but not greater than 8 mL/kg PBW), increasing the

MINI CLINI

Volume Targeted Assist/Control Ventilation

Problem

Mr. King, 54 years old, has acute pancreatitis as well as acute respiratory distress syndrome (ARDS). He is currently being ventilated in volume A/C mode with a V_T of 6 mL/kg PBW (400 mL). His respiratory rate is 26/min and his inspiratory time is 0.5 s. Gas is being delivered in a square-wave flow pattern with a peak flow of 48 L/min. Mr. King is tachycardic, with a pulse rate of 118/min, blood pressure 138/98, and SpO_2 92%. Visual assessment of the his ventilatory pattern indicates that he is using his accessory muscles with every breath. You observe the following waveform on the ventilator:



Solution

Assessment of the pressure and flow waveforms indicates that there is frequent double triggering. You have a number of choices on how to eliminate the double triggering: increasing the V_T to 8 mL/kg PBW, increasing the inspiratory time while changing the waveform to decelerating flow, changing to pressure support, or performing a number of these changes.[57,58] Only after these approaches have failed should the patient be sedated. Changing to pressure support at a pressure level that maintains the V_T below 8 mL/kg PBW may be the best option if Mr. King can maintain his ventilatory pattern. This would allow him to determine his V_T needs on a breath-by-breath basis. The V_T can simply be increased; this may work in some patients, but in others the constant V_T may still be a problem. Inspiratory time can be increased with the waveform changed to decelerating flow and the V_T increased to 8 mL/kg PBW. This may also be a viable option. Sedation is always the last choice and may not eliminate the double triggering until the patient has been sedated to total apnea.

BOX 48.6 Autotriggering

Caused by
- Circuit leaks
- Water in circuit
- Inappropriately set sensitivity
- Hyperdynamic cardiac contractions

Corrected by
- New ventilator circuit
- Removal of water from the circuit
- Appropriate setting of sensitivity

BOX 48.7 Double Triggering

Caused by
- Inadequate peak flow
- Inadequate V_T
- Short inspiratory time
- Inappropriate mode of ventilation

Corrected by
- Increased V_T (≤8 mL/kg PBW)
- Increased peak flow to match patient demand
- Increased inspiratory time to match patient's inspiratory time
- Mode changed to pressure support

V_T, Tidal volume.

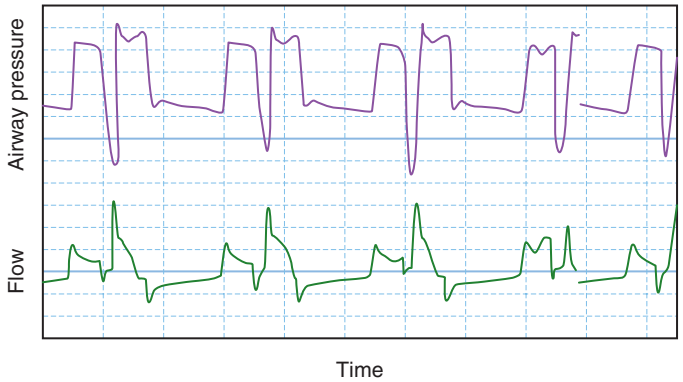


Fig. 48.11 Double Triggering (Breath Stacking). With each inspiratory effort, the patients' inspiratory time exceeds the ventilator's inspiratory time. As a result, the patient triggers a second breath without exhaling. Both tidal volume and airway pressures can be markedly increased.

inspiratory time, or changing from volume A/C to pressure A/C or pressure support.[57,58] If none of these changes eliminates the double triggering, sedation is indicated (Box 48.7).

RULE OF THUMB Double triggering is most commonly observed in volume ventilation when the set V_T and inspiratory time are less than the patient's demand. Increasing V_T or inspiratory time or changing to pressure-targeted ventilation can correct double triggering.

Reverse Triggering

Reverse triggering is a form of double triggering that occurs during controlled ventilation. It has primarily been described in patients with ARDS in whom a controlled mechanical breath

stimulates the respiratory center via stretch receptors to attempt a spontaneous breath.[38,39] The reverse trigger can occur in any mode of ventilation and can occur within the controlled breath or during the subsequent expiratory phase (Fig. 48.12). Little is known about why reverse triggering develops or its effects on the patient except that it can cause double triggering and the periodic delivery of excessive V_T. If reverse triggering occurs, alteration of V_T or inspiratory time should be attempted. Since the patient is already sedated, sedation is not the solution. More research is needed to determine the potential harm of reverse triggering, its causes, and its treatment.

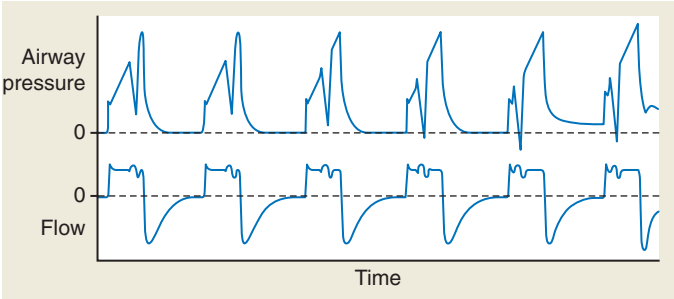


Fig. 48.12 These Waveforms Illustrate Reverse Triggering. Note that the volume-targeted breaths are all machine triggered, with no patient effort. However, within each machine breath there is a patient inspiratory effort. Reverse triggering is the stimulation of a patient effort following a machine-controlled breath.

CYCLE ASYNCHRONY

Cycle asynchrony is a result of a difference between the patient's inspiratory time and that of the ventilator.[41] Thus cycle asynchrony can result in excessively long inspiratory times (Fig. 48.13) or excessively short ones (Fig. 48.14). Theoretically, cycle asynchrony can occur in any mode of ventilation but is by far most commonly seen in pressure ventilation.[40] If the ventilator's inspiratory time is excessive compared with the patient's inspiratory time, a spike in pressure above the set level is commonly observed at the end of the pressure-targeted breath (see Fig. 48.13). If the ventilator inspiratory time is too short, a double trigger will occur with every breath (see Fig. 48.14).

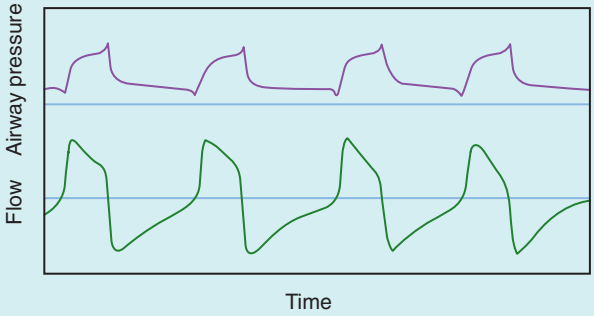
During pressure support, cycle asynchrony can be corrected by adjusting the variable that terminates inspiration or the **expiratory cycling criteria**.[44,45] Normally, pressure support is terminated when the peak flow decreases to a predetermined level. Historically, this level was 25% of peak flow.[47] However, not all patients choose to terminate inspiration at this 25% setting (Fig. 48.15). Patients with marked respiratory distress and those with chronic pulmonary disease choose to end inspiration at high terminal flows.[40] In our experience, these patients require a termination criterion set around 50%. If the termination criterion is set too low, patients will contract their abdominal muscles during the latter part of mechanical inspiration in an effort to force exhalation to occur. The clinician can identify that this is happening by an increase in the set pressure at the end of inspiration. This increase indicates that the breath is terminated by the pressure support secondary termination criterion or an

MINI CLINI

Pressure Support Ventilation

Problem

Mrs. Gonzalez, 68 years old, presents with an acute exacerbation of COPD. She has failed noninvasive ventilation and has been intubated and invasively ventilated in the pressure support mode. Her pressure support level is 12 cm H_2O with 8 cm H_2O PEEP delivering an average V_T of 6.5 mL/kg PBW (350 mL). F_iO_2 is 0.5 and respiratory rate is 28/min. She appears to be working hard to interact with the ventilator; she is using her accessory muscles to breathe. Her SpO_2 is 90% and her blood gases are PO_2 59 mm Hg, PCO_2 55 mm Hg, with a pH of 7.34. You note the following pressure and flow waveforms on the ventilator.



Solution

Mrs. Gonzalez and the ventilator are not ending inspiration at the same time. She is choosing to begin exhalation during the pressure support breath. This is shown on the airway pressure waveform as an increase in the airway pressure at the end of the pressure support breath. In addition, upon palpation of the diaphragm, you note that Mrs. Gonzalez is contracting her abdominal muscles during the inspiratory phase of the ventilator, trying to force exhalation. To correct this, the expiratory cycling criterion must be properly set. It is currently set at 25% of peak flow but should be set at a much higher percentage. You should slowly increase the expiratory cycling criterion until the airway pressure waveform does not show a spike in airway pressure at the end of the breath. To do this, slowly increase the expiratory cycling criterion in 5% increments, observing the effect on the airway pressure curve. The lowest percentage that eliminates the pressure spike is the correct setting. When this is set properly, Mrs. Gonzalez's respiratory rate should decrease and contraction of her abdominal muscles during inspiration should end.

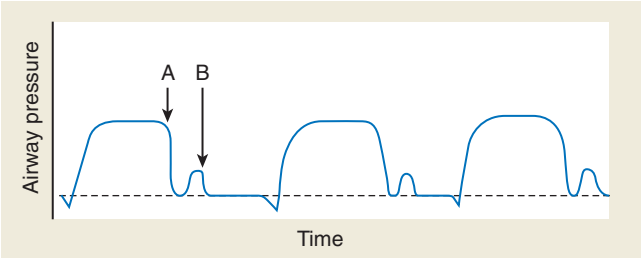


Fig. 48.13 Cycling Asynchrony in Pressure Ventilation. In this figure the patient's inspiratory time is longer than the ventilator's inspiratory time. *A* indicates the end of the ventilator's inspiratory time, and *B* indicates the end of the patient's inspiratory time. To correct this, the ventilator's inspiratory time must be increased to equal the patient's inspiratory time. In pressure support this is done by decreasing the percent cycle sensitivity and in pressure control breath by directly increasing the set inspiratory time.

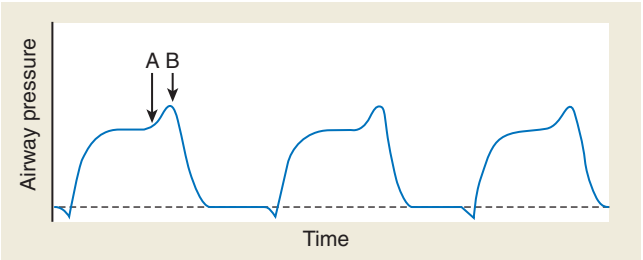


Fig. 48.14 Cycling Asynchrony in Pressure Ventilation. In this figure the patient's inspiratory time is shorter than the ventilator's inspiratory time. *A* indicates the end of the patient's inspiratory time, and *B* indicates the end of the ventilator's inspiratory time. To correct this, the ventilator's inspiratory time must be decreased to equal the patient's inspiratory time. In pressure support this is done by increasing the percent cycle sensitivity, and in pressure control breath by directly decreasing the set inspiratory time.

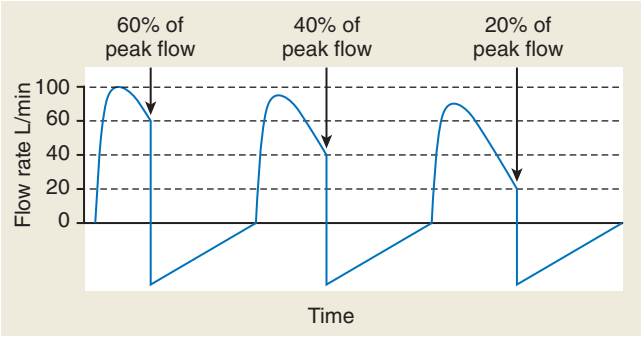


Fig. 48.15 Function of Cycling (Termination) Sensitivity (Criterion). In all three breaths the peak flow is 100 L/min. However, the first breath has the shortest inspiratory time, cycling criterion 60% (60% of peak flow). The middle breath has a longer inspiratory time, cycling criterion 40% (40% of peak flow). The last breath has the longest inspiratory time, cycling criterion 20% (20% of peak flow).

increase in airway pressure above the set level. This level is ventilator specific.[47] If the breath is ended by a spike in pressure, the termination criterion must be increased slowly until there is a smooth decrease in pressure. If the ventilator cannot adjust the termination criterion, the problem can be corrected by switching to PA/C. PA/C essentially operates during assisted breaths the same as PSV except that inspiration terminates at a set time.[40]

BOX 48.8 Cycle Asynchrony

Caused by
- Pressure assist/control or SIMV
  - Ventilator inspiratory time to short
  - Ventilator inspiratory time to long
- Pressure support
  - Expiratory cycling criteria percentage too high
  - Expiratory time criteria percentage too low
- If ventilator inspiratory time too long, corrected by
  - Decreasing ventilator inspiratory time in pressure assist/control or SIMV to eliminate the pressure spike at the end of the breath
  - Increasing expiratory cycling criteria percentage so that the breath ends sooner, eliminating the pressure spike at the end of the breath
- If ventilator inspiratory time is too short, corrected by
  - Increasing ventilator inspiratory time in pressure A/C or SIMV to eliminate the double trigger at the end of the breath
  - Decreasing expiratory cycling criteria percentage so that the breath ends sooner, eliminating the double trigger at the end of the breath

SIMV, Synchronized intermittent mandatory ventilation

If there is a spike in pressure at the end of a PA/C breath, the inspiratory time setting must be decreased until the spike disappears. In all other pressure modes, inspiratory time or termination criteria can be adjusted; make sure that the patient and ventilator end the breath at the same time.

If the termination criterion is set too high in patients with relatively healthy lungs or inspiratory time too short, double triggering can occur with every breath.[59,60] These are primarily postoperative patients or overdose patients (see Fig. 48.14). In such patients the termination criterion is decreased until the double trigger is eliminated. As opposed to the patient with high ventilatory demand who requires a termination criterion of more than 50%, these patients frequently require the termination criterion be set at only 10% to 15%. In this setting, the termination criterion is slowly decreased, followed by careful assessment until the double triggering is gone. In pressure A/C and pressure SIMV where inspiratory time is set, inspiratory time is slowly increased until the double triggering is eliminated (Box 48.8).

RULE OF THUMB Cycle asynchrony occurs most commonly in pressure ventilation when the patient's neuro-inspiratory time and the ventilator's inspiratory time are not equal.

MODE ASYNCHRONY

Mode asynchrony implies that an inappropriate mode of ventilation has been selected for a given patient. There are many biases regarding mode of ventilation and few data to support any relationship between mode and patient outcome. See Chapters 46, 47, and 49 for a detailed discussion regarding modes of ventilation. However, it is increasingly clear that asynchrony is highest in volume ventilation because of its control over the variables associated with ventilation. Of all the classic modes of ventilation, pressure support is the least confining and should result in little asynchrony. PAV and NAVA, however, can be expected to result in the least asynchrony because those modes do not control any gas delivery variable and follow the patient's desires

rather than dictating the required ventilatory pattern to the patient.[18-20,43] However, for clinicians to accept these modes of ventilation, they must be willing to accept the resultant ventilatory pattern. Most patients will breathe in a rapid, shallow manner when they are experiencing respiratory distress/failure—that is, when V_T are in the range of 4 to 6 mL/kg PBW and the respiratory rate exceeds 25/min. In spite of this pattern, both PAV and NAVA have been shown to reduce asynchrony.[18-20,43]

The mode of ventilation that can be the most problematic is SIMV. This is because of the variation in ventilatory load between mechanical and spontaneous breaths (see Chapters 47 and 49 for details). As the percentage of the total spontaneous breaths increases, the WOB also increases, not only in the spontaneous breaths but also in the mechanical breaths.[61,62] Essentially, the respiratory center cannot distinguish between mechanical and spontaneous breaths once some 50% of the breaths are spontaneous, resulting in the same level of patient work exerted during both spontaneous and mechanical breaths.[61,62] This is a major reason why SIMV has been shown to be the least effective mode in weaning patients from ventilatory support.[62,63]

PATIENT–VENTILATOR ASSESSMENT

Periodic assessment of the patient–ventilator system should occur on a regular basis. The frequency of the assessment varies from every hour to every 4 hours depending on the severity of the patient's illness. For highly unstable patients, such assessments may be done at bedside on a minute-to-minute basis. In such situations a complete assessment of both the patient and the ventilator should occur; assessing the patients' cardiopulmonary status and the function and settings of the mechanical ventilator. Depending on the patient's overall status, all of the following should be measured and documented: plateau pressure, driving pressure, and P_{100}. In addition, a prolonged review of the patient's airway pressure and flow waveforms should occur. Asynchronies are not easy to identify, and a lengthy review of waveforms may be necessary to identify their presence. Based on the finding of this assessment, adjustments to gas delivery should occur. Adjustment of V_T, peak flow, flow waveform, and inspiratory time may be necessary in volume ventilation. In pressure ventilation, rise time, inspiratory termination criteria, pressure setting, and inspiratory time may have to be adjusted. In most patients a minor adjustment of ventilator settings is necessary with each patient-ventilator assessment.

P_{100} or $P_{0.1}$ should be measured and assessed during every patient–ventilator assessment if the patient is triggering the ventilator! The P_{100} is an assessment of ventilatory drive or the level of ventilatory distress. A normal P_{100} is about −0.5 to −1.5 cm H_2O (Box 48.9).[64] The more negative the P_{100}, the greater the drive or ventilatory distress. In mechanically ventilated patients, a P100 of −0.5 to −5 cm H_2O is considered acceptable. A P_{100} of −5.1 to −10 cm H_2O generally requires significant adjustment of the way ventilation is provided and may require sedation if ventilator adjustment does not normalize the P_{100}. A P_{100} more negative than a −10 H_2O generally requires controlled ventilation.[65] Since ventilatory patterns vary from breath to breath, it is important to measure the P_{100} three or four times and establish an average value that reflects the patient's condition.[66] The P_{100}, though not a precise assessment of a patient's ventilatory distress, does provide a reasonable guide to assessment of the adequacy of ventilator setting and the need for more or less ventilatory support.

BOX 48.9 P_{100} or $P_{0.1}$

The P_{100} is an assessment of ventilatory drive or ventilatory distress.
Normal P_{100} is −0.5 to −1.5 cm H_2O
Acceptable during patient-triggered ventilation: −0.5 to −5.0 cm H_2O
Need for ventilator adjustment and possibly sedation: −5.1 to −10 cm H_2O
Requires controlled ventilation more negative than −10 cm H_2O

SUMMARY CHECKLIST

- Patient–ventilator interaction is not a problem during controlled ventilation because the patient is not interacting with the ventilator, but it is always a major issue during patient-triggered ventilation.
- Poor patient–ventilator interaction has been associated with increased length of mechanical ventilation, length of ICU stay, need for a tracheotomy, and mortality.
- A change in patient status is commonly the reason for the development of poor patient–ventilator interaction.
- Artificial airway issues can cause marked changes in patient–ventilator interaction.
- The development of a pneumothorax or tension pneumothorax is a major cause of markedly deteriorating patient–ventilator interaction.
- Whenever there is an acute severe change in the ability to provide ventilatory support, the three most probable causes are tension pneumothorax, airway obstruction, and right mainstem bronchus intubation.
- Malfunction of the mechanical ventilator can be a cause of poor patient–ventilator interaction but it is a highly unlikely cause with today's mechanical ventilators.
- The four variables that can be controlled during classic modes of mechanical ventilation are pressure, flow, volume, and time.
- The less control that is exerted by the mechanical ventilator on the patient's ventilatory pattern, the less likely it is that the patient will develop patient–ventilator asynchrony.
- The general types of asynchrony are flow asynchrony, trigger asynchrony, cycle asynchrony, and mode asynchrony.
- Asynchrony can be caused by inappropriately set sensitivity, PEEP, flow, V_T, and inspiratory time.
- Flow asynchrony is a result of the flow provided by the ventilator being inadequate to match the patient's inspiratory demand.
- Trigger asynchrony can manifest as missed triggering, delayed triggering, autotriggering, double triggering, and reverse triggering.
- Missed triggering and delayed triggering are normally a result of auto-PEEP.
- Autotriggering is normally a result of circuit leaks or fluid moving back and forth in the ventilator circuit, but can also be caused by hyperdynamic contractions of the myocardium.

- Flow asynchrony is a result of the ventilator providing less flow then the patient's respiratory center requires.
- Mode asynchrony occurs when the selected mode of ventilation does not match the patient's ventilatory demands.
- Volume ventilation can be expected to cause the most asynchrony because it controls volume, flow, and time.
- Pressure support should result in the least asynchrony of the commonly used modes of ventilation.
- PAV and NAVA cause the least asynchrony because they do not force a ventilatory pattern but follow the ventilatory pattern selected by the patient.
- Patient–ventilator assessment should include careful evaluation of airway pressure and flow waveforms and adjustment of the ventilator if asynchrony identified.
- P100 should be assessed during ALL patient-triggered patient-ventilator assessments.

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49

Initiating and Adjusting Invasive Ventilatory Support

Robert M. Kacmarek

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Discuss the goals of ventilatory support.
- Describe how to choose an appropriate ventilator to begin ventilatory support.
- Explain how to select an appropriate mode of ventilation given a patient's specific condition and ventilatory requirements.
- Choose appropriate initial ventilator settings, based on patient assessment.
- Describe how to assess a patient after initiation of ventilation.
- Discuss how to adjust ventilatory support based on oxygenation and ventilation status.
- Discuss how to ventilate using the concept of lung protective ventilation.
- Explain how to adjust the ventilator on the basis of the patient's oxygenation response.
- Explain how to adjust the ventilator on the basis of the patient's ventilation response.

CHAPTER OUTLINE

KEY TERMS

controlled ventilation
full ventilatory support
high-frequency oscillatory ventilation (HFOV)
lung protective ventilatory strategy
neurally adjusted ventilatory assist (NAVA)
partial ventilatory support
plateau pressure (P_{plat})
pressure-controlled ventilation (PCV)
pressure-regulated volume control (PRVC)
pressure support ventilation (PSV)
proportional assist ventilation (PAV)
synchronized intermittent mandatory ventilation (SIMV)
transpulmonary pressure
volume-controlled ventilation
volume support

Mechanical ventilation uses sophisticated life-support technology to maintain adequate tissue oxygenation and remove carbon dioxide (CO_2). At its most basic level, mechanical ventilation supports or replaces the normal ventilatory pump, moving air into and out of the lungs. The primary function of a mechanical ventilator is to ventilate. The main indication for mechanical ventilation is inadequate or absent spontaneous breathing.

Mechanical ventilation is not without risk, and the complications and hazards can be life-threatening. The decision to initiate mechanical ventilatory support is a serious one that requires sound clinical judgment and a clear understanding of the various approaches to ventilatory support. This chapter reviews and describes the initial set-up of the ventilator and the adjustments made in ventilatory support based on the patient's response. Techniques for patient stabilization; methods for optimizing oxygenation, ventilation, and acid–base balance; and methods for minimizing harmful side effects are described.

GOALS OF MECHANICAL VENTILATION

The goals of mechanical ventilatory support are to maintain adequate alveolar ventilation and oxygen (O_2) delivery, restore acid–base balance, and reduce the work of breathing (WOB) with minimum harmful side effects and complications.[1] Mechanical ventilation may also reduce increased myocardial work secondary to hypoxemia and an increased WOB.[1] Other physiologic objectives of mechanical ventilatory support include increasing or maintaining lung volume with positive end-expiratory pressure (PEEP) for promotion, improvement, or maintenance of lung recruitment.[1]

Lung Protective Ventilatory Strategies

Lung protective ventilatory strategies entail an approach to mechanical ventilation that includes the use of small tidal volume (V_T), low plateau pressures and driving pressures, appropriate fractional inspired oxygen (FiO_2), and appropriate levels of PEEP.[2] This approach was first described in patients with acute respiratory distress syndrome (ARDS); however, the concept of lung protection today should be applied to all patients requiring ventilatory support for acute respiratory failure. Ventilator-induced lung injury is primarily caused by an elevated transpulmonary pressure during positive pressure ventilation.[3] **Transpulmonary pressure** is the difference between alveolar pressure and pleural pressure. A safe transpulmonary pressure during mechanical ventilation is not firmly established, but most clinicians would agree that the lower the transpulmonary pressure, the less likely the development of ventilator-induced lung injury.[4] At the bedside we measure plateau pressure and driving pressure (plateau pressure – PEEP) and use these variables to assess the safety of our ventilator settings. Analysis of stress and strain applied to the lungs during ventilatory support identified 27 cm H_2O as the maximum plateau pressure without increasing the risk of significant lung injury.[4] Therefore most recommend that plateau pressure should be maintained ≤28 cm H_2O. Amato et al.[5] identified a driving pressure greater than 15 cm H_2O, increasing the risk of mortality during ventilatory support. Table 49.1 lists all of the components of a lung-protective approach to ventilatory support, which will be discussed later in the chapter. See Chapter 52 for a discussion of esophageal and transpulmonary pressure measurements. High transpulmonary pressures are associated with alveolar overdistention and lung injury.[3]

TABLE 49.1 Components of a Lung Protective Approach to Ventilatory Support

- V_T 4–8 mL/kg PBW greater P_{plat} lower V_T
- Plateau Pressure <28 cm H_2O
- Driving pressure <15 cm H_2O
- PEEP appropriate for the patient presentation
- Avoid asynchrony
- Avoid autoPEEP and air trapping
- Appropriate FiO_2 maintain PaO_2 55–80 and SpO_2 88%–95%

FiO_2, Fractional inspired oxygen; *PEEP,* positive end-expiratory pressure.

RULE OF THUMB The goals of mechanical ventilatory support are to maintain adequate alveolar ventilation and oxygen (O_2) delivery, restore acid-base balance, and reduce the WOB) with minimum harmful side effects and complications.

Plateau pressure (P_{plat}), the end inspiratory equilibration pressure, measures the mean peak alveolar pressure and is the best bedside clinical reflection of transpulmonary pressure.[2,4,6] Although P_{plat} is not an accurate measurement of transpulmonary pressure, the transpulmonary pressure during controlled ventilation never exceeds the P_{plat}.[4] P_{plat} provides an excellent bedside assessment of the level of potentially dangerous ventilating pressure. Limiting P_{plat} reduces the likelihood of ventilator-induced lung injury. Generally, the lower the P_{plat} the better the patient outcome.[2,6] Ideally, P_{plat} should be less than 28 cm H_2O;[4] however, a P_{plat} greater than 28 cm H_2O may need to be applied in patients with a morbid obesity requiring high PEEP (>20 cm H_2O) levels and in patients with decreased thoracic compliance without resulting in overdistention;[6] this is because a decrease in chest-wall compliance (massive fluid resuscitation, abdominal distention, elevated bladder pressure) increases the pleural pressure, decreasing the transpulmonary pressure. Generally, the lowest possible P_{plat} is maintained by selecting a V_T of 4 to 8 mL/kg of ideal body weight (IBW). The higher the P_{plat}, the smaller the V_T should be. Generally, a V_T greater than 10 mL/kg IBW is never indicated in critically ill patients.

Lung injury can also be caused by repetitive opening and closing of unstable lung units.[7] The application of an appropriate level of PEEP ensures that unstable lung units are maintained in the open position, reducing the likelihood of additional lung injury.

RULE OF THUMB Driving pressure has recently been linked to mortality and it has recently been demonstrated that driving pressures greater than 15 cm H_2O increase mortality.

The general trajectory of pH, PCO_2, and PO_2 during the progression of acute respiratory failure is depicted in Fig. 49.1. Table 49.2 lists the most common causes of acute respiratory failure

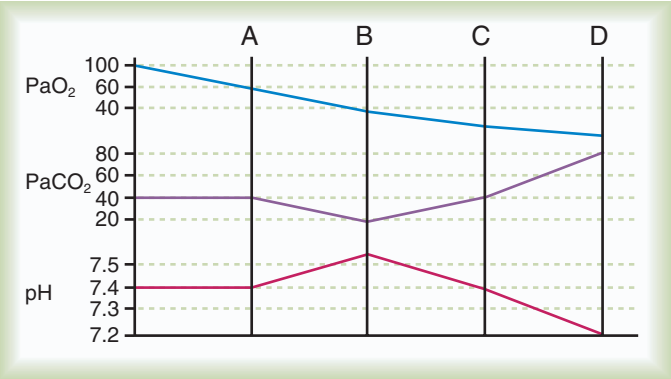

Fig. 49.1 Typical progression of acute respiratory failure. Initially, there is a decline in arterial O_2 tension and saturation. When PaO_2 decreases to approximately 60 mm Hg *(A)*, the patient begins to breathe more, $PaCO_2$ decreases, and pH increases. Early in the progression, arterial blood gas results show acute alveolar hyperventilation (uncompensated respiratory alkalosis) secondary to hypoxemia. As the patient's condition worsens, increases in ventilatory workload typically lead to the adoption of a rapid, shallow breathing pattern; although minute ventilation may remain high, effective ventilation decreases, $PaCO_2$ begins to increase, and pH begins to decrease *(B)*. At point *C*, arterial blood gas results may show normal $PaCO_2$ and pH with moderate to severe hypoxemia. If mechanical ventilation is not initiated, the patient's condition may progress to acute ventilatory failure, severe hypoxemia, and corresponding severe respiratory acidosis *(D)*.

TABLE 49.2 Most Common Causes of Acute Respiratory Failure Requiring Mechanical Ventilation in the United States and Canada

Condition	Rank	Percentage
Postoperative respiratory failure	1	17
Sepsis	1	17
Other	2	16
Heart failure	3	13
Pneumonia	3	13
Trauma	3	13
ARDS	4	9
Aspiration	5	3

ARDS, Acute respiratory distress syndrome.
Modified from Esteban A, Anzueto A, Alia I, et al: How is mechanical ventilation employed in the intensive care unit? An international utilization review. *Am J Respir Crit Care Med* 161:1450, 2000.

leading to ventilatory support in the United States and Canada. Hazards of mechanical ventilation include decreased venous return and cardiac output, patient–ventilator asynchrony (see Chapter 48), and ventilatory muscle dysfunction owing to inappropriate ventilator settings, ventilator-associated pneumonia, and ventilator-induced lung injury.[1] Box 49.1 lists the goals of ventilatory support, and Box 49.2 lists specific objectives of mechanical ventilation.

RULE OF THUMB A **lung protective ventilatory strategy** is an approach to mechanical ventilation that includes the use of small tidal volume (V_T), low plateau pressures and driving pressures, appropriate FiO_2 and appropriate levels of PEEP.

BOX 49.1 Physiologic Goals of Ventilatory Support

- Support or manipulate gas exchange.
- Maintain alveolar ventilation ($PaCO_2$ and pH).
- Maintain arterial oxygenation (PaO_2, SaO_2, SpO_2, CaO_2, and DO_2).
- Increase end-expiratory lung volume, functional residual capacity (FRC).
- Reduce or manipulate work of breathing.
- Minimize cardiovascular impairment.
- Ensure patient–ventilatory synchrony.
- Avoid ventilator-induced lung injury.

BOX 49.2 Specific Clinical Objectives of Ventilatory Support

- To reverse hypoxemia.
- To reverse acute respiratory acidosis.
- To prevent or reverse atelectasis.
- To reverse ventilatory muscle dysfunction.
- To decrease systemic or myocardial O_2 consumption.
- To maintain or improve cardiac output.
- To reduce intracranial pressure.
- To stabilize the chest.

VENTILATOR INITIATION

When the decision to begin mechanical ventilatory support is made, one must choose the mode of ventilation, select an appropriate device, and establish the initial ventilator settings. The goals of mechanical ventilation are achieved by choosing an appropriate mode of ventilation, PEEP level, FiO_2, V_T or pressure level, rate, peak flow and flow waveform, and inspiratory time. Appropriate trigger sensitivity, pressure limit, alarms, backup ventilation, and humidification must be selected. After initial ventilator setup, adjustments must be made based on the patient's response and the patient-specific clinical objectives of ventilatory support. Most patients who need mechanical ventilatory support receive invasive positive pressure ventilation; however, an increasing number of patients are being ventilated noninvasively (see Chapter 50). Next, the clinician must choose the mode of ventilation (e.g., volume assist/control [VA/C], pressure assist/control [PA/C], pressure support ventilation [PSV], **pressure-regulated volume control [PRVC]**, **volume support**, adaptive support ventilation, **proportional assist ventilation [PAV]**, or **neurally adjusted ventilatory assist [NAVA]**) and initial ventilator settings (e.g., rate, V_T or pressure level, FiO_2, PEEP). Finally, the clinician must choose appropriate alarm and apnea settings. Box 49.3 summarizes key decisions that must be made as part of the initial ventilator setup.

RULE OF THUMB Generally, a V_T greater than 10 mL/kg IBW is never indicated in critically ill patients.

Establishment of the Airway

Conventional mechanical ventilatory support requires the establishment of an artificial airway. Initially, nearly 100% of patients

BOX 49.3 Initial Ventilator Setup

Initial ventilator setup includes the following key decisions:
- Noninvasive versus invasive ventilation.
- Type and method of establishment of an airway.
- Partial versus full ventilatory support.
- Choice of ventilator.
- Mode of ventilation.
- Assist/control ventilation (volume vs. pressure) vs. pressure support.
- Other newer modes and adjuncts to ventilation.

Next, the clinician must consider key ventilatory values:
- Trigger method (pressure or flow trigger) and sensitivity.
- V_T (volume ventilation) or pressure level (pressure support and PA/C).
- Rate
- Inspiratory flow, inspiratory time, expiratory time, or I:E ratio.
- Inspiratory flow waveform.
- FiO_2
- PEEP

Last, the clinician must choose appropriate alarm and backup values:
- Low-pressure, low PEEP alarms.
- High-pressure limit and alarm.
- Volume alarms (low V_T/high V_T, high and low minute ventilation).
- High rate and low rate alarms.
- Apnea alarm and apnea ventilation values.
- High/low O_2 alarm.
- High/low temperature alarm.
- I:E ratio limit and alarm.

FiO_2, Fractional inspired oxygen; *I:E,* inspiratory-to-expiratory; *PA/C,* pressure assist/control; *PEEP,* positive end-expiratory pressure.

receiving positive pressure ventilation are intubated and, of these, 99% have oral endotracheal tubes and only approximately 1% are intubated nasally.[8,9] Approximately 5% to 10% of patients receiving mechanical ventilation have a tracheotomy performed at some point.[8,9] Airway management is described in detail in Chapter 37.

RULE OF THUMB Initial setup of ventilation parameters should include a limitation of tidal volume (4–8 mL/kg predicted body weight [PBW]), plateau (<28 cm H_2O), and driving (<15 cm H_2O) pressure in ALL patients acutely requiring mechanical ventilation.

Pressure-Controlled Versus Volume-Controlled Ventilation

The next decision to be made regarding initiation of mechanical ventilation is whether to use a pressure-targeted or volume-targeted mode of ventilation. Volume-targeted ventilation essentially includes VA/C and synchronized intermittent mandatory ventilation (SIMV). Pressure ventilation includes PA/C, SIMV, PRVC, volume support, and airway pressure release ventilation (APRV). In addition, the clinician can select the patient-controlled modes PAV or NAVA; however, most patients are initially ventilated with pressure or volume forms of ventilation. The operational capabilities of these modes are described in detail in Chapter 46, and the indications, benefits, and concerns regarding these modes are discussed in Chapter 47.

Full Ventilatory Support Versus Partial Ventilatory Support

Full ventilatory support can be defined as the application of mechanical support such that all or most of the energy necessary for effective alveolar ventilation is provided by the ventilator.[9] When a ventilator is set to deliver full ventilatory support, the patient is either passive or simply triggers the breath to initiate inspiration, allowing the ventilator to perform most of the WOB; however, it is very difficult to set the ventilator to assume all of the WOB without significantly sedating the patient. In most patient-triggered approaches to ventilatory support, patient-ventilatory synchrony is a major issue, and very careful titration of the ventilator settings is necessary to ensure synchrony and minimize patient WOB. See Chapter 48 for details on patient-ventilatory synchrony.

Partial ventilatory support implies that only a percentage of the WOB is provided by the ventilator.[9] Normally, when partial ventilatory support is indicated, SIMV, pressure support ventilation (PSV), volume support, PAV, and NAVA are the modes of choice; however, as with full ventilatory support, care in setting the ventilator is critical to ensure that patient–ventilator synchrony is maximized. Partial ventilatory support strategies minimize the loss of ventilatory muscle function, require less sedation, assist in recruiting and stabilizing alveolar units, and generally move patients closer to ventilator discontinuance than full ventilatory support approaches.

Choice of a Ventilator

After the decision is made to initiate mechanical ventilatory support, the clinician must select an appropriate ventilator. This decision should be guided by considering the features, modes available, pressure and flow capabilities, alarms and monitoring systems, and reliability, in relation to the patient needs; however, the most important feature is the clinician's familiarity with the equipment. Only a ventilator that the clinician is totally familiar with should ever be used.

INITIAL VENTILATOR SETTINGS

Initial ventilator settings are chosen based on the patient's clinical presentation and the need to provide full or partial ventilator support.

Choice of Mode

Most modern critical care ventilators include VA/C, PA/C, SIMV, and PSV and many of the newer modes of ventilation; however, some modes of ventilation are found only on a specific type of ventilator, such as PAV PB 840 and PB 980 (Medtronic, Boulder, Colorado), adaptive support ventilation and Intellivent Hamilton ventilators (Hamilton Medical, Bonaduz, Switzerland), NAVA Servo-U and Servo-i ventilators (Maquet, Inc, Wayne, New Jersey), and SmartCare Draeger ventilators (Draeger Medical, Inc, Telford, Pennsylvania).

Assist/Control Ventilation (Patient-Triggered or Time-Triggered Continuous Mandatory Ventilation)

A/C ventilation involves the patient receiving a pre-set number of machine breaths per minute at a pre-set V_T; however, the

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Selecting Initial Ventilator Settings

Problem

A 52-year-old man, 5 ft 10 in (178 cm) tall and weighing 200 lb (91 kg) is being returned from the operating room after coronary artery bypass surgery. He is being manually (bag-valve-mask) ventilated with supplemental O_2 by the anesthesiologist en route to the intensive care unit (ICU). He is apneic at this time. The patient has no history of lung disease and has never smoked cigarettes. Heart rate and blood pressure are stable, and SpO_2 during manual ventilation is 99%. What initial mode, V_T, rate, and FiO_2 should the respiratory therapist (RT) select when starting ventilatory support for this patient?

Solution

The patient is apneic at this time but is likely to resume spontaneous breathing as the anesthetic wears off and sedation is reduced. The patient is expected to resume breathing spontaneously, so volume ventilation or pressure ventilation in assist/control (A/C) is appropriate.

Initial V_T and rate should be selected to provide full ventilatory support. Generally, initial V_T of approximately 6–8 mL/kg IBW or pressure control setting to establish this V_T with a rate of 12–20 breaths/min provides an adequate starting minute ventilation for most adult patients. The formulas for estimating IBW are:

$$\text{IBW in kg (men)} = [106 + 6(H - 60)]/2.2$$
$$\text{IBW in kg (women)} = [105 + 5(H - 60)]/2.2$$

where H is height in inches.

For this patient:

$$\text{IBW} = [106 + 6(70 - 60)]/2.2 = 75.5 \text{ kg}$$

On the basis of IBW of 75.5 kg, initial V_T can be set at about 450 mL, 6 mL/kg IBW. Initial inspiratory flow should be set at 60 L/min with a decreasing ramp flow waveform to achieve an inspiratory time of approximately 0.8 s in VA/C. In PA/C, the pressure control level is set to maintain a V_T of 450 mL with an inspiratory time of 0.8 s. Initially, the rate can be set at 12/min. Owing to the fact that the patient has a normal respiratory system and that it is usual to return from the operating room with a below-normal body temperature, a low initial control rate is indicated. Trigger sensitivity (A/C) should be set so that minimal patient effort triggers the ventilator without autocycling.

Initial FiO_2 should be set at 1.0 but because of the patient's history and the presence of normal lung function, it is expected that it will be reduced rapidly as the patient recovers. Initial PEEP is set at 5 cm H_2O. In summary, appropriate initial ventilator settings for this patient are:

Mode: A/C (volume or pressure)

V_T: 6 mL/kg, 450 mL

f_{mach}: 12 breaths/min

FiO_2: 1.0 followed by immediate assessment and SpO_2 observation with titration downward as indicated to maintain an SpO_2 between 88% and 95%.

Inspiratory flow and time: 60 L/min, decreasing ramp, inspiratory time approximately 0.8 s in VA/C, pressure control set to achieve V_T 450 mL and inspiratory time 0.8 s.

Pressure limit: Adjust to 10 to 15 cm H_2O above peak inspiratory pressure (PIP) after patient connection.

Humidification: Heated humidifier to achieve temperature >35°C at the airway or an appropriate heat and moisture exchanger (HME).

BOX 49.4 Typical Values for Ventilator Initiation for Adults Receiving Volume or Pressure Assist/Control Ventilation

- Trigger sensitivity: –0.5 to –1.5 cm H_2O or 1–2 L/min set to minimize trigger work without autocycling.
- V_T: Volume ventilation 6–8 mL/kg IBW; pressure ventilation, pressure level to achieve 6–8 mL/kg IBW.
- Rate: Backup rate of ≥12–14 breaths/min if providing assisted ventilation.
- Inspiratory flow: Volume ventilation 60–80 L/min to achieve inspiratory time of approximately 0.6–1.0 s and I:E ratio of ≤1 : 2; inspiratory flow ≥80 L/min may be required to meet or exceed the patient's spontaneous inspiratory flow demand.
- Flow waveform volume ventilation: Decreasing ramp.
- Inspiratory time pressure ventilation:0.6–1.0 s.
- PEEP: 5 cm H_2O.
- Pressure limit: Start at 30–40 cm H_2O depending on approach (volume 40 cm H_2O-) and adjust after patient connection to 10–15 cm H_2O above PIP.
- Humidification: Begin with heated humidifier to provide temperature of 35°C at the airway connection or appropriate HME.

HME, heat and moisture exchanger; *IBW,* ideal body weight; *PEEP,* positive end expiratory pressure; *PIP,* peak inspiratory pressure.

patient can initiate additional machine breaths, which will be given at the pre-set V_T. AC can be delivered in either pressure-targeted or volume-targeted ventilation. Suggested initial settings for **volume ventilation** in the care of adults are listed in Box 49.4. Advantages of AC volume ventilation include the assurance that a minimum safe level of ventilation is achieved, yet the patient can still set his or her own breathing rate. In the event of sedation or apnea, a minimum safe level of ventilation is guaranteed by the selection of an appropriate backup rate, usually approximately 4 to 6 breaths/min less than the patient's assist rate but not less than the rate necessary to provide a minimum safe level of ventilation (e.g., a backup rate of at least 12 to 14 breaths/min).[9]

Owing to the fact that AC ventilation usually provides full ventilatory support, it may result in less WOB than partial support modes; however, less WOB should not be assumed just because the patient is in AC ventilation. Trigger work may be significant if inappropriate sensitivity settings are selected. In addition, when a breath is triggered, inspiratory muscle activity persists.[10,11] If the inspiratory flow rate during volume ventilation does not meet or exceed the patient's inspiratory demand, or inspiratory time is too lengthy, the patient's WOB may be greater or equaling the work of a spontaneous unassisted breath.[10,11] In pressure ventilation, lengthy inspiratory times, inadequate rise time, and improperly set pressure levels can also cause asynchrony (see Chapter 48).

If properly applied and tolerated by the patient, AC ventilation may provide ventilatory muscle rest that allows the ventilatory muscles to recover. Disadvantages of AC mode include an increase in WOB if not applied properly.[9,12] AC may also be poorly tolerated by awake, nonsedated patients because the patient may fight the ventilator or asynchronous patient-to-ventilator breathing patterns may develop. Because flow is based on patient

BOX 49.5 Advantages and Disadvantages of Pressure-Controlled Ventilation

Advantages

- Variable flow results in square pressure waveform and improves gas distribution.
- Ensures that P_{plat} cannot exceed set pressure control level.
- All alveoli are placed under the same sustained inspiratory pressure, which decreases hyperinflation of more compliant alveoli compared with volume ventilation square wave flow.
- Sustained inspiratory pressure may result in more alveolar recruitment.
- Improved gas distribution allows for lower V_T.
- Lower PIP is achieved compared with that achieved with volume ventilation with a square flow waveform.

Disadvantages

- Higher mean airway pressure can decrease venous return and decrease cardiac output if preload is inadequate.
- V_T varies depending on lung compliance, resistance, and patient effort.
- If V_T or minute ventilation alarms are not set properly, alveolar hypoventilation and acidosis may not be rapidly detected.

PIP, Peak inspiratory pressure.

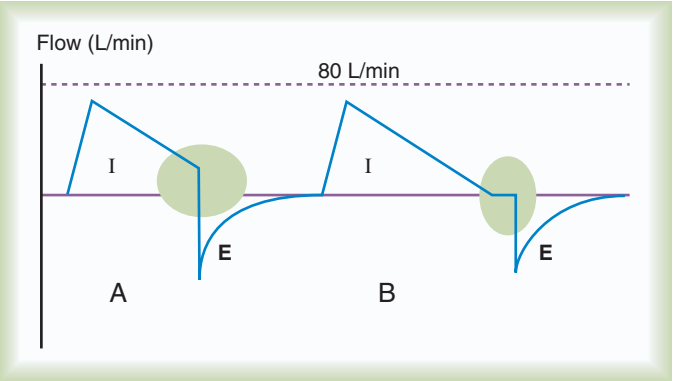


Fig. 49.2 Flow versus time waveform during pressure-controlled ventilation (PCV). *Curve A* shows a flow pattern during controlled ventilation in which inspiratory time is inadequate to ensure maximum V_T has been delivered. During inspiration, flow does not decrease to zero before exhalation occurs, so the preset pressure has not equilibrated to that in the lung. *Curve B* shows an increase in inspiratory time from *curve A.* Inspiratory flow reaches zero, maximizing V_T delivery and allowing the preset pressure to equilibrate in the lungs. Exhaled V_T is greater for *curve B* than for *curve A* despite the pressure setting not changing.

demand in pressure-targeted ventilation, synchrony is generally better achieved during PA/C than with VA/C ventilation. Advantages and disadvantages of **pressure-controlled ventilation (PCV)** are described in Box 49.5.

AC volume ventilation is the most common ventilator mode used throughout the world for the primary initial mode of ventilatory support.[7,13] Regardless of the indication for ventilatory support or the underlying disease, this mode can provide adequate ventilatory support for all indications for ventilatory support when properly adjusted and the patient is properly managed.[6,13]

Controlled Ventilation (Time-Triggered Continuous Mandatory Ventilation)

Controlled ventilation, pressure or volume, is characterized by the patient's inability to trigger breaths above the number of breaths set. Controlled ventilation is achieved using the AC mode when the patient is apneic owing to a medical condition, anesthesia, or use of sedative drugs and paralytic agents. Ventilators in use today do not prevent a patient with sufficient effort from triggering additional breaths. Controlled ventilation can only be achieved with pharmacologic agents. Advantages of controlled ventilation include eliminating WOB and complete control over the patient's ventilatory pattern. In cases where WOB is high, controlled ventilation may allow for ventilatory muscle rest, reduce O_2 consumption of the ventilatory muscles, and "free up" O_2 for delivery to the tissues.[9]

Controlled ventilation is a common initial approach in situations of severe acute respiratory failure, especially if the primary problem is hypoxemia. Fig. 49.2 depicts the effects of inspiratory time on V_T during PA/C. Disadvantages of controlled ventilation include the need for sedatives and, perhaps, paralytic drugs. All patients given paralytic drugs must be sedated adequately because paralysis does not alter the patients' perception of their surroundings. All patients' senses are active: none are affected by paralysis; only voluntary muscles are paralyzed. In addition, in the care of apneic patients, ventilator malfunction or disconnection can lead to death.

RULE OF THUMB All modes of ventilation are equally as effective and equally well tolerated in patients requiring controlled ventilation: that is when the patient is NOT triggering any breaths; however, with assisted ventilation patient-triggered breaths, volume ventilation is more likely to cause asynchronies than pressure ventilation, specifically, the development of flow asynchrony.

Synchronized Intermittent Mandatory Ventilation

SIMV is characterized by the patient receiving a pre-set number of machine breaths per minute at a pre-set V_T; however, the patient can initiate additional breaths at the PEEP level set generally without any inspiratory support, and not the pre-set volume as with AC mode. SIMV may be used as a means of providing partial or full ventilatory support.[9] With SIMV, the machine breath may be volume or pressure targeted; in adults, it is typically a volume-targeted breath. SIMV is often combined with pressure support to overcome the imposed WOB (WOB_I) during spontaneous breathing owing to the artificial airway. SIMV allows the clinician to vary the amount of support provided from minimal to full ventilatory support. Disadvantages of SIMV include possible development of respiratory muscle dysfunction, especially in patients with rapid, shallow spontaneous breathing patterns; acute hypoventilation with use of low rates if patients do not continue to do their share of breathing; and an increase in WOB secondary to lack of ventilatory support during spontaneous breaths unless pressure support is applied.[9] SIMV also delays weaning compared with spontaneous breathing trials or pressure support and, as a result, is not a recommended mode of ventilation in adults.[14,15] The advantages and disadvantages of SIMV modes are summarized in Table 49.3. Outside of the United States, SIMV is an infrequently used mode of ventilation because of the above-mentioned problems.

TABLE 49.3 Advantages and Disadvantages of Synchronized Intermittent Mandatory Ventilation

Advantages	Disadvantages
Lower mean airway pressure may result than is achieved with assist/control ventilation	SIMV with PSV may increase mean airway pressure
Ventilatory muscle activity, strength, and coordination are maintained	Ventilatory muscle fatigue may occur
Level of support to maintain adequate levels of alveolar ventilation is easy to titrate	Acute hypoventilation may occur, especially with lower machine rates (<8 to 10 breaths/min)
Weaning protocols are easy to apply	Weaning is prolonged
Spontaneous breathing, which is physiologic, is incorporated	Addition of pressure support is often required to overcome WOB_I during spontaneous breathing
Patients tend not to hyperventilate and may not fight the ventilator, as they may do with assist mode	Patients may have difficulty adjusting to the ventilator; breath stacking is common with intermittent mandatory ventilation
Sedation or paralysis is not required, as it is in control mode	Patients may experience or continue a rapid, shallow breathing pattern or continue to make spontaneous breathing efforts during delivery of a "machine breath"
Full or partial ventilatory support and level of support can be titrated according to patient's need	Patient's workload increases considerably when SIMV rate decreases to approximately 50% of full ventilatory support value

PSV, Pressure support ventilation; *SIMV,* synchronized intermittent mandatory ventilation; *WOB_I,* imposed work of breathing.

Pressure Support Ventilation

PSV is characterized by spontaneous triggering of the ventilatory at a patients totally determined rate. PSV assumes minimal control over the patient's ventilatory pattern. Specifically, only the level of pressure applied is controlled by the ventilator, with all other aspects of gas delivery controlled by the patient; however, PSV is very similar to PA/C. The primary difference is that in PSV, flow terminates the breath, whereas in PA/C, time terminates the breath. Other than this, PA/C has a backup rate, and with pressure support an apnea mode of ventilation is set.[16] PSV can reduce WOB and may improve patient–ventilator synchrony by placing more control with the patient.[17] Many clinicians use PSV simply to overcome WOB imposed by the artificial airway.[17] The PSV level required to overcome WOB_I may be estimated as follows:

$$PSV = \frac{(PIP - P_{plat}) \times \dot{V}_I \text{ spontaneous}}{\dot{V} \text{ ventilator}}$$

where PSV is the pressure support level needed to overcome WOB_I, PIP is the peak inspiratory pressure during a volume-control machine breath, P_{plat} is the plateau pressure after an inspiratory pause (usually >1 second), $\dot{V}_I$ is the patient's spontaneous peak inspiratory flow (L/s), and $\dot{V}$ ventilator is the ventilator peak inspiratory flow rate (L/s) with a square wave inspiratory flow waveform. An example of the calculations for PSV needed to overcome WOB_I is presented in Box 49.6.

BOX 49.6 Calculation of Pressure Support Ventilation Level Needed to Overcome Imposed Work of Breathing and During Synchronized Intermittent Mandatory Ventilation

- Machine delivered V_T during VA/C: 450 mL
- Machine inspiratory flow rate: 50 L/min (1 L/s)
- Flow pattern: Square wave
- PIP: 25 cm H_2O
- P_{plat}: 23 cm H_2O
- Patient's spontaneous inspiratory flow rate: 30 L/min (0.5 L/s)

$$PSV = \frac{(PIP - P_{plat}) \times \dot{V}_I \text{ spontaneous}}{\text{Ventilator inspiratory flow}}$$
$$= \frac{(40 - 30 \text{ cm } H_2O) \times 0.5 \text{ L/s}}{1 \text{ L/s}}$$
$$= \frac{10 \text{ cm } H_2O \times 0.5 \text{ L/s}}{\text{L/s}} = 5 \text{ cm } H_2O$$

PIP, Peak inspiratory pressure; *VA/C,* volume assist/control.

PSV can be, and is being, increasingly used as a primary mode of ventilation. PSV is essentially the only mode of ventilation used during noninvasive ventilation and is equal to the difference between inspiratory positive airway pressure (I-PAP) and expiratory positive airway pressure (E-PAP). It is also an acceptable mode of ventilation for any patients capable of triggering ventilatory support who have an intact ventilatory drive. Many clinicians use this mode in the initial phases of ventilatory support and following the most acute phase of ventilatory failure. The actual PSV level required is based on the desired V_T. PSV is adjusted to ensure the desired V_T (4 to 8 mL/kg, IBW) is delivered, and the rise time and termination criteria are set to avoid asynchrony. Few clinicians attempt to calculate a PSV level based on the previously listed formula.

RULE OF THUMB The use of SIMV to wean patients from ventilatory support lengthens the time mechanical ventilation is required. Patients are liberated most rapidly from ventilatory support by the use of spontaneous breathing trials.

Airway Pressure Release Ventilation

APRV is a mode of ventilation designed to allow patients to breath spontaneously without assistance at high CPAP levels that are supplemented by a change in pressure from a high level (High continuous positive airway pressure [CPAP]) to a low level (Low CPAP). The original discussions of APRV referred to it as varying pressure between 2 CPAP levels. In addition to setting the High and Low CPAP levels, the time allocated to High and Low CPAP must be set. Essentially this mode is the same as pressure control inverse ratio ventilation with the addition of patients being able to breathe spontaneously at both the High and Low CPAP levels.

APRV has been indicated in the management of trauma patients and trauma/surgical patients with ARDS, but there is currently no data indicating that APRV is better than a lung protective approach to ventilatory support using classic modes of ventilation. In fact, there is data to indicate that the outcome may be worse with APRV.

High continuous positive airway pressure. The High CPAP level is set based on the combined need to establish a high mean airway pressure to improve oxygenation and to establish a pressure gradient to facilitate CO_2 removal during the transition from High to Low CPAP. The High CPAP is usually set between 20 and 30 cm H_2O but may be set higher depending on the pathophysiology of the specific patient.

Low continuous positive airway pressure. In the classic application of APRV, the Low CPAP level is set at 0 to 5 cm H_2O. This is done because the application of PEEP during the Low CPAP periods is accomplished by creating autoPEEP. Generally, spontaneous breathing does not occur at the Low CPAP level because of short Low CPAP times; however, the Low CPAP time can be set to any level. Usually, the longer the Low CPAP time the higher the Low CPAP level owing to an inverse relationship between the Low CPAP time and the development of autoPEEP.

High continuous positive airway pressure time. Generally, the High CPAP time is set at 3 to 5 seconds to establish a rate of change to Low CPAP (mechanical respiratory rate) of about 10 to 15 /min. The lengthy High CPAP time is set to maintain a high mean airway pressure to manage oxygenation.

Low continuous positive airway pressure time. The most common method to set the Low CPAP time is to ensure that autoPEEP is established with the short time. What is currently recommended is that the Low CPAP time is determined by expiratory flow; that is, expiratory time is limited to the time needed to allow expiratory flow to decrease to 70% to 75% of peak expiratory flow. This setting insures that autoPEEP is established during the Low CPAP time period.

Concerns with airway pressure release ventilation. A number of concerns are inherent in the typical application of APRV. First, the tidal volume delivered during the change from High to Low CPAP is large, frequently above the recommended 4 to 8 mL/kg PBW and commonly above 10 mL/kg, causing lung injury. Second, PEEP is established during Low CPAP by autoPEEP. AutoPEEP is established in lung units with long time constants, not short time constants, and thus it is likely that the lung units with short time constants will collapse and reopen with reestablishment of High CPAP, causing lung injury. Third, breathing spontaneously at High CPAP requires a large change in intrathoracic pressure, potentially creating an excessive transpulmonary pressure and inducing lung injury.

High-Frequency Oscillatory Ventilation

High-frequency oscillatory ventilation (HFOV) is the primary approach to high-frequency ventilation used in adults. Respiratory rates range from approximately 3 Hz (180/min) to approximately 8 Hz (480/min), and very small V_T, often approaching anatomic dead space, is delivered.[18] Gas transport during HFOV is caused by conventional bulk flow and a number of gas-moving and mixing effects associated with the rapid frequency (see Derdak et al.[18] for details regarding gas delivery in HFOV). Although high-frequency ventilation has been shown to be safe and effective in maintaining oxygenation and ventilation in various patients,[18-20] HFOV has not been shown to be superior to conventional ventilation. In fact, two recent randomized controlled trials indicate that HFOV in adults may negatively affect outcome.[21,22] In one of these trials, those ventilated with HFOV had a higher mortality than patients managed with conventional ventilation.[21] The primary setting where HFOV has been used is in the treatment of ARDS. Recently, however, some well-conducted research has suggested that HFOV is not associated with favorable outcomes such as length of stay, ventilator days and mortality; hence HFOV is rarely used in adult ARDS patients today.

RULE OF THUMB PSV can and is increasingly being used as a primary mode of ventilation. PSV is essentially the only mode of ventilation used during noninvasive ventilation and is equal to the difference between I-PAP and E-PAP.

Initial Choice of Mode

Most patients who need mechanical ventilation in the acute care setting initially are managed with volume or pressure ventilation.[7,13] SIMV may also be used, but it has no advantage over these modes, and it has considerable disadvantages; however, there is no evidence suggesting any of the modes are more beneficial in terms of patient outcomes except that asynchrony is increased and weaning delayed with SIMV.[14,15] Consequently, the choice of initial ventilator mode is primarily one of clinician preference and patient tolerance. Once the patient is stabilized on a ventilator mode, decisions can be made regarding the use of other, newer modes of ventilation such as PRVC, volume support, adaptive support ventilation, PAV, or NAVA.

RULE OF THUMB For most patients, begin with mechanical ventilatory support with VA/C, PA/C, or PSV. When the patient is stabilized, other modes of ventilation can be considered.

Tidal Volume and Rate

V_T and machine rate should be chosen concurrently because these are the two major determinants of minute ventilation. Normal spontaneous V_T for unstressed adults is, on average, 6.3 mL/kg IBW (approximately 5 to 7 mL/kg IBW) with a respiratory rate of 12 to 18 breaths/min, establishing a minute ventilation of approximately 100 mL/kg IBW per minute.[23] Acceptable V_T for mechanical ventilation usually ranges from 4 to 8 mL/kg IBW.[1,5] V_T larger than 8 mL/kg IBW is harmful in patients with ARDS[2,24,25] and is mostly harmful to any patient in acute respiratory failure regardless of the cause of the failure.

Generally, regardless of mode, an initial V_T of 6 to 8 mL/kg IBW with a rate of 12 to 16 breaths/min is suggested for patients without acute restrictive disease.[5,26] After initiation of ventilation, the P_{plat} can be assessed, and V_T can be adjusted downward, as needed, for maintenance of a P_{plat} less than 28 cm H_2O and driving pressure less than 15 cm H_2O. A smaller initial V_T (4 to

6 mL/kg IBW) is appropriate for patients with ARDS[2,23,24] and a high P_{plat} and is usually necessary in patients with severe acute asthma. Table 49.4 lists V_T values for men and women according to calculated IBW.

RULE OF THUMB When starting ventilatory support for most adult patients, use an initial V_T of 6–8 mL/kg (IBW) and a respiratory rate of 12–16 breaths/min.

V_T times rate (f) determines minute ventilation ($\dot{V}_E$). As a rule, for adult patients, the resultant minute ventilation should be approximately 100 mL/kg IBW per minute.[9] A 70-kg adult (IBW) would have a minute ventilation of approximately 7000 mL/min. Patients with elevated CO_2 production ($\dot{V}CO_2$) or increased physiologic dead space (V_{Dphys}) need a larger minute ventilation to maintain acceptable $PaCO_2$. Minute volume should be increased by increasing the rate not the V_T.

In SIMV, the total minute ventilation is composed of spontaneous tidal volume (V_{Tsp}), spontaneous rate (f_{sp}), machine tidal volume (V_{Tmach}), and machine rate (f_{mach}). For SIMV, total minute ventilation ($\dot{V}_{ETOT}$) is described as follows:

$$\dot{V}_{ETOT} = \dot{V}_E \text{ machine} + \dot{V}_E \text{ spontaneous}$$

and

$$\dot{V}_E = (V_{Tmach} \times f_{mach}) + (V_{Tsp-average} \times f_{sp})$$

For PA/C or PSV, the delivered V_T depends on the pressure limit, the inspiratory time, and the patient's lung mechanics.

TABLE 49.4 Tidal Volume Based on Ideal Body Weight[a]

Height (in)	Height	Weight (lb)	Weight (kg)	6 mL/kg	8 mL/kg	10 mL/kg	12 mL/kg
Men							
58	4′10″	94	43	260	340	430	520
59	4′11″	100	45	270	360	450	540
60	5′0″	106	48	290	380	480	580
61	5′1″	112	51	310	410	510	610
62	5′2″	118	54	320	430	540	650
63	5′3″	124	56	340	450	560	670
64	5′4″	130	59	350	470	590	710
65	5′5″	136	62	370	500	620	740
66	5′6″	142	65	390	520	650	780
67	5′7″	148	67	400	540	670	800
68	5′8″	154	70	420	560	700	840
69	5′9″	160	73	440	580	730	880
70	5′10″	166	75	450	600	750	900
71	5′11″	172	78	470	620	780	940
72	6′0″	178	81	490	650	810	970
73	6′1″	184	84	500	670	840	1010
74	6′2″	190	86	520	690	860	1030
75	6′3″	196	89	530	700	890	1070
76	6′4″	202	92	550	740	920	1100
77	6′5″	208	95	570	760	950	1140
Women							
55	4′7″	80	36	220	290	360	430
56	4′8″	85	39	230	310	390	470
57	4′9″	90	41	250	330	410	500
58	4′10″	95	43	260	340	430	520
59	4′11″	100	45	270	360	450	540
60	5′0″	105	48	290	380	480	580
61	5′1″	110	50	300	400	500	600
62	5′2″	115	52	310	416	520	620
63	5′3″	120	55	330	440	550	660
64	5′4″	125	57	340	460	570	680
65	5′5″	130	59	350	470	590	710
66	5′6″	135	61	370	490	610	730
67	5′7″	140	64	380	510	640	770
68	5′8″	145	66	400	530	660	790
69	5′9″	150	68	410	540	680	820
70	5′10″	155	70	420	560	700	840
71	5′11″	160	73	440	580	730	876
72	6′0″	165	75	450	600	750	900

[a]Ideal body weight (lb): Men, 106 + [6(H – 60)]; women, 105 + [5(H – 60)], where H is height in inches.

TABLE 49.5 Suggested Initial Tidal Volume and Frequency for Mechanical Ventilation Based on Disease State or Condition

Patient Type	Tidal Volume (mL/kg)[a]	Frequency (breaths/min)
Adults		
Normal lungs	6–8	12–16
Neuromuscular disease, postoperative period, or with normal pulmonary mechanics in which maintaining lung volume is a concern	6–8	12–16
Acute restrictive disease, ALI/ARDS	4–8	20–35
Obstructive lung disease (COPD)	6–8	10–12[b]
Acute severe asthma exacerbation	4–6	8–12
Children		
Age 8–16 years	6–8	20–30
Age 0–8 years	6–8	25–35

[a]In all patients, maintain P_{plat} at <28 cm H_2O and driving pressure <15 cm H_2O.
[b]For patients with obstructive disease, ensure a short inspiratory time and long expiratory time to avoid air trapping and minimize auto-PEEP. Lower V_T and rate may be necessary in acute asthma to avoid further lung overinflation.
ALI, Acute lung injury; *ARDS,* acute respiratory distress syndrome; *COPD,* chronic obstructive pulmonary disease

Generally, the pressure limit is increased or decreased to achieve a target V_T while a P_{plat} of less than 28 cm H_2O and a driving pressure less than 15 cm H_2O is maintained. A good initial pressure setting is to start at 10 cm H_2O (above PEEP) and observe the resulting V_T. Pressure is increased or decreased to achieve the desired volume. As with VA/C, minute ventilation with PA/C is simply rate multiplied by tidal volume V_T($\dot{V}_E = f \times V_T$). Recommended initial V_T and frequency for various patient types are described in Table 49.5.

Patients with ARDS may need lower V_T to avoid further lung injury and a higher rate to maintain effective alveolar ventilation, while P_{plat} is maintained less than 28 cm H_2O and driving pressure less than 15 cm H_2O. Results of multicenter studies suggest V_T of 4 to 8 mL/kg IBW for patients with ARDS.[2,23,24] Set respiratory rates of 25 to 35 breaths/min may be needed in patients with ARDS to maintain adequate minute ventilation. Box 49.7 summarizes the ARDS Clinical Network guidelines for initial ventilator setup.[2]

Trigger Sensitivity

Trigger sensitivity should be set at the most sensitive level avoiding autotriggering to minimize trigger work and missed triggering. With flow triggering, the trigger should be set at 1 to 2 L/min, and with pressure triggering, the range is generally −0.5 to −1.5 cm H_2O; however, because of pin holes in disposable ventilator circuits, the sensitivity may need to be adjusted to 3 or 4 L/min or −2 cm H_2O to avoid autotriggering. The increased use of ventilator graphics packages has led to the recognition that patients' inspiratory efforts are often insufficient to trigger the ventilator.[9] Factors that can prolong ventilator response time include large V_T, low trigger sensitivity, auto-PEEP, high bias circuit flow, and abdominal paradox (Box 49.8) (see Chapter 48).

Many ventilators offer the option of a pressure or a flow trigger. With older generation intensive care unit (ICU) ventilators, flow triggering offered slightly lower trigger work than pressure triggering,[27-29] although the gain in terms of the patient's total WOB was slight. Newer ventilators with fast pressure-triggering capabilities are as sensitive as flow-triggered devices;[30,31] however, no triggering mechanism can reduce the WOB caused by auto-PEEP, which must be addressed by other means (see Chapter 48). Flow-trigger settings vary by ventilator. Generally, for flow triggering, the trigger flow should be set 1 to 2 L/min below baseline or bias flow.

BOX 49.7 Initial Ventilator Setup and Management of Oxygenation, Plateau Pressure, and pH

1. Calculate predicted (ideal) body weight as follows:
   - Men: Weight in kilograms = 50 + 2.3 (height in inches − 60)
   - Women: Weight in kilograms = 45.5 + 2.3 (height in inches − 60)
2. Select assist/control mode.
3. Set V_T to 6–8 mL/kg of predicted body weight.
4. Set initial rate to achieve baseline minute ventilation ($\dot{V}_E$). Rate only limited by the development of auto-PEEP.
5. Adjust V_T and rate to achieve pH of 7.30–7.45 while maintaining P_{plat} of ≤28 cm H_2O.
6. Set inspiratory flow rate above patient demand (may be >80 L/min).
7. For oxygenation to achieve PaO_2 of 55–80 mm Hg or SpO_2 88%–95%, set FiO_2 after establishing PEEP to the level resulting in acceptable oxygenation. Over time adjust FiO_2 to maintain oxygenation level. When FiO_2 is ≤0.5, decrease PEEP slowly 2 cm H_2O every 8 hours. If patient desaturates during PEEP decrease, reestablish PEEP.

FiO_2	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7
Low PEEP	5	5	8	8	10	10	10	12
High PEEP	12–14	14	16.0	16.0	18–20	20	20	20
FiO_2	0.7	0.8	0.9	0.9	0.9	1.0	1.0	1.0
Low PEEP	14	14	14	16	18	20	22	24
High PEEP	20	20–22	22	22	22	22	22	24

8. Check P_{plat}, SpO_2, respiratory rate, V_T, and pH (if available) at least every 4 hours and after each change in PEEP or V_T:
   - If P_{plat} is >28 cm H_2O, decrease V_T by 1-mL/kg steps (minimum 4 mL/kg).
   - If P_{plat} is <25 cm H_2O and V_T is <6 mL/kg, V_T may by increased in 1-mL/kg steps until P_{plat} is >25 cm H_2O or V_T is 6 mL/kg.
   - If P_{plat} is <20 and breath stacking occurs, V_T may be increased in 1-mL/kg increments (maximum 8 mL/kg).
9. The pH goal is 7.30–7.45.
   For acidosis management (pH < 7.30):
   - If pH is 7.15–7.30, increase the rate until pH is >7.30.
   - If metabolic acidosis is present, address the cause of the acidosis maintaining $PaCO_2$ > 25 mm Hg.
   For alkalosis management (pH > 7.45), decrease ventilator rate, if possible.

FiO_2, Fractional inspired oxygen; *PEEP,* positive end-expiratory pressure.
Adapted from National Institutes of Health (NIH) National Heart Lung and Blood Institute (NHLBI) ARDS Clinical Network Mechanical Ventilation Protocol Summary (Mechanical Ventilation Protocol Summary, revised 25 January 2005).

BOX 49.8 Factors That Can Prolong Ventilator Response Time

- Low trigger sensitivity
- Large V_T (causing air trapping)
- Abdomen–rib cage paradox
- Auto-PEEP (dynamic hyperinflation)
- High tubing compliance
- High circuit dead space
- High bias flow in the circuit
- Mechanical malfunction

PEEP, Positive end-expiratory pressure.

Inspiratory Flow, Time, and Inspiratory-to-Expiratory Ratio for Volume Ventilation

Most modern critical care ventilators allow the clinician to select peak flow, V_T, and rate *or* inspiratory time (or percentage inspiratory time, V_T, and rate). For most adults, an initial inspiratory time of approximately 0.8 second (range 0.6 to 1.0 second) with a resultant inspiratory-to-expiratory (I:E) ratio of 1:2 or lower is a good starting point. This value corresponds to an initial peak flow setting of approximately 60 L/min (range 40 to 80 L/min) and a down ramp (decelerating) or square flow waveform. Higher flow (≤100 L/min) may improve gas exchange in patients with chronic obstructive pulmonary disease (COPD), which may be a result of a longer expiratory time resulting in less air trapping.[10] (See Chapter 48.)

Inspiratory flow rate should be adjusted to ensure that the flow provided meets or exceeds the patient's spontaneous inspiratory flow[1] (see Chapter 48). A less sensitive trigger level and lower ventilator inspiratory flow tend to increase the patient's WOB. Common ventilator configurations and related controls that determine inspiratory flow, time, and I:E ratio are described in Fig. 49.3.

For ventilators with V_T, peak flow, and rate controls, inspiratory time is determined by V_T, peak flow, and flow pattern. To decrease inspiratory time, one may increase peak flow, decrease V_T, or change from a down ramp to a square wave flow pattern. Expiratory time and I:E ratio are determined by inspiratory time and rate. To increase expiratory time (and decrease I:E ratio), one may decrease the inspiratory time as described earlier or increase the expiratory time by decreasing the rate.[1]

For ventilators with V_T (or minute ventilation), percentage inspiratory time, and rate controls, the inspiratory time and V_T determine the inspiratory flow rate. On these ventilators, one can directly increase or decrease the percentage inspiratory time. At the same rate, as inspiratory time (or percentage inspiratory time) decreases, expiratory time and inspiratory flow rate increase, and I:E ratio decreases. An increase in V_T at the same percentage inspiratory time and rate also increases inspiratory flow rate with no change in I:E ratio. Box 49.9 shows the calculation of inspiratory flow rate based on percentage inspiratory time settings. To alter I:E ratio on these ventilators, one simply adjusts inspiratory percent time. Decreasing rate at the same inspiratory percent time setting does not affect I:E ratio, and both inspiratory time and expiratory time increase owing to a longer respiratory cycle. Changing the inspiratory flow waveform on these ventilators has no effect on inspiratory time, expiratory time, or I:E ratio; however, flow waveform changes affect peak and mean airway pressure.

BOX 49.9 Calculation of Inspiratory Flow Rate From Percentage Inspiratory Time

The effect of percentage inspiratory time on inspiratory flow rate can be estimated as follows:

$$\text{Inspiratory flow rate} = \frac{\text{Set minute ventilation}}{\text{Percentage inspiratory time} \times 0.01}$$

For example, a patient being treated with a Servo ventilator may have the following ventilator settings:

- Set minute ventilation = 12 L/min
- Set CMV rate = 20 breaths/min
- Resulting V_T = 12 L/20 breaths/min = 0.6 L or 600 mL
- Set time inspiratory percentage = 25%
- Set pause time percentage = 0%

$$\text{Inspiratory flow rate} = \frac{12\,\text{L/min}}{25\% \times 0.01} = \frac{12\,\text{L/min}}{0.25} = 48\,\text{L/min}$$

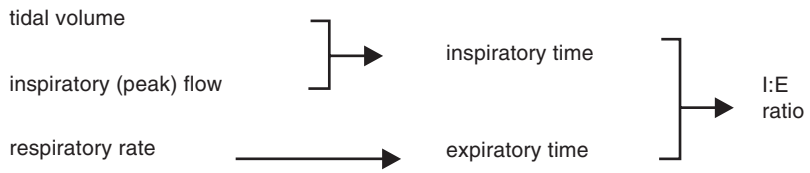
CMV, Continuous mechanical ventilation.

Flow Waveform

Flow waveform options on mechanical ventilators vary from a preset square wave to seven adjustable waveforms on older ventilators. Common choices available on current generation ventilators for waveform are square or down ramp (decreasing or "decelerating" waveform). Pressure support and pressure-controlled modes also deliver decreasing flow waveforms, but the decrease is patient-specific and not programmed into the gas delivery. The literature on clinical application of specific waveforms is mixed;[32] however, as one moves from an increasing ("accelerating") flow waveform to a square wave to a decreasing flow waveform, while holding inspiratory time constant, there tends to be a predictable decrease in peak airway pressure and a corresponding increase in mean airway pressure.[32] Increases in mean airway pressure may improve oxygenation, but may also impede venous return to the heart.[32] We suggest a decreasing, or down ramp, flow waveform when the goal is optimization of the distribution of inspired air and improvement in oxygenation. A square waveform may be useful in reducing mean airway pressure in patients with severe hypotension or cardiovascular instability. Fig. 49.4 compares the effect of ventilator flow waveforms on peak and mean airway pressure. Box 49.10 describes guidelines for selecting flow waveform during volume ventilation.

During PCV or PSV, a decreasing flow waveform is delivered. The initial peak flow is typically reached rapidly. Flow decreases throughout inspiration until the breath is terminated. With PSV, inspiration ends when the flow decreases to a preset value, typically adjustable from 5% to 85% of the peak flow in some newer ventilators. With PCV, flow continues to decrease until the inspiratory time has elapsed. In the PCV mode, increasing inspiratory time tends to increase V_T until zero flow is reached at end inspiration. Further increases in inspiratory time do not increase V_T, although distribution of inspired air may improve and mean airway pressure does increase.

A. Tidal volume, peak flow, and rate determine inpiratory time, expiratory time, and I:E ratio.



↑ tidal volume → ↑ inspiratory time → ↓ expiratory time→ ↑ I:E ratio

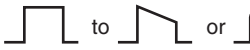
↓ tidal volume → ↓ inspiratory time → ↑ expiratory time → ↓ I:E ratio

↑ peak flow → ↓ inspiratory time → ↑ expiratory time → ↓ I:E ratio

↓ peak flow → ↑ inspiratory time → ↓ expiratory time → ↑ I:E ratio

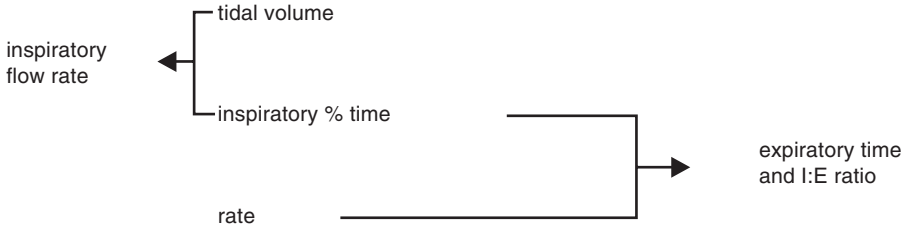
↑ rate → ↓ expiratory time → ↑ I:E ratio

↓ rate → ↑ expiratory time → ↓ I:E ratio

 to or → ↑ inspiratory time → ↓ expiratory time → ↑ I:E ratio

 or  to  → ↓ inspiratory time → ↑ expiratory time → ↓ I:E ratio

B. Tidal volume, % inspiratory time, and rate determine inspiratory flow rate, expiratory time, and I:E ratio.



↑ tidal volume → ↑ inspiratory flow rate → no change in inspiratory time, expiratory time, or I:E ratio

↓ tidal volume → ↓ inspiratory flow rate → no change in inspiratory time, expiratory time, or I:E ratio

↑ rate → ↓ expiratory time → I:E ratio constant or ↑*

↓ rate → ↑ expiratory time → I:E ratio constant or ↓*

↑ inspiratory % time → ↓ expiratory time

↓ inspiratory % time → ↑ expiratory time

*In the VC-CMV mode, ventilators with a percent inspiratory time control will maintain a constant I:E ratio with changes in rate. For the Servo 900C, 300, 300A, and Hamilton Veolar, changes in SIMV rate will alter I:E ratio in the SIMV mode, as described.

Fig. 49.3 Relationship between V_T, inspiratory flow, inspiratory time, expiratory time, and I:E ratio in various ventilator systems. (A) Effects of V_T, flow, and respiratory rate on inspiratory time, expiratory time, and inspiratory-to-expiratory (I:E) ratio. Some ventilators provide V_T, inspiratory flow, and rate control in volume control (VC) and synchronized intermittent mandatory ventilation (SIMV) modes. (B) Effects of volume, inspiratory time, and rate on inspiratory flow, expiratory time, and I:E ratio. Other ventilators provide controls for inspiratory time (or percentage inspiratory time), V_T (or minute ventilation), and rate control in the VC and SIMV modes. In the VC mode (controlled ventilation), ventilators with a percentage inspiratory time control maintain a constant I:E ratio with changes in respiratory rate. In the SIMV mode, changes in SIMV rate alter I:E ratio on these machines.

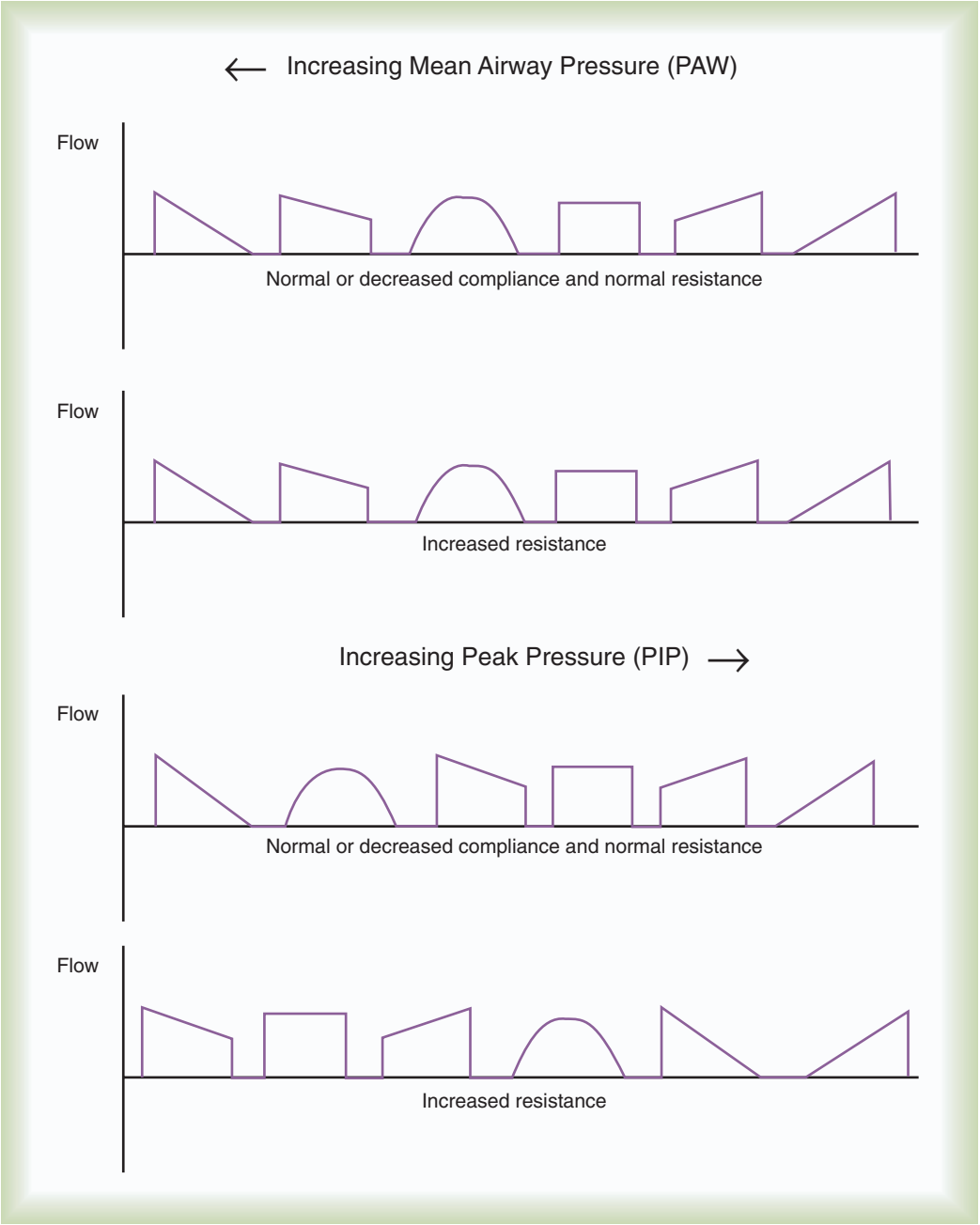


Fig. 49.4 Effect of ventilator flow waveform on peak and mean airway pressure with changing lung mechanics. Generally, flow waveforms that tend to increase mean airway pressure also decrease peak pressure *(PIP)* and vice versa. Consequently, if increasing mean airway pressure is the goal, decelerating *(down ramp)* flow waveforms may be helpful; however, in the care of patients with cardiovascular compromise, in whom reducing mean airway pressure may be helpful, a square wave may be valuable. Accelerating flow waveforms are no longer available on newer critical care ventilators. (Modified from Rau JL, Shelledy DC: The effect of varying inspiratory flow waveforms on peak and mean airway pressures with a time-cycled volume ventilator: a bench study. *Respir Care* 36:347, 1991.)

Inspiratory Pause

An inspiratory pause is rarely used for therapeutic purposes; it is normally used for estimating the plateau pressure. In addition to inspiratory time or flow, most ventilators have an option for setting an inspiratory pause or hold in the volume-control mode. From an assessment standpoint, an inspiratory pause may be used; however, from the therapeutic perspective, a brief inspiratory pause (up to 10%) has been recommended in the past for improving the distribution of the inspired air and PaO_2.[33] Use of an inspiratory pause has been suggested for administration of bronchodilators to improve medication delivery; however, in COPD patients, an inspiratory pause did not result in significant improvement in bronchodilator effectiveness.[9] If a brief inspiratory pause is used, I:E ratio and mean airway pressure

BOX 49.10 Guidelines for Selecting Inspiratory Flow Waveforms During Volume Ventilation

Constant Flow Waveform

- Alternative terms: Square wave, rectangular wave, constant flow generator.
- Advantages: High flow provided with a reduced inspiratory time and improved I:E ratio; may decrease mean airway pressure, which may be helpful in terms of venous return and cardiac output in compromised patients.
- Disadvantages: Increased PIP may lead to excessive pressure; lower mean airway pressure may affect oxygenation; inadequate peak flow may cause flow asynchrony.

Decreasing Flow Waveform

- Alternative terms: Down ramp, decelerating flow, descending ramp.
- Advantages: Lower PIP and higher mean airway pressure; this flow waveform may improve gas distribution, oxygenation, and patient–ventilator synchrony.
- Disadvantages: Increased mean airway pressure may impede venous return and cardiac output in compromised patients; in ventilators that have a peak flow control, the down ramp increases inspiratory time and I:E ratio and decreases expiratory time.

I:E, Inspiratory-to-expiratory; *PIP,* peak inspiratory pressure.

increase. An inspiratory pause of 0.5 to 2 seconds applied for a single breath is used for measurement of P_{plat} and in estimation of airway resistance (Raw):

$$\text{Raw} = \text{PIP} - P_{plat}/\text{Inspiratory flow (L/sec)}$$

where PIP is peak inspiratory pressure. An inspiratory pause should never be set in a spontaneously breathing patient except for a single breath in attempts to measure P_{plat} because it increases the level of asynchrony, causing the patient to fight the pause and to try to exhale during the pause.

An inspiratory pause can also be used for diagnostic or assessment purposes to either determine plateau pressure or ensure a full inspiration before a chest radiograph is obtained.[34] Irrespective as to whether it is used for therapeutic or diagnostic purposes, the use of an extended inspiratory pause should be limited because of the resultant increase in mean airway pressure and risk of impeding venous return and cardiac output. This is especially true in patients who are hypovolemic or hypotensive or whose condition is hemodynamically unstable.

RULE OF THUMB An end inspiratory pause should only be used to estimate the end inspiratory P_{plat}. It should never be applied continuously to a patient actively triggering the ventilator.

Oxygen Percentage (Fractional Inspired Oxygen)

FiO_2 selected on initiation of mechanical ventilation varies with the patient's condition. If little is known about the patient or if the patient's condition appears to be grave, 100% O_2 is the preferred starting point. Examples of disease states or conditions that typically warrant initial FiO_2 of 1 include acute pulmonary edema, ARDS, near drowning, cardiac arrest, severe trauma, suspected aspiration, severe pneumonia, carbon monoxide poisoning, and any disease state or condition resulting in a large right-to-left shunt. After initiation of mechanical ventilation with FiO_2 of 1, the FiO_2 should be reduced as soon as is practical to avoid O_2 toxicity and absorption atelectasis. In most patients, FiO_2 should always be adjusted to ensure PaO_2 of 55 to 80 mm Hg or SpO_2 of 88% to 95%. Recent data indicates that patients maintained on high FiO_2 resulting in $PaO_2 > 100$ mm Hg or $SpO_2 > 95\%$ have greater mortality than those maintained at an FiO_2 that maintains PaO_2 of 55 to 80 mm Hg or SpO_2 of 88% to 95%.[35,36]

Patients who have undergone previous blood gas measurement or oximetry who are doing well clinically, and patients with disease states or conditions that normally respond to low to moderate concentrations of O_2, may begin ventilation with a lower O_2 concentration (50%). These typically are patients with normal ventilation/perfusion ($\dot{V}/\dot{Q}$) or a $\dot{V}/\dot{Q}$ imbalance without shunt ($\dot{V}/\dot{Q}$ <1 but >0). Patients who often do well with low-to-moderate concentrations of O_2 include patients with acute exacerbation of COPD, emphysema, chronic bronchitis, drug overdose without aspiration, or neuromuscular disease and postoperative patients with normal lungs. For example, a patient with an acute exacerbation of COPD who needs mechanical ventilatory support may have had PaO_2 of 50 mm Hg with a nasal cannula at 4 L/min before intubation and mechanical ventilation. This patient would probably do well with FiO_2 of approximately 0.50 when adequate ventilation is restored. The patient can begin with 50% O_2 and be immediately assessed for assurance of adequate SpO_2. FiO_2 can be adjusted according to the patient's response. Many ICU patients are now managed with an FiO_2 of 21% because that is all that is needed to maintain appropriate oxygenation.

Positive End-Expiratory Pressure and Continuous Positive Airway Pressure

PEEP and CPAP are effective techniques for improving and maintaining lung volume and improving oxygenation for patients with acute restrictive disease such as pneumonia, pulmonary edema, and ARDS.[1,9] PEEP and CPAP should be cautiously applied in the treatment of patients with an already elevated functional residual capacity (FRC), such as patients with COPD or acute asthma, except at levels that are applied to offset auto-PEEP and air trapping.[9] Generally, the indication for PEEP or CPAP is inadequate arterial O_2 with moderate-to-high concentrations of O_2 caused by unstable lung units that are collapsed. PaO_2 less than 50 to 60 mm Hg with FiO_2 greater than 0.40 is a good general starting place for considering use of PEEP or CPAP.

In terms of ventilator initiation, initial PEEP or CPAP levels are usually 5 to 8 cm H_2O, even in the absence of unstable lung units or auto-PEEP. Most experts advocate for the use of 5 cm H_2O PEEP for all patients who have an artificial airway in place. Intubation results in small reductions in FRC,[1,9] which can be balanced with the application of PEEP or CPAP.

PEEP has been advocated in the presence of auto-PEEP, in particular in the care of patients with obstructive lung disease.[37] Applied PEEP in the presence of auto-PEEP is indicated only if the patient has difficulty triggering the ventilator. During controlled ventilation, increasing PEEP in the presence of auto-PEEP is usually not indicated (see Chapter 48 for auto-PEEP details). An absolute contraindication to PEEP is an uncontrolled tension

pneumothorax; however, PEEP should be cautiously applied in any patient with severe intrinsic lung disease, hypotension, and elevated intracranial pressure.

Open Lung Strategy, Recruitment Maneuvers, and Positive End-Expiratory Pressure

In the care of patients with ARDS, it is usually necessary to initiate PEEP at 10 to 15 cm H_2O;[24,25,38,39] however, many clinicians use the ARDS Clinical Network PEEP/FiO_2 tables to set PEEP initially during the establishment of ventilatory support (see Box 49.7). When patients are stabilized, the use of an open lung ventilation strategy in early-stage ARDS has been recommended.[1,5] Such a strategy incorporates V_T of 4 to 8 mL/kg IBW with either pressure-targeted or volume-targeted ventilation and a PEEP level set after a lung recruitment maneuver using a decremental PEEP trial.[1,5,40,41] The lung recruitment maneuver is intended to open collapsed lung units, and the setting of PEEP using a decremental PEEP trial is intended to apply PEEP based on the patient's lung mechanics to keep the recruited lung units open.

Although all patients with ARDS require PEEP, not all patients with ARDS respond to low-level PEEP, and patients with pulmonary (vs. nonpulmonary) causes of ARDS, such as pneumonia, may be less likely to respond to low to moderate levels of PEEP.[12] Nonpulmonary causes of ARDS (e.g., extrathoracic trauma, intraabdominal sepsis) seem to respond well to PEEP.[12] In practice, some authors have suggested that higher levels of PEEP (>15 cm H_2O) be reserved for patients with a high percentage of recruitable lung.[4] High levels of PEEP have been shown to improve outcomes in ARDS in patients with the most severe forms of ARDS (PaO_2/FiO_2 < 150 mm Hg).[42,43] (See later section on the performance of recruitment maneuvers and the setting of PEEP by decremental trial.)

Pressure Rise Time or Slope

Most newer, critical care ventilators include an inspiratory pressure rise time or pressure slope. This control functions only with pressure-limited breaths (PSV, PCV, PRVC, volume support, APRV, pressure SIMV). The purpose of this control is to adjust the rate at which flow increases from baseline to peak (see Chapter 48 for details).[44-46]

Limits and Alarms

Ventilator alarms and limits warn of ventilator malfunction and changes in patient status. Ventilator malfunction alarms include power or gas supply loss and electronic or pneumatic malfunction. These alarms are usually preset by the manufacturer.

Patient status alarms are usually set by the RT. These include maximum inspiratory pressure, low-pressure and low-PEEP alarms, high-volume, low-volume and rate alarms, O_2 and humidification alarms, and apnea alarms. After initiation of ventilation, alarms and limits are readjusted as needed. Alarms are usually set so that they warn the clinician of important changes or problems. Without proper setting, these alarms can become a nuisance by falsely signaling problems that are not real.[9]

In volume ventilation, a pressure limit should be set. Generally, before the patient is connected to the ventilator, the limit should be set at 40 cm H_2O to avoid over pressuring the system when the patient is connected. After the patient is connected to the ventilator, the peak and plateau pressures should be assessed. If P_{plat} is greater than 28 cm H_2O, consideration should be given to decreasing the set V_T. If P_{plat} is less than 28 cm H_2O, the high-pressure limit can be adjusted to 10 to 15 cm H_2O above PIP. One can decrease peak pressure by decreasing the peak flow rate, increasing the inspiratory time, changing the inspiratory flow waveform from a square to a down ramp, or decreasing the delivered V_T. For spontaneously breathing patients, inspiratory flow and time must meet or exceed the patient's inspiratory demand to ensure one does not increase the patient's WOB further (see Chapter 48 for details). Preset or adjustable alarms common to most ventilators include pressure (high-low), volume (high-low V_T, minute ventilation), apnea, O_2 percentage, and temperature. Suggested initial settings for these alarms and backup ventilator settings are presented in Table 49.6.

TABLE 49.6 Alarm and Backup Ventilation Setting of Initial Ventilatory Setup (Adults)

Low pressure	5–10 cm H_2O below PIP
Low PEEP/CPAP	3–5 cm H_2O below PEEP
High pressure limit	Max 50 cm H_2O, adjusted to 10–15 cm H_2O above PIP
Low exhaled V_T	100 mL or 50% below set V_T
Low exhaled minute ventilation	2–5 L/min or 50% below minimum SIMV or assist/control backup minute ventilation
High minute ventilation	50% above baseline minute ventilation
O_2 percentage (FiO_2)	5% above and below set O_2 percentage
Temperature	2°C above and below set temperature, do not exceed 37°C
Apnea delay	20 s
Apnea values	V_T and rate set to achieve full ventilatory support (V_T 8–10 mL/kg; rate 10–12 breaths/min) with 100% O_2

CPAP, Continuous positive airway pressure; *FiO_2,* fractional inspired oxygen; *PEEP,* positive end-expiratory pressure; *PIP,* peak inspiratory pressure.

Humidification

Humidification is required during both invasive and noninvasive mechanical ventilation. A heated humidifier or a HME should provide a minimum of 30 mg/l of water with a temperature of 30°C or greater.[47] Use of HMEs should be avoided in the care of patients with thick and or retained secretion and patients with low body temperature (<32°C), high spontaneous minute ventilation (>10 L/min), or air leaks in which exhaled V_T is less than 70% of delivered V_T.[47] Heated humidifiers may be used to deliver saturated gas at 100% relative humidity at body temperature (see Chapter 39). Current clinical practice guidelines suggest an inspired gas temperature of 35 ± 2°C.[48] The optimal humidity approach uses a heated humidifier to deliver gas in the range of 35 to 37°C at the airway and at a temperature consistent with patient comfort during noninvasive ventilation; however, in patients without primary pulmonary dysfunction and short-term ventilation, HMEs are very useful. Generally, these are postoperative patients after elective surgery, patients in the emergency department, and patients recovering from an overdose.

Periodic Sighs

Constant, monotonous tidal ventilation at a small volume (<7 mL/kg) may result in progressive atelectasis.[9,49] Periodic deep breaths or sighs delivered every 6 to 10 minutes reverse this trend.[9,49] During the 1960s and 1970s, it was common to ventilate patients with a smaller V_T (5 to 7 mL/kg) and no PEEP. As a result, an intermittent sigh function was incorporated into most volume ventilators. Sighs were programmed at 1½ to 2 times the set V_T at an interval of every 6 to 10 minutes. Sometimes, multiple sighs were included at a preset interval of up to 10 times per hour; however, because of the use of PEEP, sighs are no longer routinely included. Appropriate PEEP helps prevents the formation of atelectasis with constant small V_T. This is the primary reason why 5 to 8 cm H_2O of PEEP is routinely used on patients, including patients with healthy lungs. General guidelines for the initial ventilator settings for most adult patients are described in Box 49.11.

BOX 49.11 General Guidelines for Initial Ventilator Settings for Adult Patients

Mode
- Assist/control volume or pressure targeted
- Pressure support

Tidal Volume
- 4–8 mL/kg IBW
- Avoid overdistention
- Maintain P_{plat} <28 cm H_2O
- For COPD, V_T 6–8 mL/kg IBW in assist/control or pressure support mode with adequate expiratory time for reducing air trapping is suggested
- For ARDS, begin at 6–8 mL/kg IBW; adjust as indicated to maintain P_{plat} <28 cm H_2O
- For acute asthma, V_T 4–6 mL/kg IBW is indicated to maintain P_{plat} <28 cm H_2O

Rate
- 18 (asthma)–40 breaths/min
- Minimize auto-PEEP
- Set initial rate and V_T to maintain baseline minute ventilation (approximately 100 mL/kg IBW for most healthy adults)

PEEP
- 5 cm H_2O in most patients ventilated without acute lung injury
- 10 cm H_2O in patients with mild ARDS
- 15–20 cm H_2O in most patients with moderate to severe ARDS
- 5 cm H_2O in patients with COPD, adjust as indicated to offset effect of auto-PEEP on ventilator triggering
  0–5 cm H_2O with asthma, must evaluate the effect of applied PEEP on total PEEP. In most asthmatic patients, applying PEEP increases total PEEP.
- Trigger sensitivity –0.5 to –1.5 cm H_2O or flow trigger 1–2 L/min; minimize trigger work without autocycle
- Inspiratory flow and time 60–100 L/min
- Inspiratory time 0.6–1.0 s; inspiratory flow must meet or exceed patient's spontaneous inspiratory flow demand
- Resultant I:E ratio should be ≤1 : 2

ARDS, Acute respiratory distress syndrome; *COPD,* chronic obstructive pulmonary disease; *IBW,* ideal body weight; I:E, inspiratory-to-expiratory; *PEEP,* positive end-expiratory pressure.

ADJUSTING VENTILATORY SUPPORT

After ventilator initiation, the patient should be carefully assessed and the ventilator adjusted so that patient–ventilator synchrony is ensured; WOB is minimized; and oxygenation, ventilation, and acid–base balance are optimized while harmful cardiovascular effects are minimized. Initial patient evaluation should include physical assessment, assessment of ventilator settings, cardiovascular assessment, oximetry, and measurement of arterial blood gases (Box 49.12).

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Humidification of the Airways During Mechanical Ventilation

Problem

A mechanically ventilated patient is in the medical ICU recovering from acute respiratory failure secondary to aspiration pneumonia. The patient currently needs airway suctioning every 30–60 min according to the RT and staff nurse caring for the patient. Both caregivers note that the secretions are thick and copious. Current ventilator settings are as follows:
Mode: A/C volume ventilation
V_T: 500 mL (6.8 mL/kg IBW)
Preset rate: 16 breaths/min
Total rate: 26 breaths/min
FiO_2: 0.50
PIP: 31 cm H_2O
V_E: 13 L/min

The RT is asked to place an HME on the ventilator circuit at the "wye." Is this an appropriate action?

Solution

Humidification can be provided with either a heated humidifier or an HME. Although useful in some instances, placement of an HME would be contraindicated in this case for several reasons. Adequate humidification for a patient with an artificial airway is critical in preventing inspissation of airway secretions, injury to and destruction of the airway epithelium, and atelectasis.

The patient information in this clinical scenario points to several potential problems with use of an HME, the most obvious one being copious, thick airway secretions. The HME may not provide sufficient water vapor and heat output, and secretions could be retained. The airway secretions could be coughed into the HME, causing increased resistance to flow and possible obstruction. Because the patient has high ventilatory requirements, as evidenced by an elevated exhaled minute ventilation, it is important that the humidification system can maintain adequate heat and moisture output when demands dictate.

Other situations in which an HME should not be used are administration of aerosol treatments through the ventilator tubing circuit, high-minute ventilation (>10 L/min), and body temperature less than 32°C.

BOX 49.12 Initial Assessment of Ventilatory Support

- Inspection, palpation, and auscultation.
- Assessment of position of artificial airway and cuff inflation.
- Assessment of pulse, blood pressure, oximetry, and electrocardiogram.
- Inspection of patient–ventilator system breathing circuit, humidifier, ventilator settings, and findings.
- Analysis of arterial blood gas values.
- Inspection of chest radiograph.

Physical assessment should include general appearance, level of consciousness, signs of anxiety or dyspnea, color, extremities (temperature, edema, capillary refill, cyanosis), heart rate and blood pressure, respiratory rate and pattern, inspection of the neck for jugular venous distention, and chest examination. Use of accessory muscles, tachypnea, retractions, or paradoxical abdomen movement may indicate increased WOB. Unilateral or unequal lung expansion is associated with bronchial intubation, pneumothorax, and other unilateral disorders.

Breath sounds should be assessed for good aeration, and absent, diminished, or abnormal breath sounds should be documented. Palpation should be performed as appropriate for tracheal position, chest wall motion, and presence of subcutaneous air. Percussion of the chest should be performed for assessment of resonance, dullness, or hyperresonance. Key findings at initial assessment of a patient undergoing ventilation are described in Table 49.7.

Ventilator settings that should be assessed after initiation of mechanical ventilation include peak, plateau, and mean airway pressures; exhaled volumes (spontaneous and machine V_T, minute ventilation); respiratory rate (spontaneous and machine rate); baseline pressures (PEEP, CPAP, auto-PEEP); trigger effort; O_2 concentration; inspiratory time; flow; I:E ratio; humidification; airway temperature; and airway cuff pressure. In addition, patient-ventilator interaction should be assessed to ensure that a spontaneously breathing patient is able to trigger a breath easily and that inspiratory flow and time are such that WOB is minimized. When using pressure ventilation, the patient should also be evaluated to ensure ease of cycling to expiration. Factors that may affect patient–ventilator interaction are discussed in detail in Chapter 48.

The artificial airway should be assessed for proper placement, patency, and cuff inflation. Size, position, and depth of the endotracheal tube and cuff pressure, including volume used to inflate the cuff, should be recorded. A clean, functioning manual resuscitator with O_2 supply and suction equipment including an appropriate supply of suction catheters, sterile water or saline solution, and sterile gloves must also be placed near the bedside. Patients requiring high levels of PEEP (>5 cm H_2O) should have PEEP valves attached to the manual ventilator.

Cardiovascular assessment should include observation of heart rate, blood pressure, and electrocardiogram for the presence of arrhythmias. Tachycardia, ST segment elevation, and frequent premature ventricular contractions may indicate myocardial ischemia. If the patient has a central venous line or pulmonary arterial catheter, hemodynamic variables may be assessed, including central venous pressure, pulmonary arterial pressure, wedge pressure, and cardiac output.

Continuous monitoring with pulse oximetry is recommended for patients receiving mechanical ventilatory support in the ICU, and arterial blood gases should be measured 30 to 60 minutes after initiation of mechanical ventilation. A chest radiograph should be obtained to verify proper endotracheal tube placement and to evaluate the chest and lungs. After the initial assessment,

TABLE 49.7 Assessment of Ventilatory Support

Ancillary equipment in room	Crash cart (patient's condition unstable); cardiac monitor; chest tubes (pneumothorax, chest drainage, thoracic surgery); aortic balloon pump (heart failure); cooling blanket (fever); other
General appearance	Resting quietly, calm, relaxed (no distress); restless, anxious, distressed (pain, anxiety, inadequate oxygenation or ventilation)
Level of consciousness	Alert, awake, and oriented to person, place, and time (good mental status, neurologic function); confused (neurologic problems, hypoxia, low cardiac output, drugs); sleepy (tired, sedatives, narcotics); lethargic (exhaustion, impaired CNS status, sedation); somnolent (CNS impairment, sedation); coma (CNS malfunction, heavy sedation, severe hypoxia)
Extremities	Cyanosis (hypoxemia); pale, cold, and clammy (poor cardiac output, low blood pressure, shock); edema (fluid overload)
Respiratory rate and pattern	Normal (good cardiopulmonary status); tachypnea (pain, anxiety, hypoxemia, acidosis, CNS problems); bradypnea or apnea (severe hypoxia, CNS problems, heavy sedation, paralysis)
Head, eyes, ears, nose, and throat	Cyanotic lips and gums (hypoxemia); pupils dilated (drugs, severe hypoxia, low cardiac output, cardiac arrest); pupils dilated and fixed (brain death); pupils contracted (drugs, light); response to light (good if responsive)
Neck	Accessory muscle use (increased WOB, respiratory distress); jugular vein distention (right-sided heart failure, positive pressure impeding venous return)
Chest inspection	Right-left chest wall synchrony (normal); right-left chest wall asynchrony (right main stem intubation, pneumothorax, large unilateral pleural effusion, flail on one side); chest-diaphragm synchrony (normal); chest-diaphragm asynchrony—abdominal paradox (increased WOB, diaphragmatic fatigue)
Chest auscultation	Good bilateral breath sounds (normal); decreased breath sounds unilaterally (right main stem intubation, pneumothorax, unilateral lung disease); bilaterally decreased or absent breath sounds (inadequate or decreased ventilation, large leak, ventilator malfunction or disconnect, misplaced endotracheal tube); air leak around cuff (underinflation, cuff malfunction); wheezing (bronchospasm, tumor, narrowing of airway); bibasilar crackles in patients with congestive heart failure (pulmonary edema); rhonchi, coarse crackles (secretions in the larger airways); bronchial breath sounds (consolidation or microatelectasis)
Palpation	Subcutaneous air (pneumothorax, pneumomediastinum); tracheal shift (tension pneumothorax, large area of atelectasis); right-left chest motion symmetry (normal); right-left asymmetric breathing (unilateral disease, pneumothorax, bronchial intubation)
Percussion	Resonant over lung tissue (normal); dull (pleural effusion, lobar infiltrates, consolidation, atelectasis); hyperresonant (pneumothorax, overinflation—COPD, asthma exacerbation)
Vital signs	Normal heart rate and rhythm (normal); tachycardia (hypoxemia, pain, anxiety, distress); hypertension (anxiety, cardiovascular disease, head trauma); bradycardia (severe hypoxia, severe hypercapnia, cardiac disease); hypotension (blood loss, shock, gram-negative sepsis, heart failure)

CNS, Central nervous system; *COPD,* chronic obstructive pulmonary disease; *WOB,* work of breathing.

the method and level of ventilatory support are adjusted to optimize oxygenation, ventilation, WOB, acid–base balance, and cardiovascular status. The ventilatory adjustments for each of these areas are discussed next.

Patient–Ventilator Interaction

Patient–ventilator interaction refers to patient comfort, WOB, and synchrony during ventilator-assisted breaths. Generally, ventilatory support should be initially adjusted to minimize the WOB and to allow the ventilatory muscles to rest.[50] See Chapter 48 for a detailed discussion.

OXYGENATION

Oxygen Concentration

Initiation of treatment for most patients in the acute care setting is with 100% O_2, unless detailed information identifying the precise FiO_2 required is available. FiO_2 is titrated to achieve PaO_2 of 55 to 80 mm Hg or SpO_2 88% to 95%. Estimate of O_2 needs can be derived as follows:

$$FiO_2 = \left(\frac{PaO_2 \text{ desired}}{PaO_2/PAO_2 \text{ ratio}} + PaCO_2 \times 1.25\right) \times \frac{1}{P_B - P_{H_2O}}$$

where FiO_2 required is the FiO_2 needed to achieve a desired PaO_2, PaO_2/PAO_2 is the initial PaO_2 divided by the initial alveolar partial pressure of oxygen (PAO_2), $PaCO_2$ is the initial $PaCO_2$, PB is barometric pressure, and P_{H_2O} is water vapor pressure. A simpler but less accurate calculation is as follows:

$$\underset{\text{Initial}}{PaO_{2(1)}/FiO_2(1)} = \underset{\text{Desired}}{PaO_{2(2)}/FiO_2(2)}$$

Instead of a formula, a nomogram can be used to predict a patient's required FiO_2 (Fig. 49.5). In either case, it is suggested that O_2 levels be titrated down from 100% to minimal FiO_2 required in decrements not to exceed 20%; titration is followed by oximetry or measurement of arterial blood gases. When

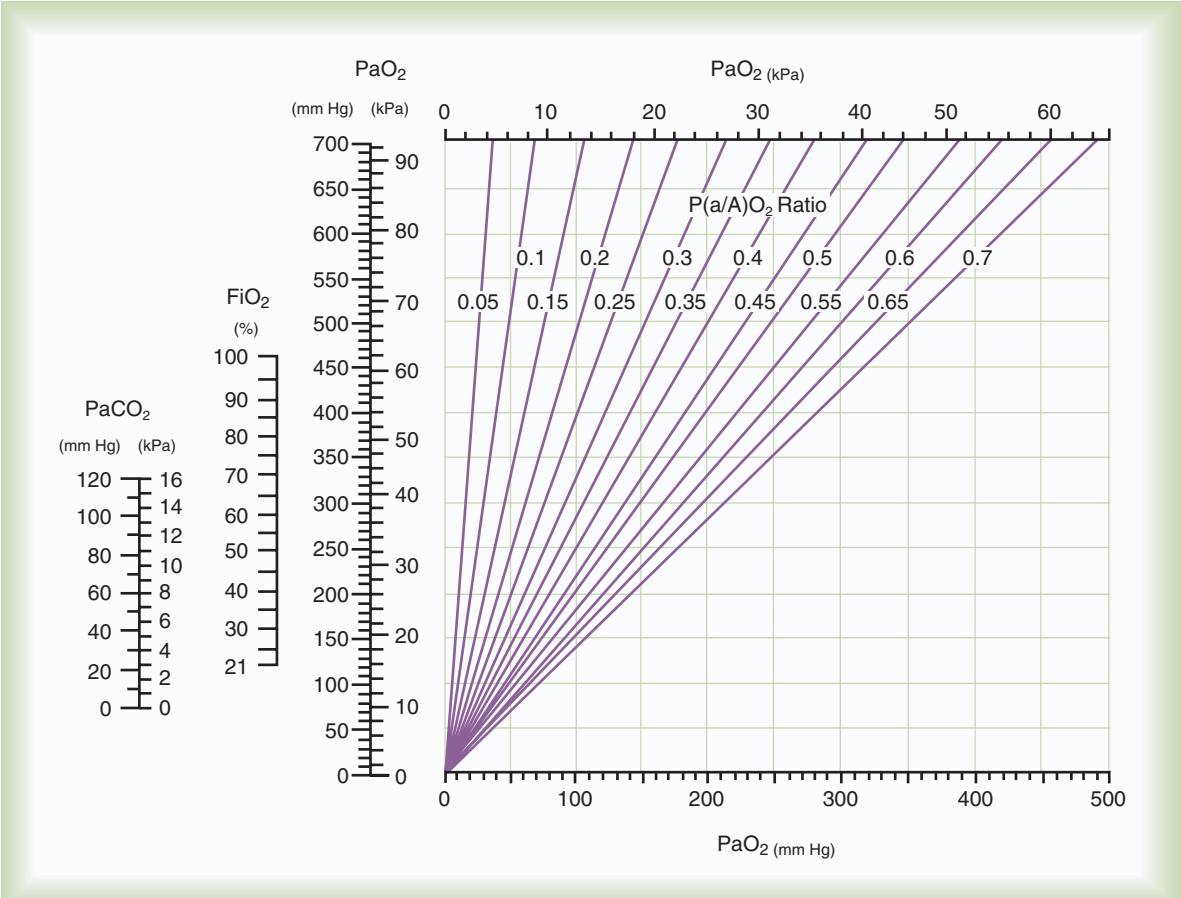

Fig. 49.5 Nomogram for computing PaO_2/PAO_2 ratio and predicting FiO_2 required for desired PaO_2. To use the nomogram, first align the patient's current $PaCO_2$ and FiO_2 *(left two columns)* with a straight edge. This line intersects the vertical line corresponding to the patient's PAO_2 *(third column)*. Draw a horizontal line from this point to the vertical line corresponding to the patient's PaO_2. The diagonal line at this point (or one interpolated from the nearest diagonal lines bracketing it) is the PaO_2/PAO_2 ratio. $PaCO_2$ of 40 mm Hg and FiO_2 of 50% give PAO_2 of approximately 310 mm Hg. If PaO_2 is 50 mm Hg, PaO_2/PAO_2 is approximately 0.15. To predict FiO_2 required for PaO_2 of 70 mm Hg, follow the diagonal line representing 0.15 up to where it intersects the vertical line representing PaO_2 = 70 mm Hg. From this point, draw a horizontal line to the left intersecting the PAO_2 column at approximately 450 mm Hg. Connect this point to the present $PaCO_2$ (40 mm Hg) and note that the line passes through the required FiO_2 of approximately 70%. (From Chatburn RL, Lough MD. *Handbook of respiratory care*, Chicago, 1990, Year Book Medical Publishers.)

titrating FiO_2 downward, the clinician should wait at least 15 to 20 minutes between changes in FiO_2 to allow O_2 levels to stabilize to a steady state. Patients with obstructive disease may need a longer period of approximately 30 minutes for equilibration after a change in FiO_2.When minimal FiO_2 is identified, further reduction in FiO_2 should be in steps of 5% to 10% followed by pulse oximetry measurements.

Once the desired PaO_2 and saturation are reached, monitoring should be continued. Generally, O_2 levels are titrated up and down as required, with adjustments in FiO_2 of 0.05 to 0.10 to maintain PaO_2 of 55 to 80 mm Hg with SpO_2 of 88% to 95%. Titration is followed by pulse oximetry.

RULE OF THUMB If a patient's oxygenation status is unknown, or if the patient's condition is unstable or critical, begin ventilatory support with FiO_2 of 100% until PaO_2, SaO_2, or SpO_2 can be assessed.

Positive End-Expiratory Pressure and Continuous Positive Airway Pressure

Various approaches to adjusting PEEP or CPAP have been suggested over the years, including minimum PEEP, optimal or best PEEP, use of PEEP tables, PEEP titrated by compliance or pressure-volume curves, and decremental PEEP trials. With acute restrictive disease, as PEEP or CPAP levels are increased, PaO_2, SpO_2, and static compliance tend to improve until the point at which lung overinflation occurs.[50,51] As mean airway pressure increases, venous return decreases. The result may be a decrease in cardiac output. Fig. 49.6 shows the physiologic factors that change during application of PEEP or CPAP. Several approaches to adjusting PEEP or CPAP are described later.

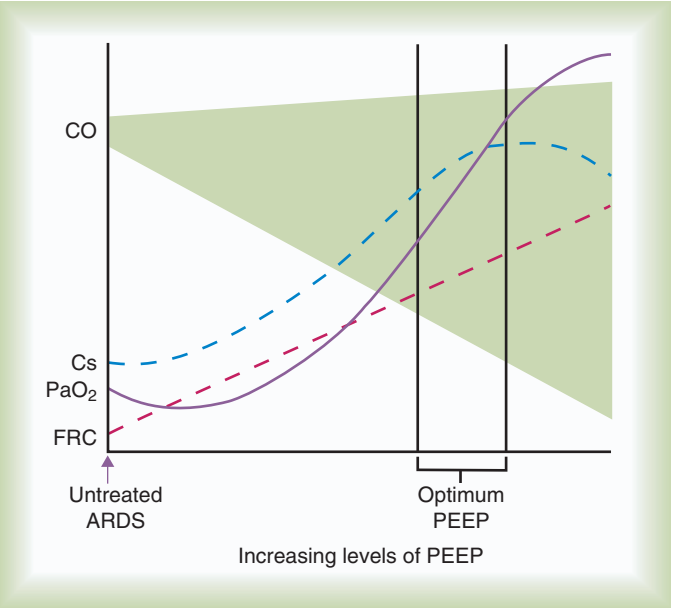

Fig. 49.6 Curves represent the physiologic factors that change during the application of positive end-expiratory pressure *(PEEP)* and continuous positive airway pressure (CPAP). As PEEP level is increased, PaO_2, functional residual capacity *(FRC)*, and static compliance (Cs) normally increase. Cardiac output (CO) *(shaded area)* can increase slightly, stay the same, or decrease. Optimum PEEP level can be expected to occur when PaO_2, FRC, and Cs are high. CO should be maintained near normal so that O_2 transport to the tissues remains high. *ARDS*, Acute respiratory distress syndrome. (Modified from Pilbeam SP: Mechanical ventilation: physiological and clinical applications, ed 3, St. Louis, 1998, Mosby.)

Minimum Positive End-Expiratory Pressure

Minimum PEEP can be defined as the minimal PEEP needed to maintain recruited lung open and achieve adequate PaO_2 (and SpO_2) with FiO_2 less than 0.6. Generally, the PEEP level needed to achieve PaO_2 of at least 60 mm Hg ($SpO_2 \geq 90\%$) with FiO_2 of 0.40 to 0.50 or less is the minimum PEEP. With this approach, the least PEEP or CPAP level needed to achieve this therapeutic end point is applied.[1]

RULE OF THUMB When titrating FiO_2 downward, the clinician should wait at least 15–20 min between changes in FiO_2 to allow O_2 levels to stabilize to a steady state. Patients with obstructive disease need a longer period of approximately 30 min for equilibration after a change in FiO_2.

Optimal or Best Positive End-Expiratory Pressure Based on Oxygen Delivery

Optimal or best PEEP may be defined as the PEEP that maximizes oxygen delivery (DO_2). Oxygen delivery is calculated as cardiac output ($\dot{Q}_T$) multiplied by oxygen content (CaO_2):

$$DO_2 = \dot{Q}_T \times CaO_2$$

For the optimal PEEP level, PEEP is increased in increments of 2 cm H_2O. Blood pressure, mixed venous O_2 levels (partial pressure of oxygen in mixed venous blood [$P\bar{v}O_2$], mixed venous oxygen saturation [$S\bar{v}O_2$], arteriovenous oxygen content difference [$C(a-\bar{v})O_2$]) cardiac output, and cardiac index are assessed. PEEP is increased incrementally until there is a decline in O_2 delivery, at which point the best or optimal PEEP has been exceeded. PEEP is adjusted down to the previous level that represents the "best" PEEP. Table 49.8 shows an example of a PEEP study for determining optimal PEEP based on O_2 delivery. In Table 49.8, as PEEP is increased from 8 cm H_2O to 10 cm H_2O to 12 cm H_2O, $P\bar{v}O_2$, $S\bar{v}O_2$, and O_2 delivery increase with no decline in cardiac output ($\dot{Q}_T$) or blood pressure; however, when PEEP is increased to 14 cm H_2O, $S\bar{v}O_2$, O_2 delivery, $\dot{Q}_T$, and blood pressure decline, indicating that optimal PEEP for this patient has been exceeded. The best PEEP for this patient would be 12 cm H_2O. Before determining PEEP using this approach, it is critical that the patient's hemodynamic status is stabilized. Patients with a compromised hemodynamic status generally do not tolerate PEEP titration without further compromise.

Compliance-Titrated Positive End-Expiratory Pressure

With the compliance-titrated technique, PEEP is increased in increments of 2 cm H_2O, and the patient's estimated static compliance (Cs) is measured:

$$Cs = \frac{\text{Volume delivered (ml)}}{P_{plat} - P_{baseline}(PEEP/CPAP)}$$

where total PEEP equals the sum of applied PEEP plus auto-PEEP.

MINI CLINI

Adjustment of Oxygen Concentration Down From 100%

Problem

At 9:00 a.m., mechanical ventilation is initiated with the following settings for a 70 kg (IBW) patient:
Mode: PA/C with the patient actively triggering the ventilator
PA/C level: 12 cm H_2O
V_T: 420 mL/ 6.0 mL/kg IBW
Rate: 20–26 breaths/min
FiO_2: 1
PEEP: 5 cm H_2O

An arterial blood gas is obtained 20 minutes after ventilator initiation:
FiO_2: 1
PaO_2: 225 mm Hg
pH: 7.42
$PaCO_2$: 40 mm Hg
HCO_3: 24 mEq/L
Base excess: +1 mEq/L

Calculated alveolar PAO_2 and PaO_2/PAO_2 ratios are:

$$PAO_2 = FiO_2(PB - P_{H_2O}) - PaCO_2 \times 1.25 = 663$$

$$PaO_2/PAO_2 = 225/663 = 0.34$$

What FiO_2 is required to achieve a target PaO_2 of 80 mm Hg?

Solution

The following equation and normal barometric pressure ($P_B = 760$), lead to the calculation:

$$FiO_2 \text{ required} = \left(\frac{PaO_2 \text{ desired}}{PaO_2/PAO_2 \text{ ratio}} + PaCO_2 \times 1.25\right) \times \frac{1}{P_B - P_{H_2O}}$$

$$= \left(\frac{80}{0.34} + 40 \times 1.25\right) \times \frac{1}{760 - 47} = 0.40$$

An alternative calculation would be:

Initial Desired

$$PaO_2/FiO_2 = PaO_2/FiO_2$$

$$225/1 = 80/FiO_2 \text{ desired}$$

$$FiO_2 \text{ desired} = 80 \times (1/225) = 80/225 = 0.36$$

What should the clinician do now?

The target O_2 concentration to achieve a PaO_2 in the range of 55–80 mm Hg (with 80 mm Hg as the specific target for the purpose of this calculation) would be approximately 40%; however, it is suggested that for adjusting down from 100% after initial ventilator setup, changes in FiO_2 be limited to 0.20 in the range of FiO_2 1–0.50 and 0.10–0.05 below FiO_2 of 0.50. Each change in FiO_2 should be followed by oximetry and patient assessment.

In this example, the FiO_2 can be decreased in a stepwise manner, as follows:

Time	FiO_2	SpO_2 (%)
9:30 a.m.	1	99
9:45 a.m.	0.80	99
10:00 a.m.	0.60	98
10:15 a.m.	0.50	97
10:30 a.m.	0.45	97
10:45 a.m.	0.40	95

Arterial blood gas on FiO_2 of 0.40 reveals a PaO_2 of 80 mm Hg.

MINI CLINI

Adjusting Fractional Inspired Oxygen

Problem

A 65 kg (IBW) patient in the ICU is receiving mechanical ventilation in the PA/C mode. The patient's arterial blood gas values and related ventilator settings are:
Mode: PA/C the patient is not breathing spontaneously.
FiO_2: 0.40
PaO_2: 50 mm Hg
PA/C level: 13 cm H_2O
V_T: 450 mL (7 mL/kg IBW)
pH: 7.4
Rate: 22 breaths/min
$PaCO_2$: 40 mm Hg
PEEP: 10 cm H_2O
HCO_3: 24 mEq/L
Base excess: +1 mEq/L

What FiO_2 would be required to increase this patient's PaO_2 to 60 mm Hg?

Solution

First, calculate the patient's current PAO_2 and PaO_2/PAO_2 ratio:

$$PAO_2 = FiO_2(P_B - P_{H_2O}) - PaCO_2/0.8$$

$$= 0.40(760 - 47) - 40/0.8$$

$$= 285 - 50 = 235 \text{ mm Hg}$$

$$PaO_2/PAO_2 = 50/235 = 0.21$$

Next, calculate the FiO_2 needed to achieve the desired PaO_2 of 60 mm Hg:

$$FiO_2 \text{ required} = \left(\frac{PaO_2 \text{ desired} + PaCO_2 \times 1.25 \times 1}{PaO_2/PAO_2 \text{ ratio } P_B - P_{H_2O}}\right)$$

$$= \left(\frac{60 + (40 \times 1.25) \times 1}{0.21760 - 47}\right)$$

$$= \frac{335.7 \times 1}{713} = 0.47$$

For this patient, if the FiO_2 is increased from 0.40 to 0.50, the PaO_2 should increase from 50 to 60 mm Hg. An alternative calculation, based on PaO_2/FiO_2 ratio, would be:

Actual Desired

$$PaO_2/FiO_2 = PaO_2/FiO_2$$

Solving for FiO_2, this becomes:

$$FiO_2 \text{ required} = PaO_2 \text{ desired} \times (FiO_2 \text{ actual}/PaO_2 \text{ actual})$$

$$= 60 \times (0.40/50) = 0.48$$

To increase this patient's PaO_2 to greater than 60 mm Hg would require increasing FiO_2 to approximately 0.50. Although FiO_2 of 0.50 or less is acceptable, as an alternative, the RT may consider increasing PEEP to 12 cm H_2O and then perform a clinical assessment, including evaluation of the effect of the increase on blood pressure, compliance, and arterial blood gases.

TABLE 49.8 Example of an Incremental Positive End-Expiratory Pressure Study[a]

Value	PEEP = 8	PEEP = 10	PEEP = 12	PEEP = 14	PEEP = 16
Time (min)	0	5	10	15	20
V_T (L)	4–8 mL/kg PBW	4–8 mL/kg PBW	4–8 mL/kg PBW	4–8 mL/kg PBW	4–8 mL/kg PBW
f (breaths/min)	22	22	22	22	22
FiO_2 (%)	60	60	60	60	60
I:E ratio	1:2	1:2	1:2	1:2	1:2
P_{peak} (cm H_2O)	30	32	35	42	50
P_{plat} (cm H_2O)	25	27	26	30	33
Cs (mL/cm H_2O)	24	27	32	29	26
SaO_2 (%)	86	92	96	95	95
Blood pressure (mm Hg)	131/78	133/82	130/79	125/74	110/69
Heart Rate	110	106	100	108	106

[a]When first reviewing a PEEP study, observe changes in the following: (1) airway pressure, (2) blood pressure, (3) heart rate, and (4) arterial oxygen (PaO_2, SaO_2). With increases in PEEP, PaO_2 and saturation improve; airway pressure may increase or decrease; compliance improves and then decreases at higher levels of PEEP. Optimum PEEP for this patient is 12 cm H_2O because it provides the best arterial oxygenation (PaO_2, SaO_2) and compliance without a decline in blood pressure or heart rate.
FiO_2, fractional inspired oxygen; *PEEP,* positive end-expiratory pressure.

Best PEEP has been exceeded at the point where an increase in PEEP is followed by a decrease in compliance. PEEP is reduced to the previous level, and this is optimal PEEP based on compliance.[51] For the example shown in Table 49.8, the best PEEP based on compliance would be 12 cm H_2O. Regional lung overdistention and declines in cardiac output can occur at levels less than compliance-titrated best PEEP, and, consequently, hemodynamic status should be optimized before any PEEP trial.

Positive End-Expiratory Pressure Titrated With Pressure-Volume Curves as Part of a Lung Protective Strategy

A lung protective strategy that has been shown to improve outcome in ARDS includes use of a low V_T (4 to 8 mL/kg) and PEEP set 2 cm H_2O above the lower inflection point (P_{flex}) on a pressure-volume curve or slow-flow pressure-volume curves to determine best PEEP. To obtain a static pressure-volume curve, the RT passively inflates the patient's lungs with varying volumes in increasing increments of 50 to 100 mL. At each end point, static pressure is obtained by means of application of an end inspiratory pause, and the resultant pressure-volume curve is plotted (Fig. 49.7). Upper and lower inflection points can typically be determined. The lower inflection point is thought to be the point at which alveolar recruitment begins. The upper inflection point indicates lung overdistention. PEEP is set at approximately 2 cm H_2O above the lower inflection point (P_{flex}). Determining PEEP level using the P_{flex} value may be done after a lung recruitment maneuver (see later). V_T is adjusted to ensure that the upper inflection point is not exceeded during inspiration.

Calculating the static pressure-volume curve is technically difficult and time-consuming.[12] An alternative is to use the slow-flow pressure-volume curve. A slow-flow curve (≤6 L/min) may also identify the lower inflection point for the purposes of setting PEEP (Fig. 49.8); however, in either case, some patients do not have a lower inflection point. In approximately 25% of patients, the P_{flex} cannot be identified from the pressure-volume curve.[25] In addition, observer variability in identifying the lower inflection point can be significant.[52]

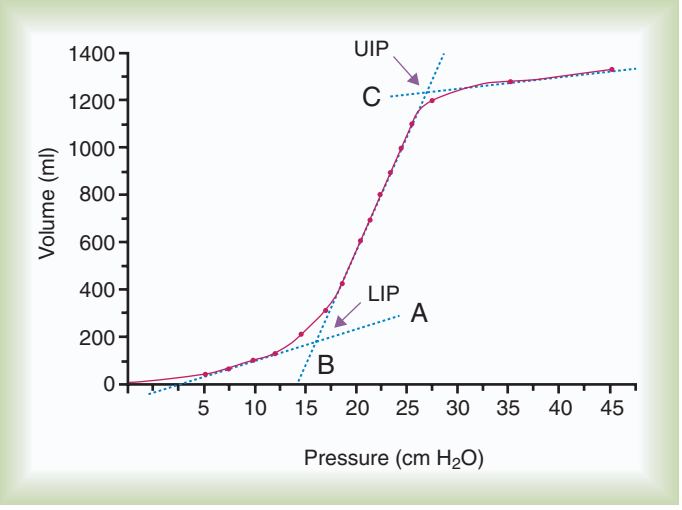

Fig. 49.7 Static pressure-volume curve of a patient with acute respiratory distress syndrome. Volume is increased in increments of approximately 100 mL, inspiratory P_{plat} is measured, and a pressure—volume curve is plotted. Straight lines (*A, B,* and *C*) are drawn tangent to the curve, and the lower inflection point *(LIP)* and the upper inflection point *(UIP)* are identified. Positive end-expiratory pressure is adjusted to approximately 2 cm H_2O above the *LIP*.

Positive End-Expiratory Pressure and Lung Recruitment Maneuvers

Various lung recruitment maneuvers have been suggested for improving $\dot{V}/\dot{Q}$ and reducing shunting in patients with ARDS. These maneuvers include several variations that incorporate CPAP[25,52,53] or the use of PCV with high PEEP levels.[54,55] Regardless of approach, before any lung recruitment maneuver is performed, the patient must be hemodynamically stable and sedated to apnea. Neuromuscular paralysis is unnecessary, but the patient must be accepting of passive ventilation at high pressures. Hemodynamic stability is crucial because of the high intrathoracic pressures established during all recruitment maneuvers, although few studies are available that indicate that pressure control recruitment maneuvers are better tolerated than CPAP recruitment

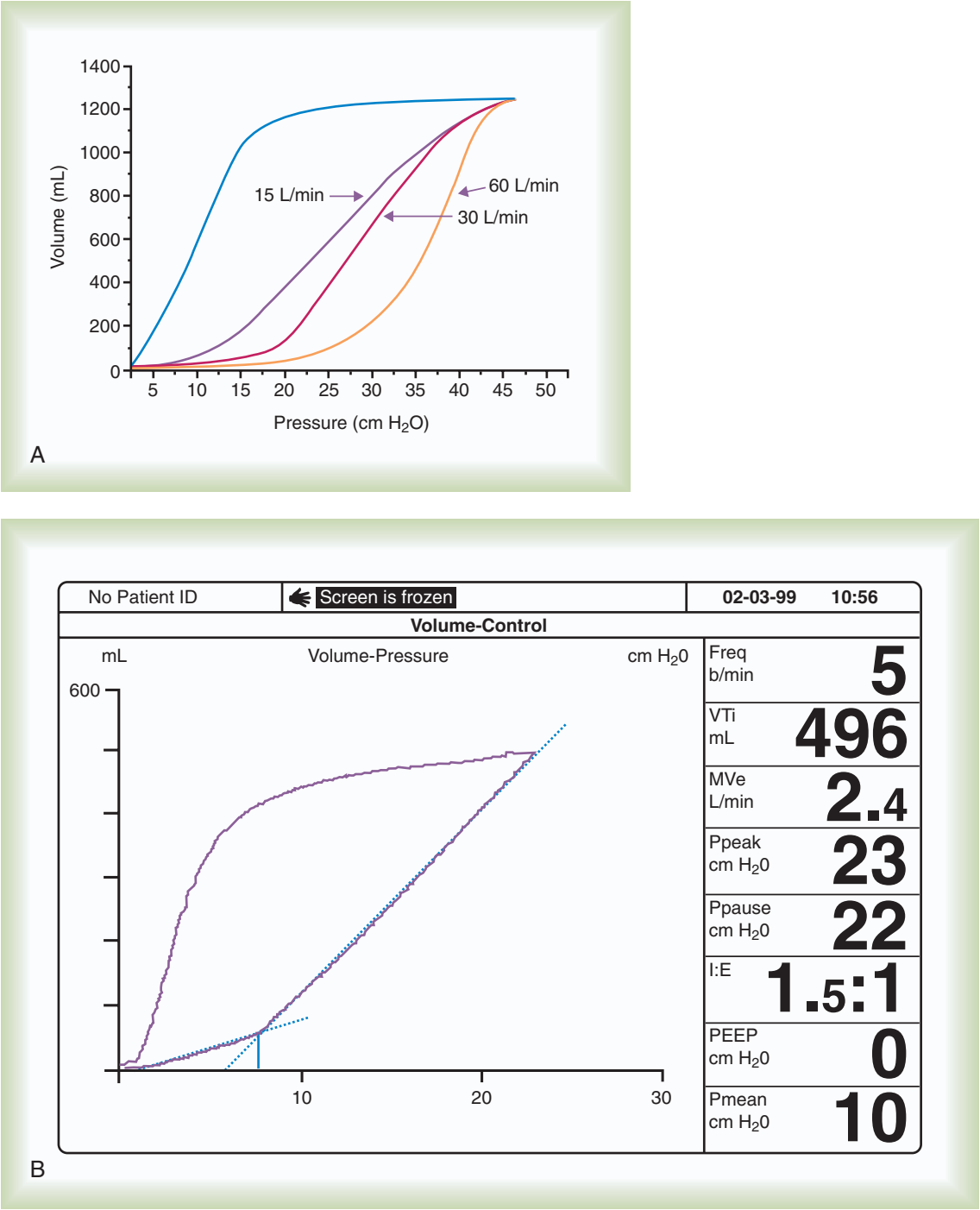

Fig. 49.8 (A) Pressure-volume curves generated by a ventilator graphics package with the flow set at 60 L/min, 30 L/min, and 15 L/min. As flow is decreased, the curve shifts to the left and more closely approximates a static pressure-volume curve. Flow of less than 6 L/min is recommended for identifying the lower inflection point (LIP) from a slow-flow pressure-volume curve. (B) Slow-flow pressure-volume curve with use of a set rate of 5 breaths/min, inspiratory-to-expiratory *(I:E)* ratio of 1.5:1, and V_T of 500 mL. LIP is approximately 8 cm H_2O. The respiratory cycle time is 12 s (cycle time = 60/f = 60/5 = 12 s). An I:E ratio of 1.5:1 results in an inspiratory time of 4.8 s. Inspiratory flow is V_T/T_i = 0.5 L/4.8 s = 0.104 L/s, or approximately 6 L/min. *PEEP*, Positive end-expiratory pressure.

maneuvers.[56,57] The original recruitment techniques applied 40 to 45 cm H_2O CPAP for 30 to 40 seconds.[25,53,58] For recruitment maneuvers to be successful, they should be performed as early as possible after the patient is stabilized on the ventilator.[53,55,58] The longer the length of mechanical ventilation before the recruitment maneuver, the greater the likelihood that the maneuver will fail. See Box 49.13 for details on the performance of lung recruitment maneuvers and decremental PEEP trials.

The most widely accepted approach to recruiting the lung is the use of PCV. With this approach, PEEP is set higher than

BOX 49.13 Performing a Lung Recruitment Maneuver and Decremental Positive End-Expiratory Pressure Trial

- General approach: PCV
- Pressure control setting: 10–15 cm H_2O
  Final PIP 40–50 cm H_2O
- Inspiratory time: 2 s
- Rate: 15–20/min
  Increase PEEP from team set level 3–5 cm H_2O every 3–5 breaths dependent on patient tolerance until PIP is reached
  Maintain at PIP 1 min then preform decremental PEEP trial
  Decremental PEEP trial
- Mode: Volume control
- PEEP: 20–25 cm H_2O
- V_T: 4–6 mL/kg IBW
- Rate: Highest rate avoiding auto-PEEP
- Ventilate until dynamic compliance stabilizes 30–45 s
- Record compliance
- Decrease PEEP by 2 cm H_2O
- Ventilate until dynamic compliance stabilizes 30–45 s
- Decrease PEEP by 2 cm H_2O
- Ventilate until dynamic compliance stabilizes 30–45 s
- Continue this until a PEEP level that results in the best compliance is identified
- Repeat the recruitment maneuver (doing a decremental PEEP trial results in derecruitment)
- Set PEEP at best compliance PEEP plus 2 cm H_2O

Before performing a recruitment maneuver, ensure that the patient is hemodynamically stable and sedated to apnea.

IBW, Ideal body weight; *PCV,* pressure-controlled ventilation; *PEEP,* positive end-expiratory pressure; *PIP,* peak inspiratory pressure.

levels required to maintain the recruited lung open, usually between 20 and 25 cm H_2O; a pressure-control level 15 cm H_2O above this is then set. Ventilation is provided with an I:E of 1:1 to 1:2 at a rate of 10 to 15 /min. All recruitment maneuvers are performed with 100% O_2. If this initial approach to lung recruitment does not open the lung, PEEP can be set higher in increments of 5 cm H_2O, and the recruitment repeated after the patient has totally stabilized from the previous maneuver (>30 minutes). The maximum safe peak pressure during a recruitment maneuver is 50 cm H_2O. Peak pressures greater than 50 cm H_2O increase the likelihood of barotraumas during the maneuver.[55,58]

The best method of establishing optimal PEEP after recruitment is a decremental PEEP trial.[53-55,59] It is best to perform the trial in volume ventilation because the easiest bedside method of identifying the optimal PEEP is to determine the best compliance PEEP. The best oxygenation PEEP can also be determined. It takes only approximately 30 to 45 seconds for the compliance to stabilize when PEEP is changed, but at least 20 minutes is required for PaO_2 to stabilize after a PEEP adjustment.

To perform the trial, PEEP should begin at 20 to 25 cm H_2O but always at PEEP higher than expected necessary to maintain the lung open. V_T during the decremental PEEP trial is usually set at 4 to 6 mL/kg IBW depending on P_{plat}. Inspiratory time is set at 0.6 to 0.8 second, and rate is at a level that does not result in auto-PEEP. First, the compliance is recorded at these settings after stabilization. Then, the PEEP is decreased 2 cm H_2O, and the compliance is again allowed to stabilize. The process is continued until the best compliance PEEP can be identified. Generally, compliance is low at the starting PEEP (20 to 25 cm H_2O) because of overdistention. As PEEP is decreased, compliance improves until it peaks and then starts to decrease because of derecruitment and atelectasis.[54] The best compliance PEEP is increased by 2 cm H_2O because the best compliance PEEP generally underestimates the best oxygenation PEEP by 2 cm H_2O.[54] After identifying the optimal PEEP level, the lung must be recruited again because derecruitment occurred during the decremental PEEP trial. After this second recruitment, PEEP is set at the optimal level determined during the decremental trial.

A recruitment maneuver should be stopped if there is a decrease in SpO_2 to less than 85%, a significant change in heart rate (>140 beats/min or <60 beats/min), a significant change in mean arterial blood pressure (<60 mm Hg or a decrease >20 mm Hg from baseline), the development of cardiac arrhythmia, or any indication that barotraumas occurred.[53] More recent meta-analyses indicate that the use of high PEEP benefits patients with moderate to severe ARDS but does not benefit patients with mild ARDS.[42,43]

Esophageal manometry. The best method of setting PEEP is ensuring that the PEEP level set results in a positive transpulmonary pressure.[60,61] Normally, the pleural pressure is negative, but in ARDS or when atelectasis is present, the pleural pressure can become markedly positive, resulting in a highly negative transpulmonary pressure unless appropriate PEEP is applied. The transpulmonary pressure that will prevent end-expiratory collapse of lung unit is approximately +2 cm H_2O.[60,61] With this approach, PEEP is best set after a lung recruitment maneuver at a level resulting in a positive end-expiratory transpulmonary pressure. PEEP set at a positive end-expiratory transpulmonary pressure of 2 cm H_2O following a recruitment maneuver is equal to the best compliance PEEP following a recruitment maneuver.

RULE OF THUMB For recruitment maneuvers to be successful, they should be performed as early as possible after the patient is stabilized on the ventilator.

Electrical impedance tomography. As discussed in detail in Chapter 52, electrical impedance tomography (EIT) is a noninvasive, radiation-free bedside approach to obtain qualitative images of the chest during ventilation.[62] Specifically, EIT can determine the percentage of lung that is collapsed and the percentage of lung that is over distended. When EIT is used during a recruitment maneuver followed by a decremental PEEP trial, it can identify the PEEP resulting in the least collapse and the least overdistension.[63] Recent research indicates that the most appropriate PEEP determined by EIT, esophageal manometry, and best compliance are all equal![63] In addition, it has been clearly established that the same PEEP level without lung recruitment results in a greater amount of collapse and overdistention than the same PEEP level following a recruitment maneuver.[63]

Positive End-Expiratory Pressure Tables

The ARDS Clinical Network study used an FiO_2-PEEP table to adjust PEEP levels.[2] Using this approach, PEEP and FiO_2 are

alternately adjusted to obtain PaO_2 of 60 to 80 mm Hg or SpO_2 90% or greater (see Box 49.7). The table offers higher and lower PEEP options. For the lower PEEP option, PEEP is set at 5 to 10 cm H_2O with FiO_2 of 0.30 to 0.70; the higher PEEP option sets PEEP at 12 to 20 cm H_2O in the same FiO_2 range. The higher PEEP option should be reserved for patients who may benefit from higher PEEP in terms of lung recruitment and who have a stable blood pressure and no barotrauma. Of all the approaches to setting PEEP, this is the approach least based on the physiology of the patient. It is a reasonable approach to establish initial PEEP, but it is generally a poor choice for further adjustment of PEEP.

Other Techniques for Improving Oxygenation

The primary techniques for optimizing oxygenation in patients receiving mechanical ventilatory support are adjusting FiO_2 and PEEP. Other techniques that may be helpful in improving arterial O_2 levels include optimizing the patient's hemodynamic status, providing good bronchial hygiene, prone positioning, pulmonary vasodilators such as Nitric Oxide and Epropostenol and extracorporeal membrane oxygenation (ECMO). Some clinicians have also used techniques to prolong inspiratory time and reverse the I:E ratio; however, approaches focused on increasing inspiratory time have not been shown to be better than properly set PEEP and are associated with marked hemodynamic compromise and poorer outcomes.[64]

Bronchial Hygiene

In many patients, turning, sitting up, and getting out of bed into a chair can be helpful in improving oxygenation. Upright positioning (30 to 45 degrees) seems to be beneficial for ventilated patients, and supine positioning may increase the risk of pneumonia, especially in patients receiving enteral feeding or with a decreased level of consciousness.[65] Elevation of the head of the bed greater than 30 degrees has been recommended in all ventilated patients to reduce the incidence of ventilator-associated pneumonia. Special rotational beds can be used to optimize PaO_2 in selected patients. Postural drainage, adequate humidification, and bronchodilator therapy may all improve oxygenation and should be considered in the care of ventilated patients when not specifically contraindicated.

Prone Positioning

Prone positioning may be an effective technique for improving oxygenation in some patients with ARDS.[66-69] Prone positioning may improve PaO_2, decrease shunt fraction, and reduce mortality in patients with severe ARDS when it is initiated early and applied for most of the day (a minimum of 12 hours).[70] Although improvement in PaO_2 may be dramatic and sustained (up to 12 hours), not all patients benefit from prone positioning. The procedure is not without risk. Care must be taken to ensure that endotracheal tubes, intravenous lines, and catheters are not blocked or dislodged. The patient may also have skin breakdown at specific pressure points (face, sternum, hips, knees), and facial or eyelid edema may occur, although the latter is primarily a cosmetic concern that resolves quickly when the patient returns to a supine or sitting position.[71] The most serious complication is corneal abrasion necessitating corneal transplantation.[71,72] Prone positioning is labor-intensive, often requiring two nurses, an RT, and a physician to "flip" the patient. If patients have to be turned in to the supine position because of an emergency (cardiac arrest), it is very difficult, frequently resulting in an unfortunate situation. Numerous early randomized controlled trials have evaluated the impact of prone positioning on survival in ARDS[66-69]; however, none of the trials have shown improved outcome. A more recent meta-analysis indicated improved survival in patients with the most severe lung injury—patients with a PaO_2/FiO_2 ratio less than 100 mm Hg.[70] A recent randomized control trial verified the meta-analysis finding.[73] As a result, prone positioning should be reserved for severe ARDS (PaO_2/FiO_2 < 100 mm Hg) and after lung recruitment and appropriate PEEP titration has been performed. Similar to all lung protective approaches to ventilatory support, prone positioning should be used early in the course of ARDS if it is to be beneficial.

The mechanism of action of prone positioning is unclear. In ARDS, dorsal lung injury tends to increase shunt and decrease $\dot{V}/\dot{Q}$, resulting in hypoxemia. Supine positioning tends to increase regional pressure in the dependent, or dorsal portions of the

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Use of Positive End-Expiratory Pressure

Problem

A 30-year-old, 80 kg (IBW) man is in the critical care unit because of blunt trauma to the chest after a motor vehicle accident. The patient's initial mechanical ventilatory support settings are as follows:

Mode: = A/C pressure ventilation, V_T: 500 mL (6 mL/kg IBW)
Rate: 20 breaths/min
FiO_2: 0.70
PA/C level: 30 cm H_2O
P_{plat}: 25 cm H_2O
PEEP: 0

Arterial blood gas analysis yielded the following results:

pH: 7.38
PaO_2: 48 mm Hg
$PaCO_2$: 36 mm Hg
SaO_2: 81%

The RT considers a recommendation that PEEP be instituted. What are the goals of this type of therapy, and what are some of the potential adverse effects of PEEP that the RT should be aware of?

Solution

The general goals of PEEP are to stabilize and maintain open alveolar units to achieve adequate oxygenation and to avoid potentially unsafe levels of FiO_2 and inflation pressure. Improvement is most commonly assessed with PaO_2 or SpO_2, compliance and measurement of blood pressure and cardiac output.

At least 5 cm H_2O PEEP should be used in all acutely ventilated patients unless the patient is too hemodynamically unstable to tolerate the use of PEEP. When PaO_2 does not respond to a high FiO_2, the condition is referred to as *refractory hypoxemia*. An appropriate initial PEEP for this patient would be 10 cm H_2O because of the patient PaO_2/FiO_2 ratio of 69, classified as severe ARDS. Arterial blood gases, P_{plat}, and blood pressure should be assessed immediately after PEEP adjustment. As the level of PEEP is increased, the RT must be alert for signs of decreased cardiac output. Measurement of effective compliance and P_{plat} is also indicated. In all cases, the lowest PEEP level that provides acceptable oxygenation should be selected.

BOX 49.14 Prone Positioning

Preparation for prone positioning includes the following:
- Adequate sedation of patient
- Clear assignment of responsibilities between team members
- Moving the patient to one side of the bed
- Checking all lines for length
- Checking the security of the endotracheal tube
- Endotracheal suctioning
- Preoxygenation with 100% O_2
- Checking all vital signs

The turn includes:
- Tipping the patient to the side
- Securing electrocardiogram leads
- Turning the patient prone
- Turning the patient's head toward the ventilator

Care after the turn includes:
- Checking artificial airway
- Checking all lines
- Checking ventilator pressure and volume
- Monitoring vital signs
- Repositioning and recalibrating pressure transducers
- The patient needs support (pillows) for each side of the chest and forehead so that the endotracheal tube and head are not compromised.

lungs. Prone positioning may improve $\dot{V}/\dot{Q}$ and reduce shunting by removing the pressure of the heart on the dorsal regions, causing regional dorsal traction, which may promote lung opening. The recommended technique for prone positioning is outlined in Box 49.14.

VENTILATION

Alveolar ventilation is determined by respiratory rate, V_T, and dead space and is described by the following equation:

$$\dot{V}_A = (V_T - V_{Dphys})f$$

where $\dot{V}_A$ is alveolar ventilation, V_T is tidal volume, V_{Dphys} is physiologic dead space, and f is respiratory frequency or rate. The relationship between arterial $PaCO_2$, alveolar ventilation ($\dot{V}_A$), and CO_2 production ($\dot{V}CO_2$) is described as follows:

$$PaCO_2 = (0.863)(\dot{V}CO_2)/\dot{V}_A$$

Arterial $PaCO_2$ is considered the best index of effective ventilation. Increases in $\dot{V}_A$ or decreases in $\dot{V}CO_2$ result in a decrease in $PaCO_2$, whereas increases in $\dot{V}CO_2$ or decreases in $\dot{V}_A$ result in an increase in $PaCO_2$. If there is no change in $\dot{V}CO_2$, the following relationships can be used to estimate the effect of changes in $\dot{V}_A$ on $PaCO_2$:

$$\underset{\text{Initial}}{PaCO_{2(1)} \times \dot{V}_{A(1)}} = \underset{\text{Desired}}{PaCO_{2(2)} \times \dot{V}_{A(2)}}$$

The foregoing predictive equation can be used during mechanical ventilation with the following modifications:

$$PaCO_{2(1)}(V_{T(1)} - V_{Dphys(1)})f_{(1)} = PaCO_{2(2)}(V_{T(2)} - V_{DSphys(2)})f_{(2)}$$

For changes in rate alone, if there is no change in $\dot{V}CO_2$ or V_{Dphys}, this becomes:

BOX 49.15 Example of the Effect of Change in $\dot{V}_A$ on $PaCO_2$

If a patient has an initial $PaCO_2$ of 50 mm Hg with a corresponding alveolar ventilation ($\dot{V}_A$) of 4 L/min, what level of alveolar ventilation is required to decrease the $PaCO_2$ to 40 mm Hg (if there is no change in $\dot{V}_ACO_2$)?

If the patient's $\dot{V}_A$ is increased from 4–5 L/min, the $PaCO_2$ should decrease from 50–40 mm Hg.

$$\underset{\text{Initial}}{PaCO_{2(1)} \times f_{(1)}} = \underset{\text{Desired}}{PaCO_{2(2)} \times f_{(2)}}$$

For changes in V_T alone, this becomes:

$$\underset{\text{Initial}}{PaCO_{2(1)} \times V_{T(1)}} = \underset{\text{Desired}}{PaCO_{2(2)} \times V_{T(2)}}$$

A major goal of mechanical ventilation is optimization of the patient's ventilation and $PaCO_2$; however, this does not mean normalization of $PaCO_2$. Acceptable arterial pH and alveolar PCO_2 are assessed by P_{plat}. For many patients, the level of ventilatory support is adjusted to achieve a $PaCO_2$ of 35 to 45 mm Hg with a pH of 7.35 to 7.45. In the care of patients with acute exacerbation of COPD and accompanying chronic ventilatory failure, the clinician may target ventilatory support to achieve the patient's "normal" $PaCO_2$ and pH. For patients with COPD and chronic hypercapnia, the target $PaCO_2$ may be 50 to 60 mm Hg with a pH of 7.30 to 7.35. In patients with severe ARDS, a $PaCO_2$ of 70 mm Hg with an acidic pH may have to be accepted to protect the lung from ventilator-induced lung injury. The sicker the patient, the more likely the clinician is to accept oxygenation and acid–base values that greatly deviate from normal. Regardless of the patient's condition, optimizing pH is more important than targeting a specific $PaCO_2$ value.[1,9] Box 49.15 presents an example of the effect of change in $\dot{V}_A$ on $PaCO_2$.

Adjusting Tidal Volume and Rate

V_T and rate may be adjusted for a desired level of ventilation as assessed by $PaCO_2$. V_T is usually based on specific patient considerations but, ideally, should never result in P_{plat} greater than 28 cm H_2O. Respiratory rate is adjusted to achieve the desired $PaCO_2$. Normal resting V_T of healthy individuals is 6.3 mL/kg IBW. In most critically ill patients, V_T should be in the range of 4 to 8 mL/kg IBW. In patients with improving respiratory function ready for extubation, V_T of 9 to 10 mL/kg IBW may be acceptable; however, V_T greater than 10 mL/kg IBW should never be selected for a critically ill patient.

Apnea (Controlled Ventilation)

In an apneic patient, precise control of $PaCO_2$ can usually be achieved with pressure or volume ventilation because the ventilator rate and V_T are determined directly or indirectly by the clinician.

Rate. In the care of apneic patients, the clinician has complete control over the patient's rate, and changes in ventilator rate can be used precisely to alter $PaCO_2$. For example, if a patient's initial rate was 18 breaths/min and resultant $PaCO_2$ was 50 mm Hg,

the rate change needed to decrease the patient's $PaCO_2$ to 40 mm Hg could be calculated as follows:

$$\begin{array}{cc} \text{Initial} & \text{Desired} \\ PaCO_{2(1)} \times f_{(1)} = & PaCO_{2(2)} \times f_{(2)} \end{array}$$

$$50 \times 18 = 40 \times f_{(2)}$$

$$f_{(2)} = (50 \times 18)/40 = 23 \text{ breaths/min}$$

For this patient, an increase in machine rate from 18 to 23 breaths/min would decrease $PaCO_2$ from 50 to 40 mm Hg. Two warnings must be kept in mind in the use of this predictive equation. First, it is assumed that $\dot{V}CO_2$ is constant. If there is an increase or decrease in $\dot{V}CO_2$, the resultant $PaCO_2$ would be different from the predicted value. Common causes of increased $\dot{V}CO_2$ in the ICU include pain, agitation, anxiety, fever, overfeeding, increased activity, and fighting the ventilator. Decreases in $\dot{V}CO_2$ may be caused by decreased activity, sedation, paralysis, anesthesia, or sleep. Second, the equation is based on the assumption that the patient is apneic. Patients who are triggering the ventilator in the A/C mode determine their own $PaCO_2$ on the basis of the assist rate. Patients in the SIMV mode who are spontaneously breathing may simply increase or decrease their level of spontaneous breathing and make $PaCO_2$ prediction difficult. In addition, the primary factor that limits the selection of rate is the development of auto-PEEP. If auto-PEEP develops, plateau pressure increases in volume ventilation and tidal volume decreases in pressure ventilation.

Tidal volume. Changes in V_T can be used to alter $PaCO_2$. For a patient 80 kg IBW receiving ventilation in the control mode with V_T of 600 mL (7.5 mL/kg) and resultant $PaCO_2$ of 30 mm Hg, the change in V_T to achieve a PaO_2 of 40 mm Hg would be calculated as follows:

$$\begin{array}{cc} \text{Initial} & \text{Desired} \\ PaCO_{2(1)} \times V_{T(1)} = & PaCO_{2(2)} \times V_{T(2)} \end{array}$$

$$30 \times 600 = 40 \times V_{T(2)}$$

$$V_{T(2)} = (30 \times 600)/40 = 450 \text{ ml}$$

For this patient, a decrease in V_T from 600 to 450 mL results in an increase in $PaCO_2$ from 30 to 40 mm Hg. This is directly altered in volume ventilation by changing the tidal volume or indirectly by decreasing the pressure control level in pressure ventilation. Several warnings should be kept in mind for changes in V_T. First, V_T should be within the preferred range for a given patient condition. In the example, new V_T (450 mL) represents 5.6 mL/kg IBW, which is an acceptable value. V_T should be small enough to avoid lung injury and maintain P_{plat} at less than 28 cm H_2O. Second, in this equation, $\dot{V}CO_2$ and V_{Dphys} are assumed to be constant because changes in $\dot{V}CO_2$ or V_{Dphys} affect $PaCO_2$. Activity, agitation, fever, and overfeeding may increase $\dot{V}CO_2$, whereas sedation, paralysis, or sleep may decrease $\dot{V}CO_2$. V_{Dphys} changes with changes in airway pressure, and increases in ventilator V_T may result in increased dead space. Development of pulmonary emboli or hemodynamic instability may abruptly increase V_{Dphys}.

Mechanical dead space. Mechanical dead space is defined as the volume of gas rebreathed as the result of a mechanical device. Large-bore tubing attached between the ventilator circuit "wye" and the patient airway connection serves as mechanical dead space, and 6 inches (15 cm) of large-bore tubing represents a volume of approximately 50 to 70 mL.

For ventilation of tracheostomy patients, 6 inches (15 cm) of mechanical dead space is often used to keep the weight of the "wye" connection and tubing off the tracheostomy tube and to give additional flexibility to the circuit for patient movement. Mechanical dead space is usually not used for endotracheally intubated patients, and the addition of mechanical dead space can serve as a cause for an increase in $PaCO_2$. Mechanical dead space is a primary concern in patients with severe ARDS in whom V_T is 4 to 6 mL/kg IBW and, as a result, $PaCO_2$ is elevated. The simple removal of mechanical dead space in these patients can, in some cases, markedly improve CO_2 elimination. HME filters are another major cause of mechanical dead space. Depending on the brand, up to 80 mL of dead space can be added by these devices.

In healthy persons, the combination of V_{Dphys} and anatomic dead space can be estimated at approximately 1 mL/lb or 2.2 mL/kg IBW. Although healthy persons have a dead space-to-tidal volume (V_D/V_T) ratio of approximately 0.20 to 0.40, a V_D/V_T ratio greater than 0.50 is common among ventilated patients.

Control of $PaCO_2$ in Synchronized Intermittent Mandatory Ventilation Mode

In the SIMV mode, machine breaths are interspersed with spontaneous breathing, and the spontaneous breaths may be PSV. $PaCO_2$ can be decreased by increasing V_T, increasing PSV for spontaneous breaths, or increasing the machine rate. Levels of $PaCO_2$ may be increased by reducing the machine rate, decreasing V_T, or decreasing the level of PSV for spontaneous breaths. As with apneic (control) ventilation, an appropriate V_T should be selected on the basis of the patient's condition and with the goal of keeping P_{plat} less than 28 cm H_2O, with V_T ideally 4 to 8 mL/kg IBW depending on the patient's pulmonary status. PSV level in the SIMV mode should be adjusted to overcome WOB_I; the usual range is 5 to 15 cm H_2O, although higher levels may be needed by patients with high resistance. PSV should be adjusted to ensure that during spontaneous breathing, WOB is not excessive. Accessory muscle use or suprasternal, intercostal, or substernal retractions during spontaneous breathing indicate the need to increase the PSV level. When appropriate V_T and PSV level are selected, the primary method for adjusting $PaCO_2$ is to increase or decrease SIMV rate.

After ventilator initiation, two different approaches may be taken. For full ventilatory support, an initial SIMV rate and V_T are selected to provide 100% of the patient's ventilatory requirements; for most adults, this means starting with V_T of 6 to 8 mL/kg IBW with SIMV rate of 15 to 20 breaths/min. Generally, a minute ventilation of approximately 100 mL/kg IBW is achieved with these initial settings. Arterial blood gas values are obtained 20 to 30 minutes after initiation of mechanical ventilation, and SIMV rate is titrated up or down in increments of 2 breaths/min until desired $PaCO_2$ is achieved. Monitoring is continued,

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Adjusting $PaCO_2$ During Volume Ventilation

Problem

A 22-year-old man, 5 ft 10 in (178 cm) tall, being treated for a drug overdose is being ventilated with the following settings:
Mode: PA/C
FiO_2: 0.40
V_T: 600 mL
Rate: 15 breaths/min
PA/C level: 15 cm H_2O
P_{plat}: 18 cm H_2O
PEEP: 5 cm H_2O

The patient's lungs are clear to auscultation and there is no evidence of aspiration. Arterial blood gas values obtained 15 min previously were:
PaO_2: 80 mm Hg
$PaCO_2$: 30 mm Hg
SaO_2: 95%
HCO_3: 24 mEq/L
pH: 7.52
Base excess: +2 mEq/L

The physician asks the RT to normalize this patient's oxygenation and ventilatory status. What should the RT do?

Solution

At this time, the patient is making no spontaneous breathing efforts. The patients' oxygenation status is fine and no adjustments are needed. In the absence of spontaneous breathing in the PA/C mode, $PaCO_2$ can be adjusted by changing machine rate (f) or PA/C level. Because the V_T is large (600 mL), the correct adjustment would be to decrease PA/C level to obtain a specific smaller V_T.

For prediction of the needed change in V_T to increase $PaCO_2$ to 40 mm Hg, the following calculation could be performed:

$$\text{Actual} \qquad \text{Desired}$$
$$V_{T(1)} \times PaCO_{2(1)} = V_{T(2)} \times PaCO_{2(2)}$$
$$V_{T(2)}\ \text{Desired} = (V_{T(1)} \times PaCO_{2(1)})/PaCO_{2(2)}$$
$$V_{T(2)}\ \text{Desired} = (600 \times 30)/40 = 458\ \text{ml}$$

If PA/C level is decreased to obtain a V_T 450 mL, $PaCO_2$ and pH should normalize.

BOX 49.16 Partial Ventilatory Support With Synchronized Intermittent Mandatory Ventilation

Mechanical ventilation is initiated in the SIMV mode for a 70 kg, spontaneously breathing 38-year-old man. Before initiation of ventilation, the patient's spontaneous rate was 30 breaths/min with a spontaneous V_T of 200 mL. Initial ventilator settings are:
V_T: 450 mL
SIMV rate: 14 breaths/min
FiO_2: 0.40
PSV: +8 cm H_2O
PIP: 20 cm H_2O
P_{plat}: 24 cm H_2O
PEEP: 8 cm H_2O

Arterial blood gases are obtained in 20 minutes, with the following results:
PaO_2: 88 mm Hg
SaO_2: 97%
pH: 7.38
$PaCO_2$: 40 mm Hg
HCO_3: 24 mEq/L
Base excess: +1 mEq/L

The decision is made to provide partial ventilatory support for this patient, and the SIMV rate is titrated as follows:

Time	V_T (mL)	SIMV Rate	Total Rate	$PaCO_2$ (mm Hg)
9:00 a.m.	450	14	20	40
9:30 a.m.	450	12	15	38
10:00 a.m.	450	10	18	38
10:30 a.m.	450	8	16	46
11:00 a.m.	450	16	20	42

The patient's condition should now be stabilized at a rate of 10 breaths/min with titration of SIMV to the patient's needs with observation and measurement of arterial blood gases. When the rate is decreased to 8 breaths/min, $PaCO_2$ begins to increase. The rate is increased to the previous setting of 10 breaths/min. Titrating the level of SIMV support to the patient's needs is not the same as weaning the patient. After improvement in the patient's condition, weaning may be tried (see Chapter 53) by daily spontaneous breathing trial.

FiO_2, Fractional inspired oxygen; *PEEP,* positive end-expiratory pressure; *PIP,* peak inspiratory pressure; *PSV,* pressure support ventilation; *SIMV,* synchronized intermittent mandatory ventilation.

and adjustments are made by increasing or decreasing SIMV rate to maintain full ventilatory support until the patient's condition improves and ventilator discontinuation is considered.

Partial ventilatory support in the SIMV mode requires a different initial approach. Ventilation begins with V_T and machine rate sufficient to provide full ventilatory support, and arterial blood gases are measured. If $PaCO_2$ is adequate, the patient is immediately challenged with a decrease in SIMV rate of 2 breaths/min. This procedure is followed by patient assessment and measurement of arterial blood gases, as indicated. If the resultant assessment values remain adequate, the patient continues to be challenged with decreases in SIMV rate until $PaCO_2$ increases. At that point, the patient's ventilatory capacity has been exceeded, and SIMV rate is returned to the previous value. Box 49.16 provides an example of titration of the SIMV rate for partial ventilatory support after ventilator initiation in a spontaneously breathing patient.

RULE OF THUMB Mechanical dead space is defined as the volume of gas rebreathed as the result of a mechanical device. Large-bore tubing attached between the ventilator circuit "wye" and the patient airway connection serves as mechanical dead space, and 6 inches (15 cm) of large-bore tubing represents a volume of approximately 50 to 70 mL.

Assist/Control Mode Volume Ventilation and $PaCO_2$

Ventilator initiation in the VA/C mode begins with selection of initial V_T and backup control rate to ensure a safe minimum level of ventilation. In PA/C, a pressure control level sufficient to establish desired V_T is selected along with a backup as in VA/C.

The patient is allowed to trigger the machine as often as desired above this backup rate, and the resultant assist rate is determined by the patient's ventilatory drive. If the respiratory drive is intact, patients tend to trigger the ventilator at an appropriate rate to achieve adequate $PaCO_2$ and pH. By allowing patients to set their own rates, the level of ventilation increases or decreases on the basis of the patient's physiologic needs. Should the patient become apneic owing to sedation or sleep, a minimum backup control rate is provided.

Because the patient determines the level of ventilation, $PaCO_2$ levels are regulated by the patient; however, problems arise when the patient triggers the ventilator at an inappropriately rapid rate. Pain, anxiety, hypoxemia, secretions in the airway, and metabolic acidosis may contribute to an excessive trigger rate and the result can be an inappropriate I:E ratio and an inadequate expiratory time. These abnormal values may increase mean airway pressure, reduce venous return, and result in auto-PEEP and overinflation and associated missed triggering of the ventilator, especially in patients with obstructive disease. Patients may fight the ventilator, resulting in high inspiratory pressure. In the event that a patient receiving ventilation in the A/C mode is triggering the ventilator at an inappropriately high rate, the first step the RT should take is to identify the cause of the increased rate. Patient anxiety may be diminished with simple reassurance and encouragement to relax and "let the machine breathe for you." Hypoxemia should be managed with appropriate O_2 therapy and PEEP, if indicated. Secretions should be removed by suctioning, and bronchial hygiene techniques should be applied. The cause of metabolic acidosis should be identified and managed, if possible.

In some patients, appropriate sedation reduced anxiety and appropriately reduces respiratory rate. Patients who begin fighting the ventilator after a previous period of calm may have a new and potentially life-threatening complication. If a patient begins fighting the ventilator, a careful assessment should be made to identify the problem. Often, careful attention to the ventilator trigger sensitivity, flow rate, volume, and pressure is helpful, and administration of analgesic and sedative agents may be needed.[12] If sedation is required, the use of intermittent sedation with daily interruption using a sedation protocol may reduce the duration of mechanical ventilation.[74,75] A last resort is pharmacologic-controlled ventilation.[12] In the presence of a metabolic acidosis, a sudden change from assisted ventilation at a rapid rate with the associated hyperventilation to controlled ventilation at a slower rate can result in severe acidosis, which can be life-threatening. Other problems with controlled ventilation include patient safety, ventilatory muscle atrophy, and prolonged muscle weakness if paralytic agents are used for a prolonged period.

Pressure Support Ventilation and $PaCO_2$

PSV is normally set at the level needed to establish a normal V_T of 4 to 8 mL/kg IBW. To increase or decrease V_T, the clinician simply increases or decreases the PSV level and observes the resultant V_T on the ventilator exhaled volume monitoring screen. Because PSV is an assist mode, the patient is allowed to trigger the ventilator as desired. The result should be an adequate $PaCO_2$ and pH. In patients with an unstable ventilatory drive or periods of apnea, PSV should be avoided.

Pressure-Controlled Ventilation and $PaCO_2$

Management of ventilation and $PaCO_2$ during PCV is similar to PSV; the only difference between these two modes in a spontaneously breathing patient is the method of breath termination. With PSV, the breath is terminated as a result of the patient's inspiratory flow decreasing to the termination cycling flow, whereas in PA/C, the breath is terminated when the inspiratory time is reached. No other real differences in these modes exist in a spontaneously breathing patient.

To increase or decrease $PaCO_2$ in the PCV mode, the RT can simply increase or decrease the pressure limit while observing the exhaled V_T on the ventilator display monitor until desired V_T is obtained. The most important problem with the use of V_T to adjust $PaCO_2$ in the PCV mode is that the peak pressure should not be increased greater than 28 cm H_2O to avoid ventilator-induced lung injury.

In a patient receiving PCV, a change in the rate affects $PaCO_2$ in the same manner as in **volume-controlled ventilation**. If V_T remains constant, an increase in rate decreases $PaCO_2$ and vice versa; however, in the PCV mode, percent inspiratory time ($\%T_i$) and I:E ratio may be fixed. If $\%T_i$ is constant, and respiratory rate is increased, actual inspiratory time decreases and V_T may also decrease. Decreases in rate ($\%T_i$ and pressure limit constant) may result in an increase in delivered V_T. The following example shows this principle.

A patient receiving ventilation in the PCV mode has a pressure control setting of 15 cm H_2O, PEEP of 5 cm H_2O, $\%T_i$ of 50%, I:E ratio of 1:1, and rate of 20 breaths/min. In this example, respiratory cycle time can be calculated as follows:

$$\text{Respiratory cycle} = 60/f = 60/20 = 3 \text{ seconds}$$

Inspiratory time (T_i) would be:

$$T_i = \%T_i \times \text{Respiratory cycle} = 0.50 \times 3 = 1.5 \text{ seconds}$$

A pressure of 25 cm H_2O applied for 1.5 seconds might achieve V_T of 400 mL for this patient.

If the rate were increased to 30 breaths/min, what would happen to respiratory cycle time, inspiratory time, and delivered V_T? Respiratory cycle and inspiratory time are calculated for a rate of 30 breaths/min as follows:

$$\text{Respiratory cycle} = 60/f = 60/30 = 2 \text{ seconds}$$

$$T_i = \%T_i \times \text{Respiratory cycle} = 0.50 \times 2 = 1 \text{ second}$$

At a constant pressure control setting of 15 cm H_2O, a decrease in inspiratory time from 1.5 seconds to 1 second may reduce delivered V_T. An increase in respiratory rate may reduce delivered V_T and increase (rather than decrease) $PaCO_2$.

When using PCV, the RT should observe the effect of inspiratory time and pressure limit on the patient's flow and volume curves as displayed by a ventilator graphics monitoring package. Generally, as inspiratory time increases at a given pressure, volume also increases until an inspiratory plateau or hold is reached. This point can be identified by observing the inspiratory flow curve. If the inspiratory flow curve decreases to zero and holds that value for a time before exhalation begins, an inspiratory plateau is present (Fig. 49.9). Further increases in inspiratory

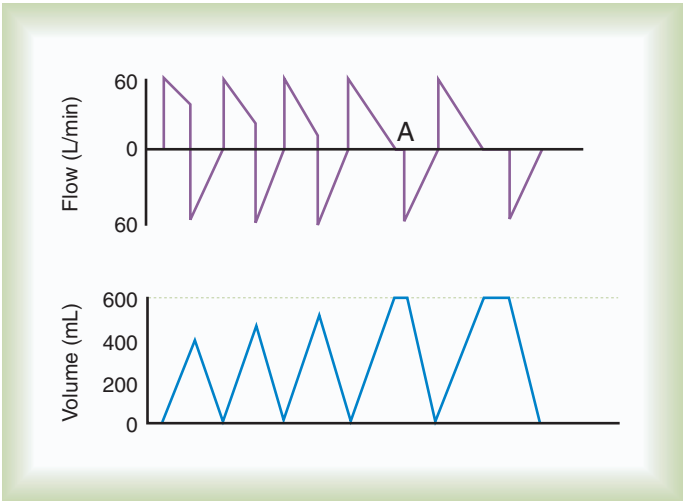

Fig. 49.9 Effect of inspiratory time and inspiratory plateau on delivered V_T in the PCV mode. Initially, as inspiratory time is increased, V_T increases. When an inspiratory plateau *(A)* is achieved, a further increase in inspiratory time does not result in increased V_T. The same effect occurs as inspiratory time is decreased. Initially, with small decreases in inspiratory time, there would be no change in V_T as long as an end inspiratory plateau was maintained. When the inspiratory time is less than that needed for an inspiratory plateau, further decreases in inspiratory time result in a decrease in V_T at the same pressure.

time do not result in additional V_T. Conversely, if an inspiratory plateau or hold is present, a decrease in inspiratory time does not decrease V_T (at the same pressure limit) until the inspiratory plateau is no longer present (see Fig. 49.9). Table 49.9 summarizes methods of altering $PaCO_2$ during volume-controlled ventilation (VCV) and PCV.

TABLE 49.9 Changing Ventilation and $PaCO_2$

Mode		
Increase	**Ventilation (↓ $PaCO_2$)**	**Decrease Ventilation (↑ $PaCO_2$)**
Volume-Controlled Ventilation		
VC-CMV control	↑ V_T; ↑ f; remove V_{Dmach}	↓ V_T; ↓ f
VC-CMV assist control	↑ V_T; ↑ f (to greater than assist rate); remove V_{Dmach}	↓ V_T; ↓ f (may require sedation, control mode)
SIMV	↑ V_T; ↑ f; add/increase PSV; remove V_{Dmach}	↓ V_T; ↓ f; reduce PSV (may require sedation)
Pressure-Controlled Ventilation		
PCV[a]	↑ ΔP; ↑ f (maintaining same T_i); remove V_{Dmatch}	↓ ΔP; ↓ f (maintaining same T_i)
PSV	↑ ΔP; remove V_{Dmatch}	↓ ΔP
Bilevel PAP	↑ IPAP (↑ ΔP); remove V_{Dmatch}	↓ IPAP (↓ ΔP)
APRV	↑ ΔP ↑ release frequency	↓ ΔP ↓ release frequency

Note: In assist (patient-triggered) mode, the patient may simply alter the trigger rate after a ventilator change, and it becomes difficult to predict the results of a ventilator change on $PaCO_2$ in the assist mode.

[a]In PCV, if $\%T_i$ is preset, an increase in respiratory rate results in a decrease in inspiratory time and may reduce V_T. If $\%T_i$ is set at 50% in PCV mode, an increase in rate from 15 to 20 breaths/min causes inspiratory time to decrease from 2 s (50% of 4 s) to 1.5 s (50% of 3 s). If the pressure limit is not changed, V_T is likely to decrease.

APRV, Airway pressure release ventilation; *IPAP,* inspiratory positive airway pressure; *PCV,* pressure-controlled ventilation; *PSV,* pressure support ventilation; *SIMV,* synchronized intermittent mandatory ventilation; *VC-CMV,* volume controlled-continuous mechanical ventilation.

$PaCO_2$ When Using Lung Protective Strategies for Acute Lung Injury and Acute Respiratory Distress Syndrome

Ventilation strategies for lung protection include low V_T, rapid respiratory rates, and permissive hypercapnia, if necessary, to avoid overdistention ($P_{plat} > 28$ cm H_2O).

Open Lung Approach

The use of a high PEEP, low V_T lung-protective strategy using V_T of 4 to 8 mL/kg and PEEP set after a lung recruitment maneuver and decremental PEEP, as discussed previously, may improve mortality in patients with persistent ARDS.[24,25] Because V_T is reduced, respiratory rate should be increased incrementally up to 35 to 40 breaths/min. The limitation on rate is the development of auto-PEEP; if auto-PEEP does not develop, the rate can be increased. The primary concern in patients with severe ARDS is acidosis; however, most patients without severe sepsis, cardiovascular dysfunction, or renal failure can tolerate severe acidosis. The ARDS Clinical Network defined the limit for acidosis as pH less than 7.15.[2] $PaCO_2$, although important, should be allowed to increase before accepting V_T that results in P_{plat} greater than 28 mm Hg. The need to allow $PaCO_2$ to increase to avoid inducing lung injury is referred to as *permissive hypercapnia*; however, the goal is not to allow the $PaCO_2$ to increase but to avoid P_{plat} that may induce lung injury. With this approach in severe ARDS, V_T is frequently 4 to 5 mL/kg IBW, and $PaCO_2$ is greater than 60 mm Hg. Table 49.10 compares the effect of acute changes in $PaCO_2$ on pH.

When applying this approach, PEEP is set after it is determined by a lung recruitment maneuver and a decremental PEEP trial, Table 49.11. V_T or pressure level is adjusted, ensuring that P_{plat} or pressure control setting is less than 28 cm H_2O. Because V_T is small, inspiratory times can be short (frequently 0.6 to 0.8 second). The respiratory rate is set to achieve CO_2 elimination, with its limit being the development of auto-PEEP. Initially, FiO_2 is set to 1.0 but then titrated downward until PaO_2 is greater than 55 mm Hg. Generally, PEEP is sustained at the set level until FiO_2 is less than 0.5, and when PEEP is decreased it should be decreased in increments of 2 cm H_2O no more frequently than approximately every 6 to 8 hours. If PaO_2 decreases when PEEP is decreased, the correct decision is to reestablish PEEP level, *not* increase FiO_2, because if this occurs, the lung is derecruited and lung volume needs to be reestablished.

When to repeat a recruitment maneuver is a difficult question to answer, and data are insufficient at this time to provide an answer; however, if the PaO_2 does not decrease after the initial lung recruitment maneuver, there is no reason to perform an additional recruitment maneuver. Suctioning may cause derecruitment and hypoxemia, and ventilator disconnection always results in derecruitment. If either of these situations occurs, the

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Adjusting Ventilation in PA/C Mode

Problem

A 70 kg (IBW) patient with ARDS is receiving PCV in the control mode with the following ventilator settings:
Pressure: 15 cm H_2O
Rate: 25 breaths/min
Inspiratory time: 0.8
FiO_2: 0.60
PEEP: 12 cm H_2O
V_T (exhaled): 425 mL

Arterial blood gas values with these ventilator settings are as follows:
PaO_2: 60 mm Hg
SaO_2: 90%
pH: 7.30
$PaCO_2$: 50 mm Hg
HCO_3: 23 mEq/L
Base excess: –2 mEq/L

The physician requests that the respiratory rate be increased to 18 breaths/min to decrease the patient's $PaCO_2$ to 40 mm Hg and normalize the pH. What should the RT do?

Solution

This patient has a PaO_2/FiO_2 ratio of 100 (60/0.60), which is consistent with the diagnosis of ARDS. Special considerations for the ventilatory management of ARDS include maintaining P_{plat} less than 28 cm H_2O. V_T is started at 8 mL/kg IBW and gradually reduced to 6 mL/kg IBW to achieve this goal and minimize ventilator-induced lung injury. Respiratory rate may be increased to maintain $PaCO_2$ and pH closer to normal, as long as volume and P_{plat} are acceptable. $PaCO_2$ may be allowed to increase if necessary to maintain P_{plat} less than 28 cm H_2O as long as pH is acceptable for the patient (usually >7.25). Oxygenation problems are managed initially with PEEP to achieve PaO_2 of 60 mm Hg or more with an acceptable FiO_2. If PEEP fails to improve PaO_2, lung recruitment maneuvers and prone positioning may be used.

For this patient, the V_T is acceptable at approximately 6 mL/kg (70 kg × 6 mL/kg = 420 mL), and P_{plat} is 27 cm H_2O. $PaCO_2$ (50 mm Hg) and pH (7.30) are acceptable, and PEEP of 12 cm H_2O may be appropriate for a patient with ARDS. To decrease $PaCO_2$, the rate could be increased as follows:

$$\text{Initial} \qquad \text{Desired}$$
$$f_{(1)} \times PaCO_{2(1)} = f_{(2)} \times PaCO_2$$
$$25 \times 50 = f_{(2)} \times 40$$
$$f_{(2)}\ \text{Desired} = (25 \times 50/40) = 31.25$$

If V_T is maintained at 425 mL, a rate of 30–32 breaths/min should bring $PaCO_2$ and pH into normal range; however, if respiratory rate is increased, air trapping and auto-PEEP may develop. If auto-PEEP develops, V_T is likely to decrease. In pressure ventilation, an auto-PEEP increase is equal to an equivalent decrease in pressure control level, decreasing V_T. The rate should be increased cautiously, constantly evaluating the impact of the rate increase on V_T. More importantly, there is no reason to try to normalize $PaCO_2$ in this patient. $PaCO_2$ of 50 mm Hg with pH of 7.30 is acceptable.

lung needs to be recruited again, but PEEP is reestablished at the previous PEEP level because the hypoxemia was *not* a result of deterioration in lung function. A recruitment maneuver and decremental PEEP trial should be repeated only if the patient's lung function deteriorates.

TABLE 49.10 Effect of Acute Changes in $PaCO_2$ on pH

$PaCO_2$	pH
80	7.16
70	7.22
60	7.28
50	7.34
40	7.40
35	7.45
30	7.50
25	7.55
20	7.60

From Malley WJ: *Clinical blood gases: assessment and intervention*, ed 2, Philadelphia, 2005, Saunders.

In all patients with severe ARDS, mechanical dead space should be eliminated, in-line suction catheters should be in place, and airway suctioning should be performed only to the level of the main stem bronchus. In addition, ideally the ventilator circuit should not be disconnected.

Other Lung Protective Strategies

Alternative techniques for facilitating CO_2 removal during lung protective ventilation in patients with ARDS include extracorporeal CO_2 removal (ECMO, see Chapter 51), reduction of CO_2 production by control of fever, avoidance of overfeeding, and neuromuscular paralysis. Patients with severe ARDS (PaO_2 < 150 mm Hg) should receive neuromuscular paralysis for the first 12 to 48 hours to allow for stabilization and titration of therapy. This has been shown to improve mortality in these patients.[48] Other authors have advocated the use of HFOV;[76–78] however, recent data in adults indicate that the use of HFOV in ARDS patients results in poorer outcome than the continued use of conventional ventilation.[21,22] As a result, HFOV cannot be recommended in the management of ARDS.

SUMMARY CHECKLIST

- P_{plat} should ideally be maintained at less than 28 cm H_2O in all patients to prevent ventilator-induced lung injury.
- Driving pressure should be maintained at less than 15 cm H_2O in all patients to prevent ventilator-induced lung injury and improve mortality.
- PEEP is used primarily to maintain lung volume, resulting in improved oxygenation and lower FiO_2 in patients with severe oxygenation problems and refractory hypoxemia.
- Initially, all acutely ill patients should be ventilated with V_T of 4 to 8 mL/kg IBW with a respiratory rate to maintain adequate CO_2 removal.
- Patients with ARDS may begin mechanical ventilation with V_T of 8 mL/kg but may need volume adjusted to less than 6 mL/kg IBW to maintain P_{plat} less than 28 cm H_2O.
- Lung protective strategies in the management of ARDS include use of lower V_T (6 mL/kg), maintaining P_{plat} less than 28 cm H_2O, permissive hypercapnia, and PEEP set above the lower inflection point on the static pressure-volume curve.

TABLE 49.11 Example of a Decremental Positive End-Expiratory Pressure Study Following a Lung Recruitment Maneuver[a]

Value	PEEP = 20	PEEP = 18	PEEP = 16	PEEP = 14	PEEP = 12
Time (s)	0	30	75	120	175
V_T (L)	4–6 mL/kg PBW	4–6 mL/kg PBW	4–6 mL/kg PBW	4–6 mL/kg PBW	4–6 mL/kg PBW
f (breaths/min)	24	24	24	24	24
FiO_2 (%)	100	100	100	100	100
I:E ratio	1:2	1:2	1:2	1:2	1:2
P_{peak} (cm H_2O)	36	34	32	30	34
P_{plat} (cm H_2O)	28	26	24	22	26
Cs (mL/cm H_2O)	24	27	32	34	28
SaO_2 (%)	96	97	98	100	98
Blood pressure (mm Hg)	131/78	133/82	130/79	125/74	110/69

[a]The best compliance PEEP is 14 cm H_2O. Because the process of doing a decremental PEEP trial results in derecruitment, the lung must be recruited again and then PEEP is set at the best compliance PEEP plus 2 cm H_2O.
FiO_2, fractional inspired oxygen; *I:E,* inspiratory-to-expiratory; *PEEP,* Positive end-expiratory pressure.

- FiO_2 should be adjusted in all patients who are mechanically ventilated to maintain PaO_2 55 to 80 mm Hg and SpO_2 88% to 95%.
- An open lung approach to mechanical ventilation includes the application of lung recruitment maneuvers, decremental PEEP trial, choosing V_T that maintains P_{plat} less than 28 cm H_2O, and accepting permissive hypercapnia.
- Inspiratory flow for most adult patients should initially be set at approximately 60 L/min or greater to achieve an inspiratory time of approximately 0.6 to 1 second.
- Patient ventilator synchrony is a major problem in patients during patient-triggered ventilation.
- In all modes of pressure ventilation, the pressure level should be set to ensure that V_T of 4 to 8 mL/kg IBW is delivered.
- When in doubt, initial FiO_2 should be set at 1.0.
- Auto-PEEP is a problem in patients with obstructive lung disease (COPD, asthma).
- In spontaneously breathing patients with COPD and auto-PEEP, applied PEEP should be added to ensure that all patient efforts result in triggering of the ventilator.
- An appropriate goal of PEEP would be to achieve PaO_2 55 to 80 mm Hg with FiO_2 less than 0.50.
- Alternative lung protective strategies in patients with ARDS include prone positioning and ECMO.
- Careful attention to acid–base homeostasis and the effect of $PaCO_2$ on pH is an essential part of ventilator management.

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Noninvasive Ventilation

Purris F. Williams

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- List the goals and benefits of noninvasive ventilation (NIV).
- Discuss indications for NIV and the relative strength of the supporting evidence for each indication.
- List the selection and exclusion criteria for successful NIV.
- List the factors that predict successful NIV.
- Describe how to recognize NIV failure and discuss when and why this is important.
- Identify the types of patient interfaces available for NIV and describe how to choose an appropriate interface for a patient.
- List common interface-related adverse effects and discuss how to avoid them.
- Discuss the types of mechanical ventilators and ventilation modes used to provide NIV.
- Discuss the causes and resolution of patient–ventilator asynchrony in NIV.
- Describe the role of the respiratory therapist during the initial application of NIV.
- Describe the ongoing ventilator management of NIV in the acute care setting.
- List potential complications associated with NIV and possible solutions.

CHAPTER OUTLINE

KEY TERMS

chest cuirass
continuous positive airway pressure (CPAP)
erythema
expiratory positive airway pressure (EPAP)
hypercapnic respiratory failure
hypoxemic respiratory failure
inspiratory positive airway pressure (IPAP)
iron lung
negative pressure ventilator
nocturnal hypoventilation
noninvasive positive pressure ventilation (NPPV)
noninvasive ventilation (NIV)
obesity hypoventilation syndrome
palliative care
pneumobelt
rocking bed
Trendelenburg position

Noninvasive ventilation (NIV) is a means of delivering ventilatory support without using an invasive artificial airway, such as an endotracheal or tracheostomy tube. NIV can be provided by applying either negative or positive pressure to the airways. Almost any type of mechanical ventilator can be used to deliver NIV, and many noninvasive patient interfaces are available. However, at the present time, NIV is almost always delivered using a positive pressure ventilator designed specifically for noninvasive use or an ICU ventilator with a noninvasive mode in conjunction with an oronasal or nasal mask. *NIV* is generally understood to include both **noninvasive positive pressure ventilation (NPPV)** and the noninvasive application of **continuous positive airway pressure (CPAP)**.

Interest in NIV has increased in recent years with the publication of findings from clinical trials using NIV in the management of respiratory failure. At the same time, technologically advanced noninvasive ventilators have been introduced. Most intensive care unit (ICU) ventilators now include a specific noninvasive mode of ventilation. Improvements in the design of noninvasive interfaces have increased patient tolerance of NIV. The net effect of these developments is that NIV has become a familiar intervention in both acute and long-term care settings.[1] This chapter reviews the evidence supporting the use of NIV to manage various disease processes and makes recommendations on the types of patients and specific techniques for its successful application.

HISTORY AND DEVELOPMENT OF NONINVASIVE VENTILATION

Many of the early devices used for NIV were developed in the 20th century during the polio epidemic. These devices are most effective when used for patients with neuromuscular disease in the absence of primary pulmonary disease.

First described in the 1930s, the **pneumobelt** consists of a rubber bladder that is strapped around the abdomen and periodically inflated by a positive pressure ventilator (Fig. 50.1).[2] This simple, innovative device is most effective when the patient is in a sitting position. Inflation of the rubber bladder compresses the abdomen. The resulting increase in abdominal pressure pushes the diaphragm upward, actively assisting exhalation. When the rubber bladder deflates, abdominal pressure drops and the diaphragm moves down with the force of gravity, facilitating inspiration.[3]

The **rocking bed** (Fig. 50.2) is a motorized bed that frequently rocks from the **Trendelenburg position** to reverse Trendelenburg position. This repetitive motion facilitates inspiration and exhalation by using gravity to move the abdominal contents and the diaphragm upward and downward.[4] Rocking beds were used in the 1950s as an alternative to negative pressure ventilators for patients following recovery from polio.[2] The device can provide adequate minute ventilation but it is not tolerated by some patients.

Negative pressure ventilators were widely used during the polio epidemic and a few are still used in the home setting.[2] A **negative pressure ventilator** generates negative pressure within a chamber that surrounds the thorax. The chest wall expands, negative pressure is created in the alveoli and inspiration occurs when air flows into the lungs. When the negative pressure is released, elastic recoil causes the lungs and chest wall to return to their normal size, resulting in passive exhalation. The first electrically powered negative pressure ventilator, known as the **iron lung** (Fig. 50.3), surrounded the entire body from the neck down. Other designs were introduced, such as the **chest cuirass**, which enclosed only the chest.[2] A disadvantage of negative pressure ventilators is that their design limits access to the patient unless ventilation is interrupted. Effective negative pressure ventilation can be challenging to achieve if the device has air leaks or does not fit properly. In addition, collapse of the upper airway can occur during inspiration when excessive negative pressure is applied.[3]

The first reported use of NPPV was in 1780, when Chaussier used a bag and face mask during resuscitation.[1] However, widespread clinical use of NPPV did not begin until much later, with the introduction of intermittent positive pressure breathing (IPPB) in 1947.[1,2] IPPB was used extensively to deliver aerosolized medications until the mid-1980s[2] when new evidence showed

Fig. 50.1 Pneumobelt, an intermittent abdominal pressure device. (From Albert RK, Spiro SG, Jett JR: *Clinical respiratory medicine*, ed 2, Philadelphia, 2004, Mosby.)

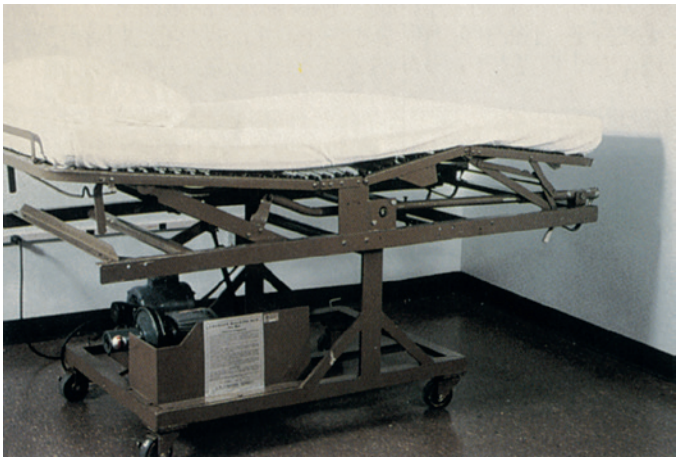

Fig. 50.2 Rocking bed.

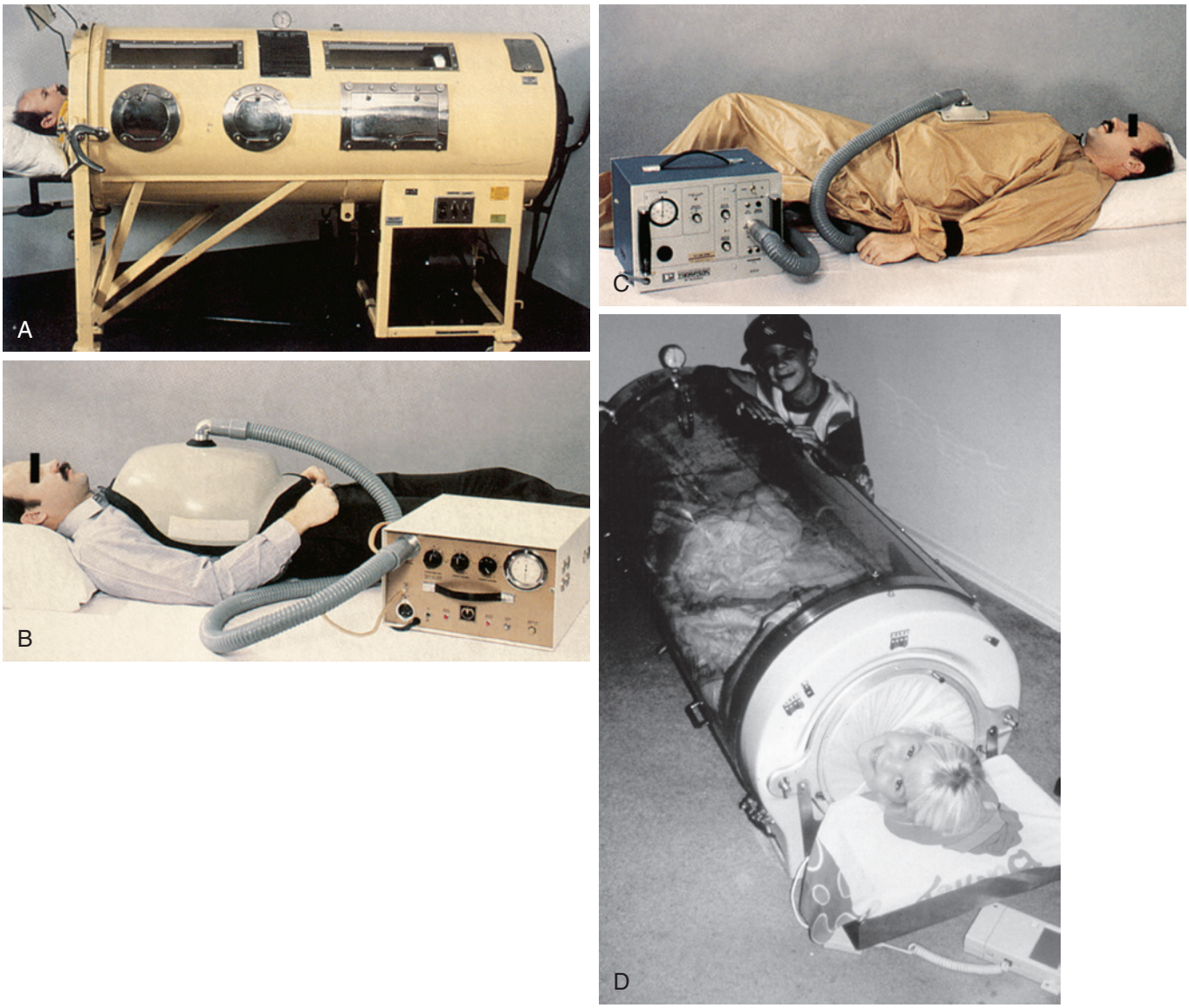

Fig. 50.3 Various devices used for negative pressure ventilation. (A) Emerson iron lung. (B) Chest cuirass. (C) Poncho wrap. (D) Porta-Lung. (A–C, From Albert RK, Spiro SG, Jett JR: *Clinical respiratory medicine*, ed 2, Philadelphia, 2004, Mosby; D, Courtesy Phillips Respironics, Murrysville, PA.)

no benefit compared to small volume nebulizers.[5] Around this time, nasal mask CPAP was suggested as a therapy for obstructive sleep apnea.[6] In 1989, NPPV was used successfully to support patients with acute respiratory failure (ARF).[7] Since then, many studies have examined the use of NIV. The next section provides evidence-based recommendations for the application of NIV in the management of respiratory failure for selected clinical conditions.

INDICATIONS FOR NONINVASIVE VENTILATION

Goals and Benefits of Using Noninvasive Ventilation

Impaired gas exchange is the hallmark of ARF. Endotracheal intubation and mechanical ventilation are often necessary to improve gas exchange in patients with severe ARF. The primary goal of NIV is to improve gas exchange without endotracheal intubation and its associated complications. The potential benefits of using NIV in the acute care setting include improved survival, less time on mechanical ventilation, shorter hospitalization, and lower rates of ventilator-associated pneumonia. In the long-term care setting, major goals are improving the patient's quality of life and relieving symptoms of hypoventilation. The goals of NIV in acute and long-term care settings are listed in Box 50.1.

The primary indication for NIV is **hypercapnic respiratory failure** due to chronic obstructive pulmonary disease (COPD) exacerbation. Hypercapnic ARF is characterized by inadequate alveolar ventilation, elevated arterial PCO_2, and respiratory acidosis. Although patients with hypercapnic ARF are the most likely to benefit from the use of NIV, it is also indicated for selected patients with hypoxemic respiratory failure or with

BOX 50.1 Goals of Noninvasive Ventilation

Acute Care Setting
- Improve gas exchange
- Avoid intubation
- Decrease mortality
- Decrease length of time on ventilator
- Decrease length of hospitalization
- Decrease incidence of ventilator-associated pneumonia
- Relieve symptoms of respiratory distress
- Improve patient–ventilator synchrony
- Maximize patient comfort

Long-Term Care Setting
- Relieve or improve symptoms
- Enhance quality of life
- Avoid hospitalization
- Increase survival
- Improve mobility

Modified from Mehta S, Hill NS: Noninvasive ventilation, *Am J Respir Crit Care Med* 163:540, 2001.

BOX 50.2 Acute and Chronic Disease Processes for Which Noninvasive Ventilation May Be Indicated

Acute Conditions
- Hypercapnic respiratory failure
- Chronic obstructive pulmonary disease (COPD) exacerbation
- Asthma
- Facilitation of extubation, especially in COPD
- Hypoxemic respiratory failure but cautiously
- Acute cardiogenic pulmonary edema
- Respiratory failure in immunocompromised patients
- End-of-life care, do-not-intubate (DNI) and comfort-measures-only (CMO) orders
- Postoperative respiratory failure
- Prevention of reintubation in high-risk patients
- Postextubation respiratory failure

Chronic Conditions
- Nocturnal hypoventilation
- Restrictive thoracic disease
- Amyotrophic lateral sclerosis (ALS)
- COPD
- Obesity-hypoventilation syndrome (OHS)

respiratory failure resulting from numerous other conditions (Box 50.2).[8–12]

Acute Care Indications

Hypercapnic Respiratory Failure

Chronic obstructive pulmonary disease. NIV is the standard of care for treatment of hypercapnic respiratory failure secondary to COPD exacerbation and should be available as first-line therapy in all institutions treating patients with COPD. Current data show that patients with COPD and ARF require intubation less often when they receive NIV. Other benefits of NIV use in this group of patients include lower risk of mortality, fewer complications, and reduced length of hospital stay.[13,14]

Early intervention with NIV should be considered before severe respiratory acidosis develops. However, NIV can be used successfully and safely in much sicker patients. Successful application of NIV has occurred in patients with hypercapnic coma and in awake, noncomatose patients.

RULE OF THUMB The use of NIV in managing COPD exacerbation is strongly supported by evidence from numerous randomized, controlled trials.

RULE OF THUMB All patients with an acute COPD exacerbation should be evaluated for NIV as an alternative to intubation and invasive mechanical ventilation. NIV is the standard of care in these patients.

RULE OF THUMB Severe hypercapnia and decreased level of consciousness should not be considered absolute contraindications to a cautious trial of NIV in selected patients. The RT should be present until the patient is alert, oriented and able to protect his or her airway.

Asthma

The evidence for using NIV for severe asthma with ARF is inconclusive.[15–19] Therefore NIV is not routinely recommended in this setting. If patients with severe asthma receive a trial of NIV, they must be monitored closely. Unless significant improvement in the symptoms of respiratory failure is evident within 1 to 2 hours, intubation should proceed without delay.

Facilitation of Weaning in Chronic Obstructive Pulmonary Disease

There is reasonable evidence that patients with COPD who were intubated for ARF and have failed at least one spontaneous breathing trial (SBT) should be considered for a trial of extubation directly to NIV.[20,21] However, early extubation to NIV does not influence weaning time for similar difficult-to-wean patients if ARF is caused by a condition other than COPD. Success is more likely for COPD patients with no exclusion criteria, for example, excessive amount of secretions and for those who have used NIV previously (and many patients with COPD are familiar with NIV from prior exacerbations). Interestingly, the failure of NIV to prevent intubation does not preclude the successful use of NIV to facilitate extubation at a later time.

RULE OF THUMB A trial of extubation directly to NIV should be considered for patients with COPD and hypercapnic ARF who are likely to receive a tracheostomy for failure to wean.

Hypoxemic Respiratory Failure

Many conditions can cause **hypoxemic respiratory failure**, defined as impaired oxygenation (PaO_2/FiO_2 ratio <300) that is refractory to supplemental oxygen (O_2). Clinical trials of NIV to manage acute hypoxemic respiratory failure have yielded conflicting results. The success of NIV depends largely on the etiology of the hypoxemia. Further study is needed to determine clearly the types of patients who would benefit from NIV.

It is important to recognize that untreated hypoxemia is a serious condition with irreversible, life-threatening implications. For this reason, clinicians should use caution during an NIV trial for a patient with hypoxemic ARF. A recurrent theme in the discussion of hypoxemic respiratory failure is that close monitoring and frequent reassessment of oxygenation during the first 1 to 2 hours are essential to the patient's safety. If NIV does not result in significant improvement, endotracheal intubation should be strongly considered.[22–25]

Acute Cardiogenic Pulmonary Edema

CPAP has been shown to reduce the need for intubation in patients with severe cardiogenic pulmonary edema. The weight of evidence in randomized controlled trials strongly suggests that NIV improves outcome in these patients compared with simple O_2 therapy. Mask CPAP should be used to treat hypoxemia associated with severe cardiogenic pulmonary edema. NPPV should be reserved for patients with both hypercapnia and hypoxemia. Extra caution is recommended for patients who present with cardiac ischemia, hemodynamic instability, arrhythmias, or depressed mental status. Patients with these risk factors should generally be intubated and invasively ventilated.[26,27]

RULE OF THUMB CPAP of 8 to 12 cm H_2O with 100% O_2 is first-line therapy in acute pulmonary edema. NPPV should be used only when hypercapnia is present.

Pneumonia

NIV has been used with mixed results in the management of severe community-acquired pneumonia. The current recommendation for the use of NIV in pneumonia is to limit its routine use to patients who also have COPD.[28] A trial of NIV may be appropriate for carefully selected patients, but caution is advised. Patients with higher severity of illness on admission or with sepsis are much less likely to be managed successfully with NIV. If a trial of NIV does not improve oxygenation within a few hours, invasive ventilation should be initiated.[28–30]

Acute Lung Injury and Acute Respiratory Distress Syndrome

High failure rates are common when NIV is used to treat acute lung injury (ALI) and acute respiratory distress syndrome (ARDS). Patients with risk factors such as severe hypoxemia, hemodynamic instability, sepsis, or metabolic acidosis are more likely to fail NIV. Other factors associated with NIV failure are ongoing dyspnea after starting NIV and large tidal volumes (> 9 mL/kg PBW) during pressure support ventilation (PSV).

The impact of NIV success or failure on survival remains unclear. NIV failure results in worse outcomes than NIV success but better than outcomes when patients are initially intubated. Most importantly, profound hypoxemia (PaO_2/FiO_2 ratio <150) is associated with increased ICU mortality in ARDS patients receiving NIV.[31–35] There is insufficient evidence to support routine NIV use in patients with ALI/ARDS. However, a closely monitored trial of NIV in carefully selected patients may be appropriate. If NIV does not markedly improve hypoxemia within 1 to 2 hours, the patient should be intubated.

Respiratory Failure in Immunocompromised Patients

NIV has long been accepted as first-line therapy for immunocompromised patients with ARF because intubation significantly increases their risk of death. The use of NIV may improve short-term survival and decrease the intubation rate when compared to standard O_2 therapy but the evidence is conflicting and relatively weak. However, recent evidence supports the efficacy of high-flow oxygen via nasal cannula (HFNC) instead of either NIV or standard O_2 therapy in reducing the intubation rate and mortality.[36–41] More work is needed to define the best approach to treating ARF in this group.

Do-Not-Intubate and Comfort-Measures-Only Orders

When NIV is provided for patients with ARF who have orders to limit life-sustaining treatments, the goals and expectations of care change. For patients with comfort-measures-only (CMO) orders, the goal is to relieve the symptoms and stress of disease through **palliative care**. The primary goal of NIV is relief of

MINI CLINI

Noninvasive Ventilation to Treat Hypoxemic Acute Respiratory Failure

Problem

A patient with acute hypoxemic respiratory failure is receiving NIV via nasal mask with a noninvasive ventilator. The ventilator is delivering PSV with peak inspiratory pressure set at 12 cm H_2O and end expiratory pressure set at 4 cm H_2O. O_2 at 10 L/min is flowing into the nasal mask. After 40 minutes on NIV, the patient's condition is only slightly improved. She continues to have signs of respiratory distress with an ineffective breathing pattern (dyspnea, tachypnea with respiratory rate 30, heart rate 120 beats/min, SpO_2 87%). She is unable to keep her mouth closed. An arterial blood gas is drawn and the PaO_2 is 53 mm Hg. List some actions that may increase this patient's chance of success using NIV.

Solutions

1. Replace the interface with an oronasal mask. A chin strap could be tried but is not likely to be successful. A mask that covers both nose and mouth provides more effective ventilator support by minimizing mouth air leaks. Dyspneic patients tend to breathe preferentially through their mouths.
2. Change to a ventilator that can deliver precise, high FiO_2 has alarms and displays calculating exhaled volumes and graphics. Bleeding in O_2 to the mask or circuit provides only low, inconsistent FiO_2. Alarms are an important safety consideration for sick, unstable patients on NIV. Waveforms and calculated volumes are useful when assessing synchrony and the effects of changing the ventilator settings.
3. Increase positive-end expiratory pressure (PEEP) to 8 to 10 to maintain alveoli open and improve severe hypoxemia; 4 cm H_2O is probably inadequate in this situation.
4. If these interventions do not result in significant improvement in oxygenation within 30 to 45 minutes, the patient should be electively intubated and ventilated. Recognizing an unsuccessful NIV trial can be challenging, However, delaying intubation in the setting of hypoxemia increases the risk of death during intubation. Such delays can result if clinicians do not recognize an unsuccessful NIV trial in the setting of hypoxemia.

dyspnea in this setting. The goals for patients with do-not-intubate (DNI) orders are to reverse the ARF and restore health. If NIV fails to achieve those goals, it can still be used to reduce dyspnea along with other palliative measures such as sedative and anti-anxiety medications and O_2 therapy.

The success of NIV in treating patients with DNI orders varies depending on the cause of the ARF. Most DNI patients survive and are discharged from the hospital when ARF is caused by COPD or cardiogenic pulmonary edema. Survival is less likely with ARF from other causes, such as pneumonia.

NIV use remains controversial in patients with CMO orders. Some clinicians have suggested that the potential hardship and stress associated with using NIV outweigh the benefits. Evidence that NIV provides relief of dyspnea in CMO patients is mixed but those with hypercapnia are more likely to improve. Patients should be asked about the intensity of their dyspnea symptoms before and after initiation of NIV and regular, periodic reassessment is recommended. If NIV is not tolerated or if the goal of reducing dyspnea is not achieved, NIV should be discontinued for any patient with a CMO order. Decisions to limit life-sustaining treatment should be mindful of the wishes of the patient and his or her loved ones. In discussions involving palliative and end-of-life care, it is important for clinicians to take the time to explain the goals of NIV, treatment options and expected outcomes to the patient.[42–47]

RULE OF THUMB Patients with DNI or CMO orders should receive NIV to reverse or improve acute respiratory failure. NIV should be removed if it causes discomfort or does not improve dyspnea in the CMO patient.

Postoperative Respiratory Failure

Several investigators have reported favorable results using NIV instead of standard O_2 therapy for ARF during the postoperative period after major abdominal or thoracic surgery.[48–50] Positive findings include improved oxygenation, fewer infections, and lower rate of intubation. Although these results are encouraging, additional randomized trials are required to define the role of NIV in the treatment of postop ARF. At the present time, there is insufficient evidence to support routine use of NIV after major surgery.

Prevention of Reintubation in High-Risk Patients

Reintubation has been associated with increased mortality, longer hospital stay, and a greater need for long-term care than in patients who are initially successfully extubated. In recent studies, randomly assigned patients at risk for reintubation to NIV or standard care showed lower reintubation rates with NIV. Patients with hypercapnia gained the most benefit from NIV. Risk factors associated with extubation failure include a diagnosis of COPD or congestive heart failure, age more than 65 years, ineffective cough and excessive secretions, upper airway obstruction, history of previous weaning failures, and the presence of comorbid conditions.[51,52]

Sufficient evidence exists to support selective application of NIV to avoid reintubation and its associated negative impact on outcome.

RULE OF THUMB NIV should be started after extubation of patients with multiple risk factors, especially patients with COPD, congestive heart failure, or hypercapnia. These patients should be monitored closely and reintubated promptly if NIV does not prevent respiratory distress.

RULE OF THUMB Recognizing NIV failure is important in patients with hypoxemic respiratory failure. Patients with severe hypoxemia have an increased risk of death during elective intubation.

Postextubation Respiratory Failure

The use of NIV to manage postextubation hypoxemic respiratory failure requires a cautious approach. Clinical trials have demonstrated uncertain efficacy when NIV is used to manage postextubation respiratory failure. Patients with COPD and hypercapnic respiratory failure or with congestive heart failure have the best chance of success using NIV in this setting. Failure is more likely if NIV is rescue management after unplanned extubation.[52,53] If hypoxemia does not significantly improve with NIV, these patients should be reintubated without delay.

RULE OF THUMB Before using NIV in the management of ARF, be sure the process causing respiratory failure is reversible, selection criteria are met, and exclusion criteria are absent.

Long-Term Care Indications

Nocturnal Hypoventilation

Nocturnal hypoventilation is common with neuromuscular diseases, severe kyphoscoliosis, COPD, obesity, and sleep apnea. Patients with these disorders can breathe spontaneously without assistance but typically have symptoms related to hypoventilation and sleep-disordered breathing. These symptoms may include excessive sleepiness during daytime hours; fatigue; morning headaches; and cognitive dysfunction, such as difficulty concentrating.[54]

Normally, the onset of sleep is characterized by an increase in $PaCO_2$ during rapid eye movement (REM) sleep. It is thought that the increased work of breathing associated with obesity and COPD or the muscle weakness caused by neuromuscular diseases results in greater levels of hypercapnia. Some of these patients are hyporesponsive to carbon dioxide (CO_2), which contributes to even more CO_2 retention. In response, the kidneys attempt to compensate by retaining bicarbonate, reducing respiratory drive further. This vicious cycle of progressively worsening hypercapnia leads to pulmonary hypertension, cor pulmonale, CO_2 narcosis, and eventually death.[54] The cycle can be stopped if breathing is assisted by NIV for 4 to 5 hours per night for 1 to 3 months. Nocturnal NIV improves sleep quality and gas exchange during waking hours. Current evidence suggests that NIV is effective because it prevents nocturnal hypoventilation and preserves ventilatory response to increases in CO_2 in patients with COPD or restrictive thoracic diseases.

Restrictive Thoracic Diseases

Restrictive thoracic diseases successfully managed with NIV include postpolio syndrome, neuromuscular diseases, chest wall

deformities, spinal cord injuries, and severe kyphoscoliosis. Patients with severe kyphoscoliosis showed improved nighttime and daytime gas exchange, fewer symptoms of hypoventilation, and increased spontaneous V_T and FVC after using NIV.[55] In patients with Pompe disease, improvement of arterial blood gas abnormalities and sleep-disordered breathing has been demonstrated after one night of NIV, though disease progression is not slowed.[56] Diaphragmatic weakness is characteristic of this disease, in contrast to most other neuromuscular diseases. NIV prolongs survival of patients with Duchenne muscular dystrophy, a rapidly progressive neuromuscular disorder. Reports from international centers treating patients with Duchenne have demonstrated that patients using NIV can avoid tracheostomy and can be managed in the home for long periods without hospitalization.[57,58]

The current recommendation for patients with restrictive thoracic disorders is to initiate NIV when patients develop symptoms of nocturnal hypoventilation.

Amyotrophic Lateral Sclerosis

Amyotrophic lateral sclerosis (ALS), also known as *Lou Gehrig disease,* is a neurodegenerative disease that affects motor neurons, resulting in progressive skeletal muscle weakness and paralysis. In the United States, one to two new cases per 100,000 people are diagnosed annually. The average survival time is 3 to 5 years after diagnosis. All patients with ALS eventually need mechanical ventilation to survive. The first signs of muscle weakness occur in the arms and legs for most patients diagnosed with ALS. Approximately a third of cases are bulbar onset, affecting the muscles used in swallowing and speaking first.[59]

Clinical trials have demonstrated a significant survival benefit and improved quality of life for patients with ALS using NIV. Four or more hours of NIV per day slows the decline in vital capacity (VC) measurements, often used an indicator of lung function. The decline occurs more slowly and survival benefit increases when NIV is used for more than 4 h/day.[60] NIV is usually initiated when VC is 50% of the predicted value adjusted for gender and height. There may be an advantage to starting NIV earlier, at 80% of the predicted VC. Regardless of the timing of its initiation, patients with functional bulbar muscles and with orthopnea are more likely to tolerate NIV and benefit from using it. All patients with ALS should be offered a trial of NIV when they show signs of nocturnal hypoventilation and declining ventilatory function.[61–63]

RULE OF THUMB Patients with restrictive thoracic disorders should have symptoms of nocturnal hypoventilation before NIV is considered.

Chronic Obstructive Pulmonary Disease With Stable Hypercapnia

The use of NIV in the management of COPD patients with stable hypercapnia is controversial. Lower $PaCO_2$ has been associated with high inspiratory positive airway pressure (IPAP) setting (18 cm H_2O), compliance with therapy (5 hours of NIV per night), and higher baseline $PaCO_2$ (55 mm Hg).[64] The use of NIV settings (higher IPAP) that target a reduction in $PaCO_2$ resulted in better NIV tolerance and longer short-term survival in a small group of patients.[65] Some evidence supports the idea that NIV in hypercapnic COPD patients following an acute exacerbation was associated with prolonging the time to readmission and death.[66] Although substantial evidence supports the role of NIV in COPD patients with ARF, strong evidence is lacking in the chronic setting. At the present time, there is not enough evidence to support routine treatment with NIV in managing stable COPD.

RULE OF THUMB NIV should be offered to all patients with ALS because it probably slows the rate of decline of lung function and lengthens survival.

Obesity-Hypoventilation Syndrome

Forty percent of adults in the US are classified as obese, and an estimated 7%, or 15.5 million people, are extremely obese (BMI >40 kg/m^2).[67] The prevalence of obesity has increased significantly in the 21st century. **Obesity hypoventilation syndrome** is a common, underdiagnosed condition in hospitalized extremely obese patients. Obesity-hypoventilation syndrome (OHS) is characterized by chronic daytime hypercapnia, sleep-disordered breathing and obesity (body mass index >30 kg/m^2) when no other known cause for hypoventilation is present.

Excess weight on the chest wall and abdomen impose a load on the inspiratory muscles, especially in sitting or supine positions. Extreme obesity decreases the compliance of the chest wall and the respiratory system and increases resistance in the airways. These changes in pulmonary mechanics can cause small airways to close completely before exhalation is complete. The result of this air trapping is the development of intrinsic PEEP, further increasing work of breathing for these patients. Patients with OHS have a defective respiratory drive with a blunted response to increased $PaCO_2$.[68]

NIV improves daytime hypercapnia and relieves symptoms associated with nocturnal hypoventilation within 1 to 4 months. Respiratory drive improves but may not return to normal. CPAP and NPPV have been shown to be equally effective in decreasing daytime $PaCO_2$ in patients with OHS, and both are generally well tolerated. CPAP is usually the first-line treatment for OHS. If hypercapnia persists with CPAP, a switch to NPPV is recommended. Typically, an IPAP setting of at least 6 cm H_2O above expiratory positive airway pressure (EPAP) is necessary to increase alveolar ventilation.[69]

SELECTING APPROPRIATE PATIENTS FOR NONINVASIVE VENTILATION

Acute Care Setting

The success or failure of NIV depends to a large degree on the clinician's clinical judgment in choosing appropriate patients. Candidates for NIV in the acute care setting should show signs and symptoms of respiratory distress and have moderately abnormal gas exchange. NIV selection criteria for ARF are detailed in Box 50.3.[2]

Candidates for NIV must have an intact respiratory drive and stable vital signs. Patients with facial anatomy or injury that prevents use of a noninvasive interface should be excluded. The

BOX 50.3 Noninvasive Ventilation Selection Criteria for Patients With Acute Respiratory Failure

Signs of Impaired Gas Exchange (at Least One of the Following)

- $PaCO_2$ >45 mm Hg and pH <7.35
- PaO_2/FIO_2 ratio <200

Signs and Symptoms of Respiratory Distress (at Least One of the Following)

- Use of accessory muscles
- Paradoxical breathing
- Respiratory rate ≥25 breaths/min
- Moderate to severe dyspnea (increased dyspnea in chronic obstructive pulmonary disease [COPD] patients)

Modified from Mehta S, Hill NS: Noninvasive ventilation, *Am J Respir Crit Care Med* 163:540, 2001.

MINI CLINI

Preventing a High-Risk Patient From Requiring Reintubation

Problem

A 74-year-old man was intubated for hypercapnic respiratory failure 3 days ago. Past medical history is significant for hypertension, coronary artery disease, COPD, and former cigarette smoker ×35 years (quit 10 years ago). He is currently on low-level PSV (PS 8, PEEP 5 cm H_2O, FiO_2 0.3). Vital signs are heart rate 80 beats/min, blood pressure 130/70 mm Hg, respiratory rate 16 breaths/min, and SpO_2 95%. Endotracheal suctioning has been performed every 2 to 3 hours for moderate to large amounts of yellow secretions. Ipratropium metered dose inhalation (MDI), 2 puffs every 6 hours, is ordered. He was placed on a spontaneous breathing trial this morning and passed; however, his ability to clear secretions is a concern. After much discussion among the patient care team, the decision was made not to extubate as planned. What are the options for clinical management?

Solutions

1. Extubate and immediately start NIV. Evidence supports using NIV to prevent reintubation in high-risk patients. Patients with hypercapnia are most likely to benefit. Other factors associated with high risk of extubation failure are age older than 65, COPD, and excessive secretions.
2. Continue aerosolized bronchodilators by delivering the MDI to a collapsible holding chamber added to the NIV circuit. Place the chamber between the exhalation port and the mask. Coordinate MDI actuation as closely as possible to the patient's own inspiration. Shake the MDI canister between each actuation to mix the propellant and the drug. These three points are important to deliver maximum medication to the patient.

patient's risk of aspiration, ability to cooperate, and volume of secretions should be considered before a decision to start NIV (Box 50.4).[2] Decreased level of consciousness due to hypercapnia should not be considered an exclusion criterion for NIV in patients with COPD.[70,71]

It is important to consider the cause of ARF because the efficacy of NIV varies depending on the underlying condition being treated. In the acute care setting, most evidence supports the use of NIV in patients with COPD exacerbations or acute cardiogenic pulmonary edema. There is less evidence supporting NIV for the other indications discussed earlier; however, it is being used more frequently for patients with DNI orders, to facilitate extubation of high-risk patients, and as a means of preventing extubation failure and reintubation (Box 50.5). Ideally, NIV should be initiated before severe ARF develops because severe hypercapnia and acidosis are predictors of NIV failure. Success is unlikely if NIV is used as rescue therapy. Significant improvements in $PaCO_2$ and pH within 2 hours of NIV are predictive of success. In some cases, clinical judgment precludes an NIV trial based on the severity of the respiratory failure or the presence of comorbid conditions. However, in many situations, a reasonable plan would be a trial of NIV for 1 to 2 hours, with close periodic reassessment and plans to intubate if the patient's condition does not significantly improve. Successful application of NIV includes short-term goals of improving gas exchange and preventing endotracheal intubation and long-term goals of improved outcome, decreased length of stay, and decreased mortality.[72,73]

BOX 50.4 Noninvasive Ventilation Exclusion Criteria for Patients With Acute Respiratory Failure

- Apnea
- Inability to protect airway/high aspiration risk
- Hemodynamic or cardiac instability
- Lack of patient cooperation
- Inability to use a noninvasive interface because of facial burns, trauma, or abnormal anatomy
- Copious amounts of secretions

Modified from Mehta S, Hill NS: Noninvasive ventilation, *Am J Respir Crit Care Med* 163:540, 2001.

BOX 50.5 Predictors of Noninvasive Ventilation Success in the Acute Care Setting

- Minimal air leak
- Low severity of illness
- Respiratory acidosis ($PaCO_2$ >45 mm Hg but <92 mm Hg)
- pH <7.35 but >7.22
- Improvement in gas exchange within 1–2 h of initiation
- Improvement in respiratory rate and heart rate

Modified from Mehta S, Hill NS: Noninvasive ventilation, *Am J Respir Crit Care Med* 163:540, 2001.

Long-Term Care Setting

Selection criteria for NIV in the long-term setting include the presence of a disorder that can be managed with NIV and one or more signs of nocturnal and daytime hypoventilation (Box 50.6). Measurable parameters should also be obtained to document a decline in pulmonary function, nocturnal hypoventilation and/or daytime hypercapnia depending on the disorder being treated. For example, measurement of VC, maximum inspiratory pressure or cough peak flow rate can be indicators of decline in a patient with neuromuscular disease. A sleep study with monitoring of end-tidal or transcutaneous CO_2 and SpO_2 is required to document nocturnal hypoventilation. Arterial blood gas analysis

documents daytime hypercapnia with elevated $PaCO_2$ and serum bicarbonate and normal pH. In long-term care settings, a follow-up examination is suggested 1 month or so after starting NIV to assure that the patient has acclimated to the device. A 2-month follow-up is recommended to determine compliance with NIV and to assess benefit.[74]

Exclusion Criteria for Noninvasive Ventilation in a Long-Term Care Setting

NIV exclusions are similar in acute and long-term settings. Cooperation on the part of the patient is a major factor when NIV is used in the management of chronic conditions. Lack of support at home can have a negative impact on compliance with NIV.

EQUIPMENT USED FOR NONINVASIVE VENTILATION

Many factors, including the choice of patient interface, ventilator, mode of ventilation, and initial ventilator settings, play a role in determining whether NIV will be successful in a given patient. This section discusses the equipment and modes of ventilation used when applying NIV.

BOX 50.6 Signs and Symptoms Associated With Nocturnal Hypoventilation

- Dyspnea during activities of daily living
- Orthopnea
- Poor sleep quality, insomnia, frequent arousals
- Morning headaches
- Daytime fatigue or sleepiness
- Decrease in energy and intellectual performance
- Recurrent complications such as hospitalizations, respiratory infections, etc.
- Signs of cor pulmonale

Patient Interfaces

Many options are available to provide a noninvasive interface between the patient and the ventilator. A primary interface requirement is compatibility with the type of ventilator to be used. Certain mask designs interfere with proper functioning of ICU ventilators. Other design considerations may include volume of dead space in the mask and the position of the exhalation port in the system. The condition to be treated, needs of certain patients, and the care setting in which NIV is used can also influence the choice of interface.

Face masks are specifically designed for use with either ICU or noninvasive ventilators (Fig. 50.4). Face masks for noninvasive ventilators have entrainment valves that prevent asphyxia if the ventilator fails or the tubing becomes disconnected. Full-face masks designed for ICU ventilators do not have this feature. In addition, noninvasive ventilators using a single-limb circuit require a leak port either in the tubing or in the mask itself (Fig. 50.5). Masks with leak ports should be used only with noninvasive ventilators because the leak interferes with the function of ICU ventilators.

Clinicians should select an interface that is the right size for the individual patient, assess mask fit and placement on the face, and reposition the mask as needed, minimizing air leaks to the extent possible. These assessments have a direct impact on patient comfort and compliance with NIV, two important factors that can influence the overall effectiveness of NIV. The most common noninvasive interfaces in the acute care setting are oronasal masks followed by nasal masks. An oronasal mask is usually the best choice when NIV is used to treat ARF.[75]

Fig. 50.4 (A) Oronasal mask designed for use with a critical care ventilator. (B) Oronasal mask with anti-suffocation valve intended for use with a noninvasive ventilator. ([A] Courtesy Phillips Respironics, Murrysville, PA. [B] Courtesy Pulmodyne, Indianapolis, IN.)

Fig. 50.5 A leak port is required with noninvasive ventilators to ensure proper function, either as shown, in the ventilator circuit, or in the nasal or oronasal mask. Occlusion of the leak port will result in ventilator malfunction. (Courtesy Pulmodyne, Indianapolis, IN.)

Fig. 50.6 (A) Nasal mask that incorporates adjustable forehead support to minimize pressure on the bridge of the nose. (B) Nasal mask designed for small size and minimal facial contact. (A, Courtesy ResMed Corp, San Diego, CA. B, Courtesy of Phillips Respironics, Murrysville, PA.)

Nasal and Oronasal Masks

Nasal and oronasal masks are typically manufactured in two parts. The body of these devices is made of clear, hard plastic. Surrounding the outer edge of the mask body is either a soft plastic or silicone lip or a cushion filled with hydrogel, silicone gel, or air. The best design has a soft inner lip that forms a seal with the patient's face. When a higher positive pressure is applied, the mask fits more closely to the face, effectively decreasing the air leak around the mask. The opposite effect occurs when resuscitation masks are used for positive pressure ventilation. Higher airway pressures tend to force this type of mask away from the face, increasing the air leak.

NIV masks incorporate straps and headgear to maintain and stabilize the mask's position on the face (Fig. 50.6). It is important to avoid tightening the straps more than necessary. A perfect seal between the mask and the face is not required because ventilators used for NIV are designed to function properly in the presence of small air leaks. Pulling the straps excessively tight is likely to result in pressure-related damage to the skin on the bridge of the nose or sometimes on the cheeks. Clinicians must be vigilant for early signs of skin damage and take steps to minimize damage and prevent development of pressure ulcers, which are a potential source of infection and for which hospitals can be penalized by oversight organizations. The first sign of pressure-related skin damage is usually an area of **erythema**, or reddened skin that persists after removal of the mask. A liquid skin barrier and a hydrocolloid patch may be applied to protect the reddened area and some hospitals are now using such precautions as part of NIV protocols.[76]

To address the problem of skin breakdown, most masks incorporate some means of minimizing pressure on the bridge of the nose. These include foam wedges used as spacers and adjustable mechanical controls that prevent the apex of the mask from being pulled too close to the face. Some masks have foam pads that rest on the forehead to help maintain proper mask positioning. An easy way to check for excessive tightness is to insert two fingers between the straps and the patient's face. If it is not easy to do this, then the straps are too tight and should be loosened slightly. A strategy for minimizing the risk of pressure ulcer formation is to alternate the use of two or more masks with different points of facial contact.

The choice of an appropriately sized mask is a key factor in patient tolerance and NIV efficacy. Most masks include sizing

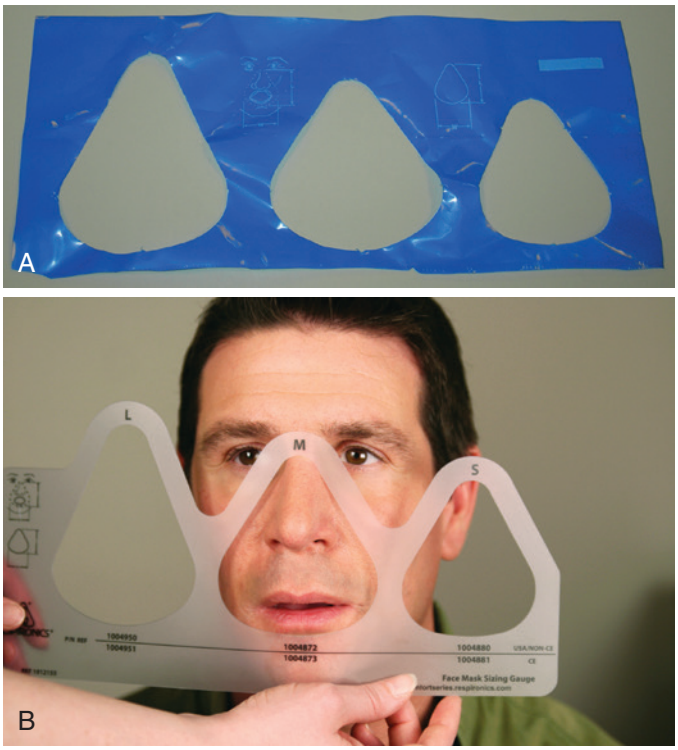

Fig. 50.7 (A) Templates help clinicians select an appropriately sized mask. (B) Oronasal masks should rest on the bridge of the nose between the eyes and in the indentation between the chin and the lower lip. (Courtesy ResMed Corp. San Diego, CA.)

Fig. 50.8 Nasal pillows are available in several designs and various sizes. (Courtesy ResMed Corp, San Diego, CA.)

templates that can be used before removing the mask from its packaging (Fig. 50.7). Nasal masks should be sized so that the cushion starts one-third of the way down from the top of the bridge of the nose, fits closely along the lateral aspects of the nose and rests above the upper lip, just under the nose. Oronasal masks fit similarly except the bottom of the mask rests in the depression above the chin and just below the lower lip. Mask sizes range from extra small to large, but for many individuals, a small or medium-small mask is a good fit. Ill-fitting masks can allow air leaks into the eyes, leading to poor tolerance. Small leaks around the mouth are generally less problematic because most ventilators used for NIV are designed to function with a baseline leak.

Nasal masks are more prone to air leaks than full-face masks, especially for patients who are mouth breathers. Chin straps are available that provide tension to help keep the mouth closed, but in practice they seldom work well. Oronasal masks are less prone to mouth leaks because both the mouth and the nose are covered. Disadvantages associated with oronasal masks include increases in dead space, risk of aspiration, and feelings of claustrophobia. Nasal masks may be better tolerated by patients with claustrophobia. Oronasal masks interfere with a patient's ability to communicate, eat, drink, and expectorate secretions without removing the mask.

In the past few years, new interfaces have been introduced in various designs, sizes, and shapes that are intended to promote patient comfort and tolerance. The respiratory therapist (RT) should be aware of all available designs to enhance the selection of a relatively comfortable, well-tolerated, correctly fitted interface through which the needed level of ventilatory support can be delivered.[77,78]

Nasal Pillows

Nasal pillows (Fig. 50.8) are round, soft cushions that fit directly into the nares. Specially designed headgear holds the prongs in place. This interface is used most often during nasal CPAP or by patients with chronic disease who do not tolerate a nasal mask. Nasal pillows are often a good option to deliver nocturnal CPAP for patients with skin breakdown on the bridge of the nose or those who prefer to sleep on their side. A newer design is the wedge-shaped mini-nasal mask that covers only the end of the nose.

Hybrid Oronasal Mask

The hybrid mask (Fig. 50.9) covers the mouth with a small mask and uses either nasal pillows connected to the top or a soft silicone lip to seal the nares. Like traditional oronasal masks, hybrid masks allow ventilation with fewer leaks. The risk of skin breakdown is reduced because the mask has no contact with the skin on the bridge of the nose. The hybrid mask feels less claustrophobic to some patients. Its design also allows patients to wear glasses during NIV.

Total Face Mask

Usage of the total face mask or full-face mask (Fig. 50.10), which covers the entire face, has increased in recent years. A soft,

Fig. 50.9 The hybrid mask covers the mouth and incorporates nasal pillows into the mask. (Courtesy InnoMed Technologies, Coconut Creek, FL.)

Fig. 50.10 The total face mask. (Courtesy Phillips Respironics, Murrysville, PA.)

flexible layer around the edge of the total mask prevents leaking without touching the bridge of the nose or cheeks. The total face mask comes in one size, which allows quick application in the emergency department or critical care unit. It is generally well-tolerated and less likely to induce feelings of claustrophobia because it does not obstruct the visual field. The total face mask is a good choice for ARF, especially for patients with severe pressure-related skin breakdown who need to continue using NIV.

Helmet

The helmet is an interface that is unavailable in the United States at the present time (Fig. 50.11). This interface surrounds the entire head like a plastic bubble and is held in place by straps under the arms. A high continuous gas flow is required to prevent CO_2 from accumulating inside the helmet during CPAP. During NIV with the helmet, CO_2 is not eliminated as effectively compared with masks, and rebreathing can occur. Triggering and cycling of the ventilator can be adversely affected because of the large internal volume and high compliance of the helmet. Interesting recent data shows that patients using the helmet tolerate higher PEEP and lower ventilating pressures for longer periods than those using an oronasal mask, suggesting a potential role for the helmet in patients with mild ARDS without hypercapnia. The helmet facilitates early mobility without interruption of NIV, which may have an impact on quality of life long after hospital discharge.[79,80] Further investigation is needed to define the best application of this interface.

Few data are available in the literature to help guide the choice of an interface for NIV. There is no perfect NIV interface that meets the needs of every patient. Success is more likely if the interface can be tolerated for long periods and only a small air leak is present. An oronasal mask is the interface of choice for patients requiring NIV for ARF. For patients who cannot tolerate an oronasal mask, a nasal mask should be tried before accepting failure.

RULE OF THUMB Use an oronasal mask for patients in ARF. If the patient is unable to tolerate a mask covering both mouth and nose, try a nasal mask before accepting NIV failure.

Types of Mechanical Ventilators and Modes of Ventilation

Three types of ventilators are used for NIV: noninvasive ventilators, critical care ventilators, and portable home care ventilators. This section describes the characteristics and function of the three types of ventilators.

Noninvasive Ventilators

Most noninvasive ventilators are electrically powered, blower-driven, and microprocessor-controlled (Fig. 50.12). These ventilators utilize a single-limb circuit with one or more small leak ports in either the circuit or the patient interface. Gas flow through the leak ports is continuous but the flow rate varies depending on the pressure in the system. The leak ports also vent exhaled

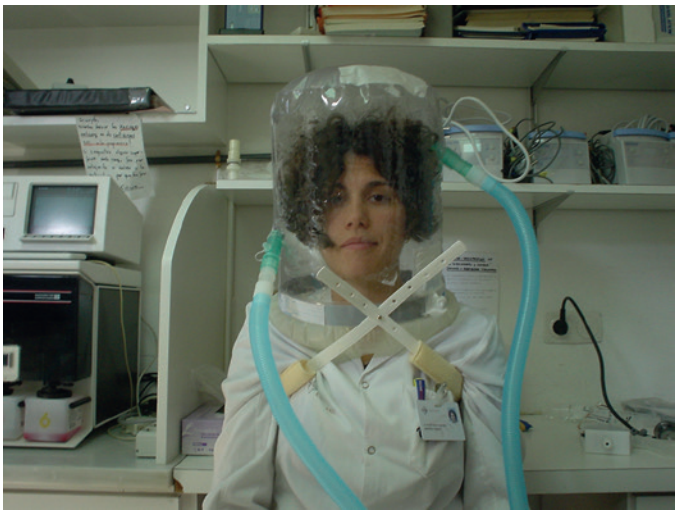

Fig. 50.11 The helmet is used in Europe to provide continuous high-flow positive airway pressure. (Courtesy Intersurgical Nederland, B.V.)

MINI CLINI

Problems With Triggering During Noninvasive Ventilation

Problem

A patient with COPD is receiving NIV with a noninvasive ventilator using a full-face mask. The ventilator settings are as follows: PSV mode, peak pressure 14 cm H_2O, PEEP 4 cm H_2O, backup rate 10 breaths/min. Arterial blood gas was obtained after 30 minutes on NIV. $PaCO_2$ was 75 mm Hg, essentially unchanged since NIV was initiated. The RT notices that the ventilator is not triggering with every patient effort, and his respiratory distress has not improved. What should the RT do?

Solutions

1. The problems of failure to trigger and ineffective ventilation could be caused by a large air leak. Determine if an air leak is present. If so, reposition, refit, or select a better fitting mask; adjust strap tension; and consider adding a forehead spacer to minimize the leak.
2. These two problems could be related to intrinsic PEEP. Carefully observe the patient and ventilator graphics, if available, for missed trigger attempts. The ventilator should trigger with every inspiratory effort by the patient. Try increasing PEEP slowly from 4 cm H_2O to 6 cm H_2O or 8 cm H_2O. If the applied PEEP from the ventilator is set to minimize the difference between end expiratory pressure and the patient's intrinsic PEEP, the ability to trigger should improve. In some ventilators, increasing or decreasing PEEP in pressure-targeted ventilation modes does not affect the peak pressure. In this case, increasing PEEP could result in a decrease in the ventilating pressure and V_T. Check the peak pressure to determine if the ventilating pressure has changed, and increase the peak pressure by the same amount as PEEP is increased. Effective ventilation is usually achieved if the exhaled V_T is approximately 4 to 6 mL/kg.

gas because no exhalation valve is present. This design maintains low resistance in the circuit throughout the breathing cycle. As a result, noninvasive ventilators are sensitive to changes in flow and pressure and can respond quickly to patient demands. The main advantage of noninvasive ventilators over other types of ventilators is the ability to trigger and cycle appropriately when small to moderate air leaks are present.

Low baseline pressure settings have been associated with significant rebreathing of CO_2 in single-limb circuits. A PEEP or **expiratory positive airway pressure (EPAP)** setting of at least 3 to 5 cm H_2O generates adequate flow to flush exhaled gas from the ventilator circuit and prevent rebreathing of CO_2. For this reason, the expiratory pressure can be set no lower than 4 cm H_2O on many noninvasive ventilators. Masks used with noninvasive ventilators typically include an anti-asphyxia valve that opens automatically in the event of power loss or circuit disconnection, minimizing CO_2 rebreathing.[81,82]

Noninvasive ventilators used in the acute care setting for patients who would otherwise need intubation should have alarms for circuit disconnection, loss of power, and battery failure if a battery is present. An internal battery is a useful feature because it allows safe transport of critical patients without interruption of NIV. Information from graphics monitoring and calculated volumes that estimate leak, V_T, and minute ventilation can help clinicians assess patient–ventilator synchrony and make appropriate adjustments to NIV settings.

Noninvasive ventilators used in a critical care setting should be capable of delivering a high, precise FiO_2. For ventilators that do not have an internal air-oxygen blender, supplemental oxygen can be administered by adding an additional flow of O_2 into the ventilator circuit or mask. However, the FiO_2 delivered by this method is inconsistent and reaches a maximum of approximately 0.5.[83,84]

Modes available on noninvasive ventilators usually include CPAP, spontaneous (pressure support), and timed (pressure assist/control). Depending on the ventilator used, the ventilating pressure is referred to as **inspiratory positive airway pressure (IPAP)**, equal to peak airway pressure, or pressure support, which is the change in pressure above PEEP. In either case, this type of breath is usually pressure-limited and flow-cycled or time-cycled (Fig. 50.13). With pressure support and spontaneous modes, inspiration is patient-triggered. With pressure assist/control or spontaneous-timed modes, inspiration is either patient-triggered or time-triggered.[85]

Critical Care Ventilators

The main problem with using older critical care ventilators to provide NIV is their inability to compensate for leaks. Air leaks around the mask can cause problems including missed trigger attempts, auto-triggering, and failure to cycle. Critical care ventilators are now available with noninvasive modes that can deliver NIV effectively, but performance of different models varies widely (Fig. 50.14). These ventilators are equipped with internal air-oxygen blenders, graphics, and alarms, and can achieve high inspiratory flow rates that meet patient demand. They generally use dual-limb circuits that prevent rebreathing of exhaled CO_2.

In a few models, the NIV mode activates only new alarms (low pressure) and deactivates low V_T and minute volume alarms. However, most models incorporate some level of leak compensation during triggering, cycling, or both. A common feature of NIV modes is the ability to set a maximum inspiratory time during PSV. This setting does not deactivate flow cycling but provides an additional limit for inspiration in the presence of a large leak.

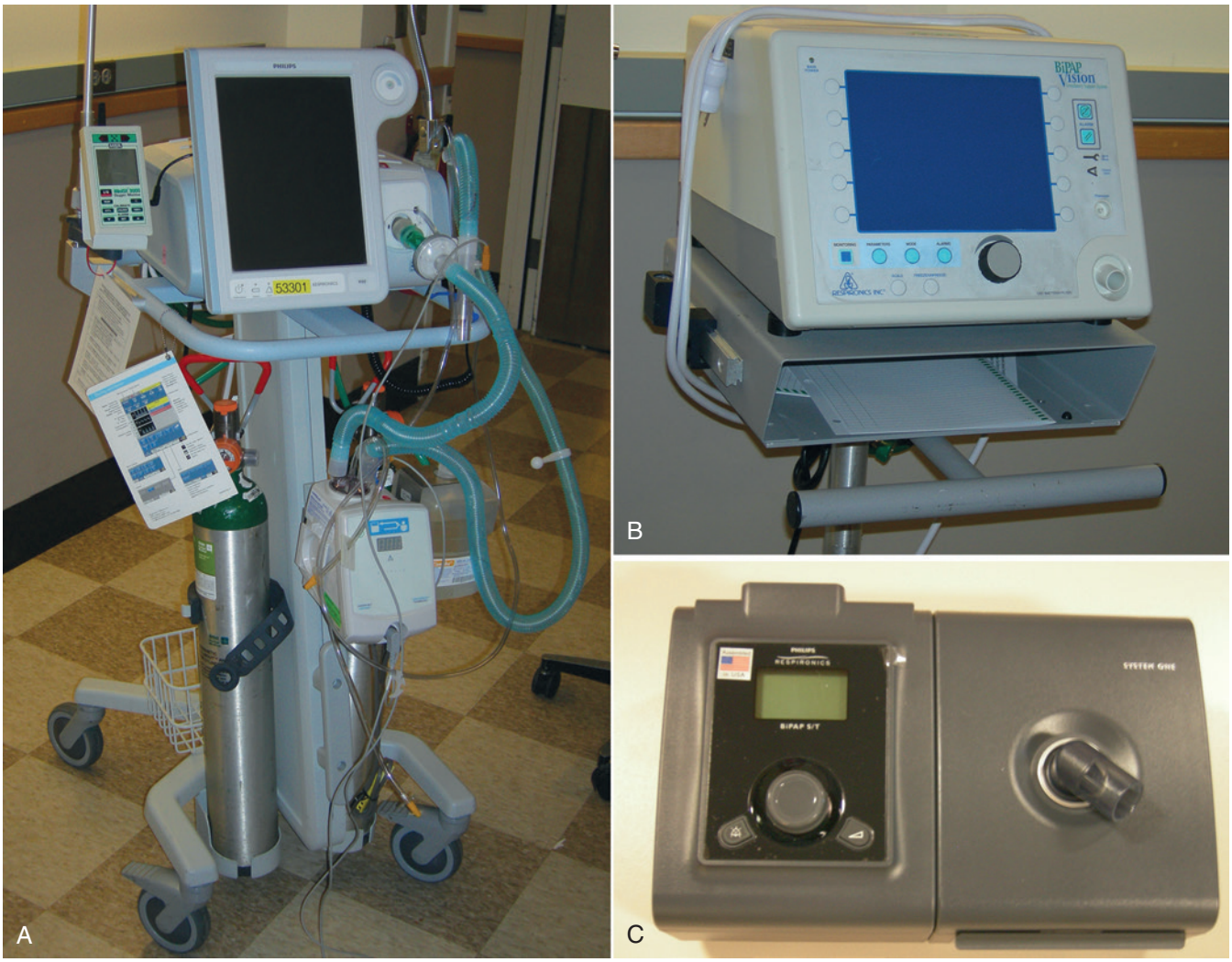

Fig. 50.12 Examples of noninvasive ventilators with monitoring and alarm capabilities. (A) Phillips Respironics V60. (B) Phillips Respironics Vision. (C) Phillips Respironics System One BiPAP S/T. (Courtesy Phillips Respironics, Murrysville, PA.)

To deliver NIV, ICU ventilators can be set in PSV mode, which is a patient-triggered, pressure-limited, flow-cycled mode. During inspiration, a high gas flow is delivered until the preset pressure limit is achieved. At that point, the flow begins to decrease until a predetermined level of flow is reached, cycling the breath to exhalation. Depending on the specific ventilator used, this flow level can be a fixed flow rate (e.g., 5 L/min) or a percentage of the peak flow (e.g., 25%). The flow-cycling mechanism of PSV can cause problems during NIV. In the presence of a large air leak, the flow may not decrease to the level necessary to cycle the breath to expiration. In this case, the patient may have to exhale actively, using abdominal muscles to increase airway pressure to cycle the ventilator to exhalation using secondary criteria.[86] This action increases work of breathing and can lead to failure of NIV.

Active exhalation can be recognized on the ventilator graphics by a spike in airway pressure at the end of the breath (Fig. 50.15). To correct this problem and allow passive exhalation to occur, the cycling criteria must be adjusted. Proper adjustment can markedly improve patient–ventilator synchrony during NIV. One method is to decrease the maximum inspiratory time setting, effectively changing the pressure-supported breath from flow-cycled to time-cycled. Time-cycled (instead of flow-cycled), pressure-limited ventilation markedly improves patient–ventilator synchrony, patient comfort, and compliance with therapy in the presence of air leaks.[87]

The second option is to adjust the expiratory sensitivity setting, which is the percentage of the peak inspiratory flow that terminates the breath. Most ICU ventilators allow adjustment of this setting over a wide range (Fig. 50.16). To prevent active exhalation, the percentage is simply increased until the spike disappears from the pressure waveform.[85–88]

PSV is the ventilation mode commonly used for NIV. Most RTs are familiar with using pressure-targeted ventilation for NIV on ventilators designed specifically for noninvasive application. The current recommendation by an international consensus conference on NIV in ARF is as follows: "Choice of mode should be based on local expertise and familiarity, tailored to the etiology and severity of the pathophysiological process responsible for ARF."[89] If a critical care ventilator is used for NIV, pressure ventilation makes sense because leak compensation is provided, triggering and cycling can be adjusted to suit patient needs, and

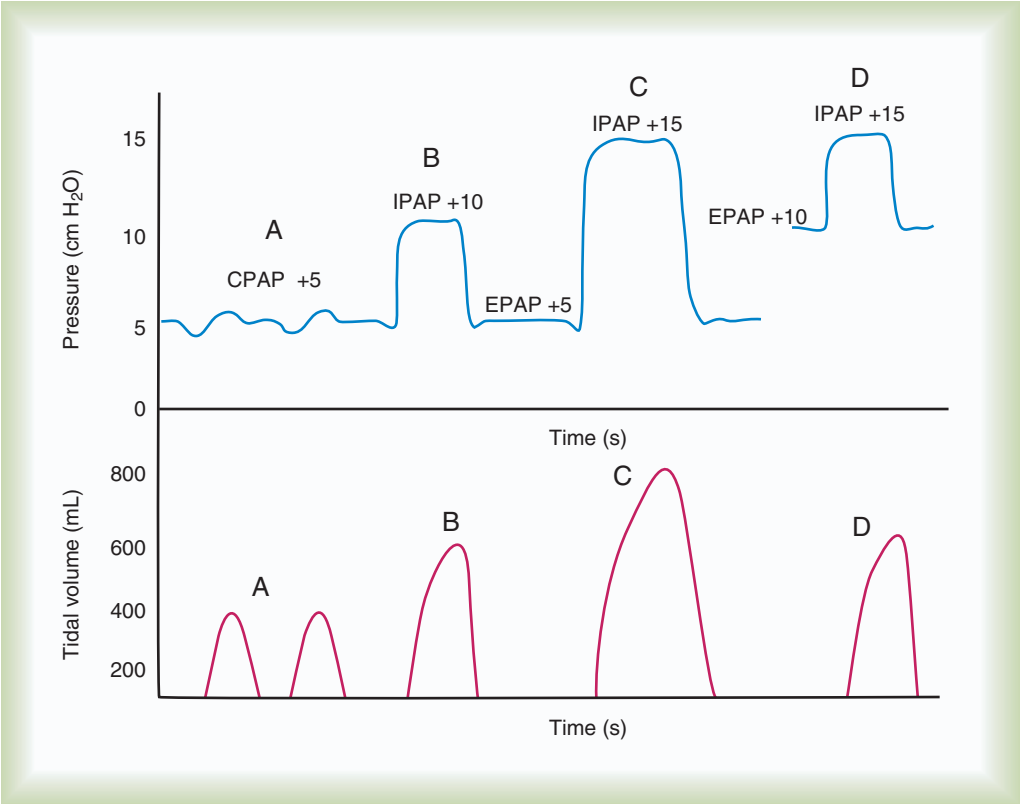

Fig. 50.13 The effects of changing noninvasive ventilator settings (inspiratory positive airway pressure *[IPAP]* and expiratory positive airway pressure *[EPAP]*). (A) Spontaneous breathing on continuous positive airway pressure *(CPAP)* of 5 cm H_2O. (B) Adding IPAP of 10 cm H_2O results in higher V_T. (C) Increasing IPAP to 15 cm H_2O delivers even higher V_T. (D) Increasing the baseline EPAP without a corresponding increase in IPAP results in lower V_T because the difference between IPAP and EPAP is less. (Copyright 2015 Covidien. All rights reserved. Used with the permission of Covidien.)

minute ventilation and end expiratory pressures are preserved. Volume-controlled modes are not recommended for NIV. Inability to compensate for the decrease in minute ventilation and loss of pressure caused by large leaks are major problems when volume-targeted modes are used for NIV.

Portable Home Care or Transport Ventilators

Most portable home care ventilators (Fig. 50.17) are electrically powered and microprocessor controlled. These devices can operate on alternating current (AC) or, if equipped with internal or external batteries, direct current (DC) power sources. The batteries can usually provide power for several hours. Batteries add a measure of safety in areas where AC power outages occur regularly. They also allow the patient to be more mobile, which may improve their quality of life. These ventilators use a single-limb or double-limb ventilator circuit with an exhalation valve that prevents rebreathing of CO_2. Updated technology has improved the performance characteristics of these ventilators to a level comparable to critical care ventilators with the added advantages of small size, light weight, and battery power that allow portability. Most newer models incorporate an NIV mode with the ability to compensate for leaks. Models with adjustable bias flow settings improve the ability of the ventilator to sense patient triggering. Additional features, such as variable termination criteria and maximum inspiratory time, are available on some of these devices to enhance breath termination in PSV.

Portable home care ventilators are currently recommended for patients who need continuous ventilatory support or high ventilating pressures, such as patients with severe chest wall deformities or obesity, or for patients who want greater mobility.[2] For acute care, these ventilators could easily be used to initiate NIV in nontraditional locations and allow transport to an emergency department or ICU without the need to interrupt ventilation.

Heated Humidifiers

An increase in nasal resistance and congestion has been reported with CPAP in patients with mouth leaks. Cold passover humidification does not provide relief but the addition of heated humidity improved nasal symptoms. To prevent the negative effect on patient compliance caused by this common complaint, and the potential accumulation of dried retained secretions in the back of the oropharynx, humidified gas, heated to a temperature that is comfortable to the patient (usually about 30°C), should be the standard when using NIV.[90]

RULE OF THUMB Heated humidity (approximately 30°C) should always be provided with NIV to avoid nasal symptoms, to avoid the accumulation of secretions in the back of the oral pharynx, and to enhance patient tolerance.

Fig. 50.14 Examples of critical care ventilators that can be used to provide noninvasive ventilation. (A) Medtronic 980. (B) Medtronic 840. (Courtesy Medtronic, Boulder, CO.)

MANAGEMENT OF NONINVASIVE VENTILATION

Initial Application of Noninvasive Ventilation

Starting NIV requires the selection of a ventilator and an interface and a significant time commitment from the RT. The patient should be seated in a chair or bed at an angle of 30 degrees or greater (Box 50.7).[2] The RT should always explain the procedure and answer any questions about NIV before placing the mask on the patient. Clinicians should recognize that dyspnea can cause feelings of anxiety and fear. For this reason, the RT or the patient should hold the mask in place when applying the mask for the first time. Holding the mask allows it to be removed quickly if the patient begins to panic or wishes to communicate. A strategy of starting with low pressures can help patients adjust to NIV more readily. Ventilating pressures should be set as low as possible initially, especially if the patient is unfamiliar with the sensation of positive pressure ventilation. Then the ventilating pressures can be adjusted in small increments over 1 to 2 minutes until exhaled V_T is 4 to 6 mL/kg predicted body weight or respiratory distress improves. During this time, the RT should assess the patient frequently, adjusting the ventilator settings to synchronize breath delivery with the patient's breathing pattern and providing instructions and coaching as required. The mask should not be strapped on until the patient is comfortable with the application of NIV and the RT has adjusted pressures to provide proper ventilation.

The specific airway pressures required to support the patient during NIV are best determined by bedside assessment of the patient's response and tolerance. They cannot be determined with accuracy before NIV is started. However, most patients require PEEP levels of 4 to 8 cm H_2O and ventilating pressure of 8 to 12 cm H_2O. Peak airway pressures greater than 20 cm H_2O are rarely required and are best avoided. Airway pressure settings greater than 20 to 25 cm H_2O can force air into the stomach through the esophagus.[91] If the patient has a nasogastric tube in place, the probability of gastric distension increases dramatically, as does the probability of NIV failure.

Final adjustment of the ventilator should deliver a V_T of approximately 4 to 6 mL/kg ideal body weight with a respiratory rate less

than 30 breaths/min. The goal of NIV is not to deliver a large V_T but rather to maintain normal ventilatory patterns with acceptable gas exchange and decrease the work of breathing. FiO_2 should be titrated to PaO_2 of at least 60 mm Hg or SpO_2 88% to 95%.

RULE OF THUMB Most patients with ARF can be stabilized with an expiratory pressure setting of 4 to 8 cm H_2O and ventilating pressure of 8 to 12 cm H_2O. Avoid using peak pressures greater than 20 cm H_2O.

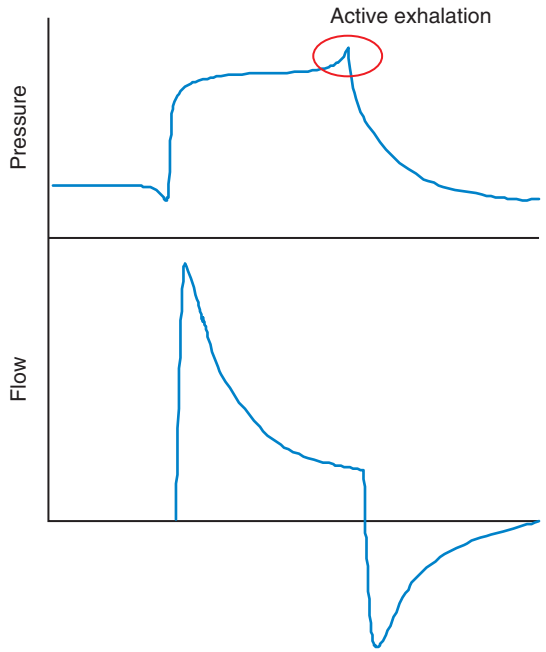

Fig. 50.15 Active exhalation is recognized by the spike on the pressure waveform at the end of inspiration. The patient uses abdominal muscles to increase airway pressure and cycle the ventilator into exhalation.

Clinical Assessment Criteria to Identify Success or Failure of Noninvasive Ventilation

Careful monitoring and frequent reassessment are very important during the first 1 to 2 hours of NIV. Successful application of NIV is easy to recognize—gas exchange improves, $PaCO_2$ decreases, pH normalizes, and PaO_2 and SpO_2 increase. Along with improvement of these measured values, the patient's clinical presentation improves; respiratory rate decreases, V_T increases, accessory muscle use decreases or is eliminated, and pulse rate and blood pressure normalize. If clinical status and gas exchange have not improved after 1 to 2 hours of NIV, intubation should be considered. This is especially true if the indication for NIV was hypoxemic respiratory failure. Evidence suggests an increased risk of cardiac arrest in patients with hypoxemic respiratory failure who do not improve after a trial of NIV for 1 to 2 hours.

Adjusting Noninvasive Ventilator Settings

Ventilator settings may need to be adjusted after the patient stabilizes and acclimates or when arterial blood gas analysis reveals gas exchange problems. Hypercapnia is addressed first by minimizing air leaks and, if necessary, by increasing the ventilating pressure. The result is an increase in the delivered V_T and minute ventilation and a decrease in $PaCO_2$. NIV is typically delivered in a spontaneous mode, where all breaths are patient-triggered and none is mandatory, so adjusting the ventilator frequency is not an option. For patients with chronic hypercapnia, ventilation should be adjusted to maintain an acceptable pH. No attempt should be made to normalize the $PaCO_2$ in such patients.

Increasing the PEEP level increases functional residual capacity (FRC), mean airway pressure, and PaO_2. Higher PEEP should also improve trigger synchrony in the setting of air trapping. In theory, decreasing PEEP should cause the opposite effects. In

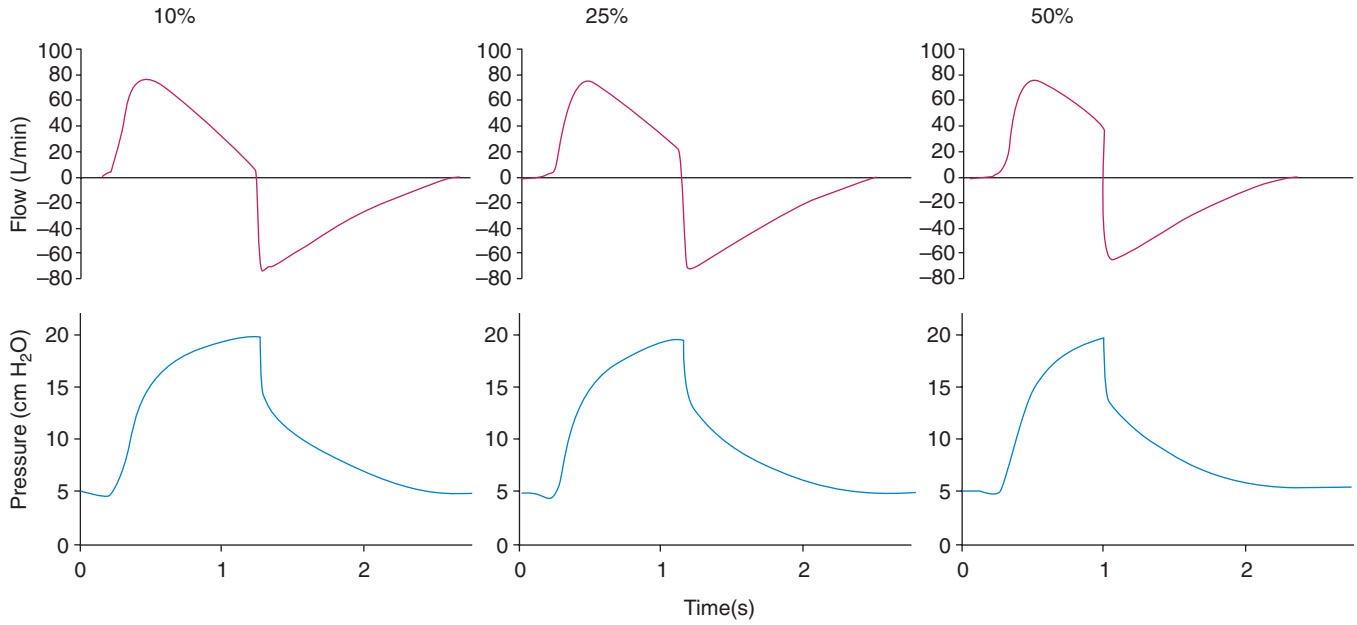

Fig. 50.16 Effects of changing the termination criteria during pressure support ventilation. Changing to a setting that ends inspiration at a higher percentage of peak flow results in shorter inspiratory time and lower tidal volume. This change is sometimes needed to improve patient–ventilator synchrony.

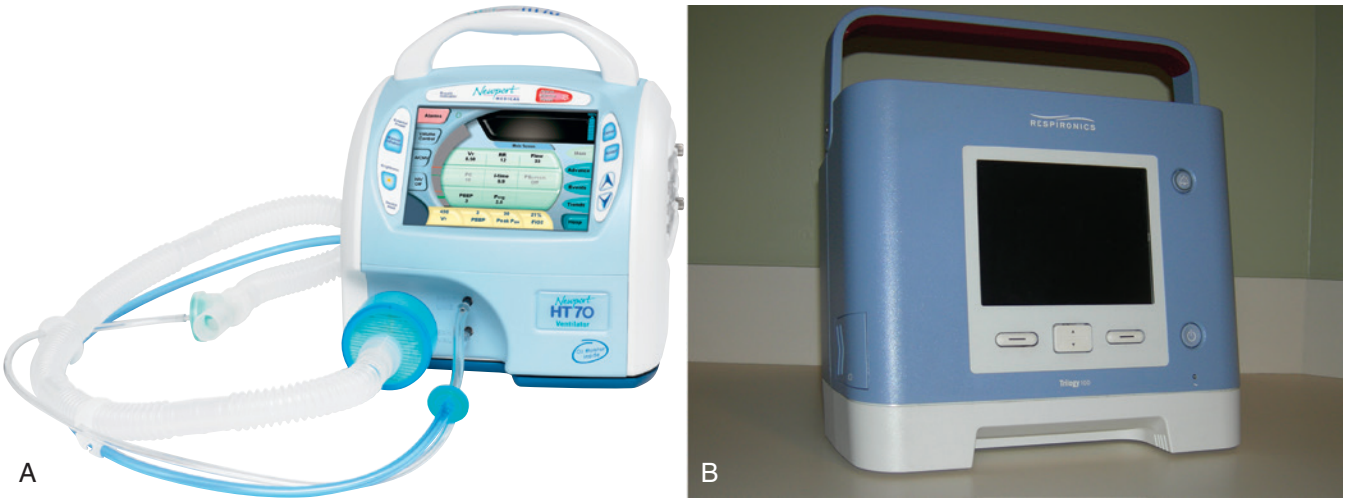

Fig. 50.17 Two examples of new generation portable ventilators that can be used in acute care, home care, or transport settings. (A) Covidien HT70. (B) Phillips Respironics Trilogy. (A, Courtesy Covidien; B, courtesy Phillips Respironics, Murrysville, PA.)

BOX 50.7 Initiation of Noninvasive Ventilation

1. Choose a location with appropriate monitoring based on the severity of the patient's condition. At a minimum, continuous pulse oximetry should be provided.
2. Position the patient with the head of the bed elevated ≥30 degrees.
3. Select a ventilator and an appropriately sized interface, assure interface compatibility with the type of ventilator to be used.
4. Turn on the ventilator and humidifier. Connect the interface to the circuit.
5. Explain the procedure and reason for therapy to the patient and answer any questions.
6. Set initial settings at a low level of support: PEEP 0–4 cm H_2O, ventilatory pressure 2–4 cm H_2O.
7. Hold the mask on the patient's face or have the patient hold the mask. Don't apply straps until he or she is familiar with the sensation of NIV. Provide coaching and encouragement
8. Adjust FiO_2 or bleed in O_2 flow to keep SpO_2 88%–95%.
9. When the patient becomes comfortable with the initial settings, assess for dyspnea and asynchrony. Increase inspiratory pressure until V_T is approximately 4–6 mL/kg predicted body weight or signs of respiratory distress improve. Increase PEEP to reduce asynchrony from missed triggers or to improve oxygenation.
10. Check for air leaks, especially around the eyes; reposition mask as required, adjust straps just tight enough to minimize air leak.
11. Reassess frequently for tolerance and efficacy of NIV (at least every 30 min) for the first 1 to 2 h.

TABLE 50.1 Expected Results of Changing Noninvasive Ventilator Settings

Setting	Adjustment	Expected Result
IPAP	↑	↑ V_T, ↑ minute ventilation, ↓ $PaCO_2$
	↓	↓ V_T, ↓ minute ventilation, ↑ $PaCO_2$
EPAP	↑	↑ FRC, ↑ PaO_2, ↓ V_T If intrinsic PEEP is present, fewer missed trigger attempts and improved patient–ventilator synchrony
	↓	↓ FRC, ↓ PaO_2, ↑ V_T, ↓ $PaCO_2$ Possible rebreathing of CO_2 with single-limb ventilator circuit if EPAP <4 cm H_2O
FiO_2	↑	↑ PaO_2; if bleeding O_2 into circuit, maximum expected FiO_2 is approximately 0.5; increasing O_2 flow >15 L/min may adversely affect triggering
	↓	↓ PaO_2
Rate control[a]	↑	↑ minute volume in timed modes, ↓ $PaCO_2$
	↓	↓ minute volume in timed modes, ↑ $PaCO_2$

[a]Rate control is generally set at 8–10 as a backup rate and not changed in spontaneous/timed mode.
EPAP, Expiratory positive airway pressure; *FRC,* functional residual capacity.

clinical practice, decreasing PEEP may not affect PaO_2 because the disease process resolves and alveolar stability improves.

If the assist/control mode is used for NIV, the rate setting should be less than the patient's spontaneous respiratory rate. Setting the rate in this manner allows the patient to maintain normal $PaCO_2$ by triggering the ventilator and provides a backup rate for safety if apnea occurs. If the patient's disease process limits the ability to trigger or breathe spontaneously, as in some neuromuscular disorders, the set rate has a direct relationship to minute ventilation and an inverse relationship to $PaCO_2$. These relationships may not always be the case in clinical practice and in a spontaneously breathing patient. Table 50.1 summarizes the effects of ventilator adjustments during NIV.

Aerosolized Medication Delivery

For patients on intermittent NIV, aerosol medications are often administered while the patient is off the ventilator. Removal of assisted ventilation from patients in ARF makes little sense and is unnecessary. Aerosol therapy can be delivered in the usual manner through an ICU ventilator used for NIV. With a noninvasive ventilator, positioning the nebulizer between the exhalation port and mask maximizes drug delivery.[92] A pressurized metered dose inhaler (pMDI) can be administered by placing an adapter or collapsible holding chamber in the same position in the circuit. Drug delivery should improve because the pMDI

MINI CLINI

Improving Patient–Ventilator Synchrony During Noninvasive Ventilation

Problem

An oncology patient with DNI orders is receiving NIV from a critical care ventilator with an oronasal mask. The ventilator is set in the PSV mode. Peak inspiratory pressure is 15 cm H_2O, PEEP is 5 cm H_2O, and flow trigger is 2 L/min. The patient has a nasogastric tube in place that is causing a large leak. The ventilator is self-triggering and fails to cycle into expiration when the patient exhales. The patient is dyspneic and appears uncomfortable.

Solutions

Large leaks can cause patient–ventilator asynchrony with ventilators that do not have leak compensation. Triggering and cycling are affected because the ventilator is unable to detect small changes in flow or pressure generated by the patient in the presence of a large leak.

1. Try to reduce the leak by repositioning the mask and placing a flat piece of gauze or hydrocolloid dressing between the mask and the nasogastric tube and another between the nasogastric tube and the patient's face.
2. Change to a critical care ventilator with a noninvasive mode or a noninvasive ventilator designed for ICU use.
3. If switching ventilators is not feasible, and a large leak is still present, adjusting the breath termination criterion or expiratory sensitivity to a higher setting can shorten inspiratory time, allowing the breath to end at a higher percentage of the peak flow.
4. If expiratory sensitivity is not adjustable, change to pressure assist/control mode. Observe the ventilator graphics to determine the patient's desired inspiratory time, and set the inspiratory time on the ventilator accordingly. Typically, critically ill patients should have inspiratory times of approximately 0.7 to 1 second (in some cases, 0.5 second).

is actuated only during inspiration. If the exhalation port is located in the mask or any other position distal to the nebulizer, much of the drug is lost via the exhalation port during both inspiration and expiration.

However, dosing for patients who need aerosolized bronchodilators should be adjusted based on patient response. The dose can safely be doubled to compensate for loss through the exhalation port and other inefficiencies.

Safe Delivery of Noninvasive Ventilation

Monitoring During Noninvasive Ventilation

In acute care or long-term care applications, clinicians must not lose sight of the goals of NIV.[2] The RT should confirm ventilator function and assess the patient on a regular basis for leaks, accessory muscle use, ventilator synchrony, comfort, and changes in vital signs and gas exchange. In the acute care setting, respiratory rate, heart rate, and gas exchange should improve within 1 to 2 hours after initiation of NIV. If there is no improvement after 1 to 2 hours on optimal settings, intubation should be considered. At a minimum, SpO_2 must be continuously monitored. In the acute care setting, continuous monitoring of heart rate and blood pressure is the safest practice. A higher level of monitoring is recommended for patients with acute hypoxemia, worsening condition, involvement of nonrespiratory organ systems, or persistent acidosis. If the patient cannot sustain ventilation independent of NIV for at least 1 hour, the same level of monitoring as any intubated patient should occur.

In the long-term care setting, improvement in gas exchange may require weeks to several months depending on daily use and compliance with the prescribed therapy.[2] Many ventilators have an internal memory card that records the hours of use and other data that can facilitate follow-up care. The patient should be assessed for complications, symptoms of hypoventilation and poor sleep quality, patient–ventilator synchrony, and other factors that affect compliance.

Patient Location

NIV can be initiated in any acute care location, including the emergency department, ICU, or general care floor. After NIV is initiated, patients should be transferred to an ICU or other inpatient location with continuous monitoring capabilities, skilled staff, and access to endotracheal intubation if required. Hypercapnic patients with COPD and a pH of 7.30 or greater and patients who can sustain ventilation without NIV for at least 1 hour can be managed safely on a general care floor. It is important that staff members be adequately trained before caring for patients on NIV. One-to-one monitoring of NIV patients for the first few hours by a trained, experienced RT, nurse, or physician is recommended.[93]

Weaning from Noninvasive Ventilation

At the present time, there is no standard approach to weaning from NIV. One weaning strategy is to decrease high levels of inspiratory and baseline pressure gradually to minimal settings as the acute disease process resolves. The length of time off the ventilator can be increased gradually as tolerated. Another approach is to continue NIV until there is a need to remove the mask. Patients often request to remove the mask after several continuous hours of NIV. The patient's ability to ventilate adequately is reassessed after 5 to 30 minutes based on tolerance. NIV is then either discontinued or restarted.

COMPLICATIONS OF NONINVASIVE VENTILATION

Serious complications of NIV, such as aspiration or pneumothorax, occur very rarely. On the other hand, undesirable side effects of NIV are more common, although less serious. Most side effects of NIV are related to the noninvasive interface, gas flow, or airway pressure. Table 50.2 lists the complications, their frequency of occurrence, and suggested remedies.

Air leaks can cause problems of various levels of concern, ranging from eye irritation and dry mouth to inability to trigger inspiration. Small air leaks should be expected during NIV. Large air leaks should be addressed immediately before they lead to patient–ventilator asynchrony or worsening gas exchange.[3] Choosing a right-sized mask for the patient can resolve or prevent many air leak problems. Changing to any mask that covers both nose and mouth resolves many problems related to large leaks through the mouth. Sometimes, ventilator settings must be adjusted if ventilation is adversely affected by the leak. Using a ventilator with leak compensation should resolve problems with leaks.

Mask-related side effects are the most common problems. Mask discomfort has been reported by up to 50%[2] of patients

TABLE 50.2 Side Effects and Complications of Noninvasive Ventilation

	Incidence[a]	Possible Solutions
Interface-Related Side Effects		
Discomfort	Common	Loosen straps Refit, reposition, or change interface
Erythema	Common	Apply skin barrier or hydrocolloid dressing or both Loosen straps, adjust forehead support, or add spacer Alternate the use of 2 masks
Claustrophobia	Infrequent	Change interface Consider anxiolytic
Pressure ulcer	Infrequent	Apply hydrocolloid dressing Change interface
Skin rash	Infrequent	Apply topical steroid or antibiotic
Air Pressure–Related or Flow-Related Side Effects		
Nasal congestion	Common	Administer inhaled corticosteroid or decongestant
Nasal dryness	Common	Avoid by using heated humidification with NIV Administer saline nasal spray
Sinus or ear pain	Common	Decrease ventilating pressure
Eye irritation	Common	Refit, reposition, or change interface
Gastric distention	Infrequent	Administer simethicone Decrease ventilating pressure
Serious Complications		
Aspiration	Rare	Avoid through careful patient selection Stop NIV, if status will allow
Pneumothorax	Rare	Decrease ventilating pressure Place chest tube, if tension pneumothorax
Hypotension	Rare	Decrease inflation pressure

[a]*Common*—occurs in 30% to 50% of patients; *infrequent*—occurs in approximately 5% to 20% of patients; *rare*—occurs in <5% of patients.
NIV, Noninvasive ventilation.
From Mehta S, Hill NS: Noninvasive ventilation, *Am J Respir Crit Care Med* 163:540, 2001.

receiving NIV, and excessive discomfort decreases patient tolerance for NIV. Switching to a correctly sized mask or loosening the straps slightly is often all that it takes to resolve this issue. Skin damage is a problem that will worsen if not addressed immediately for patients who need to continue using NIV. RTs should keep a watchful eye on reddened areas, especially on the bridge of the nose. It is important to mitigate pressure-related skin damage through the use of various barriers to protect the skin and to use strategies to decrease actual pressure applied to the skin.

Complications related to air pressure and flow, such as nasal congestion and upper airway dryness, can be minimized by providing heated humidity whenever NIV is initiated. Decongestants and saline spray are sometimes needed to relieve symptoms of congestion. Sinus and ear pain and abdominal distension may be related to high inspiratory pressure; use of the lowest effective inspiratory pressure may prevent or alleviate these concerns.

Most major complications can be avoided with careful patient selection and use of the lowest inspiratory pressure that improves the patient's gas exchange and relieves symptoms. NIV should be avoided if the patient is at high risk for aspiration or is hemodynamically unstable. The risk of aspiration increases if inspiratory pressures greater than 20 cm H_2O are used. In general, the head of the bed should be maintained at 30 degrees to reduce the risk of aspiration during NIV.

TIME AND COSTS ASSOCIATED WITH NONINVASIVE VENTILATION

The cost-effectiveness of NIV is linked to appropriate patient selection, familiarity of staff members with NIV, and the success or failure of NIV in preventing endotracheal intubation. Staff time is one of the most valuable and expensive resources in hospitals. Time required by nurses and physicians during the first 48 hours of NIV is similar to the time required for invasive mechanical ventilation, but the time required by RTs for NIV is considerably greater than for invasive mechanical ventilation. However, another study showed that the time required by RTs was significantly greater for the first 8 hours but significantly lower during the next 8 hours. The RT must be present at the bedside during initiation of NIV to properly fit and reposition the mask, provide coaching and encouragement to the patient, titrate ventilator settings upward, and assess the effects of changes in settings. As the patient acclimates and begins to show improvement, the time required to maintain NIV should decrease to a level similar to invasive ventilation.[94–96]

SUMMARY CHECKLIST

- NIV is the application of positive pressure ventilation or CPAP with a mask or other noninvasive interface to improve gas exchange or decrease the work of breathing.
- The use of NIV to manage ARF has improved patient outcomes.
- Evidence supports NIV as the standard of care for managing patients with COPD exacerbations and acute cardiogenic pulmonary edema. There is less evidence supporting other indications for NIV.
- NIV may be justified in the management of ARF if selection criteria (see Box 45.2) are present, exclusion criteria (see Box 45.3) are absent, and the disease process is reversible.
- Acute cardiogenic pulmonary edema should be managed initially with CPAP of 8 to 12 cm H_2O. NPPV should be considered only if hypercapnia is present.
- NIV is beneficial in the management of patients extubated but at risk of reintubation and patients with DNI orders.
- Patients with ALS should receive NIV because it probably prolongs their lives.
- Caution should be used in applying NIV to patients with acute hypoxemic respiratory failure.
- NIV is most successful in the acute care setting when air leaks are minimal, the patient's severity of illness is moderate, respiratory acidosis is present, and improvement in gas exchange and vital signs occurs within 1 to 2 hours after NIV initiation.

- When NIV is used for hypoxemic ARF, intubation and invasive ventilation should be initiated if gas exchange and symptoms of respiratory distress do not improve within 1 to 2 hrs of NIV.
- NIV is typically administered in the PSV mode with PEEP.
- Airway pressure during NIV should be no higher than the setting needed to achieve therapeutic goals (ideally <20 cm H_2O).
- Oronasal and nasal masks meet most patient needs but various other designs are useful to address undesired side effects (mouth leak, skin damage, discomfort).
- Using an interface that is the proper size for the patient has significant positive impact on patient comfort and compliance with NIV.
- Although any ventilator can be used for NIV, ventilators designed to compensate for leaks can be expected to perform best.
- When NIV is provided to critically ill patients, the selected ventilator should have alarms and be capable of delivering a high FiO_2 range.
- Heated humidity (about 30°C) should always be provided with NIV.
- Aerosolized drugs can be administered without interrupting NIV.
- The initiation of NIV requires significant staff time, but after patients stabilize, the time required to maintain NIV is similar to invasive ventilation.

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51

Extracorporeal Life Support

Clorinda B. Suarez and Alex George LeGassey

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Describe two primary goals of extracorporeal membrane oxygenation (ECMO).
- Describe the respiratory therapist's role as an ECMO specialist.
- List indications for initiating ECMO.
- Discuss ECMO physiology.
- Identify components of a typical ECMO circuit and their functions.
- Describe safety systems incorporated in or added to ECMO systems.
- Describe the reasons ECMO patients need to be anticoagulated.
- Describe how anticoagulation is typically monitored during ECMO.
- Identify typical sites for cannula placement for venoarterial (VA) support.
- Identify typical sites for cannula placement in venovenous (VV) support.
- Differentiate between VV, VA, extracorporeal CO_2 removal ($ECCO_2R$) and hybrid ECMO.
- Discuss the significance of ventilator support and management during ECMO.
- List risks and complications of ECMO.
- Discuss when and how to wean off ECMO support.

CHAPTER OUTLINE

KEY TERMS

activated clotting time
afterload
extracorporeal CO_2 removal ($ECCO_2R$)
extracorporeal life support (ECLS)
extracorporeal membrane oxygenation (ECMO)
cardiac output
cannulation
decannulation
hybrid
membrane pressures
oxygen content
oxygen delivery
preload
pump flow
recirculation
sweep flow
tamponade
venoarterial (VA)
venous reservoir
venovenous (VV)

Extracorporeal life support (ECLS) encompasses several forms of mechanical support, all of which involve circulating blood from a patient to outside the body, through a mechanical gas exchanger, and returning it back to the patient. The most common form of ECLS is **extracorporeal membrane oxygenation (ECMO).** There are a few general types of ECMO support: **venoarterial (VA)**, **venovenous (VV)**, and the emerging **extracorporeal CO_2 removal ($ECCO_2R$)** and **hybrid** ECMO support. Distinctions between these types will be outlined later in this chapter.

ECMO is typically considered only in conditions when maximum conventional support has not been successful in delivering oxygen, removing CO_2, or providing adequate cardiac function. ECMO itself does not heal or fix the condition but rather is life-saving support for the most severe forms of acute heart and/or lung failure. Patients can be placed on ECMO for either cardiac or respiratory support, although at times both cardiac and respiratory support are indicated. ECMO will allow the heart and/or lungs to rest and help avoid the injury that can result from high levels of conventional mechanical ventilation. The primary goals of ECMO are to provide adequate **oxygen delivery** and remove carbon dioxide while the lungs and/or heart recover, or, in some cases, until the lungs or heart can be transplanted.

RULE OF THUMB ECMO is an option for the management of severe respiratory failure or cardiogenic shock refractory to conventional treatments for patients with reversible conditions or those eligible for transplantation.

THE RESPIRATORY THERAPIST AS EXTRACORPOREAL MEMBRANE OXYGENATION SPECIALIST

ECMO is provided to patients with life-threatening conditions. These situations require intense monitoring by clinicians with good critical thinking skills, strong knowledge of cardiopulmonary physiology, and technical adeptness. Clinicians who perform this role are referred to as ECMO specialists. Respiratory therapists (RTs) are often viewed as ideal professionals for this role due to their primary training; however, state licensure laws vary on whether RTs are permitted to perform ECMO. RTs have a strong science background, a thorough understanding of cardiopulmonary physiology, and the ability to handle and manage highly technical equipment. In many ECMO centers, RTs play a significant role in the ECMO program. They assist in the initiation of ECMO, provide hour-to-hour management of the ECMO support, and provide ECMO education for the many clinical services involved in the care of ECMO patients. Experienced RTs with good critical thinking skills receive additional training to take on the role of ECMO specialist. The specific role of an ECMO specialist varies among ECMO institutions but the essential education most often provided for this role follows the Extracorporeal Life Support Organization (ELSO) (Box 51.1).

INTERNATIONAL REGISTRY

With the development of an international ECLS registry in the late 1980s, centers providing ECMO began submitting data on the patients supported in centers from around the world. Since that time patient information, including patient age, diagnosis, type of support, complications, and outcomes have been compiled by the registry. Table 51.1 shows a summary of patients entered into the registry and their outcomes.[1]

BOX 51.1 ELSO Guidelines for Training of ECMO Specialists

- Introduction to ECMO
- Physiology of the diseases supported with ECMO
- Pre-ECMO procedures
- Criteria and contraindications for ECMO
- Physiology of coagulation
- ECMO equipment
- Physiology of VA and VV ECMO
- Daily patient and circuit management
- Emergencies and complications during ECMO
- Management of complex ECMO cases
- Weaning from ECMO
- Decannulation procedures
- Post-ECMO complications

ECMO, Extracorporeal membrane oxygenation; *ELSO*, Extracorporeal Life Support Organization; *VA*, venoarterial; *VV*, venovenous.

TABLE 51.1 Number of Patients Reported to the ECLS Registry With Survival Rates in Each Category

	NEONATAL TOTAL PATIENTS	SURVIVED ECLS		SURVIVED TO DC OR TRANSFER	
Respiratory	30,934	25,990	84%	22,662	73%
Cardiac	7794	5063	64%	3281	42%
ECPR	1718	1140	66%	708	41%
Pediatric					
Respiratory	8820	5953	67%	5131	58%
Cardiac	10462	7177	68%	5447	52%
ECPR	3946	2262	57%	1675	42%
Adult					
Respiratory	16,337	10,857	66%	9649	59%
Cardiac	15,942	8865	55%	6747	42%
ECPR	4952	1896	38%	1443	29%
Total	100,905	69,203	68%	56,743	56%

Extracorporeal life support (ECLS) Registry Report, International Summary, July, 2018.

PATIENTS RECEIVING EXTRACORPOREAL MEMBRANE OXYGENATION

Newborns

In the 1980s, ECMO support was almost exclusively used for newborns with respiratory failure.[2] The primary conditions of patients placed on ECMO were meconium aspiration syndrome, respiratory distress syndrome, sepsis, congenital diaphragmatic hernia, and primary pulmonary hypertension.[2] Many of these patients also had pulmonary hypertension due to their primary condition. Improving oxygen delivery using ECMO support can greatly reduce pulmonary hypertension. ECMO was often the best option to improve oxygen delivery while the heart and lungs healed from the primary insult. According to the ECLS registry, more than 87,366 newborns have received ECMO for respiratory

BOX 51.2 Indications for Extracorporeal Membrane Oxygenation in Newborns

- Birth weight >2 kg
- Gestational age ≥34 weeks
- Maximum conventional ventilation
- Failure of optimal medical support including INO
- Lung disease considered reversible
- Absence of uncontrolled bleeding
- No uncorrectable cardiac anomalies
- No other lethal anomalies

INO, Inhaled nitric oxide.

BOX 51.3 Indications for Extracorporeal Membrane Oxygenation in Adult Patients

- Acute hypoxemic or hypercarbic respiratory failure
  - Sat <88 on FiO_2 1.0 with PEEP 15 cm H_2O
  - With plateau pressure >30 and trail of INO or epoprostenol
  - Respiratory acidosis with pH ≤7.20
- Normal RV/LV function
- Murray Score >3

PEEP, Positive-end expiratory pressure.

failure with survival rates to hospital discharge from 51% to 94% depending on the specific diagnosis.[1] Criteria for ECMO in newborns with respiratory failure are well established and are outlined in Box 51.2.[3] Contraindications for offering ECMO in the newborn population fall into two categories: absolute and relative. Absolute contraindications include lethal congenital anomalies, severe irreversible brain damage, and grade III or higher intracranial hemorrhage (ICH).[4] Relative contraindications include birth weight less than 2 kg, gestational age less than 34 weeks, irreversible organ damage (unless a transplant candidate), mechanical ventilation for greater than 10 to 14 days, as well as disease states with high probability of a poor prognosis.[4] The data collected over 25 years have been instrumental in establishing guidelines for newborn ECMO.

Development of less risky and less invasive therapies such as surfactants, nitric oxide, and improved ventilator strategies have decreased the number of newborns considered for ECMO.[5] ECMO support for newborn respiratory failure over the last few years has decreased significantly, accounting for less than 10% of total annual ECMO runs.[2]

Pediatric and Adult Patients

Although the number of newborns receiving ECMO continues to decline, ECMO cases in pediatric and adult patients are on the rise. This trend is likely due to improved strategies in ECMO management and advances in technology, which has led to better equipment for long-term support. During the past five years, the number of centers developing ECMO programs has increased greatly. Many new centers are providing ECMO primarily to pediatric and adult patients, with the largest increases in two categories: ECMO for cardiac support and ECMO as a bridge for lung transplant.[6] Unfortunately, guidelines for initiating ECMO support in pediatric and adult patients are less clear than the well-established guidelines for newborns. Criteria are generally associated with the type of support needed and are not always the same from center to center.[7] Box 51.3 provides an example of general indications for adult venoarterial extracorporeal membrane oxygenation (VA ECMO) and venovenous extracorporeal membrane oxygenation (VV ECMO). Contraindications for pediatric and adult patients generally fall into the absolute and relative categories. Some absolute contraindications typically include acute ICH or stroke, mechanical ventilation more than 7 days, in hospital CPR more than 60 minutes, irrecoverable heart disease, end stage liver disease, and contraindication to anticoagulation.[3] Some relative contraindications are advanced age, active cancer, chronic kidney disease, and multiorgan system failure more than three organs.[3]

RULE OF THUMB ECMO is inappropriate if (a) the condition is irreversible and/or (b) there is no timely, reasonable therapeutic option, and/or (c) there is a high likelihood of poor neurological outcome.[3]

PHYSIOLOGY

To understand ECMO physiology, it is essential to understand normal cardiopulmonary physiology. During normal circulation, blood is pumped from the right side of the heart to the lungs where oxygen and carbon dioxide are exchanged. From the lungs, blood is returned to the left side of the heart. The left heart then pumps oxygenated blood to the major organs and tissues. The amount of oxygen contained in blood leaving the heart is the arterial oxygen content. The absolute amount of blood pumped from the heart is **cardiac output.** Oxygen content times cardiac output equals the amount of oxygen delivered to the tissues.

Oxygen content is rarely measured directly at the bedside but it is critical in managing severely ill patients. Oxygen is carried in the blood in two forms: dissolved in plasma and in red blood cells bound to hemoglobin (as a percentage of the maximum saturation). These two components make up the total **oxygen content** in the blood. The amount of oxygen dissolved in plasma is a very minor portion of the total oxygen content. The dissolved portion is represented by the PO_2 (mm Hg) × 0.003. The majority of oxygen is bound to hemoglobin and is represented by the equation:

$$Hb \times \% \, SaO_2 \times 1.34.$$

Total oxygen content is calculated using the following equation:

$$O_2 \text{ Content } [(PO_2 \times .003) + (Hg \times SaO_2 \times 1.34)]$$

Therefore, with inadequate levels of hemoglobin, oxygen content is significantly diminished.

To understand the importance of hemoglobin, consider the following: A patient with a PO_2 of 40 mm Hg, with a typical oxygen saturation of 70% and a normal hemoglobin level (15 g), has more oxygen than a patient with a PO_2 of 100 (saturation 100%) and a low hemoglobin level (8 g). See Chapter 12 for more complete details on oxygen content and oxygen delivery.

EQUIPMENT

ECMO systems are intended to temporarily support the cardiac and pulmonary function of the patient who cannot maintain

MINI CLINI

Problem

Hemoglobin level in a patient who is bleeding has dropped from 15 to 10 g/dL. His PO_2 remains unchanged at 90 mm Hg. How much would his O_2 content change?

Calculate the change in O_2 content.

$$(PO_2 \times .003) \times (Hg \times SaO_2 \times 1.34)]$$

The O_2 content with a hemoglobin of 15 is 20.37.
The O_2 content with a hemoglobin of 10 is 13.67.

Discussion

This clearly demonstrates the importance of hemoglobin in providing adequate oxygen content. Delivery of oxygen is dependent on the oxygen content and the cardiac output. When oxygen content is low, the body will normally respond by increasing the cardiac output. Total delivered oxygen (DO_2) can be calculated using the following equation:

$$O_2 \text{ Delivery } [(PO_2 \times .003) + (Hg \times SaO_2 \times 1.34)] \times (HR \times SV) = DO_2$$

When cardiac function is impaired, the ability to increase cardiac output is altered and will result in inadequate amounts of oxygen delivered to the tissues. When this happens, anaerobic metabolism occurs and lactic acid is produced. Alternatively, carbon dioxide is produced from systemic metabolism. With normal adequate lung function and normal blood flow through the lungs, appropriate amounts of carbon dioxide are excreted and spontaneous ventilation keeps PCO_2 within acceptable ranges. When altered states of metabolism increase CO_2 production, it is imperative that the lungs are able to remove more CO_2. In diseased lungs or conditions that alter blood flow to the lungs, higher levels of CO_2 remain in the blood. When maximum conventional support fails to provide adequate delivery of oxygen to the tissue or inadequate removal of carbon dioxide occurs, a patient who has no absolute contraindications can be considered for ECMO.

MINI CLINI

Problem

The patient has a cardiac output of 5 L/min and is on 4 L/min of VA ECMO support. Eighty percent of the patient's cardiac output is therefore oxygenated by the artificial oxygenator and is 100% saturated. The patient has essentially no lung function. His SvO_2 is 65% with a PO_2 of 35 mm Hg. Twenty percent of the patient's cardiac output goes through the nonfunctional native lungs where no oxygen is added.

What is the patient's SaO_2 when blood from the ECMO-supported cardiac output and the native cardiac output mix?

Discussion

The combined saturation can be calculated by multiplying the % saturation of each portion of the cardiac output. This patient's combined saturation can be determined by multiplying the 80% (4 of 5 L/min) of the cardiac output that becomes 100% saturated by the ECMO oxygenator (0.8×1), and then multiplying the 20% (1 of 5 L/min) of the output that returns to the native lungs 65% saturated, (0.2×0.65) and adding the results of each

$$(0.8 \times 1) + (0.2 \times 0.65) = 0.93$$

The mixed saturation of this patient would be 93%. To achieve a higher saturation, a larger portion of the cardiac output could be pumped through the oxygenator and saturated to 100%. The portion of cardiac output that would remain through the native lungs would decrease. With a smaller portion of blood saturated to only 65%, the combined saturation would increase.

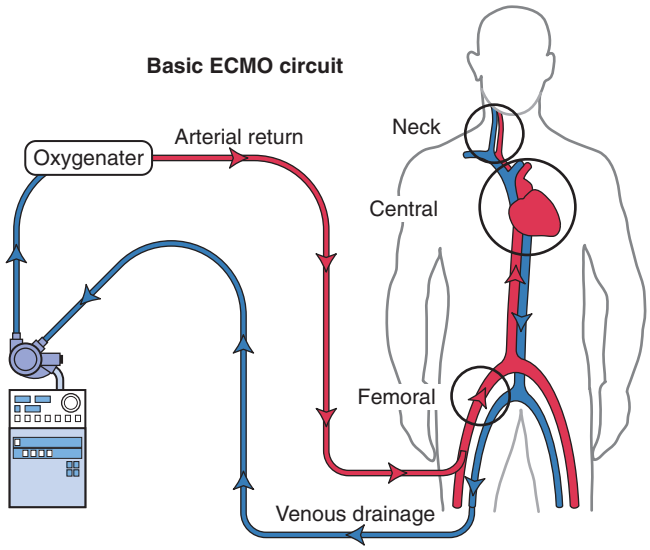


Fig. 51.1 Illustration of the blood pathway of an extracorporeal membrane oxygenation *(ECMO)* circuit. Blood drains through the circuit to a blood pump, which pushes it through an artificial lung oxygenating the blood and removing carbon dioxide (CO_2) before returning the blood to the body.

adequate tissue oxygen delivery. Basically, ECMO has the task of pumping the blood, delivering oxygen to the blood, and removing CO_2. The circuit consists of polyvinylchloride (PVC) tubing segments that have different inner diameters depending on the patient's size: ¼-inch for a neonate to ⅜-inch for pediatric/adult sized patients. Some circuits contain a heparin-based coating to reduce the response of blood to nonendothelial surfaces and to decrease the risk of clot formation. The circuit is generally custom designed using the shortest amount of tubing necessary to allow less resistance to flow and to decrease circuit volume. This is of particular importance for the newborn population because larger circuit volumes result in hemodilution and require additional transfusion of blood products. Infusion ports can be added along the tubing for infusing medications in patients who have limited intravenous (IV) access. These ports can also be an option for access when continuous veno-venous hemofiltration (CVVH) is required. Blood is drained from the patient into the circuit by either a centrifugal or roller pump. From the pump, it goes through an artificial lung, referred to as an oxygenator, where oxygen is added and CO_2 removed (Fig. 51.1).

The ECMO system is powered by the blood pump. The pump function is to draw blood in, either from a **venous reservoir** (the bladder) or directly from the venous circulation, pump it through the oxygenator, and then back into the patient. The two types of pumps frequently used are the centrifugal (or vortex) pump and the roller (or occlusive) pump.

The centrifugal pump is made up of polycarbonate cones attached to a magnetic disk that is attached to a controller (Fig. 51.2). The cones spin at an adjustable rate when attached to the controller and produce forward flow by imparting kinetic energy to the fluid (blood) in a rotating pump head. The **pump flow** provided is therefore dependent on both the patient's **preload** (the volume in the right side of the heart) and **afterload** (the

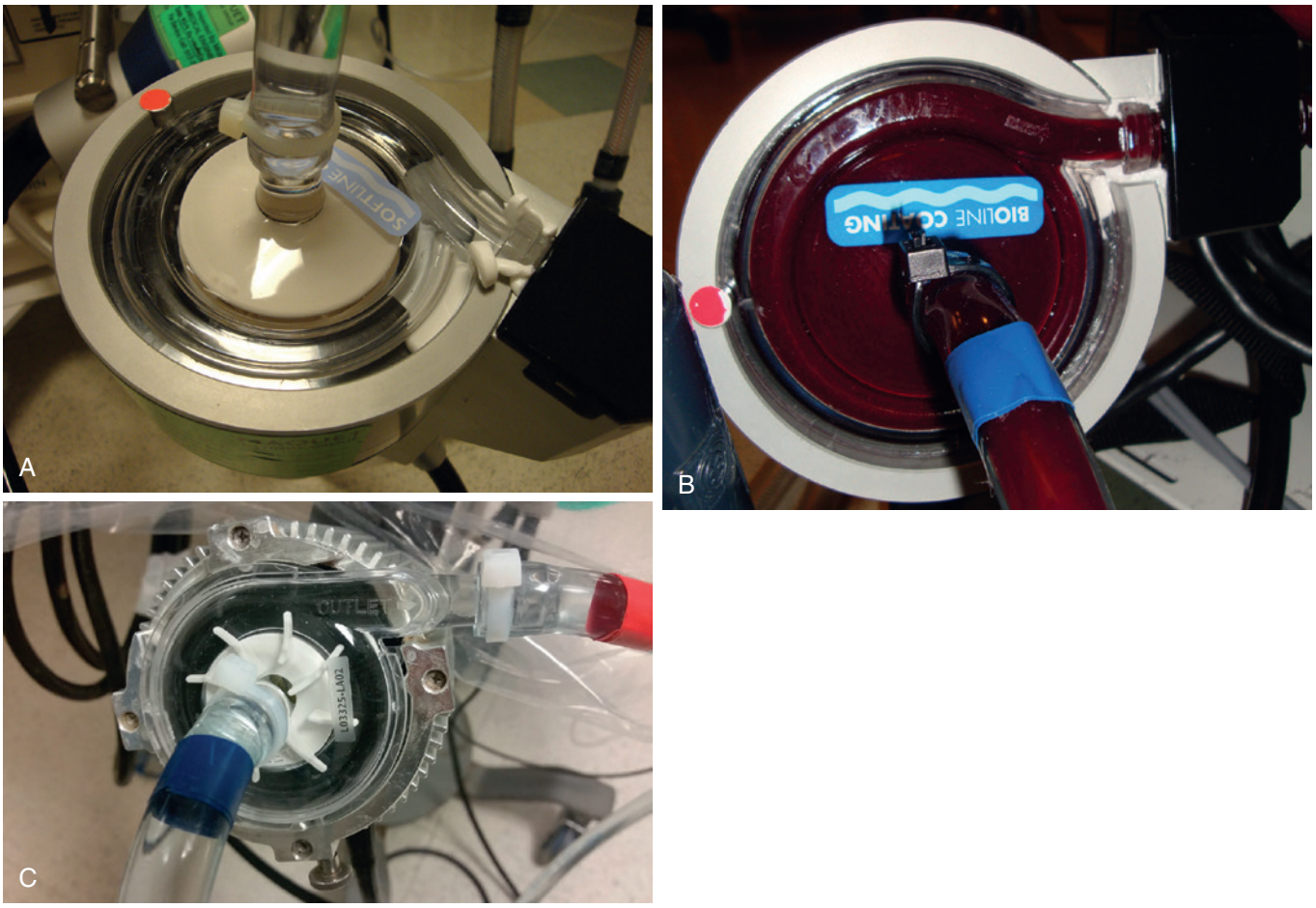


Fig. 51.2 The centrifugal pump is made up of polycarbonate cones, attached to a magnetic disk that is attached to a controller. The cones will spin at an adjustable rate when attached to the controller and produce forward flow by imparting kinetic energy to the fluid (blood) in a rotating pump head. (A) Maquet Rotaflow without blood. (B) Maquet Rotaflow with blood. (C) Abbott cetragam pump.

resistance against the pump outlet from the left side of the heart). Because the centrifugal pump is not occlusive (like the roller pump), pump flow will vary despite a set rate per minute (RPM). A decrease in preload or increase in afterload can cause a decreased pump flow. Centrifugal pumps have the advantage of not being affected by gravity for drainage. However, pump flow can change drastically at a set RPM with changes in preload and afterload. Therefore a mechanism for monitoring pump flow changes is essential. Centrifugal pumps can operate at a wide range of RPMs—often as high as 5000—but higher RPMs can result in significant hemolysis.

The roller pump functions by occluding a segment of the circuit tubing called the *raceway*. Blood is drained by gravity from a venous cannula into the venous reservoir, and then pulled into the pump at a given RPM. The pump contains two rollers positioned opposite each other. Blood is displaced by the appropriate compression of the rollers on the tubing. Roller pumps have been, for the most part, replaced by the safer, more compact centrifugal pumps and only remain at some centers to service the smaller neonatal populations.

Blood moves from the system pump to an oxygenator which functions as the lung of the ECMO system. The oxygenator contains hollow fibers for blood and gas to pass through. Gas flow, referred to as the **sweep flow,** is provided by a blender, which is flowing in the opposite direction of the blood flow (Fig. 51.3). The blender is adjusted to ensure the hemoglobin of the blood leaving the oxygenator is 100% saturated with a PO_2 greater than 250 mm Hg. As poorly saturated venous blood with very low partial pressure of oxygen is pumped into the oxygenator, it traverses through fibers that are aligned with other fibers containing gas with a high partial pressure of oxygen. Oxygen diffuses from the fibers with a high concentration of oxygen to the blood with a lower concentration. There is no CO_2 in the sweep flow. Therefore the carbon dioxide in the blood diffuses into the sweep fibers and is flushed out of the oxygenator. The higher the sweep flow is set, the more CO_2 is eliminated. There is a range of effective sweep flows along with maximum blood flow for the different sizes of oxygenators (Table 51.2). From the oxygenator, fully saturated blood with the desired carbon dioxide level is pumped back to the patient either to a vein (VV support) or to an artery (VA support). The pump speed (RPM) is adjusted to allow the appropriate amount of the patient's blood volume to be oxygenated while the sweep flow rate is adjusted to maintain the desired CO_2 level.

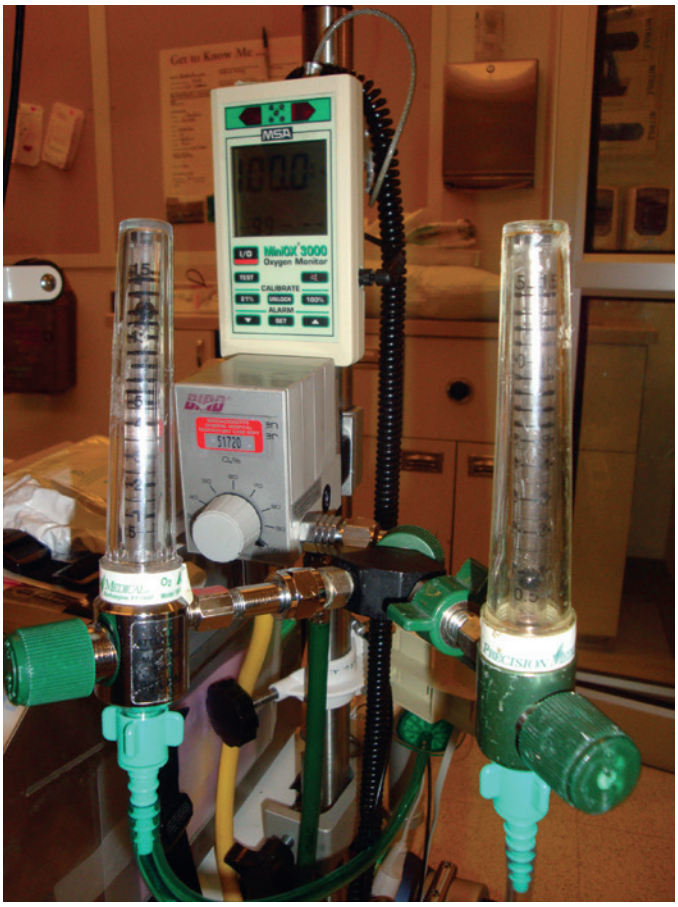


Fig. 51.3 An oxygen flowmeter is connected to the circuit blender. Sweep flow is delivered into the artificial lung delivering up to 100% oxygen. A second flowmeter allows for analysis of the actual percent of oxygen delivered.

Fig. 51.4 Blood warmer/cooler, a device that will warm or cool the blood, circulates sterile water (A) and sends the heated or cooled fluid through hoses attached to the artificial lung and surrounds the fibers containing the blood to warm or cool it (B) (right figure).

TABLE 51.2 Examples of Oxygenator Specifications

Oxygenator	Prime Volume	Maximum Sweep	Minimum Blood Flow	Maximum Blood Flow
Quadrox iD Adult	250 cc	15 lpm	500 cc/min	7 lpm
Quadrox iD Pediatric	81 cc	5.6 lmp	200 cc/m	2.8 lpm

RULE OF THUMB The ratio of sweep flow to pump flow is often 1:1. When using 4 L/min pump flow, typically the sweep flow would be initiated at 4 L/min. The oxygenator functions to provide gas exchange much like native lungs perform gas exchange—oxygen diffuses into the blood from a gas source with a higher partial pressure and CO_2 diffuses out of the blood into a gas source with a lower partial pressure.

Additional equipment used with ECMO support includes a thermoregulation device referred to as the heater/cooler (Fig. 51.4). As blood leaves the patient and circulates through the ECMO circuit, a considerable decrease in blood temperature can occur because the tubing that blood flows through is exposed to ambient temperature. Gas flow through the oxygenator is also cool, resulting in evaporative losses. Therefore, especially in neonates, active warming is required to maintain a normal body temperature. Temperature-adjusted sterile water circulates around the fibers containing blood and allows appropriate temperature control of the blood returning to the patient. These devices have the potential to maintain hypothermic states when appropriate. Recent evidence has demonstrated that mild decreases in core temperature may have a salvaging effect on the brain[8] and can be easily achieved during ECMO support.

Pressure monitoring is a standard part of the circuit. Circuit pressures are measured before and after the oxygenator and indicate the absolute pressure in the circuit along with changes in resistance across the oxygenator (Fig. 51.5). The change in resistance most often indicates development of clots within the oxygenator. Changes in pressures can alert the ECMO specialist to identify emerging situations such as kinks, clots, and, in VA support, changes in hemodynamics.

Fig. 51.5 Oxygenator/pressure monitoring. Pressure transducers are attached to ports before and after the artificial lung with reading displayed on the bedside monitor. "SP5" indicates the pressure before the oxygenator and "SP6" indicates the pressure after the oxygenator. The difference between the two pressures is an indication of the resistance to blood flow through the oxygenator. Increases in pressure difference are usually a result of clot formation.

RULE OF THUMB Monitor pre- and post-oxygenator pressures frequently. Changes will alert clinicians to clots in the oxygenator. Increases in pre-**membrane pressure** only = increased resistance within the oxygenator. Increases in pre- AND post-membrane pressures = increased resistance AFTER the oxygenator.

A pressure monitor can also be placed on the drainage line to detect excessive siphon on the system. Alarms and servo regulation can be used in association with these pressure monitors to create safer systems. Pressure monitoring is either integrated into the ECMO system or additional pressure transducers can be added.

As noted earlier, blood flow is regulated by dialing in a set RPM, which results in flow. The flow is monitored using ultrasonic devices that are either incorporated into the system or added to the circuit. Many systems will display a calculated flow but the accuracy of that flow is dependent on many factors. Flow is measured to assure appropriate occlusion when using roller pumps and to check variations in flow common with centrifugal pumps. Audible alarms are usually set to alert the ECMO specialist of changes in pump flow.

Air (bubble) detectors can be useful in identifying the presence of air in the ECMO circuit. They can be used on either the arterial or venous side of the circuit and detect inadvertent air passing through the system. These devices can function to stop support when air is detected or sound an alert. False alarms can be problematic because support to the patient is stopped and will often produce significant instability for the patient until support is resumed. The ECMO specialist must be able to immediately distinguish true presence of air bubbles from false alarms rapidly and take the appropriate action for either situation.

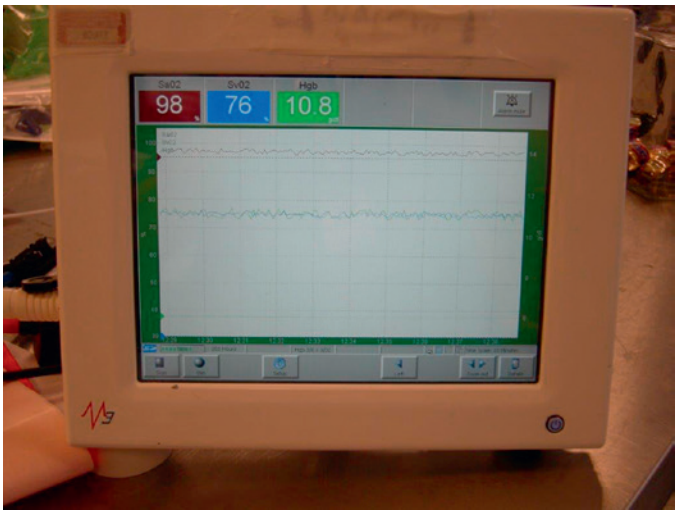


Fig. 51.6 Example of inline oxygen saturation monitoring that can be used to trend the saturation of blood draining into the extracorporeal membrane oxygenation circuit.

Additional blood parameter monitoring can be incorporated into an ECMO system through the integration of a noninvasive optical cable. These devices help trend continuous values such as venous saturations, arterial saturations, hemoglobin, hematocrit, and temperature (Fig. 51.6). They are generally considered optional, although newer consoles have integrated monitoring as standard and the use of each varies from institution to institution (Fig. 51.7).

Unlike some of the optional parameters monitored during ECMO support, monitoring of anticoagulation parameters on a routine basis is essential. The **activated clotting time** (ACT) is most often used as the primary test for anticoagulation at the bedside. The ACT is a low-cost point of care test that gives a quick assessment of anticoagulation. There are several types of devices using a small volume of blood that can determine the number of seconds it takes for blood to clot (Fig. 51.8). It is most often used in conjunction with other parameters to assess the patient's overall state of anticoagulation.

ANTICOAGULATION MANAGEMENT

Anticoagulation of the ECMO patient is a vital part of an ECMO run starting at **cannulation**. The blood's natural reaction is to activate coagulation when exposed to the nonbiologic surfaces of the cannulas and circuit. Therefore anticoagulation is essential prior to cannula insertion and throughout the ECMO course. Heparin, the most commonly used anticoagulant, is easily reversed and widely available. It is prepared from bovine lung or porcine intestines and can be monitored at the bedside. Heparin inhibits the conversion of prothrombin to thrombin and activates antithrombin III (AT III). It does not break up clots, but rather decreases the risk of their forming. A bolus of heparin is administered just prior to cannulation. ACT levels are assessed shortly after to ensure the desired levels of anticoagulation have been achieved. The bolus dose can vary based on the patient's baseline state of coagulation. Once the patient is on ECMO, periodic ACTs help assess the trend in coagulation and assist in fine-tuning the heparin

maintenance doses. The ACT can be affected by many factors including anemia, hypofibrinogenemia, hypothermia, hemodilution, thrombocytopenia, qualitative platelet abnormality, and other coagulation factor deficiencies. Reports in the literature[9] and the anticoagulation guidelines recently published from ELSO[10] suggest that using more than one parameter may be helpful in the assessment of anticoagulation during long-term support. Monitoring of additional parameters on a routine basis and implementing a guideline in response to the combined results may be useful in assessing the overall coagulation/anticoagulation status of patients requiring long-term extracorporeal support.

Fig. 51.7 Extracorporeal membrane oxygenation console with integrated pressure monitoring.

An example of an anticoagulation protocol can be seen in Table 51.3.

Heparin levels (anti Xa) may more accurately assess heparin-induced anticoagulation and are less affected by abnormal physiologic states than are ACT values. ACT levels may better reflect the overall anticoagulation status of the patient, but are not specific for heparin effects versus clotting deficiencies. The two values may be used together to better assess appropriate heparin and blood product needs. A number of studies in ECLS patients have shown a superior correlation of the anti Xa assay

MINI CLINI

Problem

The patient is being maintained on a heparin infusion to achieve the prescribed ACT range of 180–200 s. Over the past 2 h, chest tube output has increased significantly, resulting in a decrease in hemoglobin, requiring multiple blood transfusions.

Discussion

The ECMO specialist recommends lowering the desired ACT range to decrease the amount of bleeding, which can be achieved by lowering the hourly heparin infusion rate and repeating the ACT to assess the change. Vigilance in assessing the circuit for evidence of increased clot formation is essential.

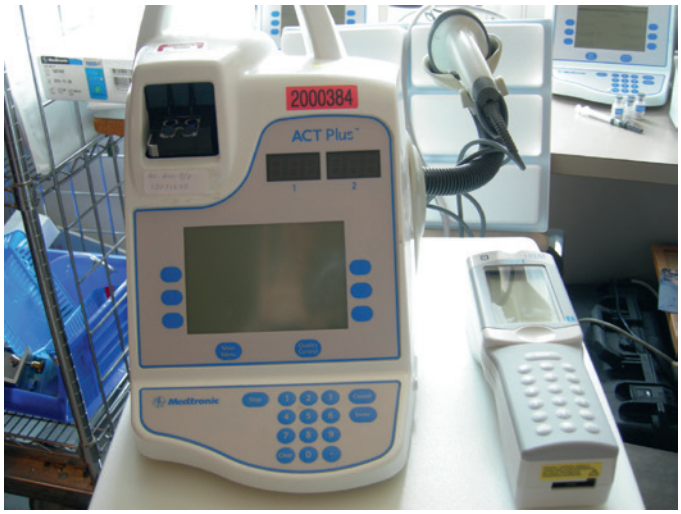


Fig. 51.8 Two types of point-of-care activated clotting time *(ACT)* devices with their cartridges. *Left*, Medtronic ACT Plus. *Right*, Abbott i-STAT ACT monitor.

TABLE 51.3 Example of Anticoagulation Protocol

Laboratory Test	Frequency	Goals	Normal
ACT	Q1 until results in desired range ×2 h, then Q4 while on heparin	As ordered, typically 160–200 (as low as 140 in bleeding patients, 200–240 at pump flows <2 L/min	90–120 s
ATIII	Pre-ECMO baseline Monday, Wednesday, and Friday at 8 AM	Level maintained >40%	40–100%
anti-Xa	Q 24 h at 8 AM	Target levels of 0.3–0.7 IU/mL	N/A
aPTT	Q 24 h	50–80 s	22–35 s
PT	Q 24 h	Normal	11–14
Fibrinogen	Q 24 h	Keep in normal range (250–300 mg/dL)	250–300
Platelets	Q 6 h	>60,000/μL	150–400/μL

ACT, Activated clotting time; *ECMO*, extra corporeal membrane oxygenation; *PT*, prothrombin time.

to heparin dose.[11] The presence of AT III in blood is also essential to achieve the desired levels of anticoagulation. AT III levels may be increased by infusing fresh frozen plasma (FFP), a blood product that contains AT III, or using recombinant AT concentrate, a concentrated form of AT III that is more effective than FFP. However, AT concentrate is significantly more costly, and therefore the cost-benefit ratio is often considered. Thermoelastogram (TEG) is an emerging method of assessing anticoagulation.[10] A small sample of blood is taken from a patient and rotated gently in a specific fashion to imitate sluggish venous flow and activate coagulation. TEG provides comprehensive whole blood hemostasis testing that can help assess bleeding and thrombotic risks, and also monitor antithrombotic therapies. Some more common coagulation values assessed during an ECMO run include prothrombin time (PT) and activated partial thromboplastin time (aPTT). The aPTT may not be as accurate at assessing anticoagulation during ECMO in newborns and small children when heparin is used as the anticoagulant.[12] However, it can be a better assessment of anticoagulation when direct thrombin inhibitors are used to anticoagulate ECMO patients who have a sensitivity to heparin.[13] Patients with sensitivity to heparin, identified by heparin-induced thrombocytopenia, may be managed on ECMO through the use of direct thrombin inhibitors, such as lipirudin and bivalrudin. When using these forms of direct thrombin inhibitors, the accuracy of ACTs is less dependable. Despite diligence with maintaining appropriate levels of anticoagulation, clot formation within the circuit remains a major complication during ECMO.[1]

RULE OF THUMB Patients receiving ECMO support require significant levels of anticoagulation, making bleeding a risk and common complication incurring during ECMO.

CANNULAS

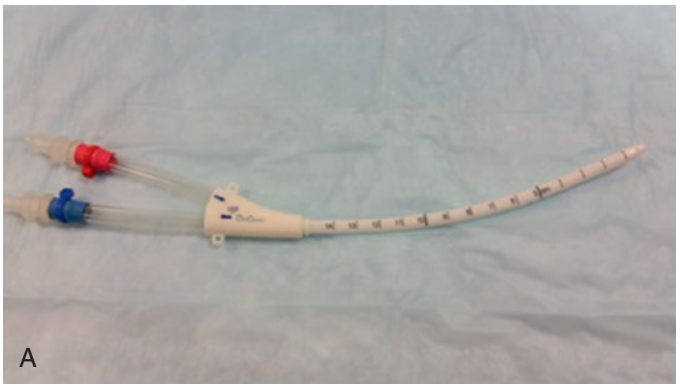
Cannulas are inserted to provide direct access to the patient. Cannula size is crucial to the amount of support an ECMO system can provide; the smaller the internal diameter of a cannula, the higher the resistance of the flow. When placing venous cannulas, the largest possible cannula should be placed to ensure adequate flows. Cannulas are sized by their outer diameter, in French units. All cannulas are tested for their pressure/flow relationship and an M number determined. The M number represents a resistive factor that can be used to approximate the expected flow at a specific pressure difference. Cannulas vary in internal size, length, port placement, size, and number (Table 51.4). This information is important to know during the cannula selection process. Selection of the appropriate cannulas is dependent on the intended insertion sites, age/size of the patient, and the type and amount of support needed. They are designed to be placed through a surgical cut-down, via sternotomy or by percutaneous insertion.

There are two types of venous cannulas: single and double lumen. Venous cannulas have several ports to allow for maximal drainage. Many are wire reinforced to decrease the potential for kinking. Some are coated to avoid an antiinflammatory response and decrease the risk of clot formation. Two types of double-lumen cannulas (DLCs) are available for VV support (Fig. 51.9). Newborn DLCs are inserted into a single vein and allow drainage of desaturated blood and return of oxygenated blood through the same vessel. They have multiple side ports to drain blood. The drainage lumen is typically larger than the return lumen, which allows for better drainage of venous blood. The return lumen has a single outlet and blood is pumped through the cannula by the positive pressure created from the pump's rotation.

The BiCaval DLC is another approach to VV support. It needs to be inserted under fluoroscopy or echocardiography guidance (Fig. 51.10) because appropriate positioning is crucial and can be difficult without imaging. The drainage ports are positioned in both the superior and inferior vena cava with the return lumen positioned at the entry of the right atrium. These DLCs are a single cannula with two lumens, the drainage lumen and the return lumen. Recirculation is expected when using a DLC. **Recirculation** occurs when oxygenated blood from the return

TABLE 51.4 Flow Characteristics of Some Cannulas

Manufacturer	Size (Fr)	Length (cm)	M#	Flow @ 100 cm H_2O
Venous Cannulas (Single Lumen)				
Biomedicus	12	25	3.55	1.5
	14	25	3.35	2
	17	50	3.4	1.9
	19	50	3.15	2.6
	23	50	2.65	5
DLP (Medtronic)	21	53	3.05	3
	28	65	2.5	5.5
RMI (Edwardlife Science Research)	20	52	3	3
	28	52	2.3	8
Venous Cannulas (Double Lumen)				
Origen	12	6	3.9V 4.7A	0.9
	15	8	3.5V 4.3A	1.6
	18	15	3.4V 3.8A	1.9
Jostra	15	3.6V 4.6A	1.4	
Coviden	14	10	3.5V 5.1A	1.6
Avalon		19	20	3.3V 3.8A
	23	29	3.1V 3.4A	2.6
	31	29	2.5V 2.8A	6
Arterial Cannulas				
Biomedicus	8	25	4.4	0.5
	10	25	4	0.9
	15	37	3.3	2.2
	17	37	3.05	3
	19	37	2.8	3.8
DLP (Medtronic)	8	23	4.5	0.4
	14	23	3.3	2.2
	16	23	3	3
	17	17	2.95	3.2
RMI (Edwardlife Science Research)	18	15	3	3
	20	25	3	3
	20	15	2.8	3.8
	22	25	3.1	2.9



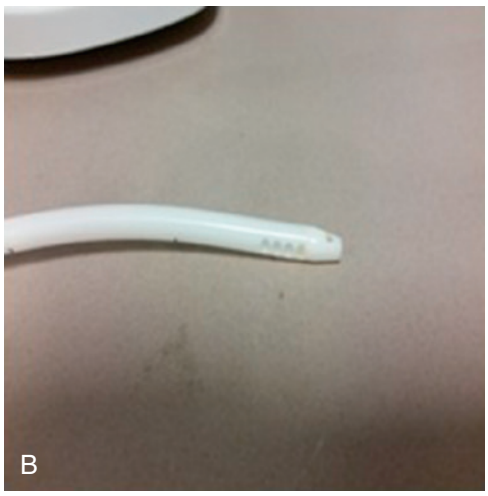


Fig. 51.9 Double-lumen, single-vessel cannulas used for venovenous extracorporeal membrane oxygenation. (A) Ports on one side of the cannula sit in the right atrium and are used to drain blood into the circuit. (B) The end return port is where blood is returned back into the respiratory therapist Atrium and directed toward the tricuspid valve.

lumen is siphoned back into the drainage side of the cannula. This is apparent when both drainage and return lines appear similar in color, with the patient showing signs of oxygen desaturation. Position is critical in a DLC to avoid recirculation. Careful monitoring of the cannula is essential. Excessive recirculation will occur if the cannula is rotated out of optimal position, resulting in inadequate support.

Arterial cannulas typically have a single outlet and they are often wire reinforced and coated. Ideal arterial cannulas should be as short as possible and have thin walls. The size inserted is based on the internal diameter of the artery selected for cannulation. The narrow diameter of the arterial cannula creates the highest amount of resistance in the ECMO circuit. It is the conduit that allows for the return of oxygenated blood back to the patient's circulation (Fig. 51.11).

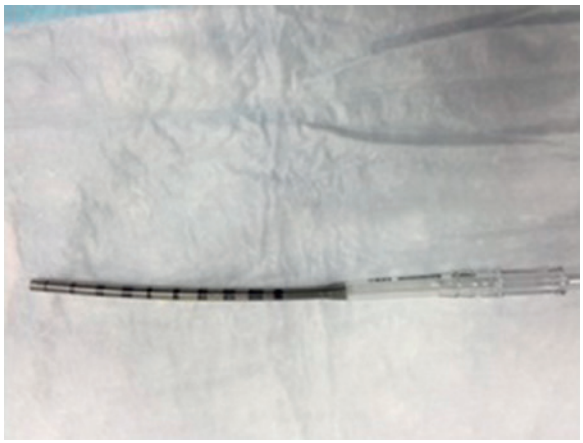


Fig. 51.11 Arterial cannula with a single end port.

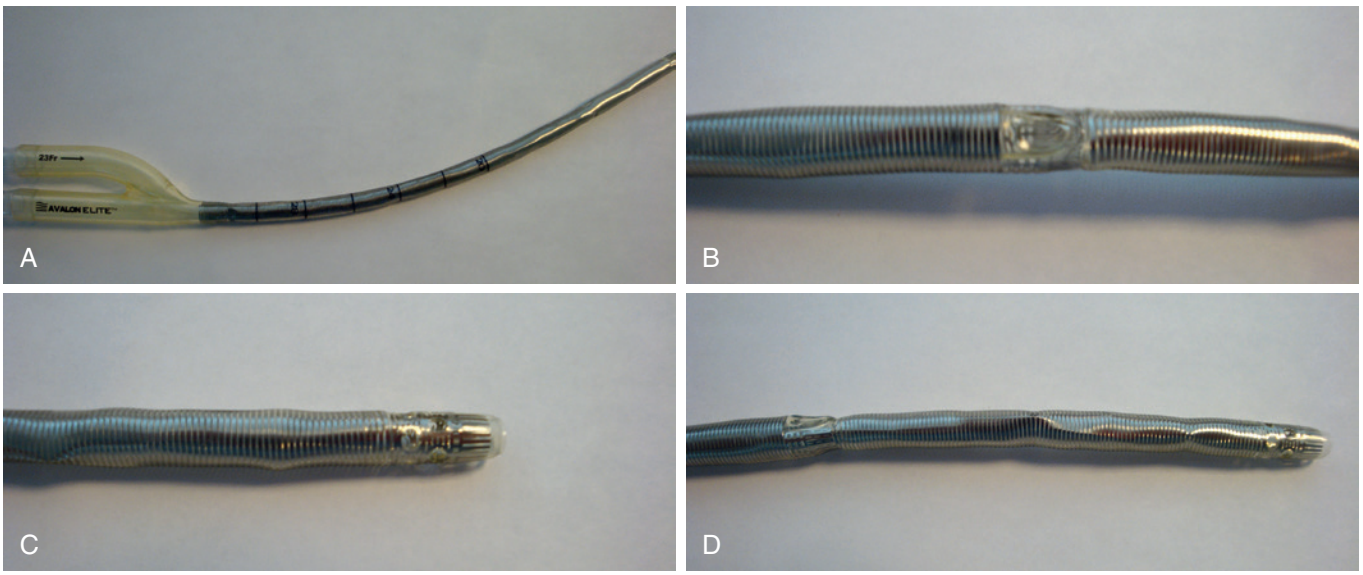


Fig. 51.10 The BiCaval double-lumen cannula is inserted under fluoroscopy or echocardiography guidance. (A) The full bicaval catheter. (B) The return port located across from entrance to right atrium. (C) Inferior vena cava drainage port. (D) Superior vena cava drainage port.

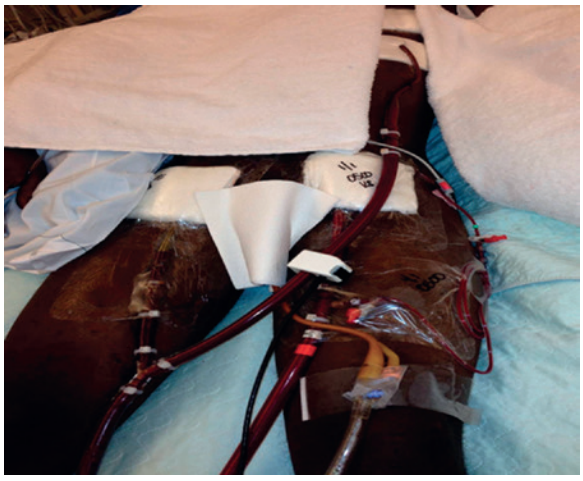


Fig. 51.12 Venoarterial extracorporeal membrane oxygenation with drainage from the right femoral vein and right atrium, with blood being returned to the left femoral artery.

TYPES OF SUPPORT

There are two primary types of ECMO support: VA and VV. VA support is partial cardiopulmonary bypass, providing both cardiac and pulmonary support. The degree of bypass depends on the underlying condition. VV does not bypass the cardiopulmonary circulation and thus only provides pulmonary support. Another emerging type is $ECCO_2R$, which is also referred to as pumpless ECMO. $ECCO_2R$ is primarily for CO_2 removal at low pump flows and requires the patient's own hemodynamics to pump blood through the oxygenator. This type of support is most effective at achieving adequate ventilation when native lung function is significantly impeded.[7]

Hybrid ECMO is also appearing in some institutions and involves extra drainage or return cannulas.

Venoarterial Extracorporeal Membrane Oxygenation

In VA ECMO a portion of the patient's blood volume is drained from the venous circulation to the ECMO circuit where gas exchange occurs (Fig. 51.12). Fully saturated blood is returned through a cannula in the arterial circulation, which results in hemodynamic support. In VA ECMO, a minimum of two cannulas are placed, with at least one in an artery and one in a vein. The cannulas can be placed by means of a surgical cut-down, through a sternotomy or percutaneously. The diameter, length, and position of the cannula will determine the potential flow that can be achieved. The typical artery accessed in the newborn would be the right common carotid artery. In larger patients, placement can be in a left or right femoral artery, axillary artery or placed transthoracically, directly into the aorta. When the femoral artery is cannulated, it is prudent to place a small reperfusion line to supplement blood flow to the lower leg and decrease the risk of limb ischemia (Fig. 51.13). In some patients, only a portion of their cardiac output is pumped through the ECMO circuit while some blood flow continues through the native circulation. The blood from the ECMO circuit returns to the patient, bypassing the heart and lungs, and mixes with the native circulation. The total oxygen content depends on the proportions of blood through the two circulations. Similarly, the measured PCO_2 in the patient's arterial circulation will be a result of the combined relatively low PCO_2 returned from the ECMO circuit and the PCO_2 in the blood coming through the native circulation. The primary advantages of VA ECMO are that it allows the heart to rest and reduces cardiac oxygen consumption while providing adequate systemic organ perfusion with oxygenated blood. There is no chance of recirculation and less ventilator support is needed. VA ECMO is best indicated for cardiogenic shock, or as a bridge to a ventricular assist device or heart transplantation. A disadvantage of VA ECMO is the need to cannulate an artery, which will require repair or ligation when support is no longer needed. See Box 51.4 for differences in VA and VV support.

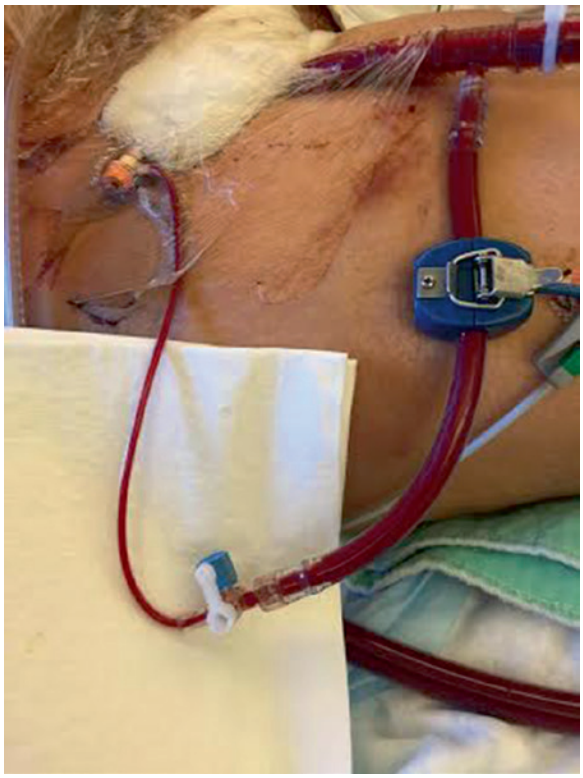


Fig. 51.13 A secondary blood return line (reperfusion line) is placed in this femoral artery cannula to supplement blood flow to the lower limb and prevent limb ischemia.

RULE OF THUMB In VA ECMO, if a femoral artery is cannulated then a distal perfusor should also be placed. Because the arterial cannula occludes much of the blood supply to the lower leg, this reperfusion will help provide blood flow to the leg. They are smaller lines, so flow should be monitored to assess for clots.

Venovenous Extracorporeal Membrane Oxygenation

As in VA ECMO, VV support involves a portion of the patient's blood volume being drained from the venous circulation to the ECMO circuit where gas exchange occurs. However, blood is returned back to the venous circulation either through the same

BOX 51.4 Characteristics of Venoarterial and Venovenous Support

Venoarterial ECMO
- Typically used for patients with cardiovascular failure
- Partial cardiopulmonary bypass
- Decreases preload
- Increases afterload
- Effects hemodynamics

Venovenous ECMO
- Typically used for patients in respiratory failure
- Can be done with multiple cannulas or a DLC
- Provides no hemodynamic support
- RV function may improve with increased S_vO_2

DLC, Double-lumen cannula; *ECMO,* extracorporeal membrane oxygenation.

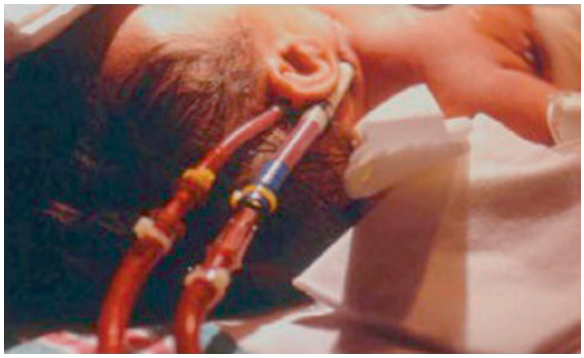


Fig. 51.14 Common cannula used for venovenous extracorporeal membrane oxygenation (VV ECMO) support in newborns. Babies are often cannulated with a double-lumen cannula through the right internal jugular for VV ECMO.

cannula via the return lumen or via a separate cannula into another vein (Fig. 51.14). The typical cannulation site for the newborn is in the right internal jugular vein. In larger patients, common sites are the right and left femoral veins, right internal jugular vein, pulmonary artery, or right atrium. Pulmonary artery and right atrium cannulations involve cannula placement via hemisternotomy or open chest surgery. Unlike VA ECMO, blood is returned to the venous circulation, therefore providing no direct cardiac support. Oxygenated blood that is lower in CO_2 returns to the venous circulation and mixes with the remaining cardiac output. The total oxygen content and measured CO_2 is a result of this mix and can be affected by the patient's mechanical ventilation settings or spontaneous minute ventilation. Two distinct advantages of VV ECMO are lower risk of cerebral air embolism and no need to ligate or repair an artery. VV ECMO is often indicated for patients with acute respiratory failure due to viral or bacterial pneumonias.[14] VV is emerging as a bridge to lung transplant.[15] ECMO in the pre–lung transplant patient allows for improved gas exchange and decreases the risk of complications from high levels of mechanical ventilation. It can also prevent further deconditioning. The patient on VV ECMO can be extubated, awake, and ambulated while waiting for available lungs.[16]

RULE OF THUMB VA ECMO is primarily used to support patients with cardiac failure. VV ECMO is used primarily to support patients with respiratory failure.

Extracorporeal Carbon Dioxide Removal

The primary goal of $ECCO_2R$ is the removal of carbon dioxide as opposed to the delivery of oxygen. This can be achieved using veno-venous support, which requires the additional use of a centrifugal pump to move the blood, or by using arterio-venous support. Arterio-venous support relies on the patient's native cardiac output to move the blood from the high (arterial pressure) system to the low (venous pressure) system, therefore eliminating the need for a centrifugal pump. There are advantages and disadvantages to both types of support. In veno-venous $ECCO_2R$, the use of a centrifugal pump generates negative pressure, which is both harmful to blood elements as well as a risk for entraining air. However, this type of support usually allows for single-site access, which allows the patient to ambulate and decreases the risk of infection from additional vessels being accessed. In arterio-venous support, the centrifugal pump is eliminated and the harmful effects on blood elements as well as risk of air is also eliminated. The disadvantage of arterio-venous support lies in the access of a major artery, which significantly increases the risk of bleeding and makes ambulation more difficult because a minimum of two vessels must be accessed.

Extracorporeal carbon dioxide removal has shown some limited benefit in patient populations of acute respiratory distress syndrome and acute-on-chronic lung disease. In the group of acute respiratory distress syndrome, the limitations of providing low tidal volume ventilation is the inability to eliminate carbon dioxide and improve the accompanying acidemia. $ECCO_2R$ may be able to provide a solution to this problem by clearing carbon dioxide and allowing for lower tidal volume ventilation as well as lower plateau pressures, both of which have been shown to improve survival. Currently, the REST-trial is undergoing enrollment in the United Kingdom to see whether lower tidal volume ventilation in combination with $ECCO_2R$ improves mortality in patients with hypoxemic respiratory failure.[17] The other patient population where $ECCO_2R$ may be considered is in patients with primary hypercapnic respiratory failure, such as chronic obstructive pulmonary disease (COPD) and asthma. This may be the most appealing patient population in its ability to avoid both noninvasive and invasive mechanical ventilation, thus avoiding the many complications that come with both. The VENT-AVOID trial is currently enrolling patients with COPD to see if there is a reduction in ventilator days by using $ECCO_2R$.[18]

Extracorporeal carbon dioxide removal is far more efficient than oxygenation, and therefore lower blood flow rates can adequately support the patient. This has some advantages as well as disadvantages. The major advantage is that the lower blood flow can allow for smaller tubing and cannulas, which allows for easier mobility of the patient as well as a smaller area for blood to come into contact with. The disadvantage of the lower blood flow rate is that it has a higher risk of forming clots in the circuit, and therefore anticoagulation may need to be

higher than in the other forms of extracorporeal support. This will then increase the risk of bleeding for the patient. Another limitation of $ECCO_2R$ is the patient population itself. Patients that have end-stage lung disease may be unable to be weaned from the circuit and discontinuing care may become difficult because most patients are awake and interactive.

Hybrid Extracorporeal Membrane Oxygenation

The use of additional drainage or return cannulas may be necessary, depending on the patient condition. Flow may be insufficient for patients with small venous drainage cannula and an additional drainage cannula may be added for increased support. If a patient is on VA ECMO and an additional drainage cannula is added, the abbreviation will be documented as VV-A. Another common type of hybrid ECMO is for patients who are cannulated in their femoral vein and artery for cardiac support. If those patients have respiratory failure in combination with their primary cardiac failure and their heart recovers before their lungs, deoxygenated blood will be ejected from their left ventricle to their brain causing cerebral hypoxia. If ventilator management cannot be optimized to correct this hypoxia, an additional return cannula can be added to their central venous system. This will provide both partial respiratory and cardiac support. The patient is supported from a respiratory standpoint by delivering fully saturated blood to the right atrium and increasing mixed venous oxygen saturation. The cardiac system also still receives a level of support by decreasing preload to a recovering heart. The abbreviation for this partial veno-venous and veno-arterial support will be V-AV. The letter to the left of the hyphen will always refer to the drainage cannula and the letter to the right of the hyphen will always refer to the return cannula. The above two descriptions are just a small example of ways to support an ECMO patient. Limitations to hybrid ECMO are based on accessible vessels as well as the experience of the surgeon.

RULE OF THUMB $ECCO_2R$ is used to treat primary hypercapnic respiratory failure without hypoxemia.

INITIATION OF SUPPORT

ECMO is frequently initiated in the intensive care unit (ICU). Specific circumstances may dictate ECMO being initiated in the operating room, cardiac catheterization lab, emergency room or many other locations in the hospital. A formal activation guideline should be established so that access to the ECMO team and equipment can be rapidly deployed.

Cannulas are inserted in the appropriate vessels and then attached to an ECMO circuit. The circuit is assembled using sterile technique, de-aired, and crystalloid primed. Newborn circuits are often primed with blood to decrease the hemodilution effect that can be encountered with a crystalloid primed circuit. The circuit is attached to the cannulas and ECMO support begins. Pump flows are adjusted according to the type of support the patient is receiving and vary based on the underlying diagnosis. Patients needing cardiac support (VA) will often need a large portion of their cardiac output supported while patients on VV support may be maintained on a relatively lower amount of pump flow. As the pump flow increases, a larger portion of the patient's desaturated blood flows through the oxygenator and returns to the patient fully saturated. Box 51.5 shows sample target pump flows for different age groups. Once pump flow is at the desired level, alarms should be set appropriately to alert the ECMO specialist of any acute changes in pump support. Sweep flow is attached to the oxygenator and adjusted based on guidelines to achieve target CO_2.

BOX 51.5 Target Pump Flows for Age Groups

- Infants: 120–150 mL/kg/min
- Children: 100–120 mL/kg/min
- Adults: 70–80 mL/kg/min
- Attempt to reach maximal flow early in run to determine buffer

RULE OF THUMB The ratio of sweep flow to pump flow is often 1:1. When using 4 L/min pump flow, typically the sweep flow would be initiated at 4 L/min.

Consideration of adjustments in ventilator support is necessary to avoid hyper- and hypoventilation. Patients' ventilator settings can gradually be weaned to "rest settings" as the sweep flow is increased. Rest settings are intended to minimize lung trauma while avoiding atelectasis. Typically, the FiO_2 from the ventilator can be reduced to 0.4 to 0.6. The goal for some long-term patients (i.e., pre–lung transplant) is often extubation to allow for activities of daily living to be maintained in conjunction with physical therapy and ambulation while on ECMO support. Circuit temperature is adjusted to maintain patients at the intended body temperature. A chest x-ray (CXR) is done to assess cannula placement. Serial blood gases and chemistries are obtained to ensure patient laboratory values are within acceptable ranges. Pump flow, sweep flow, and medications can be adjusted as needed. Blood products are transfused to maintain desired parameters. Baseline anticoagulation levels are obtained and a heparin infusion initiated at the dose necessary to achieve adequate anticoagulation. Sedation levels are adjusted to the appropriate level that will allow intermittent or continuous assessment of neurologic status. Levels of analgesia are provided as needed or as pain scores indicate. Emergency preparedness is an essential component of an ECMO start. Procedures to handle any complications during initiations should be developed for every ECMO center. Backup circuit components should be in a nearby location along with an alternative means to support the patient in the event of pump hardware failure.

MAINTENANCE OF AN EXTRACORPOREAL MEMBRANE OXYGENATION RUN

ECMO runs can be expected to last from a few days to as long as several months. An established flow sheet to document key variables should record the trends in specific parameters.

Monitoring the changes in these parameters allows the ECMO specialist to better assess a patient's progress, identify goals on a daily basis, and coordinate the best approach during the patient's course on ECMO (Box 51.6). Daily, the patient will receive a CXR to reaffirm cannula position and lung status. Periodic arterial blood gases are obtained as well as ACTs and other labs run at appropriate intervals to ensure values are maintained within the desired range. Interdisciplinary team rounds occur at the bedside daily. Every discipline should be encouraged to contribute their perspective and together a well-defined strategy is formed. It is at these rounds that clear patient goals can be identified and a plan of care is established for the day. In addition to patient trends, documentation should also be maintained on various aspects of the active ECMO system (Box 51.7). Frequent circuit assessments, from the drainage cannula through the entire system and back to the return cannula, are essential. Specialists must be mindful of the many risks and potential complications associated with extracorporeal support. Diligence with frequent inspections and evaluation of components as well as ensuring the proper backup equipment should be part of the daily task of an ECMO specialist.

Certain categories of ECMO patients may require procedures unique to their condition. Open chest cardiac patients might need to travel to the operating room (OR) for a chest washout

BOX 51.6 Extracorporeal Membrane Oxygenation Flow Sheet for Monitoring Trends in Flows, Pressures, Hemodynamics, and Pertinent Lab Values

	Date													
	Time													
	Heart rate (beats/minute)													
	Arterial pressure Sys/dia (mm Hg)													
	Mean arterial pressure (mm Hg)													
	PA pressure Sys/dia (mm Hg)													
	Mean PA pressure (mm Hg)													
	Central venous pressure (mm Hg)													
	Respiratory rate (breaths/min)													
	FiO_2/flow													
	SPO_2 (%)													
	SvO_2 (%)													
	PO_2/Hb													
	PCO_2/pH													
	ECLS flow L/min													
	RPM													
	Sweep flow L/min													
	Sweep blender $\%O_2$													
	Color change													
	Oxygenator press Pre/post (mm Hg)													
	Pre/post pressure differential (mm Hg)													
	Venous drain pressure (mm Hg)													
	Water bath temp (°C) set/measured													
	Heparin infusion (units/h)													
	Activated clotting time (ACT) sec													
	Initials													

ACT Range _____	MAP _____	SPO_2 _____	□Alarms appropriate, check Q shift +initial _____

Cannulation Date/Time	**Date Current Oxygenator Initiated**	**ECLS Type: _____ VA _____ VV**
		List cannula type, size, and site:
Signature:	Signature:	
Signature:	Signature:	

ACT, Activated clotting time; *ECLS*, extracorporeal life support; *MAT*, mean arterial pressure; *RPM*, rate per minute.

BOX 51.7 Safety Shift Checklist to Verify Availability of Appropriate Alarms and Backup Equipment

Rotaflow Shift Check List (Complete during the First Hour of Each Shift)										
Date	Time	Mode	Cream tube on Rotaflow	External drive ready for use	Back up equipment available	Change out kit	ACT cartridges exp date?	Dash alarms appropriate H/L	Initials	Comments

ACT, Activated clotting time.

or explorations to stop bleeding and, depending on the urgency, some surgical procedures may have to be done at the bedside. Bedside echocardiograms are done to assess any changes in cardiac function and sometimes to rule out **tamponade**. Cardiac catherization lab visits may also be necessary for procedures required during the ECMO run. Bronchoscopies and bronchial lavages are a little more common in patients being supported for respiratory failure. As with any ICU run, there is a potential need to travel to computed tomography (CT) scan or interventional radiology for diagnostic testing.

RULE OF THUMB During an ECMO run, vent settings should be lowered considerably to allow the lungs to recover. As the CXR improves, vent settings should be increased to evaluate if the patient might be ready to wean.

TRANSPORTING A PATIENT ON EXTRACORPOREAL MEMBRANE OXYGENATION

Most ECMO systems are designed for intrahospital transport. However, detailed guidelines should be followed when preparing for transport. These should include a fully charged battery, adequate gas supply, transport ventilator, cardiac monitors, and defibrillator. A travel kit is advisable that includes connectors, clamps, additional medications, IV fluid, and other items that might be needed on route or at the destination. Provisions for temperature control may be necessary because the blood warmer/cooler may not be supported during the transport. Travelling on ECMO carries significant risks, and teamwork is essential to successful travel. Roles should be established prior to moving. It is wise to minimize the time of the transport by clearing hallways in advance and gaining easy access to elevators. During the transport, constant assessment of the patient along with battery charge level, gas supply, and close monitoring of the circuit should be practiced. When the destination is reached, close attention to detail should be made and reestablishment of piped gas and AC power obtained as soon as possible. Intrahospital transport includes elective patient ambulation in the ICU.

Preparing a patient to ambulate on ECMO takes collaboration among all services involved (Box 51.8). An agreement must be made on destination and maximum duration of time out of the patient's room. Roles of all providers should be clear. All necessary

BOX 51.8 Guidelines for Ambulating With Patients on Venovenous Extracorporeal Membrane Oxygenation (Central-Peripheral)

I. Patient Assessment:
  a. Patient is able to participate in care
  b. Patient is able to be safely directed
  c. Demonstrates stability on ECMO
    1. Consider the following parameters
    2. Discuss with medical team if falls outside criteria

II. Prepare for Ambulation:

Hematologic	ECMO	General Considerations
No sign of bleeding over 12 h	Stability of flow, speed and sweep for 6 h	Airway clearance
Plts >50	Cannulas: sites have been stable—no migration or bleeding	Afebrile
Hgb ≥8–9		Tolerated HOB up, dangling, OOB to chair
ACT at goal		

  a. Obtain MD order for ambulation after assessment by RN, PT, RT
  b. Ensure ECMO cannulas, airway and all other lines are secured
  c. Equipment checklist:
    1. Full O_2 tank
    2. Clamps
    3. Portable SpO_2 monitor
    4. Wheelchair/recliner
    5. ECMO emergency equipment
    6. Assess battery life for all equipment
  d. Contingency plan:
    1. Identify red plug outlets
    2. Identify location of backup circuit
  e. Team discussion prior to take off to include destination & roles
    1. RN: IVs, tubing, chest tubes
    2. RT: ECMO pump/cannula (circuit), monitor flow/speed, airway
    3. PT: manages patient mobility
    4. A minimum of three staff must be present during ambulation
    5. *Each discipline to monitor hemodynamic parameters and alert team members if significant changes noted
  f. Ensure hallways are clear of obstruction
  g. Limit ambulation to within the ICU

III. Ambulate

IV. Documentation Per Each Discipline's Standards

ECMO, Extracorporeal membrane oxygenation; *HOB*, head of bed; *ICU*, intensive care unit; *MD*, physician; *OOB*, out of bed; *PT*, prothrombin time; *RN*, nurse; *RT*, respiratory therapist.

MINI CLINI

Problem

A patient in the Cardiac Care Unit coded suddenly and was placed on VA ECMO. The patient is now somewhat stabilized on ECMO but needs to travel to the Cardiac Cath Lab as soon as possible to investigate and hopefully treat the cause of the arrest. He is on a pump flow of 5l pm and sweep flow of 4l pm. He is on multiple blood pressure medications. Who should travel with this patient besides the ECMO Specialist? What other considerations should be brought to the team's attention?

Discussion

Every effort should be made to support this patient in the event an arrest reoccurs. The ECMO Specialist will be focused on the equipment that moves along with the patient. There should be a doctor from the Surgical Team available in case any cannulas are dislodged. A nurse or anesthesiologist should also be available to handle the medication pumps and help monitor the vital signs. Team members should all agree that the patient is able to travel. A dry run to the destination should be made to clear any obstacles. Back-up equipment should be brought to the Cath Lab in case of any circuit failures.

BOX 51.9 Common Complications

Mechanical Complications

- Pump failure
- Tubing rupture
- Cannula problems
- Oxygenator failure

Physiologic Complications

- Seizures
- Hemolysis
- Renal failure
- Bleeding; intracranial, surgical site
- Neurologic complications
- Arrhythmias
- Pneumothorax

equipment should be identified and checked for function prior to beginning ambulation. There should be specific reasons to abort the exercise such as tachycardia, desaturation, patient fatigue or concerns for equipment or patient safety.

RISKS AND COMPLICATIONS

ECMO poses significant risks. The complications can be classified as mechanical as a result of equipment failure or patient from clinical issues. Box 51.9 outlines ECMO complications.[1] ECMO specialists are clinicians specifically trained in all aspects of ECMO. It is essential that the ECMO specialist have a thorough understanding of ECMO physiology and ECMO patient management. These individuals must have critical thinking skills and be technically adept at assessing all components of the ECMO circuit. Monitoring and frequent inspection of the circuit and evaluating circuit functions are among the primary roles of the ECMO specialist. The risk of the many complications inherent in providing ECMO support diminishes with diligence by the specialist.

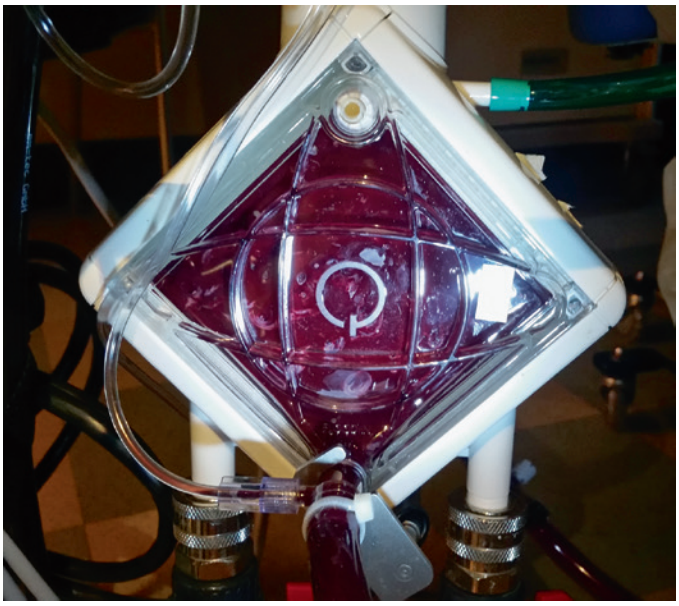


Fig. 51.15 Oxygenator with significant clot accumulation.

The most common mechanical complication during ECMO is clot formation.[1] Clots can occur anywhere in the circuit but more frequently occur in the oxygenator, at connectors, in the circuit bladder or any place with relatively low flow. Clots can result in increased resistance and may impede flow, limiting support of the patient. Clot formation within the fibers of the oxygenator will reduce gas exchange and, if significant, may require the oxygenator to be replaced (Fig. 51.15). Inadvertent **decannulation** and pump failure are other significant complications that can cause circuit interruption and require immediate attention. These conditions might result in the need for an entire circuit to be replaced. Replacement of oxygenators or circuits requires the patient to be briefly removed from support. Practitioners trained in this procedure need to maintain competency to efficiently change out the oxygenator or circuit in the least amount of time to minimize patient decompensation from interruption of support. Proper coordination with the team caring for the patient is essential during this loss of support.

Air in the circuit is a major risk during ECMO. Despite the ECMO system being a closed system, air emboli can occur when air is entrained into the system. This can occur inadvertently through cavitation—air being pulled out of a solution due to increased negative pressure—if venous return is inadequate. It can occur from drainage ports of a cannula migrating out of a vessel or from access lines, such as through the CVVH port, infusion lines or other monitoring lines. The presence of air in the circuit, if not redirected or withdrawn, may enter the patient's circulation. In VA ECMO this is particularly life threatening because air will not be filtered through the pulmonary circulation as it is in VV ECMO. As with most mechanical complications, prevention is vital.

Bleeding is a common risk of ECMO due to anticoagulation and the multiple surgical sites where bleeding can easily occur. Bleeding in the chest can lead to the complication of cardiac tamponade, an emergency needing immediate intervention,

without which the patient will not likely survive. Cannula placement in the awake and active patient on ECMO can also contribute to the occurrence of tamponade. Loss of pump flow, hemodynamic changes with a narrowing of pulse pressure, arrhythmias, and decreases in hemoglobin and hematocrit levels are symptomatic of tamponade. Bleeding from any source resulting in low pump flow causes risks not only to the patient but to the circuit as well. Lower flows result in higher potential for clot formation in a circuit. The drop in hemoglobin is also a major concern because the oxygen-carrying capacity is greatly reduced. Bleeding can occur from any surgical site, including cannula sites, chest tubes or IVs. Bleeding becomes a risk with any venopuncture, NG or OG tube placement, rectal tube placement, suctioning or anything that might cause mild trauma to the tissues. Internally, intracranial hemorrhage, GI and pulmonary bleeding are also bleeding risks associated with ECMO.

RULE OF THUMB A set up primed circuit and/or backup ECMO equipment should be kept easily accessible to the patient on an ECMO run in case any circuit complications that require a component or full circuit change.

BLOOD PRODUCTS DURING EXTRACORPOREAL MEMBRANE OXYGENATION

The most common blood product used during an ECMO run is packed red blood cells (PRBCs). PRBCs are transfused to maintain adequate levels of hemoglobin to ensure adequate oxygen carrying capacity. Typically, hemoglobin is maintained at approximately 8 to 10 g/dL. Platelets, FFP, and cryoprecipitate are often used to target specific clotting factors. Protocols identify when transfusion of each individual product is indicated. Albumin may also be used intermittently throughout the run for volume expansion.

WEANING AND DECANNULATION

Daily assessments for the possibility of weaning should be made first by considering why the patient was initially placed on ECMO and whether or not the problem has been resolved. Other questions to consider are if additional issues have been identified that either indicate the necessity to continue support or identify the need to discontinue support. Throughout the run, the team must consider if the risks of ECMO outweigh the benefits. The process of weaning off ECMO is different in VA support than in VV support. During VA weaning, the function of the heart must be assessed as increased blood flow is redirected to the native circulation. This evaluation is often accomplished via cardiac ultrasound while pump flow is decreased. At the same time, hemodynamic stability, right ventricule, left ventricule (RV, LV) function, and the degree of pulmonary hypertension should be evaluated. Ventilator support may need to be adjusted as pump flows are decreased, particularly ventilator FiO_2 to supplement the decrease in pump flow. At this time, the risk of clots developing in the circuit at the low flow states is present. Therefore the duration of the wean should be limited to no more than an hour, with close attention to anticoagulation.

MINI CLINI

Problem

A patient is cannulated for VV ECMO due to acute lung injury secondary to H1N1 flu. The patient initially required a pump flow of 4 L/min and sweep of 10 L/min to achieve the desired gas exchange. After 5 days on resting ventilator settings, an improvement in both CXR and lung compliance is noted. Additionally, PaO_2 with the ventilator FiO_2 at 1.0 is markedly improved: on day 1 it had been 50 mm Hg and after 5 days is now 220 mm Hg. What changes should be made to assess the patient's readiness to wean off of VV support?

Discussion

Gradually decreasing the sweep flow will allow assessment of the patient's native lung's ability to effectively ventilate. Simultaneously, ventilator adjustments should be made to support the transition when ECMO is discontinued. The patient is ready to be decannulated when gas exchange can be maintained without sweep flow and ventilator settings that will not induce any further lung injury (i.e., plateau pressures less than 28 and FiO_2 less than 0.6).

For the patient who requires VA ECMO for both cardiac and pulmonary support, there is the option to convert to VV ECMO if the heart function recovers before adequate lung function is achieved. The patient can be supported on VV ECMO until there is further evidence of lung improvement. Patients on VV ECMO must demonstrate improvement in their pulmonary status before weaning can be considered. This includes an increase in lung compliance, improved aeration on CXR, and the ability for effective gas exchange on conventional ventilator settings that are not likely to produce lung injury. A test to evaluate the native lung's ability to oxygenate can be achieved while maintaining the same ECMO support and obtaining an arterial blood gas with the ventilator FiO_2 at 1.0. A daily assessment using this "100% gas" can demonstrate the improvement in oxygenation. Early stages of support will not reveal much change, but as the lungs improve then significant increases in the PaO_2 will be obvious. The process of weaning off VV ECMO involves maintaining pump flow and weaning sweep flow to assess the native lung's ability to remove CO_2. Adjustments in ventilator support to accommodate the decrease in sweep flow should be made at this time. Once there is an improvement in ventilation evidenced by reasonable levels of PCO_2 on moderate ventilator settings with an improvement in the 100% oxygen gas, the sweep flow can be removed. The pump flow continues while a period of assessment off ECMO occurs to determine if the patient is ready for decannulation, with the decannulation approach determined by the cannulation sites. Percutaneously inserted cannulas may be simply withdrawn at the bedside if vascular repair is not anticipated. If surgical repair or reconstruction of the vessel is required or if the patient is centrally cannulated, decannulation will typically take place in the operating room. Post-decannulation anticoagulation is most often discontinued or adjusted to desired levels.

RULE OF THUMB Weaning from VA support is accomplished by turning down the pump flow and assessing hemodynamics. Weaning from VV support is accomplished by turning down the sweep flow and assessing gas exchange.

SUMMARY CHECKLIST

- ECMO is an option for newborn, pediatric, and adult patients with severe cardiac or respiratory failure who meet the criteria outlined in Boxes 51.2 and 51.3 and who otherwise have no absolute contraindications.
- The primary goals of ECMO are to deliver adequate amounts of oxygen, remove carbon dioxide, and, in cases of VA ECMO, provide hemodynamic support. ECMO physiology mimics native cardiopulmonary physiology in that it allows oxygen to diffuse into the blood and carbon dioxide to be removed. This is accomplished through a circuit that contains a pump and an artificial oxygenator.
- The patient is cannulated with either a double-lumen cannula or multiple single-lumen cannulas.
- During VV support, cannulas are usually placed in the right internal jugular vein, right atrium, and left or right femoral veins. In VA support, the venous cannulas are placed in the same locations as with VV support, with the arterial cannula inserted into the aorta or either femoral artery.
- Blood is either drained or siphoned into the pump, which propels it forward into an oxygenator. The oxygenator provides gas exchange before returning the blood to the patient containing hemoglobin that is fully saturated and has the desired carbon dioxide level.
- A blood warmer/cooler keeps the blood at the desired temperature and additional monitors provide clinicians with valuable information regarding circuit pressures, flows, and additional lab values. Several of the monitors can be set to sound audible alarms when the values of certain parameters are outside of the acceptable range.
- Additional safety components can be added to the ECMO system for additional blood parameter monitoring such as venous and arterial saturations, hemoglobin and hematocrit.
- The circuit and cannulas are made of materials foreign to blood. These surfaces will cause the normal activation of blood clotting reactions. Anticoagulation is necessary to decrease the risk of clots in the circuit, cannulas, and, most importantly, in the patient.
- Bedside coagulation testing is typically performed at regular intervals to keep a close watch on the level of anticoagulation, along with frequent inspection for clot development in any of the circuit components.
- A major advantage of ECMO is that ventilator support can be decreased once ECMO is initiated, thus reducing the potential of ventilator-induced lung injury. At times the ventilator can even be discontinued, reducing the potential of ventilator-associated pneumonia and allowing the patient to more actively participate in activities of daily living. This is of particular importance in the pre-transplant patient.
- As technology advances and proper candidate selection is achieved, ECMO is certain to be more frequently utilized in ICU management of the critically ill patient.
- Ambulating and/or intrahospital transports on ECMO are more common occurrences made possible by portable equipment, proper planning and team effort.

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52

Monitoring the Patient in the Intensive Care Unit

Thomas Piraino

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Discuss the principles of monitoring the respiratory system, cardiovascular system, neurologic status, renal function, liver function, and nutritional status of patients in intensive care.
- Explain why the caregiver is the most important monitor in the intensive care unit (ICU).
- Describe various measures of patient oxygenation in the ICU.
- Explain why the partial pressure of carbon dioxide ($PaCO_2$) is the best index of ventilation for critically ill patients.
- Describe the approach used to evaluate changes in respiratory rate, tidal volume, minute ventilation, $PaCO_2$, and end-tidal pressure of carbon dioxide values for monitoring purposes.
- Identify monitoring techniques used in the ICU to evaluate lung and chest wall mechanics, auto–positive end-expiratory pressure, work of breathing, and respiratory drive.
- Describe the importance of measuring transpulmonary pressure in select patients.
- Discuss the importance of monitoring peak, plateau, and driving pressures in patients receiving mechanical ventilatory support.
- Identify monitoring techniques that have become available more recently, such as lung stress and strain, functional residual capacity, stress index, electrical impedance tomography, and lung ultrasound.
- Describe the approach used to interpret the results of ventilator graphics monitoring.
- Describe the cardiovascular monitoring techniques used in the care of critically ill patients and how to interpret the results of hemodynamic monitoring.
- Discuss the evaluation of renal function, liver function, and nutritional status in the ICU.
- List and discuss the use of composite and global scores to measure patient status in the intensive care unit, such as the acute physiology, age, chronic health evaluation system for scoring the severity of illness.
- Discuss the importance of monitoring neurologic status in the ICU and the variables that should be monitored.
- Discuss monitoring and troubleshooting of the patient-ventilator system in the ICU.

CHAPTER OUTLINE

KEY TERMS

afterload
alveolar and arterial oxygen tension difference
APACHE scoring system
artifacts
bladder pressure
capnography
capnometry
cardiac output
contractility
dead space/tidal volume ratio
diaphragm ultrasound
driving pressure
electrical impedance tomography
esophageal balloon
factitious events
Fick's principle
frequency/tidal volume ratio
Glasgow Coma Scale
lung stress and strain
lung ultrasonography
maximal inspiratory pressure
maximum voluntary ventilation
mean airway pressure
Murray lung injury score
oxygen consumption ($\dot{V}O_2$)
preload
pressure-time product
respiratory inductive plethysmography
stress index
Swan-Ganz catheter
transpulmonary pressure
venous admixture
vital capacity

When patients are admitted to the intensive care unit (ICU), it is generally for the purpose of providing diagnostic and therapeutic interventions that require continuous or periodic monitoring of physiologic parameters. ICU patients often require multiple medications, fluids, and nutrition, as well as noninvasive or invasive ventilatory support for respiratory failure. The monitoring of these patients is essential to assess the effectiveness of treatment in the ICU and to minimize, limit, or prevent adverse events.

Although diagnostic procedures such as radiographic imaging can be used to monitor the progression of disease over time, this chapter focuses on the periodic and/or continuous monitoring of the respiratory system, cardiovascular system, renal function, liver function, nutritional status, and neurologic function of patients in the ICU.

PRINCIPLES OF MONITORING

The best monitoring options provide detailed, easily interpreted data, obtained noninvasively or minimally invasively with the fewest hazards and side effects. A monitoring tool that is highly invasive and carries a certain level of risk with use must provide a high level of valuable and required information to make the benefit of using it outweigh the risk.

New advancements in technology aim to make monitoring less invasive and at the same time provide the most clinically relevant data. The data provided should be accurate (reflect the true value) and precise (not vary widely when repeated). When monitoring involves images, graphs, or waveforms, the data must be easily distinguishable from **artifacts**, **factitious events**, or normal variation and still require an understanding of the overall status of the patient to understand their significance.

The best monitor in the ICU is the caregiver who understands how to use and interpret the various monitoring tools and techniques available to him or her. However, observing a monitor while ignoring the patient does not take into consideration the patient's global status. We must combine the "seen" with the "unseen" to truly understand the patient (Box 52.1).

BOX 52.1 Monitors and Monitoring Data

- Monitored values can exhibit physiologic and instrument variability.
- Monitoring devices can be noninvasive or invasive.
- Alarm systems should be set to alert caregivers properly yet avoid false alarms.
- Monitors can run continuously and measure what caregivers cannot see.
- The best monitors are caregivers who can assess and make decisions based on understanding the patient's global status.

BOX 52.2 Values Affecting Pulse Oximetry

- Motion artifact
- Environmental light (e.g., sunlight, fluorescence)
- Anemia
- Deeply pigmented skin
- Carboxyhemoglobin, methemoglobin
- Nail polish
- Blood-borne dyes

RULE OF THUMB The caregiver must understand and interpret the information provided through monitoring. The key to the proper interpretation of information is understanding how it applies to the global status of the individual patient.

HISTORY

Obtaining a history from a critically ill patient—in particular a patient with altered state of consciousness—can be difficult. However, attempting to obtain a history by speaking with the patient or family members can provide extremely useful information in the ICU. Information regarding the patient's past medical history, psychologic status, habits of smoking and alcohol use, and physical abilities is important, especially considering some of the challenges that may arise in the course of care in ICU. In particular, it is important to know how a patient's baseline state may affect the normal ranges of monitored values or the ability to be weaned quickly from mechanical ventilation.

PATHOPHYSIOLOGY AND MONITORING

The problem often faced at the bedside when one is presented with monitoring data is that clinicians may begin treating the numbers rather than the underlying pathophysiology. For example, when a patient is mechanically ventilated and the peripheral capillary oxygen saturation (SpO_2) level drops, the first step is to quickly determine whether the SpO_2 reading seems correct by confirming a good waveform or correlation with clinical findings such as the patient's appearance and objective measures such as the heart rate. If a drop in SpO_2 seems real, the respiratory therapist (RT) may recommend increasing the fraction of inspired oxygen (FiO_2) or adjusting the positive end-expiratory pressure (PEEP) in cases of refractory hypoxemia when there has been no response to moderate or high FiO_2. Treating the patient rather than the number requires the clinician to consider first if the readings seem accurate and then to address the underlying cause (Box 52.2).

RULE OF THUMB Treating the patient rather than the number requires the clinician to consider first whether the readings seem accurate and then to address the underlying cause.

The function of the lungs is the uptake of oxygen and the removal of carbon dioxide (see Chapter 12). The arterial blood gas (ABG) gives valuable information regarding the effectiveness of the gas exchange (discussed in Chapter 19). Although ABGs can be drawn at the bedside, they usually require processing outside of the patient's room, either at a point-of-care machine or by the hospital laboratory. The most common bedside monitoring surrogates for O_2 uptake and CO_2 clearance are the SpO_2 and respiratory rate (minute ventilation when the patient is mechanically ventilated). Both monitoring options have benefits, but each also has considerable limitations.

MONITORING OXYGENATION

Tissue oxygenation depends on FiO_2, inspired partial pressure of oxygen (PiO_2), alveolar oxygen tension (PAO_2), arterial oxygenation (PaO_2, SaO_2, oxygen content of arterial blood CaO_2), oxygen delivery, tissue perfusion, and O_2 uptake.

ARTERIAL PULSE OXIMETRY

ABG analysis has been the accepted method of detecting hypoxemia in critically ill patients, but obtaining arterial blood can be painful and cause complications; moreover, ABG analysis does not provide immediate or continuous data. For these reasons, SpO_2 has become the standard for a continuous, noninvasive assessment of SaO_2. However, it too has significant limitations (see Box 52.2).[1,2] SpO_2 does not measure $PaCO_2$, and patients breathing an elevated FiO_2 can retain CO_2 (increased $PaCO_2$), although SpO_2 values are acceptable. Ventilatory failure may go unnoticed unless ABGs are measured (see Chapter 19).

RULE OF THUMB There are two very important problems with relying on SpO_2 to monitor adequate respiratory function: (1) SpO_2 values reflect oxygenation, not ventilation; and (2) SpO_2 measurement is susceptible to numerous factors that can produce false values.

MINI CLINI

Trusting the Pulse Oximeter

Problem

A newborn of 32 weeks' gestation is intubated and receiving continuous positive airway pressure (CPAP) therapy. The patient appears to be in mild to moderate respiratory distress, yet her SpO_2 is 98%. Hurricane spray (20% benzocaine) had been used to reduce the irritation of the endotracheal tube. Analysis of ABG values reveals a PaO_2 of 325 mm Hg, and the co-oximeter shows a methemoglobin value of 38%.

MINI CLINI—cont'd

Trusting the Pulse Oximeter

Solution

The most common problems with the fidelity of pulse oximeter readings are motion artifacts, interference by external light sources, or malposition of the sensor. Each of these problems can be assessed easily and quickly. In this case, the clinical symptoms did not correlate with an acceptable SpO_2 value. Because adequate O_2 delivery is the ultimate goal, CO_2 and O_2-carrying ability must be considered as causes of the respiratory distress. The high methemoglobin value, most likely caused by the hurricane spray, necessitates immediate therapy with methylene blue dye. Although the pulse oximeter can be an excellent, safe means of monitoring blood oxygenation, there must be a wary vigilance regarding the values it provides.

OXYGEN CONSUMPTION

Oxygen consumption ($\dot{V}O_2$) is the volume of O_2 consumed by the body in milliliters (mL) per minute. Normal resting $\dot{V}O_2$ is approximately 250 mL/min, and $\dot{V}O_2$ increases with activity, stress, and temperature. Oxygen consumption and measurement are discussed in Chapter 12.

Alveolar-Arterial Oxygen Tension Difference

The **alveolar-arterial oxygen tension difference** ($P[A–a]O_2$) is a useful measurement of the efficiency of gas exchange. A healthy person breathing room air has a $P(A–a)O_2$ of approximately 5 to 15 mm Hg. This value increases with age to approximately 10 to 20 mm Hg in elderly adults. $P(A–a)O_2$ also increases normally with an increase in FiO_2. An abnormal increase in $P(A–a)O_2$ is associated with gas-exchange problems. This measurement is discussed in greater detail in Chapter 12.

PaO_2/FiO_2 Ratio

The PaO_2/FiO_2 ratio is easy to calculate and a reliable index of gas exchange; it is one of the commonly used oxygenation measurements in research studies involving patients in acute respiratory failure. The PaO_2/FiO_2 ratio provides an index for the effect of O_2 on PaO_2 when a range of FiO_2 settings may be prescribed. The index allows comparisons of severity between patients or when FiO_2 changes in the same patient. Every bedside clinician should be aware of the PaO_2/FiO_2 in their patients when ABG values are available. More information may be found in Chapter 12.

Murray Lung Injury Score

To monitor the severity of acute respiratory distress syndrome (ARDS), Murray and colleagues[3] developed a lung injury score. This score quantifies the injury level using the following four factors: chest radiographic findings, PaO_2/FiO_2 ratio, PEEP setting, and compliance. The **Murray lung injury score** is an example of a composite score that allows quantification of lung status according to different aspects of the injury—gas exchange, radiographic findings, and mechanics. This score is used as an index of the effectiveness of therapy or for interstudy comparisons. The method for calculating the Murray lung injury score is shown in Box 52.3. Other measures of lung injury are listed in Box 52.4.

BOX 52.3 Murray Lung Injury Score

Component	Value
Chest X-Ray	
No alveolar consolidation	0
Alveolar consolidation confined to one quadrant	1
Alveolar consolidation confined to two quadrants	2
Alveolar consolidation confined to three quadrants	3
Alveolar consolidation in all four quadrants	4
Hypoxemia Score	
PaO_2/FiO_2 >300	0
PaO_2/FiO_2 225–299	1
PaO_2/FiO_2 175–224	2
PaO_2/FiO_2 100–174	3
PaO_2/FiO_2 <100	4
PEEP Score (When Ventilated)	
PEEP ≤5 cm H_2O	0
PEEP 6–8 cm H_2O	1
PEEP 9–11 cm H_2O	2
PEEP 12–14 cm H_2O	3
PEEP >15 cm H_2O	4
Respiratory System Compliance Score (When Available)	
Compliance ≥80 mL/cm H_2O	0
Compliance 60–79 mL/cm H_2O	1
Compliance 40–59 mL/cm H_2O	2
Compliance 20–39 mL/cm H_2O	3
Compliance ≤19 mL/cm H_2O	4

The final value is obtained by dividing the aggregate sum by the number of components used.

Score

No lung injury: 0

Mild to moderate lung injury: 0.1–2.5

Severe lung injury (ARDS): >2.5

BOX 52.4 Measures of Decreased Blood Oxygenation or Lung Injury

- ↓ SpO_2
- ↓ PaO_2
- ↑ $P(A–a)O_2$ ($PAO_2–PaO_2$)
- ↓ P/F ratio (PaO_2/FiO_2)
- ↑ Shunt/venous admixture
- ↑ Murray lung injury score

Other Oxygenation Measurements

Other important measures of oxygenation (not as routinely measured), including oxygen consumption, the alveolar-arterial oxygen tension difference ($A–aO_2$), the oxygenation index (OI), and the quantification of shunt. These are covered in detail in Chapter 12.

MONITORING VENTILATION

As in the case of oxygenation, the adequacy and efficiency of ventilation is routinely evaluated in the ICU (Box 52.5). Monitoring of patients receiving mechanical ventilatory support in the ICU includes measurement of the patient's tidal volume (V_T), respiratory rate (f), and minute ventilation ($\dot{V}_E$). It is

BOX 52.5 Monitoring the Adequacy of Ventilation

- Respiratory volume and rate (V_T, f, $\dot{V}_E$)
- $PaCO_2$
- V_D/V_T
- Capnometry (not for routine use but in special situations, such as ensuring tracheal intubation and cardiac blood flow in resuscitation efforts)

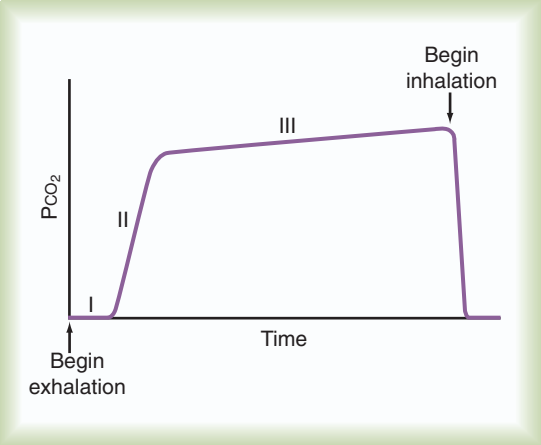

Fig. 52.1 Time-Based Capnograph. *Phase I,* anatomic dead space; *Phase II,* transition from anatomic dead space to alveolar plateau; *Phase III,* the alveolar plateau.

important to understand that the effectiveness of minute ventilation depends on alveolar ventilation ($\dot{V}_A$). Significant changes in arterial pH can still occur despite the maintenance of minute ventilation when patients have a significant change in dead space and intrapulmonary shunt.

CAPNOGRAPHY

As discussed in Chapter 19, **capnometry** is the measurement of CO_2 at the airway opening during the ventilatory cycle. **Capnography** refers to plotting CO_2 concentration against time or against exhaled volume. The normal CO_2 waveform is displayed in Fig. 52.1.

Patients for whom capnometry may be a useful monitoring tool include those with normal lungs but an unstable ventilatory drive who are breathing spontaneously or receiving low-level ventilatory support. In these patients, capnometry readings should initially be validated by comparison with $PaCO_2$. Changes in end-tidal PCO_2 ($P_{ET}CO_2$) can be used to alert the clinician to potential changes in patient ventilation. Thereafter, periodic reevaluation should be performed as the patient's clinical state changes. Capnometry has been extremely useful in emergency situations, such as to verify endotracheal intubation and assess blood flow during or after cardiac arrest. Small in-line CO_2 monitors that employ colorimetry are now routinely used to verify endotracheal intubation.[4]

Although $P_{ET}CO_2$ and $PaCO_2$ values tend to correlate at a single point in time, correlation between changes in $P_{ET}CO_2$ and in $PaCO_2$ is weaker.[5] Decreases in ventilation are reflected by increases in $P_{ET}CO_2$ and $PaCO_2$. However, with very small V_T, $PaCO_2$ increases, whereas $P_{ET}CO_2$ may decrease. Although the appropriate role of capnometry in critical care may be unclear, integration of capnometry into modern ventilators is reasonable because the primary role of the ventilator is CO_2 elimination. As a guide for clinicians, the American Association for Respiratory Care (AARC) has created a clinical practice guideline for using capnometry in ventilated patients.[6] Box 52.6 lists common causes of changes in monitored $P_{ET}CO_2$ values.

BOX 52.6 Causes of Increased and Decreased End-Tidal Carbon Dioxide Values

Increased $P_{ET}CO_2$

- Decreased effective ventilation (↓ V_T, ↓ $\dot{V}_E$, ↓ $\dot{V}_A$, ↑ $PaCO_2$)
- Increased CO_2 production ($\dot{V}CO_2$) (agitation, stress, shivering, fighting the ventilator, pain, anxiety, recovery from sedation or paralysis)

Decreased $P_{ET}CO_2$

- Increased effective ventilation (↑ V_T, ↑ $\dot{V}_E$, ↑ $\dot{V}_A$, ↓ $PaCO_2$)
- Marked decrease in effective ventilation (↓↓$\dot{V}_T$ approaching dead space volume; rapid shallow breathing)
- Decreased CO_2 production ($\dot{V}CO_2$) (sedation, sleep, cooling)
- Decrease in lung perfusion (pulmonary embolus, decreased CO)

Absent $P_{ET}CO_2$

- Apnea
- Cardiac arrest
- Ventilator disconnect or malfunction
- Airway obstruction

Volumetric CO_2 monitoring holds promise in continuously monitoring ventilation efficiency. VCO_2 can be continuously monitored in a patient being liberated from mechanical ventilation as an indicator of adequate or improving ventilatory efficiency.[7] The volumetric capnogram has been examined as a potential tool for detecting a pulmonary embolism,[8] tracking the efficiency of mechanical ventilation,[8] and calculating dead space.[9] The relationship between VCO_2 and dead space also makes it a valuable tool in the optimization of PEEP.

Dead Space

As discussed in Chapter 11, the **dead space/tidal volume (VD/VT) ratio** is a measure of the efficiency of gas exchange. This ratio is an estimate of the proportion of ventilation participating in the diffusion of CO_2. V_D/V_T can be calculated from the Enghoff modification of the Bohr equation, as follows:

$$V_D/V_T = (PaCO_2 - P_ECO_2)/PaCO_2$$

where P_ECO_2 is the CO_2 concentration in mixed expired gas.

Frequently, the V_D/V_T ratio is increased in patients with congestive heart failure, pulmonary embolism, ARDS, or pulmonary hypertension and in those undergoing mechanical ventilation. The V_D/V_T ratio has been used to evaluate patients being considered for liberation from mechanical ventilation. A V_D/V_T ratio greater than 0.60 generally requires continuation of ventilatory support. Increased V_D/V_T in the early phase of ARDS has been associated with an increased risk of death.[3,10]

MONITORING OF INSPIRED AND EXHALED GAS VOLUMES

Although the best index of effective ventilation is the measurement of $PaCO_2$, measurement of inspired and expired gas volumes is an important aspect of monitoring patients receiving mechanical ventilatory support. For patients receiving controlled mechanical ventilation, minute ventilation ($\dot{V}_E$), respiratory rate (f), and V_T are assessed by

$$\dot{V}_E = (V_T)(f) \text{ and } V_T \text{ average} = \dot{V}_E/f$$

With an adequate V_T, increases in $\dot{V}_E$ tend to increase alveolar ventilation and decrease $PaCO_2$, whereas decreases in $\dot{V}_E$ tend to have the opposite effect. However, in the presence of rapid shallow breathing with normal or elevated $\dot{V}_E$, a decrease in effective ventilation can result in an increase in $PaCO_2$. This effect is caused by ineffective shallow tidal breaths that are at or below the volume of the dead space. Spontaneous respiratory rate often is a sensitive indicator of the need for mechanical ventilation. Rates greater than 25 breaths/min in adults may indicate distress, and a rate greater than 30 breaths/min with a spontaneous V_T of less than 300 mL often indicates the need for mechanical ventilatory support in adults because a large proportion of ventilatory effort is being expended to move dead-space gases.

Inspired Versus Expired Tidal Volume During Mechanical Ventilation

Normal inspired V_T and expired V_T should be nearly the same. However, in the presence of an air leak, inspired V_T may be larger than expired V_T, and measurement of delivered V_T versus exhaled V_T may be useful in detecting and quantifying the size of a leak—a situation that may require immediate attention. When a significant mismatch between inspired and expired V_T is noticed, consider not only the possibility of a cuff leak with the endotracheal or tracheostomy tube but also check the circuit connections. Alternatively, be sure to monitor the ventilator waveform graphics and assess the patient's respiratory rate, looking for the presence of an insufficient expiratory time leading to auto-PEEP.

PEAK AND PLATEAU PRESSURES

The maximum value of pressure at the airway opening during a ventilatory cycle is routinely monitored in the ICU as peak airway pressure. Peak airway pressure greater than 50 to 60 cm H_2O is generally discouraged because high values of peak pressure carry an increased risk of lung injury and hypotension.[11] During volume-targeted modes of ventilation, an increase in peak pressure results from increased resistive pressure or increased elastic pressure from decreased lung or chest wall compliance. During pressure-targeted modes of ventilation, increased resistive pressure or increased elastic pressure results in a decrease in delivered tidal volume rather than the increase in peak or plateau pressure (P_{plat}). Measurement of P_{plat} helps to differentiate between the resistive and elastic components. The P_{plat} level should be monitored for all ventilated patients. P_{plat} ideally should not exceed 28 cm H_2O, because elevated P_{plat} increases the likelihood of developing ventilator-induced lung injury. However, the limit for P_{plat} depends on the resulting lung stress and strain.

MEAN AIRWAY PRESSURE

Mean airway pressure (MAP) represents the average airway pressure over the total ventilatory cycle. Correct measurement of this value requires continuous sampling of airway pressure at the airway opening; this is an automated feature of modern ventilators. MAP is related to mean lung volume, which correlates with oxygenation if perfusion is adequate. When MAP is increased, arterial O_2 levels often improve, but venous return and subsequently arterial pressure can be adversely affected.

In an effort to increase oxygenation while monitoring arterial pressure, the clinician can manage MAP by several means, including V_T, frequency, inspiratory-to-expiratory (I:E) ratio, and PEEP. The management of MAP relates to a concern for improving oxygenation balanced against its detrimental influence on venous return. Normally, expiratory resistance is greater than (twice) inspiratory resistance, and mean alveolar pressure normally is greater than MAP. For patients with chronic obstructive pulmonary disease (COPD) and elevated expiratory resistance, high mean alveolar volume can be significant during mechanical ventilation.

There is an understandable caution when MAP is being increased, usually by increasing PEEP, yet two ventilator modes apply dramatic increases in MAP—high-frequency oscillation and airway pressure release ventilation. The marked improvements in oxygenation seen with these modes can be attributed to high MAP. In the case of high-frequency oscillation, the lungs are never allowed to derecruit between breaths. Airway pressure release ventilation is more complicated because the lung deflates to varying unknown alveolar volumes on exhalation. In using either mode, end-expiratory alveolar lung volume status cannot easily be determined, but oxygenation is often improved.

DRIVING PRESSURE

Driving pressure is a measure of the pressure difference between P_{plat} and total PEEP (PEEP plus auto-PEEP). The swing in pressure from end-expiration to end-inspiration may be an independent stress factor on the lungs. Consider driving pressure as the amount of energy applied to the lung: the higher the energy applied to the lung, the greater the potential for lung injury. In general, the driving pressure should be kept below 15 cm H_2O.[12]

RULE OF THUMB Driving pressure is a simple bedside value obtained by determining the pressure difference between plateau pressure and total PEEP. Clinicians should attempt to keep this value below 15 cm H_2O. The use of lower tidal volume and proper levels of PEEP can help to achieve this ventilation goal.

RESISTANCE

Depending on the driving pressure measured, various resistances can be calculated, including airway, pulmonary, chest wall, and

total respiratory system resistance. An airway resistance (Raw) can be determined dynamically from simultaneous measurements of airflow and the pressure difference between the airway opening (Pao) and the alveoli (Palv) by Raw = (Pao – Palv)/flow. Because resistance changes throughout inspiration and expiration and expiratory resistance generally is greater than inspiratory resistance, instantaneous measures of resistance are not commonly performed clinically. Inspiratory resistance can be calculated simply during constant-flow volume ventilation by using a short (0.5-second) pause at the end of volume delivery. This allows for the separation of peak and plateau pressures in real time. It allows monitoring of airway status over time or after the effects of bronchodilator therapy and is determined by dividing the pressure change by the flow rate, as follows:

$$\text{Raw} = \Delta P/\Delta F = (P_{peak} - P_{plat})/\text{flow}$$

where P_{peak} is peak airway pressure and P_{plat} is plateau pressure. Automated methods of measuring expiratory resistance have been integrated into some ventilators.

In ventilated patients, a significant component of the total flow resistance is from endotracheal tubes.[13] In healthy persons, flow is relatively laminar during tidal ventilation and becomes turbulent only with increasing ventilatory demands. The flow resistance offered by the endotracheal tube increases markedly with increasing flow and varies with the size of the tube. Normal airway resistance is approximately 1 to 2 cm H_2O/L/s; however, intubated patients receiving mechanical ventilatory support typically have an airway resistance of 5 to 10 cm H_2O/L/s or more. Automated tube compensation modes have been added to mechanical ventilators to deliver flow that accounts for the added resistance of the endotracheal tube. Common causes of changes in airway resistance in mechanically ventilated patients are listed in Box 52.7.

BOX 52.7 Common Causes of Changes in Compliance and Resistance in Mechanically Ventilated Patients

Decreased Compliance
- ↓ Lung compliance (atelectasis, pneumonia, pulmonary edema, ARDS, pneumothorax, fibrosis, bronchial intubation)
- ↓ Thoracic compliance (ascites, chest wall deformity)

Increased Compliance
- ↑ Lung compliance (improvement in any of the foregoing conditions, pulmonary emphysema)
- ↑ Thoracic compliance (improvement in any of the foregoing conditions; flail chest; position change—sitting patient up)

Increased Resistance
- Small endotracheal tube, secretions plugging endotracheal tube, biting on endotracheal tube
- ↑ Bronchospasm, mucosal edema
- ↑ Secretions
- ↑ Airway obstruction
- High gas flow rate (or ↑ gas flow)

Decreased Resistance
- ↓ Improvement in any of the foregoing conditions
- ↓ Bronchodilator administration
- ↓ Suctioning and airway care
- ↓ Use of lower inspiratory gas flow rate

MINI CLINI

Airway Resistance

Problem

A patient receiving volume-assist controlled ventilation with a constant flow of 60 L/min has high peak airway pressures of 35 cm H_2O. You perform an inspiratory hold on the ventilator and determine that the plateau pressure is 22 cm H_2O. Upon auscultation you hear bilateral wheezes on exhalation. What does this finding indicate?

Solution

The patient has high airway resistance (13 cm H_2O), which could be caused by bronchospasm.

The response to any intervention, such as administering bronchodilators, can be monitored in real time by using a pause time on the ventilator of 0.2 to 0.3 seconds. This will allow a plateau pressure to be displayed in real time and breath by breath on the ventilator. The change in the difference between peak and plateau pressure will indicate a decrease in airway resistance.

MONITORING LUNG AND CHEST WALL MECHANICS

Ventilation of the lungs involves overcoming the flow-resistive, inertial, and elastic properties of the respiratory system. In a ventilated patient, change in airway pressure during ventilation is used to determine the compliance of the total respiratory system. Pressure changes measured by an esophageal balloon reflect compliance of the chest wall. The difference between the compliance of the respiratory system and chest wall is the lung compliance (lung compliance can also be measured in the passively ventilated patient using the change in **transpulmonary pressure**).

One method to assess the compliance of the respiratory system and its relation to lung volume is through the use of a pressure-volume (P-V) curve. There is normally a difference in the P-V relationship during inflation and deflation. However, a large difference between inflation and deflation, called hysteresis, typically implies that lung units have been recruited after a threshold level of pressure was applied.

To measure a static P-V curve of a ventilated patient from resting at functional residual capacity (FRC) to total lung capacity, until more recently a calibrated syringe (referred to as a supersyringe) ranging from 1.5 to 3 L was used to inject 50 to 100 mL increments into the lungs while airway pressure was recorded. A P-V curve can be measured more easily by the continuous delivery of a low flow of gas into the lung (<5 L/min) with the simultaneous recording of system pressure change. Current ICU ventilators allow the determination of an inflation P-V curve using this approach. The P-V curve is plotted as part of the ventilator graphics package with cursors available to identify specific points on the curve. Patients should be sedated during the maneuver, mostly because the flow delivered would be insufficient to satisfy

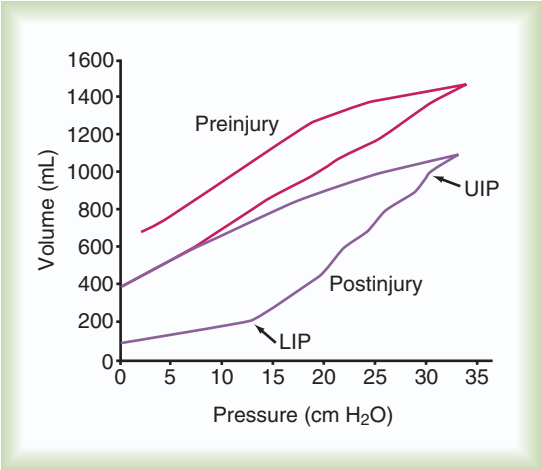

Fig. 52.2 P-V curves generated by a normal lung (preinjury) and after oleic acid injury (postinjury). In the preinjury curve, the linear relationship between pressure and volume with minimal hysteresis is evident. The postinjury curve displays marked hysteresis and two changes in compliance on the inspiratory limb: a lower inflection point *(LIP)* and upper inflection point *(UIP)*.

patient demand. Also, the amount of pressure or volume applied during the maneuver would likely cause discomfort.

The inflation P-V curve often but not always reveals two points at which the slope of the curve changes. The lower point at which the slope changes is called the lower inflection point. As depicted in Fig. 52.2, a lower inflection point may occur over the lower range of volumes, indicating a pressure above which total respiratory system compliance is improved owing to the beginning of alveolar recruitment, overcoming airway closure, or the peripheralization of secretions.[14] A recommended strategy is to set PEEP slightly above the lower inflection point with the goal of maintaining recruitment and stabilizing dependent alveoli that may otherwise sustain injury from repetitive opening, closing, and reopening during tidal ventilation. The other pressure change in the slope, called an upper deflection point, may be seen at a higher volume, indicating where compliance decreases owing to alveolar overdistension or a slowing of lung recruitment. The risk of alveolar overdistension is generally reduced if the P_{plat} is less than 28 cm H_2O in patients with ARDS.[15] More recently, attention has been focused on the deflation area of the curve and what is called the critical closing pressure, the area of the deflation curve where there is significant loss in compliance.[16] The rationale for paying attention to the critical closing pressure is that when there is a significant amount of recruitment (showing as hysteresis), the amount of pressure required to maintain an open lung may be lower than that needed during the inflation curve. The deflation area of the curve is discussed further later in this chapter.

RULE OF THUMB A P-V curve is obtained using a low-flow inflation P-V curve maneuver (flow <5 L/min). There is normally a difference in the P-V relationship during inflation and deflation. However, a large difference between inflation and deflation, called hysteresis, typically implies that the airways have been opened, and lung units have been recruited after a threshold level of pressure was applied (see Fig. 52.2).

RESPIRATORY SYSTEM COMPLIANCE

Respiratory system compliance should be routinely monitored in all ventilated patients. To attain an accurate assessment of compliance (static compliance), two maneuvers must be performed: an end-inspiratory hold and an end-expiratory hold. A short end-inspiratory hold maneuver in a passively ventilated patient allows for the equilibration of pressure across the lung and an estimation of peak alveolar pressure or the inspiratory P_{plat}. An end-expiratory hold is required to assess the total PEEP ($PEEP_{TOT}$) when auto-PEEP is present. Compliance (C) is calculated as follows:

$$C = \Delta V/\Delta P$$

where V_T (corrected for tubing compliance) is ΔV and ΔP is P_{plat}–$PEEP_{TOT}$ (driving pressure).

Normal compliance ranges from 60 to 100 mL/cm H_2O. Diseases of the lung parenchyma—such as pneumonia, pulmonary edema, or any chronic disease-causing fibrosis—cause decreased effective compliance. Acute changes—such as atelectasis, pulmonary edema, ARDS, and lung compression caused by tension pneumothorax—cause a rapid decrease in compliance. Compliance is often less than 25 to 30 mL/cm H_2O in patients with ARDS. Common causes of changes in respiratory system compliance are listed in Box 52.7. Several ventilators report breath-to-breath compliance and resistance values dynamically without the use of pause maneuvers. Monitoring of these estimates can indicate impedance problems and is useful for trending during the titration of ventilator settings (such as PEEP), but absolute values should be verified by static maneuver calculations.

CHEST WALL COMPLIANCE

In a significant proportion of patients, chest wall compliance can influence the P-V relationship during ventilation. Poor respiratory system compliance may be largely due to external pathologies of the chest wall. Normal chest wall compliance accounts for approximately 20% of the respiratory compliance but can commonly reach 50% or greater in critically ill patients. Chest wall abnormalities (including the abdomen) may cause an increase in pleural pressure both at rest and during positive-pressure ventilation. Direct measurement of pleural pressure at the bedside is highly invasive, which is why **esophageal balloon pressure** measurement is used as a surrogate (Box 52.8). Chest wall compliance (C_{CW}), by definition using esophageal pressure, is as follows:

$$C_{CW} = \Delta V/P_{esinsp} - P_{esexp}$$

where P_{esinsp} is the esophageal pressure during an end-inspiratory hold and P_{esexp} is the esophageal pressure during an end-expiratory hold.

Poor chest wall compliance (high chest wall elastance) may buffer the lung-damaging effect of elevated airway pressure by reducing end-inspiratory transpulmonary pressure (Ptp). Higher airway pressures may be required to ventilate these patients, but without the same risk of barotrauma as in patients with low pleural pressure or normal chest wall compliance. One of the

BOX 52.8 Monitoring of Esophageal Pressure

Esophageal pressure is used clinically as a surrogate for pleural pressure. The measurements are used to determine compliance of the chest wall and lung, measure work of breathing, determine the appropriateness of PEEP, and calculate lung stress. A thin esophageal catheter (approximately 2 mm in diameter) is simple to insert and poses little risk of esophageal perforation. Appropriate placement is achieved by first passing it into the stomach and then inflating the 10-cm-long balloon with approximately 0.5 to 1.0 mL of air. The catheter is carefully withdrawn until the final position of the balloon is within the lower third of the esophagus, as verified by the presence of cardiac oscillations within the pressure tracing. In adults, this is approximately 35 to 40 cm from the teeth when the balloon is inserted orally. Proper placement can also be confirmed by occluding the airway (done with an expiratory hold on the ventilator) and measuring the simultaneous deflections in pressure at the airway opening and esophageal pressure either during spontaneous efforts or by a gentle push on the chest or abdomen. The change in pressure in the airway during occlusion should be the same as the change that occurs in the esophageal pressure.

BOX 52.9 Common Causes of Elevated Pleural Pressure in the Intensive Care Unit

- Obesity
- Intra-abdominal hypertension
- Massive fluid resuscitation

most common causes of poor chest wall compliance is intra-abdominal hypertension. Regular monitoring of **bladder pressure** can be useful for confirming issues of poor chest wall compliance in the absence of esophageal pressure monitoring. Some causes of elevated pleural pressure (resulting in poor chest wall compliance) are listed in Box 52.9.

RULE OF THUMB Poor respiratory system compliance may be largely due to external pathologies of the chest wall. Normal chest wall compliance accounts for approximately 20% of the respiratory compliance but can commonly reach 50% or greater in critically ill patients. Esophageal pressure measurements are required to truly assess the impact the chest wall is having on respiratory system compliance.

TRANSPULMONARY PRESSURE

Airway pressure as measured by the ventilator does not take into consideration the pleural pressure or chest wall compliance of the patient. True distending pressure of the lung (the pressure that stretches the lung) is the transpulmonary pressure (Ptp). The appropriateness and safety of the airway pressures delivered by the ventilator, both at end-exhalation (PEEP) and end-inspiration (P_{plat}), depends on the resulting Ptp.[17]

The estimation of Ptp is commonly done through the use of esophageal pressure monitoring using the following simple equation:

$$P_{airway} - P_{es} = Ptp$$

where P_{aw} is the airway pressure and P_{es} is the esophageal pressure. Two variations are used in clinical practice, one for end-exhalation and one for end-inspiration. These variations are as follows:

$$P_{PEEP} - P_{esexp} = Ptp_{EX}$$

$$P_{plat} - P_{esinsp} = Ptp_{IN}$$

where the first equation is the transpulmonary pressure during an end-expiratory hold and the second equation is the transpulmonary pressure during an end inspiratory hold. Lung compliance (CL) can be derived from these measurements as follows:

$$C_L = \Delta V / Ptp_{IN} - Ptp_{EX}$$

Ptp_{IN} can be monitored to evaluate global lung stress and the potential for overdistension—usually allowing some liberty in accepting higher P_{plat} to deliver adequate ventilation in patients with elevated pleural pressures (stiff chest walls). It is currently unknown what the safest upper limit of Ptp_{IN} should be, as it may underestimate the stress felt in some areas of the lung, but it should be less than 20 cm H_2O of pressure. For patients with a large degree of lung inhomogeneity, efforts to maintain an even lower Ptp_{IN} should be made. The monitoring of Ptp_{EX} has been used more recently as a rationale for setting PEEP.[18] A negative Ptp_{EX} probably indicates lung closure (dependent lobe) during expiration, which can result in lung opening and closing during the ventilatory cycle. Adequate or "optimal" PEEP when measuring Ptp is the PEEP level that avoids a negative Ptp_{EX}. (See Chapter 49 for details.)

LUNG STRESS AND STRAIN

During mechanical ventilation, the lungs are exposed to positive pressure that exerts more stress and strain on the lungs than is experienced during spontaneous ventilation. This **lung stress and strain** may cause injury or extend existing lung injury along the injury/normal tissue border. When positive pressure becomes injurious, it is referred to as ventilator-induced lung injury. However, the concepts of stress and strain as applied to the lungs are not clearly defined. The physical definition of stress is a force per unit area. Strain is the deformation of a structure compared with its overall size. Hooke's law associates the two factors by the following relationship: stress = k * strain.

Working definitions for stress and strain applied to the lungs have been studied. The most common methods for assessing the pressure felt by the lung during inspiration are the directly measured method:[17]

$$Ptp_{IN} = P_{plat} - P_{pesinsp}$$

And the elastance-derived method, which requires the calculation of lung and respiratory system elastance,[19] is

$$E_L = (Ptp_{IN} - Ptp_{EX}) / \Delta V$$

$$E_{RS} = (P_{plat} - PEEP_T) / \Delta V$$

$$Ptp_{IN} = P_{plat} \times E_L / E_{RS}$$

Although these methods for Ptp_{IN} give different results, current research suggests that it is due to the pressure gradient of pleural pressure across the chest wall, and the elastance-derived method

may better reflect lung stress in the nondependent region of the lung, whereas the direct method may reflect stress in the middle of the thoracic space.[20]

Driving pressure, as previously discussed, may be an alternative measure of stress. However, when chest wall compliance is poor, it may be difficult to determine the potential for injury without measuring lung stress. Strain has been defined as V_T (the deformation) divided by FRC (the resting size of the lungs). These definitions have been associated as stress = 13.5 × strain, predicting that a stress of 27 cm H_2O (Ptp of 27 cm H_2O) and a strain of 2 (V_T of twice the FRC) reach injurious limits of ventilation.[21] The measurement of lung stress requires placement of an esophageal catheter. To measure strain, automated FRC determinations have become available on some modern ventilators.[22] Stress can also occur at lower pressures if lung units are opening and closing during the ventilator cycle.

MONITORING THE PATIENT–VENTILATOR SYSTEM

Monitoring of a patient during mechanical ventilatory support should include a physical examination (inspection, palpation, percussion, and auscultation), assessment of oxygenation and ventilation, and assessment of ventilatory load and capacity. Table 52.1 lists key physiologic monitoring data and acceptable values for patients receiving mechanical ventilation. Monitoring of all

TABLE 52.1 Physiologic Monitoring Data (Respiratory Values)

Function Assessed	Description of Value	Symbol/Formula	Acceptable Value
Oxygenation			
Lung Exchange (External)			
Adequacy	Arterial oxygen pressure	PaO_2	60–100 mm Hg
	Arterial oxygen saturation	SaO_2	≥90%
	Oxygen saturation by pulse oximeter	SpO_2	≥90%
	Transcutaneous oxygen partial pressure	$PtcO_2$	60–100 mm Hg
Efficiency	Alveolar to arterial oxygen tension gradient	$P(A–a)O_2$	<350 mm Hg (100% O_2)
	Arterial to alveolar	PaO_2/PAO_2	>0.6
	Respiratory index	$P(A–a)O_2/PaO_2$	<5
	P/F ratio	PaO_2/FiO_2	>300
	Percentage shunt	$\dot{Q}_S/\dot{Q}_T$	<15%–20%
Time exchange (internal)	Mixed venous oxygen content	$C\bar{v}O_2$	>10.0 mL/dL
	Mixed venous oxygen partial pressure	$P\bar{v}O_2$	>30 mm Hg
	Mixed venous oxygen saturation	$S\bar{v}O_2$	>65%
	Arterial-venous oxygen content difference	$C(a-\bar{v}O_2)$	<7 mL/dL
Ventilation			
Adequacy	Minute ventilation	$\dot{V}_E$	5–10 L/min
	Arterial carbon dioxide	$PaCO_2$	35–45 mm Hg (normal pH)
	Transcutaneous carbon dioxide partial pressure	$PtcCO_2$	35–45 mm Hg (normal pH)
	End-tidal carbon dioxide partial pressure	$P_{ET}CO_2$	35–43 mm Hg (4.6%–5.6%)
Efficiency	Dead space/tidal volume ratio	V_D/V_T	<0.6
	Minute ventilation vs. carbon dioxide partial pressure	$\dot{V}_E$ vs. $PaCO_2$	$\dot{V}_E$ <10 L/min with normal $PaCO_2$
Ventilatory Load			
Total impedance	Dynamic compliance	$(V_T–V_C)/(PIP–PEEP)$	35–50 mL/cm H_2O
Compliance	Effective compliance	$C_{eff} = \frac{(V_T - V_C)}{P_{plat} - PEEP}$	60–100 mL/cm H_2O
WOB	Work = kg × m/L or J/L	Work = P × V	<0.15 kg × m/L <1.5 J/L
Ventilatory Capacity			
Drive	Occlusion pressure	P0.1	<6 cm H_2O
	Mean inspiratory flow	V_T/T_i	Not established
	Diaphragm thickening fraction	TFdi	15%–30%
Strength	Vital capacity	VC	>10–15 mL/kg
	Maximal inspiratory pressure	MIP; PI_{max}	<–20 to –30 cm H_2O
	Maximum diaphragm thickening fraction	TFdi-max	>20%
Endurance	Maximum voluntary ventilation	MVV	>20 L/min or 2 × $\dot{V}_E$
	Ratio of minute ventilation to MVV	$\dot{V}_E$/MVV	<1:2
	Pressure-time index	$(Pdi/Pmax)*TI/T_{tot}$	<0.15

aspects of the patient–ventilator system is an important responsibility that must clearly be performed within the ICU. Monitoring a ventilated patient is the primary responsibility of the RT. Important areas of this responsibility include the following:

- Assessing the integrity of the airway and circuitry, including secretion clearance
- Maintaining the prescribed settings and assessing their appropriateness
- Ensuring acceptable gas exchange values
- Monitoring of respiratory system mechanics
- Evaluating the comfort and synchrony of the patient's breathing
- Setting of alarms
- Caring for any other safety issues, such as risk of unplanned extubation

A system of ensuring and documenting all aspects of safe and appropriate care must be in place. This system usually includes a manual or, more frequently, an electronic recording of all important settings, alarms, and ABG values at regular intervals. This monitoring process has been called a patient–ventilator assessment. An example of a recording form used for this purpose is shown in Fig. 52.3. Increasingly, electronic transfer of ventilator settings and monitored data is being added to the electronic medical record. The responsibility of the RT is much greater

Adult Mechanical Ventilation Flow Sheet

Patient _____
Physician _____
Diagnosis _____
Age _____ Height _____
Weight _____ Ideal body weight _____
ET tube / trach tube size _____
Tube Position (length) _____

Cuff pressure (volume) _____
□ M.O.V. □ Minimal leak
Ventilator _____ Vent. day _____
Circuit change (Date / Time) _____
Tape change (Date / Time) _____
Other therapy _____

Patient ID

Date							
Time							
Mode (A/C; SIMV, PSV, PCV, etc.)							
Set Tidal Volume / Delivered Tidal Volume							
Spontaneous Tidal Volume							
Machine Rate / Total Rate							
Minute Volume							
Peak Pressure / Static Pressure							
Mean Airway Pressure							
PEEP / CPAP [IPAP / EPAP]							
Auto PEEP							
Support / Pressure Control Level (cmH_2O)							
Sensitivity or Flowtrigger (Flowby)							
FIO2 Set / Analyzed							
Inspiratory Flow / Time							
Wave Form (⎍⎍ ⎍⎍)							
I : E Ratio							
Sigh Volume / Sigh Frequency							
Airway Temperature							
Static Compliance / Dynamic Compliance							
Airway Resistance [(PIP - PLAT / Insp. Flow L/Sec)]							
Apnea Parameters Check (Y / N)							
ALARMS — Pressure High / Low							
ALARMS — Low VT							
ALARMS — High / Low VE							
ALARMS — High rate							
BLOOD GASES — pH							
BLOOD GASES — PaO2							
BLOOD GASES — PaC02							
BLOOD GASES — Sa02 / Oximetry (Sp02)							
BLOOD GASES — Hb							
BLOOD GASES — HC03-							
BLOOD GASES — B.E.							
BLOOD GASES — Ca02							
BLOOD GASES — Pv02							
BLOOD GASES — Sv02							
BLOOD GASES — Ca02 - Cv02							
BLOOD GASES — Qs / Qt							
BLOOD GASES — Vd / Vt							
BLOOD GASES — P (ET) C02							
HEMO DYNAMICS — Pulse							
HEMO DYNAMICS — Blood Pressure (Systolic / Diastolic)							
HEMO DYNAMICS — CVP							
HEMO DYNAMICS — PAP (Systolic / Diastolic)							
HEMO DYNAMICS — PCWP							
HEMO DYNAMICS — Cardiac Output / Cardiac Index							
HEMO DYNAMICS — SVR							
HEMO DYNAMICS — PVR							
SPONTANEOUS — MIP / MEP							
SPONTANEOUS — Vital Capacity (VC)							
SPONTANEOUS — Spontaneous Volumes (VT / VE)							
SPONTANEOUS — Spontaneous Rate (f)							
SPONTANEOUS — RSBI (f/VT)							
Other							
Initials							

Fig. 52.3 Ventilator Flow Sheet.

Adult Mechanical Ventilation Flow Sheet

Respiratory Care Progress Notes

S: (pt Awareness, response, sedations / paralytics) Responds ☐ Non-responsive ☐ Sedated ☐ Paralytics ☐ See comment ☐

O: (WOB, Color, Chest Expansion, BBS, Sputum Production, latest x-ray, pertinent pt assessment concerns, lab values, fluids)

General Skin Color
- ☐ Pink
- ☐ Ashy
- ☐ Cyanotic
- ☐ Jaundice

Skin Characteristics
- ☐ Warm
- ☐ Dry
- ☐ Diaphoretic
- ☐ Cool
- ☐ Moist

Mucous Membranes
- ☐ Pink
- ☐ Ashy
- ☐ Cyanotic

Work of Breathing
- ☐ Normal
- ☐ Mild
- ☐ Moderate
- ☐ High
- ☐ Absent

Chest Excursion
- ☐ Bilateral
- ☐ Unilateral
- ☐ Diminished
- ☐ Paradoxical/Flail

Chest Configuration
- ☐ Normal
- ☐ Other _____

☐ Subcutaneous Emphysema

- ☐ Tactile Fremitus
- ☐ Tracheal Deviation
- ☐ Abdominal Distention

Nailbeds
- ☐ Pink
- ☐ Ashy
- ☐ Cyanotic

Capillary Refill
- ☐ Rapid
- ☐ Sluggish

Auscultation
1) Clear
2) Wheeze
3) Crackles
4) Rhonchi

Anterior

Posterior
A. Good Aeration
B. Diminished
C. Absent

A: (Pt history, Admit dx. & date, events leading to intubation/trach/ventilation, significant problems, etc.)

P: (Care plan , standing orders, treatments)

WEANING MECHANICS		
TIME		
VC		
I/E FORCES		
VT		
RR		
VE		
f/VT		

Pt. EVENTS / CHANGES	Time	(Reasons for changes, significant pt. events, CT Scan, chest tube placement, BP problems, codes, etc.)

Signature _____ Initials _____

Fig. 52.3, cont'd

than the task of recording values. This responsibility is care of a critically ill, vulnerable patient with respiratory failure who is being supported by a lifesaving machine. The procedure for assessing a patient–ventilator system is outlined in Table 52.2. Although the importance of monitoring the patient–ventilator system has increased, the necessity of entering and transcribing numbers into an assessment sheet is decreasing. The era of electronic transfer of monitored data directly to patients' charts is becoming the standard. All modern ventilators have the capacity for data transfer, but until standardized transfer protocols, charting formats, and archiving methods have been established, electronic monitoring of the patient–ventilator system will continue to be customized to the local setting.

Graphics Monitoring

Monitoring of graphic tracings generated during mechanical ventilation has become widely available and accepted in the ICU. A visual display of pressure, flow, and volume tracings is available on all modern ventilators. Graphic displays are possible through the development of improvements in sensing technology, integrated circuitry, and graphic–user interface. Ventilators measure inspiratory and expiratory flow and circuit pressure with pneumotachometers and transducers. The volume displays are generated through calculation of an integral of the flow tracings. All three values (flow, pressure, and volume) can be displayed and plotted against time or each other (Fig. 52.4).

Monitoring During Lung-Protective Ventilation

A lung-protective ventilation strategy that reduces the risk of pressure injury to the lungs has evolved from numerous animal studies and several key clinical studies.[23] Meticulous monitoring of the status of all mechanically ventilated patients but especially those with ARDS or patients at risk of ARDS is necessary to avoid ventilator-induced lung injury. Four principles have been

TABLE 52.2 Assessing a Patient–Ventilator System

Step	Key Points
Gather correct equipment and supplies.	Respirometer, O_2 analyzer, stethoscope, and watch with second indicator are needed. *Note:* Most modern ventilators incorporate volume-measuring devices into the system. Additional auxiliary equipment may include pulse oximeter, cuff pressure manometer, suction and airway equipment, and sterile distilled water.
Review patient record.	Note patient's admitting diagnosis or problem list, physician orders, medications, vital signs, history and physical examination findings, progress notes, results of laboratory studies, chest radiograph, blood gases, and respiratory care notes.
Enter patient area; wash hands and put on gloves.	Inattention to proper handwashing and poor aseptic technique are associated with nosocomial infection.
Identify the patient.	Wristbands may sometimes be attached to the patient's leg or to the foot of the bed. If there is no attached name band, check with the patient's nurse.
Explain what you are doing.	Communication with the patient is important; even patients who appear unaware of their surroundings may be able to hear and understand. Use broad terms, such as "I'm here to assess your breathing."
Observe overall situation and note general patient condition, including level of consciousness, condition of extremities, presence of pallor, skin color, capillary refill, airway patency, circuit connection and patency, and findings on the electrocardiogram.	Note patient's general appearance, sensorium, color, and level of activity. Note equipment in use, including ventilator, circuit, airway type, humidification, manual resuscitation bag, and related equipment and supplies Ensure that the patient's condition appears stable and that ventilation is adequate.
Drain tubing and service humidifier, if needed.	This procedure should be done before the actual ventilator check if possible.
Attend to patient's airway if necessary.	Suctioning and other airway manipulation should be done before actual ventilator check if possible; after suctioning, note volume and character of secretions. Note endotracheal or tracheostomy tube stability and position; measure tube cuff pressure and volume to inflate. If ventilator check is performed first and the patient circuit or airway is disrupted, errors may not be caught, and one of the purposes of ventilator monitoring—patient safety—is defeated.
Inspect chest and note accessory muscle use, retractions, jugular vein engorgement, bilateral symmetric chest wall movement, symmetric diaphragm–chest wall movement, respiratory rate and rhythm, and chest wall stability (flail).	Be alert for signs of respiratory distress, increased work of breathing, or patient-ventilatory asynchrony. Observe patient effort to ensure adequate trigger sensitivity and inspiratory flow rate.
Auscultate chest.	Always move stethoscope from side to side to compare right and left sides of chest. Note adventitious breath sounds (crackles, rhonchi, wheezing, bronchovesicular breath sounds). Note diminished or absent breath sounds; if breath sounds are absent, attempt to ascertain cause immediately. Water in the tubing, use of chest tubes, or PEEP may result in adventitious sounds.
Percuss chest for dullness, resonance, or hyperresonance.	Dullness may be caused by pleural effusion, atelectasis, or consolidation. Resonance is the percussion note found over normal lung tissue. Hyperresonance is associated with excess air in the chest (pneumothorax, pulmonary hyperinflation).
Note location of trachea.	Tracheal shift is associated with severe atelectasis and tension pneumothorax.
Note peak pressure, static or plateau pressure (P_{plat}), baseline pressure (PEEP/CPAP), driving pressure, pressure support level, MAP, and presence of auto-PEEP.	Sudden increase in peak airway pressure is associated with pneumothorax, secretions in the airway, bronchospasm, fighting the ventilator, biting the endotracheal tube, occlusion of the airway, and bronchial intubation. Sudden decrease in peak airway pressure is associated with reversal of any of the above-mentioned conditions, a leak in the system, or patient disconnection. MAP may be useful in predicting a decrease in CO or barotraumas; the lowest possible MAP needed to achieve adequate ventilation and oxygenation should be used. P_{plat} >28 cm H_2O is associated with the development of ventilator-induced lung injury; if P_{plat} is ≥28 cm H_2O, consider reducing delivered V_T. A driving pressure >14 cm H_2O is associated with increased risk of mortality. Consider using tidal volume 4–6 mL/kg of predicted body weight, or consider lowering PEEP.
Record exhaled volume (mL/kg predicted body weight) and respiratory frequency.	Ensure ventilator compensates for compressible volume. If volume is measured at the exhalation valve, volume loss caused by tubing compliance may be calculated and subtracted from the measured volume.

TABLE 52.2 Assessing a Patient-Ventilator System—*cont'd*

Step	Key Points
If intermittent mandatory ventilation (IMV)/SIMV system is in use, calculate delivered volume per machine breath, spontaneous volume between machine breaths, machine rate, total rate, patient spontaneous rate, and minute ventilation.	For IMV/SIMV: $V_{ISP} = \frac{\dot{V}_{Etot} - \dot{V}_{Emech}}{f_{tot} - f_{mach}}$ For assist/control: $\text{Average } V_T = \frac{\dot{V}_{Etot}}{f_{tot}}$
If a ventilator graphics package is in use, observe pressure-time, flow-time, volume-time, and P-V curves.	Mode of ventilation, patient trigger, adequacy of machine inspiratory flow, and patient–ventilator synchrony can be evaluated with a ventilator graphics package. Slow flow P-V curve can be used to assess lower and upper inflection points. Overdistension can be elevated with use of dynamic P-V curve. Flow-volume curve may be helpful in assessing effect of bronchodilator.
Note delivered FiO_2.	FiO_2 should be analyzed.
Record other ventilatory values.	Ventilatory values include inspiratory flow, inspiratory time, I:E ratio, inspiratory and expiratory positive airway pressures (IPAP and EPAP), sigh volume and rate, airway temperature, compliance and resistance, and alarm settings. Many departments chart endotracheal tube size, tube length, cuff pressure or volume, use of minimal occluding volume or minimal leak, ventilator day, circuit change, and other therapy.
Record blood gas values and related data as appropriate.	These data may include pH, PaO_2, $PaCO_2$, SaO_2, hemoglobin level, HCO_3^- level, IPAP, base excess, and CaO_2. Blood gas data should be recorded in such a way that the corresponding FiO_2, PEEP, V_T, frequency, mode, and other ventilator settings on which the sample was obtained are noted.
Record results of other physiologic monitoring of cardiopulmonary system as appropriate.	These values may include SpO_2, $PETCO_2$, $PtcCO_2$, $PtcO_2$, $\dot{Q}_S/\dot{Q}_T$, and V_D/V_T.
Record hemodynamic data as appropriate.	These values may include heart rate, blood pressure, CVP, PAP, PCWP, $\dot{Q}_T$, cardiac index, $S\dot{v}O_2$, $P\dot{v}O_2$, $CaO_2 - C\bar{v}O_2$, pulmonary vascular resistance, and systemic vascular resistance.
Record weaning values as appropriate.	These values may include spontaneous frequency, V_T, f/V_T ratio, $\dot{V}_E$ VC, and inspiratory force (MIP).
Return all alarm systems to optimal condition. Complete charting using appropriate departmental forms or computer entry systems.	Alarms include low pressure, high pressure, disconnection, and volume. Apnea values should be reviewed. Apnea values usually are set to deliver an adequate V_T, f_{mach}, and FiO_2 (100%) in the event of apnea development.

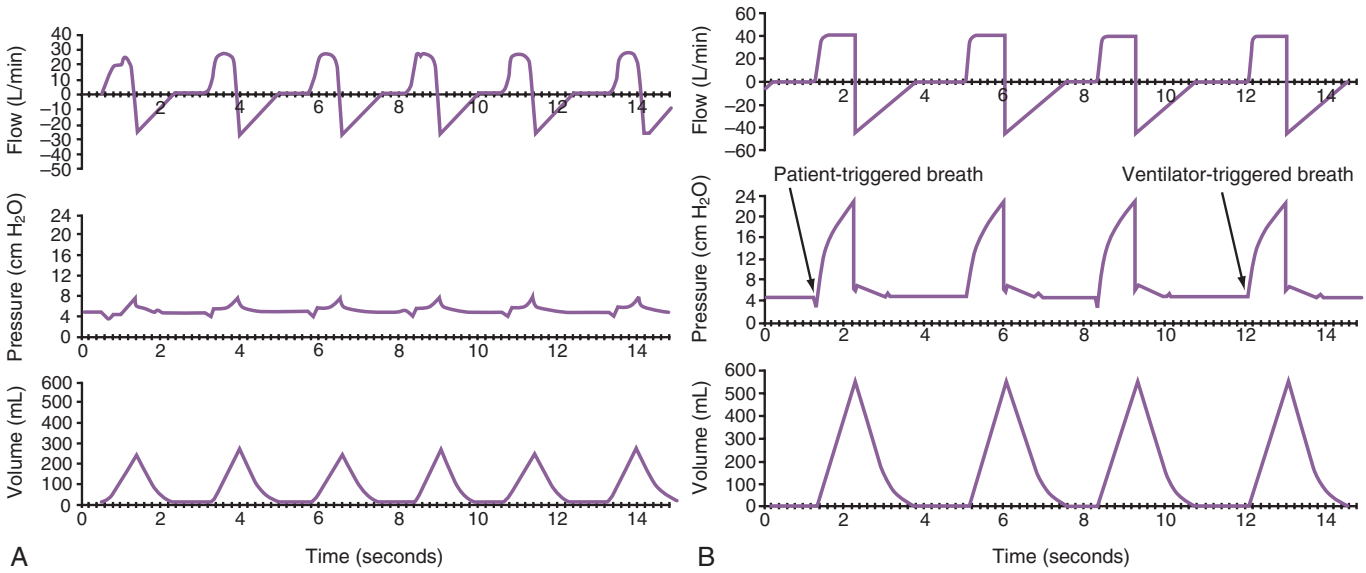

Fig. 52.4 Ventilator Graphics: Flow, Pressure, and Volume Tracings. (A) Spontaneous breathing at an elevated baseline pressure (continuous positive airway pressure [CPAP]). Flow, pressure, and volume curves show spontaneous breathing with a CPAP level of approximately 5 cm H_2O. The flow curve is sinusoidal, the pressure curve fluctuates approximately 1 to 3 cm H_2O around the baseline pressure, and the volume delivered varies. These are typical observations during spontaneous breathing. (B) Volume ventilation in the assist/control mode. Some breaths are time triggered and others are patient triggered. There is a square wave-flow pattern, and volume is constant breath to breath.

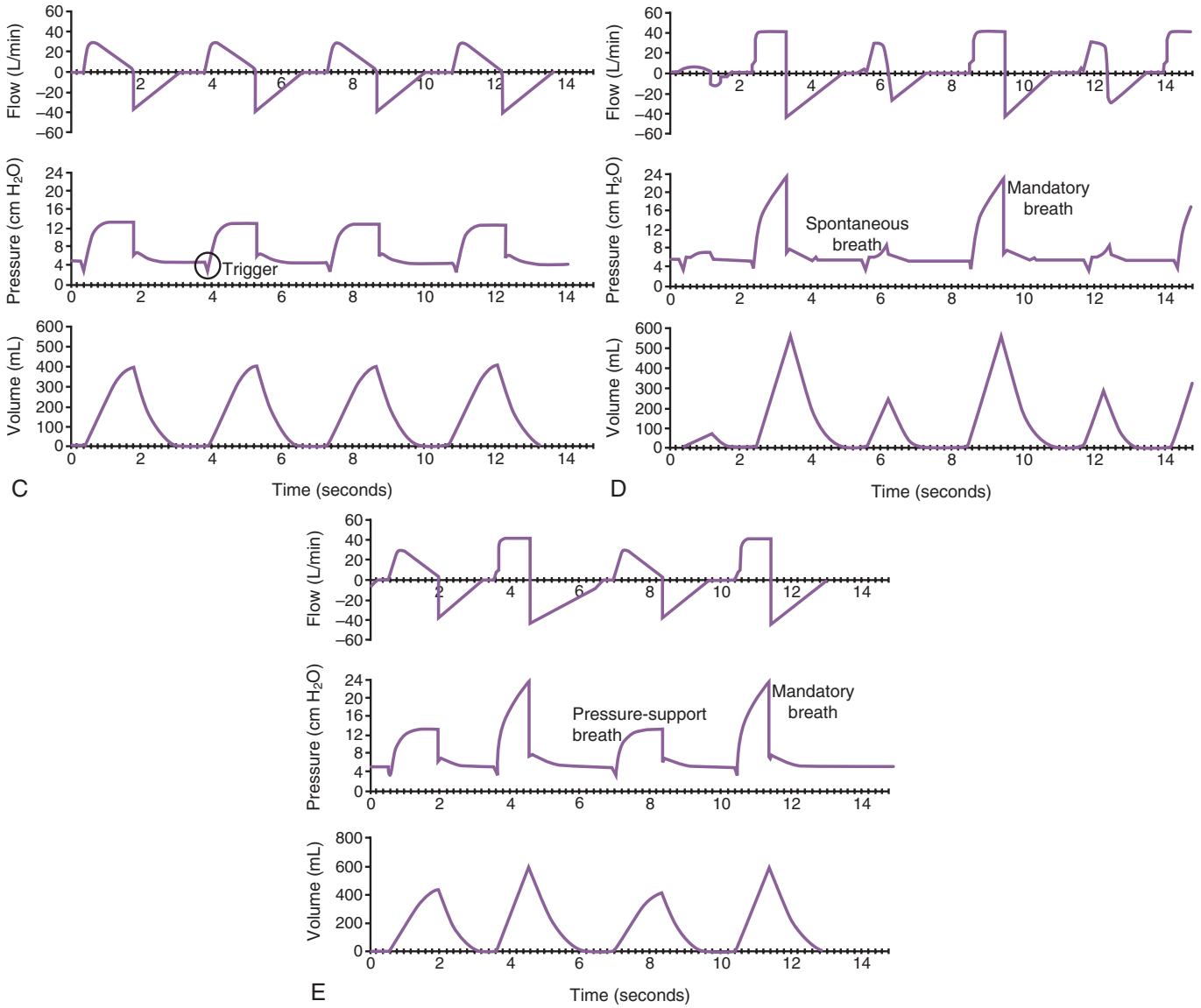

Fig. 52.4, cont'd (C) Pressure support breaths (pressure support ventilation). The patient trigger for each breath is evident. Flow is decelerating, and the pressure waveform approaches a square wave. (D) Synchronized intermittent mandatory ventilation (SIMV) with an elevated baseline positive end-expiratory pressure (PEEP). Spontaneous breathing and machine-mandatory breaths are interspersed. Spontaneous volume varies, but the SIMV breaths are constant at 600 mL. The square wave-flow pattern for mandatory breaths and sinusoidal flow during spontaneous breathing are evident. The baseline pressure (PEEP) is elevated at approximately 5 cm H_2O. (E) SIMV with pressure support. Mandatory breaths have a square flow waveform with a constant volume of 600 mL. The pressure support breaths have a decelerating flow waveform ad a pressure pattern approaching a square wave. In this example, there is also an elevated baseline of approximately 5 cm H_2O (PEEP).

confirmed: (1) reduce the risk of high-pressure exposure by limiting P_{plat} to less than 28 cm H_2O, (2) reduce the risk of excessive tidal ventilation stress by limiting driving pressure to less than 15 cm H_2O, (3) reduce V_T ventilation to 4 to 8 mL/kg of predicted body weight (PBW), and (4) maintain adequate end-expiratory lung volume with PEEP to avoid opening/closing injury.

Other considerations have received attention in monitoring patients with ARDS. Although P-V curves have been automated in ventilator algorithms, the clinical significance of curves determined from PEEP of 0 cm H_2O is questionable. However, current recommendations are to maintain ventilation on the upper portion of the deflation limb of the P-V curve to avoid alveolar derecruitment even though this position with the P-V hysteresis curve of a patient may be difficult to determine. A primary concern is to achieve adequate oxygenation in patients with lung injury, but this target can be deceptive if the price of adequate oxygenation is pressure injury to the lungs. An acceptable practice in ventilating these patients is permissive hypercapnia or pressure-protective ventilation that allows $PaCO_2$ to drift upward. This strategy is a higher frequency–lower V_T approach with the

predictable effect of decreasing pH (by increasing $PaCO_2$), which requires careful monitoring.

As previously discussed, poor chest wall or abdominal compliance must also be considered during lung-protective ventilation. This concern can be significant in obese patients. Essentially, the stiffer the chest wall or abdomen, the greater is the P_{plat} that can be established without inducing lung injury. Meta-analysis of higher versus lower PEEP suggests the use of higher levels of PEEP with patients suffering from moderate to severe ARDS, and high levels of PEEP should be used cautiously when mild ARDS is being treated.[24] Setting PEEP levels greater than 15 cm H_2O is often necessary in patients with moderate to severe ARDS to maintain oxygenation.[16] Elevated PEEP places greater importance on monitoring cardiovascular performance, plateau pressure, driving pressure, and development of barotrauma.

RULE OF THUMB Modern mechanical ventilators routinely display tracings of flow, pressure, and volume versus time. Ventilator graphics monitoring is a convenient visual method for monitoring patient–ventilator interaction. The graphic patterns allow rapid determination of mode of ventilation, breathing pattern, auto-PEEP, excessive pressure, secretions in the airway, synchrony, and triggering efforts.

STRESS INDEX

Another index involving the dynamic measurement of stress has been reported.[25] The **stress index** is a value derived from the airway pressure-time curve during constant flow delivery of a tidal breath. During constant flow (when resistance is constant), the slope of the pressure-time tracing is analyzed to evaluate the elastic properties of the lungs. The index is calculated by performing a curve fit of the slope of the pressure-time tracing, where pressure = a × time b + c. Ideally, a slope (b) of 1 indicates normal filling during lung expansion, whereas a slope greater than 1 indicates overdistension, and a slope less than 1 indicates lung recruitment (Fig. 52.5). This measure can be calculated for each delivered tidal breath, although an acceptance criterion should be used to exclude analysis of artifacts and factitious breaths. The stress index can be visually detected (without software) with good sensitivity and specificity and should be considered an additional tool for bedside monitoring of ventilator waveforms.[26]

Although the index may not determine a threshold for excessive stress or strain, it may be a useful indicator of lung response to positive pressure. If the chest wall contributes variably to airway pressure, the calculated index can be altered and deceptive.[27]

RULE OF THUMB During constant flow (when resistance is constant), the slope of the pressure-time tracing (stress index) can be analyzed to evaluate the elastic properties of the lungs. The stress index can be visually detected (without software) and should be considered an additional tool for bedside monitoring of ventilator waveforms.

MINI CLINI

Potential for Lung Injury

Problem

A patient with ARDS is being ventilated with volume assist control and constant flow. The pressure-time curve is visibly concave. Additionally, an inspiratory and expiratory pause is performed on the ventilator showing a plateau pressure of 32 cm H_2O and total PEEP of 14 cm H_2O. What could this indicate?

Solution

The patient appears to have a high stress index as demonstrated by a concave curvature of the pressure-time curve during constant flow. Also, the patient has a driving pressure of 18 cm H_2O (32 – 14 = 18). The patient is likely being ventilated near the upper inflection point of a pressure-volume curve. An attempt to lower tidal volume (if the patient does not have severe acidosis) should be made or to lower PEEP, as the patient may not be responsive to PEEP, and it is only causing overdistension of open lung regions.

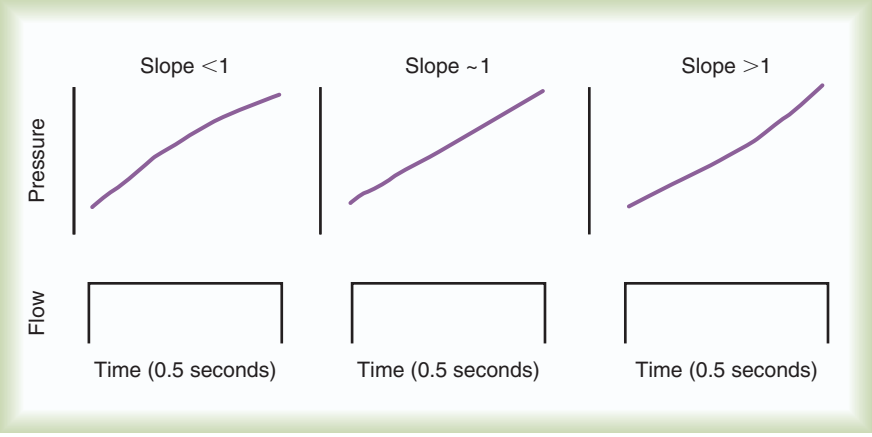

Fig. 52.5 Conceptual illustration of the dynamic pressure-time (p-t) curve. *Left,* convex curve (slope <1) indicating recruitment during the breath. *Center,* linear relationship between pressure and time (slope ~1), indicating no recruitment or overdistension. *Right,* concave curve (slope >1), indicating overdistension.

AUTO–POSITIVE END-EXPIRATORY PRESSURE (INTRINSIC POSITIVE END-EXPIRATORY PRESSURE)

PEEP is the pressure maintained in the airway by the ventilator at end-exhalation. An alveolar pressure that exists above the applied or extrinsic PEEP level at end-exhalation is termed intrinsic PEEP or auto-PEEP. At the bedside, total PEEP is the sum of extrinsic PEEP and intrinsic PEEP. Intrinsic or auto-PEEP is sometimes misunderstood when one considers "trapped" air versus breath stacking, which can occur when a patient is being passively ventilated with insufficient time to exhale. Intrinsic or auto-PEEP is often the result of small airway collapse or severe bronchospasm and can also occur when excessive tidal volume is delivered to a patient with a high ventilatory demand, causing dynamic hyperinflation when the patient has difficulty exhaling all of the excess volume.

Numerous factors, both internal and external to the patient, contribute to the development of auto-PEEP. Expiratory muscle activity can increase auto-PEEP and may interfere with attempts at assessment of auto-PEEP based solely on dynamic hyperinflation. Patients receiving mechanical ventilation for obstructive airways disease have a large degree of inhomogeneity in the emptying of lung units, and auto-PEEP can develop even at relatively low minute ventilation. Auto-PEEP is common in mechanically ventilated patients receiving high minute ventilation and occurs in patients with ARDS.[28] An increase in mean alveolar pressure owing to auto-PEEP may exacerbate the hemodynamic effects of positive-pressure ventilation and increase the likelihood of barotrauma in a manner similar to the application of PEEP. In addition, the presence of auto-PEEP makes it more difficult for the patient to trigger a ventilator-assisted breath because auto-PEEP imposes an inspiratory pressure threshold resistor, which the patient must overcome before any inspiratory flow begins.

Finally, if unrecognized, auto-PEEP leads to erroneous calculation of static lung compliance by underestimating total PEEP. Decreasing minute volume can reduce or eliminate auto-PEEP; however, minimal auto-PEEP can be benign. In addition, increasing expiratory time allows more time for airways to empty normally, thereby decreasing auto-PEEP. The use of extrinsic PEEP, when set appropriately, can partially overcome the trigger sensitivity problem seen with auto-PEEP and may provide a "stent" to allow more complete lung emptying and a decrease in patient effort, primarily in patients with dynamic airway collapse.[29] Setting PEEP slightly below the level of auto-PEEP can also help to offset the inspiratory pressure threshold by which auto-PEEP can hamper liberation from mechanical ventilation. Measuring auto-PEEP is therefore very important when liberation from mechanical ventilation is planned.

Methods for Determining Auto–Positive End-Expiratory Pressure

Dynamically, auto-PEEP varies throughout the lungs; however, all measurements of auto-PEEP reflect an average auto-PEEP level throughout the lungs. Assessment of auto-PEEP involves first its detection and then a measurement. Patients at risk for auto-PEEP include those in whom expiratory flow limitation is more common; this includes patients with COPD, obesity, heart failure, and ARDS (particularly at low PEEP).[30] Auto-PEEP may be further suspected if flow continues at end-expiration as seen on ventilator graphics monitoring (Fig. 52.6). In this case, auto-PEEP must be present unless there is active contraction of the expiratory muscles producing end-expiratory flow. The following methods are used to estimate auto-PEEP level.

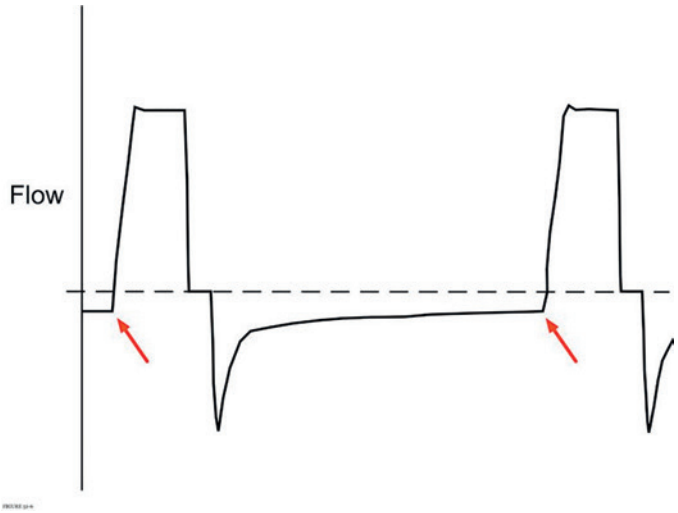

Fig. 52.6 Expiratory flow waveform that does not return to zero flow at end exhalation. Whenever this occurs, auto–positive end-expiratory pressure is almost always present.

End-Expiratory Hold by the Ventilator

Either automated or manual, an end-expiratory hold by the ventilator closes the expiratory valve at end-exhalation. The hold period must extend until the end-expiratory pressure has been stabilized; otherwise the value will be an underestimate of auto-PEEP.

Esophageal Pressure Measurements

An **esophageal balloon** is used to measure the deflection in the pleural space required to trigger the ventilator. The change in esophageal pressure from baseline to the pressure initiating flow at the airway is equal to the total PEEP that must be overcome to trigger a breath.

Using Positive End-Expiratory Pressure With Auto–Positive End-Expiratory Pressure

PEEP can be applied to a level that results in flow at end-exhalation being closer to zero (this is possible in some patients). The concept involves stenting of the airways by PEEP to allow lung emptying and a better equilibration of end-expiratory alveolar pressure with end-expiratory ventilatory circuit pressure minimizing the pressure needed to decompress the alveoli and trigger the ventilator.[29] This maneuver is essentially performed by slowly increasing applied PEEP until every patient effort triggers a ventilator breath. It is important not to exceed the patient's auto-PEEP when external PEEP is being increased. Targeting approximately

80% of the total PEEP should be sufficient to improve the patient's ability to trigger the ventilator.

MINI CLINI

Ventilator Graphics

Problem

The ventilator graphic display of a patient with COPD receiving mechanical ventilation is showing two distinct features: (1) a pressure-time tracing with spikes and dips that is generally irregular and (2) a flow-time tracing that does not reach zero flow at end expiration. What do these findings indicate?

Solution

Graphic displays of pressure and flow allow rapid identification of the presence of secretions, auto-PEEP, and asynchrony. The irregular tracing implies the presence of airway secretions. Auscultation of the lungs should be performed to assess the need for endotracheal suctioning. Without an active expiratory effort, the existence of flow at end expiration confirms the presence of auto-PEEP. Auto-PEEP can be detected in many COPD patients receiving mechanical ventilation. However, intervention to reduce or eliminate auto-PEEP may be unnecessary. Auto-PEEP should be estimated regularly. More importantly, the effects of auto-PEEP on the ability to trigger the ventilator or on cardiovascular dynamics (caused by reduced venous return) should be monitored. For reducing or eliminating auto-PEEP, adjusting the ventilator settings or bronchodilator therapy may be required. If the patient is unable to trigger every breath because of the auto-PEEP, then PEEP should be applied in steps of 1 to 2 cm H_2O until the patient is able to trigger the ventilator with every inspiratory effort.

Ventilator manufacturers have developed graphic displays that allow astute clinicians to base decisions on many more factors than gas exchange values (Box 52.10). However, the study and verification of features observed in ventilator graphics have not kept pace with the developing technology in ventilators. Ventilator graphics show many important patient–ventilator interactions, such as presence of auto-PEEP, elevated airway pressure, presence of secretions, and general pattern and dependability of supported ventilation (Fig. 52.7). The potential for expanded use of ventilator graphics awaits further investigation of the clinical importance of the graphic displays. For more details, see Chapter 48.

BOX 52.10 Purposes of Graphics Monitoring

- Confirm mode functions
- Detect inadequate flow in volume ventilation
- Detect too lengthy an inspiratory time
- Set appropriate rise time and termination criteria in pressure ventilation
- Detect auto-PEEP
- Determine patient–ventilator synchrony
- Assess and adjust trigger levels
- Measure work of breathing
- Adjust V_T and minimize overdistension
- Assess effect of bronchodilators
- Detect equipment malfunction
- Determine appropriate PEEP level

MONITORING BREATHING EFFORT AND PATTERNS

Work of Breathing

Work of breathing (WOB) is often increased in critically ill patients. Commercial systems are available for measuring WOB in ventilated patients. For measuring the WOB, changes in Ptp must be measured. The procedure requires an assessment of pleural pressure, which is normally estimated by esophageal pressure after placement of an esophageal balloon catheter. The measurement is estimated from the esophageal pressure–versus-volume curve (Fig. 52.8).

Patients with severe obstructive or restrictive lung disease "work" at levels two to three times this normal value at rest, with marked increases in work at higher minute ventilation. How much work a patient can tolerate before the ventilatory muscles fatigue is unclear. Maintaining adequate spontaneous ventilation is impossible in many patients when the workload exceeds 0.15 kg/m/L (1.5 J/L).

Monitoring WOB may be valuable in certain situations, such as liberation from mechanical ventilation. Clinicians are expected to assess a patient's WOB continually and to take appropriate action if WOB becomes excessive. Because a direct measurement of WOB requires esophageal manometry, simpler indicators are sought. Monitoring the patient's spontaneous breathing rate, V_T, and **frequency/tidal volume (f/VT) ratio** provides useful surrogates for WOB during ventilator weaning trials. Assessment of the patient's overall clinical presentation is also useful in assessing the WOB. Increased WOB is associated with a rapid shallow breathing pattern, rapid pulse rate, hypertension, and use of accessory muscles of ventilation. Values of f/V_T greater than 105 during spontaneous breathing predict failure of successful liberation from mechanical ventilation.

Pressure-Time Product

The **pressure-time product** (PTP) is the area encompassed by the esophageal pressure-time tracing during inspiration, as shown in Fig. 52.8. PTP is simpler to measure than WOB because it does not require simultaneous measurement of volume. PTP values parallel changes in effort and the O_2 cost of breathing because PTP includes a measure of the "isometric" component of muscle contraction.[31] This index includes work and effort components that may indicate endurance during a trial of liberation from mechanical ventilation.

Oxygen Cost of Breathing

The amount of O_2 consumed by the ventilatory muscles ($\dot{V}Q_2R$) is an estimate of respiratory effort at its most basic level. $\dot{V}Q_2R$ can be estimated by measurement of O_2 consumption during active breathing compared with the patient being fully supported in the control mode:

$$\dot{V}O_2R = \dot{V}O_2 \text{ active breathing} - \dot{V}O_2 \text{ apnea}$$

Normal $\dot{V}Q_2R$ is approximately 2% to 5% of total O_2 consumption; however, $\dot{V}Q_2R$ can be 30% of total O_2 consumption during hyperventilation owing to severe dyspnea. Theoretically, $\dot{V}Q_2R$ accounts for all factors that tax the respiratory muscles—that

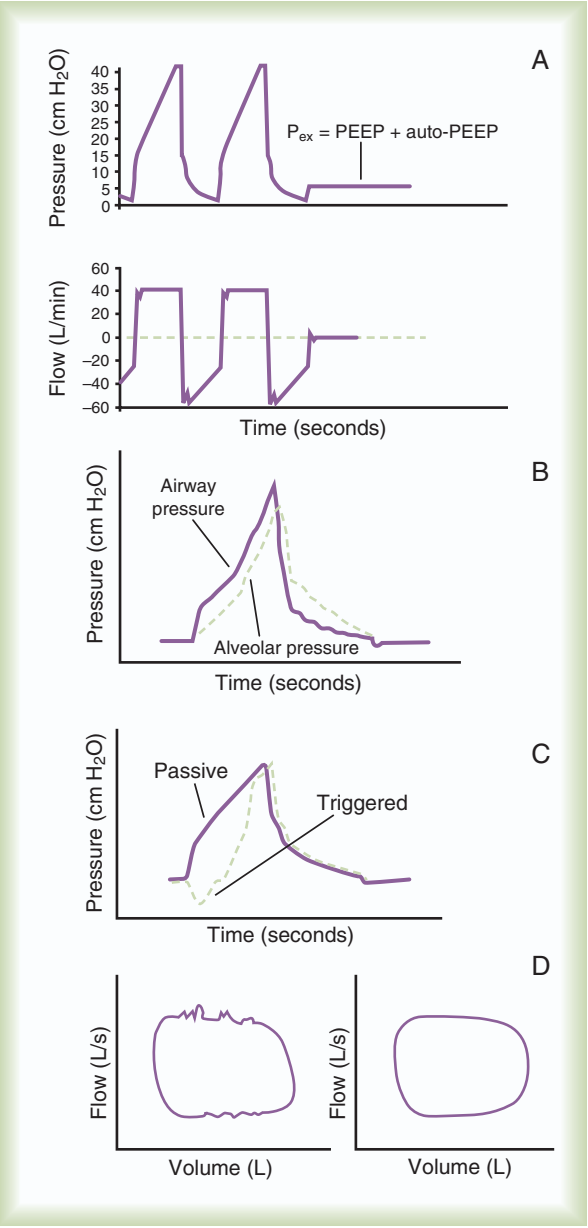

Fig. 52.7 Patient–ventilator interactions are easily identified from tracings of continuous monitoring of pressure, volume, and flow. (A) Auto–positive end-expiratory pressure (auto-PEEP). Flow and pressure tracings during ventilator-supported breaths and during end-expiratory occlusion. The airway pressure during the end-expiratory occlusion is an auto-PEEP estimate. (B) Overdistension. The upper concavity of the airway pressure-time tracing is indicative of overdistension. This example also shows alveolar pressure and its corresponding overdistension. (C) Patient effort. This is an example of mechanically ventilated passive inflation pressure and the airway pressure-time tracing deformation caused by patient effort. (D) Presence of secretions. P-V tracing of a ventilator-supported breath displays the presence of secretions. The inspiratory and expiratory limbs are irregular (not smooth) when secretions are present. An irregular airflow-time tracing can also indicate the presence of secretions.

is, the external workload and the efficiency of the conversion between cellular energy and useful work. $\dot{V}Q_2R$ is difficult to measure if the patient's condition is unstable. Other measures of respiratory muscle function are sought to assess the cost of breathing.

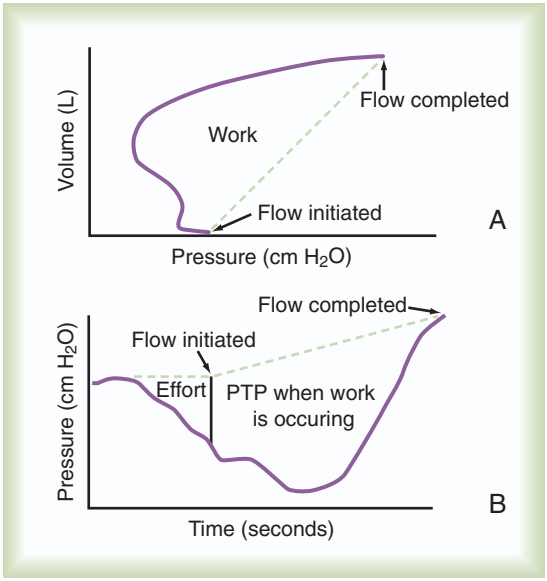

Fig. 52.8 Work of breathing (WOB) (A) and pressure time product (PTP) (B) from the same spontaneous breath of a patient receiving ventilatory support. *Dashed lines* represent a tracing of passive inflation by a ventilator-supported breath. Areas of work and PTP are not directly comparable because WOB units (pressure-volume curve [P-V]) and PTP units (pressure-time) differ. The area of effort in the total PTP area occurs before (and in addition to) the work measurement.

Assessing Ventilatory Drive

Until more recently, little attention was paid to measurement of respiratory drive during critical illness. During machine-assisted breathing, ventilatory drive can play an important role in determining the patient's energy expenditure. One study showed that patients not being liberated from mechanical ventilation often have an elevated drive to breathe and a limited ability to respond to increases in ventilatory load (e.g., increased $PaCO_2$).[32]

Airway Occlusion Pressure

A measure that has been used to index drive is the airway occlusion pressure ($P_{0.1}$ or P_{100}). $P_{0.1}$ is the pressure recorded 100 ms after initiation of an inspiratory effort against an occluded airway. $P_{0.1}$ is influenced by muscle strength and is a good measure of respiratory drive. Because the airway is occluded momentarily, there is no flow; therefore it is independent of resistance, and inhibitory reflexes cannot be influenced because there is no change in lung volume. In healthy subjects, $P_{0.1}$ is within the range of 0.5 to 1.5, but in mechanically ventilated patients, these levels can indicate excessive assistance by the ventilator.[33] Elevated $P_{0.1}$ (>5 cm H_2O) is associated with a continued need for mechanical ventilation and excessive effort. $P_{0.1}$ has also been used to detect a response to external PEEP in patients with hyperinflation and intrinsic PEEP; a decrease in $P_{0.1}$ with the application of PEEP indicates a decrease in intrinsic PEEP and WOB.[34]

In a sophisticated, commercially available system, a direct measure of the neural drive to breathe from the phrenic nerve can be measured by a catheter positioned within the esophagus. This signal is integrated into a feedback circuit in a modern ventilator. As a mode within the ventilator, flow delivery is

coordinated and augmented in response to the neural drive to breathe; this is known as neurally adjusted ventilatory assist (NAVA). (See Chapters 46 and 49 for details.)

MINI CLINI

Monitoring Patient Effort

Problem

A patient on pressure support ventilation of 10 cm H_2O with PEEP of 5 cm H_2O and FiO_2 0.55 is inspiring approximately 10 mL/kg of predicted body weight during pressure support ventilation. A P0.1 measurement is performed and demonstrates a value of 8 cm H_2O. What do these findings indicate?

Solution

The patient has an excessive amount of respiratory drive and is inspiring a high tidal volume.

This may contribute to lung injury if it continues. It is important to look at the trends of ventilator settings and minute ventilation to see if the patient is trending toward higher inspiratory effort or increasing ventilatory support needs. Additionally, look at blood work and patient temperature for any signs of infection. The solution may be to take over the work of breathing and control tidal volume with assist control ventilation until the underlying condition resolves.

RULE OF THUMB Elevated P0.1 (>5 cm H_2O) is associated with a continued need for mechanical ventilation and excessive effort. P0.1 has also been used to detect a response to external PEEP in patients with hyperinflation and intrinsic PEEP; a decrease in P0.1 with the application of PEEP indicates a decrease in intrinsic PEEP and WOB.

Diaphragm Ultrasound

Diaphragm ultrasound is a relatively new and promising method of evaluating and monitoring diaphragm function. Diaphragm excursion measurements have been used clinically in the past, but mostly during spontaneous breathing, and they are not considered to be an accurate measure of inspiratory effort when someone is receiving mechanical ventilation. The two techniques increasingly used during mechanical ventilation are the diaphragm's thickness measurement (Tdi) and the diaphragm's thickening fraction (TFdi). Changes in diaphragm thickness over time (both decreasing and increasing thickness) have been shown to be associated with prolonged mechanical ventilation. Diaphragm thinning is most likely due to atrophy, and diaphragm thickening is most likely due to excessive effort. A change in diaphragm thickness greater than 10% of baseline (after initiation of invasive mechanical ventilation) was associated with prolonged mechanical ventilation.[35] Measurement of TFdi with ultrasound is a noninvasive way of quantifying inspiratory effort. It is calculated as follows:

$$\text{Thickening fraction (\%)} = \frac{(Tdi_{peak-inspiratory} - Tdi_{end-expiratory})}{Tdi_{end-expiratory}} \times 100$$

where (Tdi-peak-inspiratory) is the diaphragm thickness at peak inspiration and (Tdi-end-expiratory) is the diaphragm thickness at end-expiration.

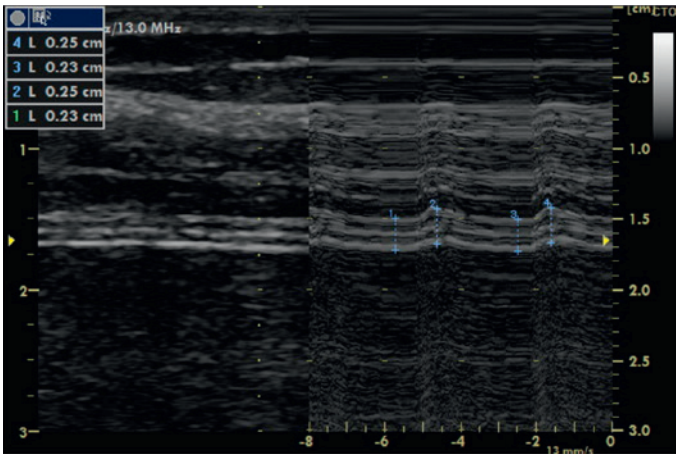

Fig. 52.9 A thickening fraction (TFdi) of 9%, indicating a weak effort from the patient. Demonstrates a TFdi of 72% to 79%, indicating excessive effort from the patient.

A TFdi between 15% and 30% has been shown to be an optimal range of inspiratory effort; inspiratory effort outside of this range (lower or higher) has been associated with an increased duration of mechanical ventilation (Fig. 52.9). Additionally, the maximum thickening fraction (TFmax) is performed without any ventilatory support or PEEP and can be used to assess diaphragm function, with a TFmax of less than 20% indicating severe diaphragm dysfunction.[36]

Rapid Shallow Breathing Index

When muscular strength is limited, patients tend to meet minute ventilation ($\dot{V}_E$) requirements by increasing frequency (f) while decreasing V_T. Although smaller breaths require less effort, rapid shallow breathing increases dead-space ventilation, causing a need for higher minute ventilation to eliminate CO_2. A very high and continuously increasing frequency (>30 breaths/min) is a sign of ventilatory muscle decompensation and potentially impending fatigue.

Considerable attention has been focused on the rapid shallow breathing index (f/V_T ratio), a simple bedside index that indicates whether mechanically ventilated patients can breathe without mechanical assistance.[29] The f/V_T ratio is easy to measure and is independent of the patient's effort and cooperation. Discontinuation of ventilator support is likely to prove successful if the f/V_T ratio is less than 105 breaths per minute per L within 1 to 2 minutes of a brief trial of fully spontaneous breathing.[37]

Respiratory Inductive Plethysmography

Respiratory inductive plethysmography is a noninvasive means of monitoring frequency, V_T, fractional duration of inspiration (Ti/Ttot), and respiratory muscle coordination. With this technique, loose elastic bands encircle the chest and abdomen. Band expansion and contraction during ventilation (spontaneous or supported) provides a volume-time plot that can also reflect short-term shifts in actual lung volume.

Monitoring Strength and Muscle Endurance

Two values commonly used for the bedside assessment of respiratory muscle strength are **vital capacity** (VC) and **maximal**

inspiratory pressure (MIP), also known as negative inspiratory force (NIF). A VC maneuver can be performed at the bedside with a simple respirometer connected to the patient's airway. Because VC is effort dependent, accurate measurements can be obtained only when the patient is conscious and cooperative. Because of an expected variability in bedside VC, three measurements should be obtained and the best result should be reported. Healthy persons are able to generate a VC of approximately 70 mL/kg. A VC less than 10 to 15 mL/kg indicates considerable muscle weakness. Spontaneously breathing patients with such weakness are unlikely to achieve liberation from mechanical ventilation, and those who are breathing spontaneously may require intubation and mechanical ventilation.

MIP is a more specific measure than VC. MIP provides information based solely on maximum output of the inspiratory muscles. A maximum stimulus is provided by total occlusion of the airway. In contrast to the VC maneuver, the MIP maneuver can be performed on unconscious or uncooperative patients. Measurement of MIP at the bedside requires an aneroid manometer with a maximum value indicator. In an effort to make the measurements more reliable, a modified technique has been described in which a one-way valve is attached to the airway to ensure that inspiratory effort is made at a low lung volume.[38] While a 20-second occlusion was maintained, the values with the one-way valve in place were approximately one-third more negative than values without such occlusion (Fig. 52.10).

Endurance: Maximal Voluntary Ventilation

Respiratory muscle fatigue (lack of endurance) may be a cause of respiratory failure. **Maximum voluntary ventilation (MVV)** is a measure used to assess respiratory muscle reserve, endurance, or fatigue. VC is measured to assess the patient's coordinated muscle function from a single breath; MVV is measured to determine the ability of a patient to sustain ventilation over time. Similar to the VC maneuver, the MVV procedure can be performed with a respirometer attached to the patient's airway as the patient is encouraged to breathe as deeply and as fast as possible over a predefined time interval (10 or 15 seconds). The value is extrapolated to a full minute.

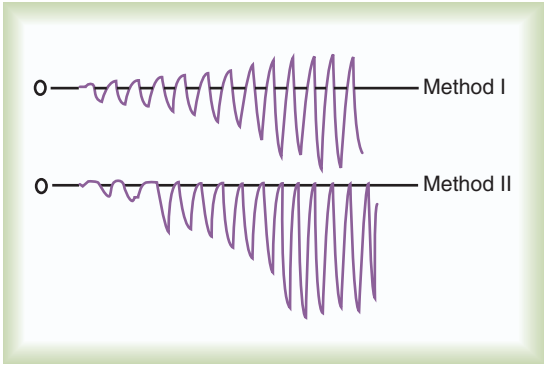

Fig. 52.10 Measurement of maximum inspiratory pressure during 25 seconds of airway occlusion. *Method I* occludes by sealing the airway to allow no movement of air. *Method II* occludes inspiratory flow but allows expiratory flow through a unidirectional valve.

Normal MVV values for adults range from 120 to 180 L/min. Values less than twice the spontaneous minute ventilation are associated with difficulty in maintaining spontaneous ventilation without mechanical assistance.[39]

RULE OF THUMB To achieve successful liberation from mechanical ventilation, the patient must have adequate gas exchange, respiratory muscle strength and endurance, and WOB that is not excessive. The process that caused respiratory failure must be partially if not completely resolved. Although numerous values have been studied to indicate the probability of successful weaning, a frequency-to-VT ratio less than 105 has been the best index of ability to achieve liberation from mechanical ventilation.

LUNG IMAGING AT THE BEDSIDE

The extent of gas exchange abnormalities is revealed by ABG values and SpO_2, but the location or source of the disorder remains unknown. The source but not the extent or type of the pathologic process can be assessed by auscultation. Localization of the disorder within the lungs is more precisely achieved by static images obtained by radiographic techniques, such as chest x-ray or computed tomography (CT). These assessments are key to directing therapeutic approaches and for tracking changes in pathology (see Chapter 21). However, thorough imaging studies frequently require transporting the patient to a radiology suite, and transport presents risks to the patient.[40] Also, the imaging is often static (not dynamically obtained throughout the ventilator cycle).

Lung imaging techniques that can be used at the bedside to actively locate regions of interest have been developed more recently. Two techniques that allow imaging of the lungs during ventilation are lung ultrasound and **electrical impedance tomography** (EIT). Each technique produces dynamic imaging of lung regions to assess the extent of injury. With lung ultrasound and EIT, there is an opportunity to perform bedside evaluation of the effects of PEEP, recruitment maneuvers, or other changes in ventilatory support.

LUNG ULTRASOUND

Ultrasound technology was traditionally thought to not be particularly helpful for imaging the lungs because air-filled lung tissue is not penetrated by ultrasound. However, the artifacts created by pathologic processes inside and outside of the lungs have led to the increasing use of **lung ultrasonography** in acute care, particularly in the emergency department. The common artifacts assessed during lung ultrasound are A-lines (horizontal lines), representing a normal artifact in air-filled lungs; B-lines (shining vertical lines), which appear when interstitial pulmonary edema is present; hyperechoic areas (brighter than normal), which appear in the presence of collapse and consolidation; and hypoechoic areas (darker than normal), which may indicate areas of pleural effusion. Pneumothorax, empyema, pleural effusions, alveolar consolidation, atelectasis, and interstitial pulmonary edema can all be assessed by lung ultrasonography; their extent can be defined and treated with the use of ultrasound. As a

diagnostic tool, lung ultrasonography is relatively inexpensive, usually available in the ICU, can be performed in 15 minutes, and does not emit ionizing radiation. There is potential for ultrasonography to evaluate the lung expansion effects on atelectatic lung tissue using recruitment maneuvers or after adjustment of PEEP in the ICU. Additionally, a "lung monitoring" scoring system has also been used to assess the daily progression of lung ultrasound findings while patients are in the ICU. The presence of A-lines contributes nothing to the score, whereas B-lines (Fig. 52.11) and consolidated areas (Fig. 52.12) are rated for severity and can be monitored daily.[41]

RULE OF THUMB Pneumothorax, empyema, pleural effusions, alveolar consolidation, atelectasis, and interstitial pulmonary edema can all be assessed by lung ultrasonography; their extent can be defined and treated with the use of ultrasound.

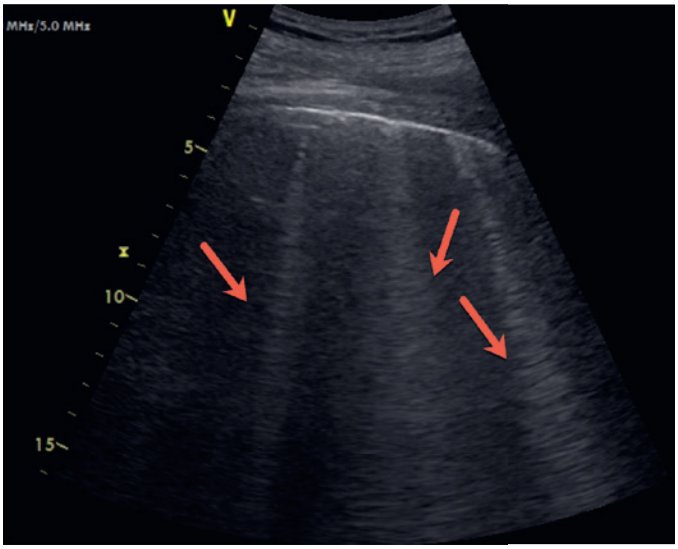

Fig. 52.11 B-lines present on lung ultrasound. The *red lines* show shining beam–like artifacts when there is interstitial pulmonary edema.

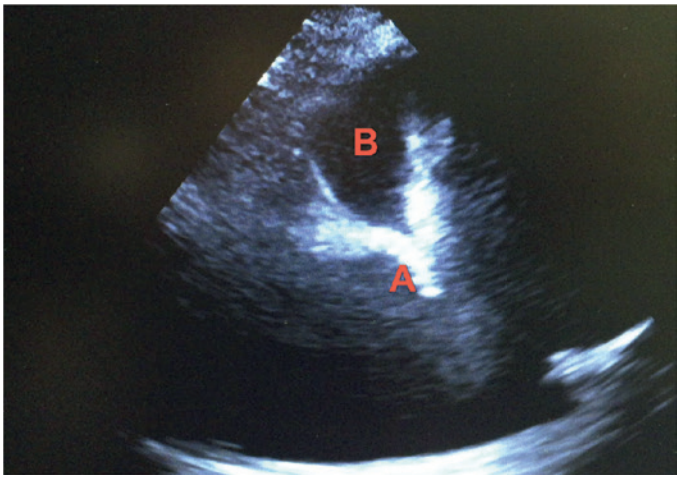

Fig. 52.12 (A) Hyperechoic area on lung ultrasound representing alveolar collapse and consolidation. (B) Hypoechoic area on lung ultrasound representing pleural effusion.

ELECTRICAL IMPEDANCE TOMOGRAPHY

EIT requires placement of electrodes (16 or 32 electrodes depending on the device used) around the chest, typically between the fourth and fifth intercostal spaces. Recent designs utilize an expandable rubber belt or adhesive strips (of various sizes) with embedded electrodes connected to a computing device with monitor. A small alternating current is sent from a reference electrode to each electrode around the chest, and impedance is measured between adjacent electrodes. The reference point rotates around the chest in a circular motion and repeats measurements approximately 50 times per second, capturing images that are reconstructed into a real-time animated graphic on the screen; this is referred to as the dynamic image. The thickness of the band is no more than a few inches, but—due to the method of sending the alternating current—it represents a lung field that is at least 14 cm in height. The images displayed represent a cross section, similar in perspective to a CT scan, looking from the foot of the bed toward the head of the bed (caudal→cranial view); the left side of the image on the screen represents the right side of the patient and right side of the image represents the left side of the patient. Global as well as regional information can be assessed.

The impact of changed ventilator settings on the distribution of ventilation can be assessed by comparing EIT images before and after the adjustment (Fig. 52.13). Trends can also be utilized to see stability of ventilator adjustments over time. With the integration of flow, volume, and pressure readings from the ventilator or pneumotach, EIT allows the monitoring of various forms of asynchrony, and built-in software can provide diagnostic tools to determine the PEEP level where overdistension and collapse are balanced. The effects of excessive spontaneous efforts causing "pendelluft" can also be seen with EIT—a new area of study providing evidence of the potential harmful effects of spontaneous breathing in patients with severe ARDS.[42,43]

EIT devices can also monitor changes in end-expiratory lung impedance (representing changes in FRC) during and after PEEP adjustment; this is particularly helpful in determining the impact of changing PEEP, particularly in patients with heterogeneous lung disease (Fig. 52.14). Modern EIT devices have also been equipped with the ability to measure the impedance of fluid distribution through the lung, allowing assessment of lung perfusion at the bedside.[44]

The ability to monitor ventilation distribution, response to PEEP, asynchrony, the impact of excessive spontaneous effort, and lung perfusion at the bedside has established an entirely new era of bedside monitoring focused on the individualization of mechanical ventilation.

CARDIAC AND CARDIOVASCULAR MONITORING

The cardiovascular system is routinely monitored in the critical care setting because patient survival depends on reliable, competent cardiac and cardiovascular performance. There is little question about the importance of monitoring electrocardiography

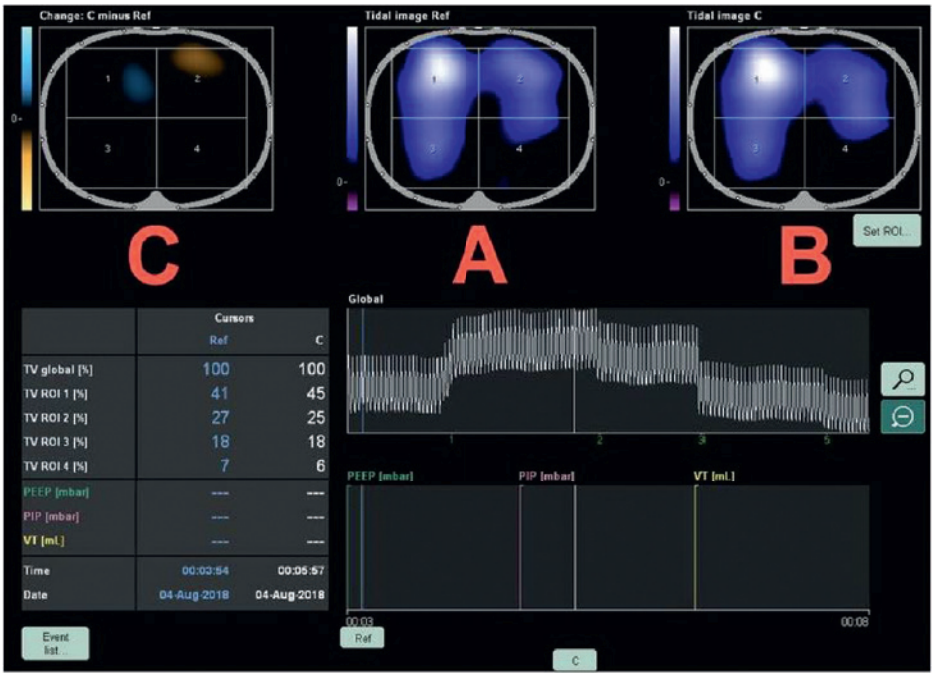

Fig. 52.13 Electrical impedance tomography (EIT) was applied to a patient with left-sided pneumonia. (A) EIT image showing the distribution of ventilation before an increase in positive end-expiratory pressure (PEEP). (B) EIT image showing the distribution of ventilation after an increase in PEEP. (C) EIT image showing the difference between A and B, where *blue* areas represent a gain in ventilation distribution the area and *orange* areas represent a loss. The increased iPEEP did appear to recruit the area affected by the pneumonia. This is evident by the lack of improvement in ventilation to the left dorsal region (region 4 in the bottom right corner of the image).

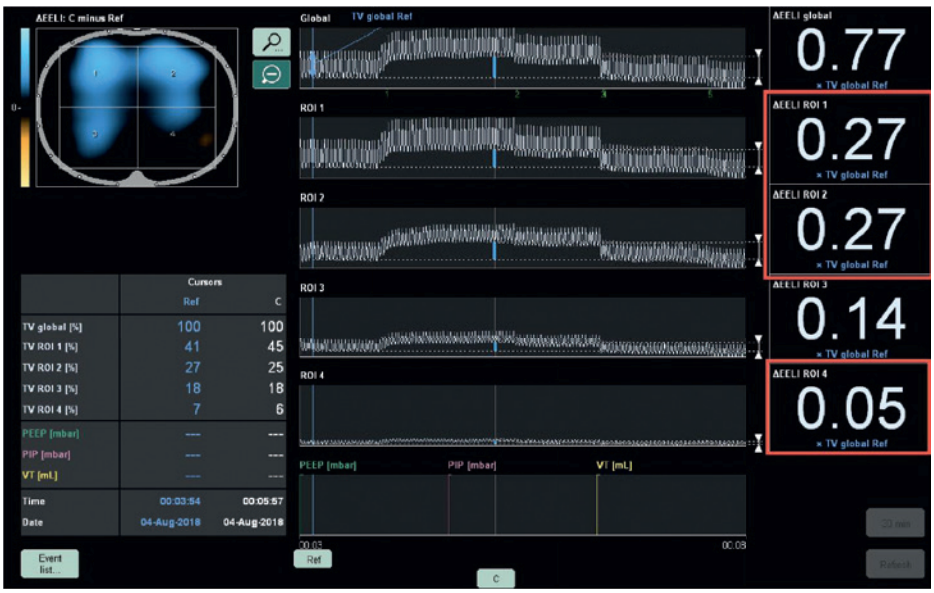

Fig. 52.14 Electrical impedance tomography trend showing the change in end-expiratory lung impedance (ΔEELI) after the increase in positive end-expiratory pressure (PEEP) described in Fig. 52.13. There was an increase in functional residual capacity (FRC) more than five times that of region 4 (the patient's left dorsal region). PEEP did not improve FRC in the affected area; therefore the area is not recruitable.

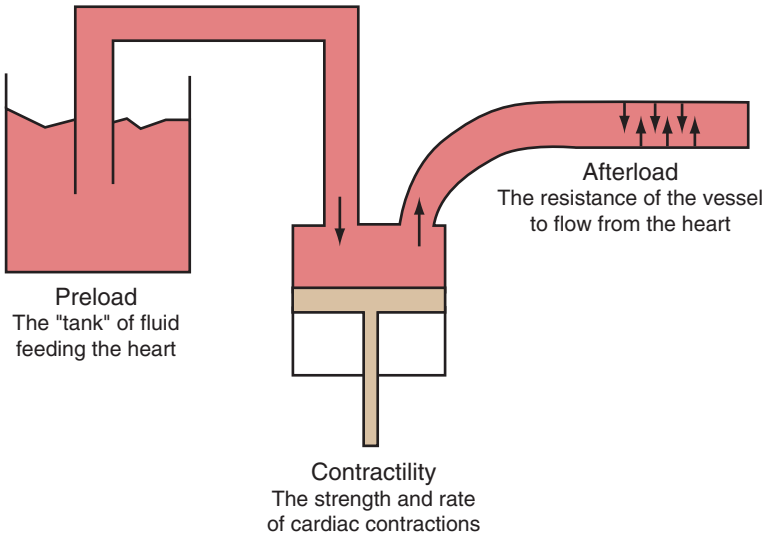

Fig. 52.15 Preload Contractility and Afterload.

(ECG), a noninvasive, continuous assessment of the performance of the conduction system of the heart. In the care of acutely ill patients, there may be clear justification for continuous monitoring of arterial blood pressure. More controversial has been the assessment of left ventricular function by right heart catheterization with measurement of pulmonary capillary wedge pressure (PCWP) and continuous monitoring of pulmonary artery pressure (PAP) (Fig. 52.15). Table 52.3 summarizes cardiovascular monitoring criteria with normal ranges and abnormal values.

ELECTROCARDIOGRAPHY

The conduction system of the heart is monitored in the ICU with a purpose different from that of the standard 12-lead ECG examination (see Chapter 18). The standard 12-lead ECG can be used to analyze disturbances in the conductive pathway that allow location and extent of injury or the source of arrhythmia. The ECG in the ICU is used primarily to detect and manage arrhythmias such as tachycardia, bradycardia, atrioventricular dissociation, ventricular tachycardia, atrial flutter, premature ventricular contractions, and ventricular fibrillation. For this purpose, there is a need for only three electrodes: right arm (or shoulder or right upper chest), left arm (or shoulder or left upper chest), and left lower chest. The deflections usually represent lead II of a standard 12-lead ECG. The direction or amplitude of the waves is of lesser concern than the rhythms being displayed.

When any arrhythmia is detected, therapy or intervention should be considered. The source of the arrhythmia often necessitates management of the underlying cause, such as O_2 therapy for hypoxemia or changes or addition to infusion therapy for fluid and electrolyte disturbances. In the ICU, certain interventions may be necessary and must be immediately available. A defibrillator must be available when ventricular fibrillation is detected.

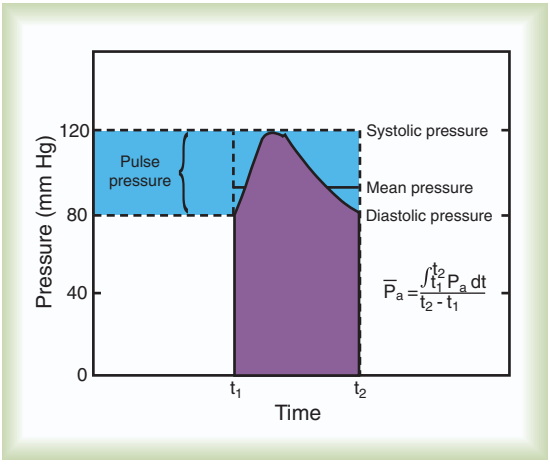

Fig. 52.16 Arterial Pressure Wave Form Systolic Pressure, Diastolic Pressure, Mean Arterial Pressure, and Pulse Pressure.

MONITORING OF ARTERIAL BLOOD PRESSURE

Arterial blood pressure is a crucial measurement for assessing the integrity of cardiovascular tone and the probability that O_2 delivery is dependable. Regulation of cardiovascular tone is under the influence of the autonomic nervous system, but there are other factors that affect blood pressure, such as fluid status or the effects of medications. Major concerns include the adequacy of O_2 delivery during hypotension and the risks of hypertension, such as increased hydrostatic pressure or stroke. Continuous monitoring of the actual blood pressure is performed by placing a catheter usually in the femoral or radial artery. Because fluid is not compressible, the catheter and connecting tubing are filled with saline solution so that the arterial pressure is transmitted to a transducer that allows display of the arterial pressure tracing (Fig. 52.16). The transducer must be properly zeroed and calibrated to reflect the true values of the deflections. The arterial line also provides access for obtaining arterial blood for ABG analysis.

TABLE 52.3 Cardiovascular Monitoring Criteria

Criterion	Normal Value (Range)	Abnormal Value
Heart rate (HR)	80 beats/min (60–100 beats/min)	>100 beats/min (tachycardia) <60 beats/min (bradycardia)
Arterial blood pressure (ABP)	120/80 mm Hg (90–140/60–90 mm Hg)	<140/90 mm Hg (hypertension) <90/60 mm Hg (hypotension)
Mean arterial blood pressure ($\overline{MAP}$)	90 mm Hg (80–100 mm Hg)	<80 mm Hg (hypotension) >100 mm Hg (hypertension)
ECG	Normal heart rate and rhythm	PR interval >0.2 s (tachycardia, bradycardia, heart block [first, second, or third degree], premature ventricular contractions, premature atrial contractions, atrial fibrillation, atrial flutter, elevated ST segment, inverted T wave, ventricular tachycardia, ventricular fibrillation, asystole)
Central venous pressure (CVP)	2–6 mm Hg	>6 mm Hg (fluid overload, right ventricular failure, pulmonary hypertension, valvular stenosis, pulmonary embolus, cardiac tamponade, pneumothorax, positive pressure ventilation, PEEP, left ventricular failure) <2 mm Hg (hypovolemia, blood loss, shock, peripheral vasodilation, cardiovascular collapse)
Pulmonary artery pressure (PAP)	25/10 mm Hg (20–35/5–15 mm Hg)	>35/15 mm Hg (PA systolic >35—pulmonary hypertension), (PA diastolic >15—left ventricular failure, fluid overload) <20/5 mm Hg (pulmonary hypotension, hypovolemia, cardiovascular collapse)
Mean pulmonary artery pressure ($\overline{PAP}$)	15 mm Hg (10–20 mm Hg)	>20 mm Hg (same as ↑ PAP) <10 mm Hg (same as ↓ PAP)
Pulmonary capillary wedge pressure (PCWP)	5–10 mm Hg (<18 mm Hg)	>18 mm Hg (left ventricular failure, fluid overload) >20 mm Hg (interstitial edema) >25 mm Hg (alveolar filling) >30 mm Hg (frank pulmonary edema) <5 mm Hg (hypovolemia, shock, cardiovascular collapse)
Cardiac output ($\dot{Q}_T$ or CO)	5 L/min (4–8 L/min)	>8 L/min (elevated) (see cardiac index) <4 L/min (decreased) (see cardiac index)
Cardiac index (CI)	2.5–4 L/min per m^2	>4 L/min/m^2 (elevated owing to stress, septic shock, fever, hypervolemia, or drugs [dobutamine, dopamine, epinephrine, isoproterenol, and digitalis]) <2.5 L/min/m^2 (left ventricular failure, myocardial infarction, pulmonary embolus, high levels of positive-pressure ventilation, PEEP, pneumothorax, blood loss, hypovolemia)
Systemic vascular resistance (SVR)	900–1400 dynes-s/cm^5 (11.25–17.5 mm Hg/L/min)	>1400 dynes-s/cm^5 (increased owing to vasoconstrictors [dopamine, norepinephrine, and epinephrine], hypovolemia, late septic shock) <900 dynes-s/cm^5 (decreased owing to vasodilators [nitroglycerin, nitroprusside, and morphine] or early septic shock)
Pulmonary vascular resistance (PVR)	110–250 dynes-s/cm^5 (1.38–3.13 mm Hg/L/min)	>250 dynes-s/cm^5 (hypoxemia, ↓ pH, $PaCO_2$, vasopressors, emboli, emphysema, interstitial fibrosis, pneumothorax) <110 dynes-s/cm^5 (pulmonary vasodilators, nitric oxide, O_2, calcium channel blockers)

CI = $\dot{Q}_T$/Body surface area.
SVR = [($\overline{MAP}$ − CVP)/CO] × 80 = dynes-s/cm^5.
PVR = [($\overline{PAP}$ − PCWP)/CO] − 80 = dynes-s/cm^5.

MONITORING OF CENTRAL VENOUS PRESSURE–RIGHT ATRIAL PRESSURE

Right atrial pressure or central venous pressure (CVP) is monitored in the ICU by placement of a central venous catheter. Right atrial pressure is normally the lowest of all the heart chamber pressures, ranging from 2 to 6 mm Hg. Mean right atrial pressure is the same as CVP. CVP is a measure of right atrial preload. Atrial preload is determined by the balance between the capacity of the cardiovascular system, its circulating volume, and the amount of venous return to the heart (see Chapter 10). Right atrial pressure also reflects right ventricular preload under normal circumstances. As a result, abnormally low right atrial pressure suggests inadequate filling of the right ventricle and is common in hypovolemia. Causes of abnormal right atrial pressure or CVP are summarized in Box 52.11.

MONITORING OF PULMONARY ARTERY PRESSURE

Placement of a right heart/pulmonary artery catheter (PAC; **Swan-Ganz catheter**) is invasive and associated with risk of pneumothorax, hemothorax, and arrhythmias. Placement of the

BOX 52.11 Causes of Increased Right Atrial and Central Venous Pressure

- Right ventricular failure (myocardial infarction, cardiomyopathy)
- Pulmonary valvular stenosis
- Tricuspid stenosis and regurgitation
- Pulmonary hypertension
- Pulmonary embolism
- Volume overload
- Compression around the heart, constrictive pericarditis, cardiac tamponade
- Increased tone of large vessels throughout the body, resulting in venoconstriction
- Arteriolar vasodilation, which increases blood supply to the venous system
- Increased intrathoracic pressure (positive-pressure breath or pneumothorax)
- Placement of transducer below the patient's right atrial level
- Infusion of solution, especially with pressure infusion pumps, into the central venous pressure line
- Left-sided heart failure

balloon-tipped 7.5-F catheter (Fig. 52.17) must be performed aseptically by an experienced clinician. The catheter is guided into the pulmonary artery while the clinician visualizes waveforms with a fluid-filled system identical to the arterial pressure monitoring system (Fig. 52.18).

Placement of a Swan-Ganz catheter allows determination of CVP, PAP, and PCWP. Data gathered with a Swan-Ganz catheter can be used to calculate thermodilution CO, pulmonary and arterial vascular resistance, and other associated indices (see Table 52.3). PAP monitoring may be helpful in the presence of shock (cardiogenic, hypovolemic, septic), left ventricular failure, myocardial infarction, pulmonary vascular disease, pulmonary edema, and ARDS. The reading and interpretation of Swan-Ganz catheter tracings can be inconsistent. There has been considerable controversy because of the risk-benefit ratio of the procedure.[45] The use of a PAC in patients without primary cardiovascular disease has decreased markedly in more recent years.

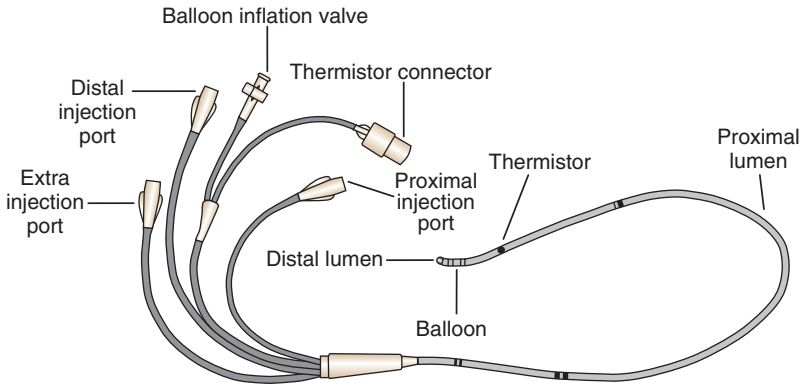

Fig. 52.17 Quadruple-Channel Pulmonary Artery Catheter. The distalmost channel (distal injection port) is for measurement of pulmonary artery pressure. Blood can be aspirated from this channel for mixed venous O_2 measurements. A second channel (balloon inflation valve) is used to inflate or deflate the distal balloon. A third channel (proximal injection port), which exits 30 cm from the catheter tip, is used for monitoring central venous pressure (right atrial pressure) and fluid infusion. The fourth channel (extra injection port), which is not present on all catheters, can be used for continuous infusion of hyperalimentation fluid.

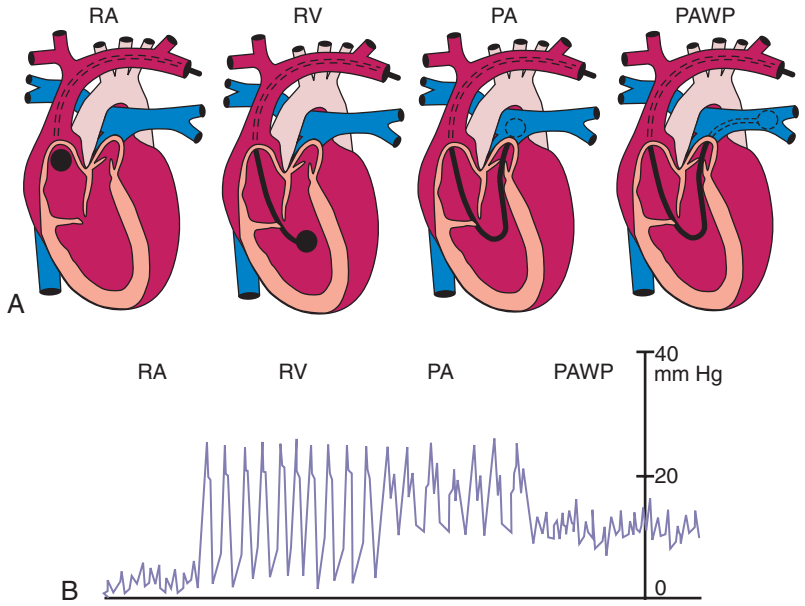

Fig. 52.18 (A) Position of pulmonary arterial catheter in the heart. (B) As monitored by pressure tracings. *PA*, Pulmonary artery; *PAWP*, pulmonary artery wedge pressure; *RA*, right atrium; *RV*, right ventricle

PRELOAD

Preload is defined as the pressure that stretches the ventricular walls at the onset of ventricular contraction. Preload can be approximated by measuring PCWP. PCWP is an estimate of left atrial pressure, which reflects left ventricular end-diastolic pressure. During left-sided heart failure, preload increases; the increase is reflected in elevated PCWP. Symptoms of congestive heart failure can sometimes be controlled with diuretic therapy.

CONTRACTILITY

Contractility is the forcefulness of the heart muscle contracting under a constant load. Numerous pharmacologic agents are used to cause a modest increase in ejection fraction (contractility) and are associated with improvement in symptoms in patients with congestive heart failure.

AFTERLOAD

Afterload is usually defined as the load against which the ventricles must contract. An increase in systemic vascular resistance increases left ventricular afterload. Although increased afterload is usually equated with increased blood pressure, the cause is better understood as the muscle tension required by the left ventricle to generate blood flow. Table 52.4 lists common conditions and associated alterations in hemodynamic variables. Table 52.5 summarizes steps to take in troubleshooting changes in monitored cardiovascular values and vital signs, including possible causes and appropriate corrective action.

CARDIAC OUTPUT

Cardiac performance is affected by preload, contractility, and afterload and is evaluated by the measurement of cardiac output (CO). The effect of cardiac pathology, medications, or mechanical ventilation on CO can be critical monitoring information. An accurate assessment of CO presents a challenge to the clinician. The physical examination (see Chapter 16) can reveal signs and symptoms of impaired cardiac performance, but a composite number provided by CO can provide more direct insight into problem and treatment options.

CO as determined by thermodilution by the use of a PAC (Swan-Ganz catheter) was the primary method of CO assessment for three decades and is considered the gold standard. The invasiveness of this method and inaccuracies in reading and interpretation led to a decrease in use of the Swan-Ganz catheter. Other methods of CO determination have become available based on algorithms that analyze the arterial pressure waveform and a rebreathing method based on **Fick's principle**. The NICO system (Philips Healthcare, Andover, MA) is a noninvasive monitor that uses Fick's principle indirectly to calculate CO by the use of volumetric capnography as well as information obtained from arterial and venous blood gases. It has some limitations, but considering its noninvasive nature, it can a useful tool when more invasive options are not feasible or safe. The FloTrac (Edwards LifeSciences. Irvine, CA) is a minimally invasive continuous CO monitor that uses the analysis of the arterial pulse contour. It requires an arterial line to function but has good correlation to the gold standard PAC.[46]

CARDIAC MUSCLE INJURY

Although heart function can be assessed by various methods, there are a number of blood tests that can indicate cardiac muscle injury. These tests include cardiac troponins, heart fatty acid–binding protein, creatinine kinase MB, and myosin light chain 1.[47]

MONITORING RENAL FUNCTION

The kidney is the main filter of waste products and the principal regulator of the volume and electrolyte composition of body

TABLE 52.4 Common Alterations in Hemodynamic Variables

	VARIABLE							
Condition	**Infiltrate on Chest Radiograph**	**BP**	**Cardiac Output**	**CVP**	**PAP**	**PCWP**	**$P\bar{v}O_2$ and $S\bar{v}O_2$**	**$C(a-\bar{v}O_2)$**
Shock								
Hypovolemic	—	↓	↓	↓	Variable	↓	↓	↑
Septic	None, one, or both sides	↓	↑	↓	N or ↓	N or ↓	N or ↑	N or ↑
Cardiogenic	One or both sides	↓	↓	↓↑	↑↑	↑↑	↓	↑
Left Ventricular Failure								
Mild	One or both sides	N or ↓	↓	N	↑	↑↑	↓	↑
Severe	One or both sides	↓	↓	N or ↑	↑↑	↑↑	↓	↑
Hypervolemic—fluid overload	One or both sides	N or ↑	N or ↑	N or ↑	↑	↑	N or ↑	N or ↓
Pulmonary embolus	None	N	Variable	↑	↑↑	N or ↓	Variable	Variable
ARDS	Both sides	Variable	Variable	Variable	Variable	N or ↓	Variable	Variable
Mechanical ventilation/PEEP	Variable	N or ↓	N or ↓	N or ↑	N or ↓	↑	N or ↓	N or ↑
Pulmonary hypertension	None	N or ↓	N or ↓	↑↑	↑↑	N	Variable	Variable

BP, Blood pressure; *CVP*, central venous pressure; *N*, normal or little or no change; *PAP*, pulmonary artery pressure; *PCWP*, pulmonary capillary wedge pressure; *PEEP*, positive end-expiratory pressure.

TABLE 52.5 Troubleshooting Changes in Vital Signs

Clue	Possible Problem	Advice
Hypotension	Hypovolemia, pump failure	Evaluate fluid balance and possible need for intravenous fluids or inotropic agents.
Hypertension	Anxiety; response to decreased PaO_2, decreased $PaCO_2$ or pain	Reassure, alleviate fear, check patient–ventilatory system; if not easily correctable, obtain and evaluate arterial blood gases.
Alteration of blood pressure with breathing	Decreased venous return (caused by changes in intrathoracic pressure)	If systolic/diastolic pressures are less than adequate perfusion levels, evaluate fluid balance; consider intravenous fluids.
New arrhythmias, tachycardia, bradycardia	Anxiety	Reassure, alleviate fear.
	Decreased PaO_2, decreased $PaCO_2$, increased $PaCO_2$	Check patient–ventilator system; if not quickly correctable, obtain and evaluate arterial blood gases.
Large swings in CVP or PCWP	Decreased venous return	Evaluate other hemodynamic values for adequacy of perfusion.
Decreased urinary output	Decreased CO	Evaluate other hemodynamic values for adequacy of perfusion.
	Hypovolemia	
Fever	Infection	Control infection; review preventive measures.
	Atelectasis	Check patient–ventilator system for secretions, plugs, slippage of tube into right main stem bronchus.
	Overheated humidifier	Check humidifier heater temperature.
Weight gain	Fluid retention	Evaluate hemodynamic values for adequacy of perfusion; consider diuresis.
Changes in respiratory rate	Altered settings	Check patient–ventilator settings.
	Change in metabolic needs	Evaluate metabolic rate.
	Anxiety	Reassure, alleviate fear.
	Sleep	Normal; metabolic rate is decreased.
Use of accessory muscles or paradoxical breathing	Increased work of breathing	Increase support level; check and change inspiratory flow.
	Patient–ventilator asynchrony	Provide pressure support ventilation. Increase sensitivity.
	Auto-PEEP	Eliminate auto-PEEP.

CO, Cardiac output; *CVP*, central venous pressure; *PCWP*, pulmonary capillary wedge pressure; *PEEP*, positive end-expiratory pressure.

fluid. Because the kidney is the primary excreter of nitrogenous waste, plasma concentrations of blood urea nitrogen (BUN) and creatinine are used to track renal function. As a general guideline, the BUN level increases 10 to 15 mg/dL/day, and the creatinine level increases 1 to 2.5 mg/dL/day after abrupt renal failure. With renal failure, the serum potassium level usually increases 0.5 mEq/L/day, and bicarbonate (HCO_3^-) level decreases approximately 1 mEq/L/day. Under the catabolic stress of burns, trauma, rhabdomyolysis (an acute and sometimes fatal disease in which products of skeletal muscle destruction produce acute renal failure), sepsis, or starvation, the rates of change in these values can double. In contrast to BUN, daily production of creatinine is relatively constant. An increasing creatinine level indicates that the rate of production exceeds clearance by means of glomerular filtration. A stable elevation in creatinine level implies that a new steady state has been achieved at a decreased glomerular filtration rate. Until the creatinine level stabilizes, the severity of acute renal dysfunction cannot be assessed reliably. The most common method of estimating glomerular filtration rate (renal function) is measurement of plasma creatinine and creatinine clearance rate. Although calculation of creatinine clearance is more accurate, the procedure entails 24-hour urine collection. The most important factor is whether the glomerular filtration rate is changing or stable, and the plasma creatinine level is tracked for most patients.

Urine volume usually reflects kidney perfusion. Polyuria and oliguria refer to a daily urine output of more than 3 L and less than 0.4 L in average-sized adults. Anuria is present when urine output is less than 50 mL/day. Polyuria should not be confused with increased urinary frequency, in which multiple small voidings occur but total output is less than 3 L/day.

RULE OF THUMB Anuria is present when urine output is less than 50 mL/day. A significant decrease in urine output can ultimately lead to difficulties in pulmonary function when patients develop a fluid overload.

MONITORING LIVER FUNCTION

Adequate liver function is essential for the survival of critically ill patients. The liver must detoxify wastes from metabolism and digestion and process poisons. Elevated results of liver function tests reflect the occurrence of liver parenchymal damage. Hepatic dysfunction may precipitate or worsen ARDS.[48] Routine indications for liver function testing in the treatment of critically ill patients include abdominal pain, jaundice, unexplained fever, nausea, malaise, failure to thrive, weight loss, and leukocytosis. Additional indications may be sought by the facilitation of acuity scoring and definition of the contribution of the liver to multisystemic organ failure.

Batteries of biochemical studies are routine in the evaluation of critically ill patients, but they reflect liver function minimally. Acute liver disease can develop in critically ill patients receiving total parenteral nutrition.[49] Liver disease may manifest as

increased liver size and tenderness. When abnormal results of liver function tests have been obtained, it is essential to determine the cause. Elevations in levels of canalicular enzymes (like alkaline phosphatase) and bilirubin should prompt a search for mechanical obstruction and appropriate imaging studies (like a liver ultrasound). Elevations of transaminase levels (e.g., alanine aminotransferase [ALT]) are unusual in cholestatic processes unless there is a superimposed ischemic event—a confounding factor in many critically ill patients. Elevated levels of aspartate aminotransferase (AST) and ALT suggest hepatic inflammation. Ischemia, viral hepatitis, and autoimmune hepatitis should be considered in the differential diagnosis of elevated AST and ALT.

NUTRITIONAL MONITORING

Assessment and monitoring of nutrition are required in the care of some critically ill patients because nutritional disorders are frequent and important determinants of outcome. Nutritional support is commonly needed by patients who have been critically ill for an extended period and those with increased metabolic demands and limited nutritional reserve.

Assessment of Nutritional Status

Early detection of malnutrition in critically ill patients, whether preexisting or a result of acute illness, enables prompt and aggressive intervention with supplemental nutrition. No single measurement or assessment tool can adequately characterize nutritional status, and the diagnosis of malnutrition is subjective. However, both functional and biochemical factors should be examined to identify whether a patient is at increased risk of malnutrition and its complications.

The functional nutritional assessment consists of the medical history, physical examination, and appraisal of muscle and organ function. However, preexisting malnutrition and dietary history may be difficult to obtain from a critically ill patient presenting to the ICU. Additionally, critically ill patients frequently have volume overload secondary to blood pressure management, which may be complicated by poor kidney function. When a patient has a fluid overload, measurement of dry weight becomes difficult to assess.

There are physical examination findings that may suggest the presence of nutritional and metabolic deficiencies. Inspection of the hair, skin, eyes, mouth, and extremities, including muscle mass and function, can all provide information about a patient's protein reserve and overall nutritional status. Serum chemistry values are important in determining the specifics of nutritional support but do not directly reflect nutritional status. Albumin, sodium, potassium, chloride, total CO_2, BUN, glucose, prothrombin time, partial thromboplastin time, iron, magnesium, calcium, and phosphate should be measured at admission and rechecked periodically. Estimation of a patient's nutritional requirements is also important to determine his or her energy or caloric needs; this applies particularly to weak patients showing signs of weaning failure. Chapter 23 provides a more detailed look at assessing patients' nutritional status.

Global Monitoring Indices

Organizing the flood of information made available by monitoring instruments is a skill and responsibility of critical care practitioners. In the ICU, the immediate concern is the welfare of the patient. Decisions frequently are based on prognosis with respect to the appropriate tests, treatments, and medications prescribed. Guiding these decisions is the weighing of risks and benefits to the patient and the responsible use of resources. Although the physician makes such decisions with all current information, specific data on the probability of survival can be estimated. In the past 30 years, prognostic indices have been derived from large clinical data sets that provide an indication of the seriousness of the patient's condition. These indices (Acute Physiology and Chronic Health Evaluation [APACHE I, II, III, and IV], Acute Physiology Score, Therapeutic Intervention Scoring System, and Burns Weaning Assessment Program) are determinations of scores from numerous monitored values obtained from isolated observations of the patient's condition, usually during the first 24 hours after hospital admission. A score may be assigned for that patient at that time, and risk of mortality can be calculated (Box 52.12).

The value of severity-of-illness scoring for individual patients is limited, and the accuracy and usefulness of physiology scoring are often questioned. Imposing a scoring system to judge intent to treat places too much emphasis on the validity of the system. Scoring systems have not been clearly associated with important outcomes such as length of stay or time on mechanical ventilation. At the present time, as a bedside tool in the care of an individual patient, scoring systems have limited value. A specific condition may "score" a 17% risk of death, but a patient has two possible outcomes: life (0%) and death (100%). The decision to withdraw or limit care would rarely be based on a score, because many other factors are involved in such a decision. Inaccuracies in predicting mortality are frequently reported. Discrepancies are probably due to patient mix differences, hospital factors, admission policies, data collection methods, and differences in quality of care. Currently, the global indices have limited use in the care of individual patients.

Global monitoring has a definite role in research. Global indices are valuable in the study of the effectiveness of new medications or therapy and the establishment of guidelines for care. When control and experimental (new treatment) groups are

BOX 52.12 Global Monitoring Indices

Indices (scores) have been developed that take into account several monitored values.

These scoring systems provide an estimate of illness acuity level and an estimate of the risk of mortality.

For clinical studies, scoring systems are required to ensure that the control and experimental groups are similar.

Scoring systems can be useful as a longitudinal monitor of acuity or a means of evaluating the effect of changes in services.

At this time, scoring systems have little value in the care of individual patients. The most commonly used acuity-of-illness scoring system is the Acute Physiology, Age, Chronic Health Evaluation II (APACHE II).

compared in a randomized, controlled trial, the severity scores of the groups must be similar, or differences in baseline condition may account for differences in results. As a tracking tool, scoring has significant value; the increasing severity of causes of ICU admissions can be followed over time with severity-of-illness scoring. The consequences of changes in services or policies or interhospital comparisons can be crudely tracked with the use of expected mortality calculations from APACHE scores. Some institutions calculate severity-of-illness scores for all patients.

ACUTE PHYSIOLOGY AND CHRONIC HEALTH EVALUATION (APACHE)

The **APACHE scoring system** was developed in 1981 to monitor severity of illness in clinical studies.[50] Studies have referenced a risk-of-mortality estimate as calculated from APACHE scoring, and such studies can be compared with similar studies in which the APACHE scoring system is used. The APACHE II scoring system assigns points to physiologic variables on the basis of whether the values are high abnormal, low abnormal, or normal. Variables rated include temperature, mean arterial pressure, heart rate, respiratory rate, PaO_2 or $P(A–a)O_2$, pH, sodium level, potassium level, creatinine level, hematocrit, white blood cell count, and Glasgow Coma Scale (GCS) score. Assigned points are added to derive a total APACHE score. There is imprecision in estimating the risk of mortality. To emphasize the importance of the neurologic examination, the scoring system is weighted toward the importance of the GCS score. Refinements of APACHE are ongoing, although the APACHE II system continues to be used more often than other systems.[51]

NEUROLOGIC MONITORING

Monitoring of the nervous system is most frequently overlooked in the ICU for several reasons. The first and most important is lack of knowledge of proper assessment of the nervous system of a ventilated, restrained, and often sedated patient in the ICU. Neurologic dysfunction is difficult to recognize in a sedated patient. Proper clinical assessment of the nervous system emphasizes the neurologic history and examination (Box 52.13).

Neurologic Status and Examination

The neurologic examination of a patient in the ICU should address several key issues. A history of an evolving focal deficit occurring over days to weeks before loss of consciousness suggests abscess, tumor, or subdural hematoma, whereas a progression to coma over minutes to hours favors a metabolic cause. Problems such as hypothyroidism, renal failure, cirrhosis, or psychiatric illness suggest greater likelihood of a metabolic cause. Uncontrolled hypertension can induce metabolic (e.g., hypertensive encephalopathy) or structural (e.g., intracerebral hemorrhage) coma. Unfortunately, patients with an altered level of consciousness often require intubation and subsequently are exposed to sedation, making neurologic assessment challenging.

The use of sedation in the ICU is often necessary when invasive mechanical ventilation is used, but its use should be guided by the needs of the patients, and patients' readiness for being awake and extubated should be assessed on a daily basis. To evaluate readiness for extubation, patients must first be rousable by voice; for this reason, sedation-agitation scales are used. Two examples of sedation-agitation scales are the Riker Sedation-Agitation Scale (SAS) and the Richmond Agitation Sedation Scale (RASS)[52,53] (Tables 52.6 and 52.7). Although these scores are not without limitations, they provide targets for sedation management and are key elements in ensuring not only that a patient can be neurologically assessed but also in gauging his or her ability to engage in various mobility exercises even while being ventilated. Daily interruption of sedation, or using minimal sedation guided by these scores, is a common and important aspect of ICU patient management.

Delirium is another common concern in ICU patients, and the routine assessment of delirium is common in daily ICU practice. Two frequently used tests recommended for assessing delirium in the ICU are the Intensive Care Delirium Screening Checklist (ICDSC) and the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU).[54] The ICDSC score is a numeric score 0 to 8 (a score of 4 or greater is associated with delirium or neurologic dysfunction) (Table 52.8).[55] The CAM-ICU score is either a positive or negative score for delirium

BOX 52.13 Neurologic Monitoring

One of the most important and frequently overlooked areas of monitoring is the neurologic examination, which includes the following:

- History
- Assessment of mental status
- Pupillary response
- Eye movement assessment
- Corneal response
- Gag reflex
- Respiratory rate and pattern
- General motor and sensory evaluations

TABLE 52.6 Riker Sedation-Agitation Scale

Score	Term	Descriptor
+7	Dangerous agitation	Pulling at endotracheal tube, trying to remove catheters, climbing over bedrail, striking at staff, thrashing sideside
+6	Very agitated	Requiring restraint and frequent verbal reminding of limits, biting endotracheal tube
+5	Agitated	Anxious or physically agitated, calms to verbal instructions
+4	Calm and cooperative	Calm, awakens easily, follows commands
+3	Sedated	Difficult to arouse but awakens to verbal stimuli or gentle shaking, follows simple commands but drifts off again
+2	Very sedated	Arouses to physical stimuli but does not communicate or follow commands, may move spontaneously
+1	Unable to rouse	Minimal or no response to noxious stimuli, does not communicate or follow commands

(Table 52.9).[56] Delirium assessments are affected by the use of sedatives and/or pain medication; therefore the discontinuation of such drugs or the use of the previously described SASs is necessary for ensuring a proper assessment.

RULE OF THUMB Daily interruption of sedation, or using minimal sedation guided by SAS or RASS scores, is a common and important aspect of ICU patient management.

TABLE 52.7 Richmond Agitation Sedation Scale

Score	Term	Descriptor
+4	Combative	Overtly combative, violent, immediate danger to staff
+3	Very agitated	Pulls or removes tube(s) or catheter(s); aggressive
+2	Agitated	Frequent nonpurposeful movement, fights ventilator
+1	Restless	Anxious but movements not aggressive, vigorous
0	Alert and calm	
–1	Drowsy	Not fully alert, but has sustained awakening (eye-opening/eye contact) to voice (>10 s), visual stimulation
–2	Light sedation	Briefly awakens with eye contact to voice (<10 s)
–3	Moderate sedation	Movement or eye opening to voice (but no eye contact)
–4	Deep sedation	No response to voice, but movement or eye opening to physical stimulation
–5	Unarousable	No response to voice or physical stimulation

Pupillary Response

Pupil size, congruency, and response to light and accommodation should be described. Pupillary light reflexes provide information regarding the status of the brain and of the sympathetic and parasympathetic nervous systems. Pupillary function is controlled by the midbrain. If pupillary function is normal, the cause of coma is either metabolic or a structural lesion located above the midbrain. Small "pinpoint" pupils usually result from pontine hemorrhage or from the ingestion of narcotics or organophosphates. Pupillary responses almost always remain intact in metabolic causes of coma. Dilated and fixed (unresponsive to light) pupils are seen in patients who have been given atropine. Midposition and fixed pupils often indicate severe cerebral damage.

Traditionally, pupillary size has been subjectively documented in critical care, but this can lead to discrepancies between clinicians. The use of a pupillometer, a device that uses an infrared camera to measure pupillary size, can improve the accuracy of measurements and avoid disagreements among clinicians. This is particularly important when sequential measurements are required to determine the progression of a pathologic process.[57]

Eye Movements

Abnormalities of extraocular movement have prognostic importance in the ICU. Normal movement of the eyes requires an intact pontomedullary–midbrain connection. The resting position of the gaze, the presence of nystagmus (rapid involuntary movements), and the response to head movements and cold tympanic membrane stimulation should be identified. Cervical spine stability must be ensured before oculocephalic maneuvers are performed. If rotation of the head (oculocephalic) and vestibular stimulation (calorics) produce no change in eye position, the pons is nonfunctional. If only the eye ipsilateral (on the

TABLE 52.8 Intensive Care Delirium Screening Checklist

Characteristic	Description	Point
Altered level of consciousness	(A) No response or (B) the need for vigorous stimulation in order to obtain any response signified a severe alteration in the level of consciousness precluding evaluation.	A dash (-) is entered and there is no further evaluation during that period.
	(C) Drowsiness or requirement of a mild to moderate stimulation for a response implies an altered level of consciousness and scores.	1 point
	(D) Wakefulness or sleeping state that could easily be aroused is considered normal and scores.	No point
	(E) Hypervigilance is rated as an abnormal level of consciousness and scores.	1 point
Inattention	Difficulty in following a conversation or instructions. Easily distracted by external stimuli. Difficulty in shifting focuses.	1 point
Disorientation	Any obvious mistake in time, place, or person scores.	1 point
Hallucination, delusion, or psychosis	Clinical manifestation of hallucination or of behavior probably due to hallucination (e.g., trying to catch a nonexistent object) or delusion, or gross impairment in reality testing.	1 point
Psychomotor agitation, or retardation	Hyperactivity requiring the use of additional sedative drugs or restraints in order to control potential danger to oneself or others (e.g., pulling out intravenous lines, hitting staff). Hypoactivity or clinically noticeable psychomotor slowing. Any of these scores.	1 point
Inappropriate speech or mood	Inappropriate, disorganized, or incoherent speech. Inappropriate display of emotion related to events or situation.	1 point
Sleep/wake cycle disturbance	Sleeping less than 4 hours or waking frequently at night (do not consider wakefulness initiated by medical staff or loud environment). Sleeping during most of the day.	1 point
Symptom fluctuation	Fluctuation of the manifestation of any item or symptom over 24 h (e.g., from one shift to another) scores.	1 point

TABLE 52.9 The Confusion Assessment Method for the Intensive Care Unit

Features and Descriptions		
I. Acute Onset or Fluctuating Course A. Is there evidence of an acute change in mental status from the baseline? B. Or, did the (abnormal) behavior fluctuate during the past 24 h, that is, tend to come and go or increase and decrease in severity as evidenced by fluctuations on the Richmond Agitation Sedation Scale (RASS) or the Glasgow Coma Scale?	**Absent**	**Present**
II. Inattention Did the patient have difficulty focusing attention as evidenced by a score of less than 8 correct answers on either the visual or auditory components of the Attention Screening Examination (ASE)?	**Absent**	**Present**
III. Disorganized Thinking Is there evidence of disorganized or incoherent thinking as evidenced by incorrect answers to 3 or more of the 4 questions and inability to follow the commands? Questions 1. Will a stone float on water? 2. Are there fish in the sea? 3. Does 1 pound weigh more than 2 pounds? 4. Can you use a hammer to pound a nail? Commands 1. Are you having unclear thinking? 2. Hold up this many fingers. (Examiner holds 2 fingers in front of the patient.) 3. Now do the same thing with the other hand (without holding the 2 fingers in front of the patient). (If the patient is already extubated from the ventilator, determine whether the patient's thinking is disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject.)	**Absent**	**Present**
IV. Altered Level of Consciousness Is the patient's level of consciousness anything other than alert, such as being vigilant or lethargic or in a stupor or coma? Alert: spontaneously fully aware of environment and interacts appropriately Vigilant: hyperalert Lethargic: drowsy but easily aroused, unaware of some elements in the environment or not spontaneously interacting with the interviewer; becomes fully aware and appropriately interactive when prodded minimally Stupor: difficult to arouse, unaware of some or all elements in the environment or not spontaneously interacting with the interviewer; becomes incompletely aware when prodded strongly; can be aroused only by vigorous and repeated stimuli, and as soon as the stimulus ceases, stuporous subject lapses back into unresponsive state Coma: unarousable, unaware of all elements in the environment with no spontaneous interaction or awareness of the interviewer so that the interview is impossible even with maximal prodding **Overall CAM-ICU Assessment (Features 1 and 2 and either Feature 3 or 4): Yes____ No____**	**Absent**	**Present**

same side of the body) to the stimulus abducts, a lesion of the medial longitudinal fasciculus should be suspected.

Corneal Responses

The corneal reflex is used to test the afferent fifth and efferent seventh cranial nerves. This test is performed by lightly touching the cornea with a cotton swab; the patient should blink both eyes in response. The presence of this response implies an intact ipsilateral fifth cranial nerve, intact central pons, and intact bilateral seventh cranial nerve. Testing must be performed bilaterally to evaluate both afferent components of the fifth cranial nerve.

Gag Reflex

The gag reflex is tested by using a tongue blade to stimulate one side of the posterior pharynx of an intubated patient. Each side should be tested separately. A normal response is bilateral movement of the posterior pharyngeal muscles and implies intact ninth and tenth cranial nerves. The ability to cough on suctioning can be tested in an intubated patient and implies an intact tenth cranial nerve and the ability of the patient to protect their airway. This test should not be attempted on nonintubated patients in the ICU because of the risk of aspiration.

Respiratory Rate and Pattern

The brain stem is the primary site of the central control of respiration. This control occurs at a subconscious level and results in rhythmic contraction and relaxation of the respiratory muscles. The most common abnormal respiratory pattern seen in patients with neurologic disorders is Cheyne-Stokes respiration, which consists of phases of hyperpnea that regularly alternate with

episodes of apnea. Breathing waxes in a smooth crescendo and, when a peak is reached, wanes in an equally smooth decrescendo. Cheyne-Stokes respiration usually has an intracranial cause, although it can be caused by hypoxemia and cardiac failure. Ataxic breathing is a marker of severe brain-stem dysfunction. Despite the nonspecificity of most breathing patterns, the respiratory pattern can provide valuable clues to the cause of coma.

Motor Evaluation

A thorough motor evaluation should be performed for all patients. The systematic approach described earlier is key to localizing the site of a pathologic process. The symmetry and pattern of the motor response to noxious stimuli and associated neurologic symptoms should be documented for all patients.

Sensory Evaluation

Assessment of light touch, pinprick, and temperature sensation can be achieved by applying a cotton swab, a clean pin, and a cold or warm object to various parts of the upper and lower extremities. Symmetry of responses between sides and between upper and lower extremities should be documented and is valuable in localizing the site of a pathologic process.

Glasgow Coma Scale

The most widely used scoring system for acute neurologic disorders is the **Glasgow Coma Scale (GCS)** (Table 52.10). The GCS score is used to test best motor response, best verbal response, and opening of the eyes. The scale goes from 3 to 15 and can be used for rapid triage. Patients with head injury and GCS scores of 13 to 15 are often admitted to a non-ICU observational unit unless neurologic examination or a CT scan reveals a lesion or abnormality that warrants ICU admission. Scores of 9 to 13 on the GCS signify a significant insult with depressed level of consciousness. Patients with head injury and GCS scores equal to or less than 8 need close monitoring and often intubation and mechanical ventilation.

TABLE 52.10 Glasgow Coma Scale

Eyes	Open	Spontaneous	4
		To verbal command	3
		To pain	2
		No response	1
Best motor response	To verbal command	Obeys	6
	To painful stimulus	Localized pain	5
		Flexion—withdrawal	4
		Flexion—decorticate	3
		Flexion—decerebrate	2
		No response	1
Best verbal response		Oriented, converses	5
		Disoriented, converses	4
		Inappropriate words	3
		Incomprehensible sounds	2
		No response	1
Total			*3–15*

Intracranial Pressure Monitoring

There are two primary reasons to measure intracranial pressure (ICP): (1) to monitor patients at risk of life-threatening intracranial hypertension and (2) to assess the effects of therapy aimed at reducing ICP. Measuring ICP during a lumbar puncture (or spinal tap) may also be useful to suggest the presence of infection (e.g., meningitis). Mean ICP of a supine patient is normally 10 to 15 mm Hg, and the ICP waveform normally undulates gently in time with the cardiac cycle. Fluctuations of the ICP waveform (>10 mm Hg) suggest a position near the critical inflection point of the cranial P-V curve. Elevations in ICP to 15 to 20 mm Hg compress the capillary bed and compromise microcirculation. At ICP levels of 30 to 35 mm Hg, venous drainage is impeded, and edema develops in uninjured tissue. Even when autoregulatory mechanisms are intact, cerebral perfusion cannot be maintained if ICP increases to within 40 to 50 mm Hg of the mean arterial pressure. When ICP approximates mean arterial pressure, perfusion stops and the brain dies.

Two categories of ICP monitoring techniques are currently available. Fluid-filled systems have external transducers, such as an intraventricular catheter and subarachnoid bolts. Solid-state systems have miniature pressure transducers that can be inserted in the lateral ventricle, brain parenchyma, or subarachnoid or epidural space.

TROUBLESHOOTING

Identification and correction of patient- and ventilator-related problems during mechanical ventilatory support are primary responsibilities of the RT. Under ideal circumstances, potential problems are identified before they occur or before they can cause harm to the patient. Potential problems with the patient include anxiety, agitation, altered mental status, fighting the ventilator, hypoxemia, hypoventilation, and the development of metabolic acidosis. The patient may experience acute changes in respiratory rate, heart rate, blood pressure, and CO_2.

Other common patient-related problems include excessive secretions, bronchospasm, and other causes of decreased compliance or increased resistance. Recognition of signs of pneumothorax, pneumomediastinum or subcutaneous emphysema, airway malfunction or leaks, and chest tube leaks should receive prompt attention.

Problems associated with the ventilator include leaks or malfunctions in the system, inappropriate ventilator settings (including trigger sensitivity and inspiratory flow rate), development of auto-PEEP, and improper humidification. Box 52.14 lists causes of sudden respiratory distress in patients receiving mechanical ventilatory support. Box 52.15 lists steps for managing sudden respiratory distress. Table 52.11 summarizes troubleshooting of the patient–ventilator system.

Pharmacologic paralysis should be considered only when no other alternatives are effective. The one exception to this guideline is the patient presenting with severe ARDS (PaO_2/FiO_2 100 mm Hg). In order to gain control of the patient's physiologic status, it is now recommended to paralyze these patients for up to 48 hours. The use of neuromuscular blocking agents can mask other patient problems, and ventilator malfunction or disconnection

BOX 52.14 Causes of Sudden Respiratory Distress in a Patient Receiving Ventilatory Support

Patient-Related Causes

- Artificial airway problems
- Movement of endotracheal tube
- Cuff herniation
- Cuff leak
- Kinking of endotracheal tube
- Foreign body
- Transesophageal fistula
- Innominate artery rupture
- Malpositioned nasogastric tube
- Secretions
- Bronchospasm
- Pneumothorax
- Pulmonary edema
- Pulmonary embolism
- Acute hypoxemia
- Blood in endotracheal tube
- Dynamic hyperinflation
- Abnormal respiratory drive
- Alteration in body posture
- Drug-induced problems
- Abdominal distention
- Agitation

Ventilator-Related Causes

- Ventilator malfunction
- Circuit malfunction
- Leaks or disconnects
- Condensate
- In-line nebulizers
- Inadequate ventilatory support
- Patient–ventilator asynchrony

From Tobin MJ, Alex CJ, Fahey PJ: Fighting the ventilator. In: Tobin MJ, editor: *Principles and practice of mechanical ventilation*, New York, 2006, McGraw-Hill.

BOX 52.15 Steps for Managing Sudden Distress in a Patient Receiving Ventilatory Support

1. Remove the patient from the ventilator.
2. Initiate manual ventilation with 100% O_2.
3. Patient improvement indicates that the ventilator is the cause of distress.
4. Lack of improvement indicates the problem is within the patient.
5. If death appears imminent, consider and manage the most likely causes; check for airway obstruction (by passing a suction catheter), a dislodged endotracheal tube, or a pneumothorax.
6. If death is not imminent, wait until the patient's condition is stable before attempting a more detailed assessment including a chest radiograph.

Modified from Tobin MJ, Alex CJ, Fahey PJ: Fighting the ventilator. In: Tobin MJ, editor: *Principles and practice of mechanical ventilation*, New York, 2006, McGraw-Hill.

TABLE 52.11 Troubleshooting the Patient–Ventilator System

Clue to Problem	Possible Cause	Corrective Action
Decreased minute ventilation or V_T	Leak around endotracheal or chest tube	Check all connections for leaks.
	Decreased patient-triggered respiratory rate	Evaluate patient.
		Check sensitivity.
		Measure auto-PEEP.
		Increase set rate.
		Change mode.
	Decreased lung compliance	Evaluate patient.
	Airway secretions	Clear airway of secretions.
	Altered settings	Check patient–ventilator system.
	Malfunctioning volume monitor	Check with external respirometer.
Increased minute ventilation or V_T	Increased patient-triggered respiratory rate	Check respiratory rate.
		Check sensitivity.
		Change mode.
	Altered settings	Check patient–ventilator system.
	Hypoxia	Evaluate patient.
		Consider ABG and SpO_2 values.
	Increased lung compliance	Decrease pressure.
		Decrease inspiratory time.
	Malfunctioning volume monitor	Check with external respirometer.
Change in respiratory rate	Altered setting	Check patient–ventilator system.
	Increased metabolic demand	Evaluate patient.
	Hypoxemia	Evaluate patient.
		Consider ABG and SpO_2 values.

Continued

TABLE 52.11 Troubleshooting the Patient–Ventilator System—*cont'd*

Clue to Problem	Possible Cause	Corrective Action
Sudden increase in peak airway pressure	Coughing	Alleviate uncontrolled coughing.
	Airway secretions or plugs	Clear airway secretions.
	Ventilator tubing kinked or filled with water	Check for kinks and water.
	Changes in patient position	Consider repositioning patient.
	Endotracheal tube in right mainstem bronchus	Verify position.
	Patient–ventilator asynchrony	Correct asynchrony.
		Check for adequate peak flow.
		Verify with waveforms.
	Bronchospasm	Identify cause and treat.
	Pneumothorax	Insert chest tube.
Gradual increase in peak airway pressure	Diffuse, reactive, or obstructive process	Evaluate for problems, such as atelectasis, increasing lung water, bronchospasm.
Sudden decrease in peak airway pressure	Volume loss from leaks in the system	Check patient–ventilator systems for leaks.
		Verify with waveforms.
		Check for active inspirations.
		Evaluate patient.
FiO_2 drift	O_2 analyzer error	Calibrate analyzer.
		Change O_2 sensor.
	Blender piping failure	Correct failure.
	O_2 source failure	Correct failure.
	O_2 reservoir leak	Check ventilator reservoir.
I:E ratio too high or too low	Altered inspiratory flow	Check flow setting and correct.
	Alteration in other settings that control I:E ratio	Check settings and correct.
	Alteration in sensitivity setting	Check setting and correct.
	Airway secretions (pressure ventilator)	Clear airway of secretions.
	Subtle leaks	Measure minute ventilation.
Inspired gas temperature too high	Addition of cool water to humidifier	Wait.
	Altered settings	Correct temperature control setting.
	Adding cool gas by small-volume nebulizer treatment	Turn off heater during treatment.
	Thermostat failure	Replace heater.
Changes in PEEP	Change in V_T	Adjust PEEP level.
	Change in compliance	Adjust PEEP level.
	Altered settings	Check settings and correct.
Changes in static pressure	Changes in lung compliance	Evaluate patient and correct if possible.
Changes in ventilator setting	Changes in these settings resulting from deliberate or accidental adjustment of dials or knobs	Determine whether current settings are the intended ones.

PEEP, Positive end-expiratory pressure.
Modified from Martz K, Joiner JW, Shepherd RM: *Management of the patient-ventilator system: a team approach*, ed 2, St. Louis, 1994, Mosby.

BOX 52.16 Pharmacologic Agents Used to Produce Sedation or Paralysis

I. Benzodiazepine tranquilizing agents
  A. Diazepam (Valium)
  B. Lorazepam (Ativan)
  C. Midazolam (Versed)
II. Sedative hypnotics and miscellaneous agents
  A. Sodium thiopental (Pentothal)
  B. Etomidate (Amidate)
  C. Haloperidol (Haldol)
  D. Propofol (Diprivan)
  E. Dexmedetomidine (Precedex)
III. Narcotic analgesics
  A. Morphine
  B. Fentanyl (Sublimaze)
IV. Neuromuscular blocking agents
  A. Nondepolarizing (competitive) agents
    1. Steroidal agents
      I. Pancuronium (Pavulon)
      II. Pipecuronium (Arduan)
      III. Rocuronium (Zemuron)
      IV. Vecuronium (Norcuron)
    2. Benzylisoquinolinium esters
      I. Atracurium (Tracrium)
      II. Cisatracurium (Nimbex)
      III. Doxacurium (Nuromax)
      IV. Metocurine (Metubine)
      V. Mivacurium (Mivacron)
      VI. Tubocurarine (Tubarine)
  B. Depolarizing agents
    1. Succinylcholine (Anectine, Quelicin)
    2. Decamethonium (Syncurine)

in the care of a paralyzed patient can be catastrophic. In addition, some patients receiving neuromuscular blocking agents in the ICU may experience prolonged neuropathy. Pharmacologic agents used to produce sedation or paralysis in the ICU are listed in Box 52.16.

SUMMARY CHECKLIST

- Caregivers must be experienced at filtering the noise from the changes in monitored variables that require attention. Caregivers must recognize false alarms. They must also discriminate real pathophysiologic changes from normal physiologic variations and variations inherent in the data.
- Because only caregivers can make choices about altering care, caregivers continue to be the most important monitors.
- Monitoring of the respiratory system includes assessment of ventilation, gas exchange, and respiratory system mechanics and function.
- Ventilation is monitored by measurement of V_T, respiratory rate, and minute ventilation and by assessment of dead space and alveolar ventilation.
- Gas exchange is routinely monitored with ABG analysis and pulse oximetry. Derived values such as V_D/V_T, $P(A–a)O_2$ difference, PaO_2/FiO_2 ratio, shunt, and lung injury score can clarify the nature and severity of gas-exchange abnormality. Arterial $PaCO_2$ is the best index of alveolar ventilation.
- Respiratory system mechanics are routinely monitored by tracking peak pressure, P_{plat}, driving pressure, auto-PEEP, compliance, and resistance.
- When any patient is being mechanically ventilated, ideally, the tidal volume should be 4 to 8 mL/kg of predicted body weight, and the plateau pressure should be less than 28 cm H_2O.
- Monitoring of transpulmonary pressure is becoming increasingly important in managing patients with decreased chest wall compliance and those with severe ARDS requiring high PEEP levels.
- Factors such as WOB, f/V_T, VC, MIP, and MVV can be extremely helpful in assessing the need to increase ventilatory support or in assessing the potential for weaning.
- Advanced monitoring techniques include EIT, diaphragm and lung ultrasound, lung stress and strain, stress index, and esophageal pressure monitoring.
- The most important responsibility of the RT in the ICU is monitoring of the patient–ventilator system.
- Monitoring of the patient–ventilator system includes overall assurance of the integrity and safety of the system. Monitoring requires complete knowledge of the ventilator settings; all aspects of ventilator function; the circuitry; airway status; gas exchange; ventilator graphics; lung mechanics; alarms; and the overall care, safety, and comfort of the patient.
- Acute changes in cardiac performance, cardiovascular status, or impulse conduction (ECG) can be life threatening; some form of monitoring of the heart, vascular system, and ECG is necessary in the care of nearly all patients in the ICU.
- Hemodynamic monitoring requires the use of invasive pulmonary arterial, central venous, and arterial catheters. Values obtained with these monitoring lines must be carefully interpreted by experienced caregivers. All ICU patients should receive ECG monitoring.
- Monitoring of changes in neurologic status is extremely important and is more often overlooked than the monitoring of other organ systems.
- The neurologic examination includes assessment of mental status, pupillary response, eye movements, corneal response, gag reflex, and respiratory rate and pattern and a general motor and sensory evaluation. ICP monitoring may be needed to detect or manage elevated ICP.
- Global index monitoring is calculation of an illness level score that is an estimate of the risk of mortality from numerous monitoring values. Illness scores are not used in the care plan for an individual patient, but scoring systems are widely used in clinical studies. The APACHE II system is among the most popular of these estimates.
- Troubleshooting the patient–ventilator system is aimed at identifying and correcting problems before they harm the patient.

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Discontinuing Ventilatory Support

Robert M. Kacmarek

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Discuss the relationship between ventilatory demand and ventilatory capacity as well as their relationship with ventilator discontinuance.
- List the factors associated with ventilator dependence.
- Explain how to evaluate a patient before attempting ventilator discontinuation or weaning.
- List acceptable values for specific weaning indices used to predict a patient's readiness for discontinuation of ventilatory support.
- Describe factors that should be optimized before an attempt is made at ventilator discontinuation or weaning.
- Describe techniques used in ventilator weaning, including daily spontaneous breathing trials, synchronized intermittent mandatory ventilation, pressure support ventilation, and other newer methods.
- Contrast the advantages and disadvantages associated with various weaning methods and techniques.
- Discuss the use of esophageal pressure, diaphragm electrical activity (EAdi), and ultrasound to assess weaning capabilities and predict weaning success.
- Discuss weaning of the morbidly obese patient.
- Discuss the new weaning guidelines provided by the ATS/ACCP.
- Describe how to assess a patient for extubation.
- List the primary reasons why patients fail a ventilator discontinuance trial.
- Explain why some patients cannot be successfully weaned from ventilatory support.

CHAPTER OUTLINE

KEY TERMS

adaptive support ventilation (ASV)
airway occlusion pressure
automatic tube compensation (ATC)
continuous positive airway pressure (CPAP)
diaphragm electrical activity (EAdi)
esophageal pressure
Intellivent
mandatory minute volume ventilation (MMV)
pressure support ventilation (PSV)
progressive mobility
prolonged mechanical ventilation (PMV)
rapid, shallow breathing index (f/V_T)
spontaneous awaking trial (SAT)
spontaneous breathing trial (SBT)
synchronized intermittent mandatory ventilation (SIMV)
ultrasound, diaphragm

The purpose of mechanical ventilation is to support the patient until the disease state or condition that caused the need for ventilatory support is alleviated or resolved. Ventilatory support can sustain life, but it cannot cure disease. Further, many complications and hazards are associated with mechanical ventilation. Consequently, ventilatory support should be withdrawn as soon as the patient is able to adequately resume spontaneous breathing.[1] All patients who are mechanically ventilated should be evaluated daily, beginning with the day of intubation, for their ability to be liberated from ventilatory support.[2,3] Frequently this evaluation is very quick, but it should be performed at least daily regardless of the patient's status.

After the problem or condition that caused the need for mechanical ventilation is resolved, most patients can be quickly and easily liberated from ventilatory support. For example, for most patients who need mechanical ventilation as a result of a drug overdose or severe asthma, for those who are recovering from postoperative anesthesia, and for those who have received ventilation for 72 hours or less, one may simply discontinue ventilation when the precipitating condition has resolved.[1,4] However, some patients require mechanical ventilation for longer periods. The term *ventilator dependent* is usually reserved for patients who need ventilatory support for lengthy periods (i.e., 2 weeks or more) or who have not responded to attempts at ventilator discontinuation. For these patients, a more prolonged ventilator discontinuation process is required.[1]

Ventilator discontinuation should be carefully timed. Premature removal from the ventilator may severely stress the cardiopulmonary system and delay the patient's recovery.[4] Premature discontinuation also exposes the patient to the hazards of reintubation. However, delays in discontinuing ventilation expose the patient to an increased risk of complications, including nosocomial pneumonia, lung injury, myocardial infarction, and death.[4]

There are three basic historical methods for discontinuing ventilatory support, which can be used alone or in combination with one another[1]:

1. **Spontaneous breathing trials (SBTs)** alternating with mechanical ventilation
2. **Synchronized intermittent mandatory ventilation (SIMV)**
3. **Pressure support ventilation (PSV)**

Other techniques that may facilitate ventilator discontinuation include the use of volume-support ventilation (VSV); **adaptive support ventilation (ASV)**/**Intellivent**; automatic tube compensation (ATC); proportional assist ventilation (PAV), which is also known as *proportional pressure support* (PPS); neurally adjusted ventilatory assist (NAVA); and **continuous positive airway pressure (CPAP)**. However, little data exist that support the use of any of these techniques except for CPAP, which seems potentially beneficial during the ventilator discontinuation process, especially in morbidly obese patients.[5]

> **RULE OF THUMB** All patients who are mechanically ventilated should be evaluated at least daily, beginning with the day of intubation, for their ability to be liberated from ventilatory support.

Techniques for predicting when patients are ready for ventilator discontinuation and weaning have been studied extensively.[4] Many weaning indices designed to predict successful ventilatory discontinuation have been proposed. Despite this, there are no universally applicable indices for predicting success. Of all the methods studied, SBTs and PSV have been shown to be the most effective methods for ventilator discontinuation and weaning. Evidence-based reviews recommend the use of at least daily SBTs.[1] Protocols for ventilator discontinuation administered by an interdisciplinary team of respiratory therapists, nurses, and physicians can be highly effective, and have been recommended.[1,4,6–10] Regardless of the method used, success is unlikely unless the precipitating problems that caused the ventilator dependency have been resolved.[1,4,10] After these problems are resolved, an organized plan or protocol should be followed, and variations from the plan should be based on each patient's response.[1,4,6]

Some patients cannot be successfully removed from mechanical ventilatory support. This group of ventilator-dependent patients poses clinical, economic, and ethical concerns.[11,12]

The term *weaning* has been used as a general term to refer to the process of discontinuing ventilatory support, regardless of the time frame or method involved. The term has also been used to refer to reductions in fractional inspired oxygen concentration (FiO_2), positive end-expiratory pressure (PEEP), and CPAP. Alternatively, the term *ventilator discontinuation or liberation* has been used to refer to the process of disconnecting a patient from mechanical ventilatory support. For the purposes of this chapter, the term *weaning* is defined as a gradual reduction in the level of ventilatory support, whereas *liberating from or discontinuing ventilatory support* refers to the overall process of removing the patient from the ventilator, regardless of the method used. In general, patients who are being considered for removal from ventilatory support fall into one of five categories:

1. Those for whom removal is quick and routine, normally the majority of ventilated patients.
2. Those who need a more systematic approach to discontinuing ventilatory support, which is normally about 15% to 20% of ventilated patients.
3. Those who require days to weeks to wean from ventilatory support, which is usually less than 5% of ventilated patients.
4. Those ventilator-dependent or "unweanable" patients, who compose less than 1% of patients who require ventilatory support.
5. Those who have no chance for survival in whom the ventilator is discontinued while comfort measures are provided, normally referred to as terminal weaning or terminal extubation.[13]

RULE OF THUMB After the problem or condition that caused the need for mechanical ventilation is resolved, most patients can be quickly and easily liberated from ventilatory support.

REASONS FOR VENTILATOR DEPENDENCE

Patients may require mechanical ventilation because of apnea, acute or impending ventilatory failure, or severe oxygenation problems that necessitate high levels of PEEP or CPAP. Regardless of the reason for initiating mechanical ventilation, patients remain dependent on the ventilator because of respiratory, cardiovascular, neurologic, or psychologic factors.[1]

Ventilatory Workload and Demand

Patients who need mechanical ventilation often have a ventilatory workload and demand that exceeds their ventilatory capacity. This is the most common cause of ventilator dependence.[1,4] The term *ventilatory workload* refers to the amount of work that the respiratory muscles are asked to perform to provide an appropriate level of ventilation. A patient's total ventilatory workload is primarily determined by the following: (1) the level of ventilation needed, (2) the compliance of the lungs and thorax, (3) the resistance to gas flow through the airways, and (4) any imposed work of breathing (WOB_I) due to ventilatory system mechanical factors.[1,4]

The level of ventilation required is determined by the following: (1) the metabolic rate, (2) the central nervous system (CNS) ventilatory drive, and (3) the ventilatory dead space. Common causes of an increased demand for ventilation include increased carbon dioxide production (i.e., fever, shivering, agitation, trauma, or sepsis) and increased dead space (i.e., pulmonary emboli or chronic obstructive pulmonary disease [COPD]). Other common causes of increased ventilatory demand include metabolic acidosis, severe hypoxemia, pain, and anxiety.

Compliance is determined by the elastic nature of the lung–thorax system. Resistance is largely related to the nature of the conducting airways. Common causes of decreased lung compliance include atelectasis, obesity, pneumonia, pulmonary edema, pulmonary fibrosis, acute lung injury, and acute respiratory distress syndrome. Thoracic compliance may be reduced because of ascites, or abdominal distention. Airway resistance increases with bronchospasm, excessive secretions, and mucosal edema.

BOX 53.1 Factors That May Increase Ventilatory Workload

Increased Ventilatory Demand: Increased Level of Ventilation Required

- Increased central nervous system drive: hypoxia, acidosis, pain, fear, anxiety, and stimulation of J receptors (e.g., pulmonary edema)
- Increased metabolic rate: increased carbon dioxide production, fever, shivering, agitation, trauma, infection, and sepsis
- Increased dead space: chronic obstructive pulmonary disease and pulmonary embolus

Decreased Compliance

- Decreased lung compliance: atelectasis, obesity, pneumonia, fibrosis, pulmonary edema, and acute respiratory distress syndrome
- Decreased thoracic compliance: ascites, abdominal distention, and pregnancy

Increased Resistance

- Increased airway resistance: bronchospasm, mucosal edema, and secretions
- Artificial airways: endotracheal tubes, tracheostomy tubes, and partial obstruction of the artificial airway or the patient airway
- Other mechanical factors: ventilator circuits, demand flow systems, and inappropriate ventilator flow or sensitivity settings

BOX 53.2 Factors That May Reduce Ventilatory Drive

- Decreased $PaCO_2$ (respiratory alkalosis)
- Metabolic alkalosis
- Pain (visceral)
- Electrolyte imbalance
- Pharmacologic depressants (narcotics, sedatives)
- Fatigue
- Decreased metabolic rate
- Increased $PaCO_2$ associated with chronic carbon dioxide retention
- Neurologic or neuromuscular disease

Mechanical factors that can increase the work of breathing (WOB) include artificial airways (i.e., endotracheal and tracheotomy tubes), partial obstruction of the airway, ventilator circuits, demand flow systems, auto-PEEP, and inappropriate ventilator flow and sensitivity settings. Factors that may increase ventilatory workload are summarized in Box 53.1.

Ventilatory Capacity

Ventilatory capacity is determined by ventilatory drive, ventilatory muscle strength, and ventilatory muscle endurance. Most patients who are being withdrawn from ventilatory support have a normal or an increased drive to breathe. Patients with neuromuscular disorders and those who are receiving sedatives, narcotics, or neuromuscular blocking agents may have a reduced or absent drive to breathe or impaired neuromuscular transmission. Patients with metabolic alkalosis, hypothyroidism, and sleep deprivation also may have a reduced ventilatory drive. Box 53.2 summarizes the factors that may reduce ventilatory drive.

Muscle strength is influenced by age, sex, muscle bulk, and overall health. Malnutrition, starvation, and electrolyte imbalances (especially involving calcium, magnesium, potassium, and

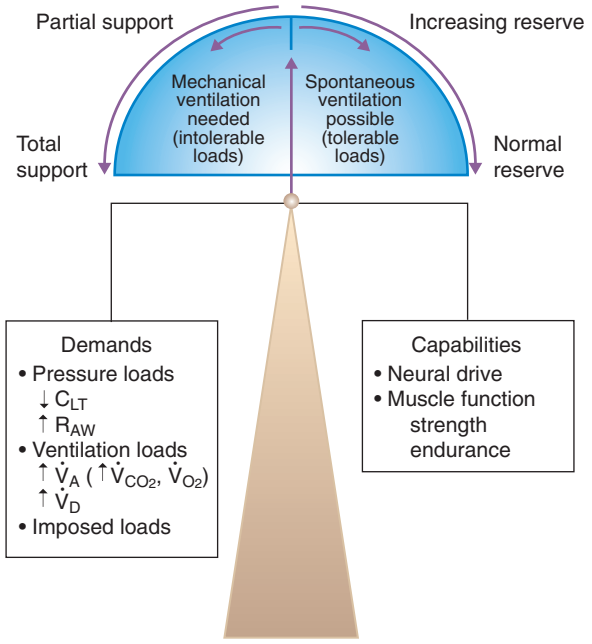

Fig. 53.1 Ventilatory failure and the need for ventilatory support depend on the balance between ventilatory muscle demands (i.e., loads) and ventilatory muscle capabilities. C_{LT}, Lung–thorax compliance; *RAW,* airway resistance, $\dot{V}$, minute alveolar ventilation; $\dot{V}$, minute dead space ventilation. (Modified from MacIntyre NR: Respiratory factors in weaning from mechanical ventilatory support. *Respir Care* 40:244–259, 1995.)

phosphate) can lead to ventilatory muscle weakness. Critical illness myopathy, critical illness polyneuropathy, and the prolonged use of neuromuscular blocking agents are major causes of the development of ventilatory muscle weakness in the intensive care unit (ICU).[14] Controlled ventilation for prolonged periods can result in ventilatory muscle discoordination and atrophy. Ventilatory muscle endurance is a function of energy supply versus demand. Energy supply is related to nutrition, perfusion, and cell energy use, whereas demand is related to the amount of work performed and is a function of minute ventilation, compliance, and resistance. Fig. 53.1 summarizes the relationship between ventilatory demands and capabilities.

RULE OF THUMB If patient workload exceeds capacity, the patient will not be successfully weaned from ventilatory support.

Global Criteria for Discontinuing Ventilatory Support

Success with liberation from ventilatory support is related to the patient's condition in four main areas[1–4]:

1. Ventilatory workload versus ventilatory capacity
2. Oxygenation status
3. Cardiovascular function
4. Psychologic factors

Simply put, when ventilatory workload or demand exceeds ventilatory capacity, successful ventilator discontinuation is unlikely. Excessive ventilatory workload may lead to ventilatory muscle fatigue. When the ventilatory muscles fatigue, they must be rested for at least 24 hours to recover.[15] Ventilatory workload increases with decreased compliance, increased airway resistance, or an increased requirement for ventilation. Ventilatory capacity can be reduced by ventilatory muscle fatigue and by a loss of muscle strength and endurance.

Other factors that may contribute to ventilator dependence include inadequate arterial oxygenation, poor tissue oxygen delivery, myocardial ischemia, arrhythmias, low cardiac output, and cardiovascular instability. Neurologic problems that may contribute to ventilator dependence include decreased central drive to breathe and impaired peripheral nerve transmission. Psychologic issues that may contribute to ventilatory dependence include the fear of removal of the life-support system, anxiety, stress, depression, and sleep deprivation. Box 53.3 summarizes the major factors that contribute to ventilator dependence.

BOX 53.3 Factors That Contribute to Ventilator Dependence

Respiratory Factors

- Ventilatory workload exceeds ventilatory capacity
- Decreased compliance: lung or chest wall
- Increased resistance: artificial airways, bronchospasm, mucosal edema, secretions, and mechanical demand flow systems
- Increased dead space: pulmonary embolus and chronic obstructive pulmonary disease
- Ventilatory muscle weakness or fatigue
- Oxygenation problems
  - ↓ $\dot{V}/\dot{Q}$
  - Increased shunt
  - ↓ DO_2
  - ↓ Oxygen extraction ratio

Nonrespiratory Factors

- Cardiovascular factors
- Myocardial ischemia
- Heart failure
- Hemodynamic instability, hypotension, and arrhythmias
- Neurologic factors
- Decreased or increased central drive to breathe
- Decreased peripheral nerve transmission
- Psychologic factors
- Fear and anxiety
- Stress
- Confusion or altered mental status
- Depression
- Poor nutrition
- Multiple-system organ failure
- Equipment shortcomings

PATIENT EVALUATION

Careful patient assessment is required to determine which patients are ready to be quickly removed from ventilatory support, which patients may need a prolonged ventilator discontinuation phase, and which patients are not yet ready for the discontinuation of ventilatory support.

An important factor to consider as part of this assessment is the length of time that the patient has been receiving mechanical ventilation. In general, those who receive support for 72 hours

BOX 53.4 Factors Associated With Readiness for the Discontinuation of Ventilatory Support

- Reversal or partial reversal of reason for instituting mechanical ventilation
- Good baseline functional status
- Ventilatory capacity that is capable of meeting ventilatory workload
- Good oxygenation status
- Good cardiovascular performance
- Good functional status of other organs and systems
- Short duration of the critical illness
- Short duration of mechanical ventilation
- No psychologic factors affecting current status

Modified from Pierson DJ: Nonrespiratory aspects of weaning from mechanical ventilation. *Respir Care* 40:263–270, 1995.

or less often can be removed quickly from the ventilator.[16,17] Those who need a longer period of support may need a more prolonged approach. Current guidelines recommend that patients who need mechanical ventilation for more than 48 to 72 hours be carefully assessed to determine the possible causes of ventilator dependence.[1,4] These include the respiratory, cardiovascular, neurologic, and psychologic causes of ventilator dependence that are listed in Box 53.3. This recommendation is especially important for the care of patients who have had unsuccessful attempts at the discontinuation of ventilation.[1,4] Factors associated with readiness for the discontinuation of ventilatory support are summarized in Box 53.4.

The Most Important Criterion

The single most important criterion to consider when evaluating a patient for ventilator liberation or weaning is whether there has been significant alleviation or reversal of the disease state or condition that necessitated use of the ventilator in the first place.[1,4,10] The clinician should determine whether the patient's condition is improving, whether the initial reason for providing ventilatory support is improved or resolved, and whether the patient's clinical condition is stable. The following specific questions for patient evaluation have been suggested[1]:

1. Is there evidence of improvement or reversal of the disease state or condition that caused the need for mechanical ventilation?
2. Is the patient's oxygenation status adequate? Specific criteria may include the following: PaO_2 of 60 mm Hg or more, FiO_2 of less than 0.40 to 0.50, PEEP of less than 5 to 10 cm H_2O; PaO_2/FiO_2 of 150 to 200 or greater; and pH of 7.25 or greater.
3. Is the patient medically and hemodynamically stable? Specific criteria may include the absence of acute myocardial ischemia or marked hypotension. Patients should have adequate blood pressure without vasopressor therapy or with only low-dose intermittently delivered vasopressor therapy (i.e., less than 5 mcg/kg/min of dopamine or dobutamine).
4. Can the patient breathe spontaneously? The patient must be able to breathe spontaneously at sufficient tidal volumes and have a sufficient drive to breathe if ventilator liberation is being considered.

If the patient's condition is improving, if the alleviation or reversal of the precipitating disease state or condition has occurred, if the patient is capable of spontaneous breathing, and if the oxygenation status and hemodynamic values are stable, then ventilator liberation should be attempted.[1]

RULE OF THUMB In general, those who receive support for 72 hours or less often can be removed quickly from the ventilator.

Weaning Indices

Mechanical ventilation is hazardous, and unnecessary delays in ventilator discontinuation increase the associated complication rate. Unfortunately, premature ventilator discontinuation may also cause serious problems, including difficulty with reestablishing the artificial airway and serious compromise of the patient's clinical status. General clinical judgment alone has been found to be a poor guide to determining whether a patient is ready for ventilator discontinuation, and as a result, more specific indicators have emerged. Specific indicators or weaning indices that clearly show whether a patient is ready to have the ventilator removed and help avoid inappropriate ventilator discontinuation have been sought. Unfortunately, none of the current weaning indices predict readiness for ventilator discontinuance with a high level of accuracy.[1,4]

Traditional discontinuation indices include the PaO_2/FiO_2 ratio, the alveolar-to-arterial partial pressure of oxygen difference [$P(A - a)O_2$], the maximum inspiratory pressure (MIP), the vital capacity (VC), the spontaneous minute ventilation (V_{Esp}), and the maximum voluntary ventilation (MVV).[3,18] Newer indices include the **rapid, shallow breathing index (f/V_T)**, **airway occlusion pressure** ($P_{0.1}$), and measures of WOB.[1,4] Although all of these values can be useful, there are enormous discrepancies in the literature regarding their accuracy with regard to the prediction of "weanability."[1,4] With respect to the more traditional discontinuation indices, VC and MIP can be highly variable, whereas minute ventilation, respiratory rate (f), and f/V_T tend to be more reliable.[1,4] However, these measures may not correlate well with discontinuation success among all patients and especially among those receiving long-term ventilatory support, the elderly, and those with major pulmonary abnormalities.[1,4,19]

A comprehensive review of related research identified a possible role for 66 specific measurements as predictors of weaning success.[4] Of these, eight values were found to be the most useful for the prediction of successful ventilator discontinuation.[1,4] Useful predictive measures included spontaneous respiratory rate, spontaneous tidal volume, f/V_T, minute ventilation, MIP, $P_{0.1}$, $P_{0.1}$/MIP, and a combined index called the *CROP (Compliance Rate Oxygenation and Plmax) score* that included compliance, respiratory rate, oxygenation, and MIP.[1,4] Unfortunately, these measures all have limitations and can falsely suggest that a patient is ready for weaning.

It is doubtful that a single index will be found that can be used for consistent discrimination between discontinuation success and failure. Moreover, none of these traditional indicators alone has proved useful for the prediction of improvements in patient outcome or in the selection of a particular discontinuation method.[5,19]

Notwithstanding these limitations, the measurement of discontinuation indices in the difficult-to-wean patient may provide guidance regarding the reasons that patients fail discontinuation trials. Many find it useful to trend these indicators daily for those patients who require lengthy weaning times.[11,16] Specific values for respiratory indices that are used to predict the successful discontinuation of ventilatory support are found in Table 53.1.

RULE OF THUMB None of the indices predicting success or failure of weaning predict with sufficient accuracy the results of a weaning trial. The trial itself is the BEST determinant of ability to be liberated from the mechanical ventilator.

Ventilation

Increased thoracic cage movement during spontaneous breathing and asynchronous chest wall–to–diaphragm movement are related to an increased workload that may lead to ventilatory muscle fatigue and failure. Tachypnea (i.e., more than 30 to 35 breaths/min in adults) is a sensitive marker of respiratory distress, but it can prolong intubation if it is used as the only criterion. One explanation for this is that when sedation is lessened to facilitate weaning, the more awake patient may become anxious about having an endotracheal tube in place and being on a ventilator, which may itself cause their tachypnea. On the other end of the spectrum, irregular spontaneous breathing or periods of apnea indicate that the patient is at risk for weaning failure. Asynchronous and rapid shallow breathing patterns—although not definitive—suggest respiratory decompensation.[19] However, decreased ventilatory variability over time (rate, V_T, minute ventilation) has been clearly shown to identify patients who will fail an SBT.[20,21]

The evaluation of patients for the presence of palpable scalene muscle use during inspiration, an irregular ventilatory pattern, palpable abdominal muscle tensing during expiration, and the inability to alter the ventilatory pattern on command can be helpful for the assessment of the potential for prolonged spontaneous ventilation. Patients with none of these signs have a very high probability of successful ventilator discontinuance. Patients with one or two of these signs usually need continued support. The presence of three or more of these signs can mean that the patient's condition is unstable and that the patient has a poor prognosis for ventilator removal.[22]

$P_{0.1}$ is the inspiratory pressure that is measured 100 ms after airway occlusion.[1,4] The $P_{0.1}$ is effort-independent, and it correlates well with central respiratory drive. Patients who have a $P_{0.1}$ more negative than −5 cm H_2O have an increased WOB; the more negative the $P_{0.1}$ the less likely it is that the patient will be able to be liberated from ventilatory support.[1,4] Daily monitoring of $P_{0.1}$ can provide very useful information on patients' ventilatory drive and WOB (see Chapter 48 for more details).[1,4]

The f/V_T is the ratio of spontaneous breathing frequency (breaths/min) to tidal volume (liters), and it has been found to be a good predictor of discontinuation success for many patients who need mechanical ventilation.[1,4,19] The f/V_T has less predictive ability for patients who need ventilatory support for longer than 8 days, and it may be less useful for predicting discontinuation success among elderly patients.[1,4] Despite these limitations, an f/V_T of less than 105 can be an accurate and early predictor of weaning outcome, and an f/V_T of 80 is associated with an almost 95% probability of successful liberation.[19] The ratio must be calculated during 1 minute of unsupported spontaneous breathing, and the

TABLE 53.1 Indices That Are Used to Predict the Success of Weaning and Ventilator Discontinuation

Measurement	Criterion
Oxygenation	
FiO_2	≤0.40–0.50
PEEP (cm H_2O)	≤5–8
PaO_2 (mm Hg)	≥60
SaO_2 (%)	≥90
SvO_2 (%)	≥60
PaO_2/PAO_2 ratio	≥0.35
PaO_2/FiO_2 ratio	>150–200
$P(A\text{-}a)O_2$ (mm Hg)	<350
$\dot{Q}_s/\dot{Q}_T$ (% shunt)	<15%–20%
No lactic acidosis, adequate $\dot{Q}_T$, blood pressure	
Ventilation	
$PaCO_2$ (mm Hg)	<50
pH	≥7.35
Ventilatory Mechanics	
Respiratory rate (f) (breaths/min)	12–30
Tidal volume (V_T) (mL/kg)	>5
Vital capacity (VC) (mL/kg)	>10–15
Static compliance (mL/cm H_2O)	>25
f/V_T	<105
Respiratory Muscle Strength	
Maximum inspiratory force (MIF) (cm H_2O)	<–20 to –30
Ventilatory Drive (Demand)	
Minute ventilation ($\dot{V}_E$) for	
• Normal PCO_2 (L/min)	<10
• V_{DS}/V_T	<0.55–0.60
• $P_{0.1}$ (cm H_2O)	<6
• $P_{0.1}$/MIP	<0.30
Work of Breathing	
Spontaneous work of breathing	<1.6 kg·m/min (<0.14 kg·m/L)
Pressure-time index	<0.15–0.18
Ventilatory Reserve	
Maximum voluntary ventilation (MVV) (L/min)	>20; more than twice the $\dot{V}_E$

Data from MacIntyre NR, Cook DJ, Ely EW, et al: Evidence-based guidelines for weaning and discontinuing ventilator support: a collective task force facilitated by the American College of Chest Physicians, the American Association for Respiratory Care, and the American College of Critical Care Medicine. *Chest* 120:375S–395S, 2001; AHRQ publication no. 01-E010, Rockville, MD, 2000, Agency for Healthcare Research and Quality; American College of Chest Physicians: *Chest* 104:1833, 1993; Burns SM et al: *Am J Crit Care* 4:4, 1995; Sharar S: *Resp Care* 40:239, 1995; Bassili HR, Deitel M: *J Parenter Enteral Nutr* 5:161, 1981.

MINI CLINI

Calculating and Interpreting the Rapid, Shallow Breathing Index

Problem

You measure the following spontaneous breathing values for two patients who are being considered for weaning from mechanical ventilation:

Patient	Rate (f) (breaths/min)	V_T (L)
A	32	0.28
B	28	0.42

For which patient is successful weaning least likely?

Solution

First, compute the rapid, shallow breathing index for each patient as follows:

Patient	Rate (f) (breaths/min)	V_T (L)	f/V_T
A	32	0.28	114
B	28	0.42	67

Patient A clearly exceeds the threshold criterion of 105 breaths/min/L, whereas patient B falls well below this criterion. All else being equal, patient A is least likely to be successfully weaned.

addition of pressure support during measurement significantly reduces the predictive value of the ratio.[19]

RULE OF THUMB Adult patients with spontaneous respiratory rates >35 breaths/min, tidal volumes of <5 mL/kg PBW, and $P_{0.1}$ more negative than –5 cm H_2O are difficult to wean.

The $P_{0.1}$/MIP ratio has been found to be a good early predictor of discontinuation success,[1,4] and it may be more useful than the MIP by itself. The f/V_T also has been found to be a better predictor of discontinuation success than the MIP alone.[1,4] However, even with f/V_T of less than 105, as many as 20% of patients have false-positive results (i.e., they cannot be discontinued from ventilation despite a favorable index) as a result of unpredictable factors such as congestive heart failure, aspiration, other comorbidities or the development of a new pulmonary lesion. In addition, some patients can be successfully discontinued from ventilatory support despite poor f/V_T values (>105).

WOB would seem to be an excellent way to gauge spontaneous ventilatory workload. Successful weaning has been found to be less likely among patients with spontaneous WOB levels of more than 1.6 kg/m/min (16 J/min) or 0.14 kg/m/L (1.4 J/L).[1,4] However, WOB may not be predictive of weaning success for specific patients.[1,4] This may be because WOB does not take into account ventilatory muscle capacity or fatigue. Consequently, WOB may be less accurate than other conventional discontinuation indices, and it is very difficult to measure at the bedside.

Oxygen cost of breathing (OCB) is the difference between oxygen consumption during spontaneous breathing and oxygen consumption during apnea (i.e., during full ventilatory support), which is determined as follows:

$$OCB = VO_{2sp} - VO_2 \text{ (controlled ventilation)}$$

VO_{2SP}, oxygen consumption during spontaneous breathing; VO_2, oxygen consumption during controlled ventilation.

After the OCB has been estimated, the relative proportion of oxygen consumed by the respiratory muscles as compared with the body as a whole can be calculated as follows:

$$\%VO_2 \text{ (Resp)} = (OCB/VO_{2sp}) \times 100$$

Both OCB and $\%VO_2$ have been correlated with the number of days required to wean patients. Patients with an OCB of 15% or less of the total VO_2 may be more likely to achieve discontinuation success.[1,4]

Pressure–time product (i.e., the area under the inspiratory pressure–time curve) and pressure–time index (PTI) may be the best measures of ventilatory workload of patients who are receiving mechanical support.[1] The PTI can be calculated as follows:

$$PTI = (\text{Mean inspiratory pressure}/MIP) \times T_i/T_{tot}$$

where MIP is maximum inspiratory pressure, T_i is the inspiratory time in seconds, and T_{tot} is the total respiratory cycle time. The T_{tot} can be calculated by dividing 60 by the respiratory rate (f) (i.e., 60/f). A PTI of more than 0.15 to 0.18 has been associated with diaphragmatic fatigue, and a PTI of more than 0.15 cannot be sustained indefinitely.[1,4] There is currently no well-accepted and reliable way to measure ventilatory muscle fatigue in patients who are receiving mechanical ventilation.

Oxygenation

Poor oxygenation status is associated with weaning failure. Arterial blood gas (ABG) analysis, pulse oximetry, and continuous mixed venous oximetry have been used to monitor and assess the oxygenation status of patients before and during a discontinuation trial. In general, a PaO_2 of more than 60 mm Hg (or of more than 55 mm Hg for patients with COPD with carbon dioxide retention) with an FiO_2 of less than 0.40 to 0.50 and a PEEP of 5 to 10 cm H_2O or less should be adequate for ventilator discontinuation. The PaO_2/FiO_2 ratio should be 150 to 200 mm Hg or more. With these values, a normal hemoglobin level, a normal oxygen saturation (SaO_2), and adequate cardiac output and tissue perfusion are assumed. Specific indices used to assess oxygenation status are found in Table 53.1.

Acid–Base Balance

Ideally the patient should have a normal acid–base balance (i.e., a pH of 7.35 to 7.45), and abnormalities in acid–base status have been corrected, if possible, before weaning. Patients with metabolic acidosis often have an increased ventilatory drive that can make weaning difficult. Patients who have metabolic alkalosis or those who have been mechanically hyperventilated for several days may have a reduced ventilatory drive. In these cases, a gradual method of discontinuing ventilatory support may be necessary: one that restores acid–base balance to normal.

Metabolic Factors

Metabolic factors primarily affect discontinuation in those patients who require long-term ventilatory support. Although nutritional factors are important for all patients, they are unlikely to affect discontinuation in those who only require short-term ventilatory

support. Nutrition should be adequate to maintain respiratory muscle mass and contractile force. Feeding should be adjusted according to individual patient needs; most patients need 1.5 to 2.0 times their resting energy expenditure. In addition, protein intake should be between 1 and 1.5 g/kg per day. Excessive carbohydrate feeding can increase carbon dioxide production and may precipitate acute hypercapnic respiratory failure. Parenteral nutrition solutions that contain amino acid formulations (e.g., arginine/lysine) can cause metabolic acidosis and thus increase ventilatory demand. Metabolic rate can increase as a result of fever or sepsis. Increased WOB, shivering, seizures, and agitation can also increase oxygen demand and should be evaluated (see Chapter 23).

Renal Function and Electrolytes

Adequate renal function is required to maintain acid–base homeostasis, electrolyte concentrations, and fluid balance. Ideally, adult patients should have an adequate urine output (i.e., more than 1000 mL/day), and there should be no inappropriate weight gain or edema.

Renal insufficiency can lead to metabolic acidosis, which increases respiratory drive. Electrolyte disorders can impair ventilatory muscle function. Key electrolytes should be normal (see Chapter 17 for details). Fluid overload can lead to congestive heart failure and pulmonary edema, which may impair pulmonary gas exchange.

Cardiovascular Function

Adequate cardiovascular function is needed to provide sufficient oxygen delivery to the tissues. Cardiac rate and rhythm and blood pressure should be evaluated. Tachycardia (i.e., a heart rate of more than 100 beats/min) and bradycardia (i.e., a heart rate of less than 60 beats/min) should be controlled. The presence of arrhythmias, hypotension (i.e., a blood pressure of less than 90/60 mm Hg), and severe hypertension (i.e., a blood pressure of more than 180/110 mm Hg) should be evaluated carefully before the discontinuation of ventilatory support is considered.

Cardiac output and index measurements as well as central venous pressure measurements may be helpful for the evaluation of cardiovascular function. Left ventricular dysfunction, myocardial ischemia, and cardiovascular instability are associated with decreased discontinuation success.[1,4] Table 53.2 provides criteria for confirming cardiovascular stability (see Chapter 10).

TABLE 53.2 Criteria for Confirming Cardiovascular Stability

Criterion	Normal Value	Values That May Be Inconsistent With Weaning
Heart rate (beats/min)	60–100	<60, >120
Blood pressure (mm Hg)	90/60–150/90	<90/60, >180/110
$\dot{Q}_t$ (L/min)	4–8	<4, >8
Cardiac index (L/min/m^2)	2.5–4	<2.1
Cardiac rhythm	No major arrhythmias present	Tachycardia, bradycardia, multiple premature ventricular contractions, heart block
Hemoglobin (g/dL)	12–15	Anemia, <8
Hematocrit	40%–50%	<35%
No angina present		
No lactic acidosis		

Psychologic Factors and Central Nervous System Assessment

Adequate CNS function is needed to ensure stable ventilatory drive, adequate secretion clearance (i.e., coughing and deep breathing), and the protection of the airway (i.e., gag reflex and swallow). In addition, the level of consciousness, dyspnea, anxiety, depression, and motivation can affect discontinuation success.[1,4]

The patient ideally is awake and alert, free of seizures, and able to follow instructions. Patients should have an intact central drive to breathe and peripheral nerve function. Brainstem strokes, electrolyte disturbances, sedation, neuromuscular blocking agents, and narcotic drugs can impair the central neurologic control of ventilation. Mental status is a good predictor of discontinuation success, and patients who are not alert are at risk for upper airway obstruction, aspiration, and secretion retention. Obtunded patients should, at a minimum, have an adequate gag reflex and cough. Decreased levels of consciousness are associated with aspiration after extubation. The level of consciousness is affected by narcotic, sedative, and analgesic drugs. Drugs with CNS depressant effects should be discontinued, if possible, before the withdrawal of ventilatory support and extubation. Protocols to reduce sedation and the daily cessation of sedative drugs may reduce weaning time[7,23] (see the section on "Spontaneous Awaking Trials"). Neuromuscular blocking agents to allow for controlled ventilation should only be administered when absolutely necessary to insure patient–ventilator interaction and for the shortest period possible.[24,25]

Psychologic factors may be among the most important nonrespiratory contributing factors that lead to ventilator dependence.[1,4] Fear, anxiety, pain, and stress should be minimized, and frequent communication among the staff, the patient, and the patient's family can be helpful. Box 53.5 summarizes nonrespiratory factors that affect discontinuation success.

Integrated Indices

Many factors are associated with discontinuation success. Integrated indices may improve prediction by combining several measures of ability to breathe without ventilatory support. Current examples of integrated indices include the CROP score, the Adverse Factor/Ventilator Score, the weaning index, and the Burns Weaning Assessment Program.[1,4] The CROP score combines measures of ventilatory load, respiratory muscle strength, and gas exchange.

The Adverse Factor/Ventilator Score combines ratings of 15 adverse factors, including hemodynamic values, infection, nutrition, and neurologic/psychiatric state, with ratings of six ventilator factors, including FiO_2, compliance, minute ventilation, and rate.[1,4] The weaning index combines measures of ventilatory strength, endurance, and efficiency of gas exchange. A weaning index of less than 4 suggests successful discontinuation from mechanical ventilation. The Burns Weaning Assessment Program

BOX 53.5 Nonrespiratory Factors That Affect Weaning

- Acid–base status
- Metabolic alkalosis: decreased ventilatory drive
- Metabolic acidosis: increased ventilatory demand
- Mineral and electrolyte balance
- Hypophosphatemia: ventilatory muscle weakness
- Hypomagnesemia: ventilatory muscle weakness
- Hypokalemia: ventilatory muscle weakness
- Hypothyroidism: decreased ventilatory drive and impaired muscle function
- Stability of other organs and systems
- Cardiac: excessive preload (e.g., overall volume overload and increased preload on discontinuation of positive pressure ventilation) and impaired contractility
- Renal: renal insufficiency and metabolic acidosis
- Hepatic: encephalopathy and protein synthesis
- Gastrointestinal: stress-related hemorrhage and ability to take enteral nutrition
- Neurologic: level of consciousness, ability to protect the airway, and clear secretions
- Effects of drugs: narcotics, benzodiazepines, other sedatives and hypnotics, muscle relaxants, and aminoglycosides
- Nutritional status
- Ventilatory muscle function
- Ventilatory drive
- Immune defense system
- Psychologic and motivational factors

Modified from Pierson DJ: Nonrespiratory aspects of weaning from mechanical ventilation. *Respir Care* 40:289, 1995.

is a 26-item assessment that combines 12 general and 14 respiratory factors into a single score.[1,4] Although integrated indices appear promising, none of these indices has emerged as superior for use in diverse patient populations. *Despite the success of these integrated indices in very specific settings, the best approach to determining if a patient can be successfully discontinued from ventilatory support is the patient's performance on a SBT.* All patients should be assessed daily, and their ability to breathe spontaneously should be the primary variable to determine if the ventilator can be discontinued.

Evaluation of the Airway

The ability to maintain a patent natural airway and the likelihood of aspiration should be evaluated as a part of the process of discontinuing ventilatory support. It is important for the clinician to separate the decision to discontinue ventilatory support from the decision to extubate. The clinician must also be aware that most weaning indices do not evaluate airway patency or protection (see the section on "Extubation"). The inability to protect or maintain the natural airway is a clear contraindication to extubation. Some patients who can be successfully removed from a ventilator should not be extubated. Although controversial, evaluating if gas moves freely around the endotracheal tube (ETT) with the cuff deflated may identify an increased likelihood of postextubation airway obstruction. If auscultation of the lateral neck does not identify gas flow around the EET, extubation should be delayed until airway edema is properly treated with steroids.

MINI CLINI

Assessment of Readiness for a Spontaneous Breathing Trial

Problem

A 64-year-old man who underwent a lung resection and who has a long history of COPD is now 24 hours postoperative, and he is being evaluated for readiness for an SBT. The data currently available for this patient include the following:

- Ventilator settings:
  - Mode pressure support 10 cm H_2O
  - Average V_T 450 mL (6.5 mL/kg ideal body weight)
- Respiratory rate of 28 breaths/min
- FiO_2 of 0.40
- PEEP of 5 cm H_2O

The patient is alert and cooperative.

The patient is not receiving any vasoactive drugs, and he is only receiving intermittent sedatives and narcotics.

Should this patient be placed on an SBT?

Solution

By 24 hours, the patient should have initially recovered from the effects of the surgical procedure. The patient's ventilator settings are offering minimal support. Because the patient is alert and able to breathe spontaneously and because he requires only intermittent sedatives or narcotics, it is very appropriate to perform an SBT on this patient.

Tracheotomy may be considered for patients who need artificial airways for an extended period.

Tracheotomy may improve patient comfort, allow for more effective suctioning, decrease airway resistance (due mainly to shorter tube length), enhance mobility, and allow the patient to eat and speak. Some patients also need high levels of sedation to tolerate the endotracheal tube. Consequently, tracheotomy should be considered for the care of patients who are likely to benefit and for those who need prolonged mechanical ventilatory support. See Chapter 37 for details about airway management and extubation.

Other patients with good airway patency and protection may be unable to maintain spontaneous breathing for prolonged periods without assistance.[26] These patients may be candidates for noninvasive ventilation (NIV) after extubation; see Chapter 50 for details.[26,27]

RULE OF THUMB The decision to discontinue ventilatory support and the decision to extubate the patient are independent decisions. Many patients may be ready for the discontinuation of one but not the other! This is particularly true of patients with airway obstruction. They may be able to ventilate but removal of the ETT results in obstruction of the upper airway.

PREPARING THE PATIENT

Optimizing the Patient's Medical Condition

Before removal of ventilatory support is attempted, the patient's oxygenation status, ventilation, cardiovascular status, and overall medical condition should be optimized. Disease-imposed ventilatory load is minimized with the management of infection, bronchospasm, and airway edema. Bronchodilator therapy should

be maximized and the appropriate use of antiinflammatory agents considered. Techniques to facilitate secretion clearance (e.g., suctioning, adequate humidification, bronchial hygiene techniques), good nutrition, and optimal positioning should be used. The patient should be rested and not fatigued nor sleep deprived, which can be common in the ICU. The patient should be allowed to sleep at night while maintained on a level of ventilatory support that ensures ventilatory muscle rest.[28] Intrinsic PEEP during mechanical ventilation may increase trigger work, and appropriate amounts of PEEP or CPAP can help overcome this problem (see Chapter 48).[1,2] Box 53.6 lists factors that should be optimized before ventilatory support is discontinued.

RULE OF THUMB Despite the success of indices of readiness for ventilator discontinuation in very specific settings, the best approach to determining if a patient can be successfully discontinued from ventilatory support is the patient's performance on a spontaneous breathing trial.

Patients' Psychologic and Communication Needs

As many as 47% of patients who spend more than 5 days in an ICU experience psychologic disturbances.[28] The cause may be the stress of critical illness, the interruption of nighttime sleep, or the use of sedatives, tranquilizers, hypnotics, narcotics, and other drugs that affect the CNS.[28] The patient's environment should be optimized; anxiety, depression, and delirium should be evaluated; and communication should be maximized.

Environmental considerations that may improve the patient's sense of well-being and outlook, reducing the likelihood of developing delirium, include reducing extraneous noise and providing clocks, calendars, pictures, a radio, a television, and, if possible, a room with windows. Daily mobility should be considered, including getting the patient up in a chair or placing the patient in the hall in a chair. Patients whose condition has been stable can sometimes even be helped to walk with the use of an E cylinder for oxygen, a transport ventilator or ICU ventilator with appropriate battery support, and two or more healthcare workers for support. The process of increasingly mobilizing ICU patients including those on mechanical ventilation is known as **progressive mobility**. Preliminary clinical research on progressive mobility is promising but it tends to be very resource-intensive.

A method for the patient to communicate with staff and visitors should be devised, if possible. Writing tablets, picture boards, and alphabet boards have been used effectively by patients to communicate with staff and visitors.

Anxiety and agitation should be minimized, and communication and encouragement may be helpful. The patient should be told what is planned and be given some control over the situation. Patients should be asked to participate and help in the weaning process. Depression or a lack of motivation may increase weaning time. If depression or delirium is present, assessment and treatment by an appropriate healthcare provider should be considered.

BOX 53.6 Factors That Should Be Optimized Before the Discontinuation of Ventilatory Support Is Attempted

- Oxygenation
- PaO_2 and SaO_2
- Anemia, if present
- Atelectasis, pneumonia, and acute pulmonary disease
- Ventilation
- Humidification
- Secretion clearance (e.g., bronchial hygiene and suctioning)
- Bronchodilator therapy
- Respiratory alkalosis
- Imposed work of breathing
- Respiratory muscle fatigue or atrophy
- Acid–base balance and electrolytes
- Metabolic acidosis (e.g., lactic acidosis and ketoacidosis)
- Metabolic alkalosis (e.g., decreased serum potassium or chloride ions, nasogastric tube, and vomiting)
- Low phosphate level
- Low magnesium level
- Cardiac and cardiovascular status
- Blood pressure and cardiac output
- Arrhythmias, if present
- Myocardial ischemia
- Left ventricular function
- Renal factors
- Kidney function
- Fluid balance
- Fever, infection, or sepsis
- Pain (i.e., minimize without over-sedation)
- Sleep deprivation
- Drugs (narcotics, sedatives, tranquilizers, hypnotics, aminoglycosides, and neuromuscular blocking agents can depress or block the ventilatory drive)
- Psychologic status
- Level of consciousness (e.g., delirium, coma)
- Agitation
- Motivation
- Fear and anxiety
- Psychologic dependence on the ventilator
- Depression
- Intensive care unit psychosis
- Hypothyroidism
- Nutritional factors
- Overfeeding (i.e., increased carbon dioxide production)
- Malnutrition or protein loss
- Consider a high-fat, low-carbohydrate diet to minimize the production of carbon dioxide
- Gastrointestinal bleeding or obstruction
- Abdominal distention or ascites
- Time of day (avoid evenings, nights, and shift changes)
- Adequate staffing
- Interruptions and disruptions
- Technical factors

Modified from Kacmarek RM, Mack CW, Dimus S: *Essentials of respiratory care*, ed 4, St. Louis, 2005, Mosby.

CAREGIVER PREPARATION

Just like careful patient preparation, caregiver preparation should occur before the onset on an SBT, the respiratory therapist needs

to be properly prepared to perform the SBT. The orders should be checked and equipment should be gathered. Specifically, oxygen therapy, NIV, and reintubation equipment should be gathered and readied for use. The patient should be carefully assessed, the ventilator alarms properly set, and the patient emotionally prepared for the SBT. Patients should be aware that the SBT is a trial and that they may fail the trial. The patient should NOT consider a failed trial as a step backward but as a part of a process to become independent of the ventilator and should know that a number of SBTs are commonly necessary before the ventilator is discontinued.

RULE OF THUMB As many as 47% of patients who spend more than 5 days in an ICU experience psychologic disturbance.

METHODS

There are three basic methods of discontinuing ventilatory support[1,4]:

1. SBTs (via the mechanical ventilator or with a T-piece) alternating with mechanical ventilatory support
2. SIMV
3. PSV

Box 53.7 summarizes evidence-based criteria and related conclusions regarding methods for ventilator discontinuation.

Rapid Ventilator Discontinuation

When the precipitating disease state or condition that necessitates support has been significantly alleviated or reversed, most patients can be rapidly removed from mechanical ventilation.[1,4] These patients typically have acceptable blood gas levels with mechanical ventilation, adequate myocardial function, and no underlying cardiovascular, pulmonary, neurologic, or neuromuscular disorders. After a careful evaluation, patients in stable condition who have been treated with a ventilator for less than 72 hours and who have a good spontaneous respiratory rate and minute ventilation may undergo an SBT on the ventilator or with a T-piece for 30 to 120 minutes.[1,4,29] If the patient does well, the endotracheal tube can then be removed if there is no reason to maintain an artificial airway.

Today, most SBTs are performed with the patient attached to a ventilator that is set with the FiO_2 unchanged, on PSV zero cm H_2O and zero CPAP. This allows for a stable FiO_2 and ongoing monitoring. Others have recommended treating the patient with a low level of PSV (i.e., 5 to 8 cm H_2O) to overcome the resistance caused by the ventilator circuit, the demand flow system, and the artificial airway.[1,4] Others may prefer simply using CPAP (i.e., 5 to 7 cm H_2O). These methods have the advantage of allowing the clinician to maintain ventilator alarm settings that can provide a margin of safety in the event of apnea or severe hypoventilation. Low levels of CPAP may be useful for maintaining lung volumes and overcoming intrinsic PEEP. Some experts recommend PSV in combination with PEEP or CPAP.[2] However, the most widely accepted guidelines recommend a simple spontaneous breathing trial for the first SBT using the ventilator at zero CPAP and PSV 0 to 8 cm H_2O.[1,4]

BOX 53.7 Agency for Healthcare Research and Quality Summary of Evidence for Criteria for Weaning From Mechanical Ventilation

- Differences in clinicians' intuitive thresholds for the reduction or discontinuation of ventilatory support have a far greater impact on the failure of spontaneous breathing trials and on reintubation than do modes of discontinuation. When clinicians set a high threshold, many patients who could tolerate weaning remain on mechanical support longer than is necessary.
- There may be an interaction between the threshold and the mode of discontinuation; in other words, one mode may be superior when the threshold is high, whereas another may be superior when the threshold is low.
- Research to date suggests that the best answer to the question of when to start discontinuation trials is to develop a protocol that can be implemented by nurses and respiratory therapists that begins testing for the opportunity to reduce support immediately after intubation and reduces support at every opportunity.
- For stepwise reductions in mechanical support, pressure support mode or multiple daily spontaneous breathing trials are superior to synchronized intermittent mandatory ventilation.
- For trials of unassisted breathing, low levels of pressure support may be beneficial in select patients.
- There may be substantial benefits to the use of noninvasive positive pressure ventilation immediately following discontinuation and extubation.
- After cardiac surgery, early extubation is achieved with a variety of interventions and intensive care unit protocols.
- Although steroids can reduce postextubation stridor in children, the impact of steroids on reintubation in children and adults remains uncertain.
- Most theoretically plausible predictors of discontinuation and extubation success have no predictive power. Those with some predictive power include the rapid, shallow breathing index, which has been most intensively studied, the $P_{0.1}$/MIP ratio, and the Compliance Rate Oxygenation and Plmax index. However, these are relatively weak predictors of discontinuation success.
- Tests are rarely useful for increasing the probability of discontinuation success; on occasion, the results can lead to moderate increases in the probability of success.
- In general, discontinuation predictors are probably found to perform poorly because physicians have already considered the results when they select patients for studies.

Modified from the Agency for Healthcare Research and Quality: *Evidence report/technology assessment Number 23 (AHRQ Publication No. 01-E010)*, Rockville, MD, 2000, Agency for Healthcare Research and Quality.

RULE OF THUMB The best initial approach to liberating a patient from mechanical ventilation is the spontaneous breathing trial. Ideally applied with zero pressure support and zero PEEP for 30 to 120 min via the mechanical ventilator so that the ventilators' monitoring of the patient continues during the SBT.

Patients Who Need Progressive Weaning of Ventilatory Support

Patients who have been receiving mechanical ventilation for more than 72 hours and those with marginal oxygenation, ventilatory, cardiovascular, or medical statuses may need a more prolonged period for ventilator discontinuation.[1,4] The most common method for accomplishing this is SBTs interspersed with continued ventilatory support.

RULE OF THUMB The most common cause of the inability to wean is an imbalance between ventilatory capability and ventilatory demand.

Spontaneous Breathing Trials

The oldest discontinuation method is an SBT via either the ventilator or T-piece, which allows for spontaneous breathing several times per day interspersed with periods of mechanical ventilatory support. For gradual weaning, initial SBTs may last only 5 to 10 minutes. Full ventilatory support is resumed for a 4-hour rest period in the assist/control or pressure-support mode. The time off the ventilator is gradually increased until the patient stays off the ventilator for an extended period. SBTs can progress rapidly to ventilator removal.

When weaning is very difficult, the process can last days or even weeks. When a T-piece is used instead of the ventilator, the patient must be more carefully monitored, because none of the ventilator alarms are active during the SBT. If distress occurs, mechanical ventilation is resumed. In no case should the patient be overstressed during the SBT, because exhaustion can delay weaning.[2,8] An example of an SBT is presented in Box 53.8.

Advantages of SBTs include the early and frequent testing of the patient's ability to breathe spontaneously without support. The use of SBTs several times per day has become unpopular, because it requires a great deal of time on the part of ICU staff, and a single daily SBT seems to be just as effective for most patients.[1,4] PSV and CPAP are sometimes used during the SBT, and patients who tolerate spontaneous breathing with a low level of PSV (i.e., 8 cm H_2O or less) should be able to tolerate extubation.[30] Current recommendations suggest a single daily trial of spontaneous breathing may be preferable to other methods of weaning.[1,4] Results of randomized, controlled studies have shown SBTs to be faster than SIMV and at least as effective as PSV.[5,29,30,31] Furthermore, performing an SBT one time per day is as effective as performing SBTs several times per day, and 30-minute trials are as effective as 120-minute trials.[1,4]

BOX 53.8 Steps for Spontaneous Breathing Trials

1. Prepare the patient psychologically.
2. Set the ventilator at zero pressure support ventilation and zero continuous positive airway pressure (CPAP).
3. Maintain the FiO_2 at the baseline FiO_2 that the patient is receiving.
4. Monitor the patient's appearance, pulse, oxygen saturation measured by pulse oximeter, and blood pressure; observe the cardiac monitor for arrhythmia. Use the ventilator to monitor respiratory rate, tidal volume, and minute ventilation.
5. If the patient tolerates the spontaneous breathing trial (SBT) for 30–120 min, consider extubation.
6. If the patient does not tolerate the SBT for at least 30 min, reestablish the ventilator settings, and allow the patient to rest for at least a few hours before reattempting another SBT.
7. If repeated SBTs over multiple days are needed, individualize the patient's schedule, depending on his or her condition. In general, the weaning schedule should be stopped during the night so that the patient can rest and sleep.

A collective task force representing the American College of Chest Physicians, the American Association for Respiratory Care, and the American College of Critical Care Medicine published in 2001 evidence-based guidelines for weaning and discontinuing ventilatory support.[1] These guidelines were based in part on a comprehensive review of the evidence collected under the direction of the U.S. Agency for Health Care Policy and Research.[4]

RULE OF THUMB Care should be taken once a patient demonstrates signs of failing the SBT. The trial should be discontinued and the patient provided ventilatory support. If patients develop ventilatory muscle fatigue during the SBT it will take more than 24 h to completely recover from that fatiguing experience, delaying ventilator liberation.

The task force made 12 specific recommendations (Box 53.9). These include the regular use of formal and carefully monitored SBTs to guide clinical decision-making regarding the discontinuation of ventilatory support.[1] Specifically, the task force recommended that, for the care of patients who need mechanical ventilation for more than 24 hours, a search for all possible causes of ventilatory dependence should be conducted and an attempt should be made to reverse or optimize each condition. Spontaneously breathing patients with evidence of reversal of the underlying condition that necessitated the ventilatory support, adequate oxygenation, and hemodynamic stability should be assessed with an SBT. Table 53.3 lists criteria to be used when determining whether patients who are receiving high levels of ventilatory support can be considered for SBTs.

TABLE 53.3 Criteria Used to Determine Whether Patients Who Are Receiving Ventilatory Support Can Be Considered for Spontaneous Breathing Trials

Criteria	Description
Objective measurements	Adequate oxygenation (e.g., PO_2 of ≥60 mm Hg with an FiO_2 of ≤0.40–0.50; PEEP of ≤5–8 cm H_2O; PO_2/FiO_2 ratio of ≥150–200)
	Stable cardiovascular system (e.g., heart rate ≤100 beats/min; stable blood pressure; no [or minimal] vasopressors)
	Afebrile (i.e., temperature about 37°C)
	No significant respiratory acidosis
	Adequate hemoglobin (e.g., ≥8–10 g/dL)
	Adequate mentation (e.g., arousable, Glasgow coma score of ≥13, no continuous sedative infusions)
	Stable metabolic status (e.g., acceptable electrolyte levels)
Subjective clinical assessments	Resolution of acute phase of disease; physician believes discontinuation is possible; adequate cough

Modified from MacIntyre NR, Cook DJ, Ely EW, et al: Evidence-based guidelines for weaning and discontinuing ventilator support: a collective task force facilitated by the American College of Chest Physicians, the American Association for Respiratory Care, and the American College of Critical Care Medicine. *Chest* 120:375S–395S, 2001.

BOX 53.9 Evidence-Based Guidelines for Weaning and Discontinuing Ventilatory Support

Recommendation 1: For patients who need mechanical ventilation for more than 24 h, a search for all of the causes that may be contributing to ventilatory dependence should be undertaken. This is particularly true for the patient who has failed attempts at withdrawing the mechanical ventilator. Reversing all possible ventilatory and nonventilatory issues should be an integral part of the ventilatory discontinuation process.

Recommendation 2: Patients who are receiving mechanical ventilation for respiratory failure should undergo a formal assessment of discontinuation potential if the following criteria are satisfied:

1. Evidence for some reversal of the underlying cause for respiratory failure
2. Adequate oxygenation (e.g., PaO_2/FiO_2 ratio of more than 150–200; requiring positive end-expiratory pressure of no more than 5–8 cm H_2O; FiO_2 of no more than 0.4–0.5) and pH of more than 7.25
3. Hemodynamic stability as defined by the absence of active myocardial ischemia and the absence of clinically significant hypotension (i.e., a condition that necessitates no vasopressor therapy or therapy with only low-dose vasopressors such as dopamine or dobutamine [<5 mcg/kg/min])
4. The capability to initiate an inspiratory effort. The decision to use these criteria must be individualized. Some patients who are not satisfying all of these criteria (e.g., patients with chronic hypoxemia values of less than the thresholds cited) may be ready for attempts at the discontinuation of mechanical ventilation

Recommendation 3: Formal discontinuation assessments for patients who are receiving mechanical ventilation for respiratory failure should be performed during spontaneous breathing rather than while the patient is still receiving substantial ventilatory support. An initial brief period of spontaneous breathing can be used to assess the capability of continuing on to a formal spontaneous breathing trial (SBT). The criteria with which to assess patient tolerance during SBTs are the respiratory pattern, the adequacy of gas exchange, hemodynamic stability, and subjective comfort. Tolerance of SBTs that last 30–120 min should prompt consideration for permanent ventilatory discontinuation.

Recommendation 4: The removal of the artificial airway from a patient who has successfully been discontinued from ventilatory support should be based on assessments of airway patency and the ability of the patient to protect the airway.

Recommendation 5: Patients who are receiving mechanical ventilation for respiratory failure who fail an SBT should have the cause of the failed SBT determined. After any reversible causes of failure are corrected and if the patient still meets the criteria listed in Table 53.3, subsequent SBTs should be performed every 24 h.

Recommendation 6: Patients who are receiving mechanical ventilation for respiratory failure who fail an SBT should receive a stable, nonfatiguing, and comfortable form of ventilatory support.

Recommendation 7: Anesthesia and sedation strategies and ventilatory management that are aimed at early extubation should be used for postsurgical patients.

Recommendation 8: Weaning and discontinuation protocols that are designed for nonphysician healthcare professionals should be developed and implemented by intensive care units (ICUs). Protocols that are aimed at optimizing sedation should also be developed and implemented.

Recommendation 9: Tracheotomy should be considered after an initial period of stabilization on the ventilator when it becomes apparent that the patient needs prolonged ventilatory assistance. Tracheotomy should then be performed when the patient appears to be likely to gain one or more of the benefits ascribed to the procedure. Patients who may derive particular benefit from early tracheotomy include the following:

- Those who need high levels of sedation to tolerate translaryngeal tubes
- Those with marginal respiratory mechanics (often manifested as tachypnea) in whom a tracheostomy tube with lower resistance may reduce the risk of muscle overload
- Those who may derive psychological benefit from the ability to eat orally, communicate by articulated speech, and experience enhanced mobility
- Those in whom enhanced mobility may assist with physical therapy efforts

Recommendation 10: Unless there is evidence for clearly irreversible disease (e.g., high spinal cord injury, advanced amyotrophic lateral sclerosis), a patient who requires prolonged mechanical ventilatory support for respiratory failure should not be considered permanently ventilator dependent until 3 months of weaning attempts have failed.

Recommendation 11: Critical care practitioners should familiarize themselves with facilities in their communities or units in hospitals that are staffed with individuals that specialize in managing patients who have prolonged dependence on mechanical ventilation. Such familiarization should include reviewing published peer-reviewed data from those units, if available. When they are medically stable for transfer, patients who have failed ventilatory discontinuation attempts in the ICU should be transferred to those facilities that have demonstrated success and safety with accomplishing ventilator discontinuation.

Recommendation 12: Weaning strategies in the patient who requires prolonged mechanical ventilation should be slow paced and should include gradually lengthening self-breathing trials.

Modified from MacIntyre NR, Cook DJ, Ely EW Jr, et al.; American College of Chest Physicians; American Association for Respiratory Care; American College of Critical Care Medicine: Evidence-based guidelines for weaning and discontinuing ventilatory support: a collective task force facilitated by the American College of Chest Physicians; the American Association for Respiratory Care; and the American College of Critical Care Medicine. *Chest* 120(6 Suppl):375S–395S, 2001.

A daily screen that includes the assessment of oxygenation, PEEP, and the use of vasopressors and sedatives should be conducted. A PaO_2/FiO_2 ratio of more than 150 to 200, a PEEP value of less than 5 to 8 cm H_2O, and a lack of a continuous infusion of vasopressors or sedatives (i.e., less than 5 mg/kg/min of dopamine) were good predictors of successful extubation and survival.[32]

The formal SBT may be performed in combination with low levels of PSV (i.e., 5 to 8 cm H_2O), CPAP (i.e., 5 cm H_2O or less), or ATC applied to just offset the imposed WOB caused by the endotracheal tube.[1] During the SBT, the patient is carefully observed for breathing comfort, anxiety, agitation, dyspnea, or diaphoresis. Respiratory rate, heart rate, blood pressure, and SpO_2 are monitored. The SBT is terminated if signs of distress are observed, including the following:

- Agitation, anxiety, diaphoresis, or a change in mental status
- A sustained respiratory rate of more than 35 breaths/min
- A sustained SpO_2 of less than 90%
- A more than 20% increase or decrease in heart rate or a heart rate of more than 120 to 140 beats/min
- A systolic blood pressure of more than 180 mm Hg or of less than 90 mm Hg

Patients with unsuccessful results of an SBT are returned to full ventilatory support for 24 hours to allow the ventilatory muscles to recover. During this period, the causes of failure are identified and corrected, if possible, and the patient is then reevaluated.

BOX 53.10 Weaning Protocol for a Spontaneous Breathing Trial

1. Verify that the patient is a candidate for ventilator discontinuation.
   a. Is there evidence of the reversal or alleviation of the disease state or condition that required mechanical ventilatory support?
   b. Is the patient able to breathe spontaneously?
   c. Has the patient's medical condition been optimized (i.e., afebrile, adequate hemoglobin, and acceptable electrolyte levels)?
   d. Are oxygenation, ventilation, and blood gas values adequate?
      - PaO_2 of at least 60 mm Hg with FiO_2 of no more than 0.40–0.50 with PEEP/CPAP of no more than 5–8 cm H_2O
      - PaO_2/FiO_2 ratio of 150–200 mm Hg or more
      - pH of 7.25 or more
   e. Is the patient awake and alert, free of seizures, and able to follow instructions?
   f. Is there evidence of hemodynamic stability? Are vasopressors only administered intermittently?
2. Prepare the patient for the SBT.
   a. Be sure that adequate personnel are present.
   b. Ensure that there are no other ongoing procedures or other major activities.
   c. Eliminate or minimize respiratory depressants (e.g., sedatives, narcotics).
   d. Suction the airway, as needed.
   e. Sit the patient up in bed, if possible.
3. Set the ventilator at zero CPAP and zero pressure support.
4. Continuously monitor the patient.
5. If any of the following occurs and are sustained, return the patient to mechanical ventilatory support:
   a. Respiratory rate of at least 35 breaths/min
   b. Oxygen saturation measured by pulse oximeter of less than 90%
   c. 20% increase or decrease in heart rate or heart rate of more than 120 beats/min
   d. Systolic blood pressure of more than 180 mm Hg or of less than 90 mm Hg
   e. Agitation, diaphoresis, or anxiety
6. Continue the trial for at least 30 min but not more than 2 h. If no signs of intolerance develop (see step 5), consider extubation.

CPAP, Continuous positive airway pressure; *PEEP*, positive end-expiratory pressure; *SBT*, spontaneous breathing trial.
Modified from MacIntyre NR, Cook DJ, Ely EW, Jr, et al; American College of Chest Physicians; American Association for Respiratory Care; American College of Critical Care Medicine: Evidence-based guidelines for weaning and discontinuing ventilatory support: a collective task force facilitated by the American College of Chest Physicians; the American Association for Respiratory Care; and the American College of Critical Care Medicine. *Chest* 120(6 Suppl):375S–395S, 2001.

If the criteria listed in Table 53.3 continue to be met, SBTs are repeated every 24 hours.[3] Patients who tolerate the formal SBT for 30 to 120 minutes are ready for ventilator discontinuance, and extubation is considered. Box 53.10 is a sample protocol for an SBT for the discontinuation of ventilatory support.

Continuous Positive Airway Pressure

CPAP is used during an SBT in many facilities. CPAP has the advantages of maintaining the lung volume during the weaning phase and thus of improving the patient's oxygenation status. Minimal levels of CPAP may be useful for reducing WOB and compensating for auto-PEEP, particularly in patients with obstructive lung disease.[1,4] CPAP is usually provided by the CPAP mode available on most mechanical ventilators. By using the ventilator in the CPAP mode, the clinician can take advantage of the alarm systems that are available. In fact, most institutions use the CPAP mode with zero CPAP level to take advantage of the ventilator alarms during weaning. This always provides an improved margin of safety as compared with the use of a T-piece and should today be the standard approach to an SBT.

Synchronized Intermittent Mandatory Ventilation

Weaning from SIMV involves the gradual reduction of the machine rate on the basis of the results of ABG analysis and patient assessment. Early claims that SIMV allowed for faster weaning times[8] have not been substantiated by subsequent studies.[29–31]

Patients who are receiving ventilation in the SIMV mode uncouple their breathing efforts from the support provided by the machine.[1,4] They continue to make spontaneous breathing efforts during the delivery of a "mandatory breath." Evidence also suggests that, once the machine cycling rate is reduced to approximately 50% of the full ventilatory support value, the patient breathes approximately as hard per cycle during the mandatory breaths as during the unsupported spontaneous breaths.[33,34] This additional work can be overcome with the use of pressure support (i.e., 5 to 10 cm H_2O). However, the addition of pressure support further complicates the weaning process. For initial ventilator setup, the SIMV rate and the tidal volume usually are set at values that are equivalent to those used during volume control-continuous mandatory ventilation (VC-CMV) or pressure control-continuous mandatory ventilation (PC-CMV). When the patient's condition has been stabilized, one of two approaches have been used. Some clinicians prefer to continue at these settings until the patient's precipitating disease state or condition has improved considerably. At that point, the rate is reduced in a stepwise manner until complete spontaneous breathing can be achieved. Other clinicians prefer to immediately reduce the level of mechanical ventilation to an SIMV rate of 4 to 8 per minute, thereby forcing the patient to perform additional WOB. From the beginning, attempts are made to reduce the SIMV rate, and the patient is challenged to provide a portion of the required ventilation. Unfortunately, research indicates that SIMV prolongs ventilatory support and that it is the least effective method of weaning from ventilatory support as compared with either SBT or PSV.[1,4,29,30,31]

Pressure Support Ventilation

PSV is a mode of ventilatory support that allows the patient to have significant control over the process of ventilatory support. The only gas-delivery variable directly controlled by the ventilator is peak airway pressure; see Chapters 46 and 49 for details.

For initial ventilator setup in the PSV mode, the beginning pressure level can be adjusted to deliver an appropriate tidal volume, which is usually approximately 4 to 8 mL/kg of the ideal body weight based on the patient's condition and the desired tidal volume. PSV is then gradually reduced to a minimal value that only compensates for the WOB imposed by the artificial

BOX 53.11 Protocol for Pressure Support Weaning

1. Verify that the patient is a candidate for ventilator discontinuation:
   - Evidence of alleviation or reversal of the disease state or condition that necessitated ventilatory support
   - Stable, spontaneous breathing pattern without irregular breathing or periods of apnea
   - Optimization of the patient's medical condition
   - Adequate oxygenation, ventilation, and acid–base balance
2. Begin with a pressure support ventilation (PSV) level that achieves a tidal volume of 4–8 mL/kg of the ideal body weight. A PSV of more than 20 cm H_2O rarely is needed. The need for a high level of PSV indicates that the patient may not be ready for ventilator discontinuation.
3. Reduce the PSV 2–4 cm H_2O as tolerated, ideally at least twice daily, and reassess the patient for signs of intolerance:
   - Rate of at least 25–30 breaths/min
   - 20% or greater increase in heart rate or a heart rate of more than 120 beats/min
   - 20% or greater increase in systolic blood pressure or systolic blood pressure of more than 180 mm Hg or of less than 90 mm Hg
   - Agitation, anxiety, and diaphoresis
4. If the patient does not tolerate a reduction in PSV, return to the previous value, and reassess.
5. Continue to reduce PSV as tolerated at least twice per day and more frequently if the patient does not have signs of distress.
6. Consider extubation when the patient is able to tolerate a PSV of 5–8 cm H_2O for 2 h with no apparent distress.

Modified from Esteban A, Frutos F, Tobin M, et al: A comparison of four methods of weaning patients from mechanical ventilation. Spanish Lung Failure Collaborative Group. *N Engl J Med* 332:345–350, 1995; and Brochard L, Rauss A, Benito S, et al: Comparison of three methods of gradual withdrawal from ventilatory support during weaning from mechanical ventilation. *Am J Respir Crit Care Med* 150:896–903, 1994.

airway.[29–31] Generally this is about 5 to 8 cm H_2O. After this reduction is accomplished, extubation can be performed directly from the low-level pressure support, or an SBT may be conducted for 30 to 120 minutes.[1,4]

PSV allows the clinician to manipulate the level of patient work, but the benefit of this to weaning is questionable.[1,4] In general, patients who can spontaneously breathe comfortably at 5 to 8 cm H_2O of PSV can be extubated without problems. However, if upper airway edema is present, WOB after extubation may be about the same as that caused by the endotracheal tube. In these cases, low levels of pressure support may give a false impression about the patient's ability to tolerate extubation (Box 53.11).[1,4]

Synchronized Intermittent Mandatory Ventilation With Pressure Support Ventilation

With SIMV, the addition of pressure support can overcome the WOB imposed during "spontaneous" breaths because of the presence of endotracheal and tracheostomy tubes, demand flow systems, and ventilator circuits. In this setting, pressure support is set to achieve the desired tidal volume during the spontaneous breaths (i.e., 4 to 8 mL/kg of the ideal body weight).

MINI CLINI

Setting Pressure Support Levels

Problem

An intubated patient is receiving mechanical ventilation in the SIMV mode with the following settings:

- V_T = 400 mL
- Rate = 12 breaths/min
- Peak inspiratory pressure = 40 cm H_2O
- Plateau pressure (P_{plat}) = 20 cm H_2O
- Ventilator inspiratory flow ($\dot{V}$) = 60 L/min (1 L/s)

The patient is breathing spontaneously with a spontaneous rate of 12 breaths/min and a spontaneous peak inspiratory flow of 30 L/min (0.5 L/s). Find the level of PSV that is needed to overcome the imposed WOB.

Solution

$$PSV = ([PIP - P_{plat}]/\dot{V}_{mach}) \times \dot{V}_{Imax}$$

$$PSV = ([40\ cmH_2O - 20\ cmH_2O]/1\ L/s) \times 0.5\ L/s$$
$$= 10\ cmH_2O$$

The calculated PSV level to overcome the imposed WOB for this patient is 10 cm.

Although it is clear that the addition of PSV during SIMV can reduce or eliminate imposed work caused by mechanical factors, it has not been shown how this affects weaning. In one study, SIMV with PSV increased tidal volume and reduced respiratory rate but did not significantly reduce weaning time or success as compared with SIMV alone.[35] On the basis of all of the weaning trials, it can be concluded that this approach to weaning can only increase the length of ventilatory support. Current guidelines recommend the use of SBT to rapidly wean patients from ventilatory support.[1,4]

RULE OF THUMB SIMV should not be used as a mode of weaning from ventilatory support. It prolongs the weaning phase and the total length of ventilatory support.

Spontaneous Awaking Trials

Concern regarding the use of sedation in critically ill patients has increased markedly during the last few years. This concern has focused on the issue of delirium.[36] The indiscriminate use of sedatives in the ICU is considered inappropriate patient management. In general, sedatives should always be considered last when trying to handle an agitated patient (Chapter 48). Something has caused the patient's agitation, and it should be addressed and corrected, if possible, before sedation is administered. In addition, it is becoming clearer that the use of excessive sedation lengthens the time of mechanical ventilation. The use of **spontaneous awaking trials (SAT)** along with daily SBT results in the faster weaning of patients from ventilatory support as well as a decrease in mortality.[37] The decrease in mortality is attributed to patients being exposed for a shorter time to the complications of mechanical ventilation. Throughout the course of mechanical ventilation, sedation should be kept to the bare minimum necessary; patient sedation should be periodically carefully assessed before additional sedation is given.[37,38] Before sedation is given the cause of the agitation should be addressed. Frequently this a result of patient–ventilator asynchrony, which can be minimized

TABLE 53.4 The Riker/Sedation Agitation Scale, the Ramsay Sedation Scale, and the Richmond Agitation Scale

Riker/Sedation Agitation Scale

Score	Level of Sedation/Agitation	Response
7	Dangerous agitation	Pulling ETT, Climbing out of bed, etc.
6	Very agitated	Does not calm, requires restraints
5	Agitated	Calms to instructions
4	Calm and cooperative	Obeys commands
3	Sedated	Difficult to verbally arouse
2	Very sedated	Arouses to physical stimuli
1	Unarousable	Minimal or no response to noxious stimuli

- Prior to conducting a SBT the SAS scale should be reduced to insure a score of 3–5, ideally 4.

The Ramsay Sedation Scale

Clinical Score	Patient Characteristics
1	Anxious, agitated, or restless
2	Cooperative, oriented, and tranquil
3	Sedated but responds to commands
4	Asleep; brisk response to light glabellar tap or loud auditory stimulus
5	Asleep; sluggish response to light glabellar tap or loud auditory stimulus
6	Asleep; no response to painful stimuli

- Prior to conducting a SBT the Ramsey Sedation Scale should be at a score of 2–4, ideally 2.

Richmond Agitation Sedation Scale (RASS)

Score	Term	Description	
	Combative	Overtly combative, violent, immediate danger to staff	
	Very agitated	Pulls or removes tube(s) or catheter(s); aggressive	
	Agitated	Frequent nonpurposeful movement, fights ventilator	
	Restless	Anxious but movements not aggressively vigorous	
	Alert and calm		
–1	Drowsy	Not fully alert, but has sustained awakening (eye-opening/eye contact) to *voice* (>10 s)	Verbal stimulation
–2	Light sedation	Briefly awakens with eye contact to *voice* (<10 s)	Verbal stimulation
–3	Moderate sedation	Movement or eye opening to *voice* (but no eye contact)	Verbal stimulation
–4	Deep sedation	No response to voice, but movement or eye opening to *physical* stimulation	Physical stimulation
–5	Unarousable	No response to *voice or physical* stimulation	Physical stimulation

SAS, Sedation Agitation Scale; *SBT*, spontaneous breathing trial.

by careful adjustment of the ventilator. One of the currently available systems to rate the level of sedation should be in use on all mechanically ventilated patients [Riker/Sedation Agitation Scale (SAS), Ramsay Sedation Scale, or Richmond Agitation Scale (RASS)] Table 53.4.

RULE OF THUMB The use of spontaneous awaking trials (SAT) along with daily SBT results in the faster weaning of patients from ventilatory support as well as a decrease in mortality.

NEWER TECHNIQUES FOR FACILITATING VENTILATOR DISCONTINUANCE

Mandatory Minute Volume Ventilation

Mandatory minute volume ventilation (MMV) was described and introduced in 1977.[39] With this mode of ventilation, the total minute volume is set, and the patient may elect to inspire all of the minute volume, part of the minute volume, or none of the minute volume spontaneously. The ventilator would automatically provide a clinician-set remainder of the minute volume. It was originally assumed that, as the patient's status improved, he or she would assume by spontaneous breathing a greater and greater percentage of the set minute volume, eventually inspiring it all spontaneously. However, this did not occur; patients generally settled into a ventilator pattern where the overall WOB was shared between the patient and the ventilator, and the patient never assumed a greater percentage of the work.[40] There is no data to support the use of MMV over SBT or PSV to wean patients from ventilatory support.

Adaptive Support Ventilation/Intellivent

ASV is a newer mode of ventilation that maintains a minimum minute ventilation with an optimal breathing pattern (tidal volume and rate) that is based on the work of Otis;[41,42] see Chapters 46 and 49 for details. ASV automatically adjusts inspiratory pressure and ventilator breath rate to achieve the target minute volume set. As the patient's status improves, the target minute

volume is reduced, and the level of pressure required for each breath diminishes. When a minimal level is reached, the patient is considered weaned from ventilatory support and ready for extubation.

Preliminary studies of ASV for the care of patients who are recovering from cardiac surgery show a reduction in the duration of mechanical ventilation as compared with an SIMV weaning protocol.[42,43] Additional data about ASV indicates that it works very well for patients who are under controlled ventilation,[44] but data from large heterogeneous groups of patients will be necessary to determine if ASV truly improves the speed of ventilator discontinuation.

A recent upgrade of ASV is referred to as Intellivent.[45] With this modification the ventilator becomes a total closed loop controller of not only ventilation but also oxygenation. Incorporated into the management algorithm are the ARDSnet PEEP/F_IO_2 tables. Thus all aspects of gas delivery are controlled. As with ASV, Intellivent works well on patients under controlled ventilation and those requiring simple postoperative ventilation, and has shown the ability to wean patients from ventilatory support.[46] However, no comparison to SBT is currently available. Intellivent use in the complex patient spontaneously triggering the ventilator is still controversial. However, one can expect this type of closed loop control of ventilation will begin to appear on other mechanical ventilators.

Computer-Based Weaning

Current versions of MMV and ASV/Intellivent are examples of computer-controlled mechanical ventilation. Several more complex systems have been developed, including Ventilation Manager, VQ-attending, ESTER, Continuous Respiratory Evaluator (CORE), KUSIVAR, and WEAN-PRO.[47] The desire to develop computer-based weaning protocols is based on two factors. First, weaning is a time-consuming and labor-intensive process. If computer control can expedite or simplify this process, considerable time and money can be saved. Second, because most weaning decisions are based on objective data, computer-based weaning protocols are relatively easy to develop.[47]

The most successful computerized application for weaning is the Smart Care approach.[48,49] The system adjusts pressure support on the basis of the patient's tidal volume, respiratory rate, and end-tidal carbon dioxide level. When the pressure support has been decreased to a predefined level, the ventilator automatically begins an SBT. If the patient fails the SBT, which is determined by changes in the patient's respiratory rate, tidal volume, and end-tidal carbon dioxide level, then the ventilator automatically reassumes ventilatory support. If the patient passes the SBT, the ventilator also returns to baseline ventilatory support but notifies the clinician that the patient is ready for ventilator discontinuation. Two studies comparing SmartCare to clinician-controlled SBT have demonstrated that patients wean faster and both the total number of days that patients are maintained in the ICU and the need for postextubation NIV are reduced with SmartCare.[48,49] One criticism of this research was that the clinician-applied SBTs were not always performed consistently. However, this is clinical reality—in the ICU there are always good intentions to do an SBT, but emergencies, new admissions, and other important job functions too often delay or prevent clinicians from performing the SBT in a timely manner. With SmartCare, if the patient meets criteria, the SBT is performed regardless of the activity in the ICU. It should be noted that at least at the time of this revision the FDA only allows SmartCare in the United States to notify clinicians of the readiness for an SBT and the patient's status during the SBT. The clinician must adjust the ventilator into and out of the SBT. In the rest of the world this is performed automatically by the ventilator. It can be expected that automated weaning systems will increasingly have a place in the care of critically ill patients.

Automatic Tube Compensation

Automatic tube compensation (ATC) is an option on newer mechanical ventilators that compensates for the flow-dependent pressure decrease across the endotracheal tube during both inspiration and expiration; see Chapters 46 and 49 for details. ATC reduces WOB and may improve patient comfort.[50] Because it compensates for the imposed WOB caused by the artificial airway, ATC has been referred to as *electronic extubation.* Patients who can breathe adequately with the addition of ATC at low peak airway pressure (i.e., <8 cm H_2O) should tolerate extubation. ATC is similar to pressure support in that an inspiratory pressure is used to compensate for imposed WOB; however, ATC varies the pressure, depending on the size of the endotracheal tube and the patient's inspiratory flow rate. Alternatively, PSV delivers a preset inspiratory pressure that may overcompensate or undercompensate imposed WOB at any given point in time. However, at this time no research indicates that ATC weans patients faster than SBTs or PSV.

Volume Support

VC is a newer mode of ventilation that combines pressure support and volume ventilation by allowing the level of pressure support to be automatically adjusted to maintain a target tidal volume. In the VC mode, inspiration is initiated by the patient. During the inspiratory phase, the pressure level is regulated to a value that is based on the previous breath's pressure-volume relationship as compared with a target tidal volume. The pressure-support level is automatically adjusted in a stepwise manner by up to ±3 cm H_2O from one breath to the next to maintain the target tidal volume.

A major problem with VC is the excessive reduction of airway pressure in the presence of high ventilatory demand, thereby increasing patient effort.[51] With most ventilators offering this mode, no lower limit to ventilating airway pressure is set, and inspiratory airway pressure can decrease all the way to the PEEP level. Volume support may offer a sort of automatic weaning from pressure support. As the patient's spontaneous tidal volume improves, the level of pressure support is automatically reduced. However, clinical trials indicate no benefit to the use of VC to wean patients.[52]

Proportional Assist Ventilation and Neurally Adjusted Ventilatory Assist

PAV and NAVA are two of the newest modes of ventilatory support.[53] These modes differ from all other modes of ventilation

since they do NOT force a ventilatory pattern. Instead they follow the ventilatory pattern desired by the patient. As a result, patient–ventilator synchrony is greater with these modes than with any of the other ventilatory modes.[54–56] Unfortunately, there are no data regarding the use of these modes to facilitate ventilator discontinuation. At this time, regardless of how these modes improve patient–ventilator interaction, the decision to discontinue ventilatory support should be made based on performance of an SBT. Future research should be able to define if these modes have a greater role in the ventilator discontinuation process.

Newer Techniques for Evaluation of Diaphragm Function and Prediction of Successful Discontinuation

Recently the use of **esophageal pressure**, **diaphragm ultrasound**, and the **diaphragmatic electromyographic signal (EAdi)** have been used to assess diaphragm function and predict performance during SBTs.[5] Normal **esophageal pressure** swings during normal resting breathing are limited, normally from about a negative 3 to 5 cm H_2O during inspiration to a positive 3 to 5 cm H_2O during exhalation, or a transpulmonary pressure of plus 3 to 5 during inspiration and a transpulmonary pressure of minus 3 to 5 during exhalation. Transpulmonary pressure is equal to alveolar pressure minus esophageal pressure. During maximum stressed increased WOB, esophageal pressure may decrease to –30 cm H_2O.[5] It is believed there is a threshold of negative pressure swing that will predict weaning failure. Currently this area has not been well researched, but expect to see more information in the near future on the use of esophageal pressure/transpulmonary pressure measurements to determine readiness to wean and the likelihood of successful weaning.

Diaphragm ultrasound can determine the thickness of the diaphragm and percent increase of diaphragm thickness during normal and stressed breathing.[57] During ventilatory support three things can happen to the diaphragm: (1) Its resting thickness can remain unchanged, (2) its resting thickness can decrease because of disuse atrophy, or (3) diaphragm thickness can increase (hypertrophy) because of excessive workload.[58] Preliminary work indicates that the greater the diaphragm thickness varies from baseline—whether atrophy or hypertrophy—the less likely the patient is to wean from ventilatory support.[58] Again, this work is preliminary, but expect to see increasing amounts of data using this technique.

Diaphragm EAdi, with the introduction of NAVA, was not only a method of providing synchrous mechanical ventilation but a method of monitoring the electrical activity of the diaphragm. The change in baseline EAdi to peak EAdi during inspiration provides an evaluation of ventilatory drive and effort.[59] As with esophageal pressure measurements and ultrasound, work is being done to determine how weaning is affected by the magnitude of the EAdi change during inspiration.

Expect to see increasing research on the use of these three techniques to assist in the evaluation of readiness to wean and the likelihood of successful extubation.

Noninvasive Ventilation/Continuous Positive Airway Pressure

A number of groups have studied the use of NIV as an adjunct to ventilator discontinuance. Essentially, NIV/CPAP has been used in this setting in three different manners:

1. Transitioning patients with COPD who failed SBTs from invasive ventilation to spontaneous breathing[60–62]
2. Supporting patients who passed SBTs but who are at high risk for failing the extubation[26,27,63]
3. Supporting patients who developed hypercarbic/hypoxemic respiratory failure after extubation[64,65]

The literature strongly supports the first two indications but does not support the third application. Refer to Chapter 50 for details regarding the application of NIV/CPAP during weaning and the use of NIV/CPAP in general.

High-Flow Nasal Cannula

As with NIV/CPAP, some patients at high risk for reintubation should receive HFNC for 24 to 48 hours post extubation.[66] In adults, HFNC establishes about 1 cm H_2O CPAP for 10 L/min flow delivered to the patient. Patients requiring support of ventilation should receive NIV, patients requiring PEEP should receive CPAP, and patients whose hypoxemia does not require a high and fixed level of PEEP to reverse atelectasis should receive HFNC.[66] See Chapters 42 and 50 for details.

Role of Mobility

If you do not move it, you lose it! This has become increasingly clear when it comes to patients in the process of weaning from ventilatory support. Mobilization of the mechanically ventilated patient should begin as soon as the patient is stabilized, requires minimal sedation, and is capable of interacting with the

MINI CLINI

Response to a Spontaneous Breathing Trial

Problem

A 70-year-old woman with a long history of congestive heart failure has been mechanically ventilated for 6 days. She has failed three previous SBTs, but today, at the end of a 45-minute SBT, her clinical presentation was as follows:

- Respiratory rate of 24 breaths/min
- Tidal volume of 300 mL (6 mL/kg ideal body weight)
- Pulse of 98 beats/min
- Blood pressure of 138/86 mm Hg

The patient did not appear to be short of breath, and she did not demonstrate excessive use of her accessory muscles of ventilation to breathe during the trial.

Should this patient's ventilatory support be discontinued?

Solution

On the basis of the given data, this patient passed her SBT and should be discontinued from ventilatory support and extubated if there is no reason for her to remain intubated. However, because of her age, history of congestive heart failure, and multiple failures of SBT, she should ideally be placed on NIV immediately after she is extubated and slowly transitioned to independent spontaneous breathing over the next 12 to 48 hours. See the following discussion below and Chapter 50.

ventilator.[67,68] Mobilization may begin simply by sitting the mechanically ventilated patient at the side of the bed. However, in many cases it may mean that the patient is walked in the hallway while receiving ventilatory support. Of course, this requires the cooperation of respiratory therapy, nursing, and physical therapy, and the use of equipment that facilitates mobilization: transport ventilator, portable suction, and walker/chair that maintains support of the patient but also allows the patient to sit and rest. Mobilization is increasingly important the longer the patient requires ventilatory support.

Respiratory Therapist–Driven Protocols

A number of studies have demonstrated that patients are weaned faster with the use of protocols than with individual physician orders.[69–72] In all of these studies, the therapists, nurses, and physicians who normally manage patients in the unit jointly developed the protocol. In addition, in the individual physician order group, the physicians who wrote the protocol also wrote the individual weaning orders. In these trials, patients weaned via protocol were extubated faster and with fewer complications.[69–72]

What these results do not mean is that therapists wean patients better than physicians. However, what they do mean is that, when an evidence-based approach to patient management is developed and followed precisely, care is generally better than with individual physician orders. The reason for this is that protocols empower the clinician at the bedside to advance care when the patient meets specific criteria without waiting for the physician to come and write an order. In many community hospitals, the wait for the physician weaning order can be lengthy, perhaps a whole shift or more. Thus, with protocols, care proceeds rapidly on the agreed-upon course. In addition, the individual bias of the caregiver does not affect the care provided. Thus the approach does not change from day to day depending on which physician is at the bedside. An example of a respiratory therapist–directed ventilatory discontinuance protocol is presented in Box 53.12.

RULE OF THUMB Therapist-driven weaning protocols result in faster weaning from ventilatory support than the writing of individual patient-specific weaning orders.

Recent ATS/ACCP Ventilation Liberation Guidelines

The American Thoracic Society and American College of Chest Physicians recently provided new guidelines for the liberation of patients from mechanical ventilation.[73] The recommendations were focused on a few areas:

(1) Acutely hospitalized patients ventilated for more than 24 hours should have their SBT performed with 5 to 8 cm H_2O pressure support. As indicated above, prior guidelines were not specific on this issue, recommending zero to 8 cm H_2O PSV. This is the single most controversial of these guidelines. The intent is that the PSV will simply overcome the added work of the artificial airway. However, there is essentially no data indicating that the use of pressure support during an SBT affects outcome compared to the use of zero pressure support.

BOX 53.12 Respiratory Therapist–Directed Weaning Protocol

- The physician's written order identifies the patient as being eligible for the respiratory therapist–directed weaning protocol.
- The timing of weaning initiation is defined as part of the protocol.
- All patients must undergo continuous oxyhemoglobin saturation monitoring by pulse oximetry.
- When the patient meets weaning criteria, the ventilator is set to zero CPAP and zero PEEP.
- The SBT continues for a minimum of 30 min to a maximum of 120 min if none of the following weaning failure conditions are present:
  - SaO_2 of less than 90% or diaphoresis
  - Spontaneous respiratory rate of at least 35 breaths/min that is sustained for at least 5 min
  - Agitation or a decreased level of consciousness
  - A heart rate increase of at least 20%
  - A blood pressure change of at least 20%
  - A cardiac output reduction of at least 30% or ventricular arrhythmia
- Results of the SBT are discussed with the unit physician
- If the SBT is well tolerated and there is no reason not to extubate the patient, the patient is extubated.

CPAP, Continuous positive airway pressure; *PEEP*, positive end-expiratory pressure; *SBT*, spontaneous breathing trial

(2) In acutely hospitalized patients ventilated for more than 24 hours sedation should be minimized throughout the ventilation period and particularly during weaning periods.

(3) High-risk patients receiving mechanical ventilation for more than 24 hours who have passed an SBT should be transitioned to NIV immediately following extubation to allow for a smooth transition to spontaneous breathing.

(4) Acutely hospitalized adults who have been mechanically ventilated for more than 24 hours should receive early mobilization in the form of a well-defined rehabilitation protocol.

(5) Acutely hospitalized adults who have been mechanically ventilated for more than 24 hours should be weaned with a well-defined ventilator liberation protocol.

(6) Before extubation of adults with high risk of postextubation stridor, a cuff leak test should be performed. For those failing a cuff leak test but otherwise ready for extubation it is recommended that systemic steroids should be administered for at least 4 hours before extubation.

SELECTING AN APPROACH

Current evidence suggests that, for ventilator discontinuance and progressive weaning from mechanical support, it is best to avoid SIMV.[1,4] It has also been suggested, regardless of approach used, that protocols administered by respiratory therapists and other healthcare workers be implemented.[3,7,11] These protocols should be designed to begin testing for the opportunity to reduce support very soon after intubation and to reduce the level of ventilatory support at every opportunity.[1,71] The approach to weaning that seems to wean patients most rapidly is the SBT. This should be the approach that is used to identify readiness for ventilator discontinuance in the vast majority of patients.[1]

In addition, NIV, CPAP, and HFNC should be considered as part of the total ventilator discontinuance process.[70]

One area that requires additional research is the role of ventilatory muscle conditioning in patients who require long-term ventilatory support. Endurance conditioning of the ventilatory muscles can be achieved by the continuous repetition of low levels of ventilatory work. Strength conditioning can be achieved by maximal ventilatory effort for short periods. In theory, PSV would allow for improving ventilatory muscle endurance, whereas intermittent SBTs would favor the development of muscle strength. Inspiratory resistive training to improve ventilatory muscle strength has been tried as an adjunct to weaning for the care of patients undergoing long-term ventilation.[14] Unfortunately, the role of ventilatory muscle rest and load in the care of difficult-to-wean patients has not been established.[14]

In summary, a single daily SBT that lasts from 30 minutes to 2 hours has been recommended as the primary approach to weaning.[1,4] If the trial is successful, extubation is considered. If the trial is unsuccessful, a period of rest is provided before another trial is attempted.[1] There are advantages and disadvantages to each of the methods used to conduct ventilator weaning. Table 53.5 compares SBT, SIMV, and PSV as weaning techniques. The best approach currently supported by the literature is an SBT. The method chosen should include careful patient assessment, and the patient's condition should be optimized before weaning. For the vast majority of patients, a protocolized approach to ventilator discontinuance is most efficient.

The Morbidly Obese Patient

In almost all trials assessing approach to mechanical ventilation and weaning, patients with a body mass index of greater that 30 to 35 were excluded. As a result, guidelines on the management of these patients are lacking (see Chapter 30). As noted, the new ATS/ACCP guidelines do not mention the use of CPAP. Increasing data indicate that CPAP should be used during the SBT and post extubation in the obese population. The larger the patient the greater the likelihood that atelectasis is a major problem requiring high levels of PEEP to stabilize the lung during mechanical ventilation. The vast majority of these patients have sleep apnea and use or should use CPAP at home. In addition, the larger the patient the greater the likelihood that the patient never sleeps in the supine position. Many sleep in a chair. As a result, it is highly likely that these large patients will fail a SBT on zero CPAP, since they require PEEP to avoid atelectasis. Thus the use of CPAP during SBT and post extubation seems most appropriate.[5] In many of these patients, the level of CPAP should be the level used on their nocturnal CPAP device, or at least 10 cm H_2O. Post extubation the amount of time spent with the CPAP can be decreased to simply sleep periods as the patient transitions to unsupported spontaneous breathing.

RULE OF THUMB Every patient at high risk of failing ventilator liberation should receive noninvasive ventilation, CPAP or HFNC, for the first 24 to 48 hours post extubation to avoid the need for reintubation.

TABLE 53.5 Comparison of Available Weaning Methods

Method	Advantages	Disadvantages
SBT	Tests patient's spontaneous breathing ability Allows periods of work and rest Weans faster than synchronized intermittent mandatory ventilation (SIMV) A single daily SBT may be as effective as multiple trials May be performed with 0–5 cm H_2O continuous positive airway pressure (CPAP), 0–8 cm H_2O PSV, or both	More staff time Abrupt transition may be difficult for some patients May overstress the patient if not monitored carefully Requires careful supervision
SIMV	Less staff time Gradual transition Easy to use Minimum minute ventilation guaranteed Sophisticated alarm systems may be used May be used in combination with PSV or CPAP	Patient–ventilator asynchrony Prolongs weaning May worsen fatigue Not a recommended approach
PSV	Less staff time Gradual transition Prevents fatigue Maintains activity of diaphragm Increased patient comfort Weans faster than SIMV Overcomes resistive work of breathing (WOB) caused by the following: Endotracheal and tracheostomy tubes Ventilator circuits Demand flow systems Patient can control cycle length, rate, and inspiratory flow Every breath is supported	Large changes in minute ventilation can occur Increased mean airway pressure as compared with SBT Tidal volume not guaranteed; low tidal volumes possible May prolong weaning

PSV, Pressure support ventilation; *SBT*, spontaneous breathing trial.

MONITORING THE PATIENT DURING WEANING

Ventilatory Status

Respiratory rate and pattern are easy to monitor and may be the most reliable indicators of patient progress during weaning.[1,4] Weaning may proceed as quickly as the patient's respiratory rate and subjective tolerance allow. However, in no case should patients be pushed beyond their physiologic limits; to do so may result in diaphragmatic dysfunction and further delay the weaning process. If the patient fatigues during a weaning trial, it will require at least 24 hours for the muscles to recover.[74,75] Dyspnea should be monitored during weaning and may be quantified with a visual analog scale or a modified Borg scale (Table 53.6).[76] The onset or worsening of discomfort, respiratory distress, fatigue, sweating, signs of increased WOB (e.g., accessory muscle use and abdominal paradox), deterioration in vital signs, or changes in mental status (e.g., agitation, anxiety, somnolence, and coma) may be signs of intolerance of a weaning trial.[1]

TABLE 53.6 Modified Borg Scale for Dyspnea

Grade	Degree of Dyspnea
0	None
0.5	Very, very slight (just noticeable)
1	Very slight
2	Slight
3	Moderate
4	Somewhat severe
5	Severe
6	Very severe
7	
8	
9	Very, very severe (almost maximal)
10	Maximal

Modified from Mahler DA: *Dyspnea*, Mt. Kisco, NY, 1990, Futura.

The single best index of ventilation remains the measurement of $PaCO_2$. However, the assessment of a patient's tolerance of an SBT should be based on clinical presentation rather than $PaCO_2$. A patient with a $PaCO_2$ of 40 mm Hg but a clinical presentation defined by a rapid, shallow breathing pattern with abdominal paradox, tachycardia, and hypertension has not passed an SBT. The results of capnography should not be used to guide the weaning of patients. End-tidal $PaCO_2$ values can be highly misleading as an estimate of effective ventilation in sick patients.[77] Gastric pH has been used as a predictor of patient status, and gastrointestinal acidosis may be an early sign of weaning failure.[78]

Oxygenation

During the SBT, FiO_2 should be the same as during ventilatory support or 10% higher. Continuous pulse oximetric (SpO_2) monitoring can provide a sensitive indicator of oxygenation status during weaning.[1] Arterial blood gas analysis for PaO_2, $PaCO_2$, and SaO_2 and the calculation of the oxygen content of the arterial blood (CaO_2) may be performed after the patient has been considered a weaning failure to determine the extent of the failure. Success, however, can be based on the SpO_2. SpO_2 monitoring during the SBT is generally the standard of care.

Cardiovascular Status

Pulse, blood pressure, and cardiac rhythm should be monitored, and arrhythmias should be assessed to determine whether weaning should be continued. Tachycardia, bradycardia, and abnormalities in blood pressure should be promptly evaluated and the patient returned to ventilatory support or a higher level of support, if indicated. Silent myocardial ischemia may occur frequently in some postoperative patients during weaning.[79] Table 53.7 summarizes changes that may occur during the withdrawal of ventilatory support.

TABLE 53.7 Changes During the Withdrawal of Ventilatory Support

Expected Change	Deleterious Change
Respiratory	
Respiratory rate minimally increased	Respiratory rate of ≥35 breaths/min
Stable $\dot{V}$	Large increase or decrease in $\dot{V}_E$
SpO_2 ≥90%	Decrease in SpO_2 to ≤90%
5–10 mm Hg swing in PaO_2	PaO_2 of <60 mm Hg
5–10 mm Hg swing in $PaCO_2$	An increase of >10 mm Hg in $PaCO_2$
pH of >7.30 and <7.50	pH of <7.30
Minimal use of accessory muscles	Increased use of accessory muscles
No paradoxical breathing	Paradoxical breathing
	Diaphoresis
	Dyspnea
Cardiovascular	
Heart rate increased by 15–20 beats/min	Persistent tachycardia of ≥120–140 beats/min
Blood pressure increased 10–15 mm Hg	Hypotension (blood pressure of <90/60 mm Hg)
	Hypertension (systolic blood pressure of >180 mm Hg)
Increased cardiac index	Decreased cardiac index
Increased stroke volume	Decreased stroke volume
	Angina
	New arrhythmias
Other	
Mental status good (i.e., awake, alert, responsive)	Anxiety, agitation, somnolence, coma

EXTUBATION

Artificial Airways and Weaning

The effect on a patient of a properly sized artificial airway on WOB is controversial.[80] However, many endotracheal tubes are partially obstructed and as a result impose a significant increase in WOB. Removing the endotracheal tube may markedly improve the patient's clinical status. There is little difference in the airway resistance of healthy adults with low minute ventilation (i.e., <8 L/min) breathing through endotracheal tubes with an internal diameter (ID) of 7.0 to 9.0 mm.[81] However, in critically ill patients decreases in ID and increases in minute ventilation increase WOB. Adults have a critical increase in workload when the tube has an ID of less than 7.0 mm.[81] It is thought that the added work due to the presence of an artificial airway may contribute to ventilator dependency among patients with borderline pulmonary function or ventilatory muscle weakness.[82]

Biofilm buildup on the inside of the endotracheal tube can cause dramatic increases in airway resistance, especially among infants and children.[83,84] Taking care to provide adequate humidification and careful suctioning can help avoid this problem.

Tracheotomy may substantially reduce the WOB of patients who need mechanical ventilatory support. The short length of tracheostomy tubes results in an overall decrease in resistance as compared with the resistance of an endotracheal tube, even though the curvature of the tracheostomy tube is greater.[1] It appears that the performance of a tracheotomy improves airway resistance and reduces the load of the ventilatory muscles. It may be the ability to avoid secretions/biofilm buildup on the inside of the tracheostomy tube that makes the difference.

Weaning and extubation should be separate decisions. Weaning indices are not predictive of the adequacy of airway patency or

BOX 53.13 Practical Guidelines for Extubation

- There is no immediate need for mechanical ventilation or intubation.
- The medical course does not suggest impending respiratory failure or other indications for mechanical ventilation.
- Procedures that require intubation and general anesthesia are not immediately planned.
- There is adequate oxygenation and ventilation with spontaneous ventilation.
- The patient's FiO_2 requirement can be achieved with a mask or a nasal cannula.
- The patient no longer needs mechanical ventilatory assistance.
- Weaning is successful.
- There is a minimal risk of upper airway obstruction.
- The patient has minimal edema or mass encroachment of the oropharynx and upper airway.
- There is adequate airway protection and a minimal risk of aspiration.
- The level of consciousness and neuromuscular function ensures a gag reflex and an adequate cough.
- Gastric contents are minimized by the discontinuation of tube feedings for 4–6 h before extubation.
- A positive gag reflex is present.
- There is adequate clearance of pulmonary secretions.
- The level of consciousness and muscular strength allow for an effective cough.
- Secretion volume and thickness are not worsening.

the need for protection of the airway. The reintubation rate among patients with prolonged postoperative ventilation as a result of respiratory failure can range from 5% to 20%.[1,4]

Patients who have been successfully extubated generally have the following characteristics: (1) the resolution of the disease state or condition; (2) hemodynamic stability; (3) the absence of sepsis; (4) adequate oxygenation status with a decreased FiO_2 and decreased PEEP or CPAP; and (5) adequate ventilatory status and $PaCO_2$. The decision to extubate should be based on the assessment of upper airway patency and protection. No one indicator is 100% sensitive and specific with regard to the prediction of successful extubation. Practical guidelines for extubation are presented in Box 53.13. Regardless of the weaning technique used, an SBT is recommended before extubation to ensure that the patient can sustain spontaneous unsupported ventilation.[1]

Some patients may be successfully extubated even if extubation criteria are not met. If the patient is at risk, trained personnel able to perform reintubation must be immediately available before extubation is attempted. At a minimum, those who perform the extubation must be prepared to provide an airway and ventilatory support if problems develop immediately after extubation. Extubation should be postponed when myocardial ischemia is present, when the patient has upper gastrointestinal hemorrhage, or when a procedure that necessitates reintubation is impending. If difficult reintubation is anticipated, trained personnel should be immediately available.

Post Extubation Complications

Many patients report hoarseness and sore throat after extubation, and patients should be advised that these symptoms may occur (see Chapter 37 for details). Other common problems after extubation include airway obstruction, increased risk of aspiration, and difficulty with secretion clearance. Patients with neurologic or neuromuscular disorders and those with excessive secretions are at increased risk after extubation. The compression of the airway as a result of a traumatic or postoperative hematoma of the neck, infectious masses or abscesses, and malignant tumors or compression after major head or neck surgery can lead to upper airway obstruction after extubation. The cuff leak test may detect airway obstruction before extubation.[85,86] An air leak of less than 11% to 12% or 110 to 130 mL has been shown to be predictive of stridor.[85,86] Box 53.13 provides a protocolized guide for extubation.

After extubation, glottic edema can result in partial airway obstruction, which can cause mild to severe stridor. Postextubation stridor occurs in 2% to 16% of patients in the ICU and should be viewed with concern.[87] Severe edema after extubation can lead to complete airway obstruction. Children, patients with epiglottitis or angioedema (i.e., dermal, subcutaneous, or submucosal edema of the face or larynx), and patients who have sustained smoke inhalation are at greater risk. Postextubation edema occurs in as many as 47% of children with trauma injuries or burns.[1,4] See Chapter 37 for detailed information about airway management and postextubation care.

RULE OF THUMB The use of CPAP during SBT and post extubation seems most appropriate for obese patients. In many of these patients the level of CPAP should be the level used on their nocturnal CPAP device or at least 10 cm H_2O.

VENTILATOR DISCONTINUANCE FAILURE

As many as 25% of patients who have been removed from ventilatory support experience respiratory distress that is severe enough to necessitate the reinstitution of mechanical ventilation. In patients who are unlikely to be successfully weaned, rapid, shallow breathing begins almost immediately after the ventilator is disconnected. As spontaneous breathing continues, respiratory mechanics worsen in these patients for reasons that are not clearly understood. Approximately half of patients who have poor results after the discontinuation of ventilation experience marked hypercapnia with rapid, shallow breathing. An unsuccessful SBT also causes considerable cardiovascular stress. Myocardial ischemia may occur frequently among ventilator-dependent patients, and it has been associated with weaning failure.[88] Critical illness polyneuropathy has been cited as a frequent cause of neuromuscular weaning failure among critically ill patients.[89] Unsuspected neuromuscular disease may be an important factor in ventilator dependency.

Inability to wean can sometimes be attributed to psychologic dependence, poor oxygenation status, or cardiovascular instability (i.e., congestive heart failure or ischemia).[1,4] However, the most common cause of the inability to wean is an imbalance between ventilatory capability and ventilatory demand. Inability to wean is usually caused by a concurrent pathologic process that necessitates treatment. Common causes of weaning failure are summarized in Box 53.14.

BOX 53.14 Common Causes of Weaning Failure

- Poor respiratory mechanics or wheezing
- Untreated cardiac disease
- Electrolyte imbalances
- Anxiety
- Secretions
- Aspiration
- Alkalosis
- Neuromuscular weakness
- Sepsis
- Excessive sedation
- Inadequate nutrition
- Opiates
- Obesity
- Thyroid disease

MINI CLINI

Patient Who Requires Long-Term Weaning

Problem

A 68-year-old man with a history of COPD was hospitalized after a motor vehicle accident. Over the course of the next 2 weeks, the patient became septic and developed acute respiratory distress syndrome. For the last week, the patient has met the criteria for an SBT, but he has failed every attempt. How should this patient's ventilator care progress from this point forward?

Solution

This patient should be classified as a difficult-to-wean patient who would benefit from a program that has been designed specifically for patients who are failing to wean. This program should systematically evaluate all systems to determine the cause of weaning failure and include the assistance of other healthcare providers, specifically physical therapy, occupational therapy, and speech and language pathology; he may also benefit from the efforts of social services. Ideally, this should take place in a unit that has been specifically designed for the difficult-to-wean patient.

PROLONGED MECHANICAL VENTILATION

Prolonged mechanical ventilation (PMV) may be required for 3% to 7% of patients who are receiving mechanical ventilation.[1,4] Patients who require a lengthy course of ventilatory support after the acute phase of their disease has resolved may be suffering from some of the items listed in Table 53.8. Any patient who is repeatedly failing SBTs should undergo a complete review of all systems to determine if something has been overlooked that may add to the patient's workload, thereby preventing them from weaning. In many patients, their pulmonary mechanics have not been optimized, and thus they are unable to assume the workload required of spontaneous breathing. In others, underlying cardiac disease may not have been properly treated. Always a concern is the patient's acid–base status. If a patient had baseline compensated respiratory acidosis, then he or she will not be able to wean if the compensation has been eliminated. Every time these patients are trialed on an SBT, their carbon dioxide levels will rise, and they will develop respiratory failure. If this is the problem, the baseline acid–base status must be slowly reestablished if these patients are to wean. In other patients, sedation, opiates, nutritional status, electrolytes, and other underlying issues many be the concern. The more carefully all systems are reviewed, the greater the likelihood that the problem will be identified and the patient weaned from ventilatory support.

BOX 53.15 Goals for Weaning After Long-Term Mechanical Ventilation

- Reduce the amount of support.
- Decrease the invasiveness of any support.
- Increase independence from mechanical devices.
- Preserve function.
- Maintain medical stability.

CHRONICALLY VENTILATOR-DEPENDENT PATIENTS

Chronically ventilator-dependent patients (i.e., <1% of those requiring ventilatory support) present ethical, economic, and practical problems.[90] From an economic point of view, the long-term care of ventilator-dependent patients in an ICU is prohibitively expensive. Often these patients are transferred to subacute or long-term care facilities, where they can be cared for in an environment that is less intrusive and more like home (see Chapter 57).[90] For cases in which the family has adequate resources, the patient may be cared for in the home. Regional weaning centers have been developed and have reported success with weaning most patients who are undergoing long-term mechanical ventilation.[1,90] Current guidelines suggest that, unless there is clear evidence of an irreversible cause of ventilator dependency (e.g., a high spinal cord injury, amyotrophic lateral sclerosis), patients should not be considered permanently ventilator dependent until 3 months of weaning attempts have failed. If the patient is unweanable, the goal should be to restore the patient to the highest level of independent function possible. For example, portable wheelchair-mounted ventilators have been effective for providing a surprising level of mobility and independence to persons who are quadriplegic. Table 53.8 describes the management of common problems among difficult-to-wean patients. Box 53.15 lists the goals for weaning of patients who are receiving long-term ventilation.

TERMINAL WEANING

The term *terminal weaning* has been used to refer to the discontinuation of mechanical ventilatory support in the face of a catastrophic and irreversible illness (see Chapter 58).[91] The decision to proceed with disconnecting the ventilator when such an act is likely to cause the death of a patient is fraught with ethical, emotional, and practical problems. The decision should be made by the family in consultation with the patient's physician and in accordance with established ethical and legal guidelines.[91] Determinants of the decision to withdraw ventilation include the patient's desire to not continue with life support, the predictions of a low chance of survival in the ICU (i.e., less than 10%),

TABLE 53.8 Management of Problems Among Difficult-to-Wean Patients

Problem	Management Strategy
Anemia	Transfuse when hemoglobin level is ≤10 g/dL and hematocrit level is ≤30% if these are thought to be factors in decreased tissue oxygenation
Increased work of breathing (WOB)	1. Tube related a. Apply pressure support or ATC b. Change the size of the small endotracheal tube c. Deflate the cuff if all breathing is spontaneous and the risk of aspiration is minimal d. Consider tracheotomy 2. Secretion related (see later) 3. Bronchospasm related a. Administer bronchodilators • β_2-agonists • Anticholinergics • Steroids b. Minimize auto-PEEP and apply PEEP to ensure triggering of ventilation. c. Manage the cause 4. Ventilator related a. Assure synchrony for machine breaths b. Eliminate auto-PEEP c. Flow-trigger ventilation with or without pressure support
Secretions, atelectasis, or plugging	1. Systemically hydrate 2. Provide adequate humidity (i.e., humidifier temperature 35°C–37°C at airway connection) 3. Maximally bronchodilate when necessary 4. Suction
Dyspnea	1. Use positioning (i.e., out of bed, dangling, and leaning forward) 2. Reassure and communicate with the patient 3. Increase endurance, alternate weaning with rest to promote endurance 4. Provide distraction
Malposition	1. Position the patient to maximize diaphragmatic excursion and to improve lung volume and gas exchange (i.e., sitting or dangling) 2. Use a rocking chair 3. Follow $\dot{V}_E$, V_T, rate, values for optimum positioning
Respiratory muscle fatigue	1. Direct management at the cause 2. Ensure adequate oxygen transport and cardiac output 3. Nourish the patient 4. Replace depleted electrolytes 5. Decrease the WOB a. Administer supplemental oxygen b. Clear secretions c. Decrease airway resistance
Hemodynamic and fluid problems	1. Administer volume replacement and drugs to increase contractility, increase or decrease preload, and decrease afterload 2. Delay weaning until the patient's cardiovascular status is stable 3. Use techniques and the mode of ventilation to decrease the mean airway pressure
Infection	1. Identify potential sites of infection 2. Remove lines early, or replace them periodically 3. Control infection 4. Nourish the patient
Metabolic problems	1. Control the cause and postpone weaning if the patient has acidosis 2. Keep the carbon dioxide level at baseline if the patient has COPD, or allow progressive renal compensation during long-term weaning 3. Provide moderate carbohydrate loading with total parenteral nutrition
Low magnesium level High magnesium level	4. Give supplements 5. Provide dialysis or calcium chloride
Low calcium level	6. Control the cause before weaning
Low phosphate level	7. Replace phosphate before weaning
Nutrition	1. Assess weight, albumin, and total lymphocyte count at admission 2. Label the degree of malnutrition, and calculate protein needs 3. Nourish the patient

Continued

TABLE 53.8 Management of Problems Among Difficult-to-Wean Patients—*cont'd*

Problem	Management Strategy
Exercise	1. Provide exercise therapy to increase muscle function, prevent contracture, and maintain joint integrity (i.e., passive-to-active range of motion and sitting to walking) 2. Increase strength during activities of daily living 3. Secure a physiotherapy consultation 4. Consider the use of an exercise bicycle 5. Encourage wheelchair rides or walks with a portable ventilator 6. Provide breathing retraining
Psychologic problems	1. Secure early psychiatric consultation 2. Allow for patient control 3. Demonstrate staff accountability and honesty 4. Provide a communication method 5. Decrease environmental stress 6. Teach relaxation methods 7. Provide mental stimulation 8. Provide recreation 9. Provide rewards for reaching short-term goals 10. Encourage self-care 11. Allow other patients to visit 12. Provide flexible visiting hours 13. Take the patient out of the ICU environment
Sleep disturbances	1. Provide a quiet environment (i.e., dim lights), reposition the patient, give a back rub, and administer sedation 2. Provide for uninterrupted sleep 3. Avoid weaning at night 4. Provide relaxation method (e.g., hypnosis, biofeedback, and progressive muscle relaxation) 5. Prescribe short-acting sedative hypnotics
Pain	1. Administer minimal analgesia

ATC, Automatic tube compensation; *COPD*, chronic obstructive pulmonary disease; *ICU*, intensive care unit; *PEEP*, positive end-expiratory pressure.
Modified from Norton LC, Neureuter A: Weaning the long-term ventilator-dependent patient: common problems and management. *Crit Care Nurse* 9:42–52, 1989.

the likelihood that future cognitive function would be severely impaired, and the continuous need for inotropes or vasopressors to maintain blood pressure.[91] After the decision has been made, the process is generally one of ventilator disconnection rather than weaning. The method of terminal weaning should be as humane and as comfortable as possible and should not be done in a way that further burdens the family.[92]

SUMMARY CHECKLIST

- The most common cause of ventilator dependence is a ventilatory workload that exceeds the patient's ventilatory capabilities.
- Other common causes of ventilator dependence include oxygenation problems, cardiovascular instability, and psychologic factors.
- The most important criterion for determining whether a patient is ready for ventilator discontinuation or weaning is a significant improvement or reversal of the disease state or condition that caused the patient to need ventilatory support.
- Factors that should be optimized before weaning include oxygenation, ventilation, acid–base balance and electrolyte levels, cardiovascular status, kidney function and fluid balance, sleep deprivation, psychologic status, nutrition, and overall medical condition.
- Weaning techniques include spontaneous breathing trials, PSV, and SIMV.
- Spontaneous breathing trials and PSV result in faster discontinuation of ventilatory support as compared with SIMV.
- The ideal approach to weaning patients is a therapist-driven protocol that makes use of an SBT.
- Esophageal pressure monitoring, diaphragm ultrasound, and diaphragm EAdi may be useful in identifying readiness for a SBT and the likelihood of successfully passing the SBT.
- The ATS/ACCP new mechanical liberation guidelines indicate that 5 to 8 cm H_2O PSV should be used during the SBT.
- When preforming an SBT on a morbidly obese patient, CPAP should be applied during the SBT and post extubation.
- The monitoring of the patient during weaning should include SpO_2, respiratory rate and pattern, dyspnea, cardiac rate and rhythm, and blood pressure assessments.
- The use of daily SATs or the maintenance of minimal sedation not only improves the speed of weaning but has also been shown to improve mortality.
- Before extubation, patients should be assessed for the ability to maintain and protect their airway and for the presence of upper airway edema.
- Common causes of weaning failure include an excessive ventilatory workload in the presence of ventilatory muscle weakness or fatigue, oxygenation problems, cardiovascular instability,

the inability to clear secretions, poor mental status, and the presence of an underlying concurrent pathologic condition that necessitates treatment.

- The goals of the weaning of long-term ventilator-dependent patients include reducing the amount of support, reducing the invasiveness of support, and increasing the patient's level of independent function.
- Only less than 1.0% of patients that require mechanical ventilation end up as long-term ventilator-dependent patients.
- The decision to terminally wean a patient should be made by the family in consultation with the patient's medical team and in accordance with established ethical and legal guidelines.

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54

Neonatal and Pediatric Respiratory Care

Daniel W. Chipman

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Describe the correct approach to assessment of the fetus and newborn infant.
- Discuss the use of oxygen therapy, bronchial hygiene therapy, aerosol drug therapy, airway management.
- Discuss resuscitation of the newborn infant experiencing respiratory or cardiac distress.
- List the components of an Apgar score.
- Identify the different pulse oximetry (SpO_2) target ranges for preterm and full-term infants and those with primary pulmonary hypertension.
- List normal blood gas values for a newborn infant.
- Discuss the administration of surfactant in premature infants.
- Differentiate low-birth-weight, very low-birth-weight, and extremely low-birth-weight infants.
- Describe the correct approach to assessment of the pediatric patient.
- Discuss the use of high-flow nasal cannulas in infants and children.
- Discuss the use of continuous positive airway pressure in infants and children.
- Discuss the use of noninvasive ventilation in infants and children.
- Discuss the basics of mechanical ventilation including high-frequency ventilation in the care of infants and children.
- Discuss the advantages and disadvantages of self-inflating, flow-inflating and T-piece resuscitators.
- List clinical situations where nitric oxide is used and discuss its basic application.
- Explain the correct approach to ventilator management for a patient in status asthmaticus.
- Discuss the use of heliox for a patient with asthma.
- Discuss the steps to ventilator discontinuance for infants and children including a safety screen and assessment of ability to breathe spontaneously.

CHAPTER OUTLINE

KEY TERMS

Apgar score
appropriate for gestational age (AGA)
continuous positive airway pressure (CPAP)
extremely low birth weight (ELBW)
grunting, flaring, and retracting
high-frequency ventilation (HFV)
inhaled nitric oxide (INO)
large for gestational age (LGA)
meconium
patent ductus arteriosus (PDA)
primary pulmonary hypertension of the newborn (PPHN)
retinopathy of prematurity (ROP)
small for gestational age (SGA)
surfactant
very low birth weight (VLBW)

Caring for infants and children is one of the most challenging and rewarding aspects of respiratory care. Competent clinical practice in this area requires knowledge of the many pathophysiologic differences among infants, children, and adults. Understanding the unique pathophysiology involved in neonatal and pediatric respiratory disorders (see Chapter 35) can assist the respiratory therapist (RT) in providing quality care to infants and children. A thorough understanding of how the respiratory system develops in the fetus is the first step toward acquiring the specialized knowledge needed to practice neonatal respiratory care (see Chapter 9). This chapter begins with an overview of neonatal and pediatric patient assessment and then describes respiratory care modalities used to treat these patients.

ASSESSMENT OF THE NEWBORN

Assessment of the newborn begins before birth with assessment of the maternal history, the maternal condition, and the status of the fetus.

Maternal Factors

Maternal risk factors include many medical, physical, and social conditions. Maternal health and individual physiology, pregnancy complications, and maternal behaviors affect the health of the fetus. Any condition that causes an interference with placental blood flow or the transfer of oxygen (O_2) to the fetus can result in an adverse outcome. The clinician must be prepared for the possibility of resuscitation at delivery. This possibility is best anticipated by identifying risk factors that relate to neonatal compromise. Table 54.1 lists maternal risks and related outcomes of which the team preparing to receive the infant should be aware when the infant is delivered.

TABLE 54.1 Maternal Condition and Neonatal Outcomes

Maternal Condition	Fetal or Neonatal Outcome
Previous pregnancy complication	Same outcome as previous fetus
Diabetes mellitus	LGA, congenital malformations, RDS, hypoglycemia
Pregnancy-induced hypertension	Prematurity, SGA (preeclampsia)
Maternal age <17 years	Low birth weight, prematurity
Maternal age >35 years	Prematurity, chromosomal defects
Placenta previa	Prematurity, bleeding, SGA
Abruptio placentae	Fetal asphyxia, bleeding
Alcohol consumption	SGA, CNS dysfunction, mental retardation, facial dysmorphology
Smoking	SGA, prematurity, mental retardation, SIDS
Drug use	Placental abruption, IUGR, prematurity, CNS abnormalities, withdrawal disorders

CNS, Central nervous system; *IUGR,* intrauterine growth restriction; *LGA,* large for gestational age; *RDS,* respiratory distress syndrome; *SGA,* small for gestational age; *SIDS,* sudden infant death syndrome.

Fetal Assessment

Fetal assessment is performed with ultrasonography, amniocentesis, fetal heart rate monitoring, and fetal blood gas analysis. Ultrasonography uses high-frequency sound waves to obtain an image of the infant in utero. This image allows the physician to view the position of the fetus and placenta, measure fetal growth, identify possible anatomic anomalies, and assess the amniotic fluid qualitatively.

Amniocentesis involves direct sampling and quantitative assessment of amniotic fluid. Amniotic fluid may be inspected for **meconium** (fetal bowel contents) or blood. In addition, sloughed fetal cells can be analyzed for genetic normality. Lung maturation can be assessed with amniocentesis. The lecithin-to-sphingomyelin ratio (L:S ratio) involves measurement of two phospholipids, lecithin and sphingomyelin, synthesized by the fetus in utero. The L:S ratio increases with increasing gestational age. At approximately 34 to 35 weeks' gestation, this ratio abruptly increases to greater than 2:1. An L:S ratio greater than 2:1 indicates stable **surfactant** production and mature lungs.[1] Phosphatidylglycerol is another lipid found in the amniotic fluid that is used to assess fetal lung maturity. Phosphatidylglycerol first appears at approximately 35 to 36 weeks' gestation. If phosphatidylglycerol is more than 1% of the total phospholipids, the risk of respiratory distress syndrome (RDS) is less than 1%.[2] A technique using three-dimensional (3D) ultrasonography for the assessment of fetal maturity has recently been described, and this may serve as a useful alternative to amniotic fluid phospholipids in analyzing fetal lung maturity.[3] Fetal heart rate monitoring includes the measurement of fetal heart rate and uterine contractions during labor. Examination of fetal heart rate changes related to uterine contractions identifies a fetus in distress. Fetal well-being is obtained by examining the variability and reactivity of the fetal heart rate. A normal fetal heart rate ranges from 120 to 160 beats/min. Fetal tachycardia can be a sign of fetal hypoxemia or could be related to other factors, such as prematurity or maternal fever. Temporary declines in fetal heart rate are called *decelerations* and can be mild (<15 beats/min), moderate (15 to 45 beats/min), or severe (>45 beats/min). Decelerations are classified by their occurrence in the uterine contraction cycle.

Fig. 54.1 illustrates the three common patterns of early decelerations, late decelerations, and variable decelerations. Early decelerations occur when the fetal heart rate decreases in the beginning of a contraction. This type of deceleration is benign and in most cases is caused by a vagal response related to compression of the fetal head in the birth canal. A late deceleration occurs when the heart rate decreases 10 to 30 seconds after the onset of contractions. A late deceleration pattern indicates impaired maternal-placental blood flow, or uteroplacental insufficiency. With variable decelerations, there is no clear relationship between contractions and heart rate. This pattern is the most common of the three and probably related to umbilical cord compression. Short periods of cord compression are generally benign, but prolonged periods of compression result in impaired umbilical blood flow and can lead to fetal distress. Fetal heart rate variability is the beat-to-beat variation in rate that occurs because of normal sympathetic or parasympathetic influences. A completely monotonous heart rate tracing may be indicative

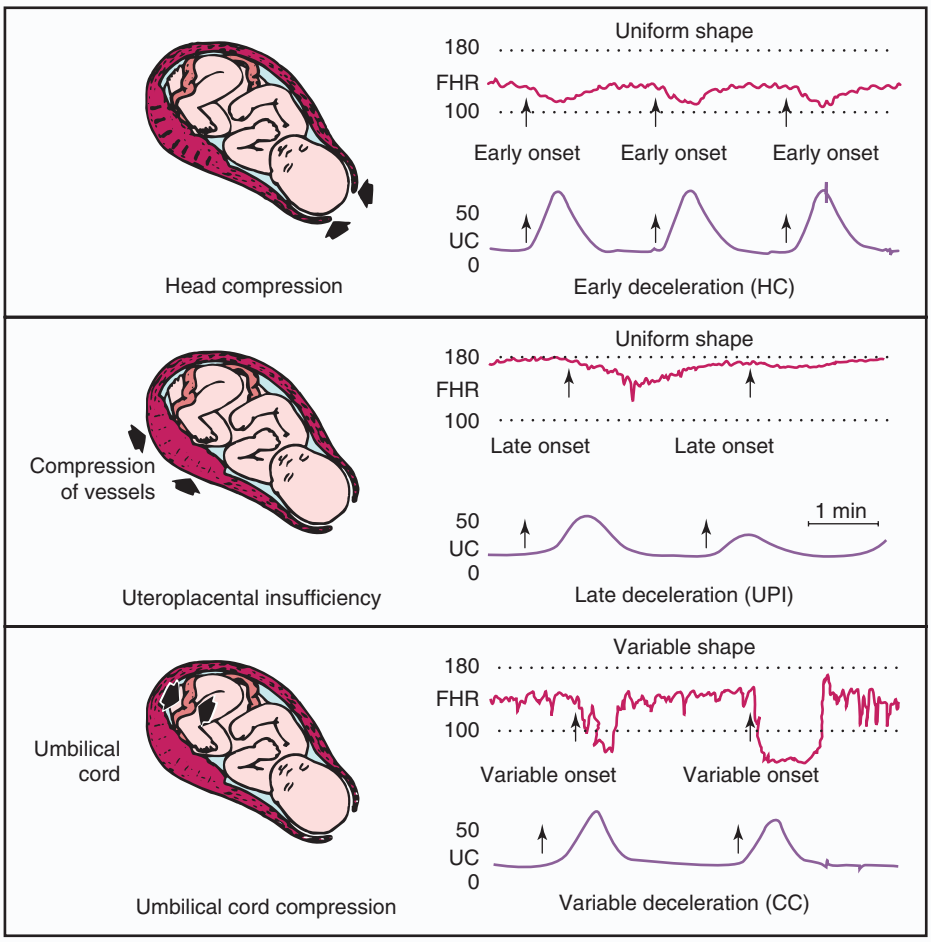

Fig. 54.1 Fetal heart rate patterns. (Modified from Avery GB, ed. *Neonatology: Pathophysiology and management of the newborn.* 2nd ed. Philadelphia: JB Lippincott; 1981.)

of fetal asphyxia. Fetal heart rate reactivity is the ability of the fetal heart rate to increase in response to movement or external stimuli. A healthy fetus has two accelerations within a 20-minute period.

In utero, the fetus receives its blood supply from the placenta. Only a small portion of the blood that enters the fetal right heart flows through the lungs. This is a result of fetal pulmonary blood vessels being constricted with a high resistance to blood flow. There are two openings in the fetal heart through which most fetal blood flows. These normal anatomic shunts in the fetus are called *patent foramen ovale* and *patent ductus arteriosus (PDA)*. Blood flows through these openings and into the umbilical vessels before returning to the mother. Pressure in the umbilical vessels is low. During the transition from fetal life to newborn life, the umbilical cord is clamped, and the infant's systemic blood pressure is increased. The infant begins to breathe, and O_2 enters the infant's blood. Oxygenated blood entering the pulmonary vessels causes the vessels to dilate and decreases pulmonary resistance. With higher systemic resistance and lower pulmonary resistance, less blood flows through the anatomic openings, and these openings begin to close. Evidence of normal transitional circulation is noted as the infant's skin turns from a bluish hue to pink over the first several minutes of life.

RULE OF THUMB Infants presenting with a monotonous heart rate or a fetal scalp pH less than 7.2 may be experiencing asphyxia.

Fetal Blood Gas Analysis

When other factors indicate potential problems during labor and delivery, fetal blood pH can be used to determine severity. Normally, fetal blood is obtained from a capillary sample taken

from the presenting body part, usually the scalp. Normal fetal capillary pH ranges from 7.25 to 7.35, with the lower values occurring late in labor. A pH less than 7.20 may indicate that the fetus is experiencing asphyxia. There is no direct correlation between fetal scalp and arterial blood pH; scalp pH should be used only to assist in interpreting clinical signs of fetal distress.

Evaluation of the Newborn

All newborns should be assessed immediately upon delivery. The American Heart Association and American Academy of Pediatrics have developed guidelines for the assessment and treatment of newborn infants. These guidelines, collectively referred to as the Neonatal Resuscitation Program (NRP) should be familiar to all caring for newborns. They cover a wide range of topics, including initial preparation and assessment, interventions such as positive pressure ventilation (PPV) and chest compressions, emergency equipment and medications, specific emergency procedures including intubation and needle decompression of the chest for pneumothoraces, postresuscitation care, and ethics and care at end of life. Special consideration is given to ethical principles associated with neonatal resuscitation and withholding resuscitation and how to help parents and staff through the grieving process.

Most newborns (>90%) do not need intervention when transitioning from intrauterine to extrauterine life. The two categories of newborns most likely to need intervention are infants born with evidence of meconium in their airway and premature infants. The need for intervention is determined by assessing for the presence of meconium, breathing or crying, muscle tone, color, and gestational age.

Meconium is the medical term for the infant's first stool. It is a sticky green-black substance that if inhaled by the infant can cause significant respiratory problems. It is more likely to be present in a term or postterm newborn than one born prematurely. Term infants delivered without evidence of meconium who are crying or breathing and have good tone should not routinely be separated from the mother. They should be dried, covered, and given to the mother and observed for breathing, activity, and color. If meconium is present and the infant is vigorous, pharyngeal suctioning with a bulb suction is appropriate. Simultaneously, the infant should be dried and placed under a warmer and assessed for signs of respiratory distress.

If meconium is present in a nonvigorous infant, stimulation should be avoided. Immediate endotracheal intubation before beginning PPV is indicated as a means to clear meconium from the airway. The endotracheal tube should be attached to a meconium aspirator, and a suction device should be regulated for −70 to −100 mm Hg. As soon as the endotracheal tube is inserted, suction should be applied to the tube, and then the endotracheal tube is withdrawn. Reintubation and repeat suctioning may be necessary if meconium is still visible in the airway. Frequent assessment of the heart rate is indicated during this process, and if the heart rate is less than 100 beats/min, bag-mask ventilation should be performed.

Preterm infants frequently need interventions. The more preterm the infant, the more likely the infant will need some level of resuscitation. If an infant is preterm, is not breathing, is not vigorous, or does not have good tone, resuscitation efforts should be initiated. Efforts are directed at warming the infant because cold stress may increase O_2 consumption and impair all subsequent resuscitation efforts.

After the infant is dried and warmed, the infant is positioned supine, with the head in a neutral position or slightly extended. A bulb syringe or 8- to 10-F suction catheter may be used for secretion removal; however, in the absence of blood or meconium, catheter suctioning should be limited because aggressive pharyngeal suctioning may cause laryngospasm or bradycardia. Suction pressure should not exceed −100 mm Hg. Once the infant is suctioned, dried, and warmed, if apnea or inadequate respirations are present, tactile stimulation may be used to encourage spontaneous breathing. Many infants respond to stimulation and need no further resuscitative efforts. If after 30 seconds, the infant has a heart rate of less than 100 beats/min or is apneic, bag-mask ventilation at a rate of 40 to 60 breaths/min should be initiated.

The *most* important and effective action in neonatal resuscitation is effective ventilation. Recommendations from the American Academy of Pediatrics are to attach a pulse oximeter to the infant, begin resuscitation efforts using room air, and assess carefully the amount of O_2 needed.[4] Effective PPV usually results in rapid improvement of heart rate. Initial ventilating pressures of 30 to 40 cm H_2O may be necessary to achieve noticeable chest movement, particularly in a preterm newborn with surfactant deficiency. Continuous assessment of the lowest pressure needed to observe the chest rise is essential throughout the resuscitation. After application of PPV for 30 seconds, the heart rate is reassessed. If the heart rate is less than 60 beats/min, chest compressions are begun and PPV is maintained. If the heart rate remains less than 60 beats/min after adequate ventilation with 100% O_2 and chest compressions for 30 seconds, appropriate medications are given. As soon as the heart rate is noted to be greater than 100 beats/min, compressions are discontinued. If spontaneous breathing is present, PPV may be gradually reduced and then discontinued. If spontaneous breathing remains inadequate or if heart rate remains less than 100 beats/min, assisted ventilation is continued via bag-mask or endotracheal tube. Fig. 54.2 outlines a newborn resuscitation algorithm and includes the targeted saturation levels for the first 10 minutes of life.

RULE OF THUMB The most important and effective action in neonatal resuscitation is to ventilate.

Apgar Score

An Apgar score is assigned at 1 minute and 5 minutes of life. The **Apgar score** is an objective scoring system used to rapidly evaluate a newborn. As shown in Table 54.2, the score has five components: heart rate, respiratory effort, muscle tone, reflex irritability, and skin color. Each component is rated according to standard definitions, resulting in a composite assessment score. In general, infants scoring 7 or higher at 1 minute are responding normally. An infant with a score of 7 may require supportive care, such as O_2 or stimulation to breathe. Infants with a 1-minute Apgar score of 6 or lower may require more aggressive support.

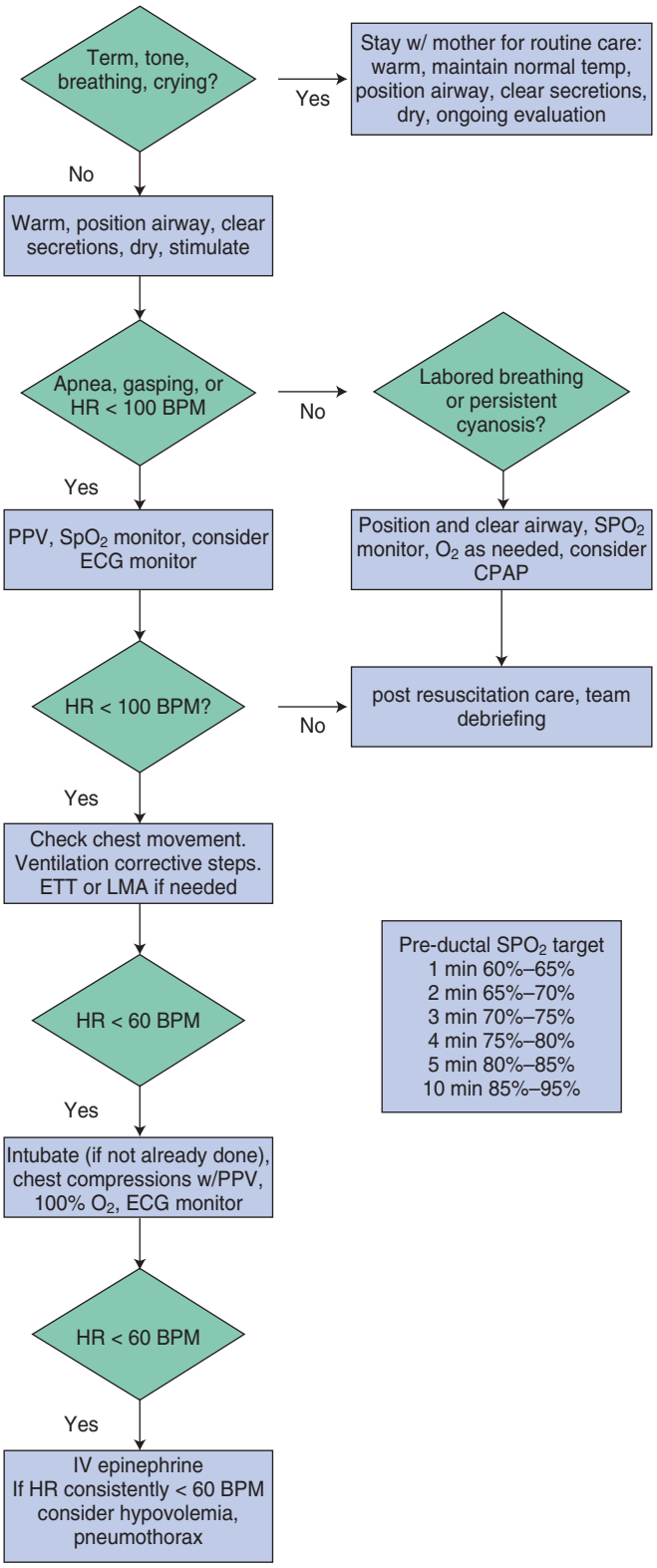

Fig. 54.2 Neonatal resuscitation algorithm. *CPAP,* Continuous positive airway pressure; *ETT,* endotracheal tube; *LMA,* laryngeal mask airways; *PPV,* positive pressure ventilation.

TABLE 54.2 Apgar Scoring System for Newborn Assessment

	SCORE		
Sign	**0**	**1**	**2**
Heart rate	Absent	<100/min	>100/min
Respirations	Absent	Slow, irregular	Good, crying
Muscle tone	Limp	Some flexion	Active motion
Reflex irritability (catheter in nares, tactile stimulation)	No response	Grimace	Cough, sneeze, cry
Color	Blue or pale	Pink body with completely blue extremities	Pink

From Koff PB, Eitzman DV, Neu J. *Neonatal and pediatric respiratory care.* 2nd ed. St Louis: Mosby; 1993.

Assessment of Gestational Age

Gestational age assessment and assessment of relationship of weight to gestational age are performed shortly after delivery. Determination of gestational age involves assessment of multiple physical characteristics and neurologic signs. Two common systems are used to determine gestational age: the Dubowitz scales and the Ballard scales. The Dubowitz scales involve assessment of 11 physical and 10 neurologic signs.[5] Physical criteria include assessment of skin texture, skin color, and genitalia. Neurologic criteria include posture and arm and leg recoil. The Ballard scales are a simplified version of the Dubowitz scales and include six physical and six neurologic signs as illustrated in Fig. 54.3. The New Ballard Scale is an updated version expanded to include extremely preterm infants. Both the Dubowitz and New Ballard scales may predict gestational age ± 14 days.[6] Soon after delivery, the newborn is stabilized and weighed, followed by determination of gestational age. Infants born between 38 weeks and 42 weeks are considered term gestation. Infants born before 38 weeks are preterm. Infants born after 42 weeks are post term.

All newborns weighing less than 2500 g are considered low birth weight. Newborns weighing less than 1500 g are considered **very low birth weight (VLBW).** Newborns weighing less than 1000 g are considered **extremely low birth weight (ELBW).** A newborn with a weight that is either too large or too small or who has been born preterm or post term has a higher risk of morbidity and mortality. As shown in Fig. 54.4, by plotting the infant's gestational age against weight, the newborn's relative developmental status can be classified. Infants whose weight falls between the 10th and 90th percentiles are **appropriate for gestational age (AGA).** Infants whose weight is greater than the 90th percentile are **large for gestational age (LGA).** Infants whose weight is less than the 10th percentile are **small for gestational age (SGA).**

RULE OF THUMB Infants weighing less than 2500 g are normally considered low-birth-weight (LBW) neonates. Infants weighing less than 1500 g are considered VLBW (very LBW) neonates, and neonates weighing less than 1000 g are considered ELBW (extremely LBW) neonates.

Neuromuscular maturity

	–1	0	1	2	3	4	5
Posture	—						—
Square window (wrist)	>90°	90°	60°	45°	30°	0°	—
Arm recoil	—	180°	140°–180°	110°–140°	90°–110°	<90°	—
Popliteal angle	180°	160°	140°	120°	100°	90°	<90°
Scarf sign							—
Heel to ear							—

Physical maturity

	–1	0	1	2	3	4	5
Skin	Sticky, friable, transparent	Gelatinous, red, translucent	Superficial peeling or rash; few visible vessels	Superficial peeling or rash; few visible vessels	Cracking; pale areas; rare visible vessels	Parchment-like; deep cracking; no visible vessels	Leathery, cracked, wrinkled
Lanugo	None	Sparse	Abundant	Thinning	Bald areas	Mostly bald	—
Plantar surface	Heel-toe 40 to 50 mm: –1; <40mm: –2	>50 mm; no crease	Faint, red marks	Anterior transverse crease only	Creases over anterior two-thirds	Creases over entire sole	—
Breast	Imperceptible	Barely perceptible	Flat areola; no bud	Stippled areola; 1- to 2-mm bud	Raised areola; 3- to 4-mm bud	Full areola; 5- to 10-mm bud	—
Eye and ear	Lids fused, loosely: –1; tightly: –2	Lids open; pinna flat, stays folded	Slightly curved pinna; soft, slow recoil	Well curved pinna; soft but ready recoil	Formed and firm; instant recoil	Thick cartilage; ear stiff	—
Genitalia, male	Scrotum flat, smooth	Scrotum empty; faint rugae	Testes in upper canal; rare rugae	Testes descending; few rugae	Testes down; good rugae	Testes pendulous; deep rugae	—
Genitalia, female	Clitoris prominent; labia flat	Prominent clitoris; small labia minora	Prominent clitoris; enlarging minora	Major and minora equally prominent	Majora large; minora small	Majora cover clitoris and minora	—

Maturity rating

Score	–10	–5	0	5	10	15	20	25	30	35	40	45	50
Weeks	20	22	24	26	28	30	32	34	36	38	40	42	44

Fig. 54.3 The Ballard gestational age assessment. (Modified from Ballard JL, et al. Assessment of gestational age, *J Pediatr.* 1979;95:769.)

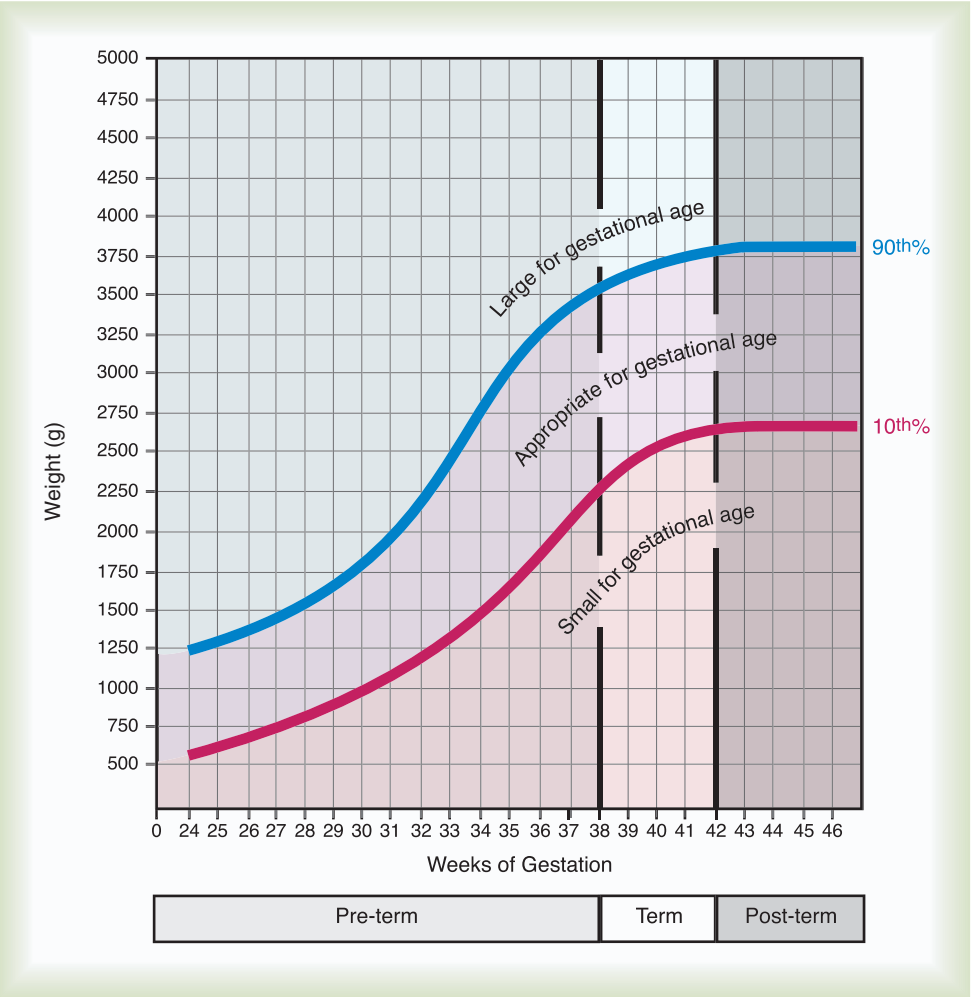

Fig. 54.4 Colorado intrauterine growth chart. (Modified from Avery GB, ed. *Neonatology: Pathophysiology and management of the newborn*. 4th ed. Philadelphia: JB Lippincott; 1994.)

By classifying infants into one of the combined categories, such as "preterm, AGA," the clinician can help to identify infants at highest risk and predict the nature of the risks involved and the likely mortality rate. Small, preterm infants are at highest risk. Compared with term infants, the lungs of these infants are not yet fully prepared for gas exchange. In addition, their digestive tracts cannot normally absorb fat, and their immune systems are not yet capable of warding off infection. Small, preterm infants also have a very large surface area-to-body weight ratio; this increases heat loss and impairs thermoregulation. Finally, the vasculature of these small infants is underdeveloped, increasing the likelihood of hemorrhage (especially in the ventricles of the brain).

RULE OF THUMB Infants born before 38 weeks' gestation are considered preterm.

Respiratory Assessment of the Infant

Not all respiratory problems occur at birth; many respiratory disorders develop after birth and may develop slowly or suddenly. RTs are commonly called on to help assess and treat infants who develop respiratory distress after birth.

Physical Assessment

Physical assessment of the infant begins with measurement of vital signs. A normal newborn respiratory rate is 40 to 60 breaths/min. The lower the gestational age, the higher the normal respiratory rate will be. A 28-week gestational age infant may normally breathe 60 times a minute, whereas the rate more typical of a term newborn is 40 breaths/min. Tachypnea (>60 breaths/min) can occur because of hypoxemia, acidosis, anxiety, or pain. Respiratory rates less than 40 breaths/min should be interpreted with previous trends of the newborn's respiratory rate. A baseline respiratory rate of 36 breaths/min in a term newborn is within normal limits; however, a respiratory rate of 36 breaths/min in a preterm newborn previously breathing at 70 breaths/min may indicate compromise. Causes of slow respiratory rates include medications, hypothermia, or neurologic impairment.

Normal infant heart rates range from 100 to 160 beats/min. Heart rate can be assessed by auscultation of the apical pulse, normally located at the fifth intercostal space, midclavicular line. Alternatively, the brachial and femoral pulses may be used. Weak

pulses indicate hypotension, shock, or vasoconstriction. Bounding peripheral pulses occur with major left-to-right shunting through a **patent ductus arteriosus (PDA).**[7] A strong brachial pulse in the presence of a weak femoral pulse suggests either PDA or coarctation of the aorta. Table 54.3 lists normal ranges of blood pressure for neonates of different sizes.

RULE OF THUMB The normal respiratory rate for a full-term infant is 40–60 breaths/min.

Chest examination in an infant is more difficult to perform and interpret than in an adult because of the small chest size and the ease of sound transmission through the infant chest. Thorough observation of the infant greatly enhances the assessment data obtained. Infants in respiratory distress typically exhibit one or more key physical signs: nasal flaring, cyanosis, expiratory grunting, tachypnea, retractions, and paradoxical breathing. Nasal flaring is seen as dilation of the ala nasi on inspiration. The extent of flaring varies according to facial structure of the infant. Nasal flaring coincides with an increase in the work of breathing. In concept, nasal flaring decreases the resistance to airflow. It also may help to stabilize the upper airway by minimizing negative pharyngeal pressure during inspiration.[8] Cyanosis may be absent in infants with anemia, even when arterial partial pressure of oxygen (PaO_2) levels are decreased. In addition, infants with elevated fetal hemoglobin levels may not become cyanotic until PaO_2 decreases to less than 30 mm Hg. Hyperbilirubinemia, common among newborns, may mask cyanosis. Grunting occurs when infants exhale against a partially closed glottis. By increasing airway pressure during expiration, grunting helps to prevent airway closure and alveolar collapse. Grunting is most common in infants with RDS, but it is also seen in other respiratory disorders associated with alveolar collapse. Fig. 54.5 illustrates the Silverman score, which is a system of grading severity of lung disease.

Retractions refer to the drawing in of chest wall skin between bony structures. Retractions can occur in the suprasternal, substernal, and intercostal regions. Retractions indicate an increase in the work of breathing, especially because of decreased pulmonary compliance. Paradoxical breathing in infants differs from paradoxical breathing normally seen in adults. Instead of drawing the abdomen in during inspiration, an infant with paradoxical breathing tends to draw in the chest wall. This inward movement of the chest wall may range in severity. As with retractions, paradoxical breathing indicates an increase in ventilatory work. Applying high-flow nasal cannula (HFNC) or continuous positive airway pressure (CPAP) to a newborn exhibiting signs of respiratory distress including **grunting, flaring, and retracting** may help to increase lung volume by preventing alveolar collapse and improve gas exchange. The benefits of HFNC and CPAP in children are discussed in more detail later.

TABLE 54.3 Normal Neonatal Blood Pressures

Weight (g)	Systolic (mm Hg)	Diastolic (mm Hg)
750	35–45	14–34
1000	39–59	16–36
1500	40–61	19–39
3000	51–72	27–46

From Whitaker K. *Comprehensive perinatal and pediatric respiratory care*. 3rd ed. Albany, NY: Delmar; 2001.

Surfactant

Surfactant production begins around the 24th week of gestation and continues through gestation. Surfactant contributes to the stability of the alveolar sacs by reducing the surface tension of the fluids that coat the alveoli. Surfactant deficiency places an

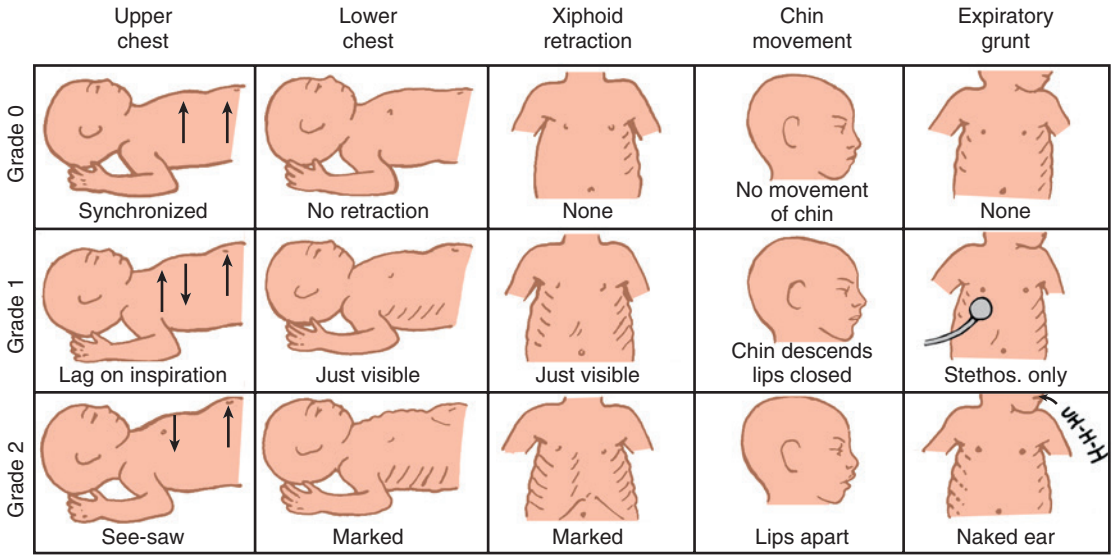

Fig. 54.5 Silverman score—a system for grading severity of underlying lung disease. (Modified from Silverman WA, Anderson DH. A controlled clinical trial of effects of water mist on obstructive respiratory signs, death rate and necropsy findings among premature infants, *Pediatrics*. 1956;17(1):1–70.)

infant at increased risk for respiratory distress. By approximately 34 weeks' gestation, most infants have produced enough surfactant to keep the alveoli from collapsing. Surfactant deficiency is due to lung immaturity. There are two specific approaches to preventing and treating surfactant deficiency. When a premature delivery is anticipated, steroids are given to the mother to help promote lung maturation. In addition, infants born before 35 weeks' gestation, especially infants born very prematurely (<30 weeks), should be assessed clinically for the need to receive exogenous surfactant. The need for surfactant is determined by assessing the infant's lung volume on chest x-ray, evaluating the inspired O_2 concentration to maintain O_2 saturations greater than approximately 88%, and clinically assessing the infant's work of breathing.

Evidence supports early surfactant replacement, immediately following delivery, for infants less than 27 weeks' gestation. Infants 27 to 30 weeks' gestation should be placed on HFNC or CPAP and evaluated clinically for the need to receive surfactant.[9–12]

Surfactant administration has also been shown to be useful in conditions in which surfactant structure and/or function has been altered. These conditions include meconium aspiration, neonatal pneumonia, pulmonary hemorrhage, and primary surfactant deficiency. See later section regarding administration of surfactant.

Blood Gas and Pulse Oximetry Analysis

Blood gas analysis is helpful in assessing respiratory distress in an infant. Many noninvasive techniques, such as transcutaneous partial pressure of oxygen ($PtcO_2$), transcutaneous partial pressure of carbon dioxide ($PtcCO_2$), end-tidal carbon dioxide (CO_2), and pulse oximetry (SpO_2), are used to obtain comparable data, although blood gas analysis is more precise when results are critical. An infant blood gas sample can be obtained from an artery or capillary. Chapter 19 summarizes the advantages, disadvantages, and complications of these sampling methods. Care must be taken in assessing the results of capillary sampling. Capillary blood gases provide information regarding only ventilation and acid–base status, and accuracy is highly dependent on technique.[13] Normal values for infant blood gases are listed in Table 54.4.

Monitoring O_2 saturation using a pulse oximeter is a standard of care for sick newborns. Saturation probes must be carefully placed on the newborn; the most common sites are the wrist, the medial surface of the palm, or the foot. Sufficient cardiac output and skin blood flow are essential to provide an accurate saturation value. The pulse rate indicated on the oximeter should correlate with the infant's actual pulse before any conclusions regarding saturation can be drawn. Intracardiac shunting and intrapulmonary shunting are causes of decreased saturation in sick infants. When interpreting saturation levels in a newborn, it is important to consider where the saturation is being monitored. Saturation probes placed on the right hand assess preductal saturations. Probes placed on other extremities indicate postductal saturation levels. Infants at risk for pulmonary hypertension should have saturation probes placed to monitor preductal and postductal saturations. A large difference (>5%) between the two readings should prompt the clinician to consider pulmonary hypertension as a potential concern. Conditions that prevent the closing of the ductus arteriosus and foramen ovale result in decreased saturation. Many congenital heart defects result in significant intracardiac shunting. Interpreting adequate saturation for a newborn requires knowledge of any cardiac defect along with the infant's pulmonary condition.

MINI CLINI

Neonatal Ventilation

Problem

A 1.8-kg, 28-week newborn is transported from the delivery room to the neonatal intensive care unit (NICU). The patient was apneic and bradycardic at birth and failed to respond to initial stimulation and resuscitation. He was intubated with a 3.0 uncuffed endotracheal tube. His heart rate increased to 120 beats/min, and he has been manually ventilated with a T-piece resuscitator at a peak inspiratory pressure (PIP) of 20 cm H_2O and Positive end-expiratory pressure (PEEP) of 7 cm H_2O during transport. When the neonate is admitted to the NICU, the respiratory therapist (RT) is asked to recommend appropriate ventilator settings.

Solution

- Mode—assist/control (A/C) pressure ventilation
- PIP—20 cm H_2O
- PEEP—7 cm H_2O
- Set respiratory rate—40 breaths/min
- Inspiratory time—0.3 s
- FiO_2—0.4

TABLE 54.4 Age-Related Values Commonly Reported for Normal Blood Gases

	Normal Preterm Infants (at 1–5 h)	Normal Term Infants (at 5 h)	Normal Preterm Infants (at 5 Days)	Children, Adolescents, and Adults
pH (range)	7.33 (7.29–7.37)	7.34 (7.31–7.37)	7.38 (7.34–7.42)	7.40 (7.35–7.45)
PCO_2 (range)	47 (39–56)	35 (32–39)	36 (32–41)	40 (35–45)
PO_2 (range)	60 (52–68)	74 (62–86)	76 (62–92)	95 (85–100)
HCO_3^- range	25 (22–23)	19 (18–21)	21 (19–23)	24 (22–26)
BE range	–4 (–5 to –2.2)	–5 9 (–6 to –2)	–3 (–5.8 to –1.2)	0 (–2 to +2)

BE, Base excess; *HCO_3^-*, bicarbonate.

Modified from Orzalesi MM, Mendicini M, Bucci G, et al. Arterial oxygen studies in premature newborns with and without mild respiratory disorders. *Arch Dis Child.* 1967;42:174. From Koff PB, Eitzman DV, Neu J. *Neonatal and pediatric respiratory care.* 2nd ed. St Louis: Mosby; 1993.

Because the patient was manually ventilated during transport, it is unclear what tidal volume (V_T) has been delivered. Initial PIP of 20 cm H_2O and PEEP of 7 cm H_2O are safe and common settings. Immediate observation of the chest would allow the RT to evaluate chest expansion and adjust PIP as required. Over the next several minutes if V_T monitoring is available, targeting V_T of 6 to 8 mL/kg would guide subsequent settings.

Set respiratory rate of 40 breaths/min is at the lower end of the normal range for this patient; however, use of the A/C mode with a time-cycled, pressure-limited breath, and appropriately set trigger sensitivity would allow the patient to establish a more comfortable respiratory rate. Adjustment of the inspiratory time may also be necessary to increase patient comfort and improve patient–ventilator synchrony. Further adjustments may be guided by $PaCO_2$. Because this patient was born prematurely, rapid assessment of pulse oximetry (SpO_2) is essential, and FiO_2 should be adjusted to maintain SpO_2 between 89% and 94%.

This patient should receive surfactant replacement therapy. The clinician may consider volume-targeted, pressure-limited ventilation (e.g., pressure-regulated volume control, volume guarantee) during and immediately after surfactant delivery. This modality may help to prevent lung overdistension until compliance has stabilized.[14–16]

Respiratory Assessment of the Pediatric Patient

Normal breathing in children is evidenced by quiet inspiration and passive expiration at an age-appropriate rate. Respiratory rates are rapid in neonates and decrease in toddlers and older children. Table 54.5 lists normal respiratory rates. The American Heart Association, in conjunction with the American Academy of Pediatrics, has developed a Pediatric Advanced Life Support (PALS) program. This program is similar to the Advanced Cardiac Life Support (ACLS) program used for adults, with a focus on the pediatric patient. The program includes such topics as primary assessment, diagnostic testing, respiratory failure and other emergencies, emergency equipment and medications including pediatric dosing guidelines, shock, cardiac arrythmia, cardiac arrest, and postresuscitation management. PALS certification should be an integral part of the curriculum for RTs specializing in care of the pediatric patient.

The initial assessment of a pediatric patient starts with evaluating airway patency. Normal heart rates are higher in younger children and decrease with age. In assessing a pediatric patient, establishing if the airway is patent or has any obstructive component is essential. Signs that suggest upper airway obstruction include increased inspiratory effort with retractions or inspiratory efforts with no airway or breath sounds.

TABLE 54.5 Normal Respiratory and Heart Rates by Age

Age	Breaths/Minute	Heart Rates
Infants (<1 year)	30–60	90–120
Toddler (1–3 years)	24–40	80–100
Preschooler (4–5 years)	22–34	70–90
School age (6–12 years)	18–30	70–90
Adolescent (13–18 years)	16–22	60–80

The clinician should assess for movement of the chest and abdomen. The clinician listens for breath sounds focusing on both inspiratory sounds and expiratory sounds. Chest or abdominal movement without breath sounds may indicate total airway obstruction, and basic life-support maneuvers are indicated. High-pitched sounds heard on inspiration (stridor) are often indicative of upper airway conditions, whereas expiratory noises are more often associated with lower airway obstruction.

Causes of stridor in children can be infections, such as croup; foreign body aspiration, particularly in a small child; congenital or acquired airway abnormalities; allergic reactions; or edema after a procedure. Inhaled epinephrine via nebulizer and intravenous steroids are commonly used to treat stridor. Common causes of lower airway obstruction are bronchiolitis and asthma. When wheezing is noted, inhaled bronchodilators are indicated. If the patient is able to use a metered dose inhaler (MDI), repeated inhalations can act quickly to improve aeration. When the patient is unable to use the MDI appropriately or when severe symptoms are present, delivering a bronchodilator with a nebulizer can bring relief. More than one nebulizer treatment often is necessary to relieve airway inflammation. A common approach is to deliver three consecutive treatments. If the patient continues to be symptomatic, continuous bronchodilator therapy may be delivered with a nebulizer attached to an infusion pump set to administer a bronchodilator continuously. Tachycardia secondary to the beta-1 effect of inhaled bronchodilators may occur. Frequent reassessment of any patient receiving continuous bronchodilator therapy is essential. Heliox, an inhaled mixture of helium and O_2 (described in the section on specialty gases), has been shown to be beneficial in cases of some airway conditions in children.

As noted in the section describing newborn assessment, use of accessory muscles, grunting, flaring, and retracting all can be signs of respiratory distress. Head bobbing, noted by chin up and neck extended during inspiration with chin falling during expiration, and seesaw respirations, indicated by the chest retracting and the abdomen expanding during inspiration, are signs of impending respiratory failure. Assessing the child's level of alertness is essential. Levels of alertness range from fully awake, agitated, minimally responsive, to unresponsive. A child's ability to protect his or her airway should be questioned in a minimally responsive or unresponsive child.

RESPIRATORY CARE

Respiratory care of infants and children incorporates approaches taken from adult practice. Important physiologic and age-related differences between adults and children require variations in the provision of respiratory care. This section focuses on neonatal and pediatric O_2 therapy, bronchial hygiene, humidity and aerosol therapy, airway management, and resuscitation.

Oxygen Therapy

Goals and Indications

O_2 should be administered as any other drug, using the lowest dose necessary to achieve the intended goal. The goal of O_2 therapy is to provide adequate tissue oxygenation. However, O_2 therapy is most frequently adjusted according to O_2 saturation

levels. A clear understanding of the limitation of O_2 saturation (See Chapter 19) is needed to interpret the saturation reading and make appropriate decisions. Infants and children receiving O_2 therapy have variable O_2 saturation target ranges depending on age and underlying condition.

Lower saturation levels are targeted in infants less than 32 weeks' gestation. There is evidence that exposure to supplemental O_2 in a premature infant is a risk factor for the development of **retinopathy of prematurity (ROP).** ROP is caused by an abnormal vascularization of the retina, which in the most severe cases leads to retinal detachment. Preterm neonates weighing less than 1500 g are most susceptible. Hyperoxia is not the only factor associated with ROP, but close monitoring and adjusting of O_2 therapy to avoid hyperoxia are crucial to decrease the risk of ROP. A specific saturation goal of 88% to 94% should be established for this age group, and O_2 should be adjusted to maintain the intended target. Avoiding very high or very low saturation levels is critical. Adjusting the delivered O_2 concentration by small increments avoids large swings in saturation levels.[17–21]

In a term infant with **primary pulmonary hypertension of the newborn (PPHN),** a higher targeted saturation level is desired to avoid further pulmonary constriction associated with hypoxemia. The position of the saturation probe needs to be considered when interpreting saturation. Intracardiac shunting can occur in the presence of PPHN. One saturation probe positioned on the upper right extremity represents preductal saturations and is indicative of the saturation of blood being delivered to the brain. O_2 saturation measured on other extremities is considered postductal and represents saturation to other parts of the body.

Newborns with certain cardiac anomalies are dependent on their intracardiac shunt through the ductus arteriosus to survive. An increased saturation in newborns promotes constriction of the ductus arteriosus. Although this constriction is normally a positive response, it may cause premature closure of the ductus arteriosus in infants with ductal-dependent congenital heart defects. An infant born with hypoplastic left heart syndrome, a defect in which the left-sided heart structures are poorly developed, relies on the patency of the ductus arteriosus for systemic blood supply. In addition, hyperoxia can increase aortic pressures and systemic vascular resistance, decreasing the cardiac index and O_2 transport in children with acyanotic congenital heart disease. The emphasis for O_2 therapy for all newborns should be to provide only as much O_2 as indicated by the infant's condition. O_2 therapy should be administered using a written care plan with specified clinical outcomes (e.g., titrate flow/FiO_2 to maintain SpO_2 89% to 92%, notify physician if FiO_2 is >0.40). An example of an oxygen therapy guideline/order is shown in Table 54.6.

Methods of Administration

The effectiveness of O_2 devices depends on the performance characteristics of the device (delivered FiO_2, flow rate, relative humidity), the interface of the device, and the tolerance of the patient for using the device. Children are often frightened and combative, making it impractical to use some O_2 administration devices. Selection of an O_2 device must be based on the degree of hypoxemia and the emotional and physical needs of the child and family (see Chapter 42 Medical Gas Therapy). O_2 can be administered to infants and children by mask, cannula, high-flow nasal cannula, or oxyhood. Table 54.7 compares the advantages and disadvantages of standard O_2 delivery methods.

Surfactant Administration

Exogenous pulmonary surfactant replacement therapy is indicated in the delivery room for infants 27 weeks' gestation or less. Surfactant should also be given to infants born at 27 to 29 weeks' gestation if they are intubated for severe RDS, surfactant deficient neonates with RDS evident by clinical presentation and term or

TABLE 54.6 Oxygen Saturation Goals

Preterm, ROP risk: on SpO_2 89%–94%
Preterm, ROP risk: on room air SpO_2 89%–100%
Preterm, 31–34 weeks: SpO_2 91%–96%
Preterm, ≥ 35 weeks or term: SpO_2 93%–100%
Pulmonary hypertension: SpO_2 96%–100%

ROP, Retinopathy of prematurity.

TABLE 54.7 Oxygen Delivery Devices

Device	Age	FDO_2	Advantages	Disadvantages
Air entrainment mask	≥3 years	High flow; 0.24–1	Precise FiO_2; good for transport; ease of application	Low relative humidity; pressure necrosis to face; difficult to fit and maintain on active child, not recommended for infants; risk of aspiration
Nasal cannula	Premature infants to adult	Low flow; 25 mL/min–6.0 L/min	Tolerated well by all ages	Inaccurate FiO_2; low relative humidity; excessive flows may cause inadvertent CPAP in infants; precise FiO_2 may be achieved with O_2 blender
Incubator	Newborns ≤28 days	<0.40 FiO_2, combine use with cannula or hood for precise FiO_2	Low FiO_2 for stable infants; neutral thermal environment for premature infants	Varying FiO_2; long stabilization time; limits access to child for patient care
Oxyhood	Premature infants to ≤6 months	0.21–1 FiO_2 with O_2 blender maintained at 30°C–34°C	Warmed and humidified gas at stable FiO_2 during routine patient care	Overheating may cause apnea and dehydration; underheating may cause O_2 consumption; inadequate flow causes CO_2 buildup; noise produced by humidification device may cause hearing loss

CPAP, Continuous positive airway pressure; *FDO_2,* delivered oxygen concentration.

MINI CLINI

Neonatal High-Flow Nasal Cannula

Problem

A baby girl 30 weeks' gestation is delivered by emergency C-section for fetal distress (nonreassuring fetal heart tracing [NRFHT]) and admitted to the neonatal intensive care unit (NICU) for issues of prematurity and moderate respiratory distress. Respiratory rate is 70 breaths/min, and pulse oximetry (SpO_2) is 84%. The respiratory therapist places a high-flow nasal cannula on the patient at 6 L/min and 40% oxygen. Respiratory rate decreases to 50 breaths/min, and SpO_2 increases to 99%.

Solution

The respiratory therapist should decrease the FiO_2 to meet SpO_2 goal of 89%–94%. The flow should be maintained at 6 L/min, the same level of continuous positive airway pressure (CPAP) which has decreased the patient's work of breathing and oxygen requirement. The flow should not be decreased until the FIO_2 requirement falls below 0.3.

postterm neonates with meconium aspiration syndrome (MAS) or pneumonia/sepsis.

The recommended first dose for treatment of RDS or MAS is 2.5 mL/kg. Repeat doses of 1.25 mL/kg may be given q12hr for a maximum of three doses. Redosing is not advised within 12 hours. Maximum total dose is 5 mL/kg.

Administration of surfactant requires intubation. It is essential to ensure the endotracheal tube is properly positioned, approximately 0.5 to 1 cm above the carina, before delivering surfactant. The dose depends on the specific brand of surfactant being administered. Close monitoring of the infant's vital signs, O_2 saturation, and compliance is necessary during and after surfactant administration. Soon after surfactant is delivered, the infant's compliance should begin to increase resulting in improved gas exchange. Ventilating pressures and FiO_2 need to be decreased to avoid lung injury and excessive partial pressure of O_2. The ventilating pressure should be decreased to the level that maintains a tidal volume (V_T) of 5 to 7 mL/kg. FiO_2 should be decreased to maintain an oxygen saturation level (SpO_2) of approximately 89% to 94% in preterm infants and to the lowest FiO_2 possible to maintain SpO_2 greater than 92% in term or postterm infants. Those with primary pulmonary hypertension should have an SpO_2 greater than 95%.

Secretion Clearance Techniques

Secretion clearance techniques that can be applied to infants and children include chest physiotherapy, positive expiratory pressure therapy, autogenic drainage, flutter therapy, and mechanical insufflation-exsufflation (MIE)[22, 23] (see Chapter 44). Secretion clearance techniques are considered when accumulated secretions impair pulmonary function and an infiltrate is visible on a chest radiograph. Secretion retention is common in children who have pneumonia, bronchopulmonary dysplasia, cystic fibrosis, bronchiectasis, and some neuromuscular diseases. Fig. 54.6 shows postural drainage and percussion positions for infants and children.

Methods

Infants and young children cannot cough on command. For this reason, secretions often must be removed by suctioning. For

MINI CLINI

Secretion Clearance Using Mechanical Insufflation-Exsufflation

Problem

A 1-year-old boy with a diagnosis of type I spinal muscle atrophy (SMA) and history of intermittent left lobe collapse is admitted to the pediatric intensive care unit. The patient's home regimen includes use of around the clock room air noninvasive ventilation (NIV), with intermittent periods off for up to an hour, 4–6 times daily. For the past week the patient has required increasing use of NIV and is unable to tolerate periods off for more than 15–20 min. He currently has an increase from his baseline NIV settings and an oxygen requirement of 3 L/min attached to his NIV device. Breath sounds reveal bilateral rhonchi with decreased aeration on the left. The patient is started on mechanical insufflation-exsufflation (MIE) therapy with an inspiratory pressure of 40 cm $H_2O \times 1$ second, expiratory pressure of –40 cm $H_2O \times 1$ s, and a 1 s rest period. This is performed for five breaths, followed by tracheal suctioning and the cycle is repeated 5 times every 2 h. After 48 h the patient has been returned to baseline NIV settings, and use of the MIE has been reduced to every 4 h. He is able to tolerate increasing periods of time, 45 min to 1 h, off NIV up to 4 times daily.

older children with excessive secretions, directed deep breathing and coughing may help to improve pulmonary clearance. The use of MIE in children with neuromuscular disease can be helpful in clearing secretions. Adjunctive therapy devices such as positive expiratory pressure, flutter, or intermittent percussive ventilation therapy have been effective in secretion clearance in patients with cystic fibrosis.[24]

Patients with SMA and other forms of neuromuscular disease are unable to generate an effective cough sufficient to mobilize retained secretions. Use of an MIE in conjunction with tracheal suctioning and increased NIV settings may provide sufficient additional respiratory support to assist patients in overcoming an acute crisis, preventing the need for intubation and invasive mechanical ventilation, allowing them to return to their baseline level of support.

Monitoring

Given the instability of most critically ill infants and children, a thorough initial assessment and ongoing patient evaluation during and after treatment are mandatory. Traditional assessment of vital signs, blood pressure, color, and breath sounds before, during, and after treatment should be supplemented with pulse oximetry monitoring if hypoxemia is suspected.

Humidity and Aerosol Therapy

Key differences in humidity and aerosol therapy in infants and children include assessment of patient response to therapy, age-related physiologic changes, and equipment application (see Chapter 39).

Humidity Therapy

In children with an intact upper airway, O_2 therapy devices, such as low-flow nasal cannulas, do not routinely need to be humidified. However, any time the upper airway is bypassed by intubation, supplemental humidification must be provided using a heated

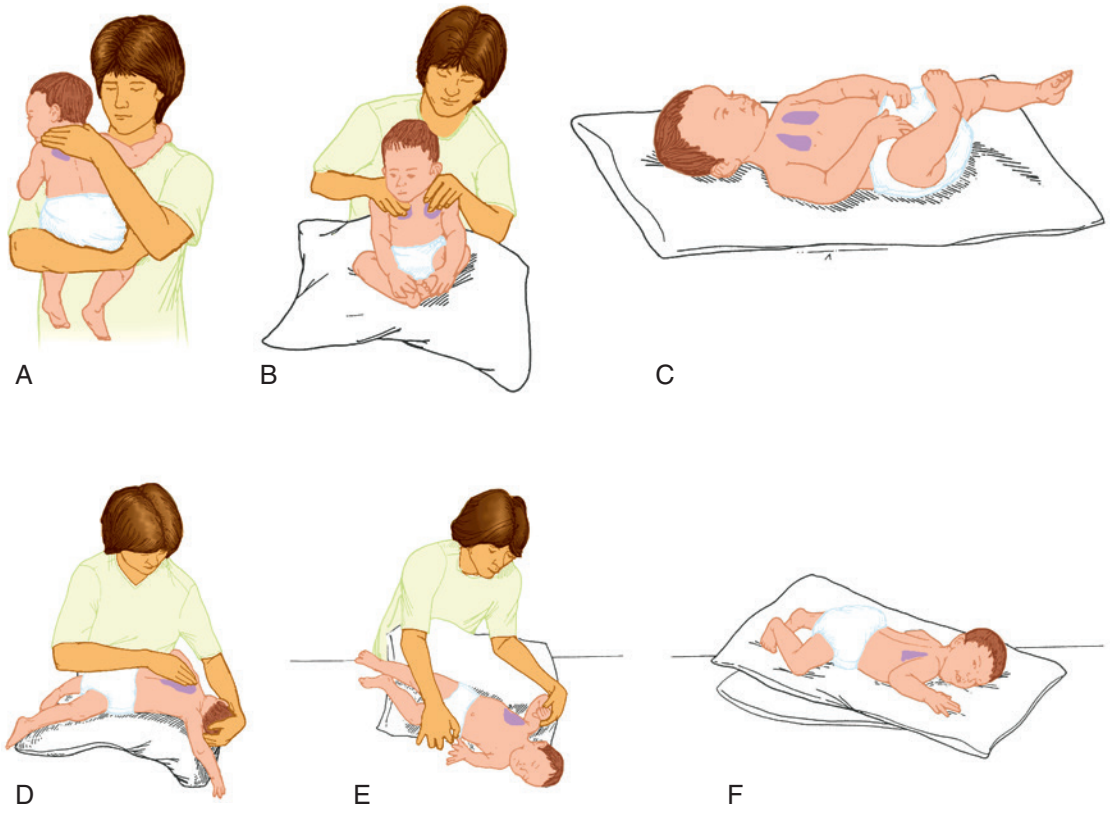

Fig. 54.6 Postural drainage and percussion positions for infant and child. Angles of drainage for infant are not as obtuse as those for child. (A) Posterior segments of right and left upper lobes are drained with patient in upright position at 30-degree angle forward. Percuss over upper posterior thorax. (B) Apical segments of right and left upper lobes are drained with patient in upright position, leaning forward 30 degrees. Percuss over area between clavicle and tip of scapula on each side. (C) Anterior segments of right and left upper lobes are drained with patient in flat, supine position. Percuss anterior side of chest directly under clavicles to around nipple area *(shaded)*. Avoid direct pressure on sternum. (D) Right and left lateral basal segments of lower lobes are drained at 30 degrees Trendelenburg. Patient lies on appropriate side, rotated 30 degrees forward. Percuss over uppermost portions of lower ribs. (E) Right and left anterior basal segments of lower lobes are drained at 30 degrees Trendelenburg. Patient lies on appropriate side with a 20-degree turn backward. Percuss above anterior lower margin of ribs. (F) Right and left superior segments of lower lobes are drained at 15 degrees Trendelenburg, with patient in prone position. Percuss below scapula in midback area.

humidifier. Humidification of inspired gases for infants and children receiving mechanical ventilation is commonly provided by a servo-controlled humidifier. Ideal features for these systems include the following: (1) low internal volume and constant water level to minimize compressed volume loss; (2) closed, continuous feed water supply to avoid contamination; (3) distal airway temperature sensor and high/low alarms. Common problems with humidifier systems include condensation in the tubing, inadequate humidification, and hazards associated with the heating coil.[25,26] Using heated wire circuits can also reduce condensation in the circuit. Frequent evaluation of the humidification system is necessary to increase the potential of adequate humidity delivered to the airway. Inadequate humidification occurs in nonheated circuits when the humidifier temperature probe is placed too far upstream from the airway connector. Variable humidification problems occur when ventilator circuits pass through an environment and then into a warmed enclosure, such as an incubator or radiant warmer.

Aerosol Drug Therapy

Drug action in infants and children differs significantly from drug action in adults because of differences in physiology, which may include immature enzyme systems, immature receptors, and variable gastrointestinal absorption (see Chapters 36 and 40). Dosing may be imprecise, and systemic effects may be hard to predict. Table 54.8 lists aerosolized medications commonly used in children.

Small volume nebulizers (SVNs), vibrating mesh nebulizers, MDIs, and dry powder inhalers (DPIs) can be used to deliver aerosolized drugs via mouthpiece or face mask to infants and children.[27] Continuous aerosol drug therapy is also used for patients unresponsive to intermittent SVN treatments. Aerosol drug administration to intubated infants and children is challenging because of the decreased deposition from baffling of small endotracheal tubes in these patients, which prevents approximately 90% of the drug from entering the lungs, regardless of delivery system. In addition, careful adjustments must be

TABLE 54.8 Commonly Used Aerosolized Medications

Medication Name	Dosage Form	Usual Child Dose	Comments
Bronchodilators			
Beta-2 Agonists			
Albuterol (Proventil, Ventolin)	MDI (90 mcg/puff)	1–2 puffs MDI q 15 min to q 6 h ± PRN	May be used 15 min before exercise to prevent exercise-induced bronchospasm; should be used as a rescue medication
	Nebs (0.5%, 5 mg/mL)	0.01–0.05 mL/kg/dose (maximum 1 mL/dose) neb q 15 min to q 6 h ± PRN	
	Rotohaler (200 mcg caps)	1–2 caps inhaled q 15 min to q 6 h ± PRN	
Levalbuterol (Xopenex)	Nebs (0.63 mg/3 mL, 1.25 mg/3 mL)	0.32–1.25 mg neb q 6–8 h ± PRN	May still cause extrapulmonary side effects including tachycardia and hypokalemia
Salmeterol (Serevent)	MDI (21 mcg/puff)	2 puffs inhalation q 12 h	Not to be used as a rescue medication; long-acting beta-2 agonist; QT_C prolongation has occurred in overdose
	DPI-Diskus (50 mcg/inhalation)	1 inhalation q 12 h	
Anticholinergic			
Ipratropium (Atrovent)	MDI (18 mcg/puff)	2 puffs inhalation q 4–6 h ± PRN	MDI is contraindicated in patients with peanut allergy; for neonates, use 25 mcg/kg/dose neb tid; may cause mydriasis if aerosolized drug gets into the eye
	Nebs (0.02%)	0.25–0.5 mg neb q 4–6 h ± PRN	
Antiinflammatory Agents			
Corticosteroids			
Beclomethasone (Beclovent, Qvar), Vanceril)	MDI (42 mcg/puff)	1–2 puffs inhalation qid or 2–4 puffs inhalation bid	Start at lower end of dosing range if patient not previously on steroids; titrate to lowest dose that is effective; always rinse mouth after each treatment
	MDI double strength (84 mcg/puff)	2 puffs inhalation bid	
Budesonide (Pulmicort)	DPI-Turbuhaler (200 mcg/inhalation)	1–2 puffs inhalation bid	May take several weeks to see benefit; not to be used as a rescue medication
	Nebs-Respules (0.25 mg/2 mL, 0.5 mg/2 mL)	0.25–0.5 mg neb bid *or* 0.5–1 mg neb qd	
Flunisolide (Aerobid, Aerobid-M)	MDI (250 mcg/puff)	2–3 puffs inhalation bid	
Fluticasone (Flovent)	MDI (44 mcg/puff, 110 mcg/puff, 220 mcg/puff)	2 puffs inhalation bid (maximum 880 mcg/d)	
	Rotadisk (50 mcg/blister)	50–100 mcg inhalation bid	
Mometasone (Asmanex)	Twisthaler (100 mcg puff, 200 mcg puff)	2 puffs inhalation bid	For use in patients 12 years and older
Ciclesonide (Alvesco)	80 mcg puff 160 mcg puff	2 puffs bid	For use in children 12 years and older
Mast Cell Stabilizers			
Nedocromil (Tilade)	MDI (1.75 mg/puff)	2 puffs inhalation qid	
Mucolytics			
N-acetylcysteine (Mucomyst)	Nebs (20%, 200 mg/mL)	3–5 mL neb qid	Consider pretreatment with albuterol 15 min before *N*-acetylcysteine secondary to bronchospasm
Dornase alfa (Pulmozyme)	Nebs (2.5 mg/2.5 mL)	2.5 mg neb qid-bid	May cause hemoptysis
Antiinfectives			
Pentamidine (Pentam)	Nebs (300 mg)	8 mg/kg/dose (maximum 300 mg/dose) neb q month	Used for PCP prophylaxis
Ribavirin (Virazole)	Powder (6 g vial)	2 g over 2 h neb q 8 h × 3–7 days *or* 6 g over 12–18 h neb q 24 h × 3–7 days	Used for RSV treatment; mutagenic, teratogenic
Tobramycin (TOBI)	Nebs (300 mg/5 mL)	300 mg neb q 12 h	Used for pseudomonal infection of the lungs

DPI, Dry powdered inhaler; *MDI,* metered dose inhaler; *Neb,* nebulizer; *PCP, Pneumocystis jiroveci* pneumonia; *RSV,* respiratory syncytial virus.

TABLE 54.9 Endotracheal Tube and Suction Catheter Sizes for Infants and Children

Age or Weight	Endotracheal Tube ID (mm)	Oral Tube Length (cm)	Nasal Tube Length (cm)	Suction Catheter (F)
Newborn				
<1000 g	2.5	9–11	11–12	6
1000–2000 g	3	9–11	11–12	6
2000–3000 g	3.5	10–12	12–14	6
>3000 g	4	11–12	13–14	8
Children				
6 months	3–4	11–12	12–14	6–8
18 months	3.5–4.5	11–13	13–15	8
2 years	4–5	12–14	14–16	8–10
3–5 years	4.5–5.5	12–15	14–17	8–10
6 years	5.5–6	14–16	16–18	10
8 years	6–6.5	15–17	17–19	10–12
12 years	6–7	17–19	19–21	10–12
16 years	6.5–7.5	19–21	21–23	10–12

Estimating formula for tube internal diameter (ID) in mm:
Tube ID = (Age + 16)/4
Tube ID = Height (cm)/20
Estimating formula for tube length in cm:
Oral: 12 + (Age/2)
Nasal: 15 + (Age/2)

TABLE 54.10 Approximate Distance From Infant's Lip to End of Inserted Oral Endotracheal Tube

Weight (kg)	Mark at Lip (cm)
<1	6.5
1	7
2	8
3	9
4	10

BOX 54.1 Complications and Hazards of Endotracheal Intubation in Infants and Children

- Palatal grooving (neonates)
- Incisal enamel hypoplasia (neonates)
- Accidental extubation
- Tube blockage
- Tracheal stenosis
- Esophageal perforation
- Tracheal perforation

made to the ventilator so that nebulizer flows do not alter delivered V_T and inspiratory pressure and interfere with triggering efforts.[28] Newer vibrating mesh type nebulizers provide a more stable particle size and do not add additional flow to the breathing circuit. As a result, there is no change in the delivered V_T and patient triggering is not affected.

Airway Management

Airway management methods in infants and children are unique because of the anatomic differences between neonates and adults. Specifically, equipment and technique must be tailored to each child according to his or her size, weight, and postpartum age. Masks, resuscitation bags, oral airways, suction catheters, laryngoscope blades, and endotracheal tubes in a wide selection of infant and child sizes are needed to account for variations in patient age and weight. Table 54.9 provides recommendations regarding endotracheal tube and suction catheter sizes for infants and children.

Intubation

Endotracheal intubation is a generally safe method of airway management in infants and children, even when used for extended periods.[29,30] Complications and hazards associated with intubation in these age groups are listed in Box 54.1. The infant's age or weight can be used to estimate proper endotracheal tube size and depth of insertion. If the tube is too small in diameter, a leak may result, decreasing delivered minute ventilation. Small endotracheal tubes have high resistance, increasing the spontaneous work of breathing for the child. An inappropriately large endotracheal tube can cause mucosal and laryngeal damage that is evident after extubation, resulting in upper airway obstruction.[31]

Most neonatal and pediatric endotracheal tubes are uncuffed. The narrowest point of the airway in an infant and small child is the cricoid cartilage. When an appropriately sized uncuffed tube is positioned in the airway, the fit of the tube in the airway "seals" the airway enough so that adequate ventilation can usually be maintained. Cuffed endotracheal tubes are an option if a large leak persists around the tube and stable ventilation cannot be maintained. Similar to adults when a cuffed tube is used, careful attention to the pressure in the cuff on the tracheal wall is essential. Because the tongue is large and the epiglottis is anatomically high in infants and small children, practitioners generally find the Miller (straight) laryngoscope blade best for intubation. Infant endotracheal tubes are small and can be easily kinked or obstructed. In addition, slight changes in the position of the endotracheal tube in movement can result in bronchial intubation.

Once a tube is inserted, immediate securing of the tube to the infant's face and ongoing evaluation of the security of the tube are essential. Proper head positioning and avoidance of cumbersome connecting apparatus help to reduce the potential of accidental extubation. Estimates of the distance the tube should be inserted into the airway based on patient weight are provided in Table 54.10. Further confirmation of correct tube position should be evaluated with a chest x-ray. Noting the infant's head position when the chest x-ray is obtained is helpful in assessing appropriate tube position in the airway. Slight changes in head position can result in the tube position sitting too high or too low in the airway. In very small infants, slight flexion of the head can move the tube into the right main stem bronchus.

Breath sounds may be of limited value in infants and small children for evaluation of tube position. Portable end-tidal CO_2 monitoring devices may be used to help assess tracheal versus

BOX 54.2 Indications for Suctioning

Absolute Indications
- Secretions visible in endotracheal tube
- Aspiration of gastrointestinal or oropharyngeal contents
- Inadvertent water aspiration from ventilator circuit

Relative Indications
- Rhonchi noted during auscultation raising suspicion of retained secretions
- Change in compliance (↓ tidal volume [V_T] at same peak pressure or ↑ pressure for same V_T)
- ↑ Work of breathing
- ↓ SpO_2 with same or ↑ FiO_2

TABLE 54.11 Appropriate Sizes and Maximum Cuff Volumes of Laryngeal Mask Airways for Varying Weights

LMA Size	Patient Weight (kg)	Maximum Cuff Volume
1	1–5	4
1.5	5–10	7
2	10–20	10
2.5	20–30	14
3	30–40	20

LMA, Laryngeal mask airways.

esophageal intubation, although they should be used only as additional assessment tools with recognition of their limitations. Factors associated with accidental extubation of infants include tension on the tube from the ventilator circuit, patient agitation, suctioning, head turning, chest physiotherapy, too short a tube distance between lip and adapter, moving the patient during procedures, and inadequately taped endotracheal tube.[32–34] Infant-sized endotracheal tube holders are available, but use of these devices is sporadic and subjective

Laryngeal mask airways (LMAs) are available as an alternative to intubation. LMAs are typically used in children when a short-term airway is indicated, such as during some surgical procedures or when endotracheal intubation cannot be accomplished and an airway needs to be established. Table 54.11 outlines appropriate sizes and maximum cuff volumes of LMAs for varying weights.

Suctioning Intubated Pediatric Patients

The goal of suctioning is to remove secretions from large airways and stimulate a cough. Although suctioning can be beneficial, significant risks are associated with the procedure, including lung derecruitment, hypoxia, hypertension, increased intracranial pressure, tracheal trauma, and infection. Absolute and relative indications for suctioning are listed in Box 54.2.

Additional considerations include the use of closed suction catheters for all mechanically ventilated patients. The closed suctioning technique helps to minimize derecruitment, which is more likely to occur during ventilator disconnections. Care should be taken to minimize the addition of mechanical dead space associated with closed suction apparatus. An increase in O_2 concentration after suctioning may be necessary but should

BOX 54.3 Complications and Hazards of Tracheal Suctioning in Infants and Small Children

- Infection
- Lung derecruitment
- Accidental extubation
- Atelectasis
- Blood pressure instability
- Increased intracranial pressure
- Cerebral vasodilation or increased blood volume
- Arterial hypoxemia
- Cerebral hypoxemia
- Hypercapnia
- Bradycardia
- Pneumothorax
- Mucosal damage

be evaluated for each patient. To reduce the risk of tracheal trauma, suction catheters should not be inserted beyond the tip of the endotracheal tube or tracheostomy tube. Routine instillation of normal saline is not recommended. Increasing ventilator support to regain volume lost during the procedure may be necessary but should be assessed each time the patient is suctioned. Because of the risks associated with suctioning, the procedure should be performed only when a clinical indication exists, not on a fixed interval.

Suctioning. Nasopharyngeal and tracheal suctioning helps to minimize aspiration, prevents endotracheal tube occlusion, and reduces airway resistance in infants and children. Suctioning is a hazardous procedure, and complications can occur. Box 54.3 lists the common complications and hazards associated with tracheal suctioning of infants and children. Tracheal suctioning of preterm infants and neonates should be performed only when clinical signs indicate a need.

Oral and pharyngeal suctioning of infants can be done with a bulb syringe. A DeLee trap or a mechanical vacuum source with catheter may be used for nasopharyngeal and nasotracheal suctioning of neonates. Equipment for suctioning larger infants and children is similar to the equipment used with adults, with modifications in vacuum pressure and catheter size. Recommended suction pressures for neonates range from approximately −70 to −100 mm Hg. With large infants and children, pressures in the range of −100 to −120 mm Hg are generally safe and effective. Catheter sizes are chosen according to the age of the patient and the size of the tracheal airway. Other techniques for averting hypoxemia include use of endotracheal tube adapters that allow preoxygenation and suctioning without disconnection of the ventilator and use of closed tracheal suction systems.[35,36]

CONTINUOUS POSITIVE AIRWAY PRESSURE

Spontaneous breathing can be supported with **continuous positive airway pressure (CPAP),** a breathing mode that maintains a constant pressure above baseline throughout inspiration and expiration. Newborn infants have increased chest wall compliance along with decreased lung compliance, which makes them

BOX 54.4 Indications for Continuous Positive Airway Pressure in Children

Respiratory Distress
- Tachypnea
- Retractions or accessory muscle use
- Grunting
- Nasal flaring
- Head bobbing

Abnormal Breathing Patterns
- Apnea of prematurity
- Obstructive sleep apnea

Lung Disease
- Decreased lung volumes on chest radiograph
- Pneumonia
- Tracheomalacia
- Pulmonary edema
- PaO_2 <50 mm Hg with FiO_2 ≥0.60

Other
- Postextubation failure

prone to developing atelectasis. CPAP maintains inspiratory and expiratory pressures above ambient, which improves functional residual capacity (FRC) and static lung compliance.[37] It is essential that the patient is able to maintain adequate minute ventilation while breathing spontaneously because ventilatory support is not provided.

CPAP is indicated when arterial oxygenation is inadequate despite elevated FiO_2. This condition is usually accompanied by certain signs of respiratory distress. CPAP is commonly used when PaO_2 is less than 50 mm Hg while the infant is breathing an FiO_2 of 0.60 or greater, provided that the $PaCO_2$ is 50 mm Hg or less and the pH is greater than 7.25. In most cases, once CPAP is applied and the FRC is restored, the oxygen requirement is significantly reduced. The indications for CPAP are described in Box 54.4.

Methods of Administration

The application of CPAP is most commonly accomplished noninvasively. In preterm and term neonates, short nasal prongs or oronasal masks are preferred. Continued improvement of interface devices has led to more consistent CPAP delivery, better patient comfort, and reduced incidence of pressure ulcers (Fig. 54.7). These interfaces include nasal masks, soft, pliable nasal CPAP cannulas, and the RAM cannula, all of which provide a comfortable interface without applying excessive pressure to maintain an effective seal.

For larger children, nasal masks, oronasal masks, nasal pillows, and other interfaces similar to interfaces used in adults may be used. In all patients, it is important to assess the patient–device interface at regular intervals to allow prevention or early detection and intervention in the event of pressure ulcers.

CPAP may be delivered using a mechanical ventilator in the CPAP mode, a CPAP driver, or continuous flow system with an underwater seal, also referred to as bubble CPAP. Mechanical ventilators provide better patient monitoring and may be connected to a central alarm system. CPAP drivers have the capability of adjusting flow to maintain set CPAP in the presence of a leak and/or increased patient inspiratory demand and typically have some type of built in disconnect alarm. The continuous flow bubble CPAP systems are the simplest and least expensive of all the devices but generally lack the ability to automatically adjust flow and do not have an integrated alarm system in the event of a patient disconnect. All are equally effective as long as the interface is appropriately sized and fitted to the patient. The choice of one device over another is often based on equipment availability or user or institutional bias. Once the delivery device has been selected, gas flow is directed though a heated humidifier into the main flow circuit and patient interface (mask, cannula, or prongs) and the temperature is allowed to stabilize. The interface is then attached to the patient and secured with appropriate head gear, transparent dressing or tape. The patient is observed for tolerance and/or adverse reactions, effectiveness of CPAP is assessed, and pressure and F_IO_2 are adjusted as necessary.

CPAP levels are selected and adjusted based on clinical observation. Initial CPAP levels are usually 5 to 7 cm H_2O and are adjusted in increments of 1 to 2 cm H_2O. The patient's SpO_2, respiratory rate, work of breathing, breath sounds, and blood pressure are monitored. The appropriate CPAP level is achieved when the respiratory rate decreases to near-normal ranges, signs of respiratory distress are lessened, and SpO_2 increases while O_2 requirements are reduced. Arterial and capillary blood gas analysis may provide additional information in determining the effectiveness of CPAP, and chest radiographs are obtained to determine the degree of lung inflation.

Weaning and eventually discontinuing CPAP are considered when oxygenation is adequate at FiO_2 less than 0.30 to 0.40, there is a sustained reduction in work of breathing, and chest radiograph and clinical assessment indicate resolution of the underlying disorder. The use of CPAP for prolonged periods in preterm infants helps to reduce the work of breathing and prevent intubation. Long-term and intermittent use of CPAP is indicated in children with obstructive airway problems, chronic lung disease, and neuromuscular disorders.

High-Flow Nasal Cannula

Supplemental O_2 administration by nasal cannula is the most comfortable and simplest means of providing O_2 for infants and children. Evidence in preterm and term neonates indicates that using a nasal cannula at flow rates of 2 to 8 L/min may be as effective as and is easier to apply than a nasal CPAP system.[38–44]

Specially designed humidification systems have been developed and allow the use of nasal cannulas at flow rates of 2 to 50 L/min.[45] These devices maximize humidification and minimize condensation accumulating in the small-diameter supply tubing. The gas should always be conditioned (warmed and humidified) for approximately 2 to 3 minutes before it is connected to the patient. High-flow nasal cannula systems have been used successfully in neonates for the same indications that CPAP has been used. Instead of titrating levels of CPAP, the flow rate is incrementally adjusted. The amount of positive pressure that the high-flow nasal cannula potentially produces cannot be

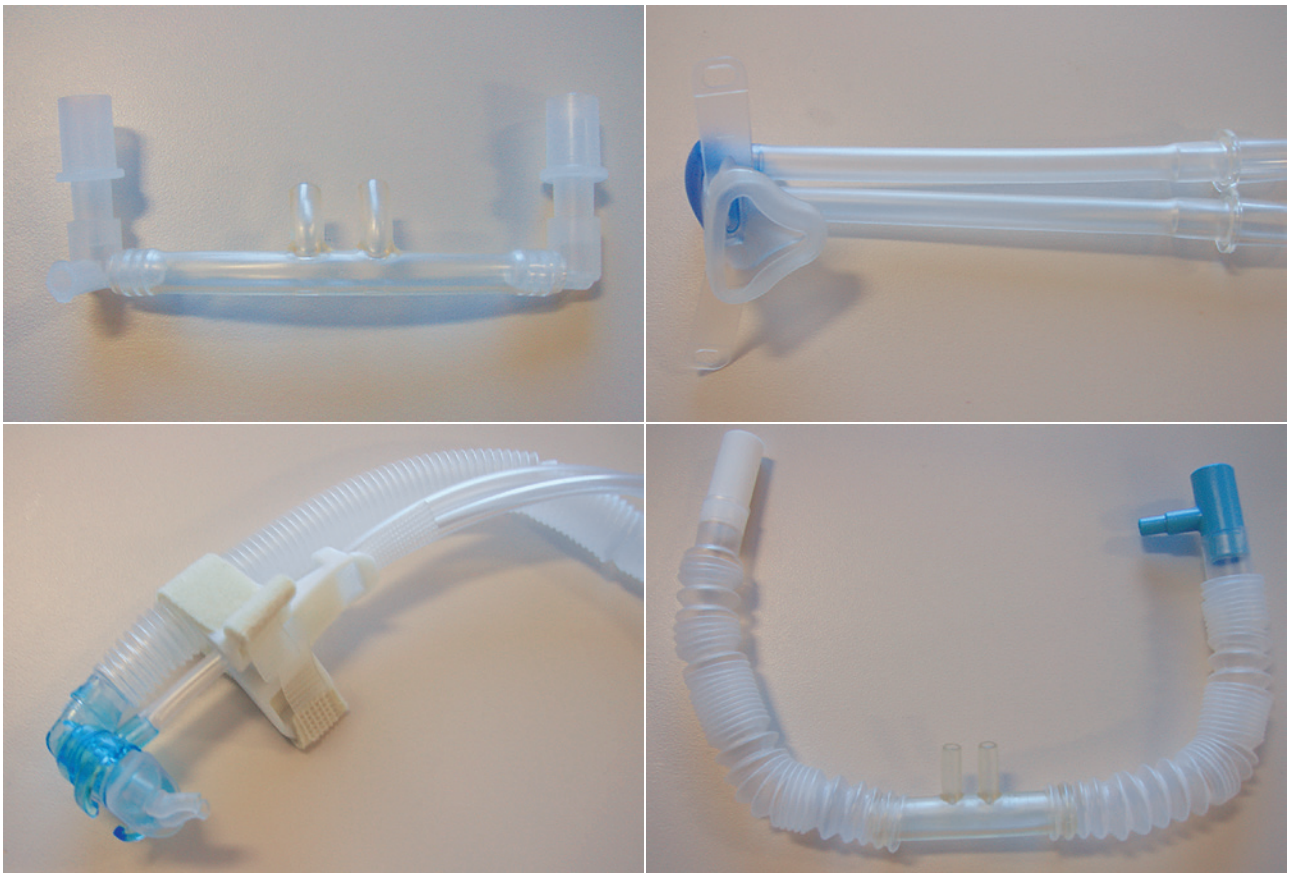

Fig. 54.7 Patient interfaces for continuous positive airway pressure or noninvasive positive pressure ventilation (NPPV).

measured, and there may be some concern that inadvertent high levels may occur, particularly if the nasal cannula fits snugly in the nares.[46,47] However, in most cases excess flow exits the patients mouth, preventing this excess pressure from being generated.

High-flow nasal cannula systems have the potential for maximizing supplemental O_2 administration because the O_2 concentration delivered to the patient should approximate the set FiO_2. This approximation occurs because the set flow meets or exceeds the patient's inspiratory demand and the anatomic reservoir of the upper airway is continuously flushed, greatly reducing the entrainment of room air. High-flow nasal cannula systems may be beneficial in stabilizing acute respiratory failure caused by hypoxemia, which may reduce the need for noninvasive or invasive assisted ventilation, such as in the case of a pulmonary exacerbation in a patient with bronchiolitis, cystic fibrosis, or congestive heart failure.

RULE OF THUMB High-flow nasal cannulas may be as effective as a continuous positive airway pressure (CPAP) device in reducing the work of breathing and improving oxygenation.

Noninvasive Ventilation

Noninvasive ventilation (NIV), also known as *noninvasive positive pressure ventilation,* has become more popular recently in neonatal patients. In the past, use of NIV was limited by the lack of available interfaces; however, these are becoming more readily available. NIV for neonates has been used successfully for premature infants in the delivery room and as an accepted mode of ventilation in the neonatal intensive care unit (NICU), where it has been used to prevent initial intubation or secondarily to prevent reintubation in the setting of extubation failure. NIV has also been used as

MINI CLINI

Pediatric High-Flow Nasal Cannula

Problem

A 10-month-old boy with a past medical history of increased temperature, runny nose, cough, and irritability is admitted to the emergency department with tachypnea, tachycardia, and use of accessory muscles. He is receiving oxygen via a non-rebreathing mask and his SpO_2 is 88%, respiratory rate 72 breaths/min, and heart rate is 140 beats/min. A clinical diagnosis of viral bronchiolitis is established.

Solution

The patient should be placed on a high-flow nasal cannula at 8 L/min and FiO_2 of 1.0. After 20 minutes his respiratory rate has decreased to 44 breaths/min, heat rate is 100 beats/min, and SpO_2 is 100%. The respiratory therapist is now able to slowly decrease the FiO_2 to 0.3, while maintaining the flow rate at 8 L/min. At this FiO_2, the respiratory therapist may attempt to decrease the flow rate. If the patient exhibits signs of increased work of breathing and/or increased oxygen requirement the flow rate should be restored to the previous setting.

a primary mode of ventilation for patients with acute respiratory failure.[48–50] However, there is scant evidence to support the use of NIV over CPAP or as a method of reducing the incidence of bronchopulmonary dysplasia. Patient triggering may be problematic given the large leaks that may occur with most patient interfaces, even with some current ventilators' "Noninvasive Modes," which generally include various forms of sophisticated leak compensation. However, there is ample evidence to support the use of both synchronized and nonsynchronized NIV in the NICU.[51,52]

Outside the NICU, NIV has been used extensively in patients of all ages, including pediatric patients.[53–56] Indications may include short-term support of hypoxemic respiratory failure, such as that seen with pulmonary edema associated with left-sided heart failure; prevention of intubation; postextubation support; and long-term support of patients with neuromuscular disease. Some limitation of available interfaces persists, particularly in smaller patients; however, most patients can be fitted without too much difficulty. As with CPAP and other noninvasive interface devices, care must be taken to prevent or minimize patient injury owing to iatrogenic pressure ulcers from a tight or poorly fitted device.

NIV may be provided with simple, single-limb devices such as bilevel positive airway pressure ventilators, or sophisticated intensive care unit (ICU) ventilators. Care must be taken whenever a single-limb circuit is used to provide sufficient positive end-expiratory pressure (PEEP) in the system to prevent rebreathing of gases (see Chapter 50).

MECHANICAL VENTILATION

Early attempts to provide assisted ventilation to infants and children were largely derived from the experiences gained in adults, including the type of ventilators used and the associated techniques. Recognition of the physiologic differences of neonates and children led to further advances in ventilator design and modes and a wider range of capabilities. Modern microprocessor controlled, critical care ventilators offer an ever-evolving array of options capable of supporting the full range of patient sizes, including ELBW infants, and physiologic conditions.[57] RTs caring for infants and children need to be familiar with their physiologic differences to select and modify the appropriate ventilatory strategy.[58–60]

Basic Principles

Conventional mechanical ventilation is the delivery of a bulk flow of humidified gas into and out of the lungs. The removal of CO_2, typically measured by PCO_2, is directly related to alveolar ventilation (frequency × V_T). Gas moves from the ventilator across an artificial airway or noninvasive interface in response to a change in pressure (pressure gradient). The magnitude of pressure required to move a volume of gas is derived from the compliance of the pulmonary system and the resistance of the airways.

Compliance is a measure of the distensibility of the lungs and is expressed as the volume change per unit of pressure change ($C = \Delta V/\Delta P$). *Resistance* is the tendency for airflow across the tracheobronchial tree to be impeded at a particular pressure per unit of gas flow ($R = \Delta P/\text{flow}$). The product of compliance and resistance is the respiratory time constant, or the measure of time necessary for the equilibration of a change in airway pressure ($TC = C \times R$). A patient with stiff or noncompliant lungs, such as a preterm infant with surfactant deficiency, has short time constants, meaning less time is required for equilibration, and filling and emptying of lungs occur faster, requiring shorter inspiratory and expiratory times. A patient with a disease characterized by impaired airflow or high resistance, such as a child with asthma, has longer time constants, in which more time is required for filling and emptying, thus longer inspiratory and expiratory times are needed.

Goals of Mechanical Ventilation

The basic goals of mechanical ventilation are to improve O_2 delivery to meet metabolic demand and eliminate CO_2, while reducing the work of breathing. The basic aim of assisted ventilation is to meet the goals while minimizing the associated deleterious effects. One approach to mechanical ventilation begins with the selection of an appropriate breath type, either pressure controlled or volume controlled, and a mode that best meets the physiologic needs of the patient's condition.[61] Box 54.5 lists the indications for mechanical ventilation in infants and children.

Modes of Ventilation and Breath Delivery Types

Historically, the most common mode of ventilation used in neonates and children was intermittent mandatory ventilation (IMV). Because early infant ventilators were unable to respond

BOX 54.5 Indications for Mechanical Ventilation

Apnea

Respiratory Failure

- $PaO_2 < 50$ mm Hg
- $PaCO_2 > 65$ mm Hg

Pulmonary Disease

- Respiratory distress syndrome
- PPHN
- Meconium aspiration syndrome
- Pneumonia
- ARDS

Neurologic and Neuromuscular

- Asphyxia
- Head trauma
- Spinal muscle atrophy
- Muscular dystrophy

Congenital Abnormalities

- Congenital diaphragmatic hernia
- Congenital heart disease

Postsurgery

- Thoracic surgery

ARDS, Acute respiratory distress syndrome; *PPHN*, primary pulmonary hypertension of the newborn.

to the small triggering efforts of these patients, mandatory timed breaths were superimposed over a continuous flow of gas. These asynchronous, mandatory breaths provided most of the ventilation, while the patient was allowed to breathe spontaneously from the continuous gas source. Eventually, technologic improvements resulted in triggering devices that provided synchronization of the mandatory breaths with patient effort synchronized intermittent mandatory ventilation (SIMV) followed by the ability to provide assist/control (A/C) and pressure support ventilation (PSV). Despite evidence that SIMV is more likely to result in patient-ventilator asynchrony, most neonatal and pediatric patients are managed by using one of these three modes or a combination (i.e., SIMV + PSV).[62–64] The most common triggering device for infant ventilators is a pneumotachygraph placed in the ventilator circuit, often proximal to the airway, which in many cases also serves as a monitoring device. The pneumotachygraph allows for the integration of a flow signal, which can be displayed as inhaled and exhaled V_T and minute ventilation. Fig. 54.8 displays graphic representations of A/C, SIMV, and PSV.

Another mode of ventilation that may be used for neonates and small children is called *neurologically adjusted ventilatory assist* (NAVA) in which the ventilator responds to electrical activity of the diaphragm (EAdi). This requires use of a special nasogastric tube with electrodes that sense EAdi. In this highly responsive mode, patient ventilator asynchronies are virtually eliminated, because ventilation is provided by adjusting the amount of airway pressure applied per 1 microvolt change in EAdi.

Proper placement of the NAVA catheter is essential for patient ventilator synchrony. Initial depth of insertion is estimated using the distance from the nose, to the ear, to the xyphoid. Further adjustment is determined from electrical activity using the ventilator's "Positioning Window." The ventilator displays an electrocardiogram (ECG) type graphic, and the catheter is manipulated to a position where there are no P waves and the ventilator tracing indicates good (green) positioning. The electrical activity from the phrenic nerve (EAdi) signals the ventilator to deliver gas to the patient at a pressure gradient determined by the NAVA level. Settings range from 0 to 15 cm $H_2O/\mu V$ with a trigger range up of 0 to 2 μV. The greater the patient's inspiratory demand, as determined by increased EAdi, the greater the level of support provided and vice versa. In the event of catheter movement or misplacement, ventilation is provided with traditional flow or pressure-triggered pressure support or pressure-controlled breaths.

In almost all cases of neonatal ventilation, the mechanical breaths delivered during SIMV and A/C are time-cycled, pressure-limited breaths. Inspiration is initiated by patient effort or timing of the set respiratory rate (whichever comes first). Based on the available flow, continuous, demand, or both, the set inspiratory pressure is reached early in the inspiratory phase and maintained throughout the remainder of the inspiratory time, after which the ventilator cycles to expiration. In many cases, appropriate setting of the *inspiratory rise time* (the speed in which gas flow is delivered controlling how rapidly set airway pressure is achieved)

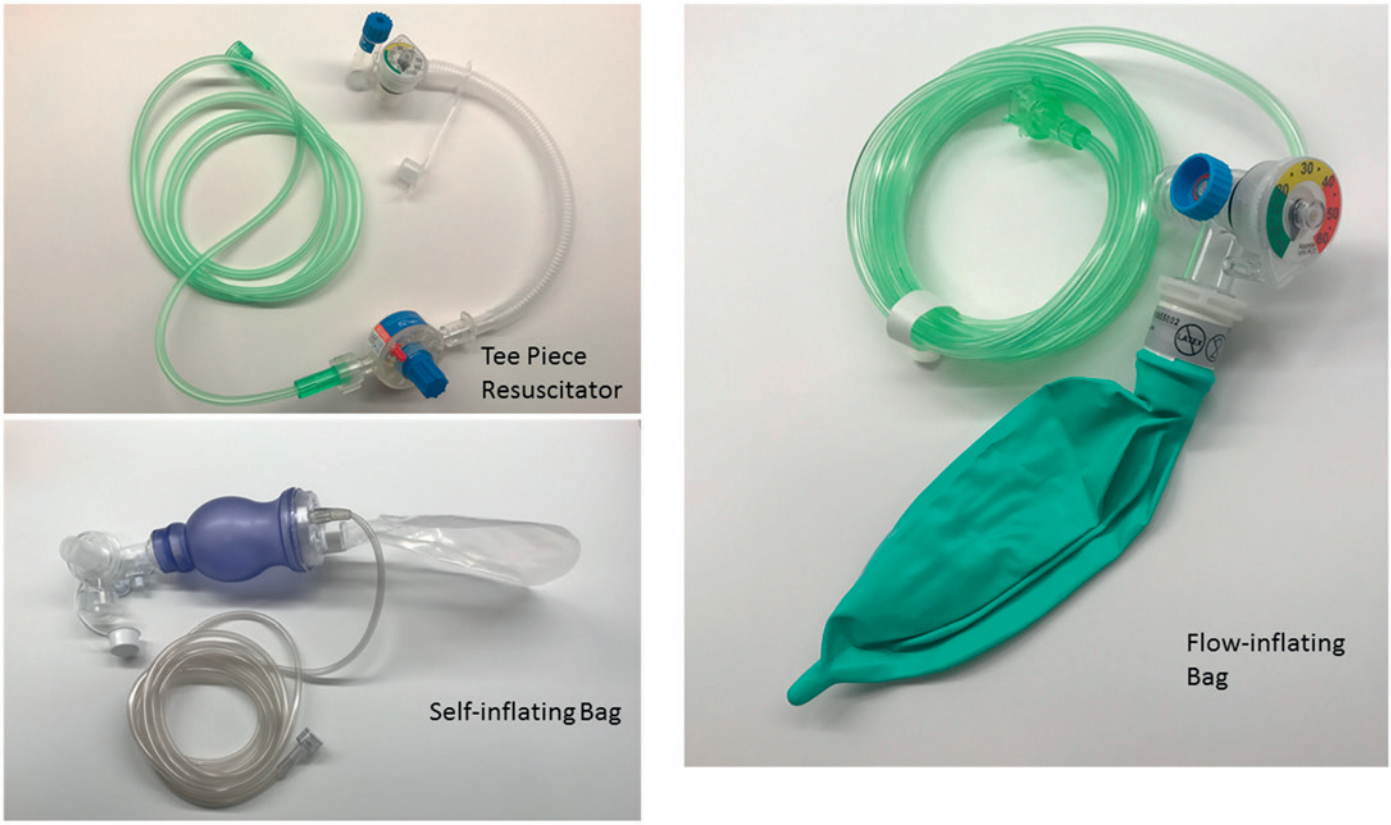

Fig. 54.8 Three types of manual (bag-mask) ventilation devices.

improves patient–ventilator synchrony. Most current-generation ventilators provide volume-targeted, pressure-limited ventilation, often referred to as *pressure-regulated volume control*, *volume guarantee, or volume control plus*. In this dual mode of ventilation, the inspiratory V_T is compared with a preset target V_T, and the inspiratory pressure on the next breath is adjusted up or down to meet the target volume. True volume-controlled breaths are rarely used for ventilating neonatal patients. (See Chapters 46, 47, and 49 for details.)

RULE OF THUMB When ventilating neonates, choose time-cycled, pressure-limited mechanical breaths.

Bag-Mask Ventilation

In all cases the ability to provide manual ventilation must be immediately available. Several manual ventilation devices exist, including traditional self-inflating bags, flow inflating bags, and T-piece resuscitators. Pediatric and infant self-inflating bags are similar to those used for adults, but contain a pressure relief (pop off) valve to prevent the application of excessive pressure. The primary advantage of these devices is the ability to provide ventilation without a gas source; the main disadvantage is the inability to allow spontaneous breathing/CPAP. A pressure manometer may be added to help regulate applied pressure. Flow inflating bags and T-piece resuscitators both require a gas source to provide ventilation. Loss of flow to the device renders it unusable. These devices allow spontaneous breathing and CPAP and include a pressure manometer to help monitor and regulate the amount of inspiratory pressure and PEEP/CPAP. The choice between the two is mostly user preference; however, the T-piece resuscitator allows better control over inspiratory and expiratory pressures and inspiratory time.[65] Fig. 54.8 shows examples of these three devices.

Pediatric patients may be ventilated with either volume-controlled or pressure-controlled breaths. The choice may be based on healthcare team or institutional preference, prior experience, and equipment availability or may be evidence-based for specific diseases (e.g., asthma).

Patients with severe status asthmaticus are among the most challenging patients to ventilate. The pulmonary time constants are increased such that it is equally difficult to inflate the lungs as it is for the patient to exhale. The inspiratory flow rate must be controlled by the clinician by means of volume-controlled ventilation, and sufficient time must be provided to allow the lungs to inflate. Expiratory time must be sufficient to allow exhalation, preventing the accumulation of trapped gas or auto-PEEP. The result is a decrease in minute ventilation, which leads to permissive hypercapnia as a lung protective strategy. $PaCO_2$ should be allowed to increase as long as the pH is ≥7.10.

The inspiratory time must be increased (up to 1 second for this patient and longer in older teenagers) to allow inspiratory gas flow to the patient. Although this increase in inspiratory time may seem counterintuitive in a patient with prolonged expiratory time constants, it is necessary to deliver gas during inspiration because the inspiratory time constant is also increased. Decreasing the inspiratory time to less than 1 second does little to prevent the development of auto-PEEP and frequently markedly decreases the level of ventilation.

In the presence of an elevated $PaCO_2$ and decreased pH, a higher FiO_2 is required to maintain SpO_2 greater than 90% owing to shifting of the oxyhemoglobin dissociation curve. FiO_2 should be set initially at 1.0 and titrated to maintain SpO_2 89% to 95%.

MINI CLINI

Pediatric Ventilation

Problem

A 12-year-old girl with asthma is admitted to the emergency department. She was intubated in the field by paramedics and is currently ventilated with a transport ventilator at the following settings:

- Mode—synchronized intermittent mandatory ventilation (SIMV)
- Tidal volume (V_T)—10 mL/kg
- Peak inspiratory pressure (PIP)—60 cm H_2O Maybe 60 to be more realistic?
- Positive end-expiratory pressure (PEEP)—0 cm H_2O
- Set respiratory rate—16 breaths/min
- Total respiratory rate—20 breaths/min
- Inspiratory time—0.25 s
- FiO_2—1.0

The paramedics inform the respiratory therapist (RT) that since the patient has been placed on the mechanical ventilator, PIP has steadily increased, blood pressure has begun to decrease, and breaths sounds consisting of bilateral inspiratory and expiratory wheezes have become increasingly diminished. What should the RT recommend?

Solution

The ventilator circuit should be immediately disconnected from the endotracheal tube allowing the patient to exhale fully. This patient should be fully sedated and possibly paralyzed to allow the RT to set and control ventilation. The ventilator settings should be set as follows:

- Mode—assist/control (A/C)
- Breath delivery type—volume controlled
- V_T—4–6 mL/kg
- Plateau pressure—maintain at ≤28 cm H_2O
- Driving pressure <15 cm H_2O
- Respiratory rate—set at whatever rate allows ventilation without an increase in auto-PEEP or increased plateau pressure or both
- Inspiratory time—1.0 s
- PEEP—5 cm H_2O
- FiO_2—1.0

Ventilator Settings and Parameters

After the mode of ventilation is selected, the RT begins to adjust the various settings associated with the mode, while keeping in mind the goals of ventilation and the patient's predicted body weight, underlying problem, and reason for mechanical ventilation.

Peak Inspiratory Pressure

For time-cycled, pressure-limited breaths, the peak inspiratory pressure (PIP) is set according to predetermined criteria (e.g., 20 to 25 cm H_2O) or by observing the pressure required to move the chest during manual ventilation with a flow inflating bag or

BOX 54.6 Interrelationship of Tidal Volume (V_T), Flow, and Time

V_T = Flow in L/s × Inspiratory time

Inspiratory time = V_T / Flow rate

T-piece resuscitator. In all cases the RT should attempt to maintain a driving pressure less than 15 cm H_2O. The delivered V_T is monitored, and adjustments may be made. Increasing the PIP normally results in an increase in V_T, whereas a decrease in PIP results in decreased V_T. In the absence of V_T monitoring, PIP may be adjusted based on subjective assessment of chest movement and auscultation of breath sounds. Efforts should be made to maintain the lowest possible pressure that delivers the target V_T. PIP greater than 28 cm H_2O and driving pressure greater than or equal to 15 cm H_2O in time-cycled, pressure-limited (pressure-controlled) breaths have been shown to increase the likelihood of ventilator-induced lung injury.

RULE OF THUMB Always strive to maintain peak inspiratory pressure (PIP) ≤28 cm H_2O and driving pressure <15 cm H_2O

Positive End-Expiratory Pressure

PEEP, referred to as the *baseline pressure,* is used to prevent alveolar collapse at end-expiration. PEEP results in improved oxygenation for a given O_2 concentration. If the PEEP is set too low, alveolar collapse may occur, resulting in decreased FRC, altered ventilation/perfusion ($\dot{V}/\dot{Q}$ matching), and hypoxemia. If the PEEP is set too high, overdistension may occur, increasing the likelihood of lung injury. Typically, PEEP is set between 5 cm H_2O and 10 cm H_2O, although higher levels may be used if necessary. PEEP is set in conjunction with PIP, and the difference between the two is often referred to as the delta P *or driving pressure*. As the delta P is increased, either by increasing PIP or decreasing PEEP, the V_T will most likely increase as well (unless overdistension occurs). Conversely, decreasing the delta P results in lower V_T.

Tidal Volume

When selecting V_T, the clinician must consider a volume that provides adequate lung inflation without overstretching the alveoli. Setting V_T too high most likely would result in lung injury. V_T of 6 to 8 mL/kg is generally considered safe in most patients. However, in some patients with extremely low lung compliance, such as patients with severe acute respiratory distress syndrome (ARDS), it may be necessary to reduce V_T to 4 to 5 mL/kg.

If the clinician chooses to deliver volume-controlled breaths, V_T is set as a control variable. Every mechanical breath delivers an identical V_T at either a preset inspiratory time or a preset flow rate. Set V_T, inspiratory time, and flow all are interrelated. If V_T is set at 300 mL and flow rate is 30 L/min (0.5 L/s), the inspiratory time is 0.6 second. See formulas in Box 54.6.

When ventilating patients with pressure-controlled breaths, V_T is not set, but it should be monitored. The clinician must compare the monitored V_T with a predetermined target and adjust the driving pressure to meet that target.

BOX 54.7 Determining Effective or Corrected Tidal Volume

Effective V_T = Delivered V_T − Compressible volume

Compressible volume = Compressible factor × (PIP-PEEP)

Example: A 12-year-old child weighing 28 kg requires assisted ventilation. Tidal volume (V_T) is set at 240 mL, peak inspiratory pressure (PIP) is 25 cm H_2O, and positive end-expiratory pressure (PEEP) is 5 cm H_2O. The compressible factor for the ventilator is 2 mL/cm H_2O.

Compressible volume = (2 ml/cm H_2O) × (25 − 5 cm H_2O) = 40 ml

Effective V_T = 240 ml − 40 ml = 200 ml

Effective V_T/kg = 200 ml ÷ 28 kg = 7.1 ml/kg

Regardless of whether the clinician chooses volume-controlled or pressure-controlled breaths, he or she must recognize that some of the V_T is compressed in the circuit and not delivered to the patient; this is referred to as *compressible volume loss*. Most current-generation ventilators automatically compensate for compressible volume loss and adjust the delivered and displayed (monitored) V_T accordingly. With older ventilators and current, less sophisticated ventilators, such as some of those used for transport, during volume-controlled breaths the clinician must calculate the compressible volume loss and increase the set V_T to deliver the desired volume to the patient. During both volume-controlled and pressure-controlled breaths, the calculated compressible volume loss must be subtracted from the ventilator displayed exhaled V_T. See Box 54.7 for calculation of compressible volume loss.

RULE OF THUMB Large tidal volume (V_T; >8 mL/kg) is likely to overstretch the lung, resulting in acute lung injury, and should be avoided. Patients with severe acute respiratory distress syndrome (ARDS) may require even lower V_T (4–5 mL/kg). In addition, peak inspiratory pressure (PIP) and/or plateau pressure should be maintained <28 cm H_2O and driving pressure ≤15 cm H_2O.

Although this patient receives NIV for nocturnal support when stable, he currently has an acute infection superimposed on chronic restrictive lung disease. Beginning NIV now may provide sufficient support to prevent intubation during this acute condition. Initial PIP of 10 to 12 cm H_2O titrated to patient comfort may provide additional support, increasing tidal volume (V_T) and allowing respiratory rate to return to baseline. Choosing an oronasal mask may prove to be a more efficient interface than the patient's usual nasal mask at this time. The set respiratory rate of 12 breaths/min is intended to be a backup rate because this patient is spontaneously breathing and should be allowed to establish his own breathing pattern. FiO_2 should be adjusted to maintain an SpO_2 of 89% to 95%.

Ventilator Rate

The ventilator rate is the set number of breaths delivered in 1 minute. During A/C ventilation, the set respiratory rate is the

MINI CLINI

Pediatric Ventilation

Problem

A 10-year-old boy with a complex medical history including trisomy 21, intractable infantile spasms, seizure disorder, and developmental delay (nonverbal) is admitted with increased difficulty breathing. His temperature on admission is 101°F, and a chest x-ray shows a left lower lobe infiltrate consistent with pneumonia. His home regimen includes nocturnal noninvasive ventilation (NIV) via nasal mask with an inspiratory pressure of 8 cm H_2O, 3 cm positive end-expiratory pressure (PEEP), and 2 L/min of O_2 added to the breathing circuit. On admission, the patient complains of shortness of breath. His respiratory rate is 40 breaths/min, and SpO_2 is 88% on a nonrebreathing mask. What should the respiratory therapist (RT) suggest?

Solution

- NIV—consider beginning NIV via oronasal mask
- Peak inspiratory pressure (PIP)—10–12 cm H_2O
- PEEP—3–5 cm H_2O
- Set respiratory rate—12 breaths/min
- FiO_2—1.0

minimum number of breaths the patient will receive and is increased if the patient triggers the ventilator at a respiratory rate faster than that which is set. The actual or total respiratory rate multiplied by V_T determines the minute ventilation, which is directly related to alveolar ventilation and PCO_2. Because V_T is usually set according to the patient's ideal or calculated body weight, adjusting minute ventilation is most often accomplished by changing the respiratory rate. The clinician must be aware of the total respiratory rate when making changes to adjust minute ventilation. If the set respiratory rate is 16 but the total respiratory rate is 22 because of patient triggering, decreasing the set rate to 12 or increasing the set rate to 18 would have no effect on minute ventilation.

Inspiratory Time

The inspiratory time is often defined as the time required to deliver V_T; however, this may be misleading. As described earlier, with volume-controlled breaths, the inspiratory time is determined by V_T and inspiratory flow rate and is the time required to deliver the preset V_T at the preset flow rate. However, with pressure-controlled breaths, the inspiratory time is set by the clinician and may be shorter, longer, or equal to the time required to deliver the breath. In the case of increased airway resistance, such as a patient with asthma, if the inspiratory time is not set long enough, flow delivery to the patient may not decelerate to zero by the end of the set inspiratory time. Under these circumstances, increasing inspiratory time would result in an increase in delivered V_T. Conversely, under the same conditions, shortening the inspiratory time would result in a decrease in delivered V_T. In the case of decreased compliance, as in pneumonia, increasing inspiratory time beyond the time necessary to allow full flow deceleration would result in an inspiratory pause or breath-hold, which may not be tolerated by the patient. Strict attention must be given to setting an inspiratory time that matches the patient's neuroinspiratory time. Failure to do so is likely to result in patient–ventilator asynchrony, making it difficult to adequately ventilate the patient and may require increased use of sedation. Some ventilators are configured such that the clinician sets inspiratory: expiratory (I:E) ratio, which along with respiratory rate will determine the inspiratory time. In such cases, changing the respiratory rate will result in a change in inspiratory time. The clinician must be aware of this and make the necessary adjustment to the I:E to restore the inspiratory time to its previous setting.

RULE OF THUMB Inspiratory time is usually set between 0.2 and 0.4 s for neonates and up to 1.0 s in teenagers. With patients who are awake and have spontaneous breathing efforts, inspiratory time must be set at a level that matches patient neuroinspiratory time to avoid patient–ventilator asynchrony.

Oxygen Concentration

The O_2 concentration or FiO_2 is kept as low as possible to avoid the risk of O_2 toxicity. Although the precise mechanisms are not fully understood, the best approach is to maintain the lowest FiO_2 possible. The immature lung is particularly susceptible to O_2 toxicity, which can result in the development of bronchopulmonary dysplasia. In a preterm infant, FiO_2 is titrated to a narrow SpO_2 range (e.g., 89% to 94%) so that retinal damage (ROP), which is caused by elevated PO_2, does not develop.[17]

RULE OF THUMB O_2 is considered a drug and should be used appropriately. High O_2 concentrations are potentially injurious and may cause O_2 toxicity in the immature lung and retinal damage in preterm infants.

Mean Airway Pressure

Mean airway pressure ($\overline{P}_{aw}$) is the average airway pressure during a 1-minute period. It is affected by changes in PIP, PEEP, inspiratory time, and respiratory rate. An increase in $\overline{P}_{aw}$ is often associated with improved oxygenation but is not without hazards. Increasing PEEP would result in increased $\overline{P}_{aw}$ and potentially increased oxygenation. However, if the PEEP is set too high, the alveoli may become overinflated, resulting in worsening $\dot{V}/\dot{Q}$ matching, and lung injury may occur.

Monitoring Mechanical Ventilation

The RT should develop a systematic approach to monitoring the effects of mechanical ventilation. Components of a ventilator assessment should include an evaluation of the artificial airway, physical examination, assessment of patient–ventilator interaction, analysis of laboratory and radiographic data, adjunct ventilator monitoring, and a systematic ventilator safety assessment including alarm function and assessment of humidification. Alarms should be connected to a central monitoring system to alert clinicians away from the bedside to a change in the patient's condition.

A flow sheet is used to prompt the user and guide the clinician through the process of assessing the patient, while serving as documentation of the ventilator settings and outputs. In the past, these flow sheets were paper and were maintained as part of the patient's medical record. Currently, most flow sheets are integrated into an electronic medical record that is readily available

MINI CLINI

Pediatric Mechanical Ventilation

Problem

A 14-month-old child, who weighs 13 kg and has a history of chronic lung disease (bronchopulmonary dysplasia), requires mechanical ventilation after surgery for correction of gastric reflux. The surgeon requests that the respiratory therapist (RT) select ventilator parameters and develop a weaning plan for this child. The child has an uncuffed 4.5 oral endotracheal tube in place. SpO_2 is 100% with manual ventilation and 100% O_2. Sedation is prescribed to keep the child comfortable but allow spontaneous breathing.

Solution

This child needs a ventilatory strategy taking into account his age, disease process, amount of sedation, and current ventilation needs. What would be the appropriate choices for his initial ventilator management in terms of mode, tidal volume (V_T), set rate, FiO_2, and positive end-expiratory pressure (PEEP) level?

- Mode—Pressure assist/control (A/C)
- Pressure level set to ensure V_T 6–8 mL/kg or 100–130 mL
- Respiratory rate—20–30 breaths/min
- FiO_2—1.0 then titrated to a SpO_2 between 89% and 95%
- PEEP—5 cm H_2O

to the entire patient care team. Although many elements of the patient–ventilator assessment may be automatically entered by means of an electronic interface and require validation only by the clinician, some data must still be entered by hand. As standardization improves and these systems become more sophisticated and interchangeable, all data, including ventilator information, laboratory values, and radiographic and other imaging data, should automatically download, eliminating transcription errors, providing a more comprehensive assessment, and allowing the clinician to focus on the patient and patient–ventilator interaction.

If this child had previously been mechanically ventilated, reviewing the preoperative settings may be helpful in deciding a ventilator plan. If not, a rationale for the suggested parameters follows.

By using the pressure A/C mode, patient–ventilator synchrony can be achieved more easily; this reduces the need for sedation later, after the pain of surgery has dissipated. The target V_T is based on current recommendations. The ventilator rate is determined by the normal respiratory rate for the age of the child, the desired PCO_2 level, and the number of assisted or triggered breaths the child is having. Because this child has chronic lung disease, a higher PCO_2 may be optimal at this time. A younger child with a higher PCO_2 and with a decreased respiratory rate may have a higher set rate. Initial FiO_2 is usually reflective of the amount currently being delivered with hand ventilation but quickly titrated to maintain a SpO_2 89% to 95%. In addition, plateau pressure should not be greater than 28 cm H_2O, and the driving pressure should not be higher than 15 cm H_2O.

Physical Examination

Examination of the patient can yield quick and useful information. The chest is examined for adequacy of chest rise, the presence of asymmetric movement and deformities, and signs of increased work of breathing such as nasal flaring, grunting, and retractions. Breath sounds are helpful in gauging the degree of air entry, verifying bilateral aeration, and identifying airflow problems and areas of diminished aeration. Skin appearance can also give the clinician a sense of the patient's perfusion—an indirect measure of cardiac output. A mottled appearance, poor capillary refill, and pale or gray color indicate poor perfusion.

Patient–Ventilator Interaction

The patient–ventilator interaction is the assessment used to determine the ease with which the patient can trigger and interact with the ventilator throughout the complete ventilatory cycle. This assessment is made by simultaneously observing the trigger indicator, waveforms, and the patient. Refinements in the trigger threshold may need to be made if there is a leak present or the work to trigger or initiate a breath is too great. Most ventilators may be flow triggered or pressure triggered. There is little difference between the two when they are set correctly. The trigger sensitivity should be set as sensitive as possible without auto-triggering. The manner in which the breath is terminated is also assessed. Pressure-supported breaths are flow cycled based on the patient's spontaneous inspiratory time and flow demand. Mechanical breaths are time cycled. Theoretically, flow-cycled, pressure-supported breaths should be more comfortable and promote improved patient–ventilator synchrony because the patient has more control over the breath than with mechanical breaths. Together, patient synchrony and comfort are determined. Patient–ventilator asynchrony occurs when the patient's efforts to breathe are unmatched with the preselected ventilator support. Airway graphics are also helpful in identifying nuances and refining ventilator settings.[66,67] Airway graphics routinely displayed are scalar waveforms of flow, airway pressure, and volume. In addition, each of these parameters can be plotted against the others. Pressure-volume and flow-volume loops can be particularly helpful in assessing alterations in work of breathing, overdistention of the lung, and compliance. Fig. 54.9 shows sample waveforms that are available on most current generation ventilators. See Chapter 48 for more detail on patient–ventilator interaction.

Additional Monitoring

The use of noninvasive monitors, particularly measurements of end-tidal CO_2 and SpO_2, has become routine. Periodic blood gas analysis is a useful tool to quantify acid–base status and to refine ventilator settings further. Other laboratory data, such as electrolytes and hematologic information, are also assessed. Periodic chest radiographs are obtained to identify suspected problems and to assess the progress of lung disease.

Patient–Ventilator Periodic Assessment

A systematic patient–ventilator assessment should be conducted periodically. Prescribed ventilator settings are confirmed and documented along with verification of ventilator outputs. Measurements of mandatory and spontaneous V_T values are made and expressed per the patient's weight to determine if targets are being achieved. Alarms must be set and tested and should detect loss of pressure, high pressure, and patient disconnection at a minimum. Additional alarms should alert

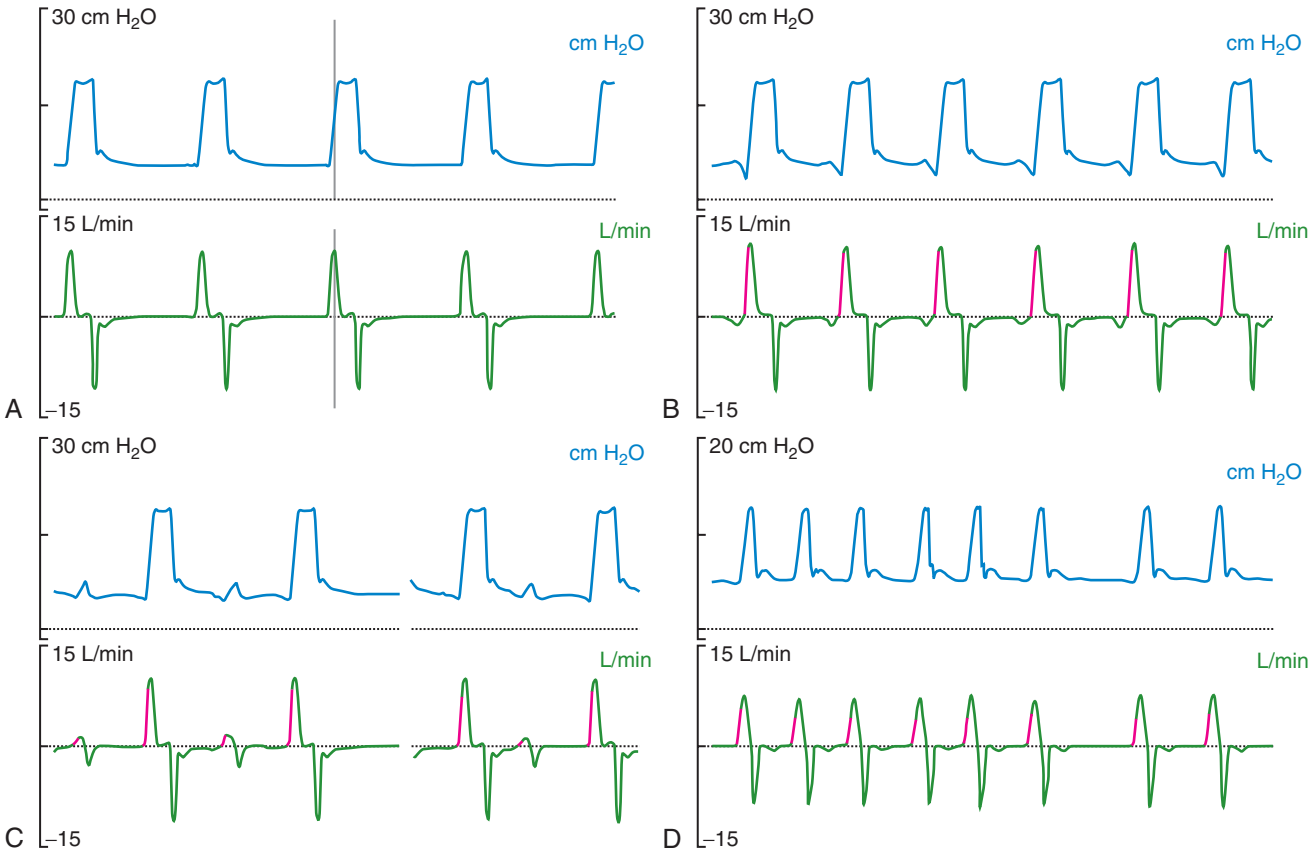

Fig. 54.9 Airway graphics. (A) Patient is apneic. Regardless of synchronized intermittent mandatory ventilation (SIMV) or assist/control (A/C) mode, all breaths are mandatory at set rate. (B) A/C mode. Total respiratory rate is determined by patient's spontaneous rate. (C) SIMV mode. Mechanical breaths are delivered at a set rate. Patient is allowed to breathe spontaneously in between mandatory breaths. (D) Pressure support ventilation mode. There are no set mandatory breaths. All breaths are pressure supported at patient's spontaneous rate.

the clinician to changes in V_T, minute ventilation, respiratory rate, and PEEP.

The humidification system is evaluated, including airway temperature and the presence of condensation in the ventilator circuit. Some visible condensation or "rain-out" is important because a completely dry circuit may be a sign of inadequate humidification, which results in thickened secretions and possible airway obstruction.

RULE OF THUMB Routine monitoring of ventilated patients is essential and should include an assessment of the patient's physiologic status, including vital signs and a systematic assessment of the patient–ventilator interaction.

Weaning From Mechanical Ventilation

Weaning or, more appropriately, liberation from mechanical ventilation is a topic that has become more standardized over the past several years in pediatric patients.[68–70] Clear guidelines for "assessment of readiness to extubate" and "spontaneous breathing trials" have become standard practice.[71] However, some controversy remains and this assessment has not yet become standard practice in neonatal patients even though there is considerable literature available to guide clinicians in this area.[72–74]

BOX 54.8 Considerations for Extubation

- Spontaneous respiratory rate appropriate for age and weight
- Absence of apnea or periodic breathing
- FiO_2 requirement ≤0.4
- Ability to protect airway
- Normal work of breathing
- Acceptable amount and consistency of respiratory secretions
- Normal vital signs
- Minimal sedation needs
- SpO_2 >90%
- Spontaneous tidal volume (V_T) >4–5 mL/kg

Considerable variation in practice exists among institutions and even among clinicians within institutions. Nevertheless, these patients should be assessed daily to determine their readiness for liberation from mechanical ventilation. Some general considerations for extubation are presented in Box 54.8. Once it is agreed that a patient may be ready for extubation, a systematic coordinated approach should be undertaken. This includes a safety screen followed by some agreed-upon evaluation of the patient's ability to breathe spontaneously without ventilatory assistance Box 54.9. If a spontaneous breathing trial is attempted, it should

BOX 54.9 Pediatric/Neonatal Ventilator Discontinuance Protocol

Step 1

Safety Screen (Lack of the Following)

- Brain death, ICP >15 mm Hg, suspected high ICP, or difficult to control ICP
- Neuromuscular blockade
- Significant hemoptysis (significant amounts of blood from endotracheal tube or tracheostomy)
- Hemodynamic instability
- Unstable airway
- FiO_2 >0.6
- PEEP ≥8 cm H_2O
- Lack of ICU team consensus
- Extracorporeal life support
- Chronic disease requiring ventilation

Issues to Address Before Extubation

- Fluid overload
- Secretions
- Neurologic impairment
- Medication requirement precludes safe extubation
- NPO time insufficient
- Unstable, unsafe, swollen airway
- Imminent procedure
- Psychosocial factors (e.g., unclear code status, assent)
- Imminent return to home hospital

Step 2

If none of the above conditions exist, the pediatric ICU team discusses the feasibility of extubation.

Consider the Following

- Stage of ventilation
  I—initial or acute stage (escalation)
  II—ventilator management stage (plateau)
  III—discontinuance stage (deescalation)
- Immediate extubation (may include reversal of sedation)
- Spontaneous breathing trial (may include some level of pressure support)
- Reduction of ventilator settings

If Spontaneous Breathing Trial Is Performed, Stop Trial at any Point for the Following

- Tachypnea, bradypnea, apnea (age appropriate)
- Excessive use of accessory muscles, nasal flaring present, subjective dyspnea (consider baseline)
- Significant, unresolved change in agitation or anxiety
- Significant tachycardia or bradycardia
- Hemodynamic changes
- Unacceptable decrease in SpO_2

Step 3

Critical care team discusses extubation plan.

ICP, Intracranial pressure; *ICU,* intensive care unit; *NPO,* nothing per mouth; *PEEP;* positive end-expiratory pressure.

be coordinated with a reduction in the level of sedation, often referred to as a *spontaneous awakening trial*. However, in some cases this may not be feasible because a reduction in sedation may result in the patient pulling the endotracheal tube (and intravenous lines, etc.) and unplanned extubation may occur. Whenever a patient is extubated, either planned or unplanned, there should be appropriate supplies, equipment, and personnel immediately available to reintubate if necessary (see Chapter 53 for details on weaning).

High-Frequency Ventilation

High-frequency ventilation (HFV) is a form of invasive mechanical ventilation that uses small V_T values (less than dead space) at rapid frequencies, up to 900 breaths/min (15 Hz). The primary goal of HFV is to provide adequate ventilation and oxygenation while limiting the development of lung injury. HFV has been used as a primary mode of ventilation, as well as a rescue therapy for patients determined to be failing conventional mechanical ventilation. Although early studies showed a beneficial effect on gas exchange compared with conventional ventilation, there has been no demonstrated improvement in outcome compared with current lung protective strategies.[75–80] In fact, studies have shown a trend toward increased mortality in patients treated with HFV.[81–83] Despite the lack of evidence supporting its use, HFV remains a controversial mode of ventilation for pediatric and neonatal patients but should be used only by clinicians expert in its clinical application and knowledgeable about its physiologic effects.

There are three basic types of HFV: high-frequency oscillatory ventilation, high-frequency jet ventilation, and high-frequency percussive ventilation. High-frequency oscillatory ventilation is the most common form of HFV. Oxygenation is achieved by inflating the patient's lungs to a high resting level, or FRC, by establishing a high $\overline{P}_{aw}$, similar to CPAP, at levels typically ranging from 16 to 30 cm H_2O. This "recruitment" improves the $\dot{V}/\dot{Q}$ ratio by opening previously collapsed alveoli. Ventilation is provided by the to-and-fro movement of a large piston in the ventilator circuit that results in high-frequency oscillations in the patient's airways. Gas exchange results from a combination of six mechanisms: bulk flow of gas, longitudinal dispersion, pendelluft, asymmetric velocity profiles, cardiogenic mixing, and molecular diffusion.

Gas exchange during high-frequency jet ventilation is believed to occur via two mechanisms—convection and diffusion. Fresh gas is injected into the endotracheal tube at a high velocity and travels down the midportion of the airways, reducing dead space. Bidirectional flow occurs as gas simultaneously travels up the outer lumen of the airways. Diffusion occurs in the lower airways as cross-sectional area increases and velocity decreases, similar to conventional ventilation.

During high-frequency percussive ventilation, a series of small, rapid breaths accompanied by air trapping are delivered that result in a steady increase in airway pressure, similar to a conventional breath. This is followed by a release phase to allow exhalation. The rapid "percussive" breaths are maintained through the entire breathing cycle, which facilitates gas exchange and simultaneously promotes movement of secretions to larger airways and eventually the trachea where they may be more easily removed.

Cardiovascular Effects

The cardiovascular effects of HFV vary with the strategy used. Using the high lung volume strategy, lung volume is recruited, and $\overline{P}_{aw}$ can be slowly reduced while maintaining alveolar

ventilation. This strategy limits the adverse side effects of PPV on cardiovascular performance and may result in increased systemic blood flow. However, if $\bar{P}_{aw}$ greater than that used during conventional ventilation is required during HFV, cardiovascular compromise may occur. Increases in intravascular volume and use of vasoactive drugs help to support mean arterial blood pressure, cardiac output, and O_2 delivery. Increases in central venous pressure or decreases in mean arterial pressure indicate decreases in systemic blood flow as a result of overdistension of the lung and inappropriately high $\bar{P}_{aw}$ after adequate intravascular volume has been established.

Weaning From High-Frequency Ventilation

When FiO_2 is equal to or less than 0.6, $\bar{P}_{aw}$ is weaned slowly. When $\bar{P}_{aw}$ is less than 15 to 18 cm H_2O, the patient may be trialed off or transitioned to conventional ventilation. Alternatively, the patient may be extubated directly from HFV once the $\bar{P}_{aw}$ and F_IO_2 have been reduced to 8 to 9 cm H_2O and 0.3, respectively.

Complications of Mechanical Ventilation

Box 54.10 summarizes the most common complications associated with mechanical ventilation in newborns and other pediatric patients.

BOX 54.10 Complications of Mechanical Ventilation in Infants and Children

- Ventilator-induced injuries
- Air leak syndromes
- Pneumothorax
- Pneumomediastinum
- Pneumopericardium
- Pneumoperitoneum
- Pulmonary interstitial emphysema
- Subcutaneous emphysema
- Parenchymal lung damage
- Bronchopulmonary dysplasia
- Cardiovascular complications
- Decreased venous return
- Decreased cardiac output
- Increased pulmonary vascular resistance
- Increased intracranial pressure
- Increased incidence of intraventricular hemorrhage
- O_2-induced injuries
- O_2 toxicity
- ROP
- Airway complications
- Accidental extubation
- Atelectasis
- Inadequate humidification
- Endobronchial intubation
- Equipment contamination
- Postintubation stridor
- Endotracheal tube plugging or kinking
- Tracheal lesions
- Infection
- Ventilator-associated pneumonia

ROP, Retinopathy of prematurity.

SPECIALTY GASES

Inhaled Nitric Oxide

Inhaled nitric oxide (INO) is a selective pulmonary vasodilator used to treat newborns who require mechanical ventilation for hypoxemic respiratory failure.[84,85] See Chapter 42 for more discussion of INO. INO improves oxygenation and reduces the need for extracorporeal membrane oxygenation (ECMO). See Chapter 51 for details. The approved indications for INO are listed in Box 54.11. INO also has been studied in preterm infants with the aim to reduce the incidence of chronic lung disease. These clinical investigations showed a modest improvement in pulmonary outcomes, but other problems associated with prematurity, such as intracranial hemorrhage, were unchanged. At the present time, INO is not routinely used in the management of respiratory failure associated with prematurity.

INO is administered in conjunction with mechanical ventilation via a specially designed delivery and monitoring system that provides precision drug dosing and safety features (Fig. 54.10). The recommended inhalation oxide (INO) dose is 20 parts per million (ppm), with an optimal response achieved when lung inflation is maximized.[86,87] When a response has been achieved and sustained, the INO dose is gradually reduced, typically by 50% each step, to a final dose of 1 ppm, at which point the drug is discontinued. During withdrawal of INO, FiO_2 is increased to minimize any recurrence of pulmonary hypertension, referred to as a rebound effect.[88]

During INO therapy, concentrations of nitric oxide and O_2 are continuously monitored. The combined exposure of nitric oxide and O_2 leads to the formation of nitrogen dioxide, which is toxic and is continuously monitored. INO doses typically used are considered to be very low and have a good safety profile. A

BOX 54.11 Indications for Inhaled Nitric Oxide

Term and near-term neonates (>34 weeks' gestation) with PPHN
- Gradient between preductal and postductal SpO_2
- Echocardiographic evidence

Congenital diaphragmatic hernia

Oxygenation index (OI) >25
- $OI = (\bar{P}_{aw} \times FiO_2/PaO_2)$

PPHN, Primary pulmonary hypertension of the newborn.

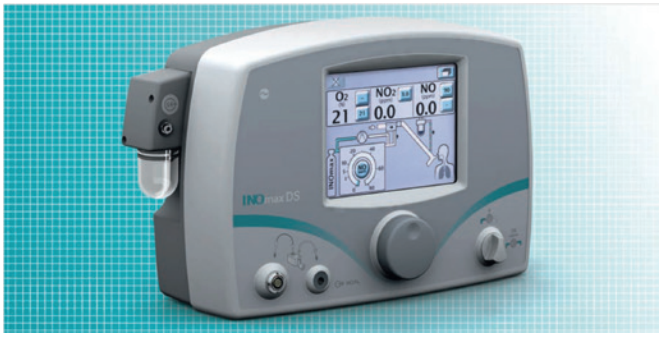

Fig. 54.10 Nitric oxide delivery system. (Ikaria INOmax DS$_{ir}$ Operator's Manual, Ikaria, Inc. 2010.)

metabolite of INO is the formation of methemoglobin as the nitric oxide molecule is bound to hemoglobin. During INO administration, the patient's ability to metabolize methemoglobin is assessed by periodically monitoring methemoglobin levels.[89]

INO should be available in any hospital that has a level III intensive care nursery. INO should be an integral part of any high-risk transport team, and it is important that non-ECMO centers have a plan for treatment failure that takes into account the distance to an ECMO center.[90] INO therapy has also been used for diagnosing and treating certain congenital heart diseases; although used in the management of ARDS, it has no effect on outcome and the oxygenation benefit is normally lost within 48 hours.[91]

Heliox

Heliox is a gas mixture of O_2 and helium (see Chapter 42). Typical concentration of a tank of heliox is 80%/20% or 70%/30% (helium/oxygen). Helium is less dense than air. Inhaling a less-dense gas can reduce the pressure needed to overcome airway resistance and results in decreased work of breathing. Heliox has been used in conjunction with other therapies in the treatment of partial large airway obstruction and asthma where airway resistance is high. It may be used to deliver bronchodilators but due to its lower density is not as efficient as air or oxygen, so a higher flow rate should be used. Heliox may serve as a temporizing measure while steroids are administered to reduce airway swelling. When high O_2 concentrations are necessary, heliox is not likely to be effective as the amount of inspired helium is diminished. Signs of decreased work of breathing, decreased use of accessory muscles, improved aeration, and decreased respiratory rate after initiating heliox are indications of its effectiveness.

NEONATAL AND PEDIATRIC TRANSPORT

Treatment of a critically ill infant or child is usually provided at a tertiary care facility. Many of these facilities have established transport teams that go to the referring facility, initiate ICU-type support, and transport the patient back to the tertiary care center. The composition of transport teams varies from one institution to another; however, typical team members include some combination of registered nurse, RT, paramedic, nurse practitioner, and physician. Regardless of the composition of the team, there are some characteristics that all transport teams should have in common.[91] All members should have exquisite assessment and critical thinking skills. They should be technically adept and have good communication skills. Each team develops minimum criteria that a team member must possess. Many teams cross-train in multiple disciplines to perform certain technical tasks. Establishing and maintaining proficiency with all skills is a must for team members.

The team essentially functions as an extension of the ICU. To do this, much of the same equipment used in the ICU is taken to the referring hospital. Establishing responsibility for assessing function and maintaining appropriate inventory is essential. Many centers use elaborate checklists to be certain not to be without necessary equipment, disposables, or medications. Teams generally prepare for the worst. Many times when the team arrives at the referring facility, the patient's condition is not the same as when the initial call for help was made. Being prepared for the worst helps in stabilizing the patient for transport. The American Academy of Pediatrics has guidelines for all ages and common conditions requiring transport to a tertiary facility. Box 54.12 lists the basic equipment and supplies needed to provide respiratory care during neonatal and pediatric transport.

BOX 54.12 Equipment and Supplies Needed to Provide Respiratory Care During Neonatal and Pediatric Transport

Equipment

- Adequate supply of O_2 and compressed air
- Air-O_2 blender
- Mechanical ventilator with circuit
- Manual resuscitator capable of giving 100% O_2 with PEEP
- Noninvasive O_2 monitor (SpO_2 or $PtcO_2$)
- O_2 analyzer
- Airway pressure monitor (electronic or mechanical)
- Electrocardiograph monitor
- Portable suction apparatus
- Laryngoscope handle
- Laryngoscope blades (sizes newborn to adult)
- Extra laryngoscope bulbs and batteries
- Stethoscope

Supplies

- Resuscitation masks (sizes 0, 1, 2, 3, 4)
- Feeding tubes (sizes 6, 8, and 10 F)
- Disposable O_2 hood
- O_2 connecting tubing
- Disposable hand held nebulizer with tubing (for bronchodilators)
- Cloth adhesive tape for taping endotracheal tubes
- Tincture of benzoin for taping endotracheal tubes
- Pulse oximeter probes (at least two, in case one fails)
- Endotracheal tubes (sizes 2.5–7)
- Stylet

PEEP, Positive end-expiratory pressure.

RULE OF THUMB A high-risk transport team must be prepared to provide the same level of care and highly trained personnel as would be available in the intensive care units (ICUs) they are transporting patients to and from.

SUMMARY CHECKLIST

- Neonatal and pediatric care is one of the most sophisticated specialty areas in the field of respiratory care. Competent practice in this area requires a firm understanding of the many anatomic and physiologic differences between infants, children, and adults.
- A critical component in the respiratory management of infants and children is thorough clinical assessment. Because of the significant anatomic and physiologic differences between adults and infants, many of the assessment techniques useful with adults do not apply to infants.
- General assessment of the infant begins before birth and involves the maternal history and the fetal and newborn status.

As a child grows and develops, more of the assessment methods used with adults become applicable.

- Respiratory care plan development is based on accurate patient information, detailed knowledge of the disease process, and current treatment guidelines and recommendations.
- Respiratory care modalities provided to pediatric and neonatal patients include: O_2, aerosol and humidity therapy, secretion management, airway care, and mechanical ventilation.
- HFNC and CPAP are commonly used to overcome atelectasis and oxygenation problems.
- In many cases HFNC may be as effective as CPAP, but the precise amount of pressure generated is unknown.
- NIV has become an acceptable choice of ventilation.
- Improved design of nasal masks and nasal prongs should help to prevent the development of pressure ulcers during CPAP and NIV.
- For mechanically ventilated patients, plateau pressure or PIP during pressure-targeted ventilation should not exceed 28 cm H_2O and driving pressure should not exceed 15 cm H_2O.
- V_T should be maintained between 4 and 8 mL/kg.
- Compressible volume loss may account for a significant portion of the small V_T used for infants and small children.
- Infants and children can be effectively managed with conventional ventilation. The use of HFV has become increasingly controversial. Mechanically ventilated infants and children should be assessed daily for readiness for liberation from mechanical ventilation.
- Nitric oxide is considered standard therapy for the management of term infants who present with PPHN and should be available in all level III NICUs.
- Surfactant replacement has become the standard of care for preterm (gestation <32 weeks) or low-birth-weight infants (<1300 g) and infants with known surfactant deficiency.
- Highly specialized transport teams are available to transport newborn and pediatric patients to tertiary care facilities.

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55

Patient Education and Health Promotion

Donna D. Gardner

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Discuss the importance of patient education
- Describe the components of a patient's culture.
- Explain the impact culture has on a patient's perception of health.
- Identify two strategies respiratory therapists may use when educating and caring for patients from different cultures.
- Reflect on your own cultural background.
- Discuss two communication strategies when teaching a patient identified as having low health literacy.
- Determine patient education goals from the patient's perspective.
- Write learning objectives in the cognitive, affective, and psychomotor domains.
- Compare and contrast the different stages of learning based on age.
- Describe learning differences between children and adults.
- Describe the methods used to evaluate patient education.
- Discuss the impact health literacy has on patient education
- Explain when to use the teach back or show me method
- Define patient centered care
- Define population health
- Describe the importance of incorporating a patient's culture into patient education.
- Discuss the chronic care model as it applies to patient centered care.
- Identify the settings that are appropriate for the implementation of health promotion activities.
- Describe the respiratory therapist's role as patient educator.

CHAPTER OUTLINE

KEY TERMS

affective domain
chronic care
cognitive domain
culture
disease management
health education
health literacy
health promotion
patient-centered care
population health
psychomotor domain
recidivism

Effective patient education is invaluable to the healthcare of society. Respiratory therapists (RTs) educate patients by providing information about their condition, disease processes, risks and benefits of treatment, medication, or procedures. They teach patients how to perform diagnostic tests, such as basic spirometry, and educate patients about health promotion issues such as tobacco cessation and taking ownership to manage their cardiopulmonary disease. RTs educate patients in all age groups, including geriatric, adult, adolescent, and pediatric patients. In certain situations, RTs educate the parents or the spouse of the patient in the hospital setting before discharge and in the home-care setting (see Chapter 57). RTs are also frequently called on to provide educational programs to patients with pulmonary diseases such as chronic obstructive pulmonary disease (COPD), asthma, and cystic fibrosis to help minimize hospitalizations and short-term readmissions. For these reasons, this chapter reviews important issues related to patient education, disease management, and health promotion.

The top three causes of death in the United States are heart disease, cancer, and chronic lower respiratory system disease, with chronic obstructive lung disease (i.e., bronchitis and emphysema) being the deadliest.[1] Public education about risk factors is the key to preventing these diseases and probably has the greatest potential for making an impact on healthcare in this country. Therefore, in the future, RTs should focus on and emphasize health promotion and disease prevention.

PATIENT EDUCATION

If we think of patient care as customer service—which it indeed is—then we cannot ignore education as a crucial component of that service. If we buy a car or a television set, for example, we expect the salesperson to educate us about the essential aspects of our purchase. We also expect this information to be provided in writing. Likewise, education is an essential component of patient care. For patients to assume or resume control of their health, they must be educated. Because they rely on the healthcare practitioner to provide this education, every respiratory care education program should include instruction regarding patient education.

RTs are able to assess patient learning needs and readiness to learn by asking patients what they know about their condition and therapies. By asking these questions, the RT will be able to identify the patient's gap in knowledge or skills to help identify where to start the patient education. There is limited time to teach patients, therefore the RT must speak in a manner the patient can understand and focus on the health problem to assist the patient becoming engaged in his/her own care.

Cultural Awareness

Behaviors, values and patterns of beliefs shared by a group is referred to as **culture.** Culture is not limited to gender, socioeconomic status, racial background, or ethnicity. Culture is learned and communicated from one generation to another. For example; families, social organizations, and religions are where individuals learn to follow the norms, traditions or customs, practices or taboos, and values of the culture that impact the thinking or behavior common to members of the group. In addition, some cultures have subcultures based on ethnicity, occupation, sexual orientation, or religion and the subculture may have its own language or behaviors. Therefore individuals may identify with more than one cultural group. (e.g., an individual may be considered "black" and be African American or Caribbean and not American nor African. Native American Indians are lumped into one group when there are over 550 different tribes in the United States).[2] RTs must be aware that culture and health perspectives go hand in hand (Table 55.1).

The health of a patient is influenced by their cultural background, which determines the individual's definition of health and how to deal with illness. A patient's culture impacts their willingness to seek healthcare when experiencing symptoms of illness and influences their actions associated with any intervention or treatment. Therefore some strategies RTs may use when educating and caring for patients from different cultures are displayed in Table 55.2.

RULE OF THUMB A person's health condition may be impacted by their culture.

Health Literacy

Health literacy is the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions.[6] Health literacy encompasses educational, social, and cultural factors that influence an individual. Entire books have been devoted to patient education and health literacy because people are neither familiar with medical terms nor how their bodies work. People with strong literacy skills may also face health literacy challenges. Low health literacy affects the patient's ability to participate in their own care, results in patient safety concerns and poor health outcomes.

RTs must be aware of the stereotypes that surround low literacy such as lower socioeconomic level, poor language, and low education levels. There are studies that correlate literacy and economic status with education level. In the United States most individuals with low literacy are Caucasian and low literacy is found in all types of individuals and not limited to one specific group or educational or socioeconomic status, which then become barriers to patient education and patient learning.[7] Because there is limited health literacy in the United States, patients may not be able to read; however, this does not provide information regarding a patient's intellect, but it may impact their ability to use a handout or pamphlet with paragraphs of words. Results from the most recent survey of literacy skills among adults has been used to develop a literacy scale that describes the different levels of health literacy in Table 55.3.[7]

Respiratory patients with low health literacy will not be able to be self-directed and navigate the healthcare system nor follow an educational program or instructions provided. Reading and comprehension may not always go hand in hand. Patients often will not voluntarily admit that they do not understand to avoid embarrassment. Therefore to determine whether a patient understands, RTs should look for clues that indicate reading or writing

TABLE 55.1 Health Perspectives for Emerging Majority Groups in the United States

Group	Traditional Definitions of Health	Traditional Definitions of Illness	Traditional Methods of Maintaining and Protecting Health	Traditional Methods of Restoring Health
American Indian and Alaska Native population	Living in total harmony with nature and being able to survive under extremely challenging situations	Illness is the price to be paid for past or future negative events. Details are specific to different nations. Illness may result from the presence of evil spirits. These types of illness are contagious with generalized symptoms	Maintain positive relationship with nature. Treat body with respect. Purification acts using water, herbal remedies and rituals	Removal of the external causative factor by a traditional healer after spiritual ceremony to determine cause and treatment. Drumming
Asian population	Living in total physical and spiritual harmony with the universe. Four major religious traditions pose variations on cultural values. Examples: respect for life, moderation of basic relationships, balance between evil and good	Human body considered as whole, with harmony between organs and superficial structures. Integration of human body within context of environment. Imbalance of ying and yang (Chinese).	Body is a gift from parents and ancestors and must be protected. Dietary practices Formal daily exercise for example, tai chi; Amulets (Chinese)	Acupuncture Applying poultices Cupping Bleeding Massage Herbal remedies Other products Use of physicians, with women treating women. Use of immunizations Important to keep the body intact (Chinese).
African population	A process of energy force, rather than a state. Consists of body, mind and spirit. State of harmony with nature. Elderly held in high regard	Process of disharmony attributed to demons and evil spirts. Pain as a sign of illness. If no pain, then illness is gone	Dietary practices Rest and clean environment Use of laxatives and cod liver oil taken internally, sulfur and molasses on back Protective materials of various substances, for example, copper or silver, dried flesh Prayer	Voodoo and magic Use of immunizations Cared for by the entire community Prayer Use of healers Pictures of catholic saints or relics Sugars and turpentine orally Poultices, herbs, minerals, oral preparations, including hot water and lemon, garlic, flannel with camphorated oil
Hispanic population	Gift from God	Imbalance in body or punishment for wrongdoing. Imbalance between hot and cold or wet and dry (definitions vary). Dislocation of body parts. Magic or supernatural causes such as evil eye. Strong emotions envy	Maintain equilibrium in the universe through behavior, diet, and work	Prayer Dietary practices of hot and cold Magical and religious rituals, artifacts frequently in Catholic and Pentecostal traditions, such as offerings confession, candles, laying on of hands. Folk, holistic healers called *curanderos*, using herbs, prayer, massage, social rapport, spiritual. Amulets

Modified from Wilson and Dorne: Impact of culture on the education of the geriatric patient.[3]

is a concern and to be sensitive to prevent any feelings of shame. Lack of understanding clues are listed in Box 55.1.

RULE OF THUMB Health literacy influences a patient's ability to adhere to self-management medication or a therapy regimen.

Patients' ability to understand health information is a prerequisite to patient adherence. Patients need to be able to read and understand the instructions, prescriptions, informed consent, and written documents to optimize their potential. Health literacy experts emphasize important behaviors to be developed for clear communication with patients (Table 55.4).

BOX 55.1 Clues Indicative of a Lack of Understanding

- Patient repeatedly is noncompliant
- Patient uses the excuse being too busy, tired, or sick to maintain attention when given instruction
- Claims that the patient did not feel like reading the information, gave the information to a family member, or lost or forgot their glasses
- Insistence on taking the information home to read
  - Demonstrates nervousness and stress, confused about the materials
  - Talks about something else and not on topic
  - Returns documents that are not complete or are illegible

TABLE 55.2 Recommended Patient Teaching for Cultural Awareness

Learn about the ethnic/cultural/religious/spiritual traditions of the patients in your clinic or healthcare facility to establish inclusion	Pay attention to body language (nonverbal communication), lack of response or expressions of anxiety that may signal the patient or family is in conflict about the education or treatment and hesitant to tell you
Arrange for language translators when necessary	Be aware of cues from the patient and/or family comprehend the teaching and assess with the cultural awareness in mind. (nodding does not guarantee understanding, ask the patient to state the information in his/her own words)
Ask the patient and family or healthcare provider open-ended questions to gain more information about their assumptions and expectations	Remain nonjudgmental when given information that reflects the values that differ from your own
Follow the advice given by the patient about appropriate ways to facilitate communication within or between the family and healthcare providers	Healthcare providers should assess their own ethnic/cultural/religious or spiritual beliefs that may not reflect the patients
Expand knowledge about sexual orientation, gender identity, and learn the definitions for Lesbian, Gay, Bi-sexual Transgender, Queer (LGBTQ) populations	Healthcare providers must be aware of their own biases and prejudices and these need to be examined and recognized

Modified from McLaughlin L, Braun K, and Siebert PS.[4,5]

TABLE 55.3 Levels of Health Literacy

Levels of Health Literacy	
Proficient	Able to perform complex activities such as searching documents to define medical terms or other information
Intermediate	Able to conduct moderately challenging task such as finding an age range for a specific vaccination from a childhood vaccination chart
Base	Able to complete simple tasks such a giving two precautions to follow if taking a specific medication, based on information in a clearly written pamphlet
Below basic	Demonstrates lower level of performance such as identifying what can be eaten or drunk before having a medical test based on a set of short instructions
Not literate in English	Not literate in English

Establishing Goals for the Patient Teaching

When considering the content to teach patients depends on the needs of the patient and the goals to be accomplished. Setting collaborative goals with the patient will direct the patient teaching. Sometimes RTs are overwhelmed with the amount of information to teach and try to cover everything, which may appear disorganized or haphazard. This type of teaching is neither efficient nor effective. The RT needs to have an organized predetermined plan with short- and long-term goals and objectives that include the patient and will be used to evaluate the patient's progress. Setting goals that are aligned with the patient's needs will contribute to successful learning activities. This can be accomplished by asking what should the patient be able to do because of this education session? What information should the patient need to carry out the instruction? These two questions have different answers for each patient. Different goals will be required for teaching respiratory patients with acute or chronic conditions and for those related to health promotion. For example, when teaching a respiratory patient how to use the prescribed controller medication for asthma in the MDI with a spacer, the short-term goals may be to fill the prescription and to take the medication correctly using the MDI with a spacer.

After this the patient needs to know the name and type of medication, when to take the medication, why the patient should take the medication as directed, what should the patient expect to occur when taking the medication (breathing is improved, and to keep taking the medicine because it is working, do not stop taking the medicine), and any special action the patient should take (if the patient stops taking the medicine the patient is more likely to have an exacerbation). Understanding the why, what, and how increases the likelihood that the patient will take the medication. Establishing long-term goals will decrease the frequency of asthma exacerbations. This information will need to be simplified and broken down into smaller or shorter time segments for the patient.

Performance Objectives

Initially it is helpful for the RT to develop learning objectives that are appropriate for the specific patient and the education topic to be addressed. These learning objectives will help the

MINI CLINI

A Hispanic parent of a child with asthma is a concerned mother who wants to do the best for her child. She is a single parent with no other family. The child is prescribed a controller medication in a metered-dose inhaler (MDI) with a spacer. The respiratory therapist (RT) teaches the mother how to use the MDI with a spacer and provides the mother with a pamphlet to use for reference. The RT also shares the importance of taking the medication twice a day every day to prevent asthma exacerbations. The mother nodded in agreement. A week later the mother and child are back in the clinic for an asthma exacerbation. The RT asks the mother about using the MDI and spacer twice daily and asked about her referring to the pamphlet. The mother nodded and smiled and informed the RT she had bought a hairless chihuahua to take the asthma away from the child. Unknowingly to the RT, in some Hispanic cultures, there is belief that a chihuahua will cure the child's asthma.[9] The RT assumed the mother would be able to read the pamphlet, understand the steps to use the MDI with a spacer, and would know that a dog is an asthma trigger. What the RT does not know is that the mother is unable to read. The RT must take time to have the patient demonstrate the use of the MDI and spacer correctly and ask questions about understanding the pamphlet or make sure there are plenty of pictures on the pamphlet that a person who is unable to read can follow, and to inquire about cultural beliefs related to the disease processes.

TABLE 55.4 Recommended Strategies for Clear Communication With Patients With Low Health Literacy

1. Assess the patient understanding at baseline before moving forward with detailed information. (This usually takes 30 s or less.) For example, for a patient newly diagnosed with asthma ask the following question; "Before we go on, could you tell me what you already know about asthma?" This will provide the respiratory therapist with an understanding of the patient's information needs and where to tailor the educational content
2. Explain using plain language or lay terms. Avoid using medical terms, jargon, or vague terms. Example say: "increased breath rate" instead of tachypnea
   Example say: "causes of asthma attacks" instead of "triggers asthma exacerbations"
   Example say: Instead of "You have asthma", say "Your breathing test results were positive for asthma"
3. Focus on 1 to 3 key points

Repeat these points throughout the education session

4. Encourage the patient to ask questions by asking open-ended questions.
   Example: ask "What questions do you have?" instead of "Do you have any questions?"
5. Use the **teach-back method** to confirm the patient understands and to make sure you have explained the information clearly to the patient; be specific when asking the patient to demonstrate back to you.
   Example: "I always ask my patient to repeat things back to me to make sure I have explained the information to them clearly. I would like you to tell me when you will take the new medication we talked about today."
   Example: "When you get home, your wife or spouse will ask you what happened today and what will you tell them?"

To confirm the patient understands how to use their medication or a different skill, ask the patent to demonstrate back to you. This usually takes 1–2 min
   For example: have the patient demonstrate how to use the puffer metered-dose inhaler (pMDI) with a spacer

6. Write down important instructions to inform the patient what they do after meeting with you
7. Provide useful patient education materials

The education materials provide the patient (and spouse or family member) with the information to reference when at home

Modified from Kripalani S, Weiss BD: Teaching about health literacy and clear communication. *J Gen Intern Med* 21(8):888–90, 2006.[8]

learner focus on more relevant topics and will help the educator clarify the teaching strategies that are needed for patient education sessions. Objectives should be stated in attainable and measurable terms so that the RT and the patient can recognize when the objective has been accomplished. Clear objectives describe what is to be accomplished and how evaluation will occur.

The format for writing an objective is as follows:

1. Begin with the phrase, "At the end of the lesson, the patient will…"
2. Write the action verb (e.g., "list," "describe," "demonstrate").
3. Write a condition, if needed (e.g., with or without the use of notes).
4. Write a standard, if needed (e.g., how fast, how accurate).

For example: At the end of the session, the patient will be given an MDI and a spacer and be able to demonstrate the correct technique for using it without error.

Action verb: "demonstrate" (from the psychomotor domain; the relevant domains are discussed later in this chapter)

Condition: "given an MDI and a spacer"

Standard: "without error"

Learning Domains

Learning occurs in three domains: **cognitive**, **psychomotor**, and **affective**. Some learning sessions will involve only one domain, whereas others may involve all three. The cognitive domain is very important, because it will address the knowledge that a patient needs regarding his or her illness and how to manage it. The psychomotor domain addresses the skills that the patient will need to acquire to perform specific treatment modalities (e.g., the use of MDIs). The affective domain involves teaching patients about the necessary attitudes and motivations for successfully living with their diseases.

MINI CLINI

Developing Learning Objectives for the Use of an Albuterol Metered-Dose Inhaler

Problem

Your 31-year-old patient is newly diagnosed with asthma, and she is being discharged tomorrow. She requires instruction regarding how to properly use her controller medication, Advair diskus, and the reliever medication albuterol metered-dose inhaler. Develop learning objectives for her and address each learning domain.

Solution

Use a variety of learning objectives, including the following:

Cognitive domain: Describe the action of albuterol on the bronchial smooth muscle; recognize when it is necessary to seek medical attention.

Affective domain: Agree that it is important not to skip a dose; verbalize willingness to use the Advair diskus daily; feel satisfaction by controlling the disease.

Psychomotor domain: Demonstrate the ability to assemble the metered-dose inhaler and the spacer; inhale slowly and deeply with an inspiratory hold.

Cognitive Domain

The cognitive domain is probably the easiest to translate into learning objectives because it involves the facts and concepts that the RT wants the patient to know and apply by the end of the education session. Objectives for the cognitive domain might include the following:

1. List the indications for oxygen therapy.
2. Discuss the importance of using the prescribed liter flow.
3. Explain the relationship between oxygen and combustion.

Any factual information that you expect the patient to understand and apply falls under the cognitive domain. Action verbs for the cognitive domain are included in Table 55.5.[10]

Psychomotor Domain

Repetition and active involvement are important when teaching a psychomotor skill. RTs who teach new skills to patients need to provide plenty of opportunity for the patient to practice the activities. Simple demonstration of the skill to the patient is not enough. To confirm performance in the psychomotor domain, have your patients provide a return demonstration. Be sure to provide help and encouragement as needed. Be patient; not everyone develops skills at the same rate.

Examples of action verbs for the psychomotor domain are included in Table 55.6.[10]

RULE OF THUMB People learn by doing. Get the learner involved.

Affective Domain

The patient's attitudes and motivations influence his or her ability to learn. It is important to remember that, with patient education, timing is everything. Patients who have recently been given a poor prognosis or who are in pain are not in an optimal position to learn. Maslow suggested a hierarchy of

TABLE 55.5 Cognitive Domain

Level	Samples	Ambiguous terms to avoid
Knowledge	Define, identify, list, label, name, state Example: List your medications.	Know, memorize
Comprehension	Describe, defend, explain, generalize, summarize Example: Describe how your medication works on your condition.	Understand, believe
Application	Apply, construct, demonstrate, calculate, operate Example: Demonstrate how you take your medication.	Realize
Analysis	Analyze, break down, contrast, differentiate, distinguish, infer Example: Distinguish between the types of pain.	Conceptualize
Synthesis	Categorize, combine, create, design, formulate, integrate, plan, revise, rearrange, write Example: Integrate diet and exercise into your rehabilitation plan.	Experience
Evaluation	Appraise, assess, compare, conclude, critique, evaluate, judge, weigh Example: Compare your level of wellness now to this time last year.	Perceive

Data from Borich GD: *Effective teaching methods*, et 3, Englewood cliffs, NJ, 1996, Merrill; Bloom BS: *Taxonomy of educational objectives, Handbook I: The cognitive domain.* New York, 1956, David McKay Co Inc.; French D, Hale C, Johnson C, et al: *Blended learning: An ongoing process for internet integration.* Austin, TX: 2003, e-Linkages, Inc and Trafford, p 231.

TABLE 55.6 Psychomotor Domain

Level	Samples	Ambiguous terms to avoid
Perception/awareness	Choose, describe, detect, distinguish, identify, relate, select Example: Identifies body language.	Perceive, comprehend, recognize
Mindset/ready to act	Begin, display, explain, move, react, show, state, volunteer Example: Shows willingness to change health behavior.	Think, understand, feel
Guided response/imitation	Copy, duplicate, imitate, trace, follow, react, reproduce Example: Follows instructions when learning crutch gait.	Appear
Mechanism/efficiency	Assemble, calibrate, manipulate, demonstrate, improve, perform, produce Example: Demonstrates proficiency in crutch gait.	Experience
Complex overt response/skilled	Assemble, calibrate, manipulate, demonstrate, improve, perform, produce Example: Performs crutch gait confidently and without hesitation.	Become familiar with
Adaptation	Adapt, alter, change, rearrange, reorganize, revise, vary Example: Adapts to new terrain and obstacles confidently when using crutches.	Conceptualize, display interest in
Origination	Arrange, combine, create, design, initiate, make, originate Example: Creates new ways to meet needs while adapting to functional limits.	Self-actualize

Data from Borich GD: *Effective teaching methods*, ed 3, Englewood cliffs, NJ: 1996, Merrill; French D, Hale C, Johnson C, et al: *Blended learning: An ongoing process for internet integration.* Austin, TX: 2003, e-Linkages, Inc and Trafford, p 231; Simpson EJ: *The classification of educational objectives in the psychomotor domain,* Washington, DC, 1972, Gryphon House.

TABLE 55.7 Affective Domain

Level	Samples	Ambiguous terms to avoid
Receive/awareness	Accept, acknowledge, alert, choose, give, attend, notice, tolerate, select Example: Acknowledges loss.	Realize, comprehend, perceive, become conscious of
Respond/display interest	Agree, assist with, aid, answer, comply, communicate, consent, volunteer Example: Consents to treatment.	Think, know, feel
Value	Adopt, behave, choose, demonstrate, commit, desire, initiate, join Example: Demonstrates a desire to change.	Understand, enjoy
Organize	Adapt, adjust, arrange, balance, compare group, rank, verify, strengthen Example: Balance work and home life.	Experience, become familiar with
Characterize/internalize values	Advocate, avoid, defend, demonstrate, exhibit, justify, resolve, support Example: Demonstrates a change in lifestyle.	Self-actualize

Data from Borich GD: *Effective teaching methods*, ed 3, Englewood cliffs, NJ: 1996, Merrill; Bloom BS: *Taxonomy of educational objectives, Handbook I: The cognitive domain.* New York, 1956, David McKay Co Inc.; French D, Hale C, Johnson C, et al: *Blended learning: An ongoing process for internet integration.* Austin, TX: 2003, e-Linkages, Inc and Trafford, p 231.

needs, and he identified physiologic needs as the most basic of human needs, followed by safety, love, esteem, and self-actualization. Lower-level needs must first be satisfied before moving on to higher-level needs. For example, if a patient is dyspneic or in pain, he or she will probably not be receptive to learning the steps that are involved in cleaning a small-volume nebulizer. It is important for RTs to assess a patient's readiness to learn by talking with the patient and his or her family and by listening to the patient's concerns. It is important to develop a relationship of trust and to be empathetic with the patient.

The RT should begin with easy-to-master facts and skills. After the patient conquers these, motivation should increase, and the patient will have a feeling of accomplishment. Motivation is also enhanced by presenting material clearly with the use of a variety of teaching methods and by relating the facts and skills to practical applications. Getting patients to see how these skills will benefit them is the key to motivation. Communicating to the patient that there is something that he or she can do to maintain or improve his or her health and sense of well-being is important.

Objectives in the affective domain—using the oxygen therapy example mentioned earlier—might include the following:

1. Express genuine concern for yourself by using your oxygen therapy correctly.
2. Commit to learn by being an active participant in the program.

Affective domain action verbs are included in Table 55.7.[10]

RULE OF THUMB Measuring the patient's commitment to caring for him/herself is essential for behavior change.

Provide Educational Resources

When using a short period of time for teaching, there is a need for the patient to repeat or practice, and therefore the patient must be given educational resources to reference about their condition. These educational resources may be in a format such as a brochure, handout, and app on a cell phone, YouTube videos, website or other technology as appropriate. The educational materials must be at a readability level that is equal to the fourth or fifth grade for most patients to understand. Because the internet is a valuable resource for patient education, make sure the websites shared are appropriate for the patient population. However, YouTube videos are not peer reviewed and may not be balanced information; therefore RTs should make sure the source is credible.

TABLE 55.8 Defined Ages Across the Lifespan

Age Range	Title
Children	
Birth to 28th day of life	Newborn, neonate
1 month to 1 year of age	Infant
1-3 years	Toddler
3-5 years	Preschooler
6-12 years or onset of puberty	School-age
13-20 years	Adolescent
Adults	
18-25	Emerging adult, young adult
30-65	Middle adult
Over 65 years	Late adulthood, older adult

Data from Potter PA, Perry AG, Stockert PA, et al: *Fundamentals of nursing*, ed 9, St Louis, 2017, Elsevier.

Teaching Children, Adolescents, Adults, and Older Adults

Teaching children and their parents, adults, and older adults requires different formats, time spans, and educational tools. This section will provide the RT with various strategies to address each age group. To be clear on age definition, refer Table 55.8.

TABLE 55.9 Teaching Methods Based on Patient's Developmental Capacity

Infant	• Keep routines (e.g., feeding, bathing) consistent. • Hold infant firmly while smiling and speaking softly to convey sense of trust. • Have infant touch different textures (e.g., soft fabric, hard plastic).
Toddler	• Use play to teach procedure or activity (e.g., handling examination equipment, applying bandage to doll). • Offer picture books that describe story of children in hospital or clinic. • Use simple words such as cut instead of laceration to promote understanding.
Preschooler	• Use role play, imitation, and play to make learning fun. • Encourage questions and offer explanations. Use simple explanations and demonstrations. • Encourage children to learn together through pictures and short stories about how to perform hygiene.
School-age child	• Teach psychomotor skills needed to maintain health. (Complicated skills such as learning to use a syringe take considerable practice.) • Offer opportunities to discuss health problems and answer questions.
Adolescent	• Help adolescent learn about feelings and need for self-expression. • Use teaching as collaborative activity. • Allow adolescents to make decisions about health and health promotion (safety, sex education, substance abuse). • Use problem solving to help adolescents make choices.
Young or middle adult	• Encourage participation in teaching plan by setting mutual goals. • Encourage independent learning. • Offer information so adult understands effects of health problem.
Older adult	• Teach when patient is alert and rested. • Involve adult in discussion or activity. • Focus on wellness and person's strength. • Use approaches that enhance patient's reception of stimuli when they have a sensory impairment. • Keep teaching sessions short.

From Potter PA, Perry AG, Stockert PA, et al: *Fundamentals of nursing*, ed 9, St Louis, 2017, Elsevier.

Teaching Children and Their Parents

Teaching children often includes educating their parents because of the dependence of the age group and the parents are considered the primary learner. Therefore the parents must be included to participate with the child as much as possible, which includes setting goals, objectives, and evaluation or feedback. Teaching parents of a child with a cardiopulmonary disease allows them to better understand the diagnosis, common signs and symptoms, and specifics associated with the treatment or care plan. The parents need to be assessed for a readiness to learn by listening for cues the parent is using to ask for more information (e.g., "I am having a really hard time getting my child to take his/her medication). Stages of learning for infants to older adults are listed in Table 55.9.

RULE OF THUMB Parents need to be communicated in a manner that is easily understood and includes their culture.

When teaching parents of toddlers, the toddler should be included in the teaching and encouraged to participate in the education activities. Toddlers are more motivated by external factors (e.g., prizes) and may need a more obvious reward system in place before learning can take place. Toddlers can grasp a cause-and-effect relationship between two things but have a very short attention span; therefore the education sessions may need to be limited to no longer than 15 to 20 minutes.

Older children may learn by example and RTs may use simple or familiar terms the child is used to using. As the child matures and enters adolescence, the parent needs to shift the responsibility to the adolescent who is able and willing to assume the responsibility. Other important issues related to differences between children and adult learners are listed in Box 55.2, and allocated time for teaching is given by age in Box 55.3. Ideally, a child can concentrate for 2 to 5 minutes per year of age.

Teaching Adolescents and Adults

When teaching adolescents and adults we need to remember they have internal motivating factors and will learn quicker if they can easily see the intrinsic value of knowing more about their illness. Some refer to this internal motivating factor as the "WIIFM (what's in it for me) concept. Adults are more independent and self-directed, and they do not like being dependent on others. Adults are task- or problem oriented and prefer practical activities such as discussion or hands on activities to drive the important points home. They also bring experience to the situation and this can be a rich resource and used to connect to new information. This suggests that

BOX 55.2 Learning Differences Between Children and Adults

Child	Adult
• Motivated by external factors like grades • Directed by others • Learning is a big part of his or her life • Trusts teacher • Has limited experience • Learns for the future • Learns quickly • Tends to learn in accordance with his or her developmental stage • Has no problem with a slow pace of learning • Subject oriented	• Motivated internally • Is self-directed • Learning is only one part of his or her life • Questions the teacher • Has rich life experiences • Learns for the present • May learn more slowly • Varies regarding learning ability • Dislikes a slow pace of learning • Problem oriented

BOX 55.3 Attention Spans for Different Ages

Toddlers:	about 4–10 min
School-aged children:	about 10–20 min
Adolescents and adults:	about 20–30 min

adults should be more involved in setting program goals and that they will readily learn skills that make them more independent.

Teaching Older Adults

Older adults may have special considerations because of functional, cognitive, and psychosocial changes that occur over time. Also, remember many older adults have comorbidities that impact coexisting conditions on the functional capacity of the individual. Quality of life or life expectancy may be considered when prioritizing content for older adults. Older adults may require more time to assimilate the information and benefit from slower paced education sessions. Also, a caregiver may need to be incorporated into the education session if the patient is not able to assume full responsibility for his/her self-care. Other important issues related to differences between children and adult learners are listed in Box 55.2, and allocated time for teaching is given by age in Box 55.3.

TEACH BACK OR ECHO METHOD

Many of the patients RTs care for have chronic diseases, and teaching these individuals about their chronic disease and self-management is best done using the teach-back method or show me method to improve the individual's understanding of the disease, and ask the individual to repeat or demonstrate back the key points of the education.[12] Asking a patient "Do you understand?" will usually elicit a response of head nodding or an answer of "yes" and will communicate to the RT the patient actually lacks comprehension about the information provided. The teach-back method was introduced to reinforce education to patients. This method has been shown to have positively affected patient adherence and self-efficacy, improved self-care, and reduced hospital readmission rates. This method includes using questions to determine what the individual understood from the education session such as "We have discussed quite a bit today, would you please tell me two things you will share with your family that we discussed today?" Or "Before you leave today, please show me how to use the puffer MDI?"[12] If the individual responds incorrectly or seems to be deficient in understanding, the RT should reinforce the positive actions or behaviors of the patient first and then repeat the information missed for clarification, or re-demonstrate the steps for the use of the equipment or medication delivery device. This cycle repeats itself until the individual can answer or demonstrate correctly. The teach-back or echo method is not a test of the individual's knowledge as much as ascertaining how well the information was taught and what needs to be reviewed. The Agency for Healthcare Research and Quality (AHRQ) created the Teach-back Observation Tool to evaluate the RT and his/her ability to use the Teach back method.

The teach-back method also allows those with low literacy levels to actively engage and for information to be reiterated. This method is useful for teaching individuals to understand treatment regimens and disease warning signs. Chronic disease management incorporates self-management strategies that are designed to assist patients and their families to better manage the disease. These programs focus on symptom recognition, self-monitoring, medication adherence, exercise, and reduction in smoking. These programs have contributed to reducing hospitalizations, readmission rates, days in the hospital, outpatient visits and healthcare utilization and costs. Box 55.4 provides recommendations for the teach-back method.

RULE OF THUMB The teach-back method reflects the respiratory therapist's ability to communicate the information correctly to the patient.

Evaluation of Patient Education

The critical question that remains when all the patient education sessions are complete is, "Has the patient learned?" Evaluation is the process that answers that question. The method used to evaluate learning is determined by the measurable learning objectives (i.e., cognitive, affective, or psychomotor). Cognitive objectives are often evaluated with the use of a written examination. Objectives in the affective and psychomotor domains are evaluated with the use of performance checklists.

RULE OF THUMB Evaluation results reflect the quality of instruction as much as the degree of learning.

BOX 55.4 Recommendations for the Teach-Back Method

Plan the approach
- Think how you will incorporate the teach-back method into the information provided
  - "We covered a lot today and I want to make sure I explained everything clearly. Let's review what was discussed. Could you tell me 3 things you agreed to do to help you control your disease?"

Chunk and check
- Do not wait until the end of the session to have the teach back session. Chunk out the information into small segments and have the patient teach it back to you. Repeat this several times during the education session

Clarify and check again
- When the teach-back method uncovers misunderstanding, explain the information again and ask the patient to teach back again until they can correctly describe in their own words or demonstrate how to use the medication or equipment again.

Start slowly and use it consistently
- Use the teach back method with every patient every time you provide education session

Practice
- Practice your delivery and make teach back part of your routine

Use this teach-back AND show me methods when using new medications or equipment by asking the patient to show you how to use these devices.
- "I have noticed many people have trouble remembering how to take their puffer metered-dose inhaler with a spacer. Can you show me how you will take your medication?"

Use handouts with the teach-back method

It is important to have written instructions for follow-up when the patient is at home. Point out the important steps by reviewing the written instructions and reinforce your patient's understanding. The patient may use the handout when teaching you.

MINI CLINI

Metered-Dose Inhaler Instruction for a Pediatric Patient

Problem

How would you change the approach to the metered-dose inhaler situation described in the previous Mini Clini if your patient was a 7-year-old boy with asthma?

Solution

Although the learning objectives may remain the same, the methods may be different. You may compare the slow, deep inspiration to getting ready to blow out the candles on a birthday cake. You may use swimming under water as an image to encourage breath holding. Use simple diagrams to show how the medication will act on the patient's lungs. If he likes sports, tell him about athletes who compete well despite having asthma (you may also use this illustration to stress the importance of controlling asthma). An abundance of resource materials is available for children with asthma; make use of them. Many local, state, and national lung associations (www.ala.org) offer such learning aids as age-appropriate books, coloring books, and puppets to make the learning process more fun for children. To utilize the teach-back and show me method ask the patient to tell you what was discussed during the education session to see if what you told the patient was clear. Also ask the patient what three things will he/she do when he/she gets home to manage his/her disease. Last, ask the patient to show you how to use the puffer MDI (pMDI) correctly. Any misunderstandings should be addressed immediately, and the patient should re-demonstrate the use of the pMDI.

Patient Education Teaching Tips

Following is a list of time-honored suggestions for improving patient education:
- Address the patient's immediate concerns first.
- Include the patient in setting the goals and objectives.
- Create an optimal learning environment. Teach in a quiet and relaxed setting.
- Avoid using medical jargon; use lay terms to explain the information
- Have patients use as many of their senses as possible during their learning session. Whenever possible, include hearing, seeing, smelling, speaking, touching, and doing.
- Keep sessions short. If the material is complex, break it down into brief segments.
- Repeat, repeat, repeat!
- Provide many opportunities for the patient to ask questions and state in their own words about the education. Also, provide ample time to practice psychomotor skills and demonstrate back to you using the teach-back method.
- Be specific when emphasizing key points.
- Be prepared.
- Be organized. People learn more quickly when they are presented with information that is well organized.
- Demonstrate enthusiasm for what you are doing. The learner can always sense your level of motivation.
- Evaluate in a nonthreatening manner and provide helpful feedback. Use evaluation as a learning tool.

HEALTH EDUCATION

Health education may have been the earliest form of organized health promotion in the United States. Health programs in schools is a result of Lemuel Shattuck's report in 1850 to the Sanitary Commission of Massachusetts, which described the value of schools helping contain communicable diseases. However, it was not until 1875 that health education became widespread. During that year, the Women's Christian Temperance Union lobbied for alcohol education in the schools. Because of these efforts, 38 states passed legislation to require this education, which later turned into tobacco, alcohol, and drug education. From that time, health education has been enhanced and expanded in schools. There are public health agencies at the local, state, national, and international levels that provide health education and care for those who would otherwise have none.

Health education is a process of planned learning that is designed to enable individuals to make informed decisions and to take responsible actions regarding their health. The primary goal of health education is behavior change, and it is designed to promote, maintain, and improve both individual and community health. Health education covers the continuum between health and disease and between prevention and treatment.

Health promotion helps people change their lifestyles through coping strategies to prevent illness in a variety of settings, from the home or school to the workplace or the healthcare agency or institution, which require different approaches to patient care planning. The RT assesses patterns and uses their assessment to facilitate an individual's maintenance of well-being toward

BOX 55.5 American Association for Respiratory Care Health Promotion and Disease Prevention Statement

Health Promotion and Disease Prevention

- The AARC acknowledges that respiratory therapists in both the civilian and uniformed/military services are integral members of the healthcare team, in hospitals, home healthcare settings, pulmonary laboratories, rehabilitation programs, and all other environments (including ICUs and critical care transport) where respiratory care is practiced.
- The AARC recognizes that education and training of the respiratory therapist is the best method by which to instill the ability to improve the patient's quality and longevity of life, and that such information should be included in their formal education and training in CoARC accredited programs.
- The AARC recognizes the respiratory therapist's responsibility to participate in pulmonary disease teaching, smoking cessation programs, pulmonary function studies for the public, air pollution alerts, allergy warnings, and sulfite warnings in restaurants, as well as research in those and other areas where efforts could promote improved health and disease prevention. Furthermore, the respiratory therapist is in a unique position to provide leadership in determining health promotion and disease prevention activities for students, faculty, practitioners, patients, and the general public in both civilian and uniformed service environments.
- The AARC recognizes the need to (1) provide and promote consumer education related to the prevention and control of pulmonary disease; (2) establish a strong working relationship with other health agencies, educational institutions, federal and state government, businesses, military, and other community organizations; and (3) monitor such activities. Furthermore, the AARC supports efforts to develop personal and professional wellness models and action plans that will inspire and encourage all respiratory therapists to cooperate on health promotion and cardiorespiratory disease prevention.

Effective 1985.
Revised 2000.
Revised 2005.

AARC, American Association for Respiratory Care; *CoARC*, Commission on Accreditation for Respiratory Care; *ICU*, intensive care unit.
From the American Association for Respiratory Care (AARC): Position statement (website): www.aarc.org/resources/position_statements/rms.html.

BOX 55.6 American Association for Respiratory Care Role Model Statement

- As healthcare professionals engaged in the performance of cardiopulmonary care, RTs must strive to maintain the highest personal and professional standards.
- In addition to upholding the code of ethics, the RT shall serve as a leader and advocate of public health.
- The RT shall participate in activities leading to awareness of the causes and prevention of pulmonary disease and the problems associated with the cardiopulmonary system. The RT shall support the development and promotion of pulmonary disease awareness programs, to include smoking cessation programs, pulmonary function screenings, air pollution monitoring, allergy warnings, and other public education programs.
- The RT shall support research to improve health and prevent disease.
- The RT shall provide leadership in determining health promotion and disease prevention activities for students, faculty, practitioners, patients, and the general public.
- The RT shall serve as a physical example of cardiopulmonary health by abstaining from tobacco use and shall make a special personal effort to eliminate smoking and the use of other tobacco products from the home and work environment.
- The RT shall strive to be a model for all members of the healthcare team by demonstrating responsibility and cooperating with other healthcare professionals to meet the health needs of the public.

Effective March 1990.
Revised March 2000.

RT, Respiratory therapist.
From the American Association for Respiratory Care: Position statement (website): www.aarc.org/resources/position_statements/rms.html.

wellness. To be effective, health education must be combined with strategies for health promotion; the two are strongly linked. In the United States, *Healthy People 2020*, the national health promotion initiative establishes national goals and provides a framework for prevention.[13] *Healthy People 2020* publishes national health objectives that identify the most significant preventable threats to health. The objectives and associated evaluation tools demonstrate progress toward the goals of attaining high-quality, longer lives, decreasing health disparities, and creating an environment—all of which promote health and improve quality of life.[13] The American Association for Respiratory Care has created a statement for health promotion and disease prevention (Box 55.5).

Although individuals must ultimately assume responsibility for their own health, promoting healthy behaviors through education is an important part of being an RT. In this capacity, the RT should serve as a role model for the public. Unless healthcare professionals' model healthy behaviors, successful health outcomes cannot be expected from the public. To this end, the American Association for Respiratory Care has created a role-model statement to encourage RTs to set a positive example for the public (Box 55.6).

Providing a good example is not enough to ensure successful health education programming. For the desired outcomes to be achieved, certain conditions must first be met. The components are remarkably like patient education requirements. The essential components of effective health education are listed in Box 55.7.

For RTs to assist patients, caregivers, or the public about the development of healthier lifestyles, greater emphasis must be placed on health promotion and disease prevention strategies Box 55.8.

HEALTH PROMOTION AND DISEASE PREVENTION

In 2015, the United States spent $3.2 trillion, or $9,990 per person, on healthcare, the highest spending by far of any developed country.[14] The top three causes of death in the United States are heart disease, cancer, and COPD. All three lead to chronic conditions and might be preventable by avoiding tobacco use, poor diet, and physical inactivity.

Current medical practice is designed to respond to the acute problems of patients by focusing on diagnosis and treatment of the presenting symptoms. Only focusing on the acute or episodic health problems creates a discrepancy when using this model of care for chronic conditions that may be prevented or

BOX 55.7 Essential Components of Effective Health Education

1. Program participants must be actively engaged in the learning process.
2. Activities must incorporate the values and beliefs of the learner. Familial, cultural, societal, and economic factors must be considered.
3. The role of the health educator is to facilitate behavioral change. Thus the learning process should be approached together by both the learner and the educator.
4. The process of predisposing an individual toward improved health as well as enabling and reinforcing health attitudes requires effort, which will only reap results over time.
5. The healthcare educator must be willing to listen nonjudgmentally to the concerns of the learners. Empathy and understanding are necessary to foster a trusting relationship.
6. The level of the learners' self-esteem and self-concept may either enhance or inhibit their ability to make decisions about their own health. The healthcare educator should be willing to provide emotional support as necessary.
7. The healthcare educator's personal characteristics have a direct impact on the outcome of the educational program. Generally, successful outcomes occur because of a confident and professional approach.

BOX 55.8 Health Promotion and Disease Prevention

- The AARC submits this paper to identify and illustrate the involvement of the RT in the promotion of health and prevention of disease and supports these activities. The AARC realizes that RTs are integral members of the healthcare team, in hospitals, home healthcare settings, pulmonary laboratories, rehabilitation programs, and all other environments where respiratory care is practiced.
- The AARC recognizes that education and training of the RT is the best method by which to instill the ability to improve the patient's quality and longevity of life, and that such information should be included in their formal education and training.
- The AARC recognizes the RT responsibility to participate in pulmonary disease teaching, smoking cessation programs, pulmonary function studies for the public, air pollution alerts, allergy warnings, and sulfite warnings in restaurants, as well as research in those and other areas where efforts could promote improved health and disease prevention. Furthermore, the RT is in a unique position to provide leadership in determining health promotion and disease prevention activities for students, faculty, practitioners, patients, and the general public.
- The AARC recognizes the need to provide and promote consumer education related to the prevention and control of pulmonary disease and to establish a strong working relationship with other health agencies, educational institutions, federal and state government, businesses, and other community organizations and to monitor such. Furthermore, the AARC supports efforts to develop personal and professional wellness models and action plans that will inspire and encourage all RT to cooperate on health promotion and disease prevention.

Effective 7/85.
Revised 3/00.

RT, Respiratory therapist.
From the American Association for Respiratory Care (AARC): Position statement (website): www.aarc.org/resources/position_statements/hpdp.html.

managed. This type of care requires refocusing on the prevention of disease by identifying risk factors and providing methods for behavioral changes. Preventative healthcare is very different from **chronic care.**

A quote from Rufus Howe is appropriate: "What a rare privilege it is to be in a position to improve the lives of others."[14a] A patient with asthma goes to the emergency department and is treated effectively and efficiently. The patient received good quality care, and, in many people's minds, the patient was "fixed." However, asthma is manageable to the point that the patient should not have to be in the emergency department. There are excellent international and national guidelines (www.GINA.org and www.NAEPP.org) that outline how to manage asthma, state the importance of patient education, and follow up with evaluating the patient inhaler technique. There are medications that control asthma and keep the patient out of this situation. Usually, the reason for the emergency visit is that the patient's asthma is not in control; this may occur because the patient is not using inhaled steroids because he or she has a poor understanding of the disease and how to manage it, because the national guidelines are not being used, or because of a combination of all these issues. Either way, this chronic disease can be better self-managed by a patient with the proper multidisciplinary education and follow-up.

The public health model attempts to reduce disease in the nation through mass education campaigns. Examples include education about the hazards of drinking and driving, tobacco use (both smokeless and smoking) education, and food labeling to indicate fat and cholesterol content. This is known as *health promotion and disease prevention*.[15] By participating in public education programs, RTs have the potential to affect the health of individuals and the population as a whole.[16] This approach is intended to look at the health disparities from infancy through to older age and to highlight opportunities to promote health and improve quality of life for all Americans.

RTs can take an active role in the development of educational materials to assist both the public and other health professionals about health promotion activities. Many medical manufacturers have also developed health promotion or education kits for a variety of diseases such as asthma, COPD, or tobacco and e-cigarettes use. These kits are generally developed with input from the medical community and from RTs. An example of an asthma program is given in Table 55.10.[12] Respiratory care educational programs need to be diligent when incorporating health promotion and disease prevention activities into all learning domains as part of their curricula.

Another specific area of health promotion that receives much attention in both hospital and public health settings is nicotine intervention. Hospitalized patients are more motivated to try to quit smoking for two reasons: the illness that resulted in the patient being in the hospital may have been made worse due to tobacco use, and hospitals have smoke-free environments. Therefore RTs should use this opportunity to promote nicotine treatments.

Nicotine intervention is a progressive, comprehensive program that incorporates a series of steps from risk identification to maintenance support. Smoking is the leading cause of preventable disease and death in the United States. January 11, 2014

TABLE 55.10 Components of an Asthma Disease Management Program

Component 1: Assessment and monitoring	Assessment: • Detailed patient history • Thorough physical examination • Spirometry to document the reversibility of airflow obstruction Monitoring: Periodic assessment and ongoing monitoring of asthma to determine if goals are being met • Minimal or no chronic and troublesome symptoms, day or night • Normal or near-normal pulmonary function • No limitations on activities • Minimal or no recurrent exacerbations of asthma • Optimal medications with minimal or no adverse side effects • Satisfaction with asthma care
Component 2: Control of the factors that contribute to asthma	Identify the allergens and irritants • House dust mites, cockroach feces, molds, and animal dander • Tobacco smoke, emissions from wood-burning stoves, strong odors and sprays, such as perfume and hairspray • Nitrogen dioxide and sulfur dioxide • Rhinitis and sinusitis • Gastroesophageal reflux disease • Viral respiratory infections • Aspirin • Sulfites Reduce exposure to the allergens and irritants, and provide medications or immunotherapy
Component 3: Pharmacologic therapy: managing asthma for the long term	Classify the asthma severity into one of the four levels based on the severity of recurrent symptoms and lung function Prescribe medications for the level of asthma • All patients with asthma need a quick-relief medication (i.e., short-acting β2-agonists) • Those with persistent asthma need daily long-term control medications to achieve control (e.g., an inhaled corticosteroid) • Start treatment in a stepwise approach (i.e., begin at a higher level to achieve rapid control; when control is achieved and sustained, cautiously step down treatment)

Component 4: Patient education for a partnership in asthma care	Patient education begins at the time of diagnosis.
	• Provide basic facts about asthma
	• Identify the roles of the medications
	• Skills: correct use of the medication delivery devices, the peak flow meter, and the symptom diary
	• Discuss environmental control measures
	• Discuss when and how to take rescue actions
	Education techniques
	• Basic facts about asthma
	  • Describe the contrast between asthmatic and normal airways
	  • Describe what happens to the airways during an asthma attack
	• Describe the roles of the medications
	  • How the medications work
	  • Long-term control: medications that prevent symptoms, often by reducing inflammation
	  • Quick relief: short-acting bronchodilators relax muscles around the airways
	Stress the importance of long-term control medications, and emphasize that the patient should not expect quick relief
	• Skills
	  • Inhaler use (patient demonstration)
	  • Spacer and holding chamber use
	  • Symptom monitoring, peak flow monitoring, and recognizing early signs of deterioration
	• Environmental control measures
	  • Identifying and avoiding indoor and outdoor environmental precipitants or exposures
	  • When and how to take rescue actions
	• Responding to changes in asthma severity (i.e., daily self-management plan and action plan)

marked the 50th anniversary of the first Surgeon General Report on smoking and health that linked smoking with lung cancer and heart disease, and the 32nd Surgeon General Report, "The Health Consequences of Smoking—50 years of progress: A report of the Surgeon General," which presents the most recent data on the consequences of smoking.[17,13] Also, in 2016, the Surgeon General's Report: E-Cigarette Use Among Youth and Young Adults is the first issued by the federal agency that comprehensively reviews the public health issue of e-cigarettes and their impact on young people.[18] This is the 33rd Report of the Surgeon General on tobacco. The Affordable Care Act's (ACA) Public Health and Prevention Fund expanded access to smoking cessation services

through most health insurance companies to include Medicaid. The ACA supports community-based programs and public education campaigns promoting prevention and helping people quit; 1.6 million smokers have tried to quit.[17,13] Safe and effective tobacco treatment enhances the success for quitting. Nicotine replacement therapies (NRT) such as nicotine gum, lozenges, or patches are available over the counter. NRT combined with behavioral therapy is more effective for tobacco cessation. Varenicline tartrate (Chantix) and bupropion (Zyban) do not contain nicotine. They are both available by prescription only.[17] Chantix interacts at the sites in the brain that are influenced by nicotine.

National, state, and local agencies, such as the American Cancer Society, the American Lung Association, and the American Heart Association offer educational materials and behavioral counseling. The educational materials that these agencies offer is available via mail, telephone, and the internet. The National Cancer Institute as part of the U.S. Department of Health and Human Services cessation initiative established a nationwide toll-free number (800-QUIT-NOW [800-784-8669]) to serve as an access point for smokers who are seeking assistance with quitting. Components of the Office of Surgeon General's tobacco cessation program is included in Tables 55.11 and 55.12.[15]

CHRONIC DISEASE MANAGEMENT AND POPULATION HEALTH

More than 190 million people have at least one chronic disease and 75 million live with two or more chronic conditions or comorbidity.[19] The key risk factors for developing a chronic disease include tobacco use, physical inactivity, poor nutrition choices, and excessive alcohol use. Also, the aging population as well as the cost of care are markedly increasing. These chronic diseases are extremely expensive and lead to unnecessary readmissions also known as **recidivism**. Short-term readmissions have always been undesirable for patients and their families. However, the Hospital Readmission Reduction Program penalizes hospitals for excessive unpreventable readmissions for diseases such as COPD and pneumonia. Hence there are financial implications for effective chronic disease management programs.

Managing chronic diseases takes more than a magic bullet, surgery, or medical rescues. They require holistic, **patient-centered care** with collaboration of an interdisciplinary team of providers (RTs, physicians, nurses, pharmacists, and other allied health providers). The team must coordinate the patient care across a continuum.

The term "**population health**" is more common and has several interpretations. The standard definition is "the health outcomes of a group of individuals, including the distribution of such outcomes within a group."[20] The people included in the population being discussed may vary depending on the situation, the organization, or the community of interest. In our hospital settings, the patient population are those individuals who use the hospital health services; in our outpatient clinics, the population are those individuals using the outpatient clinical facilities for pulmonary rehabilitation or education. Population health incorporates social determinants of health: housing, education level, economic level, race or ethnicity, and exposure to risk factors of disease. Our patients spend most of their lives outside our hospital or clinic doors and they make decisions about their health based on their culture, community, and family practices. Efforts to improve population health must include assessing the community needs, providing interventions or services for patients at risk for these chronic diseases, which may include monitoring health risk and status.

Disease management applies the best healthcare practices to a population diagnosed with a chronic illness one person at a time. The measures of health of a person with a chronic disease participating in a disease management program improves while patient satisfaction increases, mortality decreases, quality of life increases, and unnecessary medical treatment decreases, which, in turn, the cost of healthcare decreases. These disease management programs have similar components, which include a coordinated comprehensive interdisciplinary care team that has identified a process for measuring improvement. Most programs have the following attributes:

- The provision of interdisciplinary comprehensive care (i.e., health promotion, prevention, and acute care involving interdisciplinary or multidisciplinary teams—physician, RT, nurse, physical therapist (PT), occupational therapist (OT), pharmacist, and other health team members)
- A population-identification process (for a specific disease or condition)
- The use of evidence-based guidelines, protocols, and pathways
- Collaborative and coordinated components of care
- Active patient self-management and education (e.g., empowerment, behavior modification)
- Quality improvement methods to include outcomes measurement and evaluation
- The use of information technology to create a routine reporting and feedback loop

If you were interested in creating a disease management program, you would want to make sure to include these components. There are many disease management programs offered to patients with chronic diseases such as COPD, asthma, amyotrophic lateral sclerosis, and cystic fibrosis. RTs are ideal to create, coordinate, and participate as members of a disease management program. The patients whom RTs care for have chronic diseases, and these individuals need to be taught about the health risks associated with the disease, the prophylactic measures used to maintain quality health, and disease-specific respiratory therapy. For example, in a disease management program for patients with COPD, RTs would provide one-on-one counseling for tobacco cessation education (if the patient continued to use these products); discuss pulmonary rehabilitation that included exercise as well as strength and endurance training; and recognize and manage an acute situation and appropriate medication management. The RT would work with the patient to establish personal goals, including changing the person's behaviors and reducing the risks associated with the chronic disease. Outcomes such as healthcare utilization, hospital admissions, dyspnea scores, or missed school or work days, ER visits, and quality-of-life surveys would be reported for all patients with COPD. These outcome measurements are used to determine success or failure of the program for the patient population diagnosed with COPD.

TABLE 55.11 The "5 As" Model for Treating Tobacco Use and Dependence as a Chronic Disease

Ask about tobacco use	Identify and document the tobacco use status of every patient at every visit • Expand the vital signs to include tobacco use
Advise to quit	Strongly urge all tobacco users to quit Advice should be clear, strong, and personalized
Assess every tobacco user's willingness to make a quit attempt	Ask every tobacco user if he or she is willing to make a quit attempt: "Are you willing to give quitting a try?" • If the patient is willing, provide assistance • If the patient is unwilling, provide a motivational intervention • If the patient is a member of a special population (e.g., pregnant, adolescent, minority), consider providing him or her with additional information
Assist by providing counseling and medication	• Set a quit date that is ideally within 2 weeks • Tell family and friends about quitting • Anticipate challenges, including nicotine withdrawal symptoms • Remove tobacco products from the environment Recommend the use of approved medications, except when they are contraindicated or if the patient is a member of a specific population (e.g., pregnant women, smokeless tobacco users, adolescents) • Explain how the medications work to increase success with quitting and to reduce withdrawal symptoms The medications approved for this purposed by the U.S. Food and Drug Administration include the following: • Bupropion SR • Nicotine gum • Nicotine inhaler • Nicotine lozenge • Nicotine nasal spray • Nicotine patch • Varenicline Provide practical counseling (i.e., problem solving, skills training): • Abstinence: striving for total abstinence is essential (i.e., "not one puff after the quit date") • Anticipate triggers and challenges: determine how the patient will successfully overcome these (i.e., avoid the triggers) • Alcohol should be avoided because it is associated with relapse (however, reducing alcohol intake could precipitate withdrawal in alcohol-dependent persons) • Other smokers in the home: quitting is more difficult when there is another smoker in the home; patients should encourage all to quit with them or to not smoke in their presence Provide intratreatment social support • Provide a supportive clinical environment while encouraging the patient in his or her quit attempt (i.e., "My office staff and I are here to assist you") Help the patient obtain extra social support during treatment • Help the patient develop social support in his or her environment outside of the treatment by asking the patient's spouse or partner, friends, and coworkers to support the quit attempt Provide supplementary materials, including information about quit lines • Sources: Federal agencies, nonprofit agencies, national quit line network (1-800-QUIT-NOW), and local/state/tribal health departments and quit lines • Type: culturally, racially, educationally, and age appropriate for the patient • Location: readily available Recommend counseling (there are three types): Practical counseling (i.e., problem solving, skills training) • Recognize danger situations • Develop coping skills • Provide basic information Supportive treatment counseling • Encourage the patient to quit • Communicate a sense of caring and concern • Encourage the patient to talk about quitting
Arrange for follow-up contacts, either in person or via the telephone	Timing: Follow-up contact should begin soon after the quit date, preferably during the first week; a second follow-up is recommended within the first month, and follow-up should be scheduled as indicated • Actions to take during the follow-up contacts: for all patients, identify problems that have been encountered, and anticipate challenges Assess the medication use and any associated problems • Remind the patient of the support offered by quit lines • Address tobacco use at the next clinical visit • When patients have been abstinent, congratulate them on their success

TABLE 55.12 Components of a Tobacco Education Program for Those Who Are Unwilling to Quit Enhancing Motivation to Quit Tobacco: The "5 Rs"

Relevance	Encourage the patient to indicate why quitting is personally relevant and to be as specific as possible. Motivational information has the greatest impact if it is relevant to a patient's disease status or risk, to a family or social situation (e.g., having children in the home), or to health concerns, age, gender, and other important patient characteristics (e.g., prior quitting experience, personal barriers to cessation)
Risk	Ask the patient to identify potential negative consequences of tobacco use and suggest those that seem to be the most relevant to the patient. Emphasize that smoking low-tar or low-nicotine cigarettes or using other forms of tobacco (e.g., smokeless tobacco, cigars, pipes) will not eliminate these risks. Examples of risks include the following: • Acute risks: shortness of breath, exacerbation of asthma, harm to a pregnancy, impotence, infertility • Long-term risks: heart attack, stroke, lung and other cancers, chronic obstructive pulmonary disease, disability, need for extended care • Environmental risks: increased risk of lung cancer and heart disease in spouse, increased rates of smoking among children of tobacco users, sudden infant death syndrome, respiratory infections in the children of smokers
Rewards	Ask the patient to identify the potential benefits of stopping tobacco use: • Improved health • Food will taste better • Save money • Feel better • Home, car, clothing, and breath will smell better • Can stop worrying about quitting • Set an example for children • Have healthier babies and children • Reduce wrinkling and aging of skin
Roadblocks	Ask the patient to identify barriers to quitting: • Withdrawal symptoms • Fear of failure • Weight gain • Lack of support • Depression • Enjoyment of tobacco
Repetition	Repeat the motivational intervention information every time an unmotivated patient is seen

Implications for the Respiratory Therapist

Because the RT can practice as both an individual counselor and a public health advocate focused on population health, depending on the setting or circumstances, it is useful to examine the most likely settings in which the RT's health promotion and disease prevention knowledge can be put to good use.

Healthcare Institutions

Healthcare institutions in which RTs provide both health education and promotion include inpatient facilities (e.g., hospitals, skilled nursing facilities) and ambulatory care centers (e.g., physicians' offices, clinics, health insurance organizations). RTs may practice in outpatient or long-term acute care settings as well as in corporate wellness programs for staff and patients that are aimed at improving cardiopulmonary health through disease management education, which includes nutrition, medication management, and exercise (e.g., pulmonary rehabilitation, asthma management education programs).

Work Site

Healthier workers are absent from work less often; they are also more satisfied with their jobs and are more productive. This all translates into a more cost-effective workplace. RTs may find themselves involved in work-site wellness by participating in the following: (1) performing pulmonary function or blood pressure screenings; (2) developing and implementing stress management or nicotine intervention programs; and (3) consulting on policies related to smoking and occupational or environmental exposure to foreign dusts (e.g., silica, asbestos) or noxious fumes (e.g., smog).

Home

Home healthcare continues to be a rapidly growing segment of the healthcare industry. It has been proved repeatedly to be more cost-effective than hospital care. RTs can perform a wide variety of services in the patient's home, including oxygen therapy and mechanical ventilation on either a temporary or long-term basis. Generally, the focus is on prevention (i.e., preventing further decline). Patient education is of primary importance in the home so that the patient may become as self-reliant as possible (see Chapters 56 and 57).

Community

Most of the health promotion activities described earlier pertain to the individual. At the community level, the focus is on the group. Community health promotion activities provided by the RT may include the following: pulmonary function screening at health fairs, smoking cessation programs, family asthma management education programs, and COPD (i.e., better breathing) support groups. RTs who are certified in basic cardiac life-support instruction may also volunteer to perform certification in this practice for various groups.

Educational Institutions

Because many unhealthy behaviors begin during early childhood or adolescence, elementary, middle, and secondary schools are excellent places to begin health education activities. Education about smoking is one example.

Cigarette smoking is a primary risk factor that is associated with many of today's leading causes of death. Because most smoking begins during late childhood or early adolescence, schools provide the best settings in which to educate children about the dangers of tobacco. RTs are trained to provide these educational experiences. It is never too early to begin sending the antismoking message.

SUMMARY CHECKLIST

- Patient education and general approaches to health promotion are key issues in healthcare today.
- Incorporating health literacy and cultural beliefs into patient education programs affects patient compliance.
- Health literacy and cultural beliefs impact patient's decisions about their health
- Educators should use learning objectives to direct teaching strategies toward individuals or large groups of patients.
- Learning objectives call for the use of an action verb to define the performance that is expected of the patient at the end of instruction.
- Learning occurs in three domains: cognitive (knowledge), psychomotor (skills), and affective (attitudes).
- Patients tend to learn by doing. Passive participation usually does not cause a change in behavior.
- Evaluate the cognitive domain objectives with written tests. Evaluate psychomotor and affective domain objectives with a skills checklist.
- Use the teach-back method to gain an understanding of your own teaching and the patient's understanding of what was taught.
- The clinician should evaluate his or her teaching to improve.
- Population health focuses on a group of patients or people with a common disease and disease management focusing on the individual with the disease.
- The respiratory therapist can have an impact on several areas of health education and health promotion, including tobacco cessation programs, asthma education programs, pulmonary rehabilitation, and community health screenings.
- Respiratory therapists can be key players in disease management programs because of their understanding of the manifestations of the chronic cardiopulmonary diseases and their abilities to teach patients self-management with the use of the patient education tools discussed in this chapter.

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Cardiopulmonary Rehabilitation

Andres Osorio and Albert J. Heuer

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Understand and explain the definition and goals of pulmonary rehabilitation.
- Explain the rationale for exercise conditioning and psychosocial support of patients with chronic pulmonary disease.
- Understand and explain how to evaluate and select patients for pulmonary rehabilitation.
- Delineate among the different parts of a pulmonary rehabilitation program, including its implementation.
- Describe and develop educational guidelines for individuals enrolled in a pulmonary rehabilitation program.
- Understand the resources needed to develop and offer a program, including professional staffing, facilities, class size, equipment, costs.
- Review the emergence of web-based pulmonary rehabilitation.
- Describe the process and necessary documentation for reimbursement.
- Discuss the outcome measures that can be used to evaluate pulmonary rehabilitation programs.
- Understand and identify the risk factors associated with pulmonary rehabilitation.
- Understand similarities and differences between pulmonary rehabilitation and cardiac rehabilitation programs.

CHAPTER OUTLINE

KEY TERMS

6- or 12-minute walk
aerobic exercises
cardiopulmonary exercise evaluation (CPX)
comprehensive outpatient rehabilitative facilities (CORFs)
Karvonen's formula
onset of blood lactate accumulation (OBLA)
Patient Protection and Affordable Care Act (PPACA)
progressive resistance
psychosocial support
pulmonary rehabilitation
reconditioning
target heart rate
telerehabilitation
ventilatory threshold

Chronic respiratory diseases are affecting thousands of people around the world each year. This group of diseases can be defined as diseases affecting different structures of the lungs and airways. Asthma, chronic obstructive pulmonary disease (COPD), and pulmonary hypertension are part of this group. Given that COPD accounts for 6% of all deaths worldwide and almost 400,000 deaths annually are due to asthma, many organizations like the World Health Organization (WHO) are supporting programs in an effort to reduce the impact of these diseases in terms of mortality, disability, and quality of life. Not surprisingly, asthma and COPD are the main foci of these programs.[1]

Although differences in diagnoses can have an impact on treatment outcomes and survival, patients with chronic pulmonary disorders have much in common. These patients have difficulty coping with the physiologic limitations of their diseases, and these physiologic limitations cause many psychosocial problems. The result is often an unsatisfactory quality of life. The high incidence of repeated hospitalizations and the progressive disability of these patients can be reduced by well-organized programs of rehabilitative care. Hence **pulmonary rehabilitation** (PR) aims to help improve quality of life in such patients and reduce the burden of chronic respiratory diseases. In addition, with the passage of the **Patient Protection and Affordable Care Act (PPACA)** in 2010, the reduction of early hospital readmissions for various chronic diseases, including COPD, is a major concern and focus of health care today. Since PR follows hospital discharge and involves clinical monitoring and interventions, it can act as an early-warning system for patients with a deteriorating clinical status to help prevent readmissions. This chapter provides foundational knowledge regarding the goals, methods, and issues involved in providing planned programs of rehabilitation for individuals with chronic pulmonary disorders.

DEFINITIONS AND GOALS

The Council on Rehabilitation defines rehabilitation as "the restoration of the individual to the fullest medical, mental, emotional, social, and vocational potential of which he or she is capable."[2] The overall goal is to maximize functional ability and to minimize the impact the disability has on the individual, the family, and the community. The American Thoracic Society in conjunction with the European Respiratory Society characterize PR as a comprehensive intervention, based on a complete patient assessment and followed by tailored multidisciplinary therapy and education to improve the physical and emotional conditions of patients with chronic respiratory diseases and to promote adherence to healthy behaviors. The reason for the multidisciplinary approach is to have a comprehensive, goal-oriented plan of care to reduce symptoms, increase exercise tolerance, and promote independence.[3] It is important to highlight that PR does not reverse or stop progression of the disease. However, it can help address deconditioning and lack of ongoing disease management associated with chronic lung disease, therefore, improving the patient's overall quality of life.[3]

HISTORICAL PERSPECTIVE

PR is not a new concept. In 1952, Barach and colleagues recommended reconditioning programs for patients with chronic lung disease to help improve their ability to walk without dyspnea.[4] Decades passed before clinicians paid any attention to this concept because oxygen therapy and bed rest were the modality of treatment at the time. The lack of reconditioning programs resulted in a vicious cycle of skeletal muscle deterioration, progressive weakness and fatigue, and increasing levels of dyspnea.

In 1962, published results confirmed Barach's insight into the value of reconditioning.

They observed that patients with COPD who participated in physical reconditioning exhibited lower pulse rates, respiratory rates, minute volumes, and carbon dioxide (CO_2) production during exercise, without significant improvements in pulmonary function.[5] Soon thereafter, it was shown that reconditioning could improve both the efficiency of motion and O_2 consumption in patients with COPD.[6]

In 2003, Bourbeau and colleagues provided evidence that PR can reduce hospitalizations by 40% for patients with COPD exacerbations and unscheduled physician appointments by 59% when proper education is available. As a result of this and other related research, in 2006, the American College of Chest Physicians (ACCP) and the American Association of Cardiovascular and Pulmonary Rehabilitation (AACVPR) released their evidence-based guidelines relating to PR aimed at improving the way the programs are designed, implemented, and evaluated through patient outcomes.[7-12] It is currently understood that PR benefits patients with chronic obstructive and restrictive pulmonary disease in several ways. When combined with smoking cessation, optimization of blood gas results (arterial pO_2, pCO_2, and pH), and proper medication use, PR offers the best treatment option for patients with symptomatic pulmonary disease. The latest research indicates that PR decreases healthcare utilization and hospital stays, thus reducing health care cost.[8]

PHYSICAL AND PSYCHOSOCIAL BASIS

Rehabilitation must focus on the patient as a whole and not solely on the underlying disease. For this reason, effective PR programs combine knowledge from both the clinical and the social sciences. Knowledge from the clinical sciences can help quantify the degree of physiologic impairment and establish outcome expectations for reconditioning. Application of the social sciences is helpful in determining the psychological, social, and vocational impact of the disability on the patient and family and in establishing ways to improve the patient's quality of life.

Physical Reconditioning

At rest, an individual maintains homeostasis by balancing external, internal, and cellular respiration. Physical activity, such as **aerobic exercises**, increases energy demands. To maintain homeostasis during exercise, the cardiorespiratory system must keep pace. Fig. 56.1 shows how the body responds to exercise. Ventilation and circulation increase to supply tissues and cells with

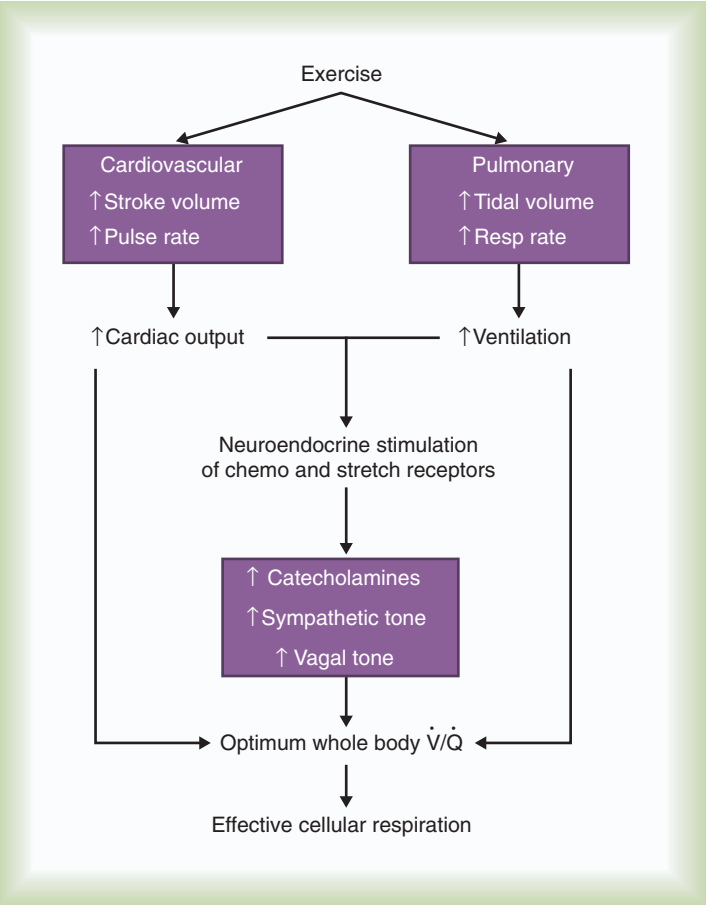

Fig. 56.1 The Body's Response to Increased Levels of Activity Such as Exercise.

additional O_2 and to eliminate the higher levels of CO_2 produced by metabolism.

As depicted in Fig. 56.2, as exercise intensity increases, both O_2 consumption and CO_2 production increase in a manner closely related to one another. If the body cannot deliver sufficient O_2 to meet the demands of energy metabolism, blood lactate levels increase above normal. In exercise physiology, this point is called the **onset of blood lactate accumulation (OBLA)**. As this excess lactic acid is buffered, CO_2 levels increase and the stimulus to breathe increases. The result is an abrupt upswing in both CO_2 and $\dot{V}_E$ (referred to as the **ventilatory threshold**). Beyond this point, metabolism becomes anaerobic, the efficiency of energy production decreases, lactic acid accumulates, and fatigue sets in.

COPD patients with impaired pulmonary function often have limited exercise capacity. Their high rate of CO_2 production during exercise results in respiratory acidosis and shortness of breath that is out of proportion to the level of activity. In addition, as ventilation increases, the rate of O_2 consumption in a patient with COPD increases significantly (Fig. 56.3). Together, these factors limit patient tolerance for any significant increase in physical activity.

PR must include physical **reconditioning**, which involves strengthening essential muscle groups, improving overall O_2 utilization and enhancing the body's cardiovascular response to physical activity as noted in Box 56.1.

Psychosocial Support

If the overall goal of PR is to improve the quality of patients' lives, physical reconditioning alone is insufficient. Psychosocial indicators are generally good predictors of morbidity in patients with COPD. As a result, a plan of care should be designed to help patients and caregivers to develop the consciousness and the psychosocial adjustment of the disease process, which is important for a successful diseases management.[13]

There is a well-established relationship between physical, mental, and social well-being in humans. However, emotional states such as anxiety and stress can aggravate an existing physical problem. The diagnosis of COPD can negatively impact an individual, especially during the late stages of the disease process, when physical limitations are more evident. There are some psychosocial challenges shared by patients with respiratory diseases, but individual differences like comorbidities and **psychosocial support** may change the impact for each particular person. Since depression, anxiety, and other disorders can negatively impact the outcome of a plan of care, early recognition of these symptoms is vital in the management of chronic diseases.[14]

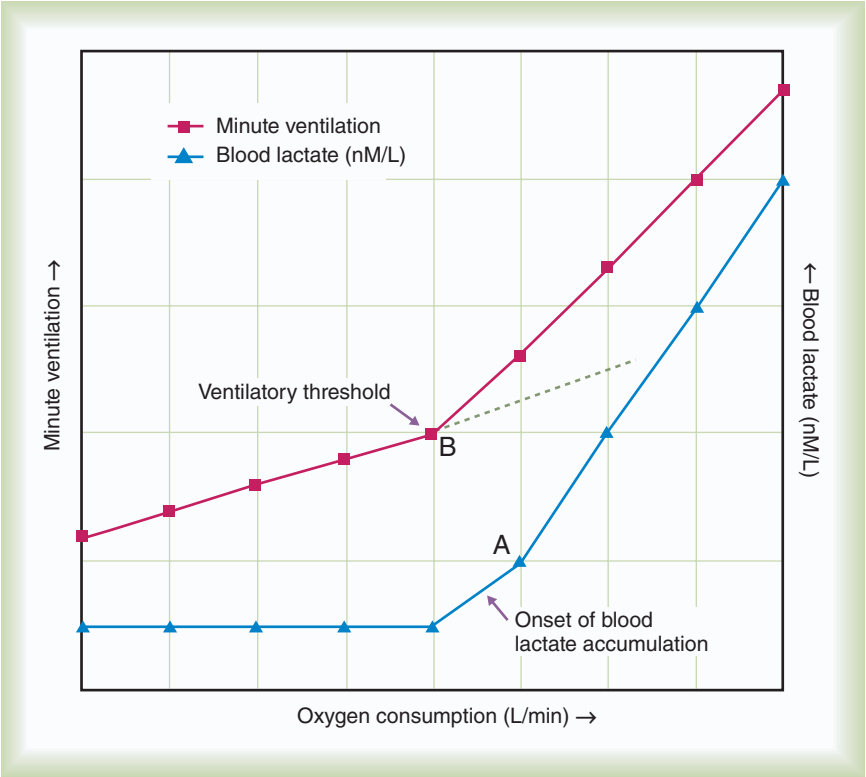

Fig. 56.2 Minute ventilation, blood lactate, CO_2 production, and O_2 consumption during graded exercise to maximum. The dashed line represents the linear extrapolation between $\dot{V}E$ and $\dot{V}O_2$ during submaximal exercise. Point A represents OBLA. At the same time, $\dot{V}E$ and $\dot{V}CO_2$ "break" from their extrapolated rate of increase and abruptly rise (point B). This is referred to as the ventilatory threshold. (Modified from McArdle WD, Katch FL, Katch VL: *Exercise Physiology: energy, nutrition and human performance*, ed 6, Baltimore, 2007, Williams and Wilkens.)

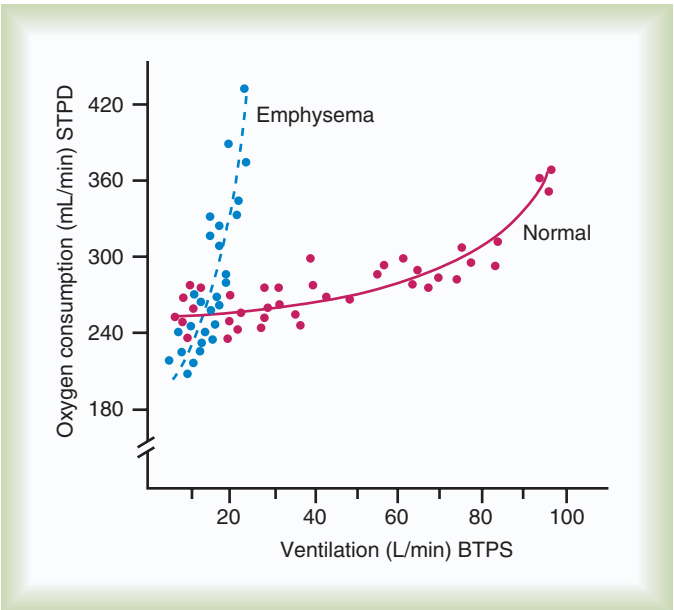

Fig. 56.3 Changes in O_2 consumption with increasing ventilation in a normal subject and in a patient with emphysema. *BTPS*, Body temperature, body pressure saturated; *STPD*, volume of dry gas at 0°C and 760 mm Hg atmospheric pressure. (Modified from Cherniack RM, Cherniack L, Naimark A: *Respiration in health and disease*, ed 3, Philadelphia, 1984, Saunders.)

BOX 56.1 Benefits From Exercise Reconditioning

Accepted Benefits

Increased physical endurance
Increased maximum O_2 consumption
Increased activity levels with:
- Decreased ventilation
- Decreased $\dot{V}O_2$
- Decreased heart rate
- Increased ventilatory threshold
- Improved blood lipids

Potential Benefits

Increased sense of well-being
Improved secretion clearance
Increased hypoxic drive
Improved cardiac function

Unproven Benefits

Prolonged survival
Improved pulmonary function test results
Decreased pulmonary artery pressure
Improved blood gases
Change in muscle O_2 extraction
Change in step desaturation

Data from references 17 and 26.

Because patients are fearful of economic loss and death, they can develop hostility toward the disease and toward the people around them. In terms of social function, the physiologic impairment of chronic lung disease combined with other variables can severely restrict a patient's ability to perform routine tasks requiring physical exertion. Moreover, patients' potential loss of confidence in their ability to care for themselves reduces feelings of dignity and self-worth.

It is here that the link between the physical reconditioning and psychosocial support components of rehabilitation becomes most evident. By increasing exercise tolerance and enhancing the body's cardiovascular response to physical activity, patients can develop a more independent and active lifestyle, thus enhancing their psychosocial well-being. For some patients, simply being able to walk to the market or play with their grandchildren can contribute to a greater feeling of social satisfaction. For others, physical conditioning may allow a return to near-normal levels of activity, including vocational pursuits.

Many patients disabled by pulmonary disease are in their economically productive years and are anxious to return to economic self-sufficiency. For these patients, occupational retraining and job placement are key ingredients of a good rehabilitation program.

STRUCTURE OF A PULMONARY REHABILITATION PROGRAM

Program Qualification

The Centers for Medicare & Medicaid Services (CMS) has provided guidelines for patients under Medicare to qualify for this program. Every healthcare insurance has its own guidelines and requirements, but they often follow CMS guidelines. Patients need to have a treating physician for the chronic respiratory disease, and the initial order is sufficient for the first 30 days of enrollment. The referring physician must certify that the patient has had a physical examination within 90 days of initial referral. The physician needs to be specific on the type of service ordering, including frequency and duration of the service. If a patient requires PR services after the certification date, the physician must certify that the patient remains capable and the benefits from continuing in the program.[15]

Documentation is a key factor for qualification and reimbursement for PR. It needs to show that a multidisciplinary plan is appropriate for the patient and has measurable and potentially obtainable objectives.[16]

Program Goals and Objectives

PR programs vary in their design and implementation but generally share common goals (Box 56.2). These general goals assist planners in formulating more specific program objectives. When determining objectives, both patients and members of the rehabilitation team should have input. These objectives should always be realistic and stated in measurable terms, because this helps monitor progress towards achieving outcomes and, ultimately, the success of the PR program. Depending on the specific needs of the participants, program objectives can include the following:

BOX 56.2 Common Goals for Pulmonary Rehabilitation Programs

- Control of respiratory infections
- Basic airway management
- Improvement in ventilation and cardiac status
- Improvement in ambulation and other types of physical activity
- Reduction in overall medical costs
- Reduction in hospitalizations
- Psychosocial support
- Occupational retraining and placement (when and where possible)
- Family education, counseling, and support
- Patient education, counseling, and support

- Development of diaphragmatic breathing skills
- Review of stress management and relaxation techniques
- Involvement in a daily physical exercise regimen to condition both skeletal and respiratory-related muscles
- Adherence to proper hygiene, diet, and nutrition
- Smoking cessation (if applicable)
- Proper use of medications, O_2, and breathing equipment (if applicable)
- Application of airway clearance techniques (when indicated)
- Participation in group support
- Provisions for individual and family counseling

When program objectives are specifically defined and structured in a measurable way, strategies should be developed to help ensure they are achieved. For example, if smoking cessation is an objective for a PR participant, then strategies such as enrollment in smoking cessation programs, the use of nicotine replacement and other medications should use and progress towards reducing and eliminating daily tobacco use should be closely monitored.

RULE OF THUMB

When program objectives are established for PR participants, they should be relevant, realistic, and measurable. In addition, strategies should be adopted to help participants achieve such objectives, and progress should be closely monitored.

Patient Evaluation and Selection

Patient selection requires comprehensive evaluation and testing. Before beginning a PR program, clinicians need to define and establish criteria for selection. They need to be aware of the patient's comorbidities and the anticipated effects of exercise on the patient's overall status as well as laboratory results.[17]

Patient Evaluation

PR programs must have a qualified physician medical director, usually a pulmonologist, to provide overall direction for the program and to help screen prospective patients.[18] Because PR is a supervised program under Medicare regulations, some programs have a supervising physician in addition to the medical director. This physician must be physically available

and accessible for consultation and emergencies at all times when the program is being provided. Non–hospital-based settings must prove compliance with the supervising physician by keeping records of policies and procedures, calendars, schedule or call logs, and records must be available for inspection by Medicare staff. [19]

Although many PR participants may share the same diagnosis and comorbidities, it is important to understand that every patient is different and that everyone requires a personalized plan of care. The patient evaluation is the foundation for a thorough plan of care, and it begins with a complete patient history and addresses medical, psychological, vocational, and social elements. A well-designed patient questionnaire and interview form often assist with this step. The patient history should be followed by a complete physical examination (see Chapter 16). A recent chest x-ray, resting electrocardiogram (ECG), complete blood count, serum electrolytes, and urinalysis provide additional information about the patient's current medical status (see Chapter 17).

To determine the patient's cardiopulmonary status and exercise capacity, both pulmonary function testing and a CPX should be performed. Pulmonary function testing includes assessment of pulmonary ventilation, lung volume determinations, diffusing capacity (DLCO). Spirometry is an essential tool during this assessment, and it should include before and after bronchodilator use to determine the severity of the airflow limitation and the stage of the chronic pulmonary disease (see Chapter 20).[20]

The **cardiopulmonary exercise evaluation (CPX)** serves two key purposes in PR. First, it is important to patient evaluation because it quantifies the patient's initial exercise capacity. This quantification provides the basis for the exercise prescription (including setting a **target heart rate**) and yields the baseline data for assessing a patient's progress over time. In addition, the CPX helps determine the degree of hypoxemia or desaturation that can occur with exercise; this provides the objective basis for titrating O_2 therapy during the exercise program. The CPX plays an important role by providing a reliable and accurate functional assessment of the patient, the lungs, cardiac function, and the muscles contributing to exercise performance. However, the CPX requires specialized equipment and as a result, is often underutilized by many clinicians despite its advantages.[21] As an alternative to the CPX, the European Respiratory Society and the American Thoracic Society have published the technical standard for field walking testing of patients with chronic respiratory diseases to guide practitioners in implementing exercise capacity evaluations. The technical standard helps to identify exercise capacity and exercise performance limitations, among other factors, and can be used as a predictor of possible hospitalizations, patient's response to treatments or therapies and survival. [22]

RULE OF THUMB

The cardiopulmonary exercise stress test (CPX) is an extremely valuable tool in screening patients for suitability for PR program participation. However, due to cost and other practical limitations associated with CPX, field exercise walking testing may be considered as an alternative for evaluating such patients.

BOX 56.3 Common Physiologic Parameters Measured During Exercise Evaluation

- Blood pressure
- Heart rate
- Electrocardiogram
- Respiratory rate
- Arterial blood gases/O_2 saturation
- Maximum ventilation ($\dot{V}E_{max}$)
- O_2 consumption (either absolute $\dot{V}O_2$ or METS)
- CO_2 production ($\dot{V}E/\dot{V}CO_2$)
- Respiratory quotient (RQ)
- O_2 pulse ($\dot{V}O_2$:heart rate)

METS, Metabolic equivalents of O_2 consumption.

Modified Borg Dyspnea Scale (With Dyspnea Descriptors)

The Modified Borg Dyspnea Scale (MBS) is another assessment tool used to evaluate patients with chronic lung disease. It is used to classify the level of dyspnea as perceived by such patients and can therefore grade the level of dyspnea by assigning the number next to the words that best describe their shortness of breath.

10	Maximal (worst possible you can imagine)
9	Very, very severe
8	Very, very severe
7	Very severe
6	Very severe
5	Severe
4	Somewhat severe
3	Moderate
2	Slight
1	Very slight
0.5	Very, very slight (just noticeable)
0	None at all

RULE OF THUMB

The Modified Borg Dyspnea scale can be quite useful in quantifying the level of dyspnea in COPD and other potential PR candidates.

The exercise evaluation procedure involves serial or continuous measurements of several physiologic parameters during various graded levels of exercise on either an ergometer or a treadmill (Box 56.3). To allow for steady-state equilibration, these graded levels are usually spaced at 3-minute intervals. Work levels are increased progressively until either: (1) the patient cannot tolerate a higher level, or (2) an abnormal or hazardous response occurs.

Blood gas and arterial oxygen saturation measurements are obtained at rest and at peak exercise. If the peak exercise puncture is unsuccessful, a sample drawn within 10 to 15 seconds of test termination usually suffices. Pulse oximetry is used to monitor and to warn clinicians of gross desaturation events during testing, including the patient's response to supplemental O_2 during exercise.

Relative contraindications to exercise testing include the following:

- Inability or unwillingness of the patient to perform the test
- Severe pulmonary hypertension or cor pulmonale
- Known electrolyte disturbances (hypokalemia, hypomagnesemia)
- Resting diastolic blood pressure greater than 110 mm Hg or resting systolic blood pressure greater than 200 mm Hg
- Neuromuscular, musculoskeletal, or rheumatoid disorders exacerbated by exercise
- Uncontrolled metabolic disease (e.g., diabetes)
- SaO_2 or SpO_2 less than 85% with the subject breathing room air
- Untreated or unstable asthma
- Angina with exercise
- Severe aortic stenosis

Exercise evaluation also can help differentiate among patients with primary respiratory or cardiac limitations to increased work capacity. Table 56.1 summarizes these key similarities and differences. Besides helping to differentiate between the underlying cause of exercise intolerance, test results can assist in placing patients in the appropriate type of rehabilitation program. For example, patients with critical cardiac and respiratory complications should receive cardiac rehabilitation before starting a pulmonary program.

To minimize patient risk during exercise evaluation, certain safety measures are implemented. First, the patient should undergo a physical examination just before the test, including a resting ECG. Second, a qualified physician or advanced practitioner (e.g., nurse practitioner or physician assistant) should be present throughout the entire test. Third, emergency resuscitation equipment (cardiac crash cart with monitor, defibrillator, O_2, cardiac and respiratory drugs, suction equipment, and airway equipment) must be readily available. Fourth, staff conducting and assisting with the procedure should be certified in basic and advanced life-support techniques. Last, the test should be terminated promptly at the patient's urging or with any adverse effect.

With regard to test preparation, patients should fast for 8 hours before the procedure. If the purpose of the test is to formulate an exercise prescription, the patient can take his or her regular medications. The patient should wear comfortable, loose-fitting clothing and footwear with adequate traction for treadmill or ergometer activity. Test conditions should be as standardized as possible to allow for comparison of results before and after rehabilitation periodically from year to year as the patient is treated and followed.

Patient Selection

Patients most likely to benefit from participation in PR are patients with persistent symptoms caused by COPD who have low maximum O_2 uptakes at baseline. Since PR is a complementary therapy for patients receiving pharmacotherapy, it should be a part of the hospital's discharge planning process after an exacerbation of the existing chronic respiratory condition. The feasibility of rehabilitation should be reviewed with the patient, physician, and respiratory therapist (RT) to educate patients and families on the benefits of the program in improving health-related quality of life and survival of people with COPD. There are studies showing that PR should be standard in the management and treatment of COPD patients.[23] Other indications for PR are listed in Box 56.4. Regardless of underlying conditions, candidates for this program should have stopped smoking. Active smokers should enroll in a smoking cessation program before starting PR. Patients are excluded from the program activities if: (1) concurrent problems limit or preclude participation in exercise, or (2) they have a very limited life expectancy (e.g., with metastatic malignancy, etc.; see Box 56.4).

Objectively, candidates for PR generally fall into one of the following groups:[24]

TABLE 56.1 Exercise Parameters Distinguishing Cardiac and Ventilatory (Chronic Obstructive Pulmonary Disease) Limitations

Parameter[a]	Cardiac[b]	COPD[b]
Maximum $\dot{V}O_2$	↓	↓
Maximum HR	N or ↓	↓
O_2 pulse	↓	N
Maximum $\dot{Q}$	↓	↓
$\dot{Q}/\dot{V}O_2$	↓	N
PaO_2	N	↓
$PaCO_2$	↓	↑
$\dot{V}E_2/\dot{V}CO_2$	↑	↑
VT	↓	N

[a] *HR*, Heart rate; $\dot{Q}$, cardiac output; $\dot{V}E_2/\dot{V}CO_2$, ratio of minute ventilation to CO_2 production; $\dot{V}O_2$, oxygen consumption; *VT*, ventilatory threshold.
[b] *N*, Normal; ↑, increased; ↓, decreased.
Modified from Lane EE, Walker JF: *Clinical arterial blood gas analysis*, St Louis, 1987, Mosby.

BOX 56.4 Indications and Contraindications for Pulmonary Rehabilitation

Indications

Symptomatic patients with COPD—usually GOLD stage III (severe) and stage IV (very severe), but stage II (moderate) may also be considered
Patients with bronchial asthma and associated bronchitis (asthmatic bronchitis)
Patients with combined obstructive and restrictive ventilatory defects
Patients with chronic mucociliary clearance problems
Patients with exercise limitations because of severe dyspnea

Contraindications

Cardiovascular instability requiring cardiac monitoring (consider cardiac rehabilitation)
Malignant neoplasms involving the respiratory system
Severe arthritis or neuromuscular abnormalities (a relative contraindication—refer to physical therapy for case-by-case review)

- Patients in whom there is a respiratory limitation to exercise resulting in termination at a level less than 75% of the predicted maximum O_2 consumption ($\dot{V}O_{2max}$)
- Patients in whom there is significant irreversible airway obstruction with a forced expiratory volume in 1 second (FEV_1) of less than 2 L or an $FEV_{1\%}$ (ratio of FEV_1 to forced vital capacity [FVC]) of less than 60% (refer to the Global Initiative on Obstructive Lung Disease [GOLD] standards for COPD severity)
- Patients in whom there is significant restrictive lung disease with a total lung capacity (TLC) less than 80% of predicted and single breath carbon monoxide diffusing capacity (DL_{CO}) less than 80% of predicted
- Patients with pulmonary vascular disease in whom the single breath DL_{CO} is less than 80% of predicted or in whom exercise is limited to <75% of maximum predicted O_2 consumption (predicted $\dot{V}O_{2max}$)

MINI CLINI

Patient Selection for Pulmonary Rehabilitation

Problem

A patient is being evaluated for possible inclusion in a pulmonary rehabilitation program. The patient undergoes a complete history and physical examination and pulmonary function testing, arterial blood gas analysis, and exercise evaluation. During the exercise test, the patient develops severe hypertension and premature ventricular contractions. The physician recommends that the patient be admitted to PR and prescribes a modified exercise routine. The RT performing the test disagrees. How should the RT proceed?

Solution

The RT should contact the department medical director for intervention. Although this patient could possibly be admitted to PR, there is a high risk that some type of adverse response might occur during the exercise component of the program. The best direction would be to treat the cardiac abnormalities first. After identifying the causes of the exercise-induced hypertension and arrhythmia, these problems can be properly treated. When the patient's cardiac status has been stabilized, the patient may be admitted to PR and safely participate in and complete the program.

Program Design

A good design helps achieve specific programming objectives with the selected group of participating patients. Key design considerations involve both format and content, with an emphasis on patient reconditioning and education.

Format

Programs can use either an open-ended or a closed design, with or without planned follow-up sessions. With an open-ended format, patients enter the program and progress through it until they achieve certain predetermined objectives. There is no set time frame. Depending on his or her condition, needs, motivation, and performance, an individual patient can complete an open-ended program over weeks or months. This format is good for self-directed patients or patients with scheduling difficulties. It also may be the best format for patients requiring individual attention. The major drawback of the open-ended format is the lack of group support and involvement. In addition, obtaining insurance reimbursement may be challenging when the program is open-ended.

The more traditional closed design uses a set time period to cover program content. These programs usually run 6 to 16 weeks, with classes meeting one to three times a week. Class sessions usually last 1 to 2 hours. Presentations are more formal, and group support involvement is encouraged. A major drawback of the closed program format is that the duration of the rehabilitation is determined by a predetermined schedule rather than by achievement of the goals.

Ultimately, insurance coverage may dictate the duration of the rehabilitation program.[25] It is important to highlight that PR may represent a cost savings for insurance companies by decreasing healthcare cost and readmissions.

There are several studies showing the benefits of PR and its long-term improvements when programs are extended. Continuation of supervised exercise training after initial PR will prevent decreasing exercise capacity.[26] Follow-up must be ongoing and available to all patients who complete the program. Frequently, this essential element of the process is difficult, especially when it is not covered by most insurance plans, but program coordinators must ensure that it is routinely scheduled. Follow-up or reinforcement could be open-ended (available during regular rehabilitation sessions and offering open attendance) or could be scheduled weekly, monthly, bimonthly, or quarterly. The important thing is to have some type of follow-up available.[27,28]

Content

The content of the rehabilitation program usually combines physical reconditioning with education activities (Table 56.2). Programs providing reconditioning or education alone are unlikely to be effective.

As shown in Table 56.2, the ideal rehabilitation session should last about 2 hours. Group size, available equipment, and group interaction also dictate session length. Patients should be advised to arrive 10 to 15 minutes before a scheduled session to allow for informal group interaction and support. Classes should begin on time and conclude promptly as scheduled. Educational presentations should be brief and to the point. Audiovisual aids or live demonstrations can enhance patient understanding and

TABLE 56.2 Sample Pulmonary Rehabilitation Session (Good)

Component	Focus	Time Frame
Educational	Welcome (group interaction)	5 min
	Review of program diaries (activities of past week)	20 min
	Presentation of educational topic	20 min
	Questions, answers, and group discussion	15 min
Physical reconditioning	Physical activity and reconditioning	45 min
	Individual goal setting and session summary	15 min
Total session		120 min (2 h)

compliance. To facilitate patient understanding, the program should be explained in plain language and avoid technical terms whenever possible. The medical staff should be aware of possible language barriers and offer educational materials in different languages when possible and should be available to facilitate understanding. A folder or notebook to record program activities and progress and gather handout materials should be maintained by each patient.

Physical Reconditioning

The physical reconditioning component of the program consists primarily of an exercise prescription with a target heart rate based on the results of the patient's initial exercise evaluation. For most patients, an initial target heart rate may be set using **Karvonen's formula** (see accompanying Rule of Thumb) or can be estimated as 20 beats/min greater than resting rate. Because of the severity of ventilatory impairment, some patients may begin exercise reconditioning without a prescribed target heart rate.

> **RULE OF THUMB**
> To set a target heart rate for patient exercise, use Karvonen's formula:
>
> $$\text{Target heart rate} = [(\text{MHR} - \text{RHR}) \times (50\% - 70\%)] + \text{RHR}$$
>
> where MHR is maximum heart rate at limit of exercise tolerance and RHR is resting heart rate.
>
> A good target exercise heart rate for a patient with COPD with MHR of 150 beats/min and RHR of 90 beats/min would be $[(150 - 90) \times 0.60] + 90 = 126$ beats/min.

Typically, the exercise prescription includes the following four related components[29,30]:

1. Lower extremity (leg) aerobic exercises
2. Timed walking (**6- or 12-minute walk**)
3. Upper extremity (arm) aerobic exercises
4. Ventilatory muscle training

To ensure success with physical reconditioning, patients must actively participate both at the rehabilitation facility and at home. While exercising, such patients should be monitored with pulse oximetry. Blood pressure measurements may also be made, but these are usually done at the start and end of each session unless a patient's condition dictates otherwise. In addition, exercise sessions should be upbeat.

To ensure compliance with the program and progress in achieving goals and objectives, a daily log or diary sheet is completed (Fig. 56.4). These log or diary forms are reviewed each time the patient attends a session. Based on this information, further individualized reconditioning goals are set.

> **RULE OF THUMB**
> Patients participating in PR should maintain a log or diary of related activities in order to monitor compliance and progress.

Lower extremity exercises may include either walking or bicycling. Patients can walk on a stationary treadmill (with set goals for distance or time and grade) or on a flat, smooth surface. Patients can bicycle on an exercise cycle. With the treadmill or stationary bicycle, patients are required to cover a certain distance or duration every day that they are in the program. Commonly, the duration is set to 30 min daily, with patients encouraged to increase both their distance and equipment tension or resistance as tolerated. Patients with significant orthopedic disabilities can participate in aerobic aquatic exercises.

Walking also improves overall conditioning; this usually takes the form of a 6- or 12-min walk performed once a day, depending on the patient's condition and tolerance. These walk exercises are a convenient way for patients to carry out a well-defined amount of activity with increasing vigor and results over a number of weeks. During the 6 or 12 min, patients should walk on flat ground for as far as possible. If dyspnea occurs, they should stop and rest, with the rest time included as part of the time interval. After resting briefly, they should try to continue walking at a comfortable pace. The objective is to walk as far as possible during the allotted time. Landmarks such as telephone poles, city blocks, or actual distance measures can be used to quantify progress. Walking indoors is an alternative during adverse weather conditions.

Aerobic upper extremity exercises improve rehabilitation outcomes for patients whose regular activities involve lifting or

Patient Log   Week # _______

Day	Flow Resistive Device	6-min or 12-min Walk	Exercycle	Other Activity	Remarks
	Setting ________ Duration ________	Distance ________ No. of stops ________	Distance _____ Duration _____	Type _______ Duration ____	
	Setting ________ Duration ________	Distance ________ No. of stops ________	Distance _____ Duration _____	Type _______ Duration ____	
	Setting ________ Duration ________	Distance ________ No. of stops ________	Distance _____ Duration _____	Type _______ Duration ____	
	Setting ________ Duration ________	Distance ________ No. of stops ________	Distance _____ Duration _____	Type _______ Duration ____	
	Setting ________ Duration ________	Distance ________ No. of stops ________	Distance _____ Duration _____	Type _______ Duration ____	
	Setting ________ Duration ________	Distance ________ No. of stops ________	Distance _____ Duration _____	Type _______ Duration ____	
	Setting ________ Duration ________	Distance ________ No. of stops ________	Distance _____ Duration _____	Type _______ Duration ____	

Fig. 56.4 Sample log or diary form on which a patient in a pulmonary rehabilitation program records daily physical reconditioning activities and exercises.

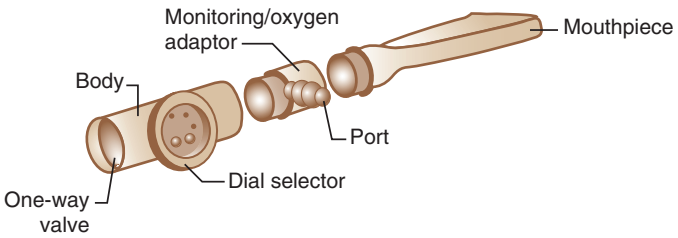

Fig. 56.5 Flow-Resistive Breathing Device.

raising the arms.[29] It is beneficial to combine upper and lower extremity exercises since they can improve exercise tolerance, provide better quality of life, increase tolerance of daily activities, and even reduce the risk of death in COPD patients.[31]

Arm ergometers or rowing machines are available for this purpose; however, simple calisthenics using either a broomstick or free weights (by prescription and with training) are a satisfactory alternative. Upper body endurance is generally more limited, with many patients capable of only 2 to 3 min of daily activity to start. This limitation is usually related to the fact that patients may revert to using accessory muscles for breathing while doing the upper body exercise. Patients need to breathe diaphragmatically and perform the exercises at the same time. Arm exercises should get progressively longer, up to 20 min if possible. Upper body conditioning helps patients perform numerous useful activities at home and can increase overall physical endurance.

Inspiratory muscle training in patients with COPD provides great clinical results by increasing functional exercise capacity, improving quality of life, and decreasing dyspnea.[32]

Ventilatory muscle training is based on the concept of **progressive resistance**. By imposing progressively greater loads on the inspiratory muscles (mainly the diaphragm) over time, the patient's strength and endurance should increase. These improvements should increase the patient's exercise tolerance.

Fig. 56.5 shows a typical inspiratory resistance breathing device. The device is an adjustable flow resistor with a one-way breathing valve. The inspiratory load is created by forcing the patient to inhale through a restricted orifice. Varying the size of this orifice varies the inspiratory load, as do changes in the patient's inspiratory flow. During expiration, gas flows unimpeded out the one-way exhalation valve. Other devices are also available. One model replaces the variable-size orifice with an adjustable spring-loaded valve. This valve ensures a constant load regardless of how quickly or slowly the patient breathes.

Because variations in breathing strategy during ventilatory muscle training can affect outcomes, proper patient evaluation, training, and follow-up are required. The RT initially measures the patient's maximum inspiratory pressure (PI_{max}) using a calibrated pressure manometer. The RT next compares the patient's maximum with established norms as noted in Table 56.3. This preliminary measure of inspiratory pressure helps to establish initial loads and provides the basis for the subsequent monitoring of patient progress.

Before beginning ventilatory muscle training, the patient should assume a position that relaxes the abdominal muscles, such as the position used for cough training. If using a flow-resistive device, the RT begins at the maximum orifice setting,

TABLE 56.3 Normal Maximum Inspiratory Pressure by Age and Sex

AGE GROUP (YEAR)	PI_{MAX} FROM RESIDUAL VOLUME ($CM\ H_2O$), MEAN ± SD	
	Male	Female
9–18	96 ± 35	90 ± 25
19–50	127 ± 28	91 ± 25
51–70	112 ± 20	77 ± 18
>70	76 ± 27	66 ± 18

From Rochester DF, Hyatt RE: Respiratory muscle failure, *Med Clin North Am* 67:573, 1983.

while measuring the inspiratory pressure generated through monitoring using the O_2 adapter (a second adapter may be needed if the patient is receiving supplemental O_2). The RT encourages the patient to breathe slowly through the device at a rate no greater than 10 to 12 breaths/min. If the patient's inspiratory pressure is less than 30% of the measured PI_{max}, the next smaller orifice is selected, with this procedure repeated until the 30% effort is consistently achieved.

At this point, the RT instructs the patient to exercise with the device in one or two regular daily sessions lasting 10 to 15 minutes. As the level of resistance becomes more tolerable over time, the patient should progressively increase the session duration up to 30 minutes. A self-maintained log of treatment times can help motivate the patient and assist the RT in subsequent progress monitoring.

Educational Component

The educational portion of the program covers topics that are both useful and necessary for the patient to achieve the goals of the plan of care (Table 56.4). Other topics can be included, depending on the program schedule, but in terms of relative importance, the ones listed in Table 56.4 generally have the highest priority.

These topics should be presented in an orderly, coherent fashion using supplementary audiovisual tools and demonstrations, where appropriate. Team members should allocate sufficient time for the class sessions themselves and for setup and breakdown of equipment.

The program facilitator or leader must ensure that sessions begin on time and encourage maximum participation by each patient. If available, health care professionals such as dietitians, occupational therapists, physical therapists, and psychologists should be invited to present their respective topics and discuss the subject matter with the group. In addition to technical knowledge, session leaders must possess group facilitation skills and be able to motivate patients to participate both in class and at home and to adhere to program guidelines.

Breathing control methods. Breathing control methods serve as the cornerstone for the physical reconditioning effort. Through structured educational sessions, patients can learn how to control their breathing efforts to ensure maximum result (ventilation) at a minimum of effort (energy expenditure). Diaphragmatic

TABLE 56.4 Typical Educational Topic Schedule for a 12-Week Pulmonary Rehabilitation Program

Session (Week)	Topic(s)	Recommended Facilitator(s)
1	Introduction and welcome; program orientation	Program administrator or rehabilitation team
2	Respiratory structure, function, and pathology	Physician or RT
3	Breathing control methods	PT or RT
4	Relaxation and stress management	Clinical psychologist
5	Proper exercise techniques and personal routines	PT or RT
6	Methods to aid secretion clearance (bronchial hygiene)	PT or RT
7	Home oxygen and aerosol therapy	RT
8	Medications—their use and abuse	Pharmacist, physician, or nurse practitioner
9	Medications—use of MDIs and spacers	RT
10	Dietary guidelines and good nutrition	Dietitian or nutritionist
11	Recreation and vocational counseling Activities of daily living	Occupational therapist
12	Follow-up planning and program evaluation Graduation	Rehabilitation team

MDIs, Metered dose inhalers; *PT*, physical therapist; *RT*, respiratory therapist.

breathing with pursed lips helps to accomplish this, but this technique requires education and daily practice on the part of the patient and continued reinforcement throughout the entire program by the group facilitator. Eupnea, another name used for deep breathing or diaphragmatic breathing, helps to use the diaphragm correctly in patients suffering from air trapping from pulmonary diseases like COPD. There are different ways to perform this technique; it can be performed lying down, sitting in a chair, or standing. The main goal of this respiratory technique is to control the diaphragm during normal breathing to decrease the work of breathing, use less oxygen during physical activities, and decrease energy consumption, which improves exercise tolerance.[33]

The COPD Foundation recommends the following steps for diaphragmatic breathing:

1. Place one hand on your abdomen. Place one hand on your upper chest.
2. Focus your breathing on your abdomen.
3. As you breathe out, the hand on your abdomen should lower.
4. As you breathe in, the hand on your abdomen should rise.
5. Breathe in through the nose. Breathe out slowly through pursed lips.
6. Practice this 2 to 3 times a day for 5 to 10 minutes. Start by doing it while lying on your back. Then try it while sitting. Then try it while standing. Finally, try it while doing an activity.

It is important that patients are instructed by the RT or trained clinician in the correct technique since diaphragmatic breathing can be difficult when combined with pursed-lips breathing.[34]

Methods of relaxation and stress management. Patients must also learn to avoid aggravation and upsetting circumstances and to adopt a more relaxed attitude about their particular life circumstances. These circumstances, including stress, affect the body, mood, and normal behavior of patients with chronic respiratory diseases. Being able to recognize these factors is going to avoid possible exacerbations and to reduce unnecessary O_2 use, conserve energy, and avoid undesirable cardiovascular and nervous responses to stress. There are multiple techniques for self-control that provide health benefits to the individual; for example, deep breathing routines, physical activities, socialization, meditation, hobbies, walking away from stressful situations, etc.[34]

Secretion clearance and bronchial hygiene techniques. This educational topic is especially helpful to patients who have secretion clearance problems associated with chronic bronchitis and bronchiectasis. Family members and friends may be invited to attend this session to acquire basic skills with these procedures and equipment, when appropriate (see Chapter 44).

Home oxygen and aerosol therapy. Preferably, an RT with home care experience should provide the educational session on home oxygen and aerosol therapy. The focus should be on the use and basic maintenance of home-care equipment and the self-administration of therapy. Patients who have not yet been prescribed this type of therapeutic regimen may be misinformed by other patients and may have questions or fears and become unreceptive to the concept. Presenting the modalities available and having patients discuss their positive experiences with respiratory home-care personnel can help alleviate the fears and anxieties of others (see Chapter 42).

MINI CLINI

Equipment Problems

Problem

The RT has been asked to check the portable concentrator (POC) for a patient who just finished a session and is ready to go home. When the nurse transferred the patient from the tank to his POC, the unit started alarming; the patient started getting anxious because of the situation and started to hyperventilate. What should the RT do to assess and solve the problem?

Solution

The solution is to return the patient to the oxygen tank, ask the nurse or a team member to work with the patient to decrease hyperventilation, and for the RT to check the POC. The RT working in a PR program should be familiar with different respiratory home-care equipment and troubleshooting techniques, since patients may bring the equipment to the program.

This scenario may have different approaches and solutions. In this case, the nurse accidentally changed the mode of the POC from continuous to pulse flow. Since the patient was exhausted from the exercise routine, the patient was breathing through the mouth and unable to trigger the POC via nasal breathing (pulse mode will sense nasal breathing and deliver oxygen), initiating an alarm. Depending on the POC, the unit may switch to previous continuous mode or alarm continuously until the situation is corrected.

Medications. Proper use of medications is another topic about which patients have numerous questions and concerns. Content should emphasize the proper use of medications, along with possible abuses and adverse effects. Participants' current prescriptions should dictate which specific drugs to cover. Common categories include β-adrenergic agents, anticholinergic agents, steroids, and diuretics. The section leader, preferably the RT, should demonstrate proper use of metered dose inhalers, including spacers or holding chambers, dry powder inhalers, and hand-held nebulizers. Sufficient time should be provided for questions and answers. Two sessions should be allotted for this topic (see Chapters 36 & 40).

Dietary guidelines. Dietary topics should focus on weight management and good nutrition as it relates to cardiopulmonary health. Emphasis should be on the importance of a sound high-protein, low-carbohydrate diet. The facilitator also should cover proper eating habits, methods of gaining and losing weight, foods to avoid, ways to increase appetite, adequate hydration, and daily menu planning. This session can stimulate patients to eat better and supply their bodies with the necessary fuel for increased energy production (see Chapter 23).

Recreational and vocational counseling. Another educational topic should be aimed at motivating the patient to participate in recreational activities and, according to his or her ability, return to work. This topic is often presented at the end of the program when patients have increased their physical endurance and are preparing for a more active and productive lifestyle.

Psychosocial and Behavioral Components

Psychological and emotional stress is a common problem for patients with moderate to severe chronic lung disease. Around 40% of COPD patients have symptoms of anxiety or depression, with a higher percentage after an Acute Exacerbation of COPD (AECOPD). The effects of AECOPD have been associated with post-traumatic stress symptoms (PTSS) and post-dramatic stress disorder (PTSD).[3] PR programs can bring in experts to cover topics related to psychosocial and behavioral therapies that provide patients with the opportunity to learn coping strategies.

RULE OF THUMB

Because anxiety and depression are often present in COPD and other patients with chronic respiratory diseases, PR education sessions should include topics related to psychosocial and behavioral therapy.

Program Implementation

In 1987, the AARC and the AACVPR jointly conducted the first national survey of PR programs. This National Pulmonary Rehabilitation Survey was published in 1988 and showed the variation existing in rehabilitation program structure, content, staffing, and cost throughout the United States.[35] In 2006, the ACCP, in conjunction with the AACVPR, released new evidence-based guidelines pertaining to the design and implementation of PR programs.[12] These guidelines are summarized below.

Staffing

PR is a multidisciplinary endeavor. PR teams generally include various health care professionals, such as RTs, nurses, physical therapists, and dietitians who plan, implement, and evaluate components of the program (Fig. 56.6). It is recommended that any staff conducting PR sessions be certified in basic life support or advanced cardiac life support in the event that a patient has an adverse response to a PR session. In addition to professional involvement, family members are needed to provide feedback and ensure that instructions and the exercise prescription are carried out at home.

RULE OF THUMB

RTs and other clinicians involved in pulmonary rehabilitation know the benefits that a well-designed program can represent for patients with pulmonary diseases, especially to recover some lost functioning. Support from the clinical staff and family members combined with early interventions may help patients in a hospital-based or home program. For COPD patients, early interventions may reduce acute exacerbation as described in the new guidelines.

It is important to highlight that the new guidelines are recommending that pulmonary rehabilitation should start 3 weeks after a hospitalization for COPD patients. The guidelines also recommend that pulmonary rehabilitation should not be started during a hospital stay. These recommendations are based on multiple studies showing the benefits of outpatient programs, especially reducing hospital readmissions, since patients may have a better quality of life and adherence to the plan of care. A well-designed home-based plan of care may help to reduce exacerbations and readmissions when patients have the correct family support.

Facilities

Location and quality of facilities can directly affect patient attendance. Patients are less likely to attend programs that are inaccessible by public transportation, have poor parking arrangements, or are physically difficult to reach. The facility must be wheelchair accessible. For elderly patients who do not drive, arrangements can be made with community organizations to provide transportation to and from the program. Ideally, the facility should provide two separate rooms for the program—one room for educational activities and one room for physical reconditioning. Rooms should be spacious and comfortable, with adequate lighting, ventilation, and temperature control. Chairs should be comfortable with good back support. Restroom facilities need to be readily accessible. A room for individual counseling is helpful, but any private office would suffice. It is also preferable to have pulmonary function testing and blood gas analysis capabilities on site. If this space is used by other departments for other functions, proper scheduling of rehabilitation sessions needs to be considered.

Scheduling

Another aspect of program implementation involves timely, advanced scheduling of the rehabilitation sessions. Class times need to be scheduled when the largest number of patients can attend; often late morning or early afternoon. Traffic patterns, bus schedules, and availability of rides are concerns that need

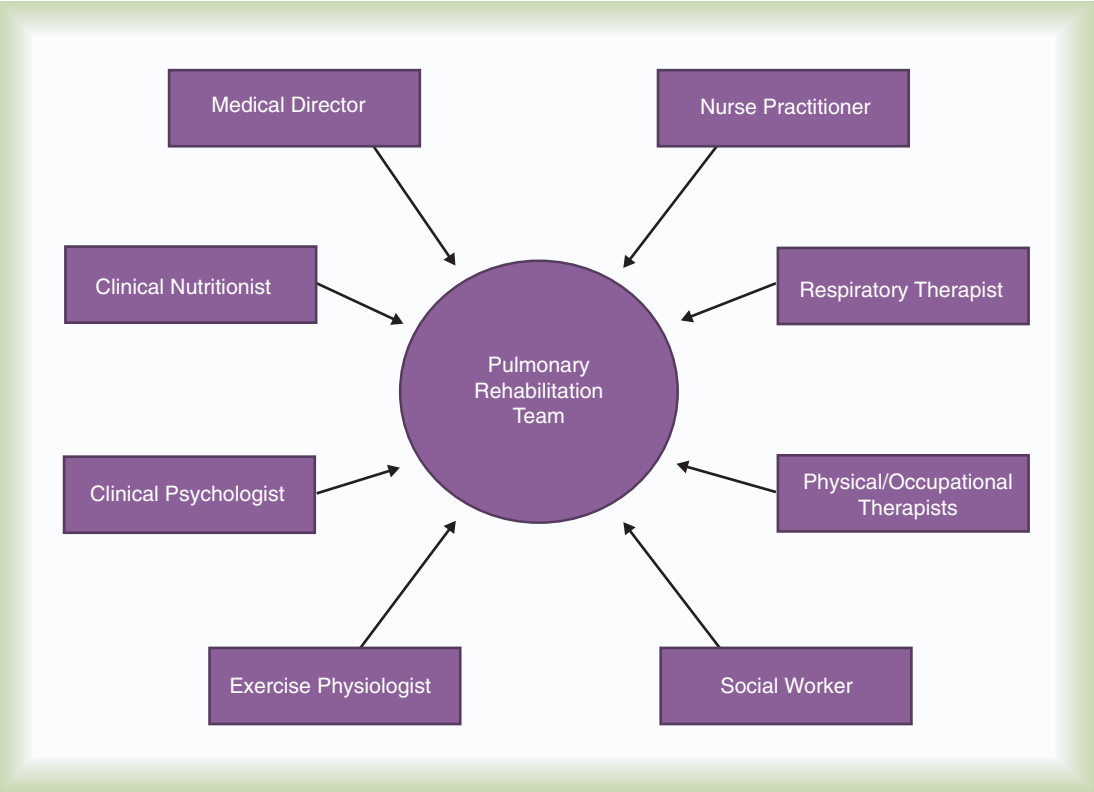

Fig. 56.6 Multidisciplinary Nature of Pulmonary Rehabilitation.

to be addressed. Proper scheduling helps to encourage participation and removes potential stumbling blocks, which could undermine the rehabilitation process.

Class Size

Class size is another issue that must be addressed. Theoretically, class size for a rehabilitation program could range from 1 to 15 participants, depending on available space, equipment, staff, and patient condition/needs. However, to foster group identity, interaction, and support, small-group discussions are encouraged. The ideal class size should range from 5 to 10 participants. Keeping the class size manageable facilitates vital group interaction processes and allows for more individualized attention. These factors help sustain motivation, reducing the likelihood of participant attrition.

Equipment

Both the instruction and the reconditioning component of the program require equipment. To meet the educational needs of the program, a whiteboard or flipchart, computer with a PowerPoint projector screen, and CD/DVD player can be very useful. Videos and formal learning packages dealing with the educational topics covered during the rehabilitation program should be available for group and individualized presentation. If possible, learning materials should be available in different languages or the predominant language in the community surrounding the location; this alternative may facilitate learning when language barriers are present.

MINI CLINI

Facilities Planning for Pulmonary Rehabilitation

Problem

The RT has been asked to assist in the planning process for starting a PR program to support a 350-bed, full-service hospital. According to the strategic plan, the physical location of the rehabilitation center is about three blocks away from the hospital. The RT has not seen the proposed site but was asked to approve a recommendation that the facility be used. What factors should the RT take into account before making a decision on site selection?

Solution

Because the hospital is currently in the planning process for starting a PR program and has not made a final facility selection, the RT is in a key position to assess, among other areas, issues related to the proposed site. Patient attendance and participation would be adversely affected if the facility is unreachable, such as at the top of a hill. If the location is in a high-crime or unsafe area with little or no security, this too would discourage patients from attending. As is true with any program, public transportation that does not permit accessibility to the proposed facility would be a limiting factor, as would little or no available parking. Numerous other facility considerations outside the actual physical location of the rehabilitation center would also need to be addressed.

Naturally, economic concerns surface when class size is considered. Although program quality must be the first priority, program viability realistically depends on the number of participants. Programs should generally be conducted with a class size that is comfortable with regard to space and staffing and that is economically feasible. Such an approach helps ensure that programs produce meaningful patient outcomes.

For physical reconditioning, stationary bicycles, treadmills, rowing machines, upper extremity ergometers, weights, pulse oximeters, and inspiratory resistance breathing devices constitute the minimum equipment requirements. The quantity of equipment needed depends on class size, available space, and financial resources available. Sufficient equipment should be on hand to keep all patients exercising and to monitor their activity. It is important to maintain equipment clean and in good working conditions for safety; dirty or malfunctioning equipment may discourage patients from attending.

Emergency O_2 and bronchodilator medications, as well as an automated external defibrillator (AED) should also be maintained in the rehabilitation area. Equipment guidelines for a class of 5 to 10 participants include the following: five stationary bicycles, two treadmills, two rowing machines, two upper extremity ergometers, five pulse oximeters for monitoring heart rate and O_2 saturation, one emergency O_2 cylinder (E), and bronchodilator medications. In addition, each patient should be supplied with an inspiratory resistance breathing device.

Because equipment can be expensive, care must be taken in its selection and purchase. Devices and appliances should be durable, easy and safe to use, simple to maintain, and not overly expensive. Initially, basic items are purchased. As a program develops and expands, equipment resources can be enhanced. Other program needs include the following:

- Maintaining individual patient manuals, including daily log forms or activity diaries
- Providing light refreshments for program participants
- Developing a communication network to announce schedule changes because of emergencies or cancellation of class sessions because of illness or weather
- Identifying available durable medical equipment providers for participants in need of specialized home care equipment
- Developing a system of charges and a mechanism for patient payment

By considering all of the factors needed for effective implementation of PR, programs have lower patient attrition and a greater chance for overall success. As programs are conducted, regular evaluations must be made by both patients and staff. Needed changes should be implemented on an ongoing basis. Only in this manner can one expect continued refinement of the process and improvement in patient outcomes.

Web-Based Pulmonary Rehabilitation

In addition to traditional face-to-face PR programs, web-based offerings known as telerehabilitation platforms are becoming a viable alternative and are now being offered by an increasing number of health service providers. Such **telerehabilitation** packages use a combination of a personal computer or device, a reliable internet connection, a patient monitoring module and relatively low-cost exercise equipment to allow patients to participate in PR. In such programs, a physician-led, multidisciplinary team, often including an RT in a central location with a digital interface, permit patients to participate in such programs from their home. Preliminary research suggests that all benefits of face-to-face PR programs, including fewer hospitalizations, can be achieved through telerehabilitation. In addition, these types of offerings have the added advantages of lower cost and the ability to include patients who are home-bound or live in remote locations and who may otherwise be excluded.[36]

RULE OF THUMB
Web-based telerehabilitation is an alternative to traditional PR programs for home-bound patients or those in remote geographic areas.

FINANCIAL CONSIDERATIONS

Costs and Fees

Rehabilitation programs usually project their fees based on the average cost per participant. According to regional labor and material prices, costs vary throughout the United States. Several factors must be considered when projecting program costs (Box 56.5). The larger the class size and the more participants involved in the overall program, the lower the per-patient cost. The aim should be to offer and conduct the highest-quality program possible at a reasonable cost that meets any existing budgetary constraints.

When determining patient charges, consideration must also be given to the type and amount of funding that has been received to offset program expenses and available insurance reimbursement. Pre-program and post-program testing and evaluations naturally generate revenues but should not be included in the formulation of program charges. However, payments for pulmonary function testing, exercise testing, arterial blood gas analysis, and other evaluations may help to keep a PR program financially viable.

Charges for an entire program or for each session must be structured in a way that does not deter patient attendance. Many patients with a chronic pulmonary disease are on a fixed income and have other living and medical expenses. A happy medium between a patient's ability to pay and program expenses must be identified. Funding from local charitable organizations, foundations, or agencies such as the American Lung Association and the COPD Foundation can help ease the financial burden. The most comprehensive and effective program available can have no impact if patients are unwilling or unable to attend and participate because of financial limitations.

Along with health care costs in general, the cost of providing PR has increased over the years. Nationwide charges for

BOX 56.5 Factors Affecting Pulmonary Rehabilitation Program Costs

- Marketing and program promotion
- Number of personnel involved in program facilitation and administration
- Space and utility expenses
- Audiovisual, exercise, and monitoring equipment (purchase and maintenance)
- Production and duplication of course materials
- Patient supplies
- Office supplies
- Refreshments
- Miscellaneous expenses
- Changes in the amount of funding and insurance coverage

PR vary, depending on program length, whether the offering is in-person or web-based, and, most importantly, insurance coverage. With most insurance plans reimbursing programs at 80% after a deductible, each patient would be responsible for the remaining 20% or copayment. The out-of-pocket amount may vary if the program is offered in a doctor's office (20% after insurance payment) or hospital outpatient program (copayment per session). Additional or supplemental medical coverage may cover this balance.

Charges for participation in these programs and inpatient rehabilitation reimbursement policies vary throughout the United States. The CMS, has published the final rules for Medicare reimbursement guidelines for **comprehensive outpatient rehabilitative facilities (CORFs)**. Under Part B of Medicare, the scope of services of a CORF includes reimbursement for outpatient activities and one home visit. Reimbursement requires that the CORF meet the conditions of participation established in section 933 of Public Law 96-499; this also includes provisions for certification of the program. To establish reimbursement mechanisms, each CORF must present its program description and anticipated results to local third-party payers.[37] The AACVPR has also developed guidelines for program design, implementation, and recognition.

By following recognized guidelines, Medicare has established an allowable charge for PR and reimburses 80% of this rate after the patient meets the annual prescribed deductible. In the past, inpatient and outpatient PR programs obtained reimbursement from third-party payers by charging for rehabilitation sessions as physical therapy exercises for COPD, reconditioning exercise sessions, office visits with therapeutic exercises, serial pulse oximetry determinations, or physician office visits. The goal was to obtain as much insurance reimbursement as possible, decreasing the financial burden on the patient (Box 56.6).[38]

RULE OF THUMB

To help ensure adequate reimbursement for PR, identify patient goals and objectives; formulate and implement an effective exercise prescription for each patient; use diagnostic codes from the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-*10*-CM); use current and proper CPT (Current Procedural Terminology) coding and documentation from patient's medical record to support the need for PR. A new revision of the ICD will be released in the near future to replace the current ICD-10-CM.

There is now a national coverage policy for PR under Medicare. Programs have to obtain reimbursement from their Medicare beneficiaries following accepted protocol, policies, and provisions specified by Medicare. Coverage is for patients with stage II, III, and IV COPD (moderate to very severe according to the GOLD standards). The programs must include five components, which must be documented in the patient's medical record:

1. Physician-prescribed exercise
2. Education and training that relate to an individual patient's needs
3. Psychosocial assessment
4. Outcomes assessment
5. Individualized treatment plan.[39]

BOX 56.6 Sources of Reimbursement for Pulmonary Rehabilitation Programs

- Nongovernment health insurance programs—private, single, or group health insurance plans
  - Health maintenance organizations (HMOs)
  - Preferred provider organizations (PPOs)
  - Medicare supplement
- Federal and state health insurance programs
  - Medicare
  - Medicaid
  - Uncompensated services (Hill-Burton)
  - Comprehensive outpatient rehabilitative facility
  - Veterans Administration benefits
  - Civilian Health and Medical Programs of the Uniformed Services (CHAMPUS)
  - Federal workers insurance
- Ancillary liability and casualty insurance programs
  - Automobile insurance—related to automobile accidents
  - Workers' compensation—related to accidents on the job
  - Business insurance coverage—related to injuries sustained on business premises
  - Homeowner's insurance—related to injuries sustained on the owner's premises
  - Malpractice insurance on providers of health care
  - Product and service liability insurance—related to injuries caused by a product or service
- Other options of reimbursement
  - Senior care
  - Rehabilitation hospitals
  - Grants

Reimbursement Qualifications

Under current guidelines, Medicare covers PR when it is determined to be medically necessary and patients meet the necessary criteria. Many insurance plans follow Medicare guidelines for eligibility and coverage:

- The patient must be diagnosed with moderate to very severe COPD (GOLD Classification II, III, & IV) or any chronic respiratory disease with disabling implications before being referred to the program by the treating physician. Pulmonary Function Test (PFT) results can be utilized to support the diagnosis in addition to the GOLD Classification.
- A physician's order. The chart must have documentation showing that a physician prescribed an exercise plan for each day.
- Documentation showing the patient completed each daily plan of care.
- Documentation showing education and training provided to the patient and specific to the patient's needs.
- Documentation showing psychosocial assessment.
- Outcome assessment after the program is completed.
- An individualized treatment plan reviewed and signed by the physician must be provided. This plan has to be reviewed by the physician every 30 days.
- Correct billing code for the services provided. For pulmonary rehabilitation, it is G0424.
- The reviewer from the insurance company has the authority to request additional documentation for determination, if

the person considerers that current documents do not support the filed claim.

According to CMS, claims for Medicare patients should be submitted to Medicare Part A for any component of PR performed during a hospital stay and claims for rehabilitation components provided on an outpatient basis must be submitted to Medicare Part B. This payment mechanism has already undergone changes and it is anticipated that Medicare will continue to change its reimbursement policy for PR in the future. It is incumbent on clinicians who provide PR to stay abreast of any changes in reimbursement policy and procedure and to make necessary adjustments to receive payment.

At the present time, there is provision to reimburse programs for two 1-hour rehabilitation sessions per patient per day up to 36 sessions. An additional 36 sessions over an extended period can be approved by the individual Medicare contractor based on patient need for continued rehabilitation and physician referral. Provision has been made for face-to-face patient sessions and for group (two or more patients) sessions. Individual sessions must be at least 31 minutes in length. If two sessions are performed on the same day, services may be reported only if the duration of the combined treatments is at least 91 minutes. It is essential that the practitioner who conducts PR is familiar with all current practices so that therapy that is provided and billed for complies with current Medicare policy, is properly documented for each patient, and is submitted in a timely manner.[38-40]

MINI CLINI

Obtaining Insurance Payment for Pulmonary Rehabilitation

Problem

The RT is asked to design and implement a PR program on an outpatient basis at her hospital. After completing the first class that ran for 12 weeks, the hospital scheduled another one. However, although the institution had been submitting bills on a timely basis to numerous insurance providers, including Medicare, no payment has been received. What is the problem, and how can it be corrected?

Solution

The insurance companies apparently either have denied claims or have not responded to the claims being submitted. There are several reasons for not receiving a payment. The most common one is improper or inaccurate claim filing. Usually Medicare provides payment or denials between 14 and 21 days after filing a claim. When insurance denies payment, it provides an explanation for the denial and sometimes with an alternative to resubmit the claim or appeal the denial. Another reason is an inefficient internal process within the insurance company (i.e., poor communication with clients, disorganized internal processes, and high workload).

The RT should work closely with the billing department at the hospital to ensure that all information is complete for each patient (i.e., correct patient identification numbers), that the hospital has the correct addresses to submit claims, and that diagnoses and procedures have been properly coded. Some insurance companies have their own coding schemes, and these must be followed accordingly. Managed care companies also require preauthorization, which must be obtained before entering any patient with a managed care plan into pulmonary rehabilitation. Finally, follow-up telephone calls are always helpful and should be conducted if payment is not received in a timely fashion.

Program Results

Patient and program outcomes must be evaluated at the conclusion of the program and periodically thereafter as described in Box 56.7. This evaluation must compare patient status before the program with current patient status and may include physiologic, psychological, and sociologic data. Common outcome measures include exercise tolerance, levels of dyspnea at rest and with exertion, and quality-of-life surveys. The data collected may support reimbursement claims or if the physician needs to order additional sessions for the patient to achieve the plan of care.

Results of PR must be communicated to the patient, referring physician, and family, if appropriate. Further goals and objectives for continued improvement may be established to provide the basis for follow-up and reinforcement activities. Tracking and documenting PR programs and patients' outcomes are important to achieve the current guidelines and to promote the benefits of the programs. For example, the AACVPR offers a registry to track the positive impact of the programs on mortality, physical activity, quality of life, etc.[41] The data can be used by providers to negotiate reimbursement rates based on the positive outcomes obtained.

If no improvements in physical or psychosocial measures occur within a class or group, program deficiencies are often the cause. Specifically, insufficient professional training in rehabilitation methods, a lack of a uniform approach, inadequate program length, and lack of follow-up are the major reasons for unsatisfactory outcomes. If a very small number of patients (i.e., one or two) from a large class show no improvement, it may be the result of a lack of patient's compliance to the plan of care.

Finally, PR has become recognized as an ideal setting for certain patients with severe chronic respiratory diseases who are able to undergo lung volume reduction or lung transplant surgery. The program can provide information before the procedure to help to educate patients about benefits, risk, and outcomes of the surgery;

BOX 56.7 Evaluation of Rehabilitation Program Outcomes

- Changes in exercise tolerance
- Before and after 6- or 12-minute walking distance
- Before and after pulmonary exercise stress test
- Review of patient home exercise logs
- Strength measurement
- Flexibility and posture
- Performance on specific exercises (e.g., ventilatory muscle, upper extremity)
- Changes in symptoms
- Dyspnea measurement comparison
- Frequency of cough, sputum production, or wheezing
- Weight loss or gain
- Psychological test instruments
- Activities of daily living changes
- Postprogram follow-up questionnaires
- Compliance improvement with pulmonary rehabilitation medical regimen
- Frequency and duration of respiratory exacerbations
- Frequency and duration of hospitalizations
- Frequency of emergency department visits
- Return to productive employment
- Other clinical and nonclinical changes

physical reconditioning helps to stabilize exercise tolerance and muscle function to improve survival and outcomes after surgery.[42]

Potential Hazards

Although most patients with COPD can expect to realize benefits through physical reconditioning and PR, certain potential hazards do exist, as follows:

I. Cardiovascular abnormalities
   A. Cardiac arrhythmias (can be reduced with supplemental O_2 during exercise)
   B. Systemic hypotension and hypertension
II. Blood gas abnormalities
   A. Arterial desaturation
   B. Hypercapnia
   C. Acidosis
III. Muscular abnormalities
   A. Functional or structural injuries
   B. Diaphragmatic fatigue and failure
   C. Exercise-induced muscle contracture
IV. Miscellaneous
   A. Exercise-induced asthma (more common in young patients with asthma than in patients with COPD)
   B. Hypoglycemia
   C. Dehydration

Proper patient selection, education, supervision, and monitoring are key factors in reducing possible hazards.

RULE OF THUMB

To help avoid potential hazards and identify contraindications, it is necessary to conduct an initial individualized assessment to identify any medical condition that may interfere with the success of the program and achieving the plan of care and goals. The assessment will help the team to determine the patient's willingness and possible adherence to the program. In all situations, patient safety must be a high priority for the PR team.

MINI CLINI

What to Expect From Pulmonary Rehabilitation

Problem

The RT is asked to consult on a 63-year-old man hospitalized with severe COPD for possible participation in an outpatient program. During the patient interview, the patient tells the RT that if the program will not cure him, he sees no reason to participate. How should the RT respond to the patient, keeping in mind his expectations of what PR should accomplish?

Solution

It is crucial for all RTs and other caregivers involved in PR to recognize that the focus of any program should attempt to treat the patient as a whole and not solely the underlying disease. A well-constructed program should be able both to quantify the extent of physiologic impairment and to assist in establishing outcome expectations for physical reconditioning. Regardless of setting or design, such programs must address the psychological, social, and vocational impact of the disability on the patient and family and seek ways to improve the patient's quality of life. In this case, the RT should describe the benefits of PR outside the traditional measures of pulmonary function. Although PR cannot affect the progressive deterioration in lung function that occurs with COPD, both education and exercise may improve the patient's ability to perform activities of daily living and exercise tolerance. In addition, effective breathing techniques may lessen the frequency and severity of "panic breathing" episodes.

CARDIAC REHABILITATION

Similar to PR, good cardiac rehabilitation programs are multidisciplinary in approach and focus. Goals include patient education promoting heart-healthy living, physical reconditioning to improve work capacity, weight loss, and a return to work when possible.

Pulmonary and cardiac rehabilitation share many similarities and differences. Similarities include the need for patient evaluation before program enrollment, patient education, the focus on exercises to increase fitness and stamina, and the need to monitor patients during exercise and for compliance. Differences include disease focus, patient age (most cardiac patients range in age from late 30s to 60s and 70s, whereas pulmonary patients for the most part are ≥50 years), and exercises used within the program. Breathing exercises to improve ventilation are essential to the pulmonary patient but are not that important to cardiac patients.

Finally, respiratory involvement in cardiac rehabilitation is significantly lower. For the most part, the RT is involved with instruction on O_2 use and may assist with patient exercise sessions during cardiac rehabilitation.

MINI CLINI

Responding to Adverse Outcomes

Problem

A 73-year-old man with stage III COPD was accepted into a PR program. Because of the severity of his disease, his preprogram CPX was stopped after 5 min because of excessive dyspnea and oxygen desaturation. He was placed on O_2 but was unable to complete the study. However, because of the desire of the patient's physician to get him into a program of pulmonary rehabilitation and the patient's desire to participate, the patient was put on home O_2 and admitted to the program. While exercising on a treadmill with supplemental O_2, the patient complained of headache and nausea. The RT stopped the exercise session and documented a significant increase in the patient's blood pressure (220/130 mm Hg). How should the RT proceed in this case?

Solution

The RT should notify the physician overseeing the program and the patient's prescribing physician (if different) immediately and document the elevated blood pressure. It is likely that the preprogram cardiopulmonary exercise test was stopped before the excessive increase in blood pressure was noted. While in PR, the patient (on supplemental O_2) was able to exercise to a level greater than that during the exercise test. This elevated blood pressure will likely result in the patient being started on some type of antihypertensive therapy and being reevaluated during another exercise test to determine the extent of his hypertensive condition. Depending on the pattern of the patient's hypertension, it is also possible that this patient will be admitted to cardiac rehabilitation first before returning to the pulmonary rehabilitation program. This case shows the importance of a thorough and complete assessment of a patient's status before any admission to PR.

CONCLUSION

A properly planned and implemented program can produce positive and measurable patient outcomes. Goals and objectives of PR should be written in these measurable terms and be explained to the patient in a clear, concise fashion to achieve

optimum therapeutic outcomes. The success of PR depends on this along with careful application of current clinical knowledge and the use of a multidisciplinary approach throughout all phases of program organization, implementation, and evaluation. Within this context, PR will help to achieve the healthcare initiatives to reduce healthcare cost and reduce readmission rates and will continue to gain greater acceptance. The role of the RT in PR will likely increase.

SUMMARY CHECKLIST

- PR has two major aims: (1) to control and alleviate disease symptoms, and (2) to help patients achieve optimal levels of activity.
- Candidates for PR are patients with moderate to very severe COPD (stage II, III, and IV according to the GOLD standards).
- Rehabilitation does not alter the progressive deterioration in pulmonary function that occurs with chronic lung disease.
- Effective rehabilitation programming requires a multidisciplinary approach and combines physical reconditioning with education and psychosocial support.
- The educational portion of a rehabilitation program should provide patients with knowledge they can use to help cope with their disease and manage symptoms better.
- Educational materials should be available in different languages when necessary.
- Increased exercise tolerance, decreased intensity of symptoms, and improved activity levels are the best-documented benefits of pulmonary rehabilitation.
- PR is still underutilized despite its documented benefits.
- Every patient must receive an initial assessment to create a personalized plan of care based on that patient's needs. Follow-up assessments are necessary to manage progress.
- The exercise evaluation provides the basis for the exercise prescription, yields the baseline data needed to assess a patient's progress, and helps determine the degree of hypoxemia or need for supplemental O_2 during exercise.
- Reconditioning should combine lower extremity and upper extremity aerobic exercises with ventilatory muscle training.
- Decisions regarding facilities, scheduling, class size, and equipment can all affect rehabilitation program outcomes.
- PR may reduce readmissions and decrease healthcare costs.
- Web-based telerehabilitation PR programs are an alternative to traditional face-to-face programs.
- Proper claim filing with proper supporting documentation will improve reimbursement.
- Cardiac rehabilitation should be considered first if a patient with pulmonary disease also has an underlying cardiac condition that needs to be addressed and appropriately managed.

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57

Respiratory Care in Alternative Settings

Albert J. Heuer and Daryl Rogers

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Describe alternative care settings in which respiratory care is often performed
- Discuss more recent developments and trends in respiratory care at alternative sites
- Identify who regulates alternative care settings
- List the standards that apply to the delivery of respiratory care in alternative settings
- Describe how to help formulate an effective discharge plan
- List factors to evaluate when alternative care sites and support services are being assessed
- Discuss how to justify, provide, evaluate, and modify oxygen (O_2) therapy in alternative care settings
- Explain how to select, assemble, monitor, and maintain O_2 therapy equipment in alternative settings
- Identify the special challenges associated with providing ventilatory support outside an acute care hospital
- Describe how to instruct patients and caregivers and confirm their ability to provide care in alternative settings
- Identify which patients benefit the most from ventilatory support outside acute care hospitals
- Identify the most appropriate device needed to treat patients in the postacute setting
- Explain how to select, assemble, monitor, and maintain portable ventilatory support and continuous positive airway pressure equipment, including applicable interfaces or appliances
- Describe proper documentation regarding patient evaluation and progress in alternative settings
- State how to ensure safety and infection control in alternative settings

CHAPTER OUTLINE

KEY TERMS

alternative (nonacute) care
Centers for Medicare and Medicaid Services (CMS)
conditions of coverage
conditions of participation
durable medical equipment (DME) supplier
durable medical equipment, prosthetics, orthotics, and supplies (DMEPOS)
home sleep test (HST)
insufflator-exsufflator
long-term acute care hospitals (LTACHs)
noninvasive ventilation (NIV)
O_2-conserving device
portable oxygen concentrator (POC)
skilled nursing facility (SNF)
transtracheal oxygen therapy (TTOT)

Although home care remains the most common alternative site for providing health care, numerous other **alternative (nonacute) care** settings—including subacute facilities, **long-term acute care hospitals (LTACHs)**, rehabilitation facilities, and **skilled nursing facilities (SNFs)**—provide respiratory care to patients.[1] Alternative health care settings offer advantages over acute care facilities—advantages that include lower costs and enhanced patient comfort. However, improper or premature discharging of patients to alternative care settings and poor care planning and implementation can erase these benefits and result in short-term readmission.

This chapter summarizes recent policy developments and discusses aspects of optimal discharge and patient care planning; it also reviews various therapeutic respiratory modalities in alternative care sites. A major alternative site is the sleep laboratory, where respiratory therapists (RTs) may conduct polysomnography, or sleep, studies. The pathophysiology, diagnosis, and treatment of disorders of sleep are covered in Chapter 34.

MORE RECENT DEVELOPMENTS AND TRENDS

There have been several developments in the area of respiratory care in alternative sites. Such changes range from governmental initiatives affecting reimbursement to enhancements involving the respiratory equipment used in such settings.

Over the past two decades, an assortment of laws and regulations were enacted that have reduced reimbursement for respiratory care in alternative settings. Furthermore, unlike the situation in many other health professions, reimbursement for the time that RTs spend in setting up the equipment and assessing and administering prescribed treatments is not generally available. This lack of reimbursement has presented challenges to organizations and agencies attempting to provide high-quality respiratory care in alternative settings.[2,3]

In addition, the federal government has introduced the **durable medical equipment, prosthetics, orthotics and supplies (DMEPOS)** competitive bidding program, awarding contracts to some respiratory care suppliers and not awarding respiratory bids to others based on selected criteria. This affected many home-care RTs, as some companies discontinued their respiratory service lines entirely or were unable to support them due to significant rate reductions. As a result, patient satisfaction suffered because of the lack of access to care.[4]

A further development stemming mainly from the aging US population is a significant increase in alternative care sites known as *assisted living facilities*. These facilities permit residents, who are generally elderly or disabled, to live in their own units either alone or with a companion and with health services available, including RTs in some facilities. Hence, these facilities are yet another alternative site at which respiratory services are provided.

RELEVANT TERMS AND GOALS

As the elderly population grows and managed care becomes the dominant delivery model, more health care services are being provided outside the acute care hospital in such settings as SNFs, LTACHs, and within homes. Rather than representing distinct entities, these alternative settings are part of an evolving continuum of care and are often elements of Accountable Care Organizations (ACOs), which are groups of doctors, hospitals, and health care providers who voluntarily come together to deliver coordinated patient care in a cost-effective manner.

Similar to the acute care setting, alternative care settings accomplish this goal through a coordinated team effort comprising many disciplines. The patient care team in alternative settings uses various specialized respiratory care services and equipment, including continuous O_2 therapy, long-term mechanical ventilation, aerosol drug administration, airway care, sleep apnea monitoring and treatment, and pulmonary rehabilitation. The respiratory equipment used within each of the major alternative settings and other relevant considerations, including patient and family education, are discussed in subsequent sections of this chapter.

Long-Term Subacute Care Hospitals

Advances in technology, research, and clinical specialization have permitted more acutely ill patients to be treated outside of large-scale acute care hospitals. Over the past decade, LTACHs have become more prevalent. These facilities provide highly focused care to patients with complex medical conditions, including patients who are ventilator-dependent and difficult to wean. LTACHs generally employ a highly experienced clinical staff, including RTs, to provide integrated interdisciplinary care using the latest equipment and evidence-based protocols. During the 20- to 30-day typical length of stay at an LTACH, many patients experience significant improvement, including successful ventilator weaning and increased functionality.[5]

Subacute Care

According to the National Association of Subacute/Post Acute Care, *subacute care* is a comprehensive level of inpatient care for stable patients who (1) have experienced an acute event resulting from injury, illness, or exacerbation of a disease process; (2) have a determined course of treatment; and (3) require diagnostic or invasive procedures but not those requiring acute care. The severity of the patient's condition typically requires active physician direction with frequent on-site visits, professional nursing care, significant ancillary services, and an outcomes-focused interdisciplinary approach employing a professional team.

The goal of acute care is to apply intensive resources to stabilize patients after severe episodic illness, whereas subacute care aims to restore the whole patient back to the highest practical level of function—ideally self-care. This holistic approach requires goal-oriented care by an interdisciplinary team, with frequent assessment of progress and a time-limited plan of care.

Although most patients receiving subacute care are elderly, all age groups can be found at these sites. Pediatric, adolescent, and adult patients requiring ventilatory support or extensive care, depending on their diagnosis, are also cared for at these sites.[6,7]

Home Care

Currently, most respiratory care in the alternative setting is provided in the home. The primary goal of home care is to provide

high-quality health care services to patients in their home settings, thus minimizing their dependence on institutional care. In regard to respiratory home care, several specific objectives are evident. Respiratory home care can contribute to the following:

- Supporting and maintaining life
- Improving patients' physical, emotional, and social well-being
- Promoting the self-sufficiency of both patient and family
- Ensuring cost-effective delivery of care
- Maximizing patient comfort near the end of life

Although not all aspects of respiratory home care have proven effective, various studies have shown that carefully selected treatment regimens can benefit patients significantly. These benefits include improved quality of life and functional performance as well as a reduction in the individual and societal costs associated with hospitalization.[8-10]

STANDARDS

Standards for the delivery of respiratory care in the subacute and home settings are derived from several different sources. First, the Clinical Practice Guidelines created and published by the American Association for Respiratory Care (AARC) offer RTs an evidence-based clinical framework for performing numerous respiratory procedures, including many procedures used in alternative care settings. Other standards are established by federal and state laws and private-sector accreditation.

Regulations

As the largest purchaser of health services, the federal government (in connection with state and local governments) plays a major role in setting standards and regulating this industry. The federal agency responsible for the overall administration of Medicare and Medicaid is the **Centers for Medicare and Medicaid Services (CMS)**. Created in 1997, CMS oversees the framework for providing health coverage to elderly adults, disabled adults, and many disadvantaged young children in the United States.[5]

As part of this structure, CMS created the Medicare Provider Certification Program. This program ensures that providers that serve Medicare beneficiaries—including hospitals, skilled nursing facilities (SNFs), LTACHs, home health agencies, and assisted living facilities—meet health and safety requirements. These requirements are called **conditions of coverage** and **conditions of participation**. Current conditions of participation emphasize quality indicators, outcome measures, and cost efficiency designed to improve the quality and effectiveness of care provided to beneficiaries.[5] Institutions undergo certification surveys by either state survey agencies or private accrediting organizations such as The Joint Commission (TJC), which is discussed in more detail in the following section.

State survey agencies are partners with the federal government and principal agents in performing institutional certification. Typically, a state survey agency is either the state department of health or state licensing authority for health care facilities. The main function of the state survey agency is to ensure that facilities providing Medicare or Medicaid services comply with state and federal health, safety, and quality standards as determined by periodic on-site inspections.

Private Sector Accreditation

The primary organization responsible for standard setting and voluntary accreditation of care providers in alternative settings is the TJC. To assist hospitals and health care organizations with the accreditation process and overall performance improvement, the TJC develops and publishes standards and National Patient Safety Goals for long-term and subacute care, home care, and assisted living facilities. The standards and goals relate to the delivery of high-quality patient care and the process and structure needed to do so. These categories include patient rights, ethics, and assessment and organizational leadership and management of information. The patient safety goals set targets for the improvement or resolution of common problems for health care organizations such as proper patient identification, medication safety, and infection control.[11,12]

Approximately 90% of all hospitals and other health care organizations voluntarily subscribe to TJC accreditation and as a result are surveyed at least every 3 years. Insufficient or unsatisfactory compliance is flagged and requires formal follow-up to ensure correction. In certain circumstances, unfavorable results may result in a facility's or organization's failing to maintain TJC accreditation.[11,12]

TRADITIONAL ACUTE CARE VERSUS ALTERNATIVE SETTING CARE

For the RT, working in the alternative care setting is distinctly different from working in an acute care hospital. Key differences involve resource availability, supervision and work schedules, documentation and assessment, and provider–patient interaction (Table 57.1).[13] Although some practitioners do not like the alternative work settings, many find the greater independence, professional team orientation, creativity, and higher level of patient and family interaction to be rewarding.

DISCHARGE PLANNING

Effective discharge planning provides the foundation for high-quality care in the alternative care setting. A properly designed and implemented discharge plan guides the multidisciplinary team in successfully transferring a respiratory care patient from the health care facility to an alternative site of care.[14] Effective implementation of the discharge plan also ensures the safety and efficacy of the patient's continuing care. In addition, CMS's Readmission Reduction Program penalizes hospitals that have high short-term readmission rates for the following diseases:

- Acute myocardial infarction (AMI)
- Chronic obstructive pulmonary disease (COPD)
- Heart failure (HF)
- Pneumonia
- Coronary artery bypass graft (CABG) surgery
- Elective primary total hip arthroplasty and/or total knee arthroplasty (THA/TKA)

As a result, it has become essential for hospitals and other health care providers to adopt and evaluate the effectiveness of evidence-based discharge protocols. In general, the key elements of such protocols include the following:

TABLE 57.1 Major Differences Between the Traditional Acute Care Setting and Alternative Settings for the Delivery of Respiratory Care Services

Area	Traditional Setting (Acute Care Hospital)	Alternative Settings (Long-Term Acute Care, Subacute Care, Home Care)
Diagnostic resources	In-house laboratory, x-ray, ABG analysis, PFT	Must rely on outside vendors to provide diagnostic tests
Equipment support	Extensive; supported by piped-in O_2 and suctioning	Limited availability; must use portable O_2 and suctioning systems
Travel requirements	None; remain in one facility	Must travel between facilities or residences
Level of supervision	Direct supervision	Respiratory care provider works independently with minimal supervision
Patient assessment	Moderate—primarily provided by attending physician or residents	Heavy—core responsibility related to care planning
Documentation requirements	Moderate—limited to medical record keeping	Heavy—includes initial justification, ongoing follow-up, and often detailed financial record keeping
Work schedule	Specific hours	Varied work schedule, often including "on-call" off hours coverage
Time constraints	More than one shift to deliver therapy	Must complete all therapy during shift or visit
Patient-family interaction	Limited treatment time available; little family interaction	One-on-one therapy; intensive family interaction
Provider interaction	Primarily attending physicians and patients' nurses	Continuous interaction with all members of professional team

ABG, arterial blood gas; *PFT,* pulmonary function testing

- Proper patient screening and evaluation
- Early identification of patients at high risk for short-term readmission
- Intensive patient and family education
- Interdisciplinary discharge planning that addresses all major potential barriers
- Patient follow-up[4]

Multidisciplinary Team

Although a physician normally initiates an order to discharge a patient to an alternative site, many other health care professionals are involved in the discharge process. Table 57.2 identifies these key professionals and their major responsibilities.[14] As with pulmonary rehabilitation (see Chapter 56), a team approach produces the best results. Communication and mutual respect for the talents and abilities of each team member are two key elements in making patient care in the alternative care setting work. Any breakdown in the system may delay or adversely affect patient discharge and the patient's physical health and mental well-being.

RULE OF THUMB To help ensure a successful discharge and confirm that a nonprofessional caregiver can perform a particular skill, the RT must go beyond demonstration and verbal confirmation of the caregiver's understanding. The RT must observe a return demonstration, whereby the caregiver properly performs the same procedural steps the RT has demonstrated. In addition, providing the caregiver with written information relating to the procedural sets and equipment setup, maintenance, and basic troubleshooting can help reinforce key areas and ensure caregiver mastery of the competency. A written competency checklist should be completed by the home-care RT to document that all details regarding equipment setup and safe use were covered. Also, most home-care companies provide 24-h coverage in the event of an emergency or if the patient or caregiver has additional questions.

TABLE 57.2 The Patient Care Team in Alternative Settings

Discipline	Responsibilities
Utilization review	Advises or recommends consideration of patient discharge, documents patient's in-hospital care
Discharge planning (social service or community or public health)	Brings all the needed elements together and ensures that a patient can be discharged to alternative care sites, makes contact with outside agencies that may assist with patient care
Physician	Writes order for patient discharge, evaluates patient's condition and prescribes needed care, establishes therapeutic objectives
Respiratory care	Evaluates patient and recommends appropriate respiratory care, provides care and follow-up
Nursing	Writes and implements nursing care plan for patient, assesses patient's status and provides necessary follow-up
Dietary and nutrition	Assesses patient's nutritional needs and writes dietary plan for patient, makes arrangements for meals as necessary
Physical and occupational therapy	Provides necessary physical therapy and recommends any additional modalities or procedures
Psychiatry or psychology	Assesses patient's emotional status and provides any needed counseling or support
Durable medical equipment supplier or home care company	Provides needed equipment and supplies and handles any emergency situations involving delivery or equipment operation

Beyond the performance of a particular skill, it is imperative for the discharge team to ensure that an adequate number of professional and nonprofessional caregivers are part of the care plan to provide appropriate patient care coverage; this is particularly true when more complicated modes, such as mechanical ventilation or multiple therapies are required by the patient. Substantial caregiver strain is often associated with the care of such patients in alternative settings. Proper assessment of the capabilities and number of potential caregivers in light

MINI CLINI

Minimizing Readmissions

Problem

A COPD patient who was admitted to the hospital for an exacerbation is now improving and is targeted for discharge in 2 days. Owing to patient quality-of-life considerations and newer financial penalties for excessive readmissions, the patient care team wishes to help minimize the likelihood of a readmission for this individual as well as similar patients. What are some of the major considerations that should be addressed in the discharge plan for this patient to help avoid a readmission?

Solution

COPD patients, especially those with moderate to severe disease, may often be deemed more clinically "fragile" and therefore especially prone to readmission. Hence it is imperative for the multidisciplinary patient care team to quickly recognize the predisposition and to carefully plan to address the major risks. Education and patient follow-up are at the core of most short-term readmission reduction protocols. In this case, the education should focus on the pathophysiology of COPD and, more importantly, the purpose and importance of each element of the care plan. Reinforcing proper medication use such as bronchodilators and steroids as well as safe use of home oxygen are priorities. Phone, computer-aided, or in-person patient follow-up should focus on continued compliance with the treatment plan, adherence to scheduled physician visits, and participation in any prescribed pulmonary rehabilitation programs. Barriers such as those related to transportation issues and assistance with activities of daily living should also be promptly identified and addressed. In some instances, transportation to physician visits, pulmonary rehabilitation sessions, or certified home-health aids can be arranged in advance by the discharge planning team or patient follow-up clinicians. Additionally, some home-care companies have developed COPD programs where RTs follow up with patients as soon as they are discharged and then complete comprehensive respiratory assessments.

of the therapy needed at home and appropriate training of such individuals can help to address this concern.

Equipment support and selected clinical services for patients receiving respiratory home care are often provided by a **durable medical equipment (DME) supplier**. DME suppliers range in size from multimillion-dollar national corporations offering a broad range of services to small local companies. Both large and small companies usually provide the following services:

- Service 24 hours, 7 days a week
- Third-party insurance processing
- Home instruction and follow-up by an RT

In addition, the patient's residence must meet safety standards and be suitable for managing the patient's specific condition. It must be free of fire, health, and safety hazards; provide adequate heating, cooling, and ventilation; provide adequate electrical service; and provide for patient access and mobility with adequate patient space (room to house medical and adaptive equipment). The selected site must be capable of operating, maintaining, and supporting all equipment needed by the patient, including both respiratory and ancillary equipment and supplies as needed, such as the ventilator, suction, O_2, intravenous therapy, nutritional therapy, and adaptive equipment.[15] Box 57.1 lists key factors one should assess in planning the discharge of a respiratory care patient to the home environment.

BOX 57.1 Assessing the Home Environment

Accessibility

- In and out of house or apartment
- Accessibility between rooms
- Doorway width and threshold heights
- Stairways
- Wheelchair mobility
- Bathroom
- Kitchen
- Carpeting
- Uneven floors

Equipment

- Available space
- Electrical power supply
- Amperage
- Grounded outlets
- Presence of hazardous appliances

Environment

- Heating and ventilation
- Humidity
- Lighting
- Living space
- Possible fire hazards
- Smoke alarms
- Fire extinguishers

A variety of equipment is available when a patient with a pulmonary disorder is discharged to an alternative setting. Many of the modalities used are discussed in other chapters throughout this textbook.

OXYGEN THERAPY IN ALTERNATIVE SETTINGS

O_2 therapy is the most common mode of respiratory care in alternative care settings. This high use is based on the fact that O_2 therapy improves both survival and quality of life in selected patient groups, especially patients with advanced COPD.[16,17] In particular, studies have shown improved nocturnal O_2 saturation, reduced pulmonary artery pressure, and lower pulmonary vascular resistance with appropriate outpatient O_2 therapy.[18-20]

Oxygen Therapy Prescription

A prescription for oxygen therapy must be based on documented hypoxemia as determined by overall clinical assessment, including an arterial blood gas or pulse oximetry. When the need for O_2 therapy is established (see Chapter 42), the physician writes a prescription for O_2 therapy, which must include the following elements:[21]

- Flow rate in L/min, concentration, or both
- Frequency of use in hours per day and minutes per hour (if applicable)
- Mode of delivery
- Duration of need

MINI CLINI

Assessing the Home Environment

Problem

A wheelchair-bound patient with a tracheostomy who requires mechanical ventilation is being discharged to the home-care setting. Inspection of the two-story home reveals front and rear elevated porch entrances, with all bedrooms upstairs. All room floors (except the kitchen and bathrooms) are covered with high-pile carpeting. The largest bedroom is 12 by 14 ft. The electrical service is rated at 75 amps, and the only grounded outlets are in the kitchen and garage. Heating is provided by a forced hot-air system; there is a single window air conditioner in the patient's bedroom.

What problems do you see, and what changes would you recommend to provide the proper home environment for this patient?

Solution

Although wheelchair-bound, this patient is still mobile. Both the elevated porch entrances and the high-pile carpeting restrict mobility. A ramp entrance must be constructed, and the carpeting must be removed or covered with a flat, hard surface material. Given the size of the patient's upstairs room and the obstacle of the stairwell, it would be best to identify a large first-story room for conversion to a bedroom. Because the patient is likely to need at least an electrical bed, ventilator, and suction machine, the electrical service capacity is inadequate and needs upgrading to ensure at least 15 to 20 amps in the patient area, with 200 amps overall. Appliance, counter, sink, and toilet heights must be assessed for easy patient access.

- Diagnosis (severe primary lung disease, secondary conditions related to lung disease and hypoxemia, related conditions or symptoms that may improve with O_2)
- Laboratory evidence (arterial blood gas analysis or oximetry under the appropriate testing conditions), as home-care companies cannot provide this testing
- Additional medical documentation (no acceptable alternatives to home O_2 therapy)

For home use, the ordering physician must authorize O_2 therapy using the CMS Certification of Medical Necessity form for O_2. After the need for long-term therapy has been documented, repeat arterial blood gas analysis or SpO_2 measurements are generally not needed. However, CMS requires that patients on home oxygen follow up with their physicians once a year, showing clinical documentation that demonstrates the need for continuation.[22]

Oxygen Qualification Criteria

In addition to a physician's prescription, in order to be eligible for reimbursement for home oxygen, patients must qualify by meeting the clinical criteria established by CMS or their health insurance companies. Such qualification criteria are largely based on arterial blood gas or pulse oximetry thresholds, as follows:

- Patients on room air while at rest and awake when tested
- Arterial oxygen saturation at or below 88%
- or
- Arterial partial pressure of oxygen (PO_2) at or below 55 mm Hg
- Patients on room air at rest while awake when tested but who have a confirmed diagnosis of congestive HF, pulmonary hypertension, or erythrocythemia with a hematocrit greater than 56%:
- Arterial oxygen saturation of 89% (or less) at rest (awake)
- or
- Arterial PO_2 of 56 to 59 mm Hg or less

Variations on these thresholds exist for patients tested under other conditions, such as while sleeping or during exercise.[22]

RULE OF THUMB In order for patients to receive reimbursement coverage for their oxygen therapy, CMS requires that they meet initial qualifications demonstrating hypoxemia and follow up with their physicians once a year, showing clinical documentation that demonstrates the need for continued services.

Supply Methods

Most alternative care sites do not have bulk O_2 storage or delivery systems. In these settings, O_2 is normally supplied from one of the following three sources[23]: (1) compressed O_2 cylinders, (2) liquid O_2 systems, or (3) O_2 concentrators. Table 57.3 summarizes the major advantages and disadvantages of each.

Compressed Oxygen Cylinders

For practical reasons, the primary use of compressed O_2 cylinders in alternative settings is either for ambulation (small cylinders) or as a backup to liquid or concentrator supply systems. Safety measures for O_2 cylinders are the same as those discussed in Chapters 41 and 42. For home use, the RT should thoroughly review these safety measures with both the patient and family members. After instruction, the RT should always confirm and document the abilities of caregivers to use the delivery system safely.

In addition to the cylinder gas, a pressure-reducing valve with a flowmeter is needed to deliver O_2 at the prescribed flow. Such a flowmeter may be preaffixed to the tank or removable. Standard clinical flowmeters deliver flows up to 15 L/min; however, flows used in alternative settings are typically in the range of 0.25 to 5 L/min. For this reason, the RT should select a calibrated low-flow flowmeter whenever possible (see Chapter 41). Home-fill stations are useful, as these cylinders have a preaffixed regulator that is filled right from an O_2 concentrator. These devices are exceptionally desirable as they are easy to use and allow patients to have portable oxygen whenever they need it simply by filling the cylinder. As in the hospital, there is usually no need to humidify nasal O_2 at flows of 4 L/min or less.[23] If humidification is needed, a simple unheated bubble humidifier can be used. Because the mineral content of tap water may be high (hard water), the water used in these humidifiers should be distilled. Otherwise the porous diffusing element may become occluded. Although complete blockage is unlikely, occlusion of the diffusing element can impair humidification and alter flow.

Liquid Oxygen Systems

Although the higher cost of liquid O_2 delivery system versus others has greatly reduced their use, they do offer some advantages and are therefore still used under certain conditions in alternative settings. One of the main advantages of a liquid O_2 system relates to the fact that 1 ft^3 of liquid O_2 equals 860 ft^3 of

TABLE 57.3 Advantages and Disadvantages of Major Alternative Oxygen Supply Systems

System	Advantages	Disadvantages
Compressed O_2	Good for small-volume user	Large cylinders are heavy and bulky
	No waste or loss	High-pressure safety hazard
	Stores O_2 indefinitely	Provides limited volume
	Widespread availability	Requires frequent deliveries
	Portability (small cylinders)	Tight valves can be a problem
Liquid O_2 system	Provides large volumes	Must be delivered as needed
	Low-pressure system (20–25 psi)	Loss of O_2 because of venting of system when not in use
	Portable units can be refilled from reservoir (up to 8-h supply at 2 L/min)	Low-temperature safety hazard
		Cannot operate ventilators or other high-pressure devices
	Valuable for rehabilitation	Some difficulty in filling portable units
O_2 concentrator	No waste or loss	Disruption in electrical service renders system inoperable
	Low-pressure system (15 psi)	Backup O_2 is needed
	Cost-effective when continual supply of O_2 is needed	Cannot operate ventilators or other high-pressure devices
		FiO_2 decreases with increasing flow
	Eliminates need for deliveries	High electricity costs possible

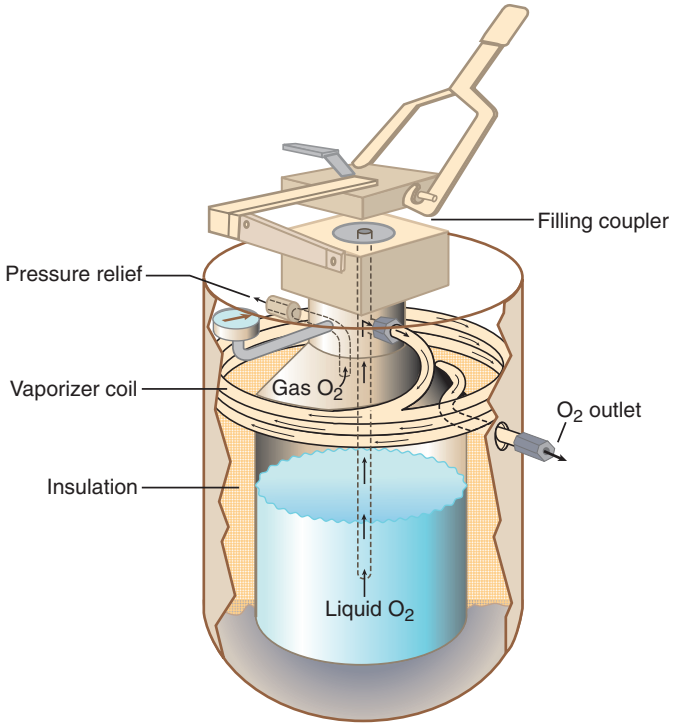

Fig. 57.1 Diagram of a personal liquid oxygen supply system. (Modified from Lampton LM: Home and outpatient oxygen therapy. In: Brashear RE, Rhodes ML, editors: *Chronic obstructive lung disease*, St Louis, 1978, Mosby.)

gas; therefore it is possible to store large quantities of oxygen in small spaces. As shown in Fig. 57.1, a typical personal liquid O_2 system is a miniature version of a hospital liquid O_2 system. Similar to its larger counterpart, this system consists of a reservoir unit similar in design to a thermos bottle. The inner container of liquid O_2 is suspended in an outer container, with a vacuum in between. The liquid O_2 is kept at approximately –300°F. Because of constant vaporization, gaseous O_2 always exists above the liquid. When the cylinder is not in use, this vaporization maintains pressures between 20 and 25 psi. When pressures increase above this level, gas vents out of the pressure relief valve.

Depending on manufacturer and model, small liquid O_2 cylinders hold 45 to 100 lb of liquid O_2. To calculate duration of flow of a liquid O_2 system, one first converts the weight of liquid O_2 in pounds to the equivalent volume of gaseous O_2 in liters. At normal liquid cylinder operating pressures, 1 lb of liquid O_2 equals approximately 344 L of gaseous O_2.

It is important for the RT to identify who is the appropriate candidate for liquid oxygen. Because of newer delivery models, most patients opt for a different stationary setup such as a concentrator coupled with a portable system.

Oxygen Concentrators

The oxygen concentrator is the primary piece of equipment used in delivering oxygen to patients in postacute settings. The output of many concentrator models has been limited to 5 L/min. However, more recently, models capable of delivering 10 L/min have been introduced, including high-intensity concentrators that deliver higher pressures and flows to patients who require high-flow devices such as Venturi or nonrebreathing masks (see Chapter 42). In addition, technologic advances have accounted for other enhancements to O_2 production and delivery devices in alternative care settings. One example is the **portable oxygen concentrator** (POC) with demand-flow conserving capabilities. Such a battery-operated unit affords the patient receiving low-flow O_2 increased mobility, and this item has been approved for use in most commercial aircrafts. In order for a patient to clinically qualify for a POC, the RT must assess the patient's saturation levels while ambulating, making sure that acceptable oxygen levels are maintained.

O_2 concentrators represent the most cost-efficient supply method for patients in alternative care settings who need continuous low-flow O_2. For home use, a concentrator running 24 hours/day increases the average monthly electrical bill by only 5% to 10%. Depending on the season, heat given off by the concentrator's compressor can also affect energy usage by increasing room temperature. Nonetheless, when used with patients receiving low-flow O_2, concentrators are just as effective in increasing blood O_2 levels as other systems. Oxygen concentrators also

require yearly preventative maintenance to make sure that they are functioning properly.[23]

Problem Solving and Troubleshooting

Technical problems with O_2 supply systems in alternative settings are similar to problems encountered in the acute care hospital (see Chapter 41). In addition to these technical problems, situations can arise where patients or caregivers fail to follow instructions properly. To avoid communication problems, verbal instructions should always be reinforced by simple written instructions for subsequent reference. In addition, the clinician should always confirm and document the ability of caregivers to use the delivery system safely, including how to troubleshoot simple problems. The ability of caregivers and patients to give an adequate return demonstration on proper equipment usage should also be recorded.

To avoid problems before they occur, the patient or caregiver should be instructed to check all O_2 delivery equipment at least once a day. The proper function of all equipment, including liter flow and connections should be checked. Oxygen concentrators have internal alarms that will audibly alert the patient if the oxygen being delivered does not have a high enough FiO_2. If the analyzed FiO_2 of the gas coming out of the oxygen concentrator is less than 95%, the problem often stems from exhausted pellet canisters, which should be replaced. In addition, air inlet filters must be cleaned weekly. In the home setting, providing the patient or caregiver with a simple checklist can help to ensure that these important tasks are performed regularly.

In contrast to the hospital setting, O_2 supply problems in the alternative care setting cannot always be addressed immediately. For this reason, the clinician must ensure that every such system has an emergency backup supply. This backup supply is normally provided by a large gaseous cylinder or, at a minimum, an E cylinder. If the primary O_2 supply of a home-care patient is by concentrator, the home-care RT should notify the electric power company in writing that life-support equipment is in use. In the event of a power outage, many utility companies will try to give priority to that location. In addition, it is important for the home-care company to notify the local fire department that a patient has oxygen in his or her home. For patients in more remote geographic areas, an emergency gasoline electrical generator is recommended. If that is not possible, several large oxygen cylinders can be left with the patient. A perfect example of contingency planning working well is when Hurricane Sandy hit New Jersey and power was out for a week or more with little to no accessibility. As a result of power company responsiveness and other backup measures, most patients were safely able to receive their oxygen therapy without interruption.

Possible physical hazards to patients and caregivers include unsecured cylinders, ungrounded equipment, mishandling of liquid (resulting in burns), and fire. Careful preliminary instruction, followed by ongoing assessment of the environment, can help to minimize these problems. Bacterial contamination of nebulizers or humidification systems is another potential problem. Infection-control procedures designed to minimize bacterial contamination are discussed later in this chapter.[23,24]

MINI CLINI

Home Safety Assessment

Problem

An RT does a home assessment on a patient who was recently prescribed long-term oxygen therapy (LTOT). The RT smells an odor similar to cigarette smoke. The patient denies smoking in the house and states that she has recently quit.

Solution

First, it is essential for the RT to perform a visual inspection of the patient's residence. This would include looking for ashtrays, matches, packs of cigarettes, burnt candles, and so on. This must all be thoroughly documented on the home assessment checklist. Second, the patient should be advised that no one, including friends and family, should be allowed to smoke in the home. Third, it is important that a "no smoking" sign is visibly present, alerting those in the home of the presence of O_2. The RT should also make sure that the patient has a working fire extinguisher and a working smoke alarm. If at any point the RT identifies that the patient is smoking, the incident should be reported to both the physician and the risk management team.

RULE OF THUMB If an O_2 concentrator cannot supply at least 85% O_2 at 5 L/min, the pellet canisters are probably exhausted and should be replaced.

Delivery Methods

The most common O_2 delivery system for long-term care is the nasal cannula. Simple O_2 masks and air entrainment masks may also be used but are much less common. To decrease O_2 use and costs, numerous O_2-conserving devices have been developed, including transtracheal O_2 catheter, reservoir cannula, and demand or pulsed-dose O_2 delivery systems.

The performance characteristics, advantages, and disadvantages of transtracheal O_2 catheters and reservoir cannulas are described in detail in Chapter 42. We focus here on the application of the transtracheal O_2 catheter and the technical aspects of demand-flow systems.

Transtracheal Oxygen Therapy

Transtracheal oxygen therapy (TTOT) is O_2 delivered via a catheter with a small orifice that is inserted through the skin and neck tissue into the trachea. As detailed in Chapter 42, this delivery method offers advantages of improved cosmetic appearance and lower flows to achieve the same therapeutic effect.

As with most modalities in alternative care settings, the success of TTOT depends mainly on effective patient education and ongoing self-care with professional follow-up. Key patient responsibilities include routine catheter cleaning and recognizing and troubleshooting common problems.[25]

Demand-Flow Oxygen Systems

A demand-flow O_2 delivery device, also known as a pulsed-dose **O_2-conserving device**, uses a flow sensor and valve to synchronize gas delivery with the beginning of inspiration.[25] These O_2-conserving devices exhibit performance comparable to that of a nasal cannula at approximately one-third to one-half the

MINI CLINI

Selecting a Long-Term Oxygen Delivery System

Problem

The following three patients require LTOT: (1) a stable home-care patient with restricted activity needing low FiO_2; (2) an active home-care patient with low FiO_2 needs who desires increased mobility; and (3) a patient in a long-term-care facility with a tracheostomy who needs moderate levels of O_2 and high humidity. Select the best O_2 delivery system for each patient.

Solution

Patient 1: Because most home-care patients who need O_2 are relatively stable and their FiO_2 needs are minimal, traditional low-flow therapy by nasal cannula (using a concentrator) is the most common and accepted approach. When it is combined with a portable gas cylinder (for backup and limited walking), this combination is ideal for patients with restricted activity.

Patient 2: For an active patient with low FiO_2 needs who desires increased mobility, a conserving device used in conjunction with a portable concentrator (coupled with a home-based concentrator) is the ideal choice. Given that selected models of reservoir cannulas are poorly accepted by some patients, the choice of conserving device usually narrows to a demand-flow/pulse-dosed system, alone or coupled with a portable concentrator.

Patient 3: Patients with artificial airways in alternative sites who need O_2 present a special problem. Because of high O_2 use and infection concerns, an O_2-powered air entrainment nebulizer is unsatisfactory. Instead, a compressor-driven humidifier with supplemental O_2 bled in at low flows from a concentrator or liquid system should be used. In this case, the RT must confirm the FiO_2 with a calibrated analyzer.

MINI CLINI

Troubleshooting a Home Oxygen Contractor

Problem

A patient calls after hours and states that his concentrator is sounding an alarm and it feels like there's no oxygen coming out.

Solution

The first thing the home-care RT should do is advise the patient to remove the oxygen cannula from the concentrator and move to the backup cylinder. This will allow the patient to troubleshoot the equipment while still receiving his oxygen therapy. There could be several different solutions to fixing the issue.

1. Ask the patient to put the cannula in a cup of water. If there is bubbling in the cup, the concentrator is delivering flow. The alarm could likely be going off because the concentrator is not taking in enough room air. The patient should then be asked to make sure that the concentrator is at least 18 in away from a wall or dresser and that the filters are clean.
2. If the alarm is sounding but no light is on, it is usually due to a loss of power. The patient should be advised to try replugging the unit. If this does not work, he or she should check the electric breaker switch on the front of the concentrator to make sure that it has not tripped.
3. If the concentrator continues to alarm, it may be a malfunction issue and the patient should contact the DME company for a replacement. Most companies have technicians available 24 h a day to replace such equipment.

flow. With these devices, most of the effective O_2 delivery occurs during the first half of inspiration. As a result, these systems deliver a synchronized pulse of O_2 delivered at the beginning (first 25%) of inspiration. Under these conditions, a properly functioning pulsed O_2 system can produce SaO_2 levels equal to levels seen with continuous flow while using 60% less O_2.[26]

In theory, demand-flow O_2 systems provide the greatest savings in O_2 use for a given level of arterial saturation. Recent improvements to demand-flow systems have made them more reliable and user friendly, addressing the major disadvantages of earlier versions. As a result of these improvements and the ability of these devices to increase the duration of flow by two or three times, they have now gained wide acceptance. This includes newer portable technology that can allow patients to use up to 10 hours of battery life before needing to recharge their concentrators. POCs also come with car chargers that will maintain and charge the concentrator.[27,28]

Selecting a Long-Term Oxygen Delivery System

As when selecting hospital-based O_2 therapy systems, the "three P's" should always be considered when selecting a long-term O_2 system: purpose, patient, and performance. The goal is always to match the *performance* of the equipment to both the objectives of therapy *(purpose)* and the *patient's* special needs. Patients requiring low-flow home O_2 and enhanced mobility should be considered for a portable concentrator alone or one with a conserving feature or a liquid O_2 setup with a pulsed-dose O_2-conserving device.

Problem Solving and Troubleshooting

Most problems with long-term O_2 delivery systems are related to patients and caregivers who fail to follow instructions or comply with the prescribed therapeutic or maintenance regimen.[23] Generally, home-based caregivers should be allowed to operate and maintain O_2 delivery devices only after they have been instructed by credentialed RTs and have demonstrated the appropriate level of skill. In no case should the patient or caregiver be allowed or instructed to alter flow settings. Instead, when in doubt, they should be taught to switch to the backup supply at the same liter flow and either contact their physician if they are feeling ill or their home-care company if they think the equipment is not functioning properly.

To be proactive and avoid complications or product failure, catheters and tubing should be replaced every 3 months, at which time a checkup by the physician is also recommended. The patient or caregiver should clean the oxygen delivery device every day, per the self-care guidelines listed in this chapter. Patients should always be instructed to put on a nasal cannula and to call the physician if any major problem occurs.

VENTILATORY SUPPORT IN ALTERNATIVE SETTINGS

Providing successful ventilatory support outside the acute care hospital requires careful patient selection and meticulous discharge planning.[29] Key factors include an interdisciplinary team approach, effective caregiver and family education, thorough assessment and preparation of the environment, and careful selection of needed equipment and supplies. Properly planned ventilatory support delivered in alternative settings can provide

TABLE 57.4 Profiles of Patient Groups Requiring Ventilatory Support in Alternative Settings

Group Description	Diseases Involved
Profile 1	
Mainly composed of neuromuscular and thoracic wall disorders; particular stage of disease process allows patient certain periods of spontaneous breathing time during the day; generally requires only nocturnal mechanical support	Amyotrophic lateral sclerosis Multiple sclerosis Kyphoscoliosis and related chest wall deformities Diaphragmatic paralysis Myasthenia gravis
Profile 2	
Requires continuous mechanical ventilatory support associated with long-term survival rates	High spinal cord injuries Apneic encephalopathies Severe chronic obstructive pulmonary disease Late-stage muscular dystrophy
Profile 3	
Usually returns home at request of patient and family; patient's condition is terminal, life expectancy is short, and patient and family wish to spend remaining time at home; patients usually pose management problems in the home because of their rapidly deteriorating conditions	Lung cancer End-stage chronic obstructive pulmonary disease Cystic fibrosis

major benefits for both the patient and family as well as yielding substantial savings in health care costs.[30]

Patient Selection

Most patients needing ventilatory support outside the acute care hospital fall into one of the following three broad categories[31]:

1. Patients unable to maintain adequate ventilation over prolonged periods (in particular, noninvasive nocturnal or intermittent use)
2. Patients requiring continuous mechanical ventilation for long-term survival
3. Patients who are terminally ill with short life expectancies

Table 57.4 provides more detailed profiles of these patient groups. In addition to adults, a growing number of ventilator-assisted children are being managed in alternative settings. The same basic principles of discharge planning and patient care as for adult patients should be followed for ventilator-assisted children.[32]

Regardless of diagnosis, patients being considered for ventilatory support in alternative settings must be medically and psychologically stable. In regard to assessing patient stability, Box 57.2 outlines the criteria developed by the American College of Chest Physicians (ACCP).[33]

Settings and Approaches

The most common setting for ventilatory support outside the acute care hospital is the home. Additional sites include long-term care facilities, including specialized long-term units such as LTACHs, designed specifically for ventilator patients.[34,35]

BOX 57.2 Criteria to Determine Patient Stability for Ventilatory Support in Alternative Care Settings

- Ability to tolerate mechanical ventilation
- Acceptable arterial blood gas results and other blood chemistry (e.g., complete blood count)
- Relatively low FiO_2 needs (generally ≤40%)
- Psychological stability
- Absence of life-limiting comorbidities, including cardiac dysfunction and arrhythmias
- Positive end-expiratory pressure should not exceed 10 cm H_2O
- Ability to clear airway secretions by cough, suction, or cough-assist device
- Tracheostomy tube as opposed to endotracheal tube for invasive ventilation
- No readmissions expected for >1 month

Based on individual evaluation of patient need, one of the following two major support approaches may be considered: (1) invasive or (2) noninvasive support. In alternative settings, invasive ventilatory support always involves application of positive pressure ventilation by tracheotomy. Noninvasive approaches include positive-pressure and very rarely negative-pressure ventilation.[36]

Standards and Guidelines

Standards and guidelines for ventilatory support outside the acute care hospital continue to evolve. The AARC developed a Clinical Practice Guideline on long-term invasive mechanical ventilation in the home, which can be found at the AARC's website (AARC.org).[37]

Special Challenges in Providing Home Ventilatory Support

Institutions that provide ventilatory support in alternative settings differ from acute care facilities mainly in their level of technology support. The home setting not only lacks this support but also must depend extensively on nontechnical, nonprofessional caregivers. For these reasons, providing ventilatory support in the home presents many special challenges.

Prerequisites

For home ventilatory support to be successful, several prerequisites must be met, including the following[38]:

- Willingness of family to accept responsibility
- Adequacy of family and professional support
- Overall viability of the home-care plan
- Stability of patient
- Adequacy of home setting
- Adequate financial stability and insurance coverage

In regard to the home setting, the same factors listed in Box 57.1 should be evaluated for patients being considered for home ventilatory support.

Planning

Successful home ventilatory support requires extensive planning, education, and follow-up by all members of the home-care team.

Basic steps in the discharge process for a ventilator-dependent patient include the following:

1. Family is consulted regarding feasibility.
2. Discharge planner coordinates efforts of team members and discharge plan is formulated.
3. Insurance has been verified and patient has coverage for services at home.
4. Team members discuss plan with family and caregivers.
5. Home layout is assessed, with necessary changes made.
6. Education and training are initiated and completed.
7. Patient and family are prepared for discharge.
8. Equipment and supplies are readied.
9. Discharge planner meets with team and makes final preparations.
10. Patient is discharged (with trial period if necessary).
11. Local power company is notified regarding the presence of life-support equipment; appropriate backup power (battery or compressed gas source) is made available.
12. Local fire department is notified regarding the presence of life-support and appropriate equipment.
13. Ongoing and follow-up care is provided by visiting nurse, RT, and other health care professionals as necessary.

Caregiver Education

To properly prepare patients, family members, and other caregivers for home discharge, a comprehensive educational program must be undertaken and completed. Essential skills that must be taught including the following[38]:

- Simple patient assessment
- Airway management, including tracheostomy and stoma care, cuff care, suctioning, cough-assist, changing artificial airways or ties
- Chest physical therapy techniques, including percussion, vibration, and coughing
- Medication administration, including oral and aerosol
- Patient movement and ambulation
- Equipment operation and maintenance
- Equipment troubleshooting
- Cleaning and disinfection
- Emergency procedures

Emergency situations that caregivers must be trained to recognize and deal with properly include the following:

- Ventilator or power failure
- Ventilator circuit problems
- Airway emergencies
- Cardiac arrest

All caregivers should successfully complete this educational process. Training generally requires a minimum of 1 to 2 weeks, over which time several education sessions can take place and cover instruction, demonstration, caregiver practice, and evaluation. Caregivers should be strongly encouraged to complete a course in basic life support, such as that offered by the American Heart Association, before the patient is discharged. Ideally, the patient should have a trial period on the actual home ventilator before discharge. In the early stages after discharge, patient follow-up by an RT likely should occur every day. As patient and caregivers become more familiar with the equipment and procedures, the frequency of follow-up visits generally decreases to about once per month.[39,40]

Invasive Versus Noninvasive Ventilatory Support

Until recently, invasive positive-pressure ventilation by tracheostomy was the default standard for long-term mechanical ventilation, especially for patients requiring 24-hour support. However, long-term tracheostomy is associated with some potential problems, including secretion retention, infection, aspiration, and ventilator-associated pneumonia as well as communication difficulties between caregivers and patients. Because many long-term care facilities treat a tracheostomy as an open wound, patient placement at certain alternative care sites is prohibited.[41] Last, invasive ventilation by tracheostomy poses significant limits on the patient's quality of life. For these reasons, noninvasive support is becoming increasingly popular in general and in alternative settings. Noninvasive ventilatory support (see Chapter 50) involves any method designed to augment alveolar ventilation without an endotracheal airway. **Noninvasive ventilation (NIV)** is usually the first choice. An individual requiring mechanical ventilation can be supported with NIV if the following conditions are met[42]:

- The patient is mentally competent, cooperative, and not using heavy sedation or narcotics.
- Supplemental O_2 therapy is generally minimal ($FiO_2 \leq 40\%$).
- SaO_2 can be maintained at greater than 90% by aggressive airway clearance techniques.
- Bulbar muscle function is adequate for swallowing and airway protection.
- No history exists of substance abuse or uncontrollable seizures.
- Unassisted or manually assisted peak expiratory flows during coughing exceed about 3 L/s.
- No conditions are present that interfere with NIV interfaces (e.g., facial trauma, inadequate bite for mouthpiece, presence of orogastric or nasogastric tube, or facial hair that can hamper an airtight seal).

Patients who can benefit from NIV generally fall into one of two categories (see Chapter 50).[43] Patients in the first category have conditions in which cessation of ventilation could lead to imminent death. This category includes both acutely ill patients (patients with asthma, acute exacerbation of COPD, or pulmonary edema) and patients requiring long-term 24-hour support (some patients with quadriplegia or patients with certain neuromuscular disorders). Patients in the second category have conditions in which NIV may offer clinical benefit but cessation is usually not life-threatening. These patients generally require only intermittent or nocturnal support and are more commonly found in alternative care settings. Patients in this category include those with chronic neuromuscular and chest wall diseases, such as amyotrophic lateral sclerosis (ALS), muscular dystrophy, and kyphoscoliosis. The application of long-term NIV for patients with obstructive disorders such as end-stage COPD or cystic fibrosis is much less common. Relative contraindications to NIV include severe upper airway dysfunction, copious secretions that cannot be cleared by spontaneous or assisted cough, and O_2 concentration requirements exceeding 40%.[43,44]

BOX 57.3 Essential Equipment and Supplies for Ventilator-Dependent Patients in Alternative Care Settings

Equipment

- Ventilator(s)
- Manual resuscitator (bag-valve-mask unit)
- Heated ventilator/humidifier with thermostat and heat and moisture exchanger
- Monitoring or alarm devices (including remote where necessary)
- 12-V battery and battery charger
- Air compressor
- O_2 source
- Power strip or surge protector
- Suction machine with backup (manual or battery)
- Stethoscope and sphygmomanometer
- O_2 analyzer
- Pulse oximeter
- Hospital bed with table
- Patient lift
- Bedside commode, urinal, or bedpan
- Wheelchair

Supplies

- O_2
- O_2 delivery devices, including manual resuscitator
- Airway interface (masks, mouthpieces, tracheostomy tubes)
- Tracheostomy tube inner cannulas
- Extra tracheostomy tubes including a tube one size smaller
- Tracheostomy care kits
- Ventilator circuits
- Bacterial filters
- Heat and moisture exchangers
- Passy Muir valve (if appropriate)
- Connecting tubing (aerosol, O_2, suction)
- Suction catheters
- Disposable gloves
- Distilled or sterile water
- Small-volume nebulizer or metered dose inhaler with ventilator adapters if appropriate
- Cleaning and disinfection supplies (10-mL syringe, 15- to 22-mm tubing adapters)

Equipment

Box 57.3 lists the essential equipment and supplies needed for ventilator-dependent patients in alternative settings.[36]

Selecting the Appropriate Ventilator

The choice of ventilator for a patient in an alternative care setting should be based on the patient's clinical need and the available support resources. In some cases, patient needs may dictate that more than one ventilator be provided.[36] A second backup ventilator should be considered for patients who cannot maintain spontaneous ventilation for more than 4 consecutive hours, for patients living in an area where a replacement ventilator cannot be secured within about 2 hours, and for patients whose care plan requires mechanical ventilation during mobility.[44] Generally ventilators chosen for care in alternative settings must be dependable and easy for caregivers to operate. If mobility is an essential element of the patient's care plan, the ventilator system selected should be portable. If the patient is receiving continuous ventilatory support in any alternative setting, external battery backup is required, and emergency AC power by way of a generator is recommended. It is also important to verify with the patient's insurance carrier as to what the financial allowance is for each piece of equipment including the accessories.

If invasive ventilation by tracheostomy is the selected approach, the best choice is a positive-pressure ventilator. The invasive route also requires a humidification system, preferably a servo-controlled heated humidifier with alarms. Patients with a tracheostomy without retained secretions may use a heat and moisture exchanger (HME) during transport or to enhance their mobility. For patients with an intact upper airway, a device capable of NIV is the first choice unless contraindicated. Box 57.4 lists the absolute contraindications to using NIV.[45]

BOX 57.4 Absolute Contraindications to Using Noninvasive Ventilation

- Need for immediate intubation
- Hemodynamic instability
- Uncooperative patient
- Facial burns or trauma
- Inadequate airway protection
- Patent tracheoesophageal fistula

TABLE 57.5 Essential, Recommended, and Optional Features of a Positive Pressure Ventilator for Use in an Alternative Care Setting

Feature	Necessity
Positive pressure tidal breaths	Essential
Mandatory rate	Essential
Flow or inspiratory-to-expiratory ratio or inspiratory time	Recommended[a]
Positive end-expiratory pressure (PEEP)	Recommended[a]
FiO_2 to 1	Optional
Patient's spontaneous breath (e.g., continuous positive airway pressure [CPAP], intermittent mandatory ventilation)	Optional
Breath-triggering mechanism (flow or pressure sensors to initiate ventilator breath)	Recommended[a]
Flow-timing interaction (e.g., pressure support)	Optional
Feedback control (e.g., pressure-regulated volume control)	Optional

[a]Essential if the patient has intact ventilatory drive and respiratory muscles or if the possibility of partial or complete ventilator independence is anticipated.

Positive Pressure Ventilators

Table 57.5 lists the essential, recommended, and optional features of positive-pressure ventilators used in alternative care settings. An *essential* feature is basic to safe and effective operation in most patient care settings. A *recommended* feature helps provide optimal patient management. An *optional* feature is possibly useful in limited situations but not needed for most patients.[45,46]

As shown in Fig. 57.2, there are many new positive pressure ventilators designed for use in alternative settings. These ventilators

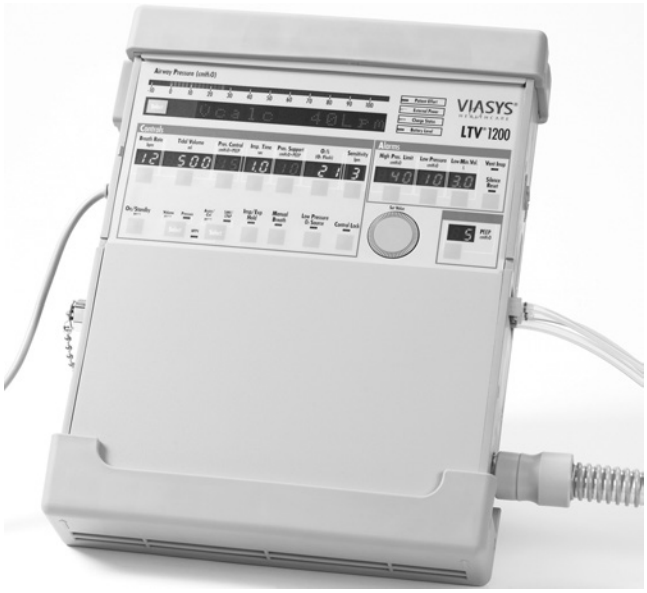

Fig. 57.2 LTV 1200 ventilator. (Courtesy Vyaire Medical, Mettawa, IL.)

Fig. 57.3 Dreamstation BiPAP. (Used with permission of Philips Respironics, Murrysville, PA.)

can be used on adults or pediatric patients weighing at least 5 kg.

Some are approximately the size and weight of a laptop computer and have many of the capabilities of much larger mechanical ventilators used in alternative sites and in acute care. These new ventilators offer ventilator-dependent patients the advantages of greater mobility and space conservation. Many of these models also offer pressure support and can provide positive end-expiratory pressure (PEEP) without having to add an adapter to the ventilator circuit.[47]

Many new positive-pressure ventilators designed for alternative care settings have an internal battery, which can provide several hours of use in the event of a power failure. For longer periods of use away from typical line power, many of these devices can run for 10 to 12 hours using an external battery.

Additionally, time-triggered or patient-triggered, pressure-limited, flow-cycled devices (pressure support with timed backup) have been successfully applied in alternative settings.[48,49] Many units are currently available (Fig. 57.3) that are specifically designed to provide this type of support, usually noninvasively by nasal or oronasal (full face) masks.

TABLE 57.6 Adverse Effects of Noninvasive Ventilation Interfaces and Possible Corrective Actions

Interface	Adverse Effect	Remedy
Nasal and oronasal masks	Discomfort	Proper fit, adjust strap tension, change mask type
	Nasal bridge redness, pressure sores, conjunctivitis	Try different size or type of mask, reduce strap tension, use forehead spacer, try nasal pillow, use artificial skin
	Acneiform rash	Cortisone cream, alternative (gel) mask
Oronasal masks	Impede speech and eating	Permit periodic removal if tolerated by patient
	Claustrophobia	Choose clear masks with minimal bulk
	Aspiration	Exclude patients unable to protect airway; nasogastric tubes for patient with nausea and abdominal distention
Mouthpieces/ lip seals	Interference with swallowing, salivary retention	Coaching, adaptation
	Pressure on lips, cheeks	Try different size or type of mask, ensure proper fit, adjust strap
	Dental deformity	Orthodontic consultation
	Aerophagia	Simethicone, coaching
	Allergic reactions	Change prosthetic materials
	Nasal air leaking	Nose clips
	Accidental disconnection	Appropriate alarms in ventilator-dependent patients

Most positive pressure ventilators can be used to provide NIV.[49,50] NIV is normally provided by pressure-targeted ventilation regardless of the cause of ventilatory failure. The newest generation of these ventilators include alarm capabilities and internal battery backup.[50]

The biggest challenge with NIV is not selecting the right ventilator but getting a good, comfortable, minimal-leak interface. Interfaces commonly found in alternative care settings include oronasal (full face) masks; nasal masks; nasal "pillows"; and simple, flanged, or custom mouthpieces. For long-term use, some patients prefer alternating between devices. A patient may prefer a simple mouthpiece for easy accessibility during the day, with a nasal mask providing support at night.[50] Table 57.6 summarizes common problems associated with NIV interfaces and how to correct them.[51]

All positive-pressure ventilators used in alternative settings must have an alarm (pneumatic or electrical) to indicate loss of power. Portable volume-cycled ventilators should also incorporate a high-pressure alarm or cycle override. For patients with conditions in which cessation of ventilation would cause death, a patient-disconnect alarm (low-pressure or low exhaled volume) must be provided.[50,51] In some settings, a remote alarm, secondary disconnect alarm, or both may be needed. A secondary alarm may be based on chest wall impedance and cardiac activity, exhaled volume, end-tidal CO_2, or pulse oximetry with alarm

capabilities. For patients in alternative settings who require only intermittent NIV, a loss-of-power alarm is generally sufficient.[50-52]

RULE OF THUMB All positive-pressure ventilators used in alternative settings must have a loss-of-power alarm. For portable volume-cycled ventilators, alarms for high pressure and loss of pressure (disconnect) are also essential.

OTHER MODES OF RESPIRATORY CARE IN ALTERNATIVE SITES

In addition to O_2 therapy and ventilatory support, other modes of respiratory care are now common in the alternative care setting. These may represent the primary therapy or may be used to supplement other modes of care. Included for discussion here are bland aerosol therapy, aerosol drug administration, airway care and clearance methods, nasal continuous positive airway pressure (CPAP), and apnea monitoring.

Bland Aerosol Therapy

The delivery of bland aerosols has been common in alternative sites for many years. Bland aerosol therapy (see Chapter 39) includes the delivery of sterile water or various concentrations of saline solution in aerosol form. The aerosol can be produced by either an ultrasonic or jet (large volume) nebulizer. If a jet nebulizer is being used, a 50-psi air compressor is also required. Supplemental O_2 is provided by either a concentrator or liquid supply system and must be analyzed with an O_2 analyzer.

Depending on the patient's condition and therapeutic objectives, bland aerosol therapy may be either continuous or intermittent. Although bland aerosol alone may have little effect on the properties of mucus or its clearance, it may be useful as an adjunct to other airway clearance procedures.

The potential problem is infection from contaminated equipment. To reduce the incidence of infection, equipment and patient delivery systems must be cleaned and changed regularly, as noted later in this chapter.[53]

Aerosol Drug Administration

As in the acute care setting, the aerosol route is popular for drug administration to respiratory patients in alternative care settings. As described in Chapter 40, drug categories commonly administered by the aerosol route include beta-adrenergic bronchodilators, anticholinergic agents, and antiinflammatory drugs.

Most pulmonary drugs are available in either metered-dose inhaler or dry-powder inhaler form. Alternatively, the caregiver can use a small-volume nebulizer powered by a low-output diaphragm compressor.[54]

Airway Care and Clearance Methods

Patients in alternative care settings with tracheostomies require both daily stoma care and tracheobronchial secretion clearance. Tracheostomy care can be provided by any trained caregiver, but tube changes should generally be performed only by an RT or a physician.

In most alternative care settings, tracheobronchial clearance (see Chapter 44) is often accomplished by suctioning, using a portable electrically powered suction pump with collection bottle and connection tubing. For suctioning of the patient at home, some patients may be taught to suction themselves. Proper suctioning procedures should also be taught to home caregivers (see Chapter 37). Education and training on proper suctioning methods may begin before patient discharge from the acute care setting, with reinforcement and follow-up as needed.[55] Daily maintenance and cleaning are required.

RULE OF THUMB For portable suction units calibrated in inches of mercury (in Hg), the following vacuum ranges are recommended (adjustment may be needed based on volume and viscosity of secretions):

Patient Category	Vacuum Setting (in Hg)
Infants	5–7
Children	7–12
Adults	12–15

Numerous methods are available for patients in an alternative care setting with an intact upper airway who need help with secretion clearance. These methods include both patient-independent and caregiver-dependent techniques (see Chapter 44).[55] Patients can be taught to apply independently coughing, forced exhalation, active cycle of breathing, and autogenic drainage methods. Caregiver assistance is required with traditional postural drainage, percussion and vibration, and directed or assisted coughing. Additional assistance can be provided by mechanical devices such as a positive expiratory pressure mask, flutter valve, intrapulmonary percussive ventilator, and high-frequency chest compression vest.

Another airway clearance method involves the use of cough-assist devices such as a mechanical **insufflator-exsufflator** or a cough-assist unit. This device, an example of which is included as Fig. 57.4, uses alternating positive and negative pressure to simulate a cough as a form of lung expansion and airway clearance therapy.

These devices can be especially effective with patients receiving NIV. The application of secretion clearance devices or techniques by nonprofessional caregivers must involve good preliminary instruction and ongoing follow-up by the RT working in any alternative site.[55]

Nasal Continuous Positive Airway Pressure Therapy

Nasal CPAP therapy has become an accepted form of home care used to treat sleep apnea–hypopnea syndrome. For Medicare reimbursement of home nasal CPAP equipment, the diagnosis of sleep apnea must be confirmed by polysomnography, also known as a *sleep study*. Private commercial insurances will typically reimburse for a **home sleep test**, also known as an "unattended sleep study" (see Chapter 34). These basic yet accurate studies measure nasal and oral airflow, respiratory effort, and oxygen saturation. With proper application and patient compliance, CPAP therapy can dramatically lessen or resolve the many problems associated with sleep apnea–hypopnea syndrome

Fig. 57.4 CoughAssist device. (Used with permission of Philips Respironics, Murrysville, PA.)

(morning headaches, daytime hypersomnolence, cognitive impairment). The patient's quality of life can be enhanced, and more severe complications, such as systemic and pulmonary hypertension and cor pulmonale, may be reduced.[56,57]

Equipment

A typical nasal CPAP apparatus consists of a flow generator capable of establishing varying levels of PEEP or CPAP, a circuit, and a patient interface (e.g., nasal mask, nasal pillows). One of the most common interfaces in alternative settings is the nasal mask. However, many patients requiring nocturnal CPAP prefer to use a full-face mask instead of a nasal mask. Most systems provide manually adjustable pressures in the range of 4 to 20 cm H_2O. Most units have a ramp feature that gradually increases the pressure to the prescribed level over a time interval to increase comfort and therapy compliance.

RULE OF THUMB For Medicare reimbursement of CPAP equipment, the diagnosis of sleep apnea must be confirmed by polysomnography, also known as a sleep study. Most insurance providers, including Medicare, will cover payment for CPAP accessories including the mask interface, tubing, and filters every 3 months.

Determining Proper Continuous Positive Airway Pressure Level

The proper CPAP level for a patient is determined by one of several methods. The most common method is to conduct the sleep study while titrating different levels of CPAP. Observed changes in the apnea-hypopnea index are correlated with the various CPAP levels. The prescribed level of CPAP is the lowest pressure at which apneic episodes are reduced to an acceptable frequency and duration.

More recently, CPAP units that automatically adjust the pressures to maintain airway patency have been commonly used. These self-titrating or auto-CPAP devices generally result in use of the lowest effective pressures and better patient compliance while also reducing the need for a subsequent sleep study and titration.[58]

Alternatively, CPAP may be titrated against pulse oximetry data. In this case, the goal is to use the lowest CPAP that maintains adequate arterial saturation (SpO_2 <90%). With changes in medical insurance policies, home sleep testing has become the preferred method for screening patients who have suspected sleep apnea. These unattended sleep study devices are used at home and are very portable. They measure nasal and oral airflow, respiratory effort, and oxygen saturations. For patients who have additional comorbidities in addition to obstructive sleep apnea, an in-lab study is recommended.[58]

Sleep Remote Telemonitoring

Technology has dramatically advanced in PAP devices. All new devices have built-in modems where a RT can remotely monitor the patient's compliance. If the patient requires a change to his or her existing parameters, the RT can adjust ramp settings, humidification, and even change the CPAP pressure. These advances in technology have helped to increase compliance by rapid intervention and adjustment to treatment.[59]

Use and Maintenance

Once proper CPAP level is determined, the patient is fitted for a mask and trained in the proper use, cleaning, and maintenance of the equipment. Typical patient instructions for self-administration of nasal or full-face mask CPAP therapy are provided in Box 57.5.

Problem Solving and Troubleshooting

Patient problems associated with nasal or full-face mask CPAP therapy include skin irritation, conjunctivitis, epistaxis, and nasal discomfort (dryness, burning, and congestion). Skin irritation is usually due to tight mask straps or a dirty patient interface. Persistent redness on the face or around the nose is the primary sign. Adjusting the straps (while maintaining a good mask seal) can help prevent irritation. In addition, the patient interface should be cleaned daily to remove dirt and facial oils. Based on medical insurance allotments, masks and nasal pillows are usually replaced every 3 to 6 months or sooner if leakage or discomfort occurs.

Conjunctivitis is probably the result of mask leakage around the bridge of the nose, which is easily corrected by ensuring a good seal in this area. Epistaxis (nosebleeds) and nasal discomfort are associated with drying of the nasal mucosa—a particular problem in cold, dry winter climates. Methods used to overcome excessive drying include in-line humidifiers, chin straps (to decrease loss of upper airway moisture), and saline nasal sprays.[60] Because none of these methods has proved satisfactory for all patients, selection should be based on individual patient acceptance and observed improvement in comfort. However, almost all patients receiving nocturnal CPAP therapy benefit from the addition of an in-line humidifier.

The most common problem with the CPAP apparatus is an inability to reach or maintain the set pressure. This problem is

BOX 57.5 Typical Patient Instructions for Self-Administration of Nasal or Full-Face Mask Continuous Positive Airway Pressure Therapy

Equipment Preparation

1. Place blower unit on a level surface (table or nightstand) close to where you sleep.
2. Ensure that the air exhaust and inlet vents are not obstructed.
3. Plug machine into a standard grounded (three-prong) electrical outlet.
4. Check air inlet filter to make sure that it is in place and free of dust.
5. Connect one end of the tubing to the interface (e.g., mask, nasal pillows).
6. Attach interface to your nose or face.
7. Adjust tightness of headgear strap to seat interface firmly onto your nose or face.
8. Turn on the blower and verify a flow of air.
9. Ensure proper fit and adjustment of mask and headgear. Air should not be leaking out around the bridge of your nose into your eyes or from the mask to your upper lip.
10. Adjust ramp feature and comfort setting if needed.
11. Continuous positive airway pressure therapy is now fully functional, but minor adjustments may be needed with ongoing use.

In the Morning

1. Remove mask by slipping the strap off the back of your head (you may leave the head strap connected between cleanings).
2. Turn off blower.
3. Wash interface every morning with a mild detergent, then rinse it with water.
4. Once dry, store interface in a plastic bag to keep it clean.
5. Empty excess water left in the humidifier.

Weekly

1. Wipe off the blower unit with a clean damp cloth.
2. Wash the head strap and circuit tubing.
3. Service the filters according to the instructions in your patient manual.
4. Wash the humidifier chamber with mild dish detergent and rinse with water.

usually due to either inadequate flow or, more commonly, system leaks. Common causes of leaks include inappropriate patient interface (mask vs. nasal pillows) or pressure loss through an open mouth. As part of their initial training, patients and caregivers should be taught how to recognize and correct these common problems. Box 57.6 outlines the procedures patients or caregivers can use to troubleshoot inadequate flows and system leaks.[61]

Follow-up with patients soon after they begin CPAP therapy is important to resolve complications promptly. If left unresolved, these issues often discourage the patient and result in decreased compliance and a return of original symptoms.[61]

For financial coverage to be provided, most medical insurance policies including CMS require that the patient be compliant with their sleep therapy within the first 90 days of treatment.

Apnea Monitoring

Apnea monitors alert clinicians and caregivers to certain life-threatening events, most notably recurrent apnea, bradycardia, and hypoxemia. At-risk infants are frequently set up on apnea monitors while they are in the hospital. After extensive family

BOX 57.6 Patient and Caregiver Instructions for Troubleshooting Continuous Positive Airway Pressure Equipment

Inadequate Flow

1. Make sure that the unit is plugged into a working electrical outlet.
2. Confirm that the unit is turned on.
3. Make sure that all connections are tight.
4. Confirm that airflow is coming from the blower.
5. Make sure that the intake/exhaust vents are not obstructed.
6. Check the blower inlet filter to confirm that air can easily enter the unit. If the filter appears obstructed, wash or replace it.
7. If there is still no flow, contact your home care provider.

Air Leaks

1. Check interface fit and readjust mask or headgear if necessary.
2. Request a chin strap to help keep patient's mouth closed.
3. If the problem is not resolved, contact the home care provider for adjustments or a different interface such as a nasal pillow.

MINI CLINI

Troubleshooting Nasal Dryness With Continuous Positive Airway Pressure

Problem

A 43-year-old obese man with documented obstructive sleep apnea has been advised by his attending physician that home CPAP therapy at night is needed. The home-care RT makes an appointment with the patient to assess his tolerance of the CPAP unit. During the visit, the patient notes that he has been experiencing nasal discomfort. How can the RT assist in problem solving with this specific complaint, and what are some of the other potential patient problems associated with CPAP therapy that the clinician should be alerted to?

Solution

CPAP devices use some type of patient interface such as a nasal mask, pillows, or full-face mask with supporting headgear. Complaints of nasal discomfort are common and are most likely due to the effects of dry airflow through the CPAP unit blower. However, other factors may aggravate the sensation of nasal irritation. Poor systemic hydration could worsen nasal mucosal drying. In addition, environmental humidity may be a factor. Cold, dry winter climates can aggravate symptoms, as can dry forced-air heating systems. In these cases, the RT might recommend increasing oral intake of fluids (if no restrictions on fluid intake), the installation of a room or heating system humidifier, or the as-needed use of a saline nasal spray. Also, almost all patients receiving nocturnal CPAP therapy benefit from the addition of an in-line humidifier. Additionally, newer CPAP machines have the option, with a physician's prescription, to add climate line tubing that delivers a consistent and comfortable temperature throughout the night, even as the room temperature and humidity levels change.

In addition to the above-mentioned factors, large leaks in the system can significantly increase flows and worsen the drying effect of these devices. Often such leaks originate from a poorly fitting patient interface. Consequently these problems can be remedied by ensuring a proper fit via repositioning the interface or switching to one of the many alternative masks or nasal pillows available today.

instruction in both equipment use and resuscitation, some of these infants may be discharged to the home with this equipment.[62]

Most apnea monitors detect both respirations and heart rate and activate audio and visual alarms when preset high or low limits are reached. Follow-up visits by the RT are usually frequent at first but occur less often as the family becomes skilled with use of the equipment and the monitoring routine. Some models record each alarm event and can be useful in monitoring the patient's progress. The "memory" of such monitors can be monitored continuously via an internet connection or via periodic downloading. Apnea monitors are usually discontinued after an infant has a negative pneumocardiogram (sleep study) or when recorded memory reveals no events during a prescribed time frame—often 2 to 4 months from the initial setup.[62]

PATIENT ASSESSMENT AND DOCUMENTATION

Alternative care sites demand extensive patient assessment and documentation. These requirements are based on both stringent reimbursement criteria and the rehabilitation orientation characterizing these settings.

Institutional Long-Term Care

In institutions providing long-term care, the assessment and documentation process involves four key components: screening, treatment planning, ongoing assessment, and discharge (Fig. 57.5).

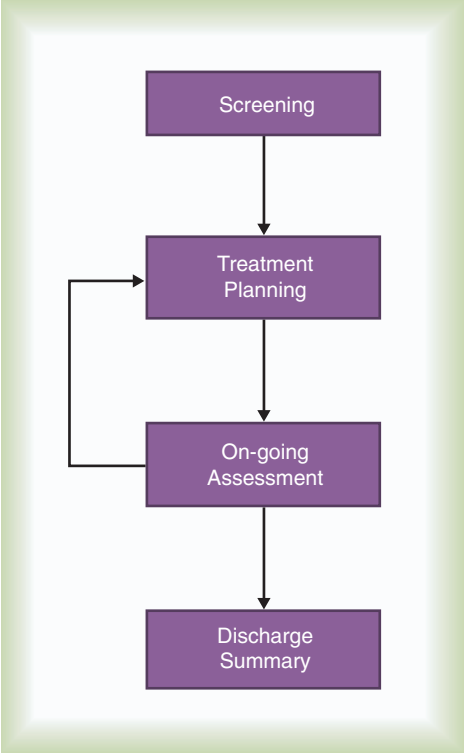

Fig. 57.5 The assessment and documentation process in institutional subacute or long-term care.

Screening

On admission to a long-term care facility, all patients with a respiratory-related admitting diagnosis should be screened by an RT. This screening is often accomplished mainly by a medical record review. During screening, the RT reviews the pertinent respiratory diagnosis, onset and severity of symptoms, current radiograph results, pulmonary function tests, arterial blood gas values, and other nonrespiratory treatment orders (e.g., physical therapy).

If the review indicates the need for a more in-depth assessment, the RT can recommend a more complete evaluation. On receipt of the appropriate orders, the RT interviews the patient and conducts a physical assessment, including inspection, palpation, auscultation, and percussion. Key clinical findings include description of breath sounds; rate, depth, and pattern of respirations; heart rate; signs of dyspnea; cough; sputum production; level of consciousness; and ability of the resident to understand and follow commands. Also noteworthy are the resident's prior respiratory status, use of supplemental O_2, pulse oximetry, skin turgor, and medications.

Treatment Planning and Ongoing Assessment

Based on the information obtained during the initial screening process, the RT and often other members of the patient care team design a specific treatment plan. A typical treatment plan includes patient demographics, assessment information, short-term and long-term goals reflective of overall rehabilitation potential, and measures to be used to achieve such goals. A treatment plan for the resident of a long-term care facility with moderate to severe COPD would likely reflect the treatment goal of correcting hypoxemia through the use of low-flow O_2 and patient monitoring.

After therapy has been initiated, the RT uses several other tools to monitor a patient's progress. In addition to regular treatment documentation, the RT should document a regular summary on each patient. This summary provides a synopsis of progress toward goal attainment, including changes in respiratory status, results of any additional tests, explanation of any patient education, and recommendations for additional therapy. Additionally, treatment plans and progress summaries become part of the resident's permanent record and are often required documentation for third-party reimbursement.

Discharge Summary

When a patient reaches his or her maximum potential, has attained all set goals, or is discharged, the RT should complete a discharge summary. The discharge summary describes the complete course of respiratory therapy, including its success or failure.

Home-Care Plan

A home-care plan must specify not only the types of care provided but also a strategy for patient follow-up. The individual making the follow-up visits is often the visiting nurse, a physical therapist, or an RT. For patients receiving respiratory care at home, follow-up by a home-care team member should occur regularly, particularly for patients on "hi-tech" equipment such as ventilators. Some patients may require more frequent follow-up, especially patients recently discharged or patients requiring

ventilatory support. Factors relevant to the frequency of home visits include the following:

- Patient's condition and therapeutic needs (objectives)
- High risk for hospital readmission
- Level of family or caregiver support available
- Type and complexity of home-care equipment
- Overall home environment
- Ability of the patient to provide self-care
- Third-party reimbursement for such visits

When a visit is made by the RT, numerous functions must be performed, including the following:

- Patient assessment (objective/subjective data and pretreatment/posttreatment data)
- Patient's compliance with prescribed respiratory home care
- Equipment assessment (operation, cleanliness, and need for related supplies)
- Identification of any problem areas or patient concerns
- Statement related to patient goals and therapeutic plan

A standard written report, consistent with the care plan, should be completed by the visiting RT. Copies are often sent to the patient's physician, the nursing agency, the home-care referral source, and any other member of the patient care team requiring this information. The report should become part of the patient's medical record and should be referred to when the patient's course and overall progress is being followed.

EQUIPMENT DISINFECTION AND MAINTENANCE

With many patients receiving respiratory care outside the hospital, the danger of infection caused by direct contact with caregivers and visitors or indirect contact with contaminated articles has grown. To help minimize home-related infection, guidelines for disinfecting home respiratory care equipment have been established. Accepted infection control techniques are based on clinical evidence, such as the evidence outlined in several of the AARC Clinical Practice Guidelines.

Collectively, these guidelines focus on sources of infection, basic principles of infection control, patients at high risk, disinfection methods, equipment processing, and care of solutions and medications. Procedures focus significantly on surveillance, prevention, and control of infection.

In regard to infection control, all guidelines and procedures mandate proper hand hygiene techniques by all caregivers—proper handwashing and use of antiseptic hand lotions. In addition, visits to the patient by friends or relatives with respiratory infections are discouraged. Relating to medical equipment suppliers, the guidelines suggest that all permanent equipment (e.g., ventilator circuits, O_2 delivery equipment, and aerosol systems) be sterilized or receive high-level disinfection before being supplied to another patient. Disposable or single-patient use equipment must be used by one patient only. It is recommended that all equipment be completely disassembled and washed first in water, followed by a soak in warm soapy water for several minutes, with equipment scrubbed as needed to remove any remaining organic material. Following this step, the equipment must be thoroughly rinsed to remove any residual soap and drained of excess water. Air drying on a clean surface or rack is recommended to minimize recontamination.

Additionally, the broad bactericidal activity exhibited by many premanufactured disinfectant solutions makes them the first choice. Other disinfection solutions to be considered include a 1:50 dilution of 5.25% to 6.15% sodium hypochlorite (household bleach) with water for a minimum of 3 minutes.

Regarding the use of water for humidification or nebulization, it is recommended that distilled water be used as a first choice. It is recommended that manufacturers' guidelines for the proper handling of specific medications be strictly followed. Detailed instructions for patients and caregivers on how to clean and disinfect selected respiratory care equipment are generally available from most manufacturers.[63,64]

SUMMARY CHECKLIST

- An increasing number of health services are being provided in alternative care settings.
- Subacute care aims achieve the highest level of patient functioning—ideally self-care.
- Standards for subacute and home health care derive from federal and state laws and private-sector accreditation, mainly TJC.
- Acute and alternative care settings differ in regard to resource availability, supervision and work schedules, documentation and assessment, and professional–patient interaction.
- Effective discharge planning (1) guides the multidisciplinary team in transferring patients to alternative sites of care and (2) ensures the safety and efficacy of the patient's continuing care.
- Alternative site caregivers must have all the competencies required to meet the patient's ventilatory and respiratory needs and provide adequate 24-hour coverage. The selected site must also be safe and suitable for the patient's specific condition.
- O_2 prescriptions for patients in alternative settings must be based on a documented diagnosis, including hypoxemia, as determined by either blood gas analysis or oximetry.
- In most alternative care sites, O_2 is normally most often supplied by concentrators with gaseous cylinders as backup and for portability.
- Most patients in alternative care settings needing O_2 use a nasal cannula; conserving devices such as portable oxygen concentrators and demand-flow O_2 systems can decrease O_2 use and costs and provide greater patient mobility.
- Because problems with long-term O_2 therapy include issues involving both people and equipment, caregivers should be allowed to operate and maintain O_2 delivery devices only after they have been properly instructed by credentialed RTs.
- Key factors needed for successful ventilatory support in alternative sites include (1) careful patient selection, (2) effective discharge planning, (3) an interdisciplinary team approach, (4) effective caregiver and family education, (5) thorough assessment and preparation of the environment, and (6) careful selection of needed equipment and supplies.
- Patients being considered for ventilatory support in alternative settings must be medically and psychologically stable.

- Most patients requiring mechanical ventilation in alternative settings can be supported with NIV if they are alert and cooperative, can maintain acceptable oxygenation without high FiO_2, and have intact airway reflexes and adequate clearance mechanisms.
- Positive-pressure ventilators used in alternative settings should be electrically powered, easy to operate, and portable (run on both AC and DC power). Loss-of-power alarms are essential, high-pressure alarms are needed on volume-cycled ventilators, and patient-disconnect (low-pressure) alarms should be provided.
- A typical nocturnal CPAP system consists of a flow generator or blower, tubing, humidification system, and nasal or full-face mask; some units can increase pressure to the prescribed level over time (ramping); others can autoadjust the CPAP level in response to apnea, hypopnea, airflow limitation, or snoring.
- The proper CPAP level can be determined by polysomnography, continuous monitoring of hemoglobin saturation, or an auto-CPAP system.
- A common problem with nocturnal CPAP systems is the inability to reach or maintain the set pressure, usually because of either inadequate flow or system leaks.
- Remote monitoring is beneficial in providing quick intervention for CPAP patients who are struggling with their therapy.
- Proper caregiver hand hygiene, limiting visits by persons with respiratory infections, providing sterile or disposable clean equipment, and proper equipment processing are the keys to infection control in such settings.

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58

Ethics and the End of Life

Ellen M. Robinson, Frederic Romain, and M. Cornelia Cremens

CHAPTER OBJECTIVES

After reading this chapter you will be able to:

- Describe the elements of the "goals-of-care framework" and state the advantages of its use in contributing to the care of seriously ill patients approaching the end of life
- Describe the ethical and legal significance of the "right to refuse life-sustaining treatment" and how it is applied in the care of seriously ill patients at the end of life
- Articulate the importance and contribution to care of clinicians taking the time to know the patient as person rather than only as a patient
- Discuss the legal and ethical approaches to end-of-life care, including the merits of the concepts of euthanasia, physician-assisted suicide, withdrawing and withholding life-sustaining treatment, and palliative sedation while also considering the distinctions between these concepts
- Describe an ethically defensible approach to the management of pain and other symptoms at the end of life in the setting of withdrawing life-sustaining treatment
- Describe and apply the rule of double effect to a clinical case
- Describe the role of the respiratory therapist as a contributing professional on an interdisciplinary team

CHAPTER OUTLINE

KEY TERMS

advance directive
assisted suicide
best interests
cardiopulmonary resuscitation
ethics consultation
euthanasia
goals of care
health care agent or durable power of attorney for health care
interdisciplinary team
life-sustaining treatment
palliative sedation
prognosis
rule of double effect
substituted judgment
values, beliefs, and preferences
withholding and withdrawing life-sustaining treatment

INTRODUCTION

Advances in life-sustaining medical technology abound, contributing to cures for desperately ill patients with a host of diseases. The field of solid organ and hematologic transplantation has progressed, providing tremendous benefit in both the extension of life and its quality to patients with oncologic diagnoses.[1] Dialysis as a **life-sustaining treatment (LST)** is now available in many forms and at various access points, even for the most critically ill patients, in the form of continuous venovenous hemofiltration (CVVH).[2] Extracorporeal membranous oxygenation (ECMO), once a therapy used only for premature infants, is now available in quaternary care centers for patients with acute cardiac, respiratory, or cardiopulmonary failure as a life-saving therapy. That is, patients with cardiopulmonary collapse, who would have died in the past, can now be offered a lifesaving treatment.[3] This is an incomplete description of the available LSTs, but it presents a snapshot of the latest advances and shows

that seriously ill patients can often have opportunities for cure or the palliation of their disease even if they are returned to a reduced yet acceptable quality of life.

Whenever a patient is seriously ill, "airway and respiration" are of prime concern. Whether the patient is being monitored for threats to the airway and oxygen exchange, receiving advanced respiratory interventions (e.g., nasotracheal suctioning), biphasic positive airway pressure (BIPAP) or other assistive respiratory therapies, being ventilated mechanically, or even receiving ECMO, the respiratory therapist (RT) plays a key role in the patient's care. Although the ability to breathe easily is taken for granted by those who are well, that is not the case for patients whose respiratory status is under threat for any length of time. In such a situation, the respiratory system is arguably the body system that the patient experiences most acutely and chronically, with a sense of anxiety regarding his or her well-being and life itself. When the patient cannot recover and is approaching the end of life, the RT plays his or her professional role by responding with competence, compassion, and knowledge of ethical practice. *To this end, the purpose of this chapter is to educate the RT regarding the key background tenets of ethical practice at the end of life as well as sound ethical approaches and considerations in the care of such patients. The RT plays a key role on the health care team, contributing a body of expertise that is unique and essential to high-quality, compassionate, and ethical patient care.*

"GOALS OF CARE" AS AN ESSENTIAL ORGANIZING FRAMEWORK

As a member of the health care team, the RT should be cognizant of the **"goals of care"** for the patient as an organizing framework in approaching a seriously ill patient's overall care. Developing goals of care requires physician leadership, including input from medical and surgical physician consultants. In addition, nurses and allied health professionals offer important contributions. RTs as allied health professionals are key in bringing forward their assessment, intervention, and the patient's response to the formulation of goals of care. "Breathing," or "taking a breath," is likely the most critical of all physiologic processes that non-comatose patients can directly experience. When a patient's breathing is compromised, his or her perception of this difficulty and its physiologic impact can cause immense distress and anxiety.

The goals-of-care framework has three components:

- The patient's medical and rehabilitative **prognosis**
- The patient's **values, beliefs, and preferences**
- Ethically and legally permissible care options

These three components provide a framework for formulating the goals of a patient's care. Attention to each component allows for a formalized approach to decision making and intervention in a patient's care as opposed to a haphazard based on momentary reactions. RTs play a significant role in this process, given their expertise in assessing and managing a patient's airway and overall oxygenation and observing the patient's response to respiratory interventions. Thus the presence and perspective of the RT on the health care team is essential to formulating goals of care that can become part of a clinically and ethically appropriate plan of care.

RULE OF THUMB A goals-of-care framework can direct purposeful versus haphazard care to seriously ill patients. This framework includes establishing the patient's medical and rehabilitative prognosis; learning the patient's values, beliefs and preferences; and considering the approaches that are ethically and legally permissible.

Medical Prognosis and Rehabilitative Prognosis

The concept of "medical prognosis" in patient care is primary and integral in addressing goals of care for a patient. Medical prognosis is defined by Merriam Webster (https://www.merriam-webster.com/dictionary/prognosis) as the "prospect of recovery as anticipated from the usual course of disease or the peculiarities of the case." In an age of advanced medical-surgical life-sustaining treatment, it is more critical than ever to address the question of medical prognosis on a regular basis within medical and interprofessional teams and with patients and families. An intentional examination of the patient's medical prognosis is the first step in a process of determining the goals of a patient's care. The following questions should be posed by or to the responsible physician:

- What is medically possible for the patient?
- Can the opinions of medical and surgical consultants be brought to bear on the "whole"?
- What is the rehabilitation potential for the patient?
- Are LSTs effective or likely to be effective in restoring the patient's functional status or at least restoring the patient to a reduced yet acceptable functional status and quality of life?

In American health care today, it increasingly seems that only the very ill are hospitalized, with multiple specialties and health professional roles involved in their care. Although the establishment of medical prognosis rests squarely within the domain of the responsible physician, it is imperative that all physicians avail themselves of disciplinary input from medical specialties, highly skilled nurses, and allied health professionals, including RTs, rehabilitation professionals, occupational therapists, physical therapists, speech-language therapists, nutrition specialists, social workers, and chaplains to gain a full picture of a given patient's response to medical/surgical interventions. Families of patients often look to the physician during a family member's prolonged illness and hospital stay for guidance about whether their loved one can get better. Speaking strictly about the "medical prognosis" without accommodating the patient's ability to rehabilitate can fall short for families, who are almost always thinking about whether their loved one can return to an acceptable level of function. Considering a patient's projected functional status as an important adjunct to medical prognosis requires the input of rehabilitation professionals whose expertise lends critical data to the patient's problems. This includes the discipline of respiratory therapy. In this way, the establishment of medical prognosis can reflect not only the patient's pathophysiology as determined by the medical examination, diagnostic tests and response to medical interventions but also how the patient is then able to function. Thus it is essential for the **interdisciplinary team** of nurses, RTs, and other allied health professionals to create a more holistic picture of what is possible for the patient.

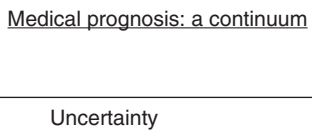


Fig. 58.1 Visual depiction of consideration of medical prognosis. (Courtesy Ellen M. Robinson.)

A patient with a primary respiratory disease process alone as well as patients with respiratory disease along with other body system disease processes may be of concern for the RT's assessment, intervention, and evaluation. It is critical for the RT to understand and appreciate the patient's patient response to intervention as well as his or her pathophysiology, medical and surgical treatment, and nursing and rehabilitation needs. All of these considerations can provide the RT with insight into the full context of the patient's medical problems. Most patients who have life-threatening conditions will have a respiratory component that requires the close attention of an RT.

Honest, transparent assessments for establishing prognosis are the responsibility of the medical and surgical physician staff, who must reevaluate the patient on a regular basis. Medical prognosis can be thought of on a continuum (Fig. 58.1), with clarity at each end: expectation of a clear recovery versus imminent death. Under such circumstances, the collective direction of care in a particular patient's case is generally evident and health professionals, physicians, and families are in agreement.

Uncertainty in medical prognosis is challenging for all involved. Time is needed to ascertain progress and setbacks, to allow interventions to take hold, and to allow the patient to declare himself or herself in a direction of recovery versus the end of life. The RT's input to team discussions is critical in all areas of prognostication, as such a specialist is an expert in airway management as well as ventilator and oxygen therapies and can speak to a patient's response to interventions in terms of benefit or burden.

The input of the RT is both objective and subjective. Objectively, the RT can report on indices that measure oxygenation, tidal volume, airway resistance, secretion management, the patient's passive or active participation, and his or her ability to cough among other important data points. Subjectively, the RT hears directly from the patient, as does the nurse, regarding pain, shortness of breath (SOB), dyspnea, and his or her overall willingness and ability to participate in interventions that are aimed at the restoration of health. The RT assesses, monitors, and responds to diseases and other issues affecting the respiratory system, the most basic functional component of human life. Thus it is critically important that RTs contribute to discussions about patient prognosis. Team huddles and meetings are vehicles designed to impart the RT's assessment and evaluation; however, if such meetings are not possible, the RT has a professional and ethical obligation to impart his disciplinary contribution—both verbally and through excellent documentation—directly to the nurses and physicians caring for the patient.

In cases where the respiratory system is failing and the patient's movement toward recovery or death is directly contingent on how he or she responds to therapy, the RT may play a critical role in team-family meetings. We recall the input of an RT into a team-family meeting when a patient suffered from unrelenting respiratory failure secondary to advanced lung cancer and was unable to be weaned from mechanical ventilation. The family insisted that the patient could be "taught" to breathe again and could "practice" doing so. The RT who was present at the team-family meeting provided a concise and compassionate explanation to the family about the innate drive to breathe, and that persons will instinctively breathe without coaching when they are able to do so. This description gave the family some sudden clarity and led to their understanding that their loved one would not be able to recover.

The practice of observing, listening, discussing, reflecting as a team and together with family can yield insights that contribute to an overall prognostic assessment from both a medical and rehabilitative perspective. Each patient's case is an ongoing narrative, particularly when the prognosis is uncertain.

RULE OF THUMB The patient's medical prognosis is a key piece of information for clinicians to consider in a goals-of-care framework. When a given patient's medical prognosis is being considered, it is also important to think about his or her potential for rehabilitation. Families are concerned mainly with their relative's potential to return to function.

Values, Beliefs, and Preferences

An "ethic of care"[4–6] is one approach that can guide ethical decision making; examples include concepts such as deontology, utilitarianism, principles, rights, virtues, and narrative ethics (see Chapter 5). An ethic of care is invoked as a framework to complement principle-based ethics, recognizing that principles provide a time-honored structure for analyzing difficult ethical problems.[7] In a goals-of-care framework, an ethic of care is made tangible by considering particulars, context, and relationships.

Particulars

It is important for all health professionals who participate in a patient's care to speak to the question, "Who is this person (and family)?" The attending physician, resident staff, and medical/surgical consultants assess and diagnose the patient's medical condition, whereas nurses assess the patient's responses using the 11 functional health patterns described by Gordon (Box 58.1).[8] Social workers assess the psychosocial domains of the patient and family, chaplains the patient's spiritual needs and priorities, rehabilitation therapists the cognitive-functional domains, nutrition specialists the patient's nutritional and metabolic needs, and RTs the patient's primary system of "respiration." All of the team members contribute vital information regarding their assessments of the patient's overall status. Regarding values, beliefs, and preferences, RTs attend to the patient's response to underlying breathing problems and respiratory therapies. The patient's ability to tolerate symptoms can often provide a window into his or her preferences. Thus it is important to consider the patient's responses within the "values, beliefs, and preferences" component of a goals-of-care framework. Questions seeking responses either directly from the patient or from his or her surrogate decision maker in building the goals-of-care framework are as follows:

BOX 58.1 Gordon's Functional Categories for the Assessment of Health Patterns

- Health perception and management
- Nutritional and metabolic issues
- Elimination
- Activity and exercise
- Sleep and rest
- Cognitive/perceptual issues
- Self-perception and self-concept
- Role relationships
- Sexuality/reproductive issues
- Coping and stress tolerance
- Values and beliefs

These issues, with input from all disciplines, are to be considered in the nursing assessment seeking to answer the question, "Who is this person living with this disease?"

Adapted from Gordon M: *Manual of nursing diagnoses*, Sudbury, MA, 2010, Jones & Bartlett Publishers.

- Who is this person (and family)?
- What is important to her/him/them?
- What would a "good day" look like for the patient and family?
- What would "intolerable days" be like for the patient?
- Quality of life—can it be projected for the patient?
- What religious, spiritual, and cultural beliefs influence end-of-life decision making?

Often a patient will come into an emergency department (ED) and then be urgently admitted to an intensive care unit (ICU), but he or she may be lacking in decision-making capacity. Under such circumstances, physicians, nurses, and health professionals seek to identify a surrogate decision maker, preferably an appointed health care agent (HCA) noted through a health care proxy or durable power of attorney for health care document or, in some cases, a legal guardian. In most states, when a power of attorney for health care does not exist or legal guardian has not been appointed, clinical teams will turn to family members. In some but not all states, a "rank order" of family members as decision makers is written into the state statute. (https://www.americanbar.org/content/dam/aba/administrative/law_aging/2014_default_surrogate_consent_statutes.authcheckdam.pdf)

Families at Massachusetts General Hospital are invited to complete a "Get to Know Me" poster (Fig. 58.2) for their loved ones who are unable to communicate. This can help familiarize clinicians with the patient, what she or he enjoyed doing, who were his or her family and friends, and also favorite movies, books, and other information of interest describing the patient. Photographs of the patient are also included on the poster. Information on this poster alone would be an insufficient contribution to the values, beliefs, and preferences component; however, it can provide bedside clinicians, including RTs, with a sense of the person who is now a critically ill patient. For the family of such a patient who is unable to communicate, hearing statements from a professional caregiver that signify familiarity with "patient as person" can be comforting. RTs who manage the patient's most vital body system, respiration, can make the patient feel safe and at ease while contributing to the decisions being made daily by the medical team.

MINI CLINI

Problem: Consider the Case of Mrs. Lake and the Concept of "Context"

Mrs. Lake, age 63, who had a recurrent glioblastoma, was raising her 12-year-old grandson. The neurology team asked for an ethics consult because Mrs. Lake was requesting or demanding additional chemotherapy, which was not indicated given her advanced disease and poor functional status. Mrs. Lake refused to assent to DNR/DNI, interventions that her physicians and the team recommended. The ethics consultant learned that Mr. and Mrs. Lake's daughter had died in a motor vehicle accident (MVA) 10 years earlier and that they had been caring for their grandson ever since. The boy loved his grandparents and was thriving in their care. One can understand how desperate Mrs. Lake and her spouse were, yet physicians and health professionals were caught in the ethical bind of wanting to protect her from harm while not breaking her spirit of self-determination. The patient was very ill, and her respiratory status was tenuous. The RT, nurse, and physicians were unsure in how to proceed.

Discussion

An urgent team meeting with a neurologist, nurses, the RT, social work, chaplaincy, and ethics consultant was held to explore approaches to the patient. It was agreed that the neurologist, nurse, RT, and social worker should meet with the patient and her spouse to compassionately explain the clinical situation and explore the best alternatives. Mrs. Lake was teary, as was her spouse, but they agreed to DNR/DNI and expressed understanding that additional chemotherapy would not be helpful. Mrs. Lake died peacefully 2 days later, at the hospital, in the presence of her spouse and grandson. In summary, the context of this patient's life and advanced disease, when understood, provided an opening for clinicians to intervene.

Context

Considering the patient's overall context as a dimension of an ethic of care can yield insight for health professionals at the end of life, and RTs, given their area of concern, must be actively involved. Where does this patient find herself or himself at this time—what is immediately confronting the patient in terms of utmost concern? What led the patient to this disease process, hospitalization, and now end-of-life situation? How is the patient responding to all of it? How is the family responding? What is the patient primarily concerned about at this time, either expressed or unexpressed? How are the patient's immediate concerns affecting the airway and the experience of respiration? To intervene appropriately and with compassion, health professionals and RTs must consider the context from which the patient comes and what is directly being experienced in order to understand patients and their concerns.

Relationships

Although the principles of biomedical ethics, specifically autonomy, represent ethical ideals, the reality is that almost all persons, particularly when ill and at the end of life, look to the relationships that are important in their lives. Otherwise, if they are not able to engage, their destiny may be affected by the relationships that they had with others in earlier times. Being bound in, enriched by, and sometimes injured by relationships is opposed to self-determination in isolation with "relational autonomy."[9,10] Patients may have significant family and friends that they care about and that care about them. It is important for health professionals to

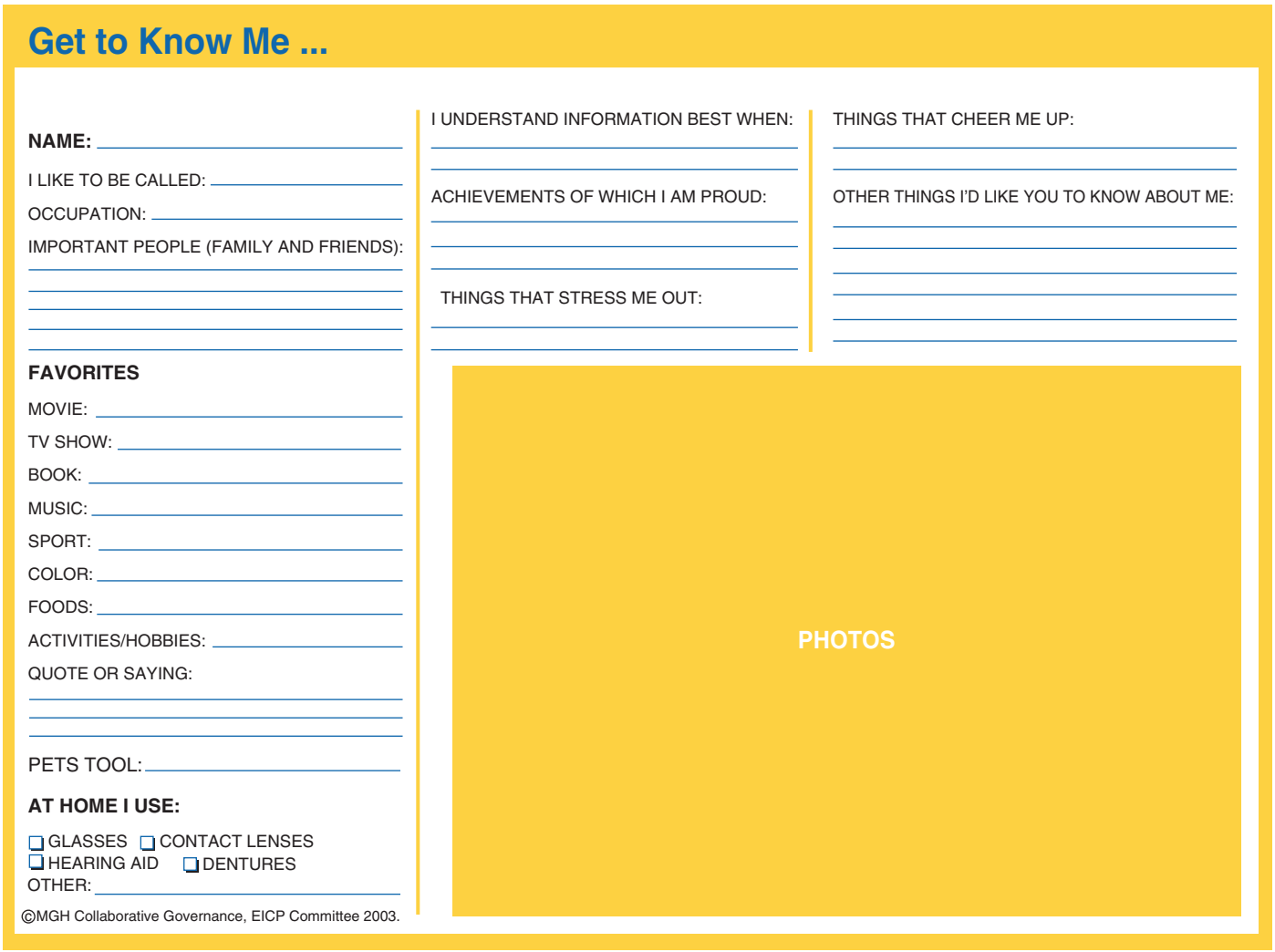


Fig. 58.2 "Get to Know Me" Poster. (Courtesy Ellen M. Robinson.)

recognize that significant family and friends may be in conflict with the patient but are still important to him or her. When health care professionals, including RTs, recognize this reality of the human condition, they can assist in working effectively with family as defined by the patient on behalf of the patient. Hopefully, in most situations, a patient's relationships can flourish even during a difficult time, serving the patient's **best interest.** There are times when relationships that are significant to the patient may not contribute to the patient's best interest and overall well-being or may authentically represent the patient's voice through "**substituted judgment,**" where the patient still loves and values these persons.

RULE OF THUMB The patient's values, beliefs, and preferences near the end of life care can be systematically uncovered in seeking to answer the question: Who is this person living with this disease? Aiming to know the patient's earlier context as well as learning about relationships that are important to the patient can also aid in this interdisciplinary assessment process.

Ethical and Legal Parameters

Refusal of Life-Sustaining Treatment

It is critical for tRTs to know what is ethically and legally permissible in the United States and their state of practice related to end-of-life care. Decision making around LST and respiratory therapies for critically ill patients is a fast-moving process that has immediate implications for the patient's life or death. As licensed health care professionals, RTs are the recipients of physician orders to be carried out on the patient's behalf; however, the RT must be aware of the ethical and legal appropriateness of a physician's orders in general as well as in terms of the specific patient case. The RT is ethically and professionally bound to question any orders that are not congruent with acceptable ethical and legal practices as well as hospital policy, which should be in synchrony with sound ethical and legal practices. One's intuition in difficult circumstances, along with a sound knowledge base, should be trusted and can lead to "speaking up" for the patient's benefit. Familiarity with hospital LST policies as well as consulting with colleagues or the RT supervisor are suggested

MINI CLINI

Problems: Complexities of Lifelong Relationships at the End of Life

The case of Mrs. Smith, an elderly woman, and Marilyn, her adult daughter, serves as an example of the complexities of lifelong relationships at the end of life. Marilyn—one of four adult children, three of whom were estranged—cared for her mother for many years. Mrs. Smith's advance directive stated her wishes against medically supplied nutrition and hydration. She had expressive aphasia due to an old stroke, was in the final weeks of life, and was refusing oral feedings. Her daughter insisted on "force feeding her," and Mrs. Smith was aspirating. Marilyn was angry and emotional, realizing that her mother was dying.

Discussion

When Marilyn left the room for a short break, the nurse said to Mrs. Smith, "I think you are both embarrassed by Marilyn's behavior, and also worried about Marilyn; please do not worry, as we understand and will take care of her." Mrs. Smith's eyes filled with tears, which streamed down her face. The nurse demonstrated to Mrs. Smith her realization that regardless of Marilyn's difficulty in accepting her mother's wishes, she knew that Mrs. Smith still loved Marilyn; it was a difficult yet important relationship that they shared. Recognition by a health care professional of this human dynamic can serve patients in protecting them from harm while also preserving family relationships at the end of life.[11]

resources, enabling the RT to talk through uncertainties and approaches in difficult situations.

A right to refuse LST exists in the United States, and this right is considered to be a bedrock of American law and ethics.[12,13] Prior to the 1960s and 1970s, medical and surgical interventions could bring a desperately ill patient only so far in terms of recovery, and death would come when the best therapies of the time were not effective. As medical technology advanced, LSTs became available to stave off death, with the intention of allowing a desperately ill patient to heal and recover. Although these can be lifesaving in many regards, there were also situations where patients would languish on life support with no hope of recovery. When LST was initiated, it was, and still often is, unclear which patients would benefit and which would merely be burdened by the treatment, with no benefit. During the early days of these LSTs, including mechanical ventilators, physicians were concerned that if the LST were terminated, it would be tantamount to murder.[14] It was often the families who requested that the LST be removed, realizing over time that their loved one was not recovering. Such was one of the major factors leading to the laws that established the legal right to refuse LST.

Several court cases initiated by family members ensued between the 1970s and 1990s, leading to the "right to refuse LST."[12,13] Themes that then emerged made explicit the parameters around refusal of LST; these are presented in Box 58.2. The case of Nancy Cruzan[15] led to the establishment of the Patient Self-Determination Act (PSDA) and the Omnibus Reconciliation Act.[16] These were the final bookend to this period of change in health law and ethics, which clearly and unequivocally established the right to refuse LST. The PSDA provides a statutory mechanism for patients to sign **advance directives** allowing their voices to be heard when they no longer have capacity to make health

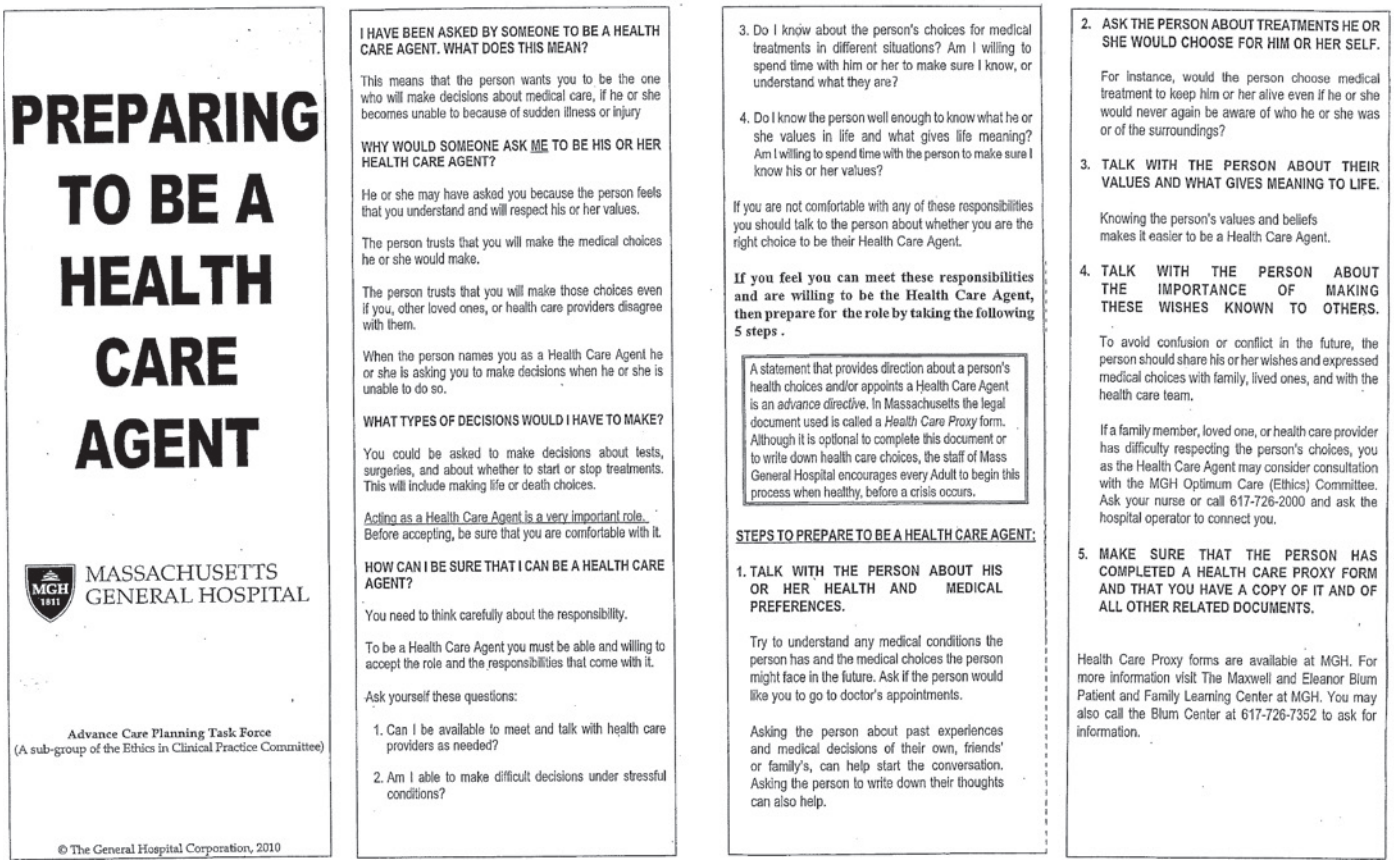
BOX 58.2 Ethics and Law at the End of Life: What Is Permissible?

- In the United States, patients have the right to refuse life-sustaining treatment.
- This right extends to the competent, once competent, and never competent person.
- The type of treatment is not determinative: analysis is necessary in terms of the benefits and burdens of life-sustaining treatment to the patient.
- Withholding and withdrawing life sustaining treatment are ethically equivalent.
- Good palliative care is supported by the US Supreme Court.
- Advance directives provide a mechanism whereby the right to refuse life-sustaining treatment can be actualized.

Data from Emanuel EJ: A review of the ethical and legal aspects of terminating medical care. *Am J Med* 84:291–301, 1988 and Cantor N: Twenty-five years after Quinlan: a review of the jurisprudence of death and dying. *J Law Med Ethics* 29:182–196, 2001.

care decisions. Individual states have specific advance directive forms, such as the Massachusetts Health Care Proxy (https://malegislature.gov/Laws/GeneralLaws/PartII/TitleII/Chapter201D). But suffice it to say that all 50 states recognize the person's right to appoint an HCA. The PSDA requires health care systems that are receiving federal monies through the Centers for Medicare and Medicaid to ask all patients upon admission if they have an advance directive; if not, they must offer to assist patients with education, counseling, and forms to complete (https://www.cms.gov/Regulations-and-Guidance/Guidance/Transmittals/downloads/R75SOMA.pdf; 2011). A patient, of course, can refuse to complete an advance directive. Overall compliance with advance directives is generally only about 33%.[17]

The history of the case law culminating in the Nancy Cruzan case, leading to the creation of the PSDA, has cemented the right to refuse LST in the American health care system. With the opportunity to identify a legally recognized surrogate decision maker through state laws, designating **an HCA or durable power of attorney for health care** decisions, persons can use their agency to name a person to speak on their behalf if a time comes when the person can no longer speak on his or her own behalf. There will be times when a patient does not have an HCA available, and physicians and health professionals will turn to close family or friends. Some states have a "rank ordering" of position in the family to turn to in such situations, as previously stated.[18] Other states, such as Massachusetts, do not have a rank ordering and seek to identify close family members and domestic partners who seem committed to the patient's care. For patients who have never had capacity (profound intellectual disability), or who do not yet have capacity (such as children), health professionals turn to court-appointed guardians or parents to make health care decisions based on the best interest of the patient. Decision making by the "best interest standard" was specified in the President's Commission Report[19] to include consideration of relief of suffering, preservation or restoration of functioning and quality, as well as extent of life sustained. Thus the right to refuse LST extends to persons with full decision-making capacity or former decision-making capacity as well as those who have never had decision-making capacity.



PREPARING TO BE A HEALTH CARE AGENT

MASSACHUSETTS GENERAL HOSPITAL

Advance Care Planning Task Force
(A sub-group of the Ethics in Clinical Practice Committee)

I HAVE BEEN ASKED BY SOMEONE TO BE A HEALTH CARE AGENT. WHAT DOES THIS MEAN?

This means that the person wants you to be the one who will make decisions about medical care, if he or she becomes unable to because of sudden illness or injury

WHY WOULD SOMEONE ASK ME TO BE HIS OR HER HEALTH CARE AGENT?

He or she may have asked you because the person feels that you understand and will respect his or her values.

The person trusts that you will make the medical choices he or she would make.

The person trusts that you will make those choices even if you, other loved ones, or health care providers disagree with them.

When the person names you as a Health Care Agent he or she is asking you to make decisions when he or she is unable to do so.

WHAT TYPES OF DECISIONS WOULD I HAVE TO MAKE?

You could be asked to make decisions about tests, surgeries, and about whether to start or stop treatments. This will include making life or death choices.

Acting as a Health Care Agent is a very important role. Before accepting, be sure that you are comfortable with it.

HOW CAN I BE SURE THAT I CAN BE A HEALTH CARE AGENT?

You need to think carefully about the responsibility.

To be a Health Care Agent you must be able and willing to accept the role and the responsibilities that come with it.

Ask yourself these questions:

1. Can I be available to meet and talk with health care providers as needed?
2. Am I able to make difficult decisions under stressful conditions?
3. Do I know about the person's choices for medical treatments in different situations? Am I willing to spend time with him or her to make sure I know, or understand what they are?
4. Do I know the person well enough to know what he or she values in life and what gives life meaning? Am I willing to spend time with the person to make sure I know his or her values?

If you are not comfortable with any of these responsibilities you should talk to the person about whether you are the right choice to be their Health Care Agent.

If you feel you can meet these responsibilities and are willing to be the Health Care Agent, then prepare for the role by taking the following 5 steps .

A statement that provides direction about a person's health choices and/or appoints a Health Care Agent is an *advance directive*. In Massachusetts the legal document used is called a *Health Care Proxy* form. Although it is optional to complete this document or to write down health care choices, the staff of Mass General Hospital encourages every Adult to begin this process when healthy, before a crisis occurs.

STEPS TO PREPARE TO BE A HEALTH CARE AGENT:

1. TALK WITH THE PERSON ABOUT HIS OR HER HEALTH AND MEDICAL PREFERENCES.

   Try to understand any medical conditions the person has and the medical choices the person might face in the future. Ask if the person would like you to go to doctor's appointments.

   Asking the person about past experiences and medical decisions of their own, friends' or family's, can help start the conversation. Asking the person to write down their thoughts can also help.

2. ASK THE PERSON ABOUT TREATMENTS HE OR SHE WOULD CHOOSE FOR HIM OR HER SELF.

   For instance, would the person choose medical treatment to keep him or her alive even if he or she would never again be aware of who he or she was or of the surroundings?

3. TALK WITH THE PERSON ABOUT THEIR VALUES AND WHAT GIVES MEANING TO LIFE.

   Knowing the person's values and beliefs makes it easier to be a Health Care Agent.

4. TALK WITH THE PERSON ABOUT THE IMPORTANCE OF MAKING THESE WISHES KNOWN TO OTHERS.

   To avoid confusion or conflict in the future, the person should share his or her wishes and expressed medical choices with family, lived ones, and with the health care team.

   If a family member, loved one, or health care provider has difficulty respecting the person's choices, you as the Health Care Agent may consider consultation with the MGH Optimum Care (Ethics) Committee. Ask your nurse or call 617-726-2000 and ask the hospital operator to connect you.

5. MAKE SURE THAT THE PERSON HAS COMPLETED A HEALTH CARE PROXY FORM AND THAT YOU HAVE A COPY OF IT AND OF ALL OTHER RELATED DOCUMENTS.

Health Care Proxy forms are available at MGH. For more information visit The Maxwell and Eleanor Blum Patient and Family Learning Center at MGH. You may also call the Blum Center at 617-726-7352 to ask for information.

Fig. 58.3 "Preparing to Be A Health Care Agent" poster. (Courtesy Ellen M. Robinson.)

When a patient has an advance directive and is unable to speak on his or her own behalf, the responsible physician is required to "invoke" the advance directive through documentation in the patient's medical record, stating that the patient does not have decision-making capacity. The HCA for the patient is ethically bound to provide the patient's voice, through the standard of "substituted judgment," which answers the question, "What would the patient say if he or she could participate in this decision-making process on behalf of himself?" Whatever the patient has discussed with the HCA that can be brought to bear in such a medical situation.[20] Substituted judgment can be thought of on a continuum, with greater and lesser degrees of knowing a patient's wishes about a specific health/illness circumstance that can be known by the HCA. Research has demonstrated that there are challenges in the surrogate decision maker role, namely that surrogates will often not be able to predict a loved one's preferences accurately or enact the intent of the role in sharing the patient's wishes versus their own wishes for the patient.[21–23] Health professionals will often be in the position to instruct a HCA in this important obligation. Hospitals can provide information to guide the HCA. Massachusetts General Hospital has an educational tool that assists in this educational process (Fig. 58.3).

The type of LST is not determinative; rather, it is the right of the patient to refuse LST regardless of the treatment in question. Treatments are not ordinary or extraordinary across the board; the treatment is analyzed within the context of what is a benefit versus a burden to the patient. Numerous LSTs are available, and they have recently multiplied. The question of whether the LST can advance a patient toward his or her goals in light of the medical prognosis is the relevant question to ask.

Within the framework of the right to refuse LST, withholding and withdrawing LSTs are rendered as ethically and legally equivalent. The concept of "time-limited trials" is useful; a treatment can be trialed, and, if deemed to be ineffective, can be discontinued.[24] From a qualitative standpoint, clinicians and families may find withdrawing LSTs, particularly medically supplied nutrition and hydration, to be emotionally challenging. However, ethical and legal equivalence in both withholding and withdrawing life support exists as a steadfast principle.

RULE OF THUMB In the United States, it is legally and ethically permissible to refuse LSTs.[12,13]

Summary

The goals-of-care framework brings to bear attention to the patient's medical and rehabilitative prognosis, then combining it with the patient's values, beliefs, and preferences within the context of ethically and legally acceptable practice. The synthesis

of prognosis, values, beliefs, and preferences and that which is ethically and legally permissible can lead to setting "goals of care" that are personalized for the patient's overall situation. Once goals are established, a plan for the patient's care is devised. As the continuum of care can range from aiming toward cure to palliation and the end of life, goals and plans may be dynamic, as a patient's condition may fluctuate. The goals-of-care framework is valuable in that it leads to purposeful and appropriate care at any given time in the patient's trajectory.

RULE OF THUMB A goals-of-care framework brings to bear attention to the patient's medical and rehabilitative prognosis, values, beliefs, and preferences within the context of ethically and legally acceptable practice.

MANAGEMENT OF PAIN AND OTHER SYMPTOMS AT THE END OF LIFE: LEGAL AND ETHICAL CONSIDERATIONS

The provision of palliative and comfort-oriented care is also both ethically and legally permissible and ought to be provided to patients in their end-of-life time when goals of care define such a pathway. The RT can develop a sound understanding and ethically defensible practice of pain and symptom management at end of life after mastering a variety of concepts, some of which define an ethically/legally defensible practice and others that are not ethically or legally defensible. Understanding definitions and distinctions between **euthanasia**, **physician-assisted suicide (PAS)**, palliative and comfort-oriented care can guide the RT in the care of patients at the end of life (Box 58.3).[25] Developing an ethically and legally defensible position is quite relevant for the RT, given that the RT's professional craft is front and center relative to decisions related to the withdrawal of LSTs such as mechanical ventilation, BIPAP, high-flow oxygen, and ECMO. When such LSTs are withdrawn, medications are rightfully ordered to ensure the patient's comfort.

BOX 58.3 Definitions of End-of-Life Concepts

Euthanasia: The act of putting to death someone suffering from a painful or prolonged illness or injury. Someone other than the patient commits the action to end the patient's life, usually by the injection of medicine.

Assisted Suicide: The means to end a patient's life is provided to the patient with knowledge of the patient's intention to use it. Physician-assisted suicide connotes that a physician will provide such means.

Palliative Sedation: The controlled and monitored use of nonopioid medications intended to lower the patient's level of consciousness to the extend necessary for relief of awareness of refractory and unendurable symptoms.

Withholding, Withdrawing, and Refusal of Life-Sustaining Treatment: Life-sustaining treatments include but are not limited to mechanical ventilation, cardiopulmonary resuscitation, chemotherapy, dialysis, antibiotics, medically supplied nutrition, and hydration.

Palliative Care: An approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness through the prevention and relief of suffering by means of the early identification and careful assessment and treatment of pain and other problems, physical, psychosocial, and spiritual.

Hospice Care: Care of patients and families at the end of life and during the last few weeks or months of life that builds on the palliative care model to minimize suffering by providing appropriate symptom management and emotional support.

Data from American Nurses' Association: *Position statement: euthanasia, assisted suicide and aid in dying,* 2013. www.nursing.org; Hospice and Palliative Nurses Association: *Palliative sedation,* Pittsburgh, PA, 2011. http://www.hpna.org/DisplayPage.aspx?Title1=Position%20Statements; and National Consensus Project for Quality Palliative Care: *Clinical practice guidelines for quality palliative care,* ed 2, Pittsburgh: PA, 2009.

Physician-Assisted Suicide

PAS was introduced into professional discourse in American medicine through some published cases in the medical literature, including the case of Diane,[26] and an anonymous piece in the Journal of the American Medical Association.[27] In Diane's case, Dr. Timothy Quill provided his patient, who had terminal cancer, with a prescription for barbiturates sufficient to end her life when she believed it was time to do so, given her fear of suffering at the end. In the anonymous piece, a resident physician described his intentional act of overmedicating a 20-year-old female patient on the night shift, who was suffering profoundly with the pain and symptoms associated with advanced gynecologic cancer. The anonymous case, arguably, could be categorized as euthanasia. The unendorsed and illegal practices of Jack Kevorkian also raised public attention to this debate; Kevorkian was ultimately arrested and convicted.[28] Thus when the US Supreme Court heard two state cases, *Vacco v. Quill*[29] and *Washington v. Glucksberg*,[30] many wondered if the court would come out in favor of "a constitutional right to die" through PAS. The court in fact did not support a constitutional right to PAS; however, it did, in an opinion authored by Justice Sandra Day O'Connor in 1997, articulate clear support for palliative care:

> *Patients near death have a right to avoid great suffering. No state laws should exist to prevent a patient who is experiencing pain from obtaining medications from qualified physicians to alleviate their suffering, even to the point of causing unconsciousness and hastening death.*
>
> ***Justice Sandra Day O'Connor (1997)***

It was stated in court opinion that the idea and practices of PAS should return to the states. In fact, as of early 2019, states that have legalized PAS include Oregon (1994), Washington (2008), Montana (2009), Vermont (2013), the District of Columbia (2016), Colorado (2016), California (2015), and Hawaii (2018). Oregon was the first state to legalize the practice, setting the model for eligibility criteria and restrictions on the practice to which other states have largely adhered (Box 58.4). Those persons who meet the criteria and request PAS may use the medication provided, and almost all patients, users or not, die under traditional hospice care.[31] Primary reasons for requesting PAS are generally not the fear of poorly managed pain; rather, it is the fear of loss of autonomy and dignity, inability to participate in the activities that made life enjoyable, existential suffering, and the unwillingness to become a burden to others.[31–34]

BOX 58.4 Requirements of the Death With Dignity Act[a]

The Death with Dignity Act (DWDA) allows terminally ill residents of Oregon to obtain and use prescriptions from their physicians for self-administered lethal medications.

Under the act, ending one's life in accordance with the law does not constitute suicide. The DWDA specifically prohibits euthanasia, where a physician or some other person directly administers a medication to end another's life.

To request a prescription for lethal medications, the DWDA requires that a patient must be

- An adult (18 years of age or older)
- A resident of Oregon
- Capable (defined as able to make and communicate health care decisions)
- Diagnosed with a terminal illness that would lead to death within 6 months

Patients meeting these requirements are eligible to request a prescription for lethal medication from a licensed Oregon physician. To receive a prescription for lethal medication, the following steps must be fulfilled:

- The patient must make two oral requests, separated by at least 15 days, to his or her physician.
- The patient must provide to his or her physician a written request signed in the presence of two witnesses.
- The prescribing physician and a consulting physician must confirm the diagnosis and prognosis.
- The prescribing physician and a consulting physician must determine whether the patient is capable.
- If either physician believes the patient's judgment to be impaired by a psychiatric or psychological disorder, the patient must be referred for a psychological examination.
- The prescribing physician must inform the patient of feasible alternatives to DWDA, including comfort care, hospice care, and pain control.
- The prescribing physician must request but may not require the patient to notify his or her next of kin of the prescription request.

To comply with the law, physicians must report to the Oregon Health Authority (OHA) all prescriptions for lethal medications. Reporting is not required if patients begin the request process but never receive a prescription. In 1999, the Oregon legislature added a requirement that pharmacists must be informed of the prescribed medication's intended use. Physicians and patients who adhere to the requirements of the Act are protected from criminal prosecution, and the choice of DWDA cannot affect the status of a patient's health care or life insurance policies. Physicians, pharmacists, and health care systems are under no obligation to participate in the DWDA.

Reporting requirements

Within **7** calendar days of writing prescription:	Patient's written request for medication/consent form Attending physician compliance form Consulting physician compliance form Psychiatric/psychological consultant compliance form (if applicable)
Within **10** calendar days of the pharmacy dispensing the lethal medications:	Pharmacy dispensing record form
Within **10** calendar days of the patient's death and/or ingestion of lethal medications:	Attending physician's follow-up form

From The Oregon Revised Statutes specify that action taken in accordance with the DWDA does not constitute suicide, mercy killing, or homicide under the law.

[a]Links to statutes can be found at https://public.health.oregon.gov/ProviderPartnerResources/EvaluationResearch/DeathwithDignityAct/Pages/ors.aspx.

Arguments and professional positions against PAS, in the opinion of some authors,[35] carry ethical weight and include erosion of trust in the medical profession, given its commitment to human dignity and care. Patients are vulnerable, given their illnesses; therefore it is imperative that health professionals can be trusted to cure when possible and, when not possible, to care for them well until death. In addition, the tools of palliative care have expanded, and teaching models and the literature are replete with strategies, even accessible for health professionals in more remote areas. given internet access and emerging telemedicine technology.

The practice of PAS will likely grow in the United States, as we have seen the expansion of it into nine states as of early 2019. Considering where the practice rests for any individual philosophically is important, especially for RTs and all health professionals, as patients and lay persons will likely ask about the arguments for and against it. Therefore all RTs should be prepared if and when PAS is legalized in their states.

Euthanasia

PAS is different from euthanasia, which is not legal in the United States. Euthanasia is defined as the active act, on the part of a health care professional, to intentionally end the life of a patient due to intolerable pain and suffering. Although euthanasia is legal in some countries such as Belgium,[36] it is not supported in the United States and is considered a criminal act punishable by law.[25]

RULE OF THUMB Euthanasia is illegal in the United States; PAS is illegal in most US states; RTs should be able to describe these practices and to distinguish between them.[25,35]

Ethically Defensible Comfort-Oriented Care

Doctrine or Rule of Double Effect

A palliative approach to care at the end of life has been a positive addition in the care of acutely and chronically ill patients when it has been determined—based on the patient's prognosis, values, beliefs, and preferences—that continuing LST in the hope for recovery is no longer an appropriate goal. The ethical approach to pain and symptom management at the end of life is best guided by the **rule of double effect**,[37,38] derived from the ethical principle of nonmaleficence and recognizing that an act can have both a good and bad effect, and that to achieve the good effect, the bad effect must be tolerated. When a well-considered decision to redirect the patient's goals of care to "comfort measures" is made and it has been decided that the burden of LST ought to be withdrawn, the responsible physician in collaboration with the interprofessional team can consider the optimal end-of-life approach given the unique specifics of the patient's condition.

The rule of double effect[37,38] provides an ethical guideline to care well for the patient (realizing that life support is no longer benefiting the patient) while also avoiding harms (pain and discomfort that may accompany the termination of life support). The rule of double effect also provides support for the ethical administration of pain and symptom management at end of life

when LSTs are not being utilized. In either clinical ethical scenario, where it is acknowledged that a patient will require pain and symptom management to ensure a peaceful death, this rule provides an ethical framework to guide practice around pain and symptom management within a sound and defensible ethical practice. Sulmasy[39] states that this moral rule has played an important role in the care of the dying, in that it allows clinicians who are opposed to euthanasia (illegal in all US states) and PAS (illegal in the majority of US states) to provide pain and symptom management while fulfilling their professional goals as health professionals and not violating their consciences. This rule should be in the "ethical parlance" of all clinicians who have professional responsibilities in caring for dying patients, as it permits the physician, pharmacist, nurse, and RT to defend their clinical actions to colleagues as well as families.

The rule of double effect provides language and reasoning that recognizes when a clinician cannot avoid all harm but can still achieve important good. The rule of double effect is invoked to justify claims that a single act (medicating a patient at the end of life) can have two foreseen effects, one good (preventing and alleviating pain and untoward symptoms) and one harmful (hastening death) is not always morally prohibited if the harmful effect is not intended. The rule of double effect has four conditions that must be satisfied in the practice of medicating a patient at the end of life. Each condition is reviewed next, integrating a tangible example of medicating a patient whose ventilator is to be withdrawn. See also Box 58.5.

1. The "nature of the act" must be good, or at least morally neutral—the act of medicating a patient at the end of life is not immoral. For example, if a "goals of care process" has led to a well-considered decision to withdraw mechanical ventilation, the patient's comfort in the process of ventilator withdrawal must be ensured. Thus the idea of providing medication to provide comfort and symptom alleviation is a good and moral act.
2. The second and perhaps most important condition is the "intention of the health professional" in the clinical situation. The goal is to "intend the good effect" while foreseeing the potential "bad effect," which must be tolerated. The good intent is to prevent or alleviate pain or untoward symptoms, such as SOB or manifestations of air hunger that might go along with the termination of ventilatory support. The intention is *not* to "kill the patient" but only to provide a dose of medicine that is clinically sound, given the patient's history with narcotics. Some may ask, "How can you really know another person's intentions?" If a physician orders 30 mg morphine IV push immediately prior to extubation in a "narcotic-naive patient," then a good intention would be questionable, as such a dose would likely go beyond anticipating the patient's discomfort and would obfuscate the patient's attempts to breathe. The RT—along with nurses, physicians, and pharmacists—can collaborate in planning how to dose a patient in such situation so as to satisfy the condition of "intention."
3. The third condition of the rule of double effect is the distinction between means and effects. Simply stated, the bad effect must not be the means to the good effect, in that the patient doesn't have to die to be free of pain and symptoms; medications can be provided that will accomplish this goal of good effect (pain and symptom relief) without the patient's immediate death from the medications.
4. The fourth condition to be met is consideration of "proportionality between good and bad effect," meaning that anticipation and treatment of a patient's distress is an ethically important value when withdrawal of LST has been agreed on as the right thing to do. Therefore there is a proportionately good reason (humane goal and value for comfort at end of life) to tolerate the "bad effect" (potential for hastening death can be foreseen) in hopes that the good effect may be realized.

BOX 58.5 Application of the Rule of Double Effect

Morphine in the treatment of dying patients in pain is generally used in a manner that satisfies the criteria for the double effect, which includes the following criteria:

1. (Nature of the act): The use of morphine is not in itself immoral.
2. (Intention of health professional): The administration of morphine is undertaken only with the intention of relieving pain, not of causing death through respiratory depression.
3. (Means vs effects): If it first kills the patient, morphine does not only relieve pain.
4. (Proportionality): The relief of pain is a proportionally grave reason for accepting the risk of hastening death.

Data from Beauchamp TL, Childress JF: *Principles of biomedical ethics*, ed 7, New York, 2013, Oxford University Press; Sulmasy DP, Pellegrino ED: The rule of double effect: clearing up the double talk. *Arch Inter Med* 159:545–550, 1999.

RULE OF THUMB The rule of double effect provides a framework for health professionals to both implement and defend their actions in the provision of pain and symptom management at the end of life.[37–39]

Pain and Symptoms at the End of Life: Clarifying the Roles of the Physician and Health Care Agent

There are times when the family member of a patient at the end of life, who may even be a legally designated surrogate, will resist the administration of pain medicines for a loved one that, per health care professional assessment, is in pain or experiencing untoward symptoms. Some families express concern that the medicine will make their loved one sleepy, and that they want the patient to be awake. In other instances, there may be a belief that suffering is redemptive and ought to be endured.[40] In such situations, a hospital chaplain may assist in exploring the origin, breadth, and depth of such religious beliefs and may discourage such a practice. In other instances, family members may not notice the objective signs of pain and symptoms or hear the patient's complaint of discomfort. In many situations, clinicians can gently inquire to better understand if there are fears or misconceptions on the part of the family and then help the family observe and understand the signs and symptoms that they, as health professionals, are noticing, and are using as the basis to

conclude that the patient, even if not conscious, might be experiencing as pain and discomfort. Clinicians have an obligation to treat a patient's pain and symptoms, and in many of the advance directives statutes, it is made clear that pain and symptom management is within the domain of the physician, not the HCA. Consider as example the section from Massachusetts General Laws Chapter 201D (Health Care Proxy Statute), Section 13: Pain Alleviation, Comfort Care Procedures states:

> *Nothing in this chapter shall preclude any medical procedure deemed necessary by the attending physician to provide comfort care or pain alleviation. Such procedures shall include but not be limited to treatment with sedatives and pain killing drugs, non-artificial oral feeding, suction and hygienic care.*

With a compassionate inquiry to the family members, clinicians can better understand their concerns and misconceptions and correct them. In rare circumstances, it may be necessary to let the family member know that the clinician's practice in assessing and medicating their loved one at end of life is, in fact, the law.

Palliative Sedation

There are times when a patient's pain and symptoms are not alleviated by the usual repertoire of medicines used at the end of life. This scenario can come up with advanced cancer or conditions such as terminal liver disease, where pain, agitation, and discomfort are unrelenting. In such situations, the practice of "palliative sedation" is permitted and its use is ethically permissible.[41,42] At Massachusetts General Hospital, a palliative care consult is required prior to instituting **palliative sedation.** As in the case of traditional end-of-life practices that are ethically defensible by meeting the criteria of the doctrine of double effect, palliative sedation, too, is an ethically defensible practice used in rare circumstances, but it is an essential tool when needed to provide comfort for a patient dying of a terminal illness with intractable pain and symptoms.

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Problem: Patient Dying of a Terminal Illness With Intractable Pain and Symptoms

Louise was in her early forties, with advanced cervical cancer that had metastasized along the nerve pathways and bones of her pelvis. She had excruciating pain, for which she was treated as an outpatient for several months by palliative care physicians, who had tried every advance in pain medication and procedures that was available—including nerve blocks, injections, and other therapies—to no avail. Finally, the patient was admitted to the hospital, where the chronic pain service and acute pain service were consulted, joining palliative care to collaborate in treating Louise's pain, again to no avail.

Discussion

Palliative sedation was proposed to Louise and her spouse, and they accepted it, along with declining medically supplied nutrition and hydration. Her cancer was advanced and could not be cured. Louise was treated with midazolam (Versed), ketamine, fentanyl, methadone, and haloperidol (Haldol) in the ICU, where she was sedated to the point of sleep. She died 48 hours later.

Withdrawal of Life-Sustaining Treatment

The discussion about the right to refuse LST and the parameters that surround it can create a pathway to a peaceful death for a patient at the end of life, even in the ICU setting. One prospective study in France revealed that 50% of ICU deaths involved withholding or withdrawing LSTs.[43] The RT is therefore in a key role in the process, given that mechanical ventilation and other aggressive respiratory therapies are very often part of, if not central, in terms of withdrawal. Different approaches to terminating mechanical ventilation are ethically defensible and can be tailored to the individual patient and family's needs. It is important to ask the family of their past experiences with deaths of loved ones, as past experiences may explain current fears. Some families may fear that their loved ones will experience great distress as LST is withdrawn.

Once consensus is reached that withdrawal of LSTs is the right action plan given the patient's goals of care, the physician, nurse, and RT can collaborate on the best approach given the specific patient's condition and family situation. A comprehensive narrative review of practices[44] reveals practice variations in the withdrawal of LSTs, although consensus exists regarding the domains to address in planning and executing withdrawal of LST in each case, including planning for withdrawal, assessment of distress, consideration of pharmacologic management of distress, and the approach to discontinuation of treatment and monitoring.[45]

Campbell[46] reviewed eight published accounts of ventilator withdrawal, citing terminal weaning and extubation as common practices; she and others argue for extubation whenever possible to promote comfort and clear visualization of the patient's face for the family's benefit, often after a long ordeal of critical illness.[47] In general, the physician, RT, and nurse should make a recommendation regarding the specific approach to terminating LST. The RT is well positioned to contribute assessment information regarding respiratory mechanics, tidal volumes, respiratory rate, minute ventilator, negative inspiratory force (NFI), P0.1. An rapid shallow breaths index (RSBI) rapid shallow breathing index can also be determined from the patient's spontaneous exhaled tidal volumes, respiratory rate, and use of accessory muscles; such data may contribute to a best prediction of how the patient might fare in the ventilator withdrawal process.[48] Long and colleagues[49] conducted an observational analysis to determine time to death after terminal withdrawal of mechanical ventilation and found, in their study of 330 patients, that predictors to shorter time to death included higher positive end-expiratory pressure, extubation prior to death, and presence of diabetes, whereas higher mean arterial pressure predicted a longer time to death. The median time to death in their cohort was 0.58 hours, with an interquartile range of 0.22 to 2.25 hours.

Some families prefer to see all tubes and lines removed so that they can see their loved one's face as intact. In this instance, the patient's endotracheal tube along with nasogastric and orogastric tubes are removed and the patient's face, upper and lower airways, and nasal passages are cleared of secretions to enhance the patient's appearance, recognizing these will likely be the family's final moments with their loved one. Families are most often

asked to step out of the room while the actual extubation process is performed. Some families, however, may prefer not to have their loved one extubated, opting rather that the patient's sedating medications be titrated to ensure comfort without any sign of respiratory distress or struggle until the patient expires with the endotracheal tube in place. Some families prefer not to have the ventilator removed from the patient until there are no detectable signs of spontaneous respirations. In such instances, it is acceptable to allow the patient to remain connected to the ventilator until cardiac arrest occurs. This requires that the RT be present throughout the entire process, as the ventilator will undoubtedly sound an alarm once assist/control ventilator modes are no longer in use and the patient's respiratory efforts become fewer and more distant during the dying process.

In some cases, family members may feel torn between the need to alleviate respiratory distress and a belief that assenting to ventilator withdrawal will precipitate the death of their loved one.

Communication with members of the family is essential in preparing them for the withdrawal process. Much care is taken to avoid using terms such as *agonal respirations*, as the family may conclude that *agonal* may imply that their loved one is truly suffering. The family must be reassured that when palliation is appropriately applied, this breathing pattern is a reflexive and normal part of the dying process rather than indicative of respiratory distress.[50]

Although the sudden discontinuation of LSTs such as CVVH, ECMO, vasocopressors, and antibiotics may not cause patient distress and discomfort, a sudden or abrupt discontinuation of mechanical ventilator support and a significant decrease in oxygen even with anticipatory medication provided can sometimes lead to patient discomfort, and the appearance of such can be quite distressing, especially to family members who have an emotional bond with the patient or inexperience with the ICU setting. Therefore it may be of benefit to the patient that a gradual ventilator wean and removal of oxygen and mechanical ventilation be considered. However, gradual and prolonged mechanical ventilator wean should be considered only in situations where the patient is clearly dyspneic and the mechanical ventilatory support is maintained as a temporizing measure to relieve the patient's dyspnea while palliation is optimized to allow for a less turbulent ventilator withdrawal process where the patient's distress can be managed more effectively. An overall guiding principle is that the sequence and process for terminal ventilator wean should be as rapid as the patient's respiratory status and anxiety level will allow. Prolonging the process of withdrawal can contribute to patient distress and family anxiety, especially if the family had been anticipating a quick end to the process.[50]

Generally, exubation to room air is standard. There are, however, times when it seems important to the family that oxygen be administered, such as by nasal cannula or face mask. Quinn-Lee and associates[51] surveyed attitudes, beliefs, and practices of oxygen use at the end of life and found that 96% of the respondents' facilities had a standard comfort-care protocol for the end of life that offered oxygen regardless of the patient's respiratory status. Over 40% of respondents in this survey stated a belief that the use of oxygen prolongs the dying process. Reasons that study participants cited to not provide oxygen included the belief that oxygen administration could be a possible irritant, could prolong death, and was not a factor in providing comfort to patient, family, or clinicians. It remains unclear whether oxygen administration prolongs death; however, it is clear that for some patients who do not exhibit breathing difficulty, it may not be beneficial to administer oxygen near the end of life.[52] For some families, providing oxygen may be reassuring, and if it is not causing the patient undue distress, it seems that responding to the family's request would be reasonable.

Noninvasive positive pressure ventilation (NPPV) can sometimes be applied following extubation or for patients who use continuous positive airway pressure (CPAP) or BIPAP to alleviate SOB.[53] Health care professionals may be apprehensive about the use of NPPV on patients whose goals of care are focused on comfort measures only.[54] However, as long as it is acknowledged that NPPV is being employed for comfort as opposed to a bridge to recovery, all can better understand its utility. NPPV can be a source of comfort for many patients as their respirations may be labored at the end of life and NPPV can relieve them of the burden of having to do all the work of breathing. NPPV is also utilized to help patients maintain some level of alertness and afford them some ability to communicate in the waning moments of life, a priority for patients and families in some situations.[55] The RT needs to adjust BIPAP or CPAP settings to patient's comfort so that NPPV does not become a burden. Whatever approach is utilized to terminally wean a patient from a mechanical ventilator, clear and constant communication with the family before, during, and after the procedure with the family is imperative.

RULE OF THUMB Providing end-of-life care when the management of pain and symptoms is required and LSTs will be withdrawn requires RTs, physicians, and nurses to be in close communication with one another as well as with the patient, if able, and family. Personalization of a plan for ventilator withdrawal should take into consideration ethically and legally acceptable standards of care.

Special Situations

Status Epilepticus

The ventilator-dependent patient who is in status epilepticus—often after a devastating brain injury requiring seizure-suppressive medications, some of which may depress respiratory effort—presents a unique challenge in end-of-life care. The ethical dilemma of stopping seizure suppressive medicines to give the patient an opportunity for respiratory effort versus continuing seizure suppressive medications, realizing that respiratory effort will be subdued, must be addressed. Most critical care physicians believe that allowing a patient, albeit comatose, to be unmedicated with status epilepticus is a harm to the patient and inhumane. Such patients on seizure-suppressive medicines that can also suppress respiratory drive at the time of ventilator withdrawal could theoretically experience a sensation of air hunger but be unable to initiate a breath. Such patients should therefore have these medicines continued, with the addition of narcotics to alleviate any potential air hunger or anxiety.[56–58] Palliative care services should be consulted in such cases.

MINI CLINI

Problem: Withdrawal of Lifesaving Treatment in a Patient With Anoxic Brain Injury

Jane had a pulseless electrical activity (PEA) arrest after massive hemoptysis leading to anoxic brain damage. She was in the ICU for 8 days, receiving high doses of sedative medications and multiple antiepileptic infusions to achieve burst suppression, given her myoclonic status and persistent electroencephalographic signatures of marked and irreversible cortical injury. The medical and neurology teams, in collaboration with interprofessional clinicians and Jane's HCA, agreed that the most appropriate goals of care would be to withdraw LST and allow Jane to die, given her very poor neurologic prognosis and prior wishes. Jane required high-dose continuous infusions of propofol, pentobarbital, and midazolam to control her ongoing abnormal electroencephalographic and myoclonic activity. When these medications were slightly reduced, she would manifest seizure activity.

Discussion

The physicians, nurse, and RT asked if it was ethically permissible to continue these antiepileptic medications while withdrawing the ventilator, as such medications could further suppress the patient's respiratory drive and ultimately hasten her death. Based on the principle of nonmaleficence, from which the doctrine of double effect is derived, it was determined to be ethically defensible, compassionate, and good medical practice at the end of life to continue the antiepileptic medications. The doctrine of double effect specifies the principle of nonmaleficence when a clinician (physician, nurse, pharmacist, and RT) cannot avoid all harms and still achieve important good.[37,39] The rule of double effect was invoked to justify claims that a single act having two foreseen effects, one good and one harmful, it is not morally prohibited if the harmful effect is not intended.

Four criteria of double effect offer a pathway for analysis in Jane's case:

The nature of the act must be good or morally neutral: For Jane, who is in a state of severe irreversible cortical injury manifesting as abnormal high-frequency electroencephalographic activity and intermittent myoclonic activity that can only be suppressed with multiple medication infusions, there is both a humane desire and professional obligation to alleviate this state. Although she may not "experience or appreciate" this state, given her devastating and irreversible brain injury, physicians, in their obligation "to do no harm," must alleviate it as best they can—thus the "nature of the act" to alleviate the condition of epileptiform activity is morally good.

Presence of good intention: The physician's intention is to eradicate seizure activity for the patient's benefit. The physician's intention is not to directly end the patient's life. The bad effect, that the patient's death may be hastened, is foreseen but not intended.

Distinction between means and effects: The provision of high-dose seizure-suppressive medication is required only if a patient's seizures are not responsive to lesser doses/types of medicine. However, the titration of such medications and addition of other medications are justified in pursuit of the good effect (seizure eradication) and not as a means to the patient's death.

Proportionality between the good effect and the bad effect must exist: The good effect (seizure suppression) must outweigh the bad effect (hastening death). The bad effect is permissible only if a proportionate reason is present that compensates for this foreseen bad effect. Allowing Jane to be in a state of myoclonus as she is dying is inappropriate and against the standards of humane end-of-life care.

Therefore continuing Jane's antiepileptic medications even when ventilator support is withdrawn meets the four criteria specified in the doctrine of double effect and is thus not only ethically permissible but also recommended as compassionate, competent end-of-life care. The intention of her physicians is to control her seizures and minimize her suffering, not to hasten her death. Discontinuation of antiepileptic medications that have been required to suppress Jane's seizures has great potential to further her suffering; thus it would be an action that cannot be tolerated.

Patient Receiving Paralytics

Some patients require paralytic medicines to promote concordance with mechanical ventilation, which allows the patient to obtain the maximal benefit from mechanical ventilation toward recovery. In time, for some patients, when progress is absent and recovery does not seem possible, the goals of care change and decisions to withdraw mechanical ventilation and other LSTs are appropriate. The ethical ideal is to wean the individual from paralytic agents before proceeding with the withdrawal of mechanical ventilation to both allow the patient the opportunity to initiate respiration postwithdrawal and to ensure that the patient does not experience air hunger without the ability to initiate a breath. There may be *rare instances*, however, when the patient's overall condition precludes tolerating the time to wean paralytics; in such *rare circumstances*, as when a patient's hemodynamic status is deteriorating rapidly, the patient's comfort should be assured with adequate sedating medicines in the process of ventilator withdrawal.[50,59] Similar reasoning by the rule of double effect applies in the earlier section titled "Status Epilepticus."

RULE OF THUMB Careful ethical consideration must be given to patients at the end of life who have intractable pain and symptoms requiring palliative sedation, patients in status epilepticus, and those who have been receiving paralytics. RTs must know ethically and legally acceptable practices in these circumstances.[42,50,56–59]

ETHICAL CONFLICT AT THE END OF LIFE

Many end-of-life decisions are reached daily at bedside and in a hospital's family meeting rooms. For the vast majority, a consensus can be reached without issue or disagreement. A patient's medical prognosis formulated by physicians and an interprofessional team is most often accepted by family. Once presented with all the facts, most families and patients concur with the physician's recommendation and the plan is adapted to accommodate unique family, religious and cultural practices. In a small percentage of cases the differences are often the result of incongruence in the family's wishes and what the clinicians deem medically appropriate.

Although case law and ethical standards have settled the right to refuse LST, there remain many reasons for ethical conflict

over LST when patients are approaching the end of life. Conflict can be present within families, within the health care team, or between families and the health care team. Some conflicts can be addressed through therapeutic use of the interprofessional team, particularly when there is good medical and nursing leadership in an ICU setting. At times, however, the conflict is such that bona fide ethics expertise, via an "ethics consult," may be sought to facilitate resolution of the conflict. It should be noted that any professional, patient, or family member can request an ethics consult. The goal of an ethics consult is to mitigate conflict by hearing the views of all stakeholders, assessing values, and helping build compromise or consensus on behalf of the patient.[60,61] The RT, as a member of the health care team, is a stakeholder in any case where ethical conflict exists and therefore has a rightful place at the table of negotiations and consensus building.

In the setting of difficult conflict at the end of life, **ethics consultation** is beneficial to health professionals, patients, and families. As of 1992, The Joint Commission on Accreditation of Hospitals and Organizations (JCAHO)[62] has required that health care organizations have a mechanism for clinicians, patients, and/or families to convey their ethical concerns.[63] When ethical concerns are related to patient care, most hospitals look toward the clinical ethics consultation service and committee. Although membership on ethics committees varies, in general there are at minimum one or more persons on the committee who have recognized expertise in ethics.[64] Ethics committees that are multidisciplinary—including community members—offer patients, families, and clinicians the "best practice" model for ethics consultation.[65] Increasingly, ethics consultation is a recognized professionalized activity, with the American Society of Bioethics and Humanities (ASBH) having recently defined criteria for health care ethics consultation.[66]

Ethics consultants are charged with responding to requests by clinicians, patients, and/or families when there is conflict. In our institution, requests are primarily about conflict at the end of life. Ethics consultants review the medical record and obtain the views of stakeholders in the case, which usually includes physicians, nurses, allied health professionals, and patients and their families. Ethics consultants may request to meet with the health care team and then with the team and family as well as the patient if able to participate. In our review of 7 years of ethics consultation, three main reasons for requests included moral support or affirmation of a plan, a surrogate decision maker's continued request for LST, and clarification of patient values and preferences.[67] Overall, the goal is to mitigate conflict, build consensus, honor patient wishes when possible, and protecting a patient from harm.

Ethics consultants possess a body of knowledge that assists them in their application of ethical theory and approaches; they are familiar with medical diagnoses and treatments, communication techniques and skills; can tolerate complex emotions; and have overall compassion for others.[61,68] In addition, ethics consultants are knowledgeable about case law, federal and state statutes, professional position statements, hospital policy, and empirical data that can contribute to an ethical analysis and recommendations.

Particular attention to the experiences of patients and families in nondominant cultures is also very important in the ethics consultation process. Persons of nondominant cultures may begin with a preconceived notion that clinicians cannot be trusted to look after their loved one's best interest. They often ask questions such as, "Can I trust them to do all they can for my loved one?" As Romain and Courtwright[69] explain, distrust in health care is manifest in different ways, and one area that has not been extensively explored is in decision making over continuing or withdrawing life-sustaining treatment. When health professionals make recommendations to stop LST or assert that there are no additional treatment options, long-standing distrust in the medical system may manifest as disbelief and refusal to accept the recommendations. Patients and families of all backgrounds should be treated respectfully, translated as equally without prejudice. Respect for human dignity and attention to the goals of the professions serves as the foundational pillars of ethics in health care.[70]

RULE OF THUMB The JCAHO mandates that health care organizations have a mechanism available to patients, families, and clinicians who encounter ethical problems. Interdisciplinary collaboration with excellent team-patient-family communication prevents many ethical conflicts; however, ethics committees and ethics consultation services exist to assist in the mitigation of ethical conflict.[60–62]

Professional Position Statements, Empirical Data, and Hospital Policy Provide Support in Ethical Conflict

There are tools available that assist clinicians and ethics consultants in formulating recommendations in practice and in situations of conflict. Professional position statements and empirical data provide evidence that can guide actions in clinical/ethical conflicts and speak to the fact that researchers and ethicists have considered the kinds of ethical problems that emerge. Clinicians and ethics consultants who draw on empirical evidence and professional position statements can demonstrate to patients and families that the end-of-life recommendations they make have a basis in evidence-based practice and professional thought beyond the institution at hand. Many institutions, such as Massachusetts General Hospital, have utilized empirical evidence and professional positions on topics in end-of-life care into hospital policy, which guides such care in the institution. Some examples follow.

The Heart Rhythm Society's[71] has issued a statement titled Expert Consensus Statement on Management of Cardiovascular Implantable Electronic Devices (CIEDs) in patients nearing end-of-life; it states that these devices—which include pacemakers, automatic implantable cardiac defibrillators (AICD), and in principle, mechanical cardiac support (MCS)—can be turned off or withdrawn when the burden of these therapies is greater than the benefit. Guided by and consistent with established case law in end-of-life care that defines the right to refuse LST [12,13] or the termination of these devices after an analysis of "goals of care" for a patient is bedrock of ethical and legal practice. Clinicians can "conscientiously object" to carrying out this "legally

BOX 58.6 Massachusetts General Hospital's Life-Sustaining Treatment Policy

Doing No Harm: The responsible physician always has an overriding responsibility to protect the patient from harm. In some clinical situations, the responsible physician may determine, after exploring and documenting a patient's values and beliefs and in conjunction with clinicians involved in the patient's care, that attempting cardiopulmonary resuscitation (CPR) would be more harmful than beneficial for the patient. In such situations, the responsible physician may decide not to offer CPR. In two such situations, the responsible physician may follow guidelines for entering appropriate code status orders, which may include do not resuscitate (DNR), do not intubate (DNI), or both.

Situation 1: The responsible physician should consider protecting a patient who is imminently dying from CPR's potential harms by not offering CPR and entering the appropriate orders. In this situation, the responsible physician may decide but is not required to obtain a second opinion about not offering CPR from another senior or experienced physician or from the optimal core committee (OCC) and also may request advice from the Office of General Counsel (OGC).

Situation 2: The responsible physician may also consider not offering CPR to a patient who is not imminently dying but has no reasonable chance of surviving CPR to the point of leaving the hospital. In this case if, after careful discussion with the patient or surrogate, the patient or surrogate does not assent to the plan, orders to withhold CPR should be entered only if another senior or experienced physician and a consultant from the OCC concur with the plan and only if this concurrence has been documented in the medical record.

In either circumstance, the responsible physician who decides not to offer CPR should inform the patient or surrogate of this decision and its rationale and ensure that the patient will continue to receive the highest possible quality of care.

Courtesy Ellen M. Robinson.

and ethically permissible procedure to terminate these devices" but must not abandon the patient and thus are obligated to identify a clinician who can do it for the patient. The RT will find it useful to be aware of this position statement, as a knowledge deficit regarding the termination of these devices persists among physicians and health care professionals in practice.

ECMO is utilized for adults with cardiac and respiratory failure due to conditions such as acute, serious influenza; acute respiratory distress syndrome (ARDS); interstitial lung disease; and cardiogenic shock as well as other life-threatening illnesses leading to cardiopulmonary collapse.[72] Although outcomes vary, given the patient's index condition and accompanying comorbidities, for some patients the provision of ECMO can clearly be lifesaving. At our institution, an ethics consult is placed for each patient receiving ECMO for the purposes of identifying any ethical conflict early.[73] RTs are key professionals in ECMO therapy in that they are responsible for administering the therapy and being present at the patient's bedside. Therefore their engagement with emerging ethical issues in these cases is essential.

The Renal Physicians' Association has published a document titled "Shared Decision Making in Appropriate Initiation and Withdrawal from Dialysis."[74] It identifies 10 recommendations that guide practice in goals of care for the patient in consideration of ethically appropriate use of dialysis and withholding or withdrawing dialysis.

The question of administration of **cardiopulmonary resuscitation** (CPR) often comes up at the end of life. Clinicians become increasingly concerned when a patient is imminently dying and DNR has not yet been agreed on by the family. Empirical evidence provides a framework for the ineffectiveness of CPR for the seriously ill.[75,76] Hospitals have adopted policies to limit offering CPR to patients who are clearly at the end of life based on this empirical evidence, showing that CPR in such instances has largely had poor outcomes. When the physician believes that the patient cannot benefit from CPR, she or he should consider not offering it as a LST.[77] At our institution, experience in using a "Do no harm, or medically indicated DNR/DNI policy" has been largely positive, and in most cases the family appreciates that they have been relieved of the burden of decision making. The case of Ms. Yates demonstrates the benefits that the policy can have.

At times there are situations when conflict about withdrawing LST is intractable and ethics consultation is not able to bring about resolution. To address such conflicts, some quaternary care institutions have written or adopted "resolving intractable conflict" policies that are due process approaches to attempt to resolve issues involving the continued use of LST. These policies are guided by or adhere to principles in a five-society position statement entitled "Responding to Requests for Potentially Inappropriate Treatments in ICUs." Those who collaboratively wrote this statement included the American Thoracic Society, the American Association of Critical Care Nurses, the American College of Chest Physicians, the European Society of Critical Care Medicine, and the Society of Critical Care Medicine.[78]

Empirical evidence can also guide ethics consultation analyses and recommendations in situations of feeding options for patients with advanced dementia, cases in which RTs may well be involved due to aspiration risk and sequelae. When a person with dementia struggles with dysphagia and aspiration, family members may believe that medically supplied nutrition and hydration can help their loved one meet his or her nutritional needs. In fact, the evidence suggests otherwise, in that patients with feeding tubes are also at risk for aspiration, along with a host of other complications including aspiration pneumonia, esophageal perforation, infection, tube blockages and dislodgements, physical or pharmacologic restraint due to agitation/attempts to remove a feeding tube, and deprivation of the pleasure of food and social interaction of feeding.[79–81] Such evidence leads to a general recommendation against tube feeding for persons with advanced dementia, a position supported by the American Geriatrics Society.[82] For such patients, ethics consultation can often provide much-needed empirical data to support both medical teams and families in their decision making against medically supplied nutrition and hydration.

RULE OF THUMB Empirical data, professional position statements, and hospital policy are resources that help patients, families. and clinicians make sound clinical/ethical decisions. Ethics consultants are experts; they know the relevant sources of information and when such might be applicable.[71,74–82]

MINI CLINI

Problem: Cardiopulmonary Resuscitation in a Patient at the End of Life

Ms. Yates, a 60-year-old Asian woman of Buddhist tradition, had metastatic breast cancer that had been diagnosed 6 years earlier. Ms. Yates had been cared for at a premier care cancer center and had benefited from cancer treatments; however, her oncologist informed her and her son, Kyle, who was also her HCA, that no further treatment could be offered given her advanced disease. Primarily driven by her son, Mrs. Yates was taken to yet another quaternary care institution, seeking treatment. She was hospitalized and her disease was found to be similarly advanced, metastatic, and no longer responsive to cancer treatment. Ms. Yates was oxygen-dependent, her functional status had declined significantly, and she had recently endured pathologic fractures of bones in her left arm and right leg.

Kyle and his sister, Lee, were almost always present in their mother's hospital room. Lee sat quietly and did not speak often. Ms. Yates had demonstrated to health professionals signs of acceptance that she was in her end-of-life time; however, when Kyle was present, she would nod in agreement to what he said about continuing treatment. Kyle had a job as a computer programmer but gave it up 6 years earlier to care for his mother. Lee shared with a social worker that although Kyle was very good at programming, he did have difficulty getting along with his supervisor and coworkers.

Discussion

Kyle was struggling with the fact that his mother had a terminal condition and a very limited life expectancy. Reportedly, Kyle was unable to accept that further life-sustaining measures, including CPR, would be both nonbeneficial and burdensome interventions for his mother. Furthermore, Ms. Yates was often uncomfortable, had difficulty breathing, and grimaced and moaned with basic nursing care. Morphine would be the most effective treatment for her symptoms; however, in the setting of a full code, nurses were hesitant to give her medication that could depress her breathing. The attending physician heard the nurses' concerns and requested an ethics consult for the question regarding limiting CPR in the setting of advanced metastatic breast cancer, nonresponsiveness to treatment, and declining functional status.

Given that Ms. Yates was at the end of life, the ethics consultants, based on a hospital policy, recommended the following: physicians are bound by the first ethical principle of their roles as doctors, which is to do no harm. In a situation such as this, CPR should not be offered, with the explicit goal of protecting the patient from harm (Box 58.6).

Kyle was angry when the attending physician told him of the medically indicated DNR/DNI—he resisted it and began talking about wanting to transfer his mother to yet another hospital. Physicians and nurses persuaded him to "stay the course." In a day or so, Kyle seemed accepting of the DNR/DNI and stopped requesting transfer. His mother's status deteriorated further, and she was transitioned to comfort measures, receiving morphine for difficult breathing and a generalized appearance of discomfort. Within a few days, the nurse suggested to Kyle and Lee that their mother was getting closer to death, and given Ms. Yates's Buddhist faith, that the Buddhist chaplain be called. The chaplain led a chanting service at Ms. Yates's bedside, and Kyle and Lee seemed comforted by it. They prayed together that Ms. Yates might have a peaceful transition and that all her family members be well.

The nurse attending the patient's death documented the following:

Kyle reported that he was so happy that his mother passed peacefully and that he now understands and appreciates what the staff who had cared for her were trying to tell him. He reports that he now realizes how much she had been suffering for so many months.

THE RESPIRATORY THERAPIST AS ETHICAL PRACTITIONER

Respiratory therapists should not make assumptions about a patient's or family's wish or preferences and how their unique cultural backgrounds may shape how they arrive at certain decisions. In such cases an RT will be present throughout and will be well positioned to show understanding, empathy, and respect to all patients and families. In times of serious illness, RTs can comfort patients and families as they imagine walking in their patient's and families' shoes, bearing in mind the vulnerability of both patient and family. A patient on a gurney who is critically ill or at the end of life can lose all sense of dignity, being surrounded by strangers who are providing care. It is therefore important for practitioners to learn who the person being treated is and thus responding to that person as an individual rather than simply a patient. The way a therapist explains the ability or failure to wean from mechanical ventilation can either calm a family member's anxiety or cause distress. Distress may ensue if the explanation is void of compassion even when it is correct. A family can more easily accept that their relative cannot be liberated from the ventilator if the explanation is communicated with empathy. Health professionals including RTs do not communicate only with words but also with their body language and attitude. The RT can convey a genuine sense of compassion by using terms that a layperson can understand, as opposed to medical jargon. While interacting with patients and families, the RT must strive to not appear rushed and preoccupied and not seem eager to be somewhere else.

When faced with a critical illness and with end-of-life decisions, patients and families do not want technically precise answers to their questions; rather, they want explanations that will bring clarity to their understanding delivered in an empathic manner—a manner that leaves the door open for continued conversation. Like physicians, nurses, and social workers, the RT is in a unique position to comfort families in times of grief. The RT is attending the patient's most vital function, respiration. RTs, whose disciplinary expertise is unique, essential, and highly valued, can also demonstrate compassion as they administer their professional craft to seriously ill patients and their families. Practicing within an ethical comportment of virtue[83] (see Chapter 5) calls the RT to be discerning, compassionate, trustworthy, manifesting a sense of integrity, having the "good of the patient" always in mind.

Dr. Edmund Pellegrino[83] cautioned health professionals that virtuous practice can be under threat, as physicians and health professionals respond to increasing economic pressures confronting health care, among other factors that can, unabated, compete with ethical and quality patient care. A health professional must bear in mind, in training and practice, what, in fact, called her or him to the vocation of the health professions. Being cognizant of the mission and objectives of the health care institution of your practice and asking, "is this organization's mission in concert with my professional-philosophical beliefs about patient care?" is a place to begin when interviewing for positions. As a licensed RT in practice, intentionally observing the care delivered and ethical climate in the organization as well as experiencing how the RT role is supported in the delivery of care, allows the RT

to reflect on his or her own professional philosophy of care and how it can or cannot be enacted in the practice setting. Are there opportunities to ask questions in patient cases? Are the health professionals collaborative and inclusive of the RT? Are practice and legal and ethical standards upheld in usual care aimed toward recovery and in end-of-life care? Health professionals who are rooted in character ethics are needed in moral transactions between professionals as well as the patients and families they serve. Sick persons are vulnerable and therefore must rely on and trust their physicians, nurses, and allied health professionals in setting goals and providing goal-appropriate, competent, and compassionate care. It is important to know that the physician, the nurse, and the RT as providers of intimate care to vital body systems are expected to be intrinsically predisposed to do the right thing for the patients they serve.[84]

RULE OF THUMB RTs are bound to practice ethically, always placing patient well-being above all and respecting the dignity of each patient they serve.

Finally, as an RT practicing in health care organizations—be they ICUs, general units, or long-term care facilities—it is essential to be a participating member of an interprofessional team.[85] Health professionals cannot practice in isolation—doing so can harm the patient, denying the patient of the multiple benefits that collaborative teamwork can provide, not to even speak of the benefits it affords each professional on a team. Seeking to know the patient in the context of her or his medical and rehabilitative prognosis as well as ethically and legally permissible strategies in end-of-life care can enhance the RT's role and professional satisfaction in providing high-quality, ethical, collaborative care.

SUMMARY CHECKLIST

- The approach to a seriously ill patient's care should be goal directed and intentional and should include consideration of the patient's prognosis and values, beliefs, and preferences within the context of what is legally and ethically permissible in the jurisdiction in which the patient is receiving treatment and care.
- In the United States, case law has accrued, building the right to refuse LST as a legal right and ethically permissible action. This right applies to the person with decision-making capacity, former decision-making capacity, or never having had decision-making capacity. LST may be withheld or withdrawn within the framework of legal and ethical permissibility. This right applies to any LST; it is analyzed in terms of benefits and burdens to the patient considering his or her goals of care.
- Good pain and symptom management at the end of life is both legally and ethically permissible. The rule of double effect provides an ethical and time-honored framework for analyzing the ethics of pain and symptom management at the end of life.
- Withdrawal of LST, in particular mechanical ventilation, requires a careful interdisciplinary process of assessment, intervention, and evaluation. The RT is a key professional in this process, given his or her expertise in the assessment and management of the patient's airway. The unique characteristics of the patient's condition should be considered as physicians, nurses, and RTs make plans for withdrawing the patient's mechanical ventilation.
- Special situations at the end of life include patients with status epilepticus, those with intractable pain and symptoms in need of palliative sedation, and those on paralytics; all such patients require careful ethical analysis with an interdisciplinary team collaboration.
- Physician and nursing leadership and interdisciplinary team collaboration can often assist in mitigating ethical conflict at the end of life. However, when conflict is challenging, ethics consultation can assist interdisciplinary teams, patients, and families in navigating to an ethical consensus.
- Professional position statements, empirical data regarding clinical-ethical decision making, and hospital LST policies can guide clinicians in sound decision making with patients and families at the end of life.
- RTs are key members of the interdisciplinary health care team with expertise that is not duplicated by other professional disciplines. Thus their disciplinary perspective into clinical/ethical decision making with and on behalf of seriously ill patients approaching the end of life is essential.

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GLOSSARY

A

***a* waves** occur when the atria contract, causing a slight increase in both atrial and ventricular pressures within 0.1 second. (Chapter 10)

AARC abbreviation for the *American Association for Respiratory Care (AARC),* the primary voluntary professional association for respiratory therapists. (Chapters 1 and 2)

abdominal compartment syndrome arises when the abdomen has become a fixed compartment, with increased pressure resulting in ischemia and organ dysfunction. (Chapter 16)

abdominal paradox abnormal breathing pattern seen as a sinking inward motion of the abdomen with each inspiratory effort; a sign of diaphragm fatigue. (Chapter 16)

abdominal thrust external pressure forcefully exerted on the abdomen, under the diaphragm, to expel obstructing objects from the upper airway. (Chapter 37)

absolute humidity actual mass or content of water in a measured volume of air, usually expressed in grams per cubic meter or pounds. (Chapters 6 and 39)

accessory muscles of breathing occurs when muscles of the neck, back, and abdomen assist the diaphragm and the internal and external intercostal muscles in respiration, especially in some breathing disorders or during exercise. (Chapter 9)

accountable care organizations (ACOs) groups of doctors, hospitals, and healthcare providers who voluntarily come together to deliver coordinated patient care. (Chapter 3)

accreditation a process of review that allows healthcare organizations to demonstrate their ability to meet regulatory requirements and standards established by a recognized accreditation organization such as The Joint Commission. (Chapter 2)

accuracy determined by how precisely a measuring instrument indicates a known reference value. (Chapter 20)

acid a compound that yields hydrogen ions (H^+) when it is dissolved in an aqueous solution. (Chapters 13 and 14)

acidemia a state in which arterial blood is more acidic than normal (pH < 7.35). (Chapter 14)

acid-fast bacterium type of bacteria that resists decolorizing by acid after accepting a stain. (Chapter 17)

acinus any small, sac-like structure, particularly one found in a gland. (Chapter 9)

activated clotting time the amount of time it takes blood to form a clot. (Chapter 51)

active compression decompression (ACD) uses a hand-held suction device, applied mid-sternum, to compress the chest then actively decompress the chest after each compression during CPR. (Chapter 38)

active compression decompression device a hand-held suction device, applied mid-sternum, which compresses the chest then actively decompress the chest after each compression during CPR. (Chapter 38)

active cycle of breathing technique (ACBT) the use of repeated cycles of breathing control, thoracic expansion, and forced expiration technique. (Chapter 44)

active transport the movement of molecules across membranes in a direction opposite to that expected because of diffusion or osmotic pressure. (Chapter 13)

acute chest syndrome a syndrome that develops in patients with sickle cell disease. The chief complaints are acute chest pain, cough, and shortness of breath caused by the sickling of red blood cells. (Chapter 12)

acute coronary syndrome (ACS) a term comprising three types of coronary artery diseases associated with gradual and/or sudden obstruction of the coronary arteries.

acute exacerbation of COPD state of worsening of chronic obstructive pulmonary disease, often defined by the need to increase medication or escalate care. (Chapter 25)

acute hypoxemic respiratory failure (AHRF) respiratory compromise characterized by severely decreased oxygenation that develops over a relatively short period of time. (Chapter 29)

acute lung injury (ALI) a condition characterized by alveolar flooding caused by an acute insult (e.g., sepsis). Normally a rapidly developing bilateral pulmonary process of noncardiac origin with ratio of a PaO_2 to FiO_2 greater than 200 mm Hg but less than 300 mm Hg. (Chapter 29)

acute respiratory distress syndrome (ARDS) a respiratory disorder characterized by respiratory insufficiency and hypoxemia; triggers include gram-negative sepsis, O_2 toxicity, trauma, pneumonia, and systemic inflammatory responses. (Chapter 29)

adaptive support ventilation (ASV) a mode of ventilation guided by evaluation of the patient's lung mechanics; the ventilator tries to impose a ventilatory pattern that results in the least amount of patient work. (Chapter 53)

adenocarcinoma a type of cancer characterized by glandular structures. (Chapter 32)

adenosine triphosphate (ATP) The most common "energy currency" of cells; a molecule that stores a lot of energy in its phosphate bonds. These bonds are broken to release the energy needed to drive all the physiological mechanisms that maintain life. (Chapter 23)

adhesion a band of scar tissue binding anatomic surfaces that are normally separate from each other. Adhesions most commonly form in the abdomen after abdominal surgery, inflammation, or injury. (Chapter 6)

adiabatic a process in which no heat is gained or lost by the system. (Chapter 6)

adrenergic of or pertaining to the sympathetic nerve fibers of the autonomic nervous system that use epinephrine or epinephrine-like substances as neurotransmitters; any chemical or drug that mimics the effect of these neurotransmitters. Also called a *sympathomimetic drug; catecholamine*. (Chapter 36)

Advanced Cardiac Life Support (ACLS) emergency medical procedures beyond basic life support; they include the establishment of an intravenous fluid line, defibrillation, drug administration, control of cardiac arrhythmias, and use of ventilatory equipment. ACLS usually requires direct or indirect supervision by a physician. (Chapter 38)

advanced directive a document in which an individual specifies what medical care he or she wishes to receive in the future should he or she no longer be able to make such decisions. It may be in the form of a living will or a durable power of attorney. (Chapters 5, 16 and 58)

adventitious lung sounds abnormal lung sounds. (Chapter 16)

aerobic exercise any physical activity that requires increased cardiac output and ventilation to meet the increased O_2 demands of the skeletal muscles. (Chapter 56)

aerophagia the swallowing of air. (Chapter 47)

aerosol a suspension of solid or liquid particles in a gas. (Chapter 40)

aerosol output the weight or mass of aerosol particles produced by a nebulizer per unit time or volume. (Chapter 40)

affective domain a learning domain addressing the area of emotion, mood, or feeling. (Chapter 55)

afterload the load against which an activated muscle must try to shorten; greater afterloads result in lower velocities. (Chapters 10, 51, and 52)

aging growing older. (Chapter 40)

agonal breathing irregular, gasping breaths often seen during cardiac arrest. (Chapter 16)

agonist a chemical substance or drug that has affinity for a receptor and exerts a desired or expected effect (as opposed to an antagonist). (Chapter 36)

air bronchograms lucent tubular shadows running through areas of consolidation. (Chapter 21)

airway hyperresponsiveness a state of the airways that causes them to constrict abnormally in response to stress or insults (e.g., exercise, inhaled materials such as dust or allergens). (Chapter 25)

airway inflammation a localized protective response to pathogens occurring within the routes for passage of air into and out of the lungs and involving the release of mediators including mast cells, eosinophils, macrophages, epithelial cells, and T lymphocytes. (Chapter 25)

airway obstruction a state of abnormally slowed expiration characterized most commonly by a decrease in FEV_1. (Chapter 25)

airway occlusion pressure inspiratory pressure generated 100 msec after airway occlusion; P0.1 (the negative airway pressure generated during the first 100 msec of an occluded inspiration) is effort independent and is thought to be a good measure of central respiratory drive. (Chapter 53)

airway pressure release ventilation (APRV) a form of pressure ventilation that uses two levels of continuous positive airway pressure in an intermittent mandatory ventilation breathing pattern. (Chapter 29)

airway resistance a measure of the impedance to ventilation caused by the movement of gas through the airways; abbreviated as Raw, airway resistance is computed as the change in pressure along a tube divided by the flow. (Chapter 11)

airway stents devices designed for internal splinting of the airway lumen to help reduce airway obstruction from malignant or benign processes that compress the airway from the outside. (Chapter 22)

alae the lateral surfaces of the external nose; the alae may flare out during respiratory distress. (Chapter 9)

albumin the largest constituent protein in plasma. (Chapter 23)

alkalemia a decreased hydrogen ion concentration in the blood; as applied to arterial blood, denotes pH greater than 7.45. (Chapter 14)

alpha-1 antitrypsin deficiency an inherited disorder that may cause emphysema and liver disease. (Chapter 25)

alternative (nonacute) care a site in which healthcare is provided to patients outside of acute care hospitals. It includes skilled nursing, long-term and rehabilitation facilities, as well as homecare. (Chapter 57)

alveolar-arterial oxygen tension difference ($P[A-a]O_2$) the difference between the alveolar and arterial PO_2, usually about 5 to 10 mm Hg when a person is breathing room air. (Chapter 52)

alveolar-capillary membrane a thin tissue barrier through which gases are exchanged between the alveolar air and the blood in the pulmonary capillaries. (Chapter 9)

alveolar dead space alveoli that are ventilated but not perfused. The condition may exist when pulmonary circulation is obstructed, as by a thromboembolus. (Chapters 11 and 12)

alveolar period the development of mature alveoli accompanied by capillary proliferation around their outside walls. (Chapter 9)

alveolar shunt alveolar units that are closed to ventilation but still perfused. (Chapter 12)

alveoli small outpouching of walls of alveolar space through which gas exchange between alveolar air and pulmonary capillary blood occurs. (Chapter 9)

alveolopleural fistula an abnormal communication between the alveoli and the pleura, often associated with pneumothorax. (Chapter 27)

ambulation the process of helping a bedridden patient begin to sit up, stand, and walk around independently. (Chapter 3)

American Academy of Sleep Medicine a professional society for the subspecialty of sleep medicine which accredits sleep medicine facilities in the United States. (Chapter 2)

American Association for Respiratory Care (AARC) a professional association of RTs. (Chapters 1 and 2)

American Respiratory Care Foundation (ARCF) a nonprofit organization formed to support research, education, and charitable activities in respiratory care. (Chapter 1)

American Society for Testing and Materials (ASTM) A nongovernment agency that establishes performance standards for various types equipment and materials. (Chapter 39)

American Society of Anesthesiologists (ASA) an educational, research, and scientific association of physicians organized to maintain the standards of the medical practice of anesthesiology. (Chapter 2)

American Standard Safety System (ASSS) specifications adopted in the United States and Canada for threaded high-pressure connections between compressed gas cylinders and their attachments. (Chapter 41)

American Thoracic Society (ATS) a nonprofit organization focused on improving care for pulmonary diseases, critical illnesses and sleep-related breathing disorders. (Chapter 2)

ampere the basic unit of electrical energy current; equivalent to the amount of electrons flowing when 1 volt of electromotive force is applied to a circuit with 1 ohm of resistance. (Chapter 3)

amyotrophic lateral sclerosis (ALS) a degenerative disease of the motor neurons often characterized by atrophy of the muscles of the hands, forearms, and legs, eventually involving most of the body including the muscles of respiration. (Chapter 33)

analyte a chemical substance that is being measured as in a broad test. (Chapters 17 and 19)

analyzer a person or device that evaluates some submitted material (e.g., a machine that measures blood chemistry components). (Chapter 19)

anatomic dead space airways and lung tissue which does not participate in gas exchange. (Chapter 9)

anemia an abnormal condition characterized by a reduction in the number of circulating red blood cells or the amount of normal hemoglobin available to carry O_2. (Chapters 17 and 23)

anergy lack of activity; an immunodeficient condition characterized by a lack of or diminished reaction to an antigen or group of antigens. This state may be seen in advanced tuberculosis and other serious infections, AIDS, and some malignancies. (Chapter 23)

angina a spasmodic, cramp-like choking feeling. (Chapter 16)

angina pectoris severe chest pain, often also spreading to the shoulders, arms, and neck, caused by an inadequate blood supply to the heart. (Chapter 10)

angle of Louis a slightly oblique angle where the manubrium articulates with the body of the sternum. (Chapter 9)

anion gap a measurement that provides a quick way of determining whether a decrease in HCO_3^- is caused by a disruption of normal anion balance or the presence of an abnormal acid anion. (Chapter 17)

anions negative ions that migrate to the anode (positive electrode) in an electrolyte solution; negative ions. (Chapter 13)

ankylosing spondylitis a chronic inflammatory disease of unknown origin, first affecting the spine and adjacent structures and commonly leading to eventual fusion (ankylosis) of the involved joints. (Chapter 33)

antagonist in pharmacology, a drug that has affinity but produces no effect; an antagonist can be competitive (forms reversible bond with receptor) or noncompetitive (forms irreversible bond). (Chapter 36)

anterior nares openings to the nose; nostrils. (Chapter 9)

anthropometrics the science of measuring the human body—height, weight, and size of component parts, including skin folds—to study and compare the relative proportions under normal and abnormal conditions. Also called *anthropometric measurement*. (Chapter 23)

antiadrenergic pertaining to blocking of the effects of impulses transmitted by the adrenergic postganglionic fibers of the sympathetic nervous system. (Chapter 36)

antibiotic therapy treatment of infections with antimicrobial agents, such as the penicillins. (Chapter 24)

anticholinergic of or pertaining to the blockade of acetylcholine receptors resulting in the inhibition of transmission of parasympathetic nerve impulses. (Chapter 36)

antiseptic a substance that tends to inhibit the growth and reproduction of microorganisms. (Chapter 4)

APACHE scoring system the *Acute Physiology and Chronic Health Evaluation* scoring system; used to assess the severity of illness in critically ill patients. (Chapter 52)

apexes uppermost regions. (Chapter 9)

Apgar score A score evaluating an infant's physical condition, usually performed 1 minute and 5 minutes after birth. It is based on a rating of five factors that reflect the infant's ability to adjust to extrauterine life. (Chapter 54)

apnea absence of spontaneous breathing. (Chapter 15)

apnea of prematurity a disorder in preterm infants, probably of central nervous system origin, characterized by frequent apneic pauses lasting longer than 20 seconds and often associated with cyanosis, pallor, hypotonia, or bradycardia. (Chapter 34)

apneustic breathing a pattern of respiration characterized by a prolonged inspiratory phase followed by expiratory apnea. (Chapters 15 and 16)

apneustic center a localized collection of neurons in the pons located at the level of the vestibular area that moderates the rhythmic activity of the medullary respiratory centers. (Chapter 15)

appropriate for gestational age (AGA) a term describing newborn—whether delivered prematurely, at term, or later than term—whose size, growth, and maturation are normal for gestational age. (Chapter 54)

argon plasma coagulation a medical endoscopic procedure used to stop bleeding or remove tumor tissue. (Chapter 22)

arterial blood pressure the force exerted by the heart against the systemic arteries as the blood moves through them. (Chapter 16)

arterialized blood blood that resembles the blood in arteries (e.g., from the finger or earlobe capillaries). (Chapter 19)

arteriovenous anastomosis a communication between an artery and a vein, either as a congenital anomaly or as a surgically produced link between vessels. (Chapter 10)

artifact an aberration resulting from interference or technical failure. An artifact does not represent a normal or so-called physiologic change. (Chapter 52)

asbestosis a restrictive lung disease caused by prolonged exposure to asbestos fibers; it is associated with a high incidence of malignant lung tumors and pleural abnormalities. (Chapter 26)

assault any conduct that creates a reasonable apprehension of being touched in an injurious manner; no actual touching is required to prove assault. (Chapter 5)

assist/control (A/C or ACV) volume ventilation continuous mandatory ventilation in which the minimum breathing rate is predetermined but the patient can initiate mechanical ventilation at an increased rate. (Chapter 49)

assisted breath a breath whose delivery is aided by a mechanical device. (Chapter 46)

assisted suicide a situation in which the means to end a patient's life is provided to the patient with knowledge of the patient's intention to use it. Physician-assisted suicide connotes that a physician provides such means. (Chapter 58)

Association for the Advancement of Medical Instrumentation (AAMI) a nonprofit organization founded in 1967 by a diverse community of approximately 7000 professionals. (Chapter 2)

asthma a respiratory disorder characterized by recurring episodes of paroxysmal dyspnea, including wheezing on expiration or inspiration, caused by constriction of the bronchi, coughing, and viscous mucoid bronchial secretions. The episodes may be precipitated by the inhalation of allergens or pollutants, infection, cold air, vigorous exercise, or emotional stress. Also called *bronchial asthma*. (Chapter 25)

asthma-COPD overlap syndrome a condition in which a patient has symptoms of both asthma and chronic obstructive pulmonary disease (COPD). (Chapter 25)

atelectasis collapse of the distal lung parenchyma. (Chapters 21 and 43)

atelectrauma lung injury as a result of alveolar collapse secondary to inappropriate positive end-expiratory pressure settings. (Chapter 47)

atmospheric pressure absolute (ATA) a measure of pressure used in hyperbaric medicine; 1 ATA equals 760 mm Hg or 101.32 kPa. (Chapter 42)

atomizer a device that produces an aerosol suspension of liquid particles without using baffles to control particle size. (Chapter 40)

atria the upper two of the heart's four chambers; the right atrium received deoxygenated blood from the inferior and supervior vena cava, and the left atrium receives oxygenated blood from the pulmonary veins. (Chapter 10)

atrial kick the propulsion of blood resulting from contraction of the atrium. (Chapters 10 and 18)

atrioventricular (AV) rings the right and left fibrous rings of heart (anuli fibrosi cordis) which surround the atrioventricular and arterial openings. (Chapter 10)

atrioventricular (AV) valves thin structures that are composed of endocardium and connective tissue, which are located between the atria and the ventricles of the heart. (Chapter 10)

atrophy the loss of muscle mass as a result of disuse. (Chapter 48)

ATPS abbreviation for *ambient temperature, ambient pressure, saturated* (with water vapor). (Chapter 6)

attending title applied to the responsible most senior physician caring for the patient in an academic medical center. (Chapter 3)

atypical pathogens select organisms in *Legionella* species, *Chlamydophila pneumoniae,* and *Mycoplasma pneumoniae* that cause pneumonia. (Chapter 24)

auditory pertaining to the sense of hearing. (Chapter 3)

autogenic drainage (AD) modification of directed coughing, beginning with low lung volume breathing, inspiratory breath holds, and controlled exhalation and progressing to increased inspired volumes and expiratory flows. (Chapter 44)

automatic external defibrillator (AED) a portable automatic device designed to perform defibrillation on patients outside of a hospital. (Chapter 38)

automatic tube compensation (ATC) a mode of ventilation that attempts to maintain tracheal pressure equal to end-expiratory pressure during both inspiration and expiration. (Chapter 53)

automaticity the heart's ability to generate its own intrinsic electrical rhythm. (Chapters 10 and 18)

autonomy the ability or tendency to function independently. (Chapter 5)

auto-PEEP pressure above atmospheric remaining in the alveoli at end-exhalation due to air trapping. Also called *intrinsic PEEP*. (Chapter 45)

autoregulation automatic control of a mechanical or physiologic system; necessitates both a sensing mechanism (to measure what is regulated) and a feedback loop (to respond to changes). (Chapter 47)

autotriggering triggering of a ventilator by any phenomenon that is not a result of the patient making an inspiratory effort. Most commonly a result of a small circuit leak. (Chapter 48)

Avogadro constant the number of constituent particles (usually molecules, atoms or ions) that are contained in one mole, the international (SI) unit of amount of substance. (Chapter 6)

Avogadro's law law in physics stating that equal volumes of all gases at a given temperature and pressure contain the identical number of molecules. (Chapter 6)

azotemia the buildup of excess nitrogenous waste products in the blood, usually secondary to renal failure. (Chapter 23)

B

bactericidal term describing substances with the ability to kill microorganisms. (Chapter 4)

bacteriostatic term describing substances with the ability to restrain the growth of microorganisms. (Chapter 4)

baffle a surface in a nebulizer designed specifically to cause impaction of large aerosol particles, leading either to further fragmentation or removal from the suspension via condensation back into the reservoir. (Chapter 40)

baffling the process of removing large water particles from suspension in a jet nebulizer so that the particles entering the patient's airways are of a uniform therapeutic size. (Chapter 39)

bands bundles of fibers, as seen in striated muscle that encircle a structure or bind one part of the body to another. (Chapter 17)

baroreceptor one of the pressure-sensitive nerve endings in the walls of the atria of the heart, the vena cava, the aortic arch, and the carotid sinus. (Chapter 10)

barotrauma physical injury sustained as a result of exposure to ambient pressures above normal, most commonly secondary to positive-pressure ventilation (e.g., pneumothorax, pneumomediastinum). (Chapters 29 and 45)

barrel chest an abnormal increase in the anteroposterior diameter of the chest caused by hyperinflation of the lungs. (Chapter 16)

basal metabolic rate (BMR) the amount of energy used in a unit of time by a fasting, resting subject. BMR, determined by the amount of O_2 used, is expressed in calories consumed per hour per square meter of body surface area or per kilogram of body weight. Also called *basal energy expenditure (BEE)*. (Chapter 23)

base a compound that yields hydroxyl ions [OH^-] when it is dissolved in an aqueous solution. (Chapters 13 and 14)

base excess (BE) the difference between the normal buffer base (NBB) and the actual buffer base (BB) in a whole-blood sample, expressed in mEq/L; a normal BE is +2 mEq/L. (Chapter 14)

basic chemistry panel (BCP) or basic metabolic panel a panel including the predominant electrolytes sodium (Na^+), potassium (K^+), chloride (Cl^-), and total CO_2/bicarbonate (CO_2) as well as glucose. (Chapter 17)

basic life support (BLS) cardiopulmonary resuscitation designed to reinstitute either circulatory or respiratory function without the use of equipment or drugs. (Chapter 38)

battery (legal) unconsented touching of an individual that causes injury. (Chapter 5)

benchmarking establishing the relationship between an organization's ability to perform at a given level to that of other comparable organizations. (Chapter 7)

beneficence the principle requiring that health providers go beyond doing no harm and actively contribute to the health and well-being of their patients. (Chapter 5)

benevolent deception actions in which the truth is withheld from the patient for his or her own good. (Chapter 5)

Bernoulli principle a principle stating that as flow increases, the pressure in the fluid will decrease along with its potential energy. (Chapter 6)

best interests UN Convention on the Rights of the Child, "…all actions concerning children, whether undertaken by public or private social welfare institutions, courts of law, administrative authorities or legislative bodies, the best interests of the child shall be a primary consideration". (Chapter 58)

bibliographic database a collection of reference sources often used in research. (Chapter 8)

bilevel positive airway pressure (bilevel PAP) spontaneous breath mode of ventilatory support that allows separate regulation of the inspiratory and expiratory pressures. (Chapter 34)

Biot respiration breathing characterized by irregular periods of apnea alternating with periods in which four or five breaths of identical depth are taken. (Chapter 16)

biotrauma inflammation of the lungs in response to inappropriate mechanical ventilation that promotes alveolar overdistention in inspiration and derecruitment on exhalation. (Chapter 47)

biovariable targeting scheme a ventilation mode that continuously monitors and makes changes based on patient and ventilator variables to mimic the natural variability of breathing. (Chapter 46)

biphasic automated external defibrillation a treatment to correct a potentially lethal heart rhythm by delivering a shock to the heart in two directions, via changing the polarity of the electrodes in the latter part of the shock delivery. (Chapter 38)

bladder pressure pressure established in the bladder. (Chapter 52)

blood-brain barrier the anatomic-physiologic feature of the brain thought to consist of walls of capillaries in the central nervous system that surround astrocytic glial membranes. This barrier separates the parenchyma of the central nervous system from blood. The blood-brain barrier prevents or slows the passage of some drugs and other chemical compounds, radioactive ions, and disease-causing organisms such as viruses from the blood into the central nervous system. (Chapter 15)

blunt trauma nonpenetrating trauma that may result in pulmonary contusion. (Chapter 30)

Board of Directors a board of directors is a group of people who jointly supervise the activities of an organization, such as the American Association for Respiratory Care (AARC). (Chapter 2)

Board of Medical Advisors (BOMA) the medical advisory group for the American Association for Respiratory Care. (Chapters 1 and 2)

body humidity absolute humidity in a volume of gas saturated at a body temperature of 37°C; equivalent to 43.8 mg/L of water in the air. (Chapter 39)

body mass index (BMI) formula for determining obesity, calculated by dividing a person's weight in kilograms by the square of the person's height in meters. (Chapter 23)

Bohr effect effect of variations in blood pH on the affinity of hemoglobin for O_2. (Chapter 12)

boiling point temperature at which the vapor pressure of a liquid exceeds atmospheric pressure. (Chapter 6)

Bourdon gauge fixed-orifice variable-pressure flowmeter. (Chapter 41)

Boyle's law law stating that with constant temperature, volume and pressure are indirectly proportional. That is, as the pressure is increased, the volume will decrease. (Chapter 6)

brachytherapy a method to deliver short-distance radiation therapy to a tumor via a bronchoscope. (Chapter 22)

bradycardia an abnormal decrease in heart rate. (Chapter 16)

bradypnea an abnormal decrease in breathing rate. (Chapter 16)

breach of contract failure, without legal excuse, to carry out the terms of a legal agreement. (Chapter 5)

breath-actuated nebulizer aerosol device responsive to the patient's inspiratory effort that reduces or eliminates aerosol generation during exhalation. (Chapter 40)

breath-enhanced nebulizer nebulizer that entrains room air in direct relation to the patient's inspiratory flow. (Chapter 40)

breathlessness distressful sensation of uncomfortable breathing that may be caused by certain heart conditions, strenuous exercise, or anxiety. (Chapter 16)

bronchial washings and brushings material sampled during bronchoscopy, specifically from instilling and withdrawing saline into the lung (washings) or inserting a brush into the lung. (Chapter 22)

Bronchial thermoplasty (BT) a nonpharmacologic treatment modality for asthma. (Chapter 22)

bronchiectasis abnormal condition of the bronchial tree characterized by irreversible dilation and destruction of the bronchial walls. (Chapters 25 and 44)

bronchiolitis acute infection of the lower respiratory tract causing expiratory wheezing, respiratory distress, inflammation, and obstruction of the bronchioles; bronchiolitis is usually caused by respiratory syncytial virus (RSV) and is most common in infants less than 2 years old. (Chapter 35)

bronchoalveolar lavage (BAL) technique used to obtain specimens from the alveolar level of the lung. BAL is performed by instilling a small volume (up to 50 mL) of normal saline solution deep into the airways and then suctioning it back. (Chapter 22)

bronchodilator a substance, especially a drug, that relaxes contractions of the smooth muscle of the bronchioles to improve ventilation to the lungs. Pharmacologic bronchodilators are prescribed to improve aeration in asthma, bronchiectasis, bronchitis, and emphysema. (Chapter 25)

bronchophony abnormal voice sounds heard over lung consolidation. (Chapter 16)

bronchopleural fistula any air communication from the lung to the pleural space. (Chapter 27)

bronchopneumonia acute inflammation of the lungs and bronchioles characterized by chills, fever, high pulse and respirator rates, bronchial breathing, cough with purulent bloody sputum, and chest pain. (Chapter 41)

bronchopulmonary dysplasia (BPD) a chronic respiratory disorder characterized by scarring of lung tissue, thickened pulmonary arterial walls, and mismatch between lung ventilation and perfusion. It often occurs in infants who have been dependent on long-term mechanical ventilation. (Chapters 35 and 42)

bronchoscopy the process of passing a bronchoscope into the airways for diagnostic testing or therapeutic purposes. (Chapter 22)

bronchospasm abnormal contraction of the smooth muscle of the bronchi, resulting in acute narrowing and obstruction. (Chapter 25)

brownian diffusion primary mechanism for deposition of small particles (<3 µm), mainly in the respiratory region where bulk gas flow ceases and most aerosol particles reach the alveoli by diffusion. (Chapter 12)

BTPS abbreviation for *body temperature, ambient pressure, saturated* (with water vapor). (Chapter 6)

buffer base total blood buffer capable of binding hydrogen ions; normal buffer base ranges from 48 to 52 mEq/L. (Chapter 14)

buffering the process of removing H^+ or OH^- in solution to minimize change in pH. (Chapter 13)

bulbar palsy a disease affecting the glossopharyngeal, vagus, accessory and hypoglossal nerves and is due to lower motor neuron pathology. (Chapter 33)

buoyancy the property that enables certain objects to float in water. (Chapter 6)

business intelligence (BI) a set of tools that permit the capture, storage, and transformation of data into useful and actionable information. (Chapter 7)

C

c wave upward bulging of the arteriovenous valves during this phase causes a slight upswing in atrial pressure graphs. (Chapter 10)

cachexia general ill health and malnutrition characterized by weakness and emaciation. (Chapter 16)

cachexic the state of being of general ill health and suffering from malnutrition. (Chapter 23)

calibration media types of equipment used to test and ensure that the output of an analyzer (blood gas) is both accurate and linear across the range of measured values. (Chapter 19)

canalicular stage in fetal development, this is the stage beginning at week 16 and continuing until week 26. (Chapter 9)

canals of Lambert openings that connect alveoli with secondary respiratory bronchioles. (Chapter 9)

cannulation the process of placing a catheter in an artery or vein. (Chapters 51)

capacity the range or limit of how much can be measured or stored in a space; it can also mean the combination of two or more lung volumes. (Chapter 20)

capillary action the basis for blood samples obtained by using a capillary tube. (Chapter 6)

capnography the process of obtaining a tracing of the proportion of CO_2 in expired air using a capnograph. (Chapters 19, 22, and 52)

capnometry measurement of CO_2 in a volume of gas, usually by methods of infrared absorption or mass spectrometry. (Chapters 19 and 52)

carbon monoxide poisoning poisoning as a result of exposure to carbon monoxide that allows the attachment of carbon monoxide to hemoglobin, preventing the attachment of O_2 to hemoglobin. (Chapter 30)

carboxyhemoglobin the compound produced by the chemical combination of hemoglobin with carbon monoxide. (Chapter 12)

cardiac output the volume of blood pumped per minute by the heart. (Chapters 10, 51 and 52)

cardiac tamponade compression of the heart caused by the collection of blood, fluid, or gas under pressure in the pericardium. (Chapter 10)

cardiopulmonary exercise evaluation (CPX) exercise-based assessment of a patient before pulmonary rehabilitation designed to determine the patient's exercise capacity and risk for desaturation. (Chapter 56)

cardiopulmonary resuscitation (CPR) basic emergency procedure for life support consisting of artificial respiration and manual external cardiac massage. (Chapters 38 and 58)

cardiorenal syndrome the combination of kidney failure resulting from a cardiac condition, frequently poor cardiac output. (Chapter 31)

cardioversion the use of electrical energy to bring an abnormal heart rhythm back to normal. (Chapter 38)

carina bifurcation of the trachea into the right and left main stem bronchi. (Chapter 9)

case report a detailed report of the symptoms, signs, diagnosis, treatment, and follow-up of an individual patient or an individual subject in clinical research. (Chapter 8)

catabolism a form of metabolism involving the breakdown of complex molecules in living organisms to form simpler ones to release of energy. (Chapter 23)

catecholamine any one of a group of sympathomimetic compounds composed of a catechol molecule and the aliphatic portion of an amine. (Chapter 36)

cation a positively charged ion. (Chapter 13)

cellular respiration the process whereby cells convert chemical energy in the three energy-yielding nutrients (CHO, protein, lipids) to the high-energy phosphorylated nucleotides comprising the currency of life. (Chapter 23)

Centers for Disease Control and Prevention (CDC) the federal agency under the U.S. Department of Health and Human Services whose main purpose is to protect public health and safety through the control and prevention of disease, injury, and disability in the United States and internationally. (Chapter 4)

Centers for Medicare and Medicaid Services (CMS) a federal agency within the US Department of Health and Human Services that administers the Medicare program and works in partnership with state governments to administer Medicaid. (Chapters 2 and 57)

central cyanosis abnormal discoloration of the skin distributed in central structures like the nose and lips. (Chapter 16)

central line–associated bloodstream infection a serious infection that occurs when microns enter the bloodstream through the central line. (Chapter 7)

central neurogenic hyperventilation breathing characterized by persistent hyperventilation driven by abnormal neural stimuli. (Chapter 16)

central neurogenic hypoventilation condition in which the respiratory centers do not respond appropriately to ventilatory stimuli, such as CO_2. It also is associated with head trauma and brain hypoxia as well as narcotic suppression of the respiratory center.

central sleep apnea absence of breathing as the result of medullary depression that inhibits respiratory movement, which becomes more pronounced during sleep. (Chapter 34)

central venous pressure (CVP) right atrial pressure. (Chapter 10)

cephalization increased visualization of pulmonary blood vessels on a chest radiograph in the nondependent regions of the lung; often a sign of left heart failure. (Chapter 21)

channel a passageway or groove that conveys fluid, such as the central channels that connect the arterioles with the venules. (Chapter 3)

Charles law a law stating that with pressure constant, the volume of a gas is directly proportional to its temperature. (Chapter 6)

chemoreceptor a sensory nerve cell activated by changes in the chemical environment surrounding it; the chemoreceptors in the carotid artery are sensitive to PCO_2 in the blood, signaling the respiratory center in the brain to increase or decrease ventilation. (Chapters 10 and 15)

chemotherapy treatment of infections and other diseases with chemical agents. (Chapter 32)

chest cuirass a device that fits over the thorax that is designed to deliver negative-pressure ventilation. (Chapter 50)

chest physical therapy (CPT) a group of therapeutic techniques designed to aid in the clearance of secretions, improve ventilation, and enhance the conditioning of the respiratory muscles; includes positioning techniques, chest percussion and vibration, directed coughing, and various breathing and conditioning exercises. (Chapter 44)

chest radiograph an x-ray image of the chest; a posteroanterior view and a lateral, or side, view are routinely obtained. (Chapter 21)

chest tube a tube inserted to monitor the rate of bleeding and determine whether the source is arterial or venous. (Chapter 27)

chest x-ray an image produced by passing x-rays through the chest to a photographic film or detector. (Chapter 21)

Cheyne-Stokes respiration an abnormal breathing pattern with periods of progressively deeper breaths alternating with periods of shallow breathing and apnea. (Chapter 16)

CHF abbreviation for *congestive heart failure;* an abnormal condition that reflects impaired cardiac output caused by myocardial infarction, ischemic heart disease, or cardiomyopathy. (Chapters 10 and 29)

chlorofluorocarbons (CFCs) gaseous chemical compounds that were originally used to power metered-dose inhalers; they are now no longer used. (Chapter 40)

cholinergic of or pertaining to nerve fibers that elaborate acetylcholine at the myoneural junctions. (Chapter 36)

chordae tendineae cordis are fibrous cords of connective tissue that connect the papillary muscles to the tricuspid valve and the bicuspid valve in the heart. (Chapter 10)

chorionic villi vascular projections arise from the chorion of the embryo and penetrate the uterine endometrium. (Chapter 9)

chronic bronchitis a common debilitating pulmonary disease characterized by a greatly increased production of mucus by the glands of the trachea and bronchi that results in a cough with expectoration for at least 3 months of the year for more than 2 consecutive years. (Chapter 25)

chronic care medical care which addresses pre-existing or long-term illness. (Chapter 55)

chronic cough a cough that lasts approximately eight weeks or longer in adults, or four weeks in children. (Chapter 16)

chyle a cloudy liquid product of digestion taken up by the small intestine. Consisting mainly of emulsified fats, chyle passes through finger-like projections in the small intestine, called *lacteals,* and into the lymphatic system for transport to the venous circulation at the thoracic duct in the neck. (Chapter 27)

chylothorax pleural fluid collection that is high in triglycerides, usually from disruption of the thoracic duct. (Chapter 27)

cilia tiny hair-like projections that line mucus-producing structures. Generally they operate in a wave-like motion to move mucus along the structure. (Chapter 9)

ciliary dyskinetic syndromes conditions in which respiratory tract cilia do not function properly. (Chapter 40)

Clara cells nonciliated cuboidal cells with apical granules. (Chapter 9)

clinical decision support (CDS) health information technology that builds on the foundation of an electronic health record to provide specific information, intelligently filtered and organized, at appropriate times to enhance health and healthcare. (Chapter 7)

clinical simulation the simulation of an actual clinical scenario using actors, manikins, and paper and pencil. (Chapter 7)

clinical staff first-line providers of respiratory care but also responders to rapid response alerts, codes, and disaster/fire emergencies. (Chapter 2)

closed buffer system a buffer system in which all components of acid-base reactions remain in the system. Products accumulate and reach equilibrium with reactants, and chemical activity ceases (no further buffering activity can take place). Closed buffer systems in the body include nonbicarbonate buffers, such as those involving plasma proteins, hemoglobin, and phosphates. (Chapter 14)

closed-loop ventilation limited, proprietary, computerized closed-loop weaning software packages that automate weaning according to set physiologic parameters. (Chapter 7)

clubbing bulbous swelling of the terminal phalanges of the fingers and toes, often associated with certain chronic lung diseases. (Chapter 16)

Coanda effect a phenomenon in hydrodynamics whereby a fluid in motion may be attracted or held to a wall. (Chapter 6)

CoBGRTE group a nationally based organization that supports the advancement of Respiratory Care education at the bachelor's and graduate degree level. (Chapter 2)

cognitive domain level of the mind comprising the processes of comprehension, judgment, memory, and reasoning. (Chapter 55)

cohesion attractive force between like molecules. (Chapter 6)

cohorting the grouping of individuals who share a common characteristic, such as the same age or sex or a common infection. (Chapter 4)

coinvestigators individuals who have a range of roles spanning screening/entering subjects into the study (including obtaining informed consent, if applicable), collecting and analyzing data, and finally assisting with writing the abstract and manuscript for publication. (Chapter 8)

cold shock cardiorespiratory reflexes reflexes activated by water temperatures below 25°C. A breathing pattern characterized by gasping followed by hyperventilation and shallow breathing at total lung capacity. (Chapter 30)

collateral circulation redundant circulation in an area of tissue or an organ that supplies blood to the tissue by more than one path. (Chapter 19)

colloids substances containing large molecules that attract and hold water; also a dispersion or gel. (Chapter 13)

Committee on Accreditation for Respiratory Care (CoARC) the committee that establishes standards and oversees approval of educational programs in respiratory care. (Chapter 1)

competencies measurable or observable skills, knowledge, behaviors, or abilities to perform a job or task. (Chapter 3)

community-acquired pneumonia an acute inflammation of the lungs contracted from the environment (as distinguished from nosocomial, or hospital-acquired, pneumonia). (Chapter 24)

compensatory justice calls for the recovery of damages resulting from the harmful action of others. (Chapter 5)

complete blood count a determination of the number of red and white blood cells per cubic millimeter of blood. A complete blood count is one of the most routinely performed tests in a clinical laboratory and one of the most valuable screening and diagnostic techniques. (Chapter 17)

compliance the volume change per unit of applied pressure. (Chapters 11 and 20)

Comprehensive Outpatient Rehabilitation Facility (CORF) a Medicare-approved facility that provides a broad scope of ambulatory rehabilitation services as defined in section 933 of Public Law 96-499. (Chapter 55)

compression atelectasis collapse of a part of the lung as a result of an external force compressing the lung. (Chapter 43)

computed tomography (CT) radiographic technique that produces a film that represents a detailed cross section of tissue structure. (Chapters 21 and 32)

computerized physician order entry (CPOE) a system by which medical orders can be electronically transmitted to the electronic health record saving time and reducing transcription errors resulting from illegible handwriting. (Chapter 7)

condensation change of state from gas to liquid, as with the condensation of water vapor. (Chapter 6)

conditions of coverage/participation a certificate awarded to institutions that meet specific standards of quality and safety as determined by the Centers for Medicare and Medicaid Services. (Chapter 57)

conduction transfer of heat by the direct interaction of atoms or molecules in a hot area that contact atoms or molecules in a cooler area. (Chapter 6)

confidentiality nondisclosure of certain information except to another authorized person. (Chapter 5)

congestive heart failure (CHF) an abnormal condition that reflects impaired cardiac pumping; caused by myocardial infarction, ischemic heart disease, or cardiomyopathy that results in either pulmonary or systemic edema. (Chapters 10 and 29)

conjugate base the base associated with the weak acid in a buffer system. (Chapter 14)

connective tissue disease a group of acquired disorders that have in common diffuse immunologic and inflammatory changes in small blood vessels and connective tissue. The causes of most of these diseases are unknown. Also called *collagen vascular disease*. (Chapter 26)

consequentialism the idea of judging an act to be right; an ethical viewpoint in which decisions are based on the assessment of consequences. (Chapter 5)

conservative fluid management a strategy of administering fluids that attempt to minimize fluid excess over output. (Chapter 29)

consultant a person who may give advice before, during, or after a study. (Chapter 8)

contact precautions safeguards designed to reduce the risk for transmission of epidemiologically important microorganisms by direct or indirect contact. (Chapter 4)

continuing respiratory care education education sought by respiratory therapists after graduation. (Chapter 7)

continuous mandatory ventilation (CMV) a system of mechanical ventilation in which the patient is allowed to initiate breathing but the ventilator delivers a set volume or pressure with each breath. The ventilator can also be programmed to initiate breathing if the patient's breathing slows beyond a certain point or stops entirely. (Chapter 46)

continuous positive airway pressure (CPAP) a method of ventilatory support whereby the patient breathes spontaneously without mechanical assistance against threshold resistance, with pressure above atmospheric maintained at the airway throughout breathing. (Chapters 34, 43, 50, 53, and 54)

continuous quality improvement (CQI) a process-based, data-driven approach that attempts to enhance the quality of care and patient safety. (Chapter 7)

continuous spontaneous ventilation (CSV) a method of delivering ventilatory support in which the patient determines when a breath is initiated and when it is terminated. (Chapter 46)

contractility the property of muscle tissue to shorten in response to a stimulus, usually electrical. (Chapters 10 and 52)

control system the system used to determine how a mechanical ventilator delivers gas (e.g., targeting schemes). (Chapter 46)

controlled ventilation the use of an intermittent positive-pressure breathing unit or other respirator that has an automatic cycling device that replaces spontaneous respiration. (Chapter 48)

convection heat transfer through the mixing of fluid molecules at different temperature states via thermal currents. (Chapter 6)

convection currents Fluid movements carrying heat energy. (Chapter 6)

coronary artery diseases (CAD) a condition in which the arteries that supply blood to heart muscle become hardened and narrowed. (Chapter 10)

coronary circulation the heart's circulatory system. (Chapter 10)

coronary sinus a large vessel wherein veins gather together which passes left to right across the posterior surface of the heart. (Chapter 10)

corticosteroid any one of the natural or synthetic hormones associated with the adrenal cortex that influence or control key processes of the body, such as carbohydrate and protein metabolism, electrolyte and water balance, and function of the cardiovascular system and kidneys. (Chapter 26)

costal cartilage fibrous tissues that connect the ribs to the sternum and to each other anteriorly. (Chapter 9)

costal groove a channel containing the thoracic artery, vein, and nerve and supplying blood flow and innervation to that region of the chest wall. (Chapter 9)

costophrenic angle an acute angle where the costal pleura meets the diaphragm. (Chapter 9)

cough a forceful expiratory effort designed to expel mucus and other foreign material from the upper airway. (Chapter 16)

crackles a discontinuous type of adventitious lung sound. (Chapter 16)

creatine phosphate a molecule that serves as a rapidly mobilizable reserve of high-energy phosphates in skeletal muscle and the brain to recycle adenosine triphosphate, the energy currency of the cell. (Chapter 23)

creatine phosphokinase (CPK) an enzyme found in your heart, brain, and skeletal muscles which leaks into the blood when muscle tissue is damaged. (Chapter 17)

creatinine a chemical waste product that's produced by your muscle metabolism and which is filtered by the kidneys. High levels are suggestive of kidney insufficiency or failure. (Chapter 23)

creatinine-height index (CHI) a method of estimating the amount of skeletal muscle mass. (Chapter 23)

credentialing the process of obtaining a recognized designation from the National Board of Respiratory Care (NBRC) which permits individuals obtaining it to apply for licensure and practice respiratory care and/or be recognized for expertise in a clinical specialty. (Chapter 2)

credentials the recognized designations from the National Board of Respiratory Care (NBRC) which permits individuals to apply for licensure and practice respiratory care and/or be recognized for expertise in a specialty area. (Chapter 2)

cricoid cartilage a ring of cartilage forming the lower border of the larynx. (Chapter 9)

critical temperature the highest temperature at which a substance can exist as a liquid, regardless of pressure. (Chapter 6)

critical test value a test result that requires its immediate communication to a physician. (Chapter 17)

croup an infectious disorder of the upper airway occurring chiefly in infants and children; it normally results in subglottic swelling and obstruction. (Chapters 41 and 42)

cryogenic related to a very low temperature. (Chapter 41)

cryotherapy treatment using the application of cold temperatures, as for airway lesions during bronchoscopy. (Chapter 22)

culture behaviors, values, and patterns of beliefs shared by a group. (Chapter 55)

current a flowing or streaming movement; a flow of electrons along a conductor in a closed circuit; an electrical current. (Chapter 3)

cuvette a small transparent tube or container with specific optical properties. The chemical composition of the container determines the vessel's use, such as Pyrex glass for examining materials in the visible spectrum or silica for examining materials in the ultraviolet range. (Chapter 19)

cyanide toxicity a result of the inhalation of gas produced by the burning of nitrogenous material. Cyanide combines with cytochrome oxide, the last receptor of the electron transport chain, which prevents the utilization of O_2. (Chapter 30)

cyanosis a bluish discoloration, especially of the skin and mucous membranes, due to excessive concentration of deoxyhemoglobin in the blood caused by deoxygenation. (Chapter 16)

cyanocobalamin chemical that reduces the half-life of the toxic compound that results from the reaction of cyanide with cytochrome oxide. (Chapter 30)

cycle asynchrony a lack of coordination of the ending of a patient's inspiration with the ending of the ventilator inspiration. (Chapter 48)

cystic fibrosis an autosomal recessive disease characterized by pancreatic insufficiency, abnormally thick secretions from the exocrine glands, and increased concentration of sodium and chloride in the sweat glands; known in Europe as *mucoviscidosis*. (Chapters 25 and 35)

cytochrome oxidase an oxidizing enzyme that contains iron and a porphyrin and is found in the mitochondrial membrane. (Chapter 30)

D

Dalton's law in physics, law stating that the total pressure exerted by a mixture of gases is equal to the sum of the pressures exerted by the individual gases if they were present alone in the container. (Chapter 6)

D-dimer small protein fragment found in the blood when fibrin clots are dissolving. (Chapter 17)

dead space respired gas volume that does not participate in gas exchange; may be anatomic, alveolar, or mechanical. (Chapter 12)

dead space/tidal volume ratio (V_D/V_T) percentage of tidal volume that does not participate in gas exchange, usually approximately 30% to 35%. (Chapter 52)

decannulation removal of a cannula or tube that may have been inserted during a therapeutic or surgical procedure. (Chapters 37 and 51)

decremental positive end-expiratory pressure (PEEP) trial progressively decreasing the amount of PEEP to assess oxygenation and hemodynamic status immediately following a recruitment maneuver. (Chapter 30)

deep breathing/directed cough movements used to improve pulmonary gas exchange or to maintain respiratory function, especially after prolonged inactivity or general anesthesia. (Chapter 43)

deep venous thrombosis (DVT) a blood clot that forms in the deep veins, usually of the legs. (Chapter 28)

defendant a person denying the party against whom relief or recovery is sought in an action or suit; also, the accused in a criminal case. (Chapter 5)

defibrillation termination of ventricular fibrillation by delivering a direct electrical countershock to the patient's precordium. (Chapter 38)

density mass per unit volume. (Chapter 6)

departmental director in respiratory therapy, this must be a highly skilled respiratory therapist; an energetic, forward-thinking, innovative individual who has as his or her primary goal high-quality patient care and the continued development of the department and the profession of respiratory care. (Chapter 2)

depolarization reduction of a membrane potential to a less negative value; in cardiac fibers, this results in the release of calcium ions into the myofibrils and activates the contractile process. (Chapter 18)

deposition testimony of a witness taken on interrogatories, either oral or in writing. (Chapter 40)

dermatomyositis a condition characterized by inflammation of the muscles and/or skin. (Chapter 33)

dewpoint temperature at which water vapor condenses back to its liquid form. (Chapter 6)

diagnosis the process of identifying the underlying cause for signs and symptoms, as in naming a patient's disease. (Chapter 16)

diameter-indexed safety system (DISS) specifications established to prevent accidental interchange of low-pressure (<200 psig) medical gas connectors. DISS is used in respiratory care to connect equipment to a low-pressure gas source. (Chapter 41)

diaphoresis secretion of sweat, especially profuse secretion associated with an elevated body temperature, physical exertion, exposure to heat, and mental or emotional stress. (Chapter 16)

diaphragm a large dome-shaped muscle that separates the thorax from the abdomen; the primary muscle of ventilation. (Chapter 9)

diaphragm dysfunction inability of the diaphragm to contract normally. (Chapter 48)

diaphragm electrical activity (EAdi) a minimally invasive bedside technology to detect diaphragmatic activity to facilitate the neurally adjusted ventilatory assist (NAVA) mode of mechanical ventilation. (Chapter 53)

diaphragm ultrasound a relatively new and promising method of evaluating and monitoring the function of the diaphragm. (Chapter 52)

diastolic pressure baseline blood pressure in the arteries during ventricular relaxation. (Chapter 16)

dicrotic notch a phenomenon caused by the elastic recoil of the arteries. (Chapter 16)

diet-induced thermogenesis the increase in energy expenditure above basal fasting level divided by the energy content of the food ingested and which is commonly expressed as a percentage. (Chapter 23)

differential diagnosis distinguishing among several diseases which share the similar signs and symptoms. (Chapter 16)

diffusing capacity of the lung (DL) the number of milliliters of gas that transfer from the lungs to the pulmonary blood per minute for each 1 mm Hg partial pressure difference between the alveoli and pulmonary capillary blood. (Chapter 20)

diffusing capacity of the lung to alveolar volume ratio ($DLCO/V_A$) index of the diffusing capacity for each 1 L of lung volume and an index of the functional alveolar surface area available for diffusion. (Chapter 20)

diffusing capacity of the lung-to–effective total lung capacity ratio index of the diffusing capacity normalized to the total lung capacity, useful to distinguish between interstitial lung disease and extrathoracic causes of restriction. (Chapter 20)

diffusion the process whereby molecules move from areas of high concentration to areas of lower concentration. (Chapter 6)

diluent a substance, generally a fluid, that makes a solution or mixture less concentrated, less viscous, or more liquid. (Chapter 13)

dilute solution a solution that contains a small amount of solute in relation to solvent. (Chapter 13)

dilution equation an equation used to determine the final concentration of a solution in which the original volume multiplied by the original concentration are equal to the final volume multiplied by the final concentration. (Chapter 13)

disease management an integrated process for the care of patients with a particular chronic disease. Generally, a multidisciplinary group of practitioners, most of whom are nonphysicians, provides this care. (Chapters 3 and 55)

disinfection the process of destroying at least the vegetative phase of pathogenic microorganisms by physical or chemical means. (Chapter 4)

distributive justice the just and proper allotment of the benefits and burdens in a society, such as taxes and subsidies. (Chapter 5)

Donnan effect of increasing osmotic pressure within the capillary. (Chapter 13)

dorsal respiratory groups (DRGs) groupings of cells in the medulla oblongata that are active in controlling inspiration. (Chapter 15)

double effect the idea that many good actions have both good and bad effects. (Chapter 5)

double triggering the activation of a second ventilator-delivered breath without exhalation after the first breath. This normally occurs when tidal volume is too small and inspiratory time is too short. (Chapter 48)

downstream reference to a point more distal from the source in a stream of flowing fluid. (Chapter 41)

driving pressure the pressure driving a fluid from one point to another. During mechanical ventilation, this is the difference between plateau pressure and positive end-expiratory pressure. (Chapters 29, 46, 47, and 52)

droplet nuclei residue of evaporated water droplets; owing to their small size (0.5 to 12 mm), droplet nuclei can remain suspended in the air for long periods. (Chapter 4)

droplet precautions safeguards designed to reduce the risk for the droplet transmission of infectious agents. (Chapter 4)

drug signaling the mechanism by which a drug exerts its effect on receptors. (Chapter 36)

dry drowning drowning that occurs without water entry into the lungs as a result of reflex laryngeal spasm. (Chapter 30)

dual targeting scheme a classification of ventilatory modes that allows the ventilator to switch between volume control and pressure control during each breath cycle. (Chapter 46)

Duchenne muscular dystrophy (DMD) an abnormal congenital condition characterized by progressive symmetric wasting of the leg and pelvic muscles; it predominantly affects males and accounts for 50% of all muscular dystrophy diseases. (Chapter 33)

ductus arteriosus a vascular channel in the fetus that joins the pulmonary artery directly to the descending aorta; it normally closes after birth. (Chapters 9 and 35)

ductus venosus a vascular channel in the fetus passing through the liver and joining the umbilical vein with the inferior vena cava; before birth, it carries highly oxygenated blood from the placenta to the fetal circulation. (Chapter 9)

durable medical equipment (DME) supplier a company that provides medical equipment to patients in the home. (Chapter 57)

durable medical equipment, prosthetics, orthotics, and supplies (DMEPOS) the collection of medical devices bundled together and designated to satisfy quality standards by the Centers for Medicare and Medicaid Services. (Chapter 57)

dynamic compression collapse of airways caused by a pressure gradient that occurs normally in diseased airways with breathing or forced breathing. (Chapter 11)

dynamic hyperinflation an increase in functional residual capacity above the elastic equilibrium volume of the respiratory system; causes include increased flow resistance, short inspiratory time, and increased postinspiratory muscle activity; see also *auto-PEEP*. (Chapters 11 and 45)

dysoxia abnormal metabolic state in which the tissues are unable to properly use the O_2 made available to them. (Chapter 12)

dyspnea difficult or labored breathing as perceived by the patient. (Chapter 16)

dysrhythmias abnormal heart rhythms. (Chapter 18)

E

ECLS extracorporeal lung support, the same process as extracorporeal membrane oxygenation. (Chapter 29)

ECMO extracorporeal membrane oxygenation is the process whereby blood is removed from the body, pumped through a membrane to exchange CO_2 for O_2, and then returned to the body. (Chapter 29)

ectopic beat impulse that originates in the heart at a site other than the sinus node. (Chapter 18)

ectopic foci origination of a heartbeat from some place in the heart other than the sinoatrial node. (Chapter 18)

educational coordinator a person tasked with individually assessing the educational needs of the respiratory therapists within the department and assigning resources to help reduce educational deficiencies. (Chapter 2)

effective total lung capacity single-breath technique distributes a gas mixture through unobstructed airways to an alveolar volume. (Chapter 20)

egophony physical examination finding of increased resonance of voice sounds when auscultating the chest (e.g., due to lung consolidation). (Chapter 43)

ejection fraction the percentage of blood that is pumped (or ejected) from the ventricles of the heart with each contraction, often separated into the right (ventricular) and left (ventricular) ejection fractions. (Chapter 10)

elastance the tendency of matter to resist a stretching force and recoil or return to its original size or form after deformation or expansion; the reciprocal of compliance. Also called *elasticity*. (Chapters 11 and 46)

elasticity ability of tissue to regain its original shape and size after being stretched, squeezed, or otherwise deformed. Muscle tissue is generally regarded as elastic because it is able to change size and shape and return to its original condition. (Chapter 11)

electrical impedance tomography (EIT) the process by which mapping of the lung is obtained by a series of electrodes placed around the chest that sequentially emit low level current. The variability among the impedance to the current between electrodes is used to map lung volume. (Chapter 52)

electrocardiogram (ECG) an important diagnostic tool used to measure the electrical activity of the heart. (Chapter 18)

electrochemical refers to processes where electrical changes drive chemical processes. (Chapter 19)

electrolyte solution a solution in which this dissociation occurs. (Chapter 13)

electromagnetic navigational bronchoscopy a bronchioscopic technique that facilitates accurate navigation to sample peripheral pulmonary target lesions. (Chapter 22)

electronic health record (EHR) the sum of all medical records produced for a patient during the different encounters with various healthcare entities throughout his or her lifetime and which are available across the continuum of care in all geographic locations. These data are stored in an electronic system. (Chapter 7)

electronic medical record (EMR) a system whereby the medical record is stored in a computer (rather than on paper records). (Chapter 7)

embryonic period the first 8 weeks of pregnancy. (Chapter 9)

E-medicine the use of computerized or digital technology to enhance efficiency and effectiveness of healthcare in general and more specifically patient care. (Chapter 7)

emitted dose the mass of drug leaving the mouthpiece of a nebulizer or inhaler as aerosol. (Chapter 40)

emphysema a destructive process of the lung parenchyma leading to permanent enlargement of the distal air spaces; classified as either centrilobular (CLE), which mainly involves the respiratory bronchioles, or panlobular (PLE), which can involve the entire terminal respiratory unit. (Chapter 25)

empyema pus within the pleural space. A Gram stain of the pleural fluid will show bacteria. (Chapters 21, 27)

end-diastolic volume (EDV) the volume of blood remaining in the ventricles just prior to contraction. (Chapter 10)

endobronchial biopsy sampling of an abnormality seen within the bronchus on bronchoscopy. (Chapter 22)

endobronchial intubation the purposeful or accidental placement of an endotracheal tube into a main stem bronchus, usually the right main stem bronchus. (Chapter 48)

endotracheal tubes artificial airways that pass through the oropharynx or nasopharynx into the trachea. (Chapter 37)

end-systolic volume (ESV) the volume of blood in the ventricles at the end of contraction, or systole. (Chapter 10)

enterprise software packages computer software used by a whole health system. (Chapter 7)

epicardium tissue that covers the outer surface of the heart and great vessels. (Chapter 10)

epiglottis flat cartilage that extends from the base of the tongue backward and upward. (Chapter 9)

epiglottitis acute, often life-threatening infection of the upper airway, which leads to severe obstruction secondary to supraglottic swelling; caused primarily by *Haemophilus influenzae* type B and affecting mainly children under 5 years of age. (Chapter 35)

epistaxis to bleed from the nose. (Chapter 9)

equal pressure point (EPP) during forced exhalation, the point along an airway where the pressure inside its wall equals the intrapleural pressure; upstream beyond this point, the pleural pressure exceeds the pressure inside the airway, tending to promote bronchiolar collapse. (Chapter 11)

equilibrium constant a constant determined by the amount of a buffer that dissociates in solution. It identifies the pH at which the buffer is most effective. (Chapter 14)

equivalent weight weight of an element in any given unit (e.g., grams) that displaces a unit weight of hydrogen from a compound or combines with or replaces a unit weight of hydrogen. (Chapter 13)

erythema reddish discoloration of a tissue, usually referring to the skin and one of the features of inflammation. (Chapter 50)

erythrocytes red blood cells. (Chapter 17)

esophageal balloon a catheter with an elongated balloon placed in the esophagus used to measure pressure change that is reflective of pleural pressure change. (Chapter 52)

esophageal pressure pressure measured inside the esophagus, often with a catheter. (Chapter 53) –

essential nutrients nutrients required for normal body functioning that cannot be synthesized by the body. (Chapter 23)

ethics consultation consultation with a group often consisting of ethicists and others regarding difficult management decisions, frequently regarding end-of-life issues. (Chapter 58) consultation with a group often consisting of ethicists and others regarding difficult management decisions, frequently regarding end-of-life issues

eustachian tubes bilateral tubes that connect the nasopharynx to the middle ear and mastoid sinus. (Chapter 9)

euthanasia the act of putting to death a person (or animal) suffering from a painful or prolonged illness or injury. Someone other than the patient commits the action to end the patient's life, usually by the injection of medicine. (Chapter 58)

evaporation change in state of a substance from a liquid to a gaseous form occurring below its boiling point. (Chapter 6)

evidence-based medicine an approach to medical practice intended to optimize decision making by emphasizing the use of evidence from well-designed research projects. (Chapter 8)

excessive daytime sleepiness sleepiness during the day to an abnormal extent, sometimes associated with narcolepsy. (Chapter 34)

excitability the ability of cells to respond to electrical, chemical, or mechanical stimulation. (Chapter 10)

expiratory cycling criteria the criteria employed by the ventilator to transition from inspiration to exhalation. In pressure support ventilation, this is usually flow. (Chapter 48)

expiratory positive airway pressure (EPAP) the application of positive pressure to the airway during exhalation. Compare with *inspiratory positive airway pressure*. (Chapter 50)

expiratory reserve volume the total amount of gas that can be exhaled from the lung after a quiet exhalation. (Chapter 20)

external nares the external openings of the nasal passages. (Chapter 9)

external respiration the part of the respiratory process that involves the exchange of gases in the alveoli of the lungs. (Chapter 9)

extracellular outside of the cell. (Chapter 13)

extracorporeal carbon dioxide removal ($ECCO_2R$) the procedure whereby blood is passed from the patient through an external membrane, which filters CO_2 to support ventilation. (Chapter 29, 51)

extracorporeal life support (ECLS) several forms of mechanical support, all of which involve circulating blood from a patient to outside the body through a mechanical gas exchanger and returning it back to the patient. (Chapter 51)

extracorporeal membrane oxygenation (ECMO) the procedure whereby venous blood is pumped outside the body to a heart-lung machine for oxygenation and returned to the body. (Chapters 29 and 51)

extrapolated volume The volume exhaled before the zero time point. (Chapter 20)

extremely low birth weight (ELBW) describes a neonate weighing less than 1 kg at birth. (Chapter 54)

extubation the process of withdrawing a tube from an orifice or cavity of the body. (Chapter 37)

exudate fluid oozing from cells and tissues. (Chapter 30)

exudative relating to the oozing of fluid and other materials from cells and tissues, usually as a result of inflammation or injury. (Chapter 42)

exudative pleural effusion any pleural effusion high in protein or lactate dehydrogenase, which implies inflammation or vascular injury on the pleural surface. (Chapter 27)

F

factitious events values that are real but "out of range" and often temporary, such as the elevation in airway pressure during a cough. (Chapter 52)

false ribs of the 12 pairs of ribs forming a large part of the thoracic skeleton, the first 7 are called *true ribs* and the next 5 are called *false ribs;* the first 3 attach to the ribs above and the last 2 are free. (Chapter 9)

fasciotomy a surgical procedure that cuts away the fascia to relieve tension or pressure. Used to treat burn patients with severe scar formation. (Chapter 30)

fatigue the inability of a muscle to carry its normal load. (Chapter 48)

febrile describing a person who has a fever. (Chapter 16)

feedback in communication theory, information produced by a receiver and perceived by a sender that informs the sender of the receiver's reaction to the message. Feedback is a cyclic part of the process of communication that regulates and modifies the content of messages. (Chapter 3)

Fellow of the American Association for Respiratory Care (FAARC) a person who has been recognized for the AARC for sustained and substantial contributions to the field of respiratory care. (Chapter 1)

fenestrated an opening into a structure; from the Latin *fenestra,* meaning "window." (Chapter 37)

fetal hemoglobin (HbF) hemoglobin variant that has a greater affinity for O_2 than adult hemoglobin; HbF is gradually replaced over the first year of life by HbA. (Chapter 12)

fetal lung fluid a unique combination of plasma ultrafiltrate from the fetal pulmonary microcirculation, components of pulmonary surfactant, and other fluids from pulmonary epithelial cells and the developing fetus. (Chapter 9)

fetal period the remaining 32 weeks of pregnancy. (Chapter 9)

fetid foul smelling. (Chapter 16)

fever abnormal elevation of body temperature owing to disease. (Chapter 16)

fiberoptic bundles individual coated fibers (or fibers formed into ribbons or bundles) that have a tough resin buffer layer; they are used to transmit light from a light source to view the airways through a bronchoscope. (Chapter 22)

fibrous pericardium a tough, loose-fitting, inelastic sac surrounding the heart. (Chapter 10)

Fick equation an equation for computing cardiac output based on knowledge of O_2 consumption and the arteriovenous O_2 content difference. (Chapters 12 and 52)

Fick's first law of diffusion law for determining the rate of gaseous diffusion across biologic membranes. (Chapter 12)

filling density ratio between the weight of liquid gas put into a cylinder and the weight of water the cylinder could contain if full. (Chapter 41)

fine-particle fraction particles that are small enough to reach the lower respiratory tract. (Chapter 40)

fissures narrow clefts or slits; the lines that divide or separate the lobes of the lung glottis. (Chapter 9)

fixed (nonvolatile) acid titratable, nonvolatile acid representing the by-product of protein catabolism; examples include phosphoric acid and sulfuric acid. (Chapter 14)

flammable the ability of a substance to burn or ignite, causing fire or combustion. (Chapter 41)

flexible bronchoscopy a bronchoscopy that is flexible in structure, allowing it to be placed deep into the respiratory tract. (Chapter 32)

floating ribs last two rib pairs that are free at their ventral extremities. (Chapter 9)

flow asynchrony asynchrony as a result of the ventilator not providing sufficient flow to meet the patient's inspiratory demand. Most commonly occurs in volume ventilation. (Chapter 47)

flowmeter device operated by a needle valve that controls and measures gas flow according to the principles of viscosity and density. (Chapter 41)
flow resistance the difference in pressure between the two points along a tube, divided by the actual flow. (Chapter 6)
fluvial or brackishwater sea water used in reference to drowning. (Chapter 30)
fomites nonliving material, such as bed linens or equipment, which may transmit pathogenic organisms to a person who comes into contact with the object. (Chapters 4 and 24)
foramen ovale opening in the septum between the right and the left atria in the fetal heart. This opening provides a bypass for blood that would otherwise flow to the fetal lungs. After birth, the foramen ovale closes. (Chapters 9 and 10)
forced expiratory technique (FET) modification of the normal cough sequence designed to facilitate clearance of bronchial secretions while minimizing the likelihood of bronchiolar collapse. (Chapter 44)
forced expiratory volume in 1 second (FEV_1) the maximum volume of gas that the patient can exhale during the first second of the forced vital capacity maneuver. (Chapter 20)
forced expiratory volume in 1 second–to–vital capacity ratio (FEV_1/FVC) the percent of the measured forced vital capacity that can be exhaled in 1 second. (Chapter 20)
forced expiratory volume in 1/2 second ($FEV_{0.5}$) the maximum volume of gas that the patient can exhale during the first half-second of a forced vital capacity maneuver. (Chapter 20)
forced vital capacity (FVC) the maximum volume of gas that the subject can exhale as forcefully and as quickly as possible. (Chapter 20)
formalism ethical viewpoint that relies on rules and principles. (Chapter 5)
fractional distillation the process of separating the components of a liquid mixture according to their boiling points via the application of heat; the primary commercial process used to produce O_2. (Chapter 41)
Frank-Starling principle rule stating that the more a muscle fiber is stretched, the greater the tension the fiber generates when contracted. (Chapter 10)
frequency/tidal volume ratio (f/V_T) ratio of the tidal volume in milliliters divided by the respiratory rate. (Chapter 52)
full ventilatory support ventilatory support modes in which the ventilator provides all of the patient's minute ventilation requirements. (Chapter 49)
functional residual capacity (FRC) the total amount of gas left in the lungs after a resting expiration. (Chapter 20)

G

gallop rhythm an abnormal heart sound that resembles the gallop of a horse; it most often indicates heart failure. (Chapter 16)
gas absorption atelectasis collapse of airways due to hyperoxygenation and nitrogen washout. (Chapter 43)
gaseous diffusion the process whereby gas molecules move from an area of high partial pressure to an area of low partial pressure. (Chapter 12)
gastric inflation the introduction of air into the stomach and intestines. (Chapter 38)
gastroesophageal reflux disease (GERD) a condition characterized by the abnormal movement of stomach contents into the esophagus or mouth; acid from the stomach may be aspirated into the lung and cause asthma-like symptoms. (Chapter 35)
geometric standard deviation (GSD) describes the variability of particle size in an aerosol distribution set at 1 standard deviation above and below the median. (Chapter 40)
gladiolus the body of the sternum. (Chapter 9)
Glasgow Coma Scale (GCS) scale used to score the level of conscious awareness in patients suspected of having an acute brain injury. (Chapters 30 and 52)
glomerular filtration rate the volume of water filtered out of the plasma through glomerular capillary walls into Bowman's capsule in the kidney per unit of time. (Chapter 30)
glottis the variable opening between the vocal cords. (Chapter 9)
gluconeogenesis the process of converting liver glycogen stores into glucose. (Chapter 23)
glucose a simple sugar which is an important energy source in living organisms and is a component of many carbohydrates. (Chapter 17)
goals of care an organizing framework for a seriously ill patient's overall care. (Chapter 58)
Graham's law law stating that the rate of diffusion of a gas through a liquid (or the alveolar-capillary membrane) is directly proportional to its solubility coefficient and inversely proportional to the square root of its density. (Chapter 6)
ground the connection between the electrical circuit and the ground, which becomes a part of the circuit. (Chapter 3)
grunting an expiratory sound caused by the sudden closure of the glottis during exhalation to maintain functional residual capacity and prevent alveolar atelectasis. (Chapter 9)
grunting, flaring, and retracting (GFR) the respiratory pattern observed in infants in marked respiratory distress. The neonate makes a grunting sound during breathing with flaring of the nostrils. (Chapter 54)
Guillain-Barré syndrome idiopathic, peripheral polyneuritis characterized by lower extremity weakness that progresses to the upper extremities and face; may lead to flaccid paraplegia and marked respiratory muscle weakness. (Chapter 33)

H

Haldane effect influence of hemoglobin saturation with O_2 on CO_2 dissociation. (Chapter 12)
Hamburger phenomenon the shifting of Cl ions out of the red blood cell as HCO ion is formed in the cell by hydrolysis (combination of CO_2 with H_2O). (Chapter 12)
hard palate the anterior roof of the oral cavity. (Chapter 9)
Harris-Benedict equation equation used to estimate the caloric expenditure in normal individuals under conditions of minimal activity. (Chapter 52)
healthcare agent and durable power of attorney for healthcare a named individual who has been given authority by another person to make decisions regarding her/his healthcare when the individual is not competent to make those decisions. (Chapter 58)
healthcare-associated infection (HAI) an infection that develops from a hospital or other healthcare environment. (Chapter 4)
health education the process of planned learning opportunities designed to enable individuals to make informed decisions about and act to promote their own health. (Chapter 55)
health informatics the systematic application of information and computer science and technology to clinical or public health practice. (Chapter 7)
Health Information Technology for Economic and Clinical Health Act (HITECH Act) part of a national strategy for building a national health information infrastructure that, among other things, began providing incentives to hospitals, physicians, and other health service providers who demonstrate that they are meaningfully using their electronic health records by meeting predefined standards. (Chapter 7)
health literacy the degree to which individuals can obtain, process, and understand basic health information to make appropriate health decisions and recommendations. (Chapter 55)
health promotion the combination of educational, organizational, economic, and environmental support necessary for behavior conducive to health; includes both disease prevention and wellness activities. (Chapter 55)
Healthcare Infection Control Practices Advisory Committee a federal advisory committee appointed to provide advice and guidance to government agencies regarding the practice of infection control and strategies for surveillance, prevention, and control of healthcare-associated infections, antimicrobial resistance and related events in United States healthcare settings. (Chapter 4)
heart failure the condition that occurs when a person's heart is weakened and not able to pump blood the way it should, causing the ejection fraction (EF) to fall below normal, healthy levels. (Chapter 10)
heart rate (HR) the number of heartbeats per unit of time, usually expressed as beats per minute. (Chapter 10)
heat and moisture exchanger (HME) a device that recirculates moisture from exhaled gas to humidify the next inhaled breath. (Chapter 39)
heave a precordial impulse that may be felt (palpated) in patients with cardiac or respiratory disease. (Chapter 16)
heliox a low-density therapeutic mixture of helium with at least 20% O_2; used in some centers to treat large airway obstruction. (Chapter 41)

heliox therapy a treatment used to reduce the work of breathing, especially in patients with severe acute asthma or upper airway obstructions, until the primary problem can be resolved. (Chapter 42)

hematemesis the vomiting of blood. (Chapter 16)

hematocrit the packed red blood cell volume in relation to total blood volume, expressed as a percentage. (Chapter 17)

hematology the branch of medicine involved in the study of blood morphology, physiology, and pathology. (Chapter 17)

hemolysis rupture of red blood cells. (Chapter 17)

hemoptysis the coughing up of blood from the lungs. (Chapter 16)

hemothorax accumulation of blood in the pleural cavity. (Chapter 27)

Henderson-Hasselbalch (H-H) equation an equation enabling the determination of pH as a measure of acidity (using pK_a, the negative log of the acid dissociation constant) in biological and chemical systems. (Chapter 14)

Henry's law in physics, a law stating that the solubility of a gas in a liquid is proportional to the pressure of the gas if the temperature is constant and if the gas does not chemically react with the liquid. (Chapter 6)

hepatomegaly abnormal enlargement of the liver; usually a sign of disease. (Chapter 16)

Hering-Breuer inflation reflex a parasympathetic inflation reflex mediated via the lung's stretch receptors that appears to influence the duration of the expiratory pause occurring between breaths. (Chapter 15)

Hertz (Hz) a unit derived from time which measures frequency in the International System of Units (SI). A frequency of 1 hertz means that something happens once a second. (Chapter 44)

heterodispersing referring to an aerosol consisting of particles of varying diameters and sizes. (Chapter 40)

high-flow nasal cannula (HFNC) a variation of the standard nasal cannula that can deliver both FiO_2 and relative humidity greater than 90% by using heated, humidified O_2 with flows up to 50 L/min. These systems have been shown to successfully treat moderate hypoxemia through a combination of a high FiO_2, distending PAP, and meeting or exceeding the patient's minute ventilation. (Chapters 42 and 43)

high-efficiency particulate air/aerosol filters a filter which is capable of filtration to a standard. Specifically, HEPA is an acronym for "High Efficiency Particulate Air" or "High Efficiency Particulate … the filter to capture 99.97% of the 0.3-micron (0.000012-inch) particles in the air. (Chapter 4)

high-flow system O_2 therapy equipment that supplies inspired gases at a consistent preset O_2 concentration. (Chapter 42)

high-frequency chest wall compression (HFCWC) a mechanical technique for augmenting secretion clearance; small gas volumes are alternately injected into and withdrawn from a vest by an air-pulse generator at a fast rate, creating an oscillatory motion against the patient's thorax. (Chapter 44)

high-frequency oscillatory ventilation (HFOV) a type of mechanical ventilation which utilizes a respiratory rate greater than four times the normal value and very small tidal volumes. (Chapters 49)

high-frequency ventilation (HFV) ventilatory support provided at rates significantly higher than normal breathing frequencies. (Chapters 29 and 54)

hilum vertical opening on either side of the mediastinum through which all the airways and pulmonary vessels pass. (Chapter 9)

home sleep test (HST) a test done in the patient's home (vs. in a sleep laboratory) to assess for sleep-disordered breathing, e.g., simplified with monitoring oxygen and breathing effort. (Chapter 57)

homeostasis relative constancy in the internal environment of the body, naturally maintained by adaptive responses that promote healthy survival. (Chapter 17)

Hoover sign inward movement of the lower lateral margins of the chest wall with each inspiratory effort owing to a low, flat diaphragm as seen in emphysema. (Chapter 16)

Hospital Readmission Reduction Program (HRRP) a Medicare value-based purchasing program that reduces payments to hospitals with excess readmissions. (Chapter 24)

hospital-acquired or nosocomial infection infection acquired at least 72 hours after hospitalization, often caused by *Candida albicans, Escherichia coli,* hepatitis viruses, herpes zoster virus, *Pseudomonas,* or *Staphylococcus.* (Chapter 4)

hospital-acquired pneumonia (HAP) a lower respiratory tract infection that develops in hospitalized patients more than 48 hours after admission and excludes community-acquired infections that are incubating at the time of admission. (Chapter 24)

huff coughing a type of forced expiration with an open glottis to replace coughing when pain limits normal coughing. (Chapter 44)

humidifier a device that adds molecular water to gas. (Chapter 39)

humidity deficit a condition associated with a BH less than 100% that represents the amount of water vapor the body must add to the inspired gas to achieve saturation at body temperature (37°C). (Chapter 6)

hydrofluoroalkane (HFA) the current gaseous chemical compound used to power metered-dose inhalers. (Chapter 40)

hydrophilic having a tendency to mix with, dissolve in, or be wetted by water. (Chapter 13)

hydrophilic drugs drugs with strongly polar groups that readily interact with water. (Chapter 30)

hydrophobic pertaining to the property of repelling water molecules, a quality possessed by nonpolar radicals or molecules that are more soluble in organic solvents than in water. (Chapter 39)

hydropneumothorax a pneumothorax that is partially filled with fluid. (Chapter 21)

hydrostatic relating to the pressure of fluids or to their properties when in equilibrium. (Chapter 27)

hydrostatic pressure pressure caused by the weight of fluid; related to the volume of fluid in a container and the effects of gravity. (Chapter 13)

hydrostatic pulmonary edema pulmonary edema caused by an increase in hydrostatic (water) pressure. (Chapter 29)

hygrometer an instrument that directly measures the relative humidity of the atmosphere or the proportion of water in a specific gas or gas mixture without extracting the moisture. (Chapters 6 and 39)

hygroscopic attracting or absorbing moisture from the air. (Chapters 39 and 40)

hyperbaric oxygen (HBO) therapy therapeutic application of O_2 at pressures greater than 1 atm (or 760 mm Hg). Also called *hyperbaric oxygenation.* (Chapter 42)

hypercalcemia greater than normal amounts of calcium in the blood, most often resulting from excessive bone resorption and release of calcium, as occurs in hyperparathyroidism, metastatic tumors of bone, Paget disease, and osteoporosis. (Chapter 13)

hypercapnia the abnormal presence of excess amounts of CO_2 in the blood (in arterial blood, PCO_2 >45 mm Hg). (Chapter 14)

hypercapnic respiratory failure inability to breathe characterized by the abnormal accumulation of carbon dioxide in the blood. (Chapter 50)

hypercapnic respiratory failure (type II) the inability to maintain normal removal of CO_2 from the tissues; may be indicated by $PaCO_2$ greater than 50 mm Hg in an otherwise healthy individual. See *ventilatory failure.* (Chapter 45)

hyperglycemia an abnormally elevated blood glucose level most often resulting from either diabetes or severe sepsis. (Chapter 17)

hyperkalemia greater than normal amounts of potassium in the blood. (Chapters 13 and 17)

hypernatremia a greater than normal concentration of sodium in the blood caused by excessive loss of water and electrolytes secondary to polyuria, diarrhea, excessive sweating, or inadequate water intake. (Chapter 17)

hyperoxemia higher than normal levels of oxygen in the blood. (Chapter 42)

hyperoxic acute lung injury the condition formerly known as oxygen toxicity. (Chapter 42)

hyperphosphatemia elevated serum levels of phosphate. (Chapter 13)

hypersensitivity pneumonitis an inflammatory form of interstitial pneumonia resulting from an immunologic reaction in a hypersensitive person. The reaction may be provoked by various inhaled organic dusts, often containing fungal spores. The disease can be prevented by avoiding contact with the causative agents. Also called *extrinsic allergic alveolitis.* (Chapter 26)

hypertension high blood pressure. (Chapter 16)

hypertonic solutions with more tonicity (more oncotic pressure and higher concentration as a result of less water). (Chapter 13)

hyperventilation ventilation greater than necessary to meet metabolic needs; signified by PCO_2 less than 35 mm Hg in the arterial blood. (Chapter 11)

hypocalcemia low serum levels of Ca^{2+}. (Chapter 13)

hypocapnia the presence of lower than normal amounts of CO_2 in the blood (in arterial blood, PCO_2 <35 mm Hg). (Chapter 14)

hypoglycemia a lower than normal amount of glucose in the blood, usually caused by administration of too much insulin, excessive secretion of insulin by the islet cells of the pancreas, or dietary deficiency (normal blood glucose levels range from 70 to 105 mg/dL). (Chapter 17)
hypokalemia a condition in which an inadequate amount of potassium, the major intracellular cation, is found in the circulating bloodstream. (Chapters 13 and 17)
hyponatremia a lower than normal concentration of sodium in the blood, caused by inadequate excretion of water or by excessive water in the circulating bloodstream. (Chapter 17)
hypoperfusion decreased pumping of the heart resulting in inadequate organ perfusion. (Chapter 31)
hypopharynx the lower portion of the upper airway between the oropharynx and the larynx. (Chapter 9)
hypoplastic lungs underdeveloped lungs. (Chapter 9)
hypotension an abnormal condition in which the blood pressure is inadequate for normal perfusion and oxygenation of the tissues. (Chapter 16)
hypothermia an abnormal and dangerous condition in which the temperature of the body is less than 32°C, usually caused by prolonged exposure to cold. (Chapters 16 and 39)
hypothesis a proposed explanation for a phenomenon to be proven or disproven through well-founded research. (Chapter 8)
hypotonic having a tonicity less than that of normal saline (0.9% NaCl). (Chapter 13)
hypoventilation ventilation less than necessary to meet metabolic needs; signified by PCO_2 greater than 45 mm Hg in the arterial blood. (Chapter 11)
hypovolemia an abnormally low circulating blood volume. (Chapter 16)
hypoxemia an abnormal deficiency of O_2 in the arterial blood. (Chapters 12 and 42)
hypoxemic respiratory failure the inability to maintain normal oxygenation in the arterial blood. (Chapter 50)
hypoxemic respiratory failure (type I) inability to breathe characterized by lower than normal blood oxygen levels. (Chapter 45)
hypoxia an abnormal condition in which the O_2 available to the body cells is inadequate to meet metabolic needs. (Chapter 12)
hysteresis the failure of two associated phenomena to coincide, as in the observed difference between the inflation and deflation volume-pressure curves of the lung. (Chapter 11)

I

ideal body weight the optimal weight associated with maximum life expectancy for a given height. (Chapter 23)
idiopathic pulmonary fibrosis the formation of scar tissue in the connective tissue of the lungs without known cause resulting in severe chronic restrictive lung disease. (Chapter 26)
impedance threshold device a valve used in cardiopulmonary resuscitation (CPR) to decrease intrathoracic pressure and improve venous return to the heart. (Chapter 38)
impulse-conducting system Purkinje fibers within the heart muscle that conduct impulses controlling the contractions of the atria and ventricles. (Chapter 18)
incentive spirometry the process of encouraging a bedridden patient to take deep breaths to avoid atelectasis; most often done with the use of an incentive spirometer that provides feedback to the patient when a predetermined lung volume is reached during inspiration. (Chapter 43)
indirect calorimetry measurement of the amount of energy a body consumes (in kcal) by determining the consumption of O_2 and production of CO_2. (Chapter 23)
inertial impaction the deposition of particles by collision with a surface; primary mechanism for pulmonary deposition of particles greater than 5 mm in diameter. (Chapter 40)
infiltrates fluids that pass through body tissues into a space or virtual space, as seen in the lung. (Chapter 21)
information retrieval gathering information, often from an electronic medical record. (Chapter 7)
informed consent permission granted based on full knowledge of the possible consequences of participating, often used in the context of participating in a research study. (Chapter 5)
inhaled mass the mass of the particles inhaled from an aerosol. (Chapter 40)
inhaled nitric oxide (INO) gas that is administered to decrease pulmonary hypertension. (Chapter 54)
innominate artery rupture a rupture of the innominate artery usually as a result of a tracheostomy tube eroding the tissue leading to the artery and eventually causing the artery to rupture. (Chapter 48)
inotropic support a way of enhancing cardiac output, either by medication or mechanically. (Chapter 31)
insensible nonmeasurable. (Chapter 13)
inspiratory capacity (IC) the maximum amount of air that can be inhaled from the resting end-expiratory level or functional residual capacity; sum of the tidal volume and inspiratory reserve volume. (Chapter 20)
inspiratory positive airway pressure (IPAP) application of positive pressure to the airway during inspiration. (Chapter 50)
inspiratory reserve volume (IRV) maximum volume of air that can be inhaled after a normal quiet inspiration. (Chapter 20)
inspiratory-to-expiratory ratio (I/E) the relationship between the time involved in inhalation versus that related to the exhalation portion of the breathing cycle, expressed as a proportion. (Chapter 29)
inspissated describing a fluid that is thickened or hardened through the absorption or evaporation of the liquid portion, as can occur with respiratory secretions when the upper airway is bypassed. (Chapters 39)
inspissation the process of becoming thickened, often referring to mucus. (Chapter 44)
Institutional Review Board an administrative body established to protect the rights and welfare of human research subjects recruited to participate in research activities conducted under the auspices of the **institution** with which it is affiliated. (Chapter 8)
insufflator-exsufflator a mechanical device that provides an artificial cough by alternately applying positive pressure and negative pressure to the airway. (Chapter 57)
intelligent targeting scheme a ventilator control system that uses artificial intelligence programs such as fuzzy logic, rule-based expert systems, and artificial neural networks. (Chapter 46)
intellivention the ability of a mechanical ventilator to utilize programmed algorithms to either make or recommend setting changes, including those related to weaning and discontinuance. (Chapter 53)
interatrial septum the wall separating the two atria in the heart. (Chapter 10)
intercostal nerves the nerves serving the intercostal muscles. (Chapter 9)
interdisciplinary collaboration working together by individuals in different medical disciplines, e.g., respiratory therapists with nurses and/or doctors. (Chapter 58)
intermittent mandatory ventilation (IMV) mode of mechanical ventilatory support in which the patient receives a preset number of machine breaths per minute set by time. The patient is allowed to breathe spontaneously as often as desired in between machine breaths. Depending on the base rate, IMV can provide partial or full ventilatory support. (Chapter 46)
intermittent positive-pressure breathing (IPPB) the application of positive-pressure breaths to a patient for a relatively short period (10 to 20 minutes). (Chapter 43)
internal respiration the exchange of O_2 and CO_2 at the tissue level. (Chapter 9)
International Council for Respiratory Care (ICRC) a diverse group of worldwide health professionals addressing issues affecting educational, medical, and professional trends in the global respiratory care community. (Chapters 1 and 2)
International Organization for Standardization an international standard-setting body composed of representatives from various national standards organizations. (Chapter 39)
interstitial fluid fluid between cells but outside of the vascular spaces. (Chapter 13)
interstitial lung disease (ILD) respiratory disorder characterized by a dry, unproductive cough and dyspnea on exertion. X-ray films usually show fibrotic infiltrates in the lung tissue, usually in the lower lobes. (Chapters 21 and 26)
interventricular septum the wall in the heart separating the right and left lower chambers (ventricles). (Chapter 10)
intervillous spaces an embryologic term describing the space between the structures (villi)containing the vessels of the mother and the embryo. (Chapter 9)

intracellular fluid fluid within cells. (Chapter 13)
intrapulmonary percussive ventilation (IPV) airway clearance technique that uses a pneumatic device to deliver a series of pressurized small volume breaths at high rates (1.6 to 3.75 Hz) to the respiratory tract, usually via a mouthpiece; usually combined with aerosolized bronchodilator therapy. (Chapter 44)
intubation passage of a tube into a body aperture; commonly refers to the insertion of an endotracheal tube within the trachea. (Chapter 37)
intuitionism an ethical viewpoint that holds that there are certain self-evident truths, usually based on moral maxims such as "treat others fairly." (Chapter 5)
invasive characterized by a tendency to spread or infiltrate; also refers to the use of diagnostic or therapeutic methods requiring access to the inside of the body. (Chapter 19)
ionic electrovalent; relating to or containing matter in the form of charged atoms or groups of atoms. (Chapter 13)
iron lung full-body negative-pressure ventilator. (Chapter 50)
ischemia decreased oxygen supply. (Chapter 10)
isohydric buffering a buffering process where the H ion produced by one buffer system is immediately buffered by another, such as the buffering of H ion by hemoglobin when H ion is formed by the combination of CO_2 and H_2O in the red blood cell. (Chapter 14)
isothermic saturation boundary (ISB) the point at which inspired gas becomes fully saturated to 100% relative humidity at body temperature. (Chapter 39)
isotonic describing a solution having the same concentration of solute as another solution and exerting the same amount of osmotic pressure as that solution, such as an isotonic saline solution that contains an amount of salt equal to that found in the extracellular fluid. (Chapter 13)

J

jet entrainment the design principle used in simple O_2 masks with variable FiO_2 settings. (Chapter 6)
Jidoka a joining of automation and human intelligence that results in a higher level of quality control. (Chapter 3)
Joint Commission a private nongovernment agency that establishes guidelines for the operation of hospitals and other healthcare facilities, conducts accreditation programs and surveys, and encourages the attainment of high standards of institutional medical care in the United States; formerly Joint Commission on Accreditation of Healthcare Organizations (JCAHO). (Chapter 2)
Joule-Thompson phenomenon effect phenomenon of expansion cooling. (Chapter 6)
J receptors C fibers in the lung parenchyma near the pulmonary capillaries, also called juxtacapillary receptors. (Chapter 15)
jugular venous distention abnormal distention of the jugular veins, most often caused by heart failure. (Chapter 16)
justice principle of fair and equal treatment for all, with due reward and honor. (Chapter 5)

K

Karvonen formula a simple formula used to set a target heart rate for patients during exercise. (Chapter 56)
Kerley B lines thin lines seen near the pleural edge on a chest film as a result of increased pulmonary capillary pressures. (Chapter 21)
key performance indicators specific measures which are used to determine the level of quality outcomes within a healthcare setting. (Chapter 7)
kilocalorie a unit of energy equal to 1000 calories. (Chapter 23)
kinetic energy energy a body possesses by virtue of its motion. (Chapter 6)
Krebs cycle (tricarboxylic acid [TCA] cycle) the sequence of reactions occurring inside the mitochondrion by which most living cells generate energy during the process of aerobic respiration. (Chapter 23)
Kussmaul breathing type of breathing observed during severe metabolic acidosis whereby patients breathe rapidly and deeply, similar to the breathing of a normal person during strenuous exercise. (Chapter 16)
Kussmaul sign paradoxical increase in venous pressure with distention of the jugular veins during inspiration, as seen in constrictive pericarditis or mediastinal tumor. (Chapter 16)
kwashiorkor a disease involving protein-energy malnutrition due to the stress of disease and the resulting increase in catabolic rate. (Chapter 23)
kyphoscoliosis abnormal condition characterized by anteroposterior and lateral curvature of the spine. (Chapter 33)

L

L/S ratio the ratio of lecithin to sphingomyelin in amniotic fluid, a test of fetal amniotic fluid to assess for fetal lung immaturity. (Chapter 9)
lactate anion of lactic acid. (Chapter 17)
Lambert-Eaton syndrome a disorder of neuromuscular conduction commonly associated with an underlying malignancy that leads to muscle weakness, frequently with sensory deficits that can often be improved by repetitive muscle contraction against pressure. (Chapter 33)
laminar flow a pattern of flow consisting of concentric layers of fluid flowing parallel to the tube wall at linear velocities that increase toward the center. (Chapter 6)
Laplace law principle of physics that the tension on the wall of a sphere is the product of the pressure times the radius of the chamber and that the tension is inversely related to the thickness of the wall. (Chapter 6)
large cell carcinoma type of lung cancer characterized by large cells. (Chapter 32)
large for gestational age (LGA) refers to an infant whose fetal growth was accelerated and whose size and weight at birth are above the 90th percentile of appropriate-for-gestational-age infants, whether delivered prematurely, at term, or later than term. (Chapter 54)
laryngectomy the surgical removal of the larynx. (Chapter 37)
laryngopharynx one of the three regions of the throat, extending from the hyoid bone to the esophagus. (Chapter 9)
larynx organ of the voice that is part of the upper air passage connecting the pharynx with the trachea. It accounts for a large bump in the neck called the *Adam's apple* and is larger in men than in women, although it remains the same size in boys and girls until puberty. (Chapter 9)
laser photocoagulation a means of using a laser with a bronchoscope to stop the bleeding in the airway. (Chapter 22)
latent heat of fusion the amount of heat at a substance's melting point required to change 1 g of the substance from a solid to a liquid. (Chapter 6)
latent heat of vaporization the amount of heat at a substance's boiling point required to change 1 g of the substance from a liquid to a gas. (Chapter 6)
law of continuity law saying that the velocity of a fluid moving through a tube varies inversely with the available cross-sectional area. (Chapter 6)
laws of thermodynamics laws that describe the relation between temperature and the kinetics of matter changing its state. (Chapter 6)
lean management a business management philosophy that focuses on eliminating waste or non–value-added activities. (Chapter 3)
learning management systems computerized web-based platforms that are used to offer courses and other learning resources. (Chapter 7)
left ventricular aid a mechanical pump that is implanted in patients with heart failure to help the heart pump blood. (Chapter 10)
left ventricular heart failure poor pumping of the heart involving the left ventricle. (Chapter 31)
leukocytes white blood cells. (Chapter 17)
leukocytosis abnormal increase in the number of circulating white blood cells. (Chapter 17)
leukopenia a low white blood cell count. (Chapter 17)
leukotriene class of biologically active compounds that occur naturally in leukocytes and produce allergic and inflammatory reactions similar to histamine. They are thought to play a role in the development of allergic and autoallergic diseases such as asthma, rheumatoid arthritis, inflammatory bowel disease, and psoriasis. (Chapter 36)
libel false accusation written, printed, or typewritten or presented in a picture or a sign that is made with malicious intent to defame the reputation of a person who is living or the memory of a person who is dead, resulting in public embarrassment, contempt, ridicule, or hatred. (Chapter 5)
licensure the granting or regulation of licenses, as for professionals. (Chapter 2)
life-sustaining treatment treatment that is preventing imminent death, such as mechanical ventilation, blood pressure-sustaining medications, cardiopulmonary resuscitation. (Chapter 58)

linearity refers to the accuracy of the instrument over its entire range of measurement, or its capacity. (Chapter 20)
lipophilic drugs drugs that can readily dissolve in lipid substances. (Chapter 30)
living will advance declaration by a patient that indicates agreement between a patient and physician to withhold heroic measures if the patient's condition is found to be irreversible. (Chapter 5)
loaded breathing breathing under conditions where breathing is challenged, as by a superimposed resistance to inspiration. (Chapter 46)
lobar atelectasis a collapsing of the airways and or alveoli limited to one lung segment. (Chapter 43)
long-term subacute care hospitals (LTACHs) facilities that provide highly focused care to patients with complex medical conditions outside of traditional acute care hospitals, including patients who have been ventilator-dependent and are difficult to wean. (Chapter 57)
loud P-2 abnormally loud closure of the pulmonic valve as part of S_2; usually caused by pulmonary hypertension. (Chapter 16)
lower confidence a statistical concept defining the lower range of normal. (Chapter 3)
lower respiratory tract infection any infectious disease of the left and right bronchi and the alveoli. (Chapter 24)
low-flow system a variable performance O_2 therapy device that delivers O_2 at a flow that provides only a portion of the patient's inspired gas needs. Also called *variable performance system*. (Chapter 42)
L/T ratio the lung availability of an aerosol divided by the total system availability of the aerosol. (Chapter 35)
lung protective ventilation (LPV) the use of low tidal volumes to help prevent ventilator-induced lung injury. (Chapter 29)
lung-protective ventilatory strategy an approach to mechanical ventilation that attempts to avoid overdistention of the lung and recruitment and derecruitment of unstable lung units with each breath. (Chapter 49)
lung stress and strain the force applied per unit area. As applied to the respiratory system it is equal to transpulmonary pressure. (Chapter 52)
lung ultrasonography the use of ultrasound technology to view lung structures. (Chapter 52)
lymphadenopathy of or pertaining to a disease of the lymph nodes; refers also to the visualization of enlarged lymph nodes on radiographs. (Chapter 16)
lymphangioleiomyomatosis rare disorder of abnormal smooth muscle tissue proliferating around small airways and leading to severe obstruction and destruction of alveoli with resultant thin-walled cyst formation. (Chapter 26)

M

machine-cycled a breath that is turned off by the ventilator. (Chapter 46)
machine-triggered a breath that is initiated by the ventilator. (Chapter 46)
macroshock shock from an electrical current of 1 mA or greater that is applied externally to the skin. (Chapter 3)
magnetic resonance imaging (MRI) an imaging technique using the magnetic disturbance of tissue to obtain images. (Chapter 32)
Mallampati classification one of the most commonly used methods to identify the ability to visualize the vocal cords and glottis and therefore assess the degree of difficulty clinicians may encounter during intubation. (Chapter 22)
malpractice in law, professional negligence that is the proximate cause of injury or harm to a patient, resulting from a lack of professional knowledge, experience, or skill that can be expected in others in the profession or from a failure to exercise reasonable care or judgment in the application of professional knowledge, experience, or skill. (Chapter 5)
mandatory ventilatory support breath either initiated or ended by the machine. (Chapter 46)
mandatory minute volume ventilation (MMV) variation of the intermittent mandatory ventilation mode of ventilatory support in which the ventilator keeps the total minute volume constant. (Chapter 52)
manifold a pipe with many connections; in medical gas storage, a collection of gas cylinders linked together for purposes of bulk storage and usually including at least one reserve bank and other safety systems, such as low-pressure alarms. (Chapter 41)
manubrium the upper triangular portion of the sternum. (Chapter 9)
marasmus protein-energy malnutrition caused by starvation. (Chapter 23)
mass the physical property of matter that gives it weight and inertia; an aggregate of cells clumped together, such as a tumor. (Chapter 32)
mass median aerodynamic diameter (MMAD) measure of central tendency that describes the particle diameter in micrometers in medical aerosols and pertains to cascade impaction. (Chapter 40)
maximal voluntary ventilation measure of maximum spontaneous breathing capabilities. Measures over 15 sec converted to minute ventilation/minute. (Chapter 20)
maximum expiratory pressure (MEP) measure of the output of the expiratory muscles against a maximum stimulus measured in cm H_2O positive pressure. (Chapter 45)
maximum inspiratory pressure (MIP) measure of the output of the inspiratory muscles against a maximum stimulus, measured in cm H_2O negative pressure. Also known as *negative inspiratory force (NIF)* or *maximum inspiratory force (MIF)*. (Chapter 45)
maximum voluntary ventilation (MVV) maximum volume of air in liters per minute that a patient can breathe during a 12- to 15-second period. It is a very patient-dependent test. Formerly called the *maximum breathing capacity (MBC)*. (Chapters 45 and 52)
mean airway pressure (MAP) the average pressure applied to the airway. (Chapters 47 and 52)
mechanical insufflation-exsufflation a mechanical device that provides an artificial cough by alternately applying positive pressure and negative pressure to the airway, also referred to as an *in-exsufflator*. (Chapter 44)
mechanical support enhancement of cardiac output using a device, e.g., an intraaortic balloon pump. (Chapter 31)
meconium material that collects in the intestines of a fetus and forms the first stools of a newborn. (Chapter 54)
meconium aspiration syndrome inhalation of meconium by a fetus or newborn; this can block the air passages and cause failure of the lungs to expand. (Chapter 35)
mediastinum the portion of the thoracic cavity lying in the middle of the thorax (between the two pleural cavities); extends from the vertebral column to the sternum and contains the trachea, esophagus, heart, and great vessels of the circulatory system. (Chapters 9 and 21)
medical director responsible for assisting and advising the department director on the management of the respiratory therapy department. (Chapter 2)
medical instrumentation devices/instruments designed specifically for use in medicine. (Chapter 2)
melting point characteristic temperature at which the solid and liquid forms of a substance are in equilibrium. (Chapter 6)
membrane pressures the pressure across an oxygenator used in an extracorporeal membrane oxygenation circuit. (Chapter 51)
meniscus the top part of a liquid where its edges form a curved surface. (Chapter 6)
Merit-based Incentive Payment System (MIPS) a salary raise program based on performance of the employee not longevity. (Chapter 7)
meta-analysis a systematic review of the available literature. (Chapter 8)
metabolic acidosis nonrespiratory processes resulting in acidemia. (Chapter 14)
metabolic alkalosis nonrespiratory processes resulting in alkalemia. (Chapter 14)
metabolic cart a specific device desing to evaluate metabolic function, frequently used to dedermine daily caloric needs. (Chapter 23)
metabolism systemic inflammatory response syndrome characterized by increased total caloric requirements, hyperglycemia, triglyceride intolerance, increased net protein catabolism, and increased macronutrient and micronutrient requirements. (Chapter 23)
methemoglobin abnormal form of hemoglobin in which the iron component has been oxidized from the ferrous to the ferric state. (Chapter 12)
methemoglobinemia abnormal condition characterized by high levels of methemoglobin in the blood and reduction in O_2-carrying capacity; may be caused by nitrite poisoning or ingestion of a certain oxidizing agent or a genetic defect in the enzyme NADH methemoglobin reductase (an autosomal dominant trait). (Chapters 12 and 22)
m-health a system focused on incurring overall medical health, not just the management of acute incidents. (Chapter 7)
micronutrients nutrients that appear in the body in very small quantities. (Chapter 23)
microshock shock from a usually imperceptible electrical current (<1 mA) that is allowed to bypass the skin and follow a direct, low-resistance pathway into the body. (Chapter 3)

minute ventilation total lung ventilation per minute, the product of tidal volume and respiration rate. It is measured by expired gas collection for a period of 1 to 3 minutes; normal rate is 5 to 10 L/min. (Chapters 11 and 20)

missed triggering the inability of a patient to trigger the ventilator during a particular inspiratory effort—usually a result of auto-PEEP or too large a tidal volume with a rapid respiratory rate. (Chapter 48)

mitral valve the heart valve between the left atria and left ventricle. (Chapter 10)

mode any one of many categories of mechanical ventilation that are determined by a number of characteristics, including how the breath is initiated and how the inhalation ceases and exhalation starts. (Chapter 46)

mode asynchrony the selection of a mode of ventilation that does not synchronously interact with the patient's inspiratory efforts. (Chapter 48)

moderate sedation a form of sedation used for certain procedures such a bronchoscopy, whereby patients can respond to verbal stimuli and maintain protective airway reflexes. (Chapter 22)

modified Allen test the most common technique to determine the adequacy of ulnar circulation. (Chapter 19)

molal solution a solution containing 1 mole of solute per kilogram of solvent or 1 mmol/g solvent. (Chapter 13)

molar solution 1 mole of solute per liter of solution or 1 mmol/mL of solution. (Chapter 13)

molar volume the volume of solvent needed to establish a 1 molar solution. (Chapter 13)

monitor to observe and evaluate a function of the body closely and constantly; a mechanical device that provides a visual or audible signal or a graphic record of a particular function, such as a cardiac monitor or a fetal monitor. (Chapter 19)

monodispersing referring to an aerosol in which particles are of uniform size. (Chapter 40)

morbid obesity a state of having a body mass index greater than 45 kg/m^2. (Chapter 30)

mucociliary escalator a term used to define the process in which the cilia of the airways continually move mucus from the lower respiratory tract to the oral cavity. (Chapter 9)

mucoid resembling mucus. (Chapter 16)

mucous plugging the partial or complete occlusion of the airway by thick mucus. (Chapter 44)

multiple organ dysfunction syndrome (MODS) a condition in which dysfunction of many different organs occurs, usually accompanying ALI. (Chapter 29)

murmur an abnormal heart sound created by turbulent blood flow through a narrowed or incompetent heart valve. (Chapter 16)

Murray lung injury score a score used to define the severity of injury in patients with acute respiratory distress syndrome (ARDS). (Chapter 52)

muscarinic stimulating the postganglionic parasympathetic receptor; pertaining to the poisonous activity of muscarine. (Chapter 36)

muscle fatigue a condition involving loss of the capacity to develop force or velocity of a muscle resulting from muscle activity overload, which is reversible by rest. (Chapter 44)

myasthenia gravis a disorder of neuromuscular conduction that leads to muscle weakness of the skeletal muscles, particularly the muscles of the face, throat, and respiratory system. Weakness and respiratory failure can occur rapidly as muscle strength decreases with repetitive contraction against a load. (Chapter 33)

myocardial infarction (MI) damage to the heart caused by a lack of blood flow to the myocardial tissue. (Chapter 10)

myogenic control the relationship between vascular smooth-muscle tone and perfusion pressure. (Chapter 10)

myotonic dystrophy a type of muscular dystrophy. (Chapter 33)

N

nanomole a quantity equal to 10^{-9} of a mole. (Chapter 13)

narrow-band imaging an imaging technique used in conjunction with bronchoscopy, where light of specific blue and green wavelengths is used to enhance the detail of certain aspects of the surface of the mucosa. (Chapter 22)

nasal flaring dilation of the alae nasi on inspiration; an early sign of an increase in ventilatory demands and the work of breathing, especially in infants. (Chapter 35)

nasopharynx the upper portion of the airway behind the nasal and oral cavities. (Chapter 9)

National Association for Medical Direction of Respiratory Care A medical association focused on the provision of respiratory care. Medical directorship of a respiratory care program required for membership. (Chapter 2)

National Asthma Educator Individual who has been certificeid to provide asthma education, requires passing a test. (Chapter 2)

National Board for Respiratory Care (NBRC) the national credentialing agency for respiratory care practitioners and pulmonary function technologists. (Chapters 1 and 2)

nebulizer a device that produces an aerosol suspension of liquid particles in a gaseous medium using baffling to control particle size. (Chapters 39 and 40)

needle capping device a safety device used to prevent or minimize needlestick injuries when capping a syringe needle (as required after blood gas sampling). (Chapter 19)

negative feedback loop exists when the output of a system acts to oppose changes to the input of the system, with the result that the changes are attenuated and output is balanced. (Chapter 10)

negative inotropism indicator of a decrease in the contractility of the heart. (Chapter 10)

negative-pressure ventilation approach to ventilation in which negative pressure is intermittently applied to the chest surface in an effort to cause inflation of the lungs. (Chapter 50)

negligence omission to do something that a reasonable person, guided by ordinary considerations, would do. (Chapter 5)

neovascularization formation of new capillary beds. (Chapter 42)

neurally adjusted ventilatory assist (NAVA) an approach to ventilation based on the electromyelographic (EMG) activity of the diaphragm. Airway pressure is increased proportional to the change in EMG activity. No control variable is set. (Chapters 48 and 49)

neutropenia an abnormal decrease in the number of neutrophils in the blood. (Chapters 17 and 36)

neutrophilia an absolute elevation in neutrophils. (Chapter 17)

nitric oxide (NO) an inhaled gas used to reduce pulmonary artery pressure and improve arterial oxygenation. (Chapter 42)

nitrogen balance the appropriate amount of nitrogen in the body, the balance between nitrogen and other nutrients. (Chapter 23)

nocturnal hypoventilation elevated $PaCO_2$ and accompanying decline in O_2 saturation that occurs in response to a progressive decrease in minute ventilation occurring during sleep, most often in the rapid-eye-movement stage. (Chapter 50)

nodule small node; small node-like structure. (Chapter 32)

nonflammable unable to support combustion. (Chapter 41)

nonhydrostatic pulmonary edema pulmonary edema that is caused by something other than an increase in blood pressure. (Chapter 29)

noninvasive pertaining to a diagnostic or therapeutic technique that does not require the skin to be broken or a cavity or organ of the body to be entered, such as obtaining a blood pressure reading by auscultation with a stethoscope and sphygmomanometer. (Chapter 19)

noninvasive positive-pressure ventilation (NPPV) positive-pressure ventilation without endotracheal intubation or tracheotomy, usually via a form-fitting mask (also referred to as noninvasive ventilation or NIV). (Chapters 50)

noninvasive ventilation mechanical ventilation performed without intubation or tracheostomy, usually using a mask. (Chapters 25, 43, 45, 50, and 57)

nonmaleficence principle that obligates healthcare providers to avoid harming patients and actively to prevent harm where possible. (Chapter 5)

nonpolar covalent a bond between molecule that does not have polarity. (Chapter 13)

non–small cell carcinoma a major category of histologic types of lung carcinomas, including adenocarcinoma of the lung, large cell carcinoma, and squamous cell carcinoma. Treatment depends on the stage of development of the cancer at the time of initial presentation. The treatme nt of choice for otherwise physically fit patients with early stages of disease is resection. (Chapter 32)

Non–ST-segment-elevation myocardial infarction (NSTEMI) a myocardial infarction that does not show the normal ECG changes, specifically no elevation is the ST segment of the ECG. (Chapter 10)

normal solution a solution that contains the gram-equivalent weight of a reagent per liter; denoted by the symbols N/I or N. (Chapter 13)

normometabolic the normal level of metabolic function in a healthy individual. (Chapter 23)
nosocomial acquired in the hospital (often defined as more than 48 hours after hospital admission), often referring to infections. (Chapter 4)
nosocomial pneumonia an infectious inflammatory process of the lung parenchyma contracted in the hospital. (Chapter 24)
null hypothesis that the probability of two events are equal. (Chapter 8)

O

O_2-conserving device an O_2 delivery system that minimizes the amount of O_2 actually delivered to a patient while also maintaining the FiO_2. (Chapter 57)
obesity hypoventilation a general syndrome involving chronic hypercapnia and hypoxemia, sleep apnea, and decreased respiratory center responsiveness to CO_2. Complications, primarily owing to chronic hypoxemia, include polycythemia, pulmonary hypertension, and cor pulmonale. (Chapter 34)
obesity hypoventilation syndrome a common underdiagnosed condition in hospitalized extremely obese patients. (Chapter 30 and 50)
observational cohort study a study in which there is just observation of the subjects with no specific intervention. (Chapter 8)
obstructive pulmonary disease any respiratory disease characterized by decreased airway size and increased airway secretions. (Chapter 20)
obstructive sleep apnea (OSA) a condition in which five or more apneic periods (lasting at least 10 seconds each) occur per hour of sleep and characterized by occlusion of the oropharyngeal airway with continued efforts to breathe. (Chapters 30, 33 and 34)
obturator device used to block a passage or a canal or to fill in a space, such as the obturator used to insert a tracheostomy tube. (Chapter 37)
occupational interstitial lung disease (ILD) ILD resulting from an occupational exposure; asbestosis is a common example. (Chapter 26)
Occupational Safety and Health Administration (OSHA) a federal agency of the United States that regulates workplace safety and health. (Chapter 4)
ohm a unit of measurement indicating the degree of resistance to the flow of electricity. (Chapter 3)
oligohydramnios conditions that lead to inadequate fetal breathing and low amounts of amniotic fluid formation. (Chapter 9)
onset of blood lactate accumulation (OBLA) the point at which blood lactate levels increase above normal when the body cannot deliver sufficient O_2 to meet the demands of energy metabolism; a term used in exercise physiology. (Chapter 56)
open buffer system the bicarbonate buffer system is an open system because H_2CO_3 can be removed as CO_2 is broken down into H_2O and CO_2 as long as ventilation removes CO_2. (Chapter 14)
optical fluorescence the use of fluorescent dyes illuminated with light of a specific wavelength for the measurement of respiratory gases. (Chapter 19)
optimal targeting scheme a scheme for mechanical ventilator gas delivery that targets an optimal approach to delivering ventilation to the patient based on predetermined variables. (Chapter 46)
optode fluorescent chemosensor useful in measuring pH or gas tensions in arterial or mixed venous blood. (Chapter 19)
organizing pneumonia (OP) the new term for bronchiolitis obliterans organizing pneumonia, which generally occurs in the setting of connective tissue disease. (Chapter 26)
oropharynx the portion of the pharynx located closest to the mouth. (Chapter 9)
orthodeoxia a decrease in PaO_2 owing to changes in position. (Chapters 16 and 45)
orthopnea labored breathing in the reclining position. (Chapter 16)
oscillation back-and-forth motion; vibration or the effects of mechanical or electrical vibration. (Chapter 44)
osmolality a measure of the concentration of a solute in a solution. (Chapter 13)
osmotic pressure a force produced by solvent particles across semipermeable membranes. (Chapter 13)
output the specific measurements made or computed by an instrument. (Chapter 20)
oxidizing the process of combining or causing to combine with O_2 to remove hydrogen or to increase the valence of an element through the loss of electrons. (Chapter 41)
oximetry a noninvasive method for monitoring how saturated a person's hemoglobin is with oxygen and other gases. (Chapter 19)
oxygen consumption (VO_2) the amount of O_2 consumed per minute; the normal value is 200 mL/min. (Chapter 52)
oxygen content the amount of oxygen carried in the blood. (Chapter 51)
oxygen delivery the amount of oxygen actually available for delivery to the tissues. (Chapter 51)
oxyhemoglobin a chemical combination resulting from the covalent bonding of O_2 to the ferrous iron pigment in hemoglobin. (Chapter 12)

P

P wave the wave of depolarization that occurs in the atria, the wave just preceding the QRS complex. (Chapter 18)
P_{100}or $P_{0.1}$ the amount of negative pressure a patient generates in the first 100 milliseconds of inspiration. (Chapter 48)
P_{50} a symbol quantifying variations in the affinity of Hb for O_2. It is the partial pressure of O_2 at which the Hb is 50% saturated, standardized to a pH level of 7.40. (Chapter 9)
pack-years a method of determining the number of cigarettes a patient has smoked over time. The number of packs of cigarettes a person smoked is divided by the number of years during which he or she has smoked. (Chapter 16)
palate a bony plate that separates the nasal cavity from the oral cavity. (Chapter 9)
palatine folds a double web on each side of the oral cavity. (Chapter 9)
palliative care care only designed to relieve suffering, usually instituted in patients with DNI medical states. (Chapter 50)
palliative sedation the controlled and monitored use of nonopioid medication intended to lower the patient's level of consciousness to the extend necessary for relief of awareness of refractory and unendurable symptoms. (Chapter 58)
Pancoast syndrome a combination of signs associated with a tumor in the apex of the lung; these signs include neuritic pain in the arm, atrophy of the muscles of the arm and the hand, and Horner syndrome they are caused by the damaging effects of the tumor on the brachial plexus and sympathetic ganglia. (Chapter 32)
PaO_2/FiO_2 ratio the PaO_2 divided by the FiO_2, indicative of the severity of lung injury. (Chapter 52)
paradoxical breathing motions a breathing pattern in which the chest wall expands first followed by the abdomen. (Chapter 33)
paraneoplastic syndrome effect of tumors remote from the tumor site and often mediated by reactions to tumor products or immune response to the tumor. (Chapter 32)
parenteral patient feeding that involves directly delivering food into the venous circulation. (Chapter 23)
parenteral nutrition (PN) a way of nourishing a patient when all other attempts at feeding are unsuccessful or not recommended. (Chapter 23)
paresthesia a subjective sensation experienced as numbness, tingling, or a "pins and needles" feeling. (Chapter 14)
parietal pleura a thin membrane covering the surface of the chest wall, mediastinum, and diaphragm that is continuous with the visceral pleura around the lung hilum. (Chapters 9 and 27)
partial pressure the pressure exerted by a single gas in a mixture. (Chapter 6)
partial ventilatory support modes of ventilatory support in which the patient must contribute to the total minute volume with spontaneous breathing. (Chapter 49)
Pascal's principle law stating that a confined liquid transmits pressure equally in all directions. (Chapter 6)
PASS an acronym for Pull the pin, Aim the nozzle, Squeeze the handle, Sweep the nozzle across the base of the fire. (Chapter 3)
passive refers to the delivery of medical care that the patient is not directly involved with. Controlled mechanical ventilation is passive ventilation. (Chapter 47)
patent ductus arteriosus (PDA) a common cardiovascular anomaly of infants in which the ductus arteriosus either fails to close or reopens after birth. (Chapter 9 and 54)
patient-cycled cycling of the mechanical ventilator in which the patient determines the end of the breath. (Chapter 46)
Patient Protection and Affordable Care Act (PPACA) legislation that changed many aspects of the American healthcare system by expanding healthcare coverage to many uninsured people, prohibiting the exclusion of

preexisting conditions, creating an exchange for purchasing health insurance coverage, increasing the scope of coverage for certain types of preventive care, and many other provisions. (Chapter 56)

patient-triggered the initiation of a mechanical breath as a result of patient effort. (Chapter 46)

patient-centered care care that is always focused on what is best for the patient not the caregiver. (Chapter 25)

patient-ventilator asynchrony lack of coordinated gas delivery between the patient and the ventilator. (Chapters 47 and 48)

peak expiratory flow rate (PEFR) maximum expiratory flow rate in liters per second. (Chapter 20)

pedal edema swelling of the ankles, usually secondary to heart failure. (Chapter 16)

Pediatric Advanced Life Support (PALS) advanced resuscitation beyond the ABC's of basic resuscitation delivered to pediatric patients. (Chapter 38)

peer review the articles published in journals. (Chapter 8)

peer review organization (PRO) an elaborate system to evaluate the quality and appropriateness of care given to Medicare beneficiaries. (Chapter 3)

penetrating trauma chest trauma that is caused by a bullet, knife, or other weapon which makes a singular entry into the chest. Normally pulmonary contusion does not occur with penetrating trauma. (Chapter 30)

percent body humidity the ratio of a saturated gas's actual water vapor content to its capacity for same at body temperature (37°C). (Chapter 6)

percent solution the weight of solute per weight of solution. (Chapter 13)

percent total body surface area (%TBSA) the percent of the body surface that is affected. Normally used to identify the extent of body surface burns. (Chapter 30)

performance improvement a measurement of the results of a process and then changing it to enhance future results. (Chapter 3)

pericardial effusion an abnormal amount of fluid between the layers. (Chapter 10)

pericardial fluid a thin layer of fluid. (Chapter 10)

pericarditis inflammation of the pericardium that results in a clinical condition. (Chapter 10)

pericardium fibrous, serous sac that surrounds the heart and roots of the great vessels. (Chapter 10)

peripheral cyanosis a bluish tinge of the extremities often caused by low arterial blood oxygen content or poor circulation. (Chapter 16)

permissive hypercapnia the purposeful increase in $PaCO_2$ to insure lung protection. (Chapter 29)

persistent pulmonary hypertension of the newborn (PPHN) a clinical syndrome seen in infants soon after birth and characterized by abnormally increased pulmonary vascular resistance. (Chapter 35)

pharmacodynamic phase mechanisms of drug action that cause effects on the body. (Chapter 36)

pharmacokinetic phase time, course, and disposition of a drug in the body. (Chapter 36)

pharyngeal airways devices that maintain the patency of the pharyngeal structure. (Chapter 37)

pharynx the throat—a tubular structure approximately 13 cm long that extends from the base of the skull to the esophagus and is situated immediately in front of the cervical vertebrae. The pharynx serves as a passageway for the respiratory and digestive tracts and changes shape to allow the formation of various vowel sounds. (Chapter 9)

phlegm mucus from the tracheobronchial tree. (Chapter 16)

photoplethysmography light-emitting technology used to detect changes in blood flow. (Chapter 19)

phrenic nerves paired nerves that originate as branches of spinal nerves C3-5, pass down along the mediastinum, and innervate the diaphragm. (Chapter 9)

physician assistant (PA) an individual academically and clinically prepared to practice medicine under the supervision of a licensed doctor of medicine or osteopathy. Within the physician-PA relationship, PAs exercise autonomy in medical decisions and provide a wide range of diagnostic and therapeutic services. Training programs average 25 to 27 months. National certification is available to graduates of approved training programs. (Chapter 1)

physiologic dead space an area of the respiratory system that includes the anatomic dead space together with the space in the alveoli occupied by air that does not contribute to the O_2-CO_2 exchange. (Chapter 11)

picture archiving and communication systems a medical imaging technology that permits storage and convenient access to images. (Chapter 7)

piezoelectric crystal a transducer capable of converting electrical energy into the physical energy of high-frequency vibrations. (Chapter 39)

pin-indexed safety system (PISS) part of the American standard safety system, this system's specifications apply only to the valve outlets of small cylinders, up to and including size E, that use a yoke-type connection. (Chapter 41)

plaintiff a person who brings an action; a person who seeks remedial relief for an injury to his or her rights. (Chapter 5)

plan-do-study-act cycle (PDSA) part of a continuous quality improvement program. (Chapter 3)

plasma colloid osmotic pressure (oncotic pressure) the osmotic pressure exerted by proteins that remain in the intravascular compartment, which draws water and small solute molecules back into the capillaries. (Chapter 13)

plateau pressure (P_{plat}) pressure in the patient's airway during mechanical ventilation resulting from the application of an end-inspiratory hold. This is equal to the average peak alveolar pressure. (Chapters 47 and 49)

platypnea the opposite of orthopnea; an abnormal condition characterized by difficult breathing in the standing position that is relieved in the lying or recumbent position. (Chapters 16 and 45)

plethysmograph a device for measuring pressure; in pulmonary physiology, a chamber in which the subject sits while lung pressures and volumes are being measured. (Chapter 11)

pleural effusion an abnormal collection of fluid in the pleural space. (Chapters 21 and 27)

pleural fluid a clear fluid with a pH of 7.60 to 7.65 that has few cells, a small amount of protein (about 1 g/dL), and glucose and electrolytes in concentrations that approximate those of plasma. (Chapter 9)

pleural friction rub friction during breathing that produces a creaking or grating sound. (Chapter 16)

pleural space the space between the parietal and pleural membranes. (Chapter 9)

pleurisy pain that comes from the pleural surface, usually as a direct result of a viral infection, but the term has been generalized to any condition (e.g., pulmonary embolism) causing pleural pain. Synonymous with *pleurodynia*. (Chapters 9 and 27)

pleurodesis a procedure of fusing the parietal and visceral pleura to prevent the formation of pleural fluid or the recurrence of pneumothorax. (Chapter 27)

pneumobelt a ventilatory assist device that applies positive pressure to the abdominal contents during expiration. (Chapter 50)

pneumomediastinum the presence of air or gas in the mediastinal tissues, which may lead to pneumothorax or pneumopericardium. (Chapter 21)

pneumonia an inflammatory process of the lung parenchyma, usually infectious in origin. (Chapter 24)

pneumotachometer any device for measuring gas flow. (Chapters 11 and 20)

pneumotaxic center a center in the upper part of the pons that rhythmically inhibits inspiration independently of the vagi. (Chapter 15)

pneumothorax the presence of air or gas in the pleural space of the thorax; if this air or gas is trapped under pressure, tension pneumothorax exists. (Chapters 16, 21 and 27)

point-of-care testing the analysis of body fluids at the bedside as opposed to conventional laboratory testing. (Chapters 7 and 19)

Poiseuille's law the physical law describing the difference in pressure required to produce a given flow under conditions of laminar flow through a smooth tube of a fixed size. (Chapter 6)

polar covalent molecular compounds dissolved in water or other solvents to produce ions (ionization); electrolytes may be weak or strong, depending on degree of ionization; polar covalent solutions are weak electrolytes or conductors ~~polarize and are good conductors~~. (Chapter 13)

polycythemia an abnormal increase in the number of erythrocytes in the blood; termed *secondary* if attributable to defined causes other than direct stimulation of the bone marrow, as occurs in chronic hypoxemia. (Chapters 6 and 17)

polymyositis a condition characterized by the inflammation of many muscles. (Chapter 33)

population health the health outcomes of a group of individuals, including the distribution of such outcomes within a group. (Chapter 55)

pores of Kohn small openings between adjacent alveoli. (Chapter 9)
portable oxygen concentrator (POC) a portable device that produces oxygen by the removal of nitrogen form room air. Used by many patients requiring continuous home oxygen therapy. (Chapter 57)
portals a means by which authorized users can gain access to computerized medical records and health resources. (Chapter 8)
positive end-expiratory pressure (PEEP) the application and maintenance of pressure above atmospheric at the airway throughout the expiratory phase of positive-pressure mechanical ventilation. (Chapters 29 and 45)
positive expiratory pressure (PEP) an airway clearance technique in which the patient exhales against a fixed-orifice flow resistor to help move secretions into the larger airways for expectoration via coughing or swallowing. (Chapters 43 and 44)
positive inotropism an increase in the contractility of muscle tissue. (Chapter 10)
positron emission tomography (PET) a computerized radiographic technique that uses radioactive substances to examine the metabolic activity of various body structures. The patient either inhales or is injected with a metabolically important substance such as glucose, which is carrying a radioactive element that emits positively charged particles, or positrons. When the positrons combine with electrons normally found in the cells of the body, gamma rays are emitted. The electronic circuitry and computers of the PET device detect the gamma rays and construct color-coded images that indicate the intensity of metabolic activity throughout the organ involved. (Chapter 32)
postural hypotension a sudden decrease in arterial blood pressure caused by a change in position; it most often occurs when a hypovolemic patient moves from the reclining position to the upright position. (Chapter 16)
potential energy energy contained in a body as a result of its position in space, its internal structure, and stresses imposed on it. (Chapter 6)
preanalytic error an error that occurs outside of the actual testing procedure. (Chapter 19)
precision the accuracy of an instrument during the measurement of a particular substance. (Chapters 19 and 20)
precordium the region of the thorax immediately in front of the heart. (Chapter 16)
preexperimental an evaluation designed to refine the actual protocol for an experiment. (Chapter 8)
preload pressure stretching the ventricular walls at the onset of ventricular contraction. (Chapters 10, 51, and 52)
pressure the amount of force applied to a specific area. (Chapter 6)
pressure-controlled ventilation (PCV) a mode of ventilatory support in which mandatory support breaths are delivered to the patient at a set inspiratory pressure. (Chapters 46 and 49)
pressure gradient the pressure difference between two points in a system. (Chapter 11)
pressure support ventilation (PSV) a mode of ventilatory support designed to augment spontaneous breathing; patient-triggered, pressure-limited, flow-cycled ventilation. (Chapters 49 and 53)
pressure-regulated volume control (PRVC) pressure-limited ventilation in which inspiratory time and a backup rate are set and a tidal volume is targeted. (Chapter 49)
pressure-time index the product of pressure generated during inspiration and the time that it is applied, an index of patient effort. (Chapter 45)
pressure-time product (PTP) product of pressure over a time interval, usually pleural pressure times inspiratory time during breathing. (Chapter 52)
primary lobule the terminal bronchiole and the cluster of respiratory bronchioles that it supplies. (Chapter 9)
primary pulmonary hypertension of the newborn (PPHN) a form of pulmonary hypertension that occurs in the absence of other heart or lung diseases and is characterized by diffuse narrowing of the pulmonary arterioles without obvious reason. (Chapter 54)
primary spontaneous pneumothorax pneumothorax occurring without underlying lung disease. (Chapter 27)
principal investigator the one who is ultimately responsible for completing a study in compliance with all applicable rules and regulations and for adhering to the protocol approved by the institutional review board (IRB). (Chapter 8)
process control a method of quality control that uses detailed information about a process to optimize outcomes. (Chapter 3)
prodrug inactive or partially active drug that is metabolically changed in the body to an active drug. (Chapter 36)
proficiency testing (PT) process of comparing measurements of a known value from different sources to establish a level of accuracy. (Chapter 19)
prognosis an estimation of a patient's outcome based on the severity of illness and the ability to treat the problem. (Chapter 58)
progressive mobility the process of increasingly mobilizing intensive care unit patients, including those on mechanical ventilation. (Chapter 53)
progressive resistance a method of increasing the strength of a weak or injured muscle by gradually increasing the resistance against which the muscle works, as by using graduated weights over a period of time. Also called *graduated resistance*. (Chapter 56)
prolonged mechanical ventilation (PMV) a lengthy process of mechanical ventilatory support. No precise length has been determined but most would consider longer than 3 weeks prolonged ventilatory support. (Chapter 53)
prone positioning the face-down position, often used during mechanical ventilation to help improve ventilation and oxygenation. (Chapter 29)
propellant something that propels or provides thrust, such as the propellant in a metered-dose inhaler. (Chapter 40)
proportional assist ventilation (PAV) a mode of ventilation without any control variable that delivers gas in proportion to the patient's actual inspiratory effort. (Chapters 48 and 49)
protein-energy malnutrition (PEM) a wasting condition resulting from a diet deficient in protein, energy (calories) or both. (Chapter 23)
protocol-based oxygen therapy oxygen therapy based on a predefined guideline that directs therapy without specific physician orders. (Chapter 42)
pseudoglandular stage an early stage of development of the lungs or any organ before the actual development of glands. (Chapter 9)
pseudorestriction an abnormality that appears at first to be a result of a restriction but is not even though its presentation is similar to a restriction. (Chapter 20)
psig abbreviation for pounds per square inch-gauge—the pressure above atmospheric registered on a meter or gauge. (Chapter 41)
psychomotor domain the area of observable performance of skills that require some degree of neuromuscular coordination. (Chapter 55)
psychosocial support needs of or pertaining to the mental, emotional, and social aspects of human existence or development. (Chapter 56)
PubMed a free computerized search engine that facilitates access to peer-reviewed articles, abstracts, and references related to the life sciences. (Chapter 8)
pulmonary arterial hypertension (PAH) an increase above normal levels in blood pressure in the pulmonary vasculature. (Chapter 28)
pulmonary artery (PA) catheter a catheter placed in the pulmonary artery designed to measure pressures reflective heart function. (Chapter 19)
pulmonary contusion the internal pulmonary bleeding and edema resulting from blunt trauma, generally localized to the area adjacent to the trauma. (Chapter 30)
pulmonary edema a condition in which excessive amounts of plasma enter the pulmonary interstitium and alveoli, usually accompanied by severe respiratory distress, tachypnea, and hypoxemia. (Chapter 29)
pulmonary embolism (PE) blockage of a pulmonary artery by foreign matter. The obstruction may be fat, air, tumor tissue, or a thrombus usually arising from a peripheral vein (most frequently from the deep veins of the legs). A pulmonary embolism is detected by chest x-ray, pulmonary angiography, and radioscanning of the lung fields. (Chapter 28)
pulmonary hypertension (PH) a condition characterized by abnormally high pulmonary artery pressures (i.e., mean pulmonary artery pressures >22 mm Hg). (Chapter 28)
pulmonary Langerhans cell histiocytosis (PLCH) a condition characterized by an abnormal proliferation of Langerhans cells accompanied by interstitial markings on the chest film and dyspnea. (Chapter 26)
pulmonary rehabilitation an organized multidisciplinary approach to improving the functional status of patients with chronic obstructive pulmonary disease, usually including education, exercise, aerosolized medication, and O_2 therapy. (Chapter 56)
pulmonary surfactant a surface-active lipoprotein formed by type II cells, which reduces surface tension and facilitates alveolar expansion during inhalation. (Chapter 9)

pulmonary vascular resistance (PVR) the resistance of blood flow through the pulmonary vascular system. (Chapter 10)
pulse co-oximetry a pulse oximetry that is capable of measuring carboxyhemoglobin and methemoglobin. (Chapter 19)
pulse pressure the difference between the systolic and diastolic pressures, which is normally 30 to 40 mm Hg. (Chapter 16)
pulseless electrical activity (PEA) a serious condition characterized by a disassociation between the electrical and mechanical activity of the heart. In essence, the electrical ECG pattern on the monitor generates neither mechanical activity of the heart nor a pulse. (Chapter 10)
pulsus alternans a pulse alternating between strong and weak heartbeats. (Chapter 16)
pulsus paradoxus an abnormal decrease in pulse pressure with each inspiratory effort. (Chapter 16)
pump flow the flow of blood pumped through on an extracorporeal membrane oxygenation system in liters per minute. (Chapter 51)
purulent consisting of or containing pus. (Chapter 16)
***P* value** a statistical value the indicates the difference between two variables or outcomes, a $p < 0.05$ indicates that the probability of the two variables being equal in less than 5%. (Chapter 8)

Q

quality assurance any evaluation of services provided and the results achieved compared with accepted standards. (Chapter 3)
quality control a planned, systematic approach to designing, measuring, assessing, and improving performance. (Chapter 19)
quality improvement the enhancement of a process, structure, product and/or organization to more closely adhere to best practices, reduce errors, and achieve intended outcomes. (Chapter 3)
quasi-experimental research designs that lack full control of all variables but where there is an effort to compensate with other controls. (Chapter 8)
qui tam Latin for suing for one's self. (Chapter 5)

R

RACE acronym for Rescue patients in the immediate area of the fire. Alert other personnel about the fire so they can assist in the rescue and can relay the location of the fire to officials. Contain the fire. Evacuate other patients and personnel in the areas around the fire who may be in danger if the fire spreads. (Chapter 3)
radiation treatment of neoplastic disease by using x-rays or gamma rays, usually from a cobalt source, to deter the proliferation of malignant cells by decreasing the rate of mitosis or impairing the synthesis of deoxyribonucleic acid. (Chapter 6)
radiograph x-ray image. (Chapter 21)
radiolucent of or pertaining to a substance or tissue that readily permits the passage of x-rays or other radiant energy. Compare with *radiopaque*. (Chapter 21)
radiopaque of or pertaining to a substance or tissue that does not readily permit the passage of x- rays or other radiant energy. Compare with *radiolucent*. (Chapters 21 and 37)
radiotherapy treatment with radiation. (Chapter 32)
rales an abnormal breath sound also known as "crackles," which is discontinuous and can be further characterized as "fine rales" associated with congestive heart failure or "coarse rales" most often associated with air moving through secretions in the airways. (Chapter 16)
random error variability of a measurement outside of accepted limits that occurs in a nonreproducible fashion. (Chapter 19)
randomized controlled trial a clinical trial where the new treatment is received by one group and a second comparative group receives the standard approach to care. (Chapter 8)
rapid shallow breathing index (f/V_T) a patient's spontaneous respiratory rate (f) in breaths per minute divided by the spontaneous tidal volume in liters. Values greater than 100 are associated with poor weaning outcomes. (Chapter 53)
ratio solution the amount of solute to solvent expressed as a proportion (e.g., 1:100). (Chapter 13)
reabsorption the active or passive transport of filtrate substances that moves them from the tubule lumen back into the tubule cell and into the blood of nearby capillaries (Chapter 14). The rebound effect withdrawal of NO resulted in the development of hypoxemia and pulmonary hypertension, perhaps worse than they were before therapy was started. (Chapter 42)
recidivism a circumstance where the same behavior is repeated and repeated in spite of attempts to correct the problem. (Chapter 58)
recirculation the movement of blood from one cannula to another in an extracorporeal membrane oxygenation (ECMO) circuit—specifically, blood being infused into a patient by a venous return catheter that is immediately removed from the patient by the venous drainage catheter during venovenous ECMO. (Chapter 51)
reconditioning physical activity to strengthen essential muscle groups, improve overall O_2 use, and enhance the body's cardiovascular response to physical activity. (Chapter 56)
recruitment maneuvers an intermittent intervention used on mechanically ventilated patients involving the very brief but repeated use of high ventilation pressures to expand previously collapsed alveoli. (Chapter 30)
reducing valve a valve that reduces gas pressure. (Chapter 41)
reexpansion pulmonary edema a type of pulmonary edema that forms after the rapid reexpansion of a lung that has been compressed with pleural fluid or pneumothorax. (Chapter 27)
reference range the acceptable range for a laboratory value measured during calibration or validation of an operation. (Chapter 17)
refractory period the period during which the myocardium cannot be stimulated. (Chapter 10)
regulator a device that controls both pressure and flow. (Chapter 41)
regurgitation the backward flow of blood through an incompetent valve of the heart. (Chapter 10)
reimbursement criteria the specific criteria required for reimbursement. (Chapter 56)
relative humidity (RH) the amount of moisture in the air compared with the maximum amount that the air could contain at the same temperature. (Chapter 6)
reliability how likely a particular tests is to have the same outcome if repeated. (Chapter 20)
repolarization a process by which the cell is restored to its resting potential. (Chapter 18)
research a scientific and systematic exploration of new knowledge. (Chapter 8)
reservoir system an O_2 delivery system providing a reservoir O_2 volume that the patient taps into when the patient's inspiratory flow exceeds the device flow. (Chapter 42)
residual drug volume medication that remains in a small-volume nebulizer after the device is no longer producing mist. (Chapter 40)
residual volume (RV) the volume of gas remaining in the lungs after a complete exhalation. (Chapter 20)
res ipsa loquitur "the thing speaks for itself"; a rule of evidence whereby the negligence of an alleged wrongdoer may be inferred from the fact that an event actually occurred. (Chapter 5)
resistance impedance to flow in a tube or conduit; quantified as ratio of the difference in pressure between the two points. (Chapters 3 and 46)
respirable mass proportion of aerosolized drug of the proper particle size to reach the lower respiratory tract. (Chapter 40)
respiratory acidosis hypoventilation resulting in acidemia. (Chapter 14)
respiratory alkalosis exists when low $PaCO_2$ decreases dissolved CO_2, raising the pH and leading to alkalemia. (Chapter 14)
respiratory alternans alternation between use of the diaphragm for short periods and use of the accessory muscles to breathe, indicative of end-stage respiratory muscle fatigue. (Chapters 16 and 45)
respiratory bronchioles bronchioles approximately 0.4 mm in diameter that have walls formed largely from flattened squamous epithelia and a thin outer layer of connective tissue. (Chapter 9)
respiratory care the healthcare discipline that specializes in the promotion of optimal cardiopulmonary function and health. Also called *respiratory therapy*. (Chapter 1)
***Respiratory Care* journal** a professional journal with an editorial board and editor in chief who are researchers and either respiratory therapists or physicians. (Chapter 2)
respiratory care practitioner a health professional with special training and experience in the treatment and rehabilitation of patients with

respiratory disorders. The respiratory care practitioner typically does not diagnose but must be able to assess patients in various clinical settings. (Chapter 1)

respiratory distress syndrome (RDS) a condition of respiratory distress in newborns, usually caused by the inadequate production (owing to immaturity) of surfactant. (Chapter 33)

respiratory hygiene/cough etiquette a state in which the respiratory tract is kept as free as possible from contaminants such as bacteria and other microbes. (Chapter 4)

respiratory inductive plethysmograph a device that, by measuring changes in the diameter of the chest and abdomen, can estimate inhaled and exhaled tidal volume. (Chapter 52)

respiratory quotient (RQ) the relationship between oxygen utilization and carbon dioxide production, normally equal to 0.8. (Chapter 23)

respiratory therapist (RT) a graduate of a Council on Accreditation of Allied Health Education Programs/Committee on Accreditation for Respiratory Care (CAAHEP/CoARC) accredited school designed to qualify the graduate for the registry examination of the National Board for Respiratory Care (NBRC). (Chapter 1)

respiratory therapy any treatment that maintains or improves the function of the respiratory tract. (Chapter 1)

resting energy expenditure (REE) caloric needs of the body estimated from O_2 consumption and CO_2 production, usually expressed in kcal/24 hour. (Chapter 23)

restrictive pulmonary disease **a pulmonary disease that primarily causes a** restriction of lung expansion. (Chapter 20)

retinol-binding protein a protein that is responsible for transporting vitamin A from the liver to other tissue. (Chapter 23)

retinopathy of prematurity (ROP) an abnormal ocular condition that occurs in some premature or low-birth-weight infants who receive O_2. Previously called *retrolental fibroplasias*. (Chapters 42 and 54)

retractions repetitive sinking inward of the skin around the chest cage with each inspiratory effort. (Chapter 16)

reverse triggering stimulation of the respiratory center to inspire after the delivery of a controlled positive e

Reynolds number a calculated valve that helps to determine if gas flow will be laminar or turbulent. (Chapter 6)

right-to-left shunt anatomic bypass in which blood flows from the venous to the arterial side of the circulation, bypassing the lungs; this lowers both the O_2 content and PO_2 of the arterial blood. (Chapter 12)

right ventricular heart failure poor pumping of the heart involving the right ventricle. (Chapter 31)

rise time the time it takes for the ventilator flow to reach its maximum flow. Rise time is a control variable available in all pressure-targeted modes. Functionally it changes the slope of the flow increase from baseline to maximum. (Chapter 48)

rocking bed a bed that rocks back and forth, moving the abdominal contents up and down facilitating inspiration and expiration. (Chapter 50)

root-cause analysis a process by which the underlying primary, secondary, and other notable causes of a medical error or other safety issue are identified, followed by the creation and implementation of an action plan. (Chapter 7)

rule of double effect a rule derived from the ethical principle of nonmaleficence, recognizing that an act can have both good and bad effects, and that to achieve the good effect, the bad effect must be tolerated. (Chapter 58)

rule utilitarianism moral reasoning approach based not on which act has the greatest utility, but on which rule would promote the greatest good if it were generally followed. (Chapter 5)

S

saccular stage the stage at which more terminal bronchioles and their associated acini form and develop from 26 weeks to birth. (Chapter 9)

sarcoidosis a chronic disorder of unknown origin characterized by the formation of tubercles of nonnecrotizing epithelioid tissue. (Chapter 26)

saturated solution a solution in which the solvent contains the maximum amount of solute it can take up. (Chapter 13)

scholarship the sharing of methods and findings of existing research and knowledge through presentations at professional events as well as publication in textbooks and journal articles. (Chapter 8)

scientific experiment a systematic evaluation of a specific substance, process or treatment that determines if the substance, process or treatment is legitimate. (Chapter 8)

scientific method usually thought of as a series of steps that lead from question to answer (and then usually to more questions). (Chapter 8)

scintigraph a photograph showing the distribution and intensity of radioactivity in various tissues and organs after administration of a radiopharmaceutical. (Chapter 40)

scope of practice the application of technology and the use of protocols across all care sites including but not limited to the hospital, clinic, physician's office, rehabilitation facility, skilled nursing facility and patient's home. (Chapter 2)

screening preliminary procedure, such as a test or examination, to detect the most characteristic sign or signs of a disorder that may require further investigation. (Chapter 32)

secondary spontaneous pneumothorax pneumothorax that occurs because of underlying lung disease. (Chapter 27)

sedimentation primary mechanism for the deposition of particles 1 to 5 mm in diameter in the central airways, when particles slow and settle out of suspension. (Chapter 40)

segs segmented neutrophils, the mature form of circulating neutrophils. (Chapter 17)

semilunar valves valves that separate the ventricles from their arterial outflow tracts, the pulmonary artery, and the aorta. (Chapter 10)

sensible measurable, as of water loss (e.g., losses from urine and the gastrointestinal tract). (Chapter 13)

sensitivity a test's ability to detect disease or its absence. (Chapter 20)

sensorium general term referring to the locus of a patient's consciousness. (Chapter 16)

serous pericardium the inner serous portion of the myocardium consisting of 2 layers the visceral and parietal layers. (Chapter 10)

servo targeting scheme a ventilator controlling scheme that continually evaluates the ventilator response and readjusts operation until it is on target. (Chapter 46)

servo-controlled heating system in a humidifier, heating unit that monitors the temperature of gas delivered to the patient, adjusting the power to the heater based on the difference between the temperature setting and the temperature monitored by a thermistor probe placed downstream from the humidifier at or near the patient airway connection. (Chapter 39)

severe obesity the state of having a body mass index greater than 40 kg/m^2. (Chapter 30)

shock a condition in which perfusion to vital organs is inadequate to meet metabolic needs; includes hypovolemic, cardiogenic, septic, anaphylactic, and neurogenic forms. (Chapter 16)

sickle cell hemoglobin the presence of hemoglobin S, causing the hemoglobin cell to form a sickle shape. (Chapter 12)

signs objective manifestations of illness, such as an increased respiratory rate and heartbeat. (Chapter 16)

silhouette in imaging, a sign obscuring of the margins of adjacent structures because they have the same density. (Chapter 21)

silicosis a lung disorder caused by continued long-term exposure to the dust of an inorganic compound, silicon dioxide, which is found in sands, quartzes, and many other stones; chronic silicosis is marked by widespread fibrotic nodular lesions in both lungs. (Chapter 26)

situs inversus a condition in which a patient's chest or abdominal contents are reversed. (Chapter 21)

Six Sigma a set of management techniques intended to improve business processes by reducing the probability of errors or defects. (Chapter 3)

six or twelve-minute walk a test that involves walking and an established protocol to assess a patient's level of physical conditioning. (Chapter 56)

skilled nursing facility (SNF) an institution or part of an institution that meets the criteria for accreditation established by the sections of the Social Security Act that determine the basis for Medicaid and Medicare reimbursement for skilled nursing care. Such care includes rehabilitation and various medical and nursing procedures. (Chapter 57)

skinfold measurement a measurement used to determine the percent body fat. (Chapter 23)

slander any words spoken with malice that are untrue and prejudicial to the reputation, professional practice, commercial trade, office, or business of another person. (Chapter 5)

sleep-disordered breathing periods of an absence of attempts to breathe during sleep. (Chapter 34)

sleep-related hypoventilation a syndrome in which CO_2 increases during sleep. (Chapter 33)

small cell cancer a malignant, usually bronchogenic epithelial neoplasm consisting of small, tightly packed round, oval, or spindle-shaped epithelial cells that stain darkly and contain neurosecretory granules and little or no cytoplasm. Many malignant tumors of the lung are of this type. Also called oat cell carcinoma or small cell carcinoma. (Chapter 32)

small for gestational age (SGA) a new born infant whose weight is low for his/her gestational age. (Chapter 54)

sniff nasal inspiratory pressure the amount of inspiratory pressure a patient can generate during the process of sniffing. (Chapter 45)

Society of Critical Care Medicine the primary American professional organization promoting critical care medicine. (Chapter 2)

soft palate structure composed of mucous membrane, muscular fibers, and mucous glands suspended from the posterior border of the hard palate forming the roof of the mouth. (Chapter 9)

sol layer the inner layer of mucus, which is much more fluid-like. (Chapter 9)

solitary pulmonary nodule (SPN) a pulmonary parenchymal opacity smaller than 3 cm in diameter that is totally surrounded by aerated lung. (Chapter 21)

solubility coefficient (gas) volume of gas that can be dissolved in 1 mL of a given liquid at standard pressure and specified temperature. (Chapter 6)

solute substance dissolved in a solution. (Chapter 13)

solution mixture of one or more substances dissolved in another substance. The molecules of each of the substances disperse homogeneously and do not change chemically. A solution may be a gas, a liquid, or a solid. (Chapter 13)

solvent any liquid in which another substance can be dissolved. (Chapter 13)

specific gravity ratio of the density of a substance to the density of another substance accepted as a standard. The usual standard for liquids and solids is water. A liquid or solid with a specific gravity four times the density of water at the same temperature. Hydrogen is the usual standard for gases. (Chapter 6)

specificity addresses a test's ability to detect disease or the absence of it. (Chapter 20)

spectrophotometry procedure for the measurement of color in a solution by determining the amount of light absorbed in the ultraviolet, infrared, or visible spectrum, widely used in clinical chemistry to calculate the concentration of substances in solution. (Chapter 19)

spiral arteries small arteries that temporality supply blood to the endometrium of the uterus during the luteal phase of the menstrual cycle. (Chapter 9)

spirometer sometimes used as a generic term for all volume-measuring and flow-measuring devices. (Chapter 20)

spirometry the measurement of air entering and leaving the lungs—includes measurement of several values of forced airflow and volume during inspiration and expiration. (Chapter 20)

splinting the process of immobilizing, restraining, or supporting a body part. (Chapter 44)

spontaneous awaking trial a trial of sedation removal or reduction performed prior to a spontaneous breathing trial. (Chapter 53)

spontaneous breath ventilatory support breaths initiated and ended by the patient. (Chapter 46)

spontaneous breathing trial (SBT) a trial of spontaneous breathing independent of the ventilator. (Chapter 53)

sporicidal a substance that is destructive to the spore form of bacteria. (Chapter 4)

sputum mucus from the respiratory tract that has passed through the mouth. (Chapter 16)

squamous cell carcinoma a type of lung cancer characterized by cells that appear plate-like. (Chapter 32)

ST-segment elevation myocardial infarction (STEMI) a myocardial infarction demonstrating ECG changes, specifically an elevation of the ST-segment of the ECG. (Chapter 18)

staging system See *TNM staging*. (Chapter 32)

standard bicarbonate plasma concentration of HCO_3^- measured in milli-equivalents per liter that would exist if PCO_2 were normal (40 mm Hg). (Chapter 14)

standard precautions guidelines recommended by the US Centers for Disease Control and Prevention to reduce the risk of transmission of blood-borne and other pathogens in hospitals. Standard precautions apply to (1) blood; (2) all body fluids, secretions, and excretions excluding sweat regardless of whether they contain blood; (3) nonintact skin; and (4) mucous membranes. (Chapter 4)

Starling equilibrium the filtration of fluid across a membrane as a result of equilibration of osmotic and hydrostatic forces across the membrane. (Chapter 13)

stenosis narrowing of a valve or vessel. (Chapters 10 and 37)

sterilization complete destruction of all microorganisms, usually by heat or chemical means. (Chapter 4)

sternal angle the fused connection between the manubrium and the body of the sternum, also known as the angle of Louis. (Chapter 9)

sternum elongated flattened bone forming the middle portion of the anterior thorax. (Chapter 9)

stomata small holes within the parietal pleura that are the main route whereby pleural fluid can exit. (Chapter 27)

STOP-BANG Assessment Tool a quick bedside process to evaluate the presence of sleep apnea. (Chapter 34)

STPD standard temperature and pressure dry; condition of a volume of gas at 0°C and 760 mm Hg and containing no water vapor (dry). It should contain a calculable number of moles of a particular gas. (Chapter 6)

strain-gauge pressure transducers a pressure-measuring device that records pressures by the expansion and contraction of a flexible metal diaphragm connected to electrical wires. (Chapter 6)

stress index an index used to determine whether, during mechanical controlled inhalation, there is overdistention or recruitment of collapsed lung. This is determined by the slope change in the airway pressure curve during volume-controlled square-wave ventilation. (Chapter 52)

strict liability a theory in tort law that can be used to impose liability without fault, even in situations where injury occurs under conditions of reasonable care. The most common cases of strict liability involve the use of dangerous products or techniques. (Chapter 5)

stridor a high-pitched, continuous type of adventitious lung sound heard from the upper airway. (Chapter 16)

stroke a condition characterized by the sudden onset of a neurologic deficit. (Chapter 33)

stroke volume the volume of blood ejected by the left ventricle during each contraction. (Chapter 10)

study subjects people (or animals or even inanimate objects) that meet the entry criteria and are enrolled in the study. (Chapter 8)

subatmospheric pressure pressure below ambient. (Chapter 11)

subcutaneous emphysema an accumulation of air in the subcutaneous tissues owing to leakage from the lung. (Chapter 16)

sublimation term describing the phase transition from a solid to a vapor without becoming a liquid as an intermediary form. (Chapter 6)

substituted judgment judgements or decision made by a third party based on that individuals knowledge of the desires of the patient. (Chapter 58)

suctioning process of mechanically aspirating airway secretions. (Chapter 37)

sudden infant death syndrome (SIDS) the leading cause of death in infants less than 1 year old in the United States. Commonly called *crib death*. (Chapter 35)

sulci surface grooves at the boundaries of the heart chambers. (Chapter 10)

superobesity the state of having a body mass index of greater than 50 kg/m^2. (Chapter 30)

supervisors/lead therapists often more experienced, more highly credentialed therapists who are more highly educated. (Chapter 2)

supplemental oxygen O_2 delivered at concentrations exceeding 21% to increase the amount of O_2 circulating in the blood. (Chapter 25)

suprasternal notch a shallow depression that forms from the superior edge of the manubrium. (Chapter 9)

surface tension the tendency of a liquid to minimize the area of its surface by contracting. This property causes liquids to rise in a capillary tube; it also affects the exchange of gases in the pulmonary alveoli and alters the ability of various liquids to wet another surface. (Chapters 6 and 11)

surfactant a surface-acting agent that forms a monomolecular layer over pulmonary alveolar surfaces. These agents prevent alveolar collapse at lower lung volumes by reducing alveolar surface tension. (Chapter 54)

surgical resection the partial removal of an organ or tissues by surgical means. (Chapter 32)

surveillance a (bacteriologic) ongoing process designed to ensure that infection control procedures are working; generally involves equipment, microbiologic identification, and epidemiologic investigation. (Chapter 4)
suspension dispersion of large particles suspended in a fluid medium; without physical agitation, the particles eventually settle out. (Chapter 13)
Swan-Ganz catheter a catheter that is positioned in the pulmonary artery to measure pressures in the heart and pulmonary circulation and can be used to determine the patient's circulatory status. (Chapter 52)
sweat chloride an analysis of the sodium chloride content of sweat used in the diagnosis of cystic fibrosis. (Chapter 17)
sweep flow the flow of gas in a direction opposite the flow of blood through an extracorporeal membrane oxygenation oxygenator to remove CO_2 and add O_2. Normally the gas is O_2 but on occasion small amounts of CO_2 are added. (Chapter 51)
symptoms the sensations or subjective experiences of some aspect of an illness, such as breathlessness. (Chapter 16)
synchronized cardioversion the delivery of countershock synchronized with the heart's electrical activity. (Chapter 38)
synchronous intermittent mandatory ventilation (SIMV) a mode of ventilatory support using periodic assisted ventilation with spontaneous breathing in between. Assisted breaths are responsive to patient demand. (Chapters 49 and 53)
syncope temporary unconsciousness; fainting. (Chapter 16)
systematic error nonrandom statistical error that affects the mean of a population of data and defines the bias between the means of two populations. (Chapters 19 and 52)
systolic pressure peak blood pressure occurring in the arteries during ventricular contraction. (Chapter 16)
systemic vasodilation relaxation of the arterial blood vessels in the systemic circulation. (Chapter 31)

T

T wave a wave following the QRS complex on an ECG that donates repolarization of the ventricles of the heart. (Chapter 10)
tachycardia an abnormally elevated heart rate. (Chapter 16)
tachyphylaxis a phenomenon in which the repeated administration of some drugs results in a marked decrease in effectiveness. (Chapter 36)
tachypnea an abnormal elevation of breathing rate. (Chapter 16)
tamponade (cardiac) the accumulation of blood in the pericardial sac, increasing pericardial pressure and reducing cardiac output. (Chapter 51)
target heart rate the heart rate achieved at 65% of a patient's maximum O_2 consumption during an exercise evaluation, used for aerobic conditioning. (Chapter 56)
targeting scheme the approach used by a particular mode to achieve the various targets active during ventilation. (Chapter 46)
telemedicine the use of electronic and telecommunication technologies to support healthcare at a geographically different location from that of the patient, thus increasing access to specialty patient care. (Chapter 7)
telemonitoring the monitoring of a patient's clinical condition through a computerized connection to a healthcare facility. (Chapter 7)
telerehabilitation the use a combination of a personal computer or device, a reliable internet connection, a patient monitoring module, and relatively low-cost exercise equipment to allow patients to participate in pulmonary rehabilitation. (Chapter 56)
tension the pressure exerted by gases dissolved in liquids. (Chapter 6)
tension pneumothorax air in the pleural space that exceeds atmospheric pressure, causing outward expansion of the ribs, downward depression of the diaphragm, mediastinal shift, and hypotension. (Chapters 27, 30 and 48)
terminal bronchioles the smallest conducting airways that supply gas to the respiratory zone of the lung. (Chapter 9)
tetralogy of Fallot a congenital cardiac anomaly that consists of four defects: pulmonic stenosis, ventricular septal defect, malposition of the aorta so that it arises from the septal defect or the right ventricle, and right ventricular hypertrophy. (Chapter 35)
thebesian veins veins in the thoracic in which flow through them is part of the normal anatomic shunting of blood past the heart. (Chapter 10)
therapeutic index difference between the minimum therapeutic and minimum toxic concentrations of a drug. (Chapter 40)
thermal conductivity a measure of gas concentrations in a sample calculated by detecting the rate at which different gases conduct heat. (Chapter 6)
thermodynamics the science of the interconversion of heat and work. (Chapter 6)
thiosulfate a compound ($S_2O_3^{2-}$) that is an oxyanion of sulfur used in treating carbon monoxide poisoning. (Chapter 30)
thoracentesis surgical perforation of the chest wall and pleural space with a needle for diagnostic or therapeutic purposes or for the removal of a specimen for biopsy. (Chapter 27)
thoracic flap or flail chest two or more ribs broken in two or more places, creating an unstable segment of the chest wall. (Chapter 30)
thoracic gas volume (TGV) a technique that measures lung volume. (Chapter 20)
thoracic inlet the opening into the thorax formed by first ribs and the upper sternum. (Chapter 9)
thoracic pump a term used to describe the negative and positive intrathoracic pressure changes during breathing that assist venous return of blood to the heart. (Chapter 10)
Thorpe tube a variable- orifice constant-pressure flowmeter. (Chapter 41)
thrill a fine palpable vibration felt accompanying a cardiac or vascular murmur. (Chapter 16)
thrombocytes the smallest cells in the blood; they are formed in the red bone marrow and some are stored in the spleen. Platelets are disc shaped, contain no hemoglobin, and are essential for the coagulation of blood and in maintenance of hemostasis. (Chapter 17)
thrombocytopenia an abnormal condition in which the number of blood platelets is reduced, usually associated with neoplastic diseases or an immune response to a drug. (Chapter 17)
thyroid cartilage a cartilage forming most of the upper portion of the larynx, generally referred to
as the Adam's apple a common term for the larynx. (Chapter 9)
tidal pressure tidal volume scaled by elastance or compliance. (Chapter 46)
tidal volume (V_T) volume of air that is inhaled or exhaled from the lungs during effortless breath. (Chapters 11, 20)
time constant mathematical expression describing the relative efficacy of lung unit filling and emptying and computed as the product of compliance times resistance (measured in seconds). (Chapters 11, 46 and 47)
tissue oxygen sensing the monitoring of the O_2 saturation or PO_2 at the tissue level. (Chapter 52)
tonsillectomy removal of the tonsils. (Chapter 9)
tort a legal wrong committed on a person or property independent of contract. (Chapter 5)
total bilirubin a substance produced by the liver from the breakdown of destroyed red blood cells (RBCs). (Chapter 17)
total lung capacity (TLC) the total amount of gas in the lungs after a maximum inspiration. (Chapter 20)
trachea the large main intrathoracic airway. (Chapter 9)
tracheal malacia softening of the tracheal cartilages. (Chapters 48)
tracheal stenosis a narrowing of the tracheal diameter. (Chapter 48)
tracheal tugging the effect of an aortic aneurysm in which the trachea is pulled downward with each heart contraction. (Chapter 16)
tracheoesophageal fistula a congenital malformation or an abnormality associated with disease in which there is an abnormal tube-like passage between the trachea and the esophagus. (Chapters 37 and 48)
tracheoinnominate artery fistula a fistula (connection between the trachea and the innominate artery). (Chapter 37)
tracheomalacia softening of the cartilaginous rings, which causes collapse of the trachea during inspiration and expiration. (Chapter 37)
tracheostomy an opening through the neck into the trachea, through which an indwelling tube may be inserted. (Chapter 37)
tracheostomy tubes artificial airways that are surgically placed directly into the trachea. (Chapter 37)
tracheotomy procedure by which an incision is made into the trachea through the neck below the larynx to gain access to the lower airways. (Chapter 37)
transairway pressure the difference between airway pressure and alveolar pressure. (Chapters 11 and 47)
transairway pressure gradient the pressure gradient between the mouth and alveoli that moves air into and out of the lung. (Chapter 11)

transalveolar pressure the difference between alveolar pressure and pleural pressure. (Chapter11)

transbronchial biopsy a lung tissue specimen obtained through a needle insertion, bronchoscopy, or surgery. (Chapter 22)

transbronchial needle aspiration the technique of sampling lung tissue through a bronchoscope that involves passing a thin needle through a bronchus. (Chapters 22 and 32)

transcellular fluid fluid that normally moves from the extravascular space into the cells. (Chapter 13)

trans–chest wall pressure the difference between the pleural space and the body surface. Also called transthoracic pressure. (Chapters 11 and 47)

transdiaphragmatic pressure (P_{di}) the pressure change across the diaphragm associated with breathing. (Chapter 47)

transient tachypnea of the newborn (TTN) the periodic increase in respiratory rate that is commonly observed in low-birth-weight infants. (Chapter 35)

transposition of the great arteries a congenital cardiac condition characterized by an anatomic abnormality in which the aorta arises from the right ventricle and the pulmonary artery arises from the left ventricle. (Chapter 35)

transpulmonary of or pertaining to the difference in a parameter (e.g., pressure) between the alveoli and pleural space. (Chapter 10)

transpulmonary pressure the difference between the alveolar pressure and intrapleural pressure of the lungs. (Chapters 47, 49 and 52)

transpulmonary pressure difference the difference between intraalveolar and intrapleural pressure, or the pressure acting across the ling from the pleural space to the alveoli. (Chapter 11)

transpulmonary pressure gradient the pressure gradient between the mouth and the pleural space that allows inspiration and expiration. Normally positive at end expiration and negative at end inspiration. (Chapter 11)

transrespiratory pressure the difference between the alveolar pressure and pressure on the body surface. (Chapters 11 and 47)

transthoracic needle biopsy the technique of obtaining a biopsy specimen of lung tissue by passing a needle into the chest, often guided by imaging. (Chapter 32)

transthoracic pressure of or pertaining to the difference in a parameter (such as pressure) between the pleural space and body surface. (Chapter 47)

transthoracic pressure difference (P_{TT}) the difference between the pleural space and the body surface. Also called trans–chest wall pressure. (Chapter 11)

transthyretin a transport protein in the serum and cerebrospinal fluid that carries the thyroid hormone (T4) and retinal binding protein bound to retinal. (Chapter 23)

transtracheal oxygen therapy (T_{TOT}) the administration of O_2 via a low-flow catheter inserted directly into the trachea. (Chapter 57)

transudate the fluid that moves out of a cell or tissue as a result of a concentration/pressure gradient. (Chapter 30)

transudative pleural effusion a pleural effusion low in protein and lactate dehydrogenase, usually caused by congestive heart failure, nephrosis, or cirrhosis. (Chapter 27)

traumatic brain injury a general term referring to any class of either focal or diffuse lesions that can result from head trauma; these lesions include injury to the nerve body (axon), hypoxic brain damage, swelling, hemorrhage, contusions, laceration, and infection. (Chapter 33)

Trendelenburg position the position in which the head is low and the body and legs are on an inclined plane. (Chapter 50)

trepopnea shortness of breath experienced by a patient while side lying. (Chapter 16)

tricuspid valve the valve on the right side of the heart. (Chapter 10)

trigger the inspiratory force a patient must generate to initiate a breath on a mechanical ventilator. (Chapter 46)

trigger asynchrony a lack of coordination between the patient's inspiratory effort and the response of the mechanical ventilator. (Chapter 48)

trigger delay a delay in ventilator response to a patient's inspiratory effort. (Chapter 48)

tripod sign the use of the elbows on a hard surface to support the movement of the chest wall and lung during breathing. This position gives a mechanical advantage to the accessory breathing muscles of the upper chest and neck. (Chapter 16)

troponin a protein in the striated cell ultrastructure that modulates the interaction between actin and myosin molecules. It is believed to be part of the calcium-binding complex of the thin myofilaments. The level of blood troponin is used to identify the presence of a myocardial infarction. (Chapter 17)

troponin I a protein similar to CPK-2; troponin I levels peak 12 to 16 hours after a myocardial infarction. It is associated with cardiac muscle damage. (Chapter 17)

true ribs the first seven ribs on each side of the thorax, called true ribs. (Chapter 9)

true-experimental experiment that attempts to prove the null hypothesis incorrect, that is that there is a difference between two treatments, substances, or devices. (Chapter 8)

tuberculosis a chronic granulomatous infection caused by an acid-fast bacillus, *Mycobacterium tuberculosis*. It is generally transmitted by the inhalation or ingestion of infected droplets and usually affects the lungs, although infection of multiple organ systems occurs. (Chapter 24)

tumor, node, metastasis (TNM) staging staging system based on a size of the tumor *(T)*, the presence and position of abnormal lymph nodes *(N)*, and the presence or absence of metastasis (or spread beyond the primary tumor site) *(M)*. (Chapter 32)

turbinates bony structures that extend from the lateral walls of the interior nasal passages. (Chapter 9)

turbulent flow flow of a fluid that does not occur in a straight line; flow in which molecules tumble over each other. (Chapter 6)

type I pneumocyte cuboidal, secretory epithelia that line the blind tubules of the acinus cells. (Chapter 9)

type II pneumocyte pneumocyte granular cells that are highly active and form part of the lining of the alveoli. These cells secrete surfactant and other substances. (Chapter 9)

U

ultrasonic nebulizer (USN) an aerosol generator in which an electrical signal is used to produce high-frequency vibrations in a container of fluid. The vibrations break up the fluid into aerosol particles. (Chapter 39)

ultrasound, diaphragm the actual diaphragm of an ultrasonic nebulizer that transmits ultrasonic waves to a liquid to form an aerosol. (Chapter 53)

ultrathin bronchoscopy a bronchoscope that has a smaller than usual diameter and circumference to permit insertion into small airways. (Chapter 22)

upper airway stimulation a newer way of treating obstructive sleep apnea which involves implantation of a nerve stimulator to maintain upper airway patency. (Chapter 34)

upper confidence a term used to define upper acceptable limit of a value during a statistical analysis. (Chapter 3)

upstream reference to a point closer to the source in a stream of flowing fluid. (Chapter 41)

uvula a small cone-shaped process suspended in the mouth from the middle of the posterior border of the soft palate. (Chapter 9)

uvulopalatopharyngoplasty (UVPPP) a surgical procedure used in treating severe obstructive sleep apnea, which involves shortening of the soft palate and removal of the uvula and tonsils. (Chapter 34)

V

v wave a rapid decrease in atrial pressures. (Chapter 10)

vagovagal reflexes reflexes caused by the stimulation of parasympathetic receptors in the airways that can result in laryngospasm, bronchoconstriction, hyperpnea, and bradycardia; often associated with mechanical stimulation, as during procedures such as tracheobronchial aspiration, intubation, or bronchoscopy. (Chapter 15)

validity meaningfulness, or the ability to accurately measure what an instrument or procedure was intended to measure. (Chapter 20)

vallecula the anatomic depression immediately beyond the base of the tongue. (Chapter 9)

value-based purchasing (VBP) a system of reimbursement by the government Centers for Medicare and Medicaid Services to hospitals and healthcare providers that is partially based on their ability to meet a predefined set of standards. (Chapter 7)

values, beliefs, and preferences what an individual considers an acceptable ethical standard based on their prior experiences, knowledge and cultural beliefs. (Chapter 58)

van der Waals forces forces that maintain a solid's shape because their atoms are kept in place by strong mutual attraction. (Chapter 6)

vaporization a process whereby matter in its liquid form is changed into its vapor or gaseous form. (Chapter 6)

vasoconstriction narrowing of the blood vessels. (Chapter 10)

vasodilation widening or distention of blood vessels, particularly arterioles, usually caused by nerve impulses or certain drugs that relax smooth muscle in the walls of the blood vessels. (Chapter 10)

vasopressor a medication that causes constriction of the blood vessels, generally used to increase blood pressure. (Chapter 36)

VCV acronym for *volume-controlled ventilation,* a mode of ventilatory support in which volume (or flow × time) serves as the cycle variable. (Chapters 46 and 49)

venoarterial (VA) an approach to ECMO in which blood is removed from the body on the venous side of circulation and returned on the arterial side, used to support heart function. (Chapter 51)

venous admixture mixing of venous blood with arterial blood, resulting in a decrease in the O_2 content of the latter; occurs in anatomic and physiologic shunting. (Chapters 12 and 52)

venous reservoir the capacity of the venous system to pool large volumes of blood. (Chapter 51)

venous thromboembolism (VTE) a clot that spreads from one venous bed to another, such as from the leg veins to the lung. (Chapter 28)

venovenous (VV) approach to ECMO in which blood is removed from the venous circulation but also returned to the venous circulation used to manage lung disease. (Chapter 51)

ventilation/perfusion (V/Q) ratio ratio of pulmonary alveolar ventilation to pulmonary capillary perfusion, both measured quantities being expressed in the same units. (Chapter 12)

ventilation/perfusion (V/Q) scan a scan of the lungs and pulmonary circulation, thus distribution of ventilation is identified but also distribution of perfusion providing the relationship between ventilation and perfusion of the whole lung and regions of the lung. (Chapter 28)

ventilator-associated events a method of determining the quality of mechanical ventilation by evaluating changes associated with the management of hypoxemia. (Chapter 24)

ventilator-associated pneumonia a lower respiratory tract infection that develops more than 48 to 72 hours after endotracheal intubation. (Chapter 24)

ventilator-induced diaphragmatic dysfunction a very common condition among critically ill patients that results in weaning failure and long-term respiratory impairment. (Chapter 33)

ventilator-induced lung injury (VILI) lung injury that occurs as a result of excessive pressure and/or volume during mechanical ventilation. (Chapter 29)

ventilatory threshold during exercise, the point at which increased levels of lactic acid result in increased CO_2 production and minute ventilation; the respiratory quotient (RQ) equals or exceeds 1.0, indicating that CO_2 production equals or exceeds O_2 consumption; at this point, metabolism becomes anaerobic, decreasing energy production and increasing muscle fatigue. (Chapter 56)

ventral respiratory groups (VRGs) groupings of cells in the medulla oblongata that are active in controlling both inspiration and expiration. (Chapter 15)

Venturi effect the flow of a gas through a constriction and the subsequent drop in pressure at the constriction. (Chapter 6)

veracity a principle that binds the healthcare provider and the patient to tell the truth, creating an environment of trust and the mutual sharing of information. (Chapter 5)

very low birth weight (VLBW) describing a newborn who weighs less than the 95% percentile of weight for newborns. (Chapter 54)

virtue ethics the viewpoint that asks what a virtuous person would do in a similar circumstance; it is based on personal attributes of character or virtue rather than on rules or consequences. (Chapter 5)

virucidal an agent that destroys or inactivates viruses. (Chapter 4)

visceral pleura a thin membrane covered by mesothelial cells that covers the entire surface of the lung, dipping into the lobar fissures. (Chapters 9 and 27)

viscosity internal force that opposes flow of a fluid, either a liquid or a gas. (Chapter 6)

vital capacity (VC) the total amount of air that can be exhaled after a maximum inspiration; the sum of the inspiratory reserve volume, tidal volume, and expiratory reserve volume. (Chapters 20 and 52)

volatile acid an acid that can be excreted in its gaseous form; physiologically, carbonic acid is a volatile acid; approximately 24,000 mmol/L CO_2 is eliminated from the body daily via normal ventilation. (Chapter 14)

voltage the expression of electromotive force in terms of volts. (Chapter 3)

volume-median diameter (VMD) the median diameter of an aerosol particle measured in units of volume. (Chapter 40)

volume support pressure-limited ventilation in which tidal volume is targeted. (Chapter 49)

volumetric capnography a way of measuring the volume of exhaled carbon dioxide to assess a patient's ventilatory status. (Chapter 19)

volutrauma alveolar overdistention and damage caused by ventilation with high peak inflation pressures. (Chapters 29 and 47)

W

water vapor pressure the pressure exerted by water in its gaseous state. (Chapter 6)

weight-per-volume (W/V) solution defined as the weight of solute per volume of solution. (Chapter 13)

wet drowning drowning due to the entry into the lungs of a large amount of water. (Chapter 30)

wheezes high-pitched, continuous type of adventitious lung sound. (Chapter 16)

withholding and withdrawing life-sustaining treatment based on the patient's wishes either discontinuing or not initiating treatment that is considered life-sustaining. (Chapter 58)

work of breathing (WOB) the amount of force needed to move a given volume into the lung with a relaxed chest wall; mathematically, work is the integral of pressure × volume. (Chapter 45)

X

xiphoid process the pointed lower portion of the sternum. (Chapter 9)

Z

zone valve on/off piping valve that controls medical gas distribution to a prespecified zone of a building. (Chapter 41)

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ABBREVIATIONS

Δ	change in
μ	micro-
μg	microgram
μm	micrometer
μV	microvolt
A	alveolar
a	arterial
AARC	American Association for Respiratory Care
ABG(s)	arterial blood gas(es)
A/C	assist/control
ACBT	active cycle of breathing technique
ADH	antidiuretic hormone
AIDS	acquired immunodeficiency syndrome
AII	airborne infection isolation
ALI	acute lung injury
ALV	adaptive lung ventilation
ANP	atrial natriuretic peptide
AOP	apnea of prematurity
APRV	airway pressure release ventilation
ARDS	acute respiratory distress syndrome
ARF	acute respiratory failure
ASV	adaptive support ventilation
ATC	automatic tube compensation
ATM	atmospheric pressure
ATPD	ambient temperature and pressure, dry
ATPS	ambient temperature and pressure, saturated with water vapor
auto-PEEP	unintended positive end expiratory pressure
AV	arteriovenous
AVP	arginine vasopressin
B	barometric
BAC	blood alcohol content
BE	base excess
bilevel PAP	bilevel positive airway pressure
BiPAP	registered trade name for bilevel PAP device
BP	blood pressure
BPD	bronchopulmonary dysplasia
BSA	body surface area
BTPS	body temperature and pressure, saturated with water vapor
BUN	blood urea nitrogen
C	compliance
c	capillary
C′	pulmonary-end capillary
°C	degrees of Celsius
C_aO_2	arterial content of oxygen
$C(a-\bar{v})O_2$	arterial-to-mixed venous oxygen content difference
CC	closing capacity
cc	cubic centimeter
$Cc'O_2$	content of oxygen of the ideal alveolar capillary
C_D	dynamic characteristic or dynamic compliance
CDC	U.S. Centers for Disease Control and Prevention
CDH	congenital diaphragmatic hernia
CDS	clinical decision support
CHF	congestive heart failure
CI	cardiac index
CINAHL	Cumulative Index to Nursing and Allied Health Literature
C_L	lung compliance (also C_{Lung})
cm	centimeters
cm H_2O	centimeters of water pressure
CMS	Centers for Medicare and Medicaid Services
CMV	controlled (continuous) mandatory or mechanical ventilation
CNS	central nervous system
CO	carbon monoxide
CO_2	carbon dioxide
CoARC	Committee on Accreditation for Respiratory Care
COHb	carboxyhemoglobin
COLD	chronic obstructive lung disease
COPD	chronic obstructive pulmonary disease
CPAP	continuous positive airway pressure
CPG	Clinical Practice Guideline
CPOE	computerized physician order entry
CPP	cerebral perfusion pressure
CPPB	continuous positive pressure breathing
CPPV	continuous positive pressure ventilation
CPR	cardiopulmonary resuscitation
CPT	chest physical therapy
CPU	central processing unit
CQI	continuous quality improvement
CRCE	continuing respiratory care education
C_s	static compliance
CSF	cerebrospinal fluid
CSV	continuous spontaneous ventilation
CT	computed tomography
C_T	tubing compliance (also C_{tubing})
CV	closing volume
CvO_2	venous oxygen content
$C\bar{v}O_2$	mixed venous oxygen content
CVP	central venous pressure
D	diffusing capacity
d	diameter
DC	discharges, discontinue
DC-CMV	dual controlled–continuous mandatory ventilation
DC-CSV	dual controlled–continuous spontaneous ventilation
DIC	disseminated intravascular coagulation
DLCO	diffusing capacity of the lung
Dm	diffusing capacity of the alveolocapillary membrane
DO_2	oxygen delivery
DPAP	demand positive airway pressure
DPPC	dipalmitoyl phosphatidylcholine
DVT	deep venous thrombosis
E	elastance
EAdi	electrical activity of the diaphragm
$ECCO_2R$	extracorporeal carbon dioxide removal
ECG	electrocardiogram
ECLS	extracorporeal life support
ECMO	extracorporeal membrane oxygenation
EDV	end-diastolic volume
EE	energy expenditure
EEP	end expiratory pressure
EHR	electronic health record
EIB	exercise-induced bronchospasm
EMR	electronic medical record
EPAP	end positive airway pressure
ERV	expiratory reserve volume
ET	endotracheal tube
E_TCO_2 or $etCO_2$	end-tidal CO_2
F	fractional concentration of a gas
°F	degrees Fahrenheit
f	respiratory frequency, respiratory rate
FDA	U.S. Food and Drug Administration
FEF	forced expiratory flow

FEF_{max}	maximal forced expiratory flow achieved during FVC
FEF_X	forced expiratory flow, related to some portion of FVC curve
FET_X	forced expiratory time for a specified portion of FVC
FEV_1	forced expiratory volume at 1 second
$FiCO_2$	fractional inspired carbon dioxide
FIF	forced inspiratory flow
F_iO_2	fractional inspired oxygen
FIVC	forced inspiratory vital capacity
FRC	functional residual capacity
FVC	forced vital capacity
FVS	full ventilatory support
f/V_T	rapid shallow breathing index (frequency divided by tidal volume)
G_{aw}	airway conductance
GCS	Glasgow Coma Scale
g/dl	grams per deciliter
GERD	gastroesophageal reflux disease
$[H^+]$	hydrogen ion concentration
HAI	health care–associated infection
HAP	hospital-acquired pneumonia
Hb	hemoglobin
HBO	hyperbaric oxygen (therapy)
HCAP	health care–associated pneumonia
HCH	hygroscopic condenser humidifier
HCO_3^-	bicarbonate
H_2CO_3	carbonic acid
H_2O	water
He	helium
He/O_2	helium/oxygen mixture; heliox
HFFI	high-frequency flow interrupter
HFJV	high-frequency jet ventilation
HFNC	high-flow nasal cannula
HFO	high-frequency oscillation
HFOV	high-frequency oscillatory ventilation
HFPPV	high-frequency positive pressure ventilation
HFPV	high-frequency percussive ventilation
HFV	high-frequency ventilation
HHb	reduced or deoxygenated hemoglobin
HMD	hyaline membrane disease
HME	heat and moisture exchanger
HMEF	heat and moisture exchange filter
HR	heart rate
HRRP	Hospital Readmission Reduction Program
ht	height
Hz	hertz
I	inspired
IBW	ideal body weight
IC	inspiratory capacity
ICP	intracranial pressure
ICU	intensive care unit
ID	inner diameter
I:E	inspiratory-to-expiratory ratio
ILD	interstitial lung disease
IMPRV	intermittent mandatory pressure release ventilation
IMV	intermittent mandatory ventilation
INO	inhaled nitric oxide
IPAP	inspiratory positive airway pressure
IPPB	intermittent positive pressure breathing
IPPV	intermittent positive pressure ventilation
IPV	intrapulmonary percussive ventilation
IR	infrared
IRB	institutional review board
IRDS	infant respiratory distress syndrome
IRV	inspiratory reserve volume
IRV	inverse ratio ventilation
IV	intravenous
IVC	inspiratory vital capacity
IVH	intraventricular hemorrhage
IVOX	intravascular oxygenator
kcal	kilocalorie
kg	kilogram
kg-m	kilogram-meters
kPa	kilopascal
KPI	key performance indicator
L	liter
LAP	left atrial pressure
lb	pound
LBW	low birth weight
LED	light-emitting diode
LFPPV-$ECCO_2R$	low-frequency positive pressure ventilation with extracorporeal carbon dioxide removal
LMS	learning management system
LPV	lung protective ventilation
LTACH	long-term acute care hospital
LV	left ventricle
LVEDP	left ventricular end-diastolic pressure
LVEDV	left ventricular end-diastolic volume
LVSW	left ventricular stroke work
m^2	meters squared
MABP	mean arterial blood pressure
MAlvP	mean alveolar pressure
MAP	mean arterial pressure or mean airway pressure
MAS	meconium aspiration syndrome
max	maximal
MDI	metered dose inhaler
MDR	multidrug resistant
MEP	maximum expiratory pressure
mEq/L	milliequivalents per liter
metHb	methemoglobin
mg	milligram
mg%	milligram percent
mg/dl	milligrams per deciliter
MI	myocardial infarction
MICP	mobile intensive care paramedic
MI-E	mechanical insufflation-exsufflation
MIF	maximum inspiratory force
MIGET	multiple inert gas elimination technique
min	minute
MIP	maximum inspiratory pressure
MIPS	Merit-based Incentive Payment System
mL	milliliter
mm	millimeter
mm Hg	millimeters of mercury
MMAD	median mass aerodynamic diameter
mmol	millimole
MMV	mandatory minute ventilation
mo	month
MODS	multiple organ dysfunction syndrome
MOV	minimal occluding volume
$mP_{aw} - P_{\overline{aw}}$	mean airway pressure
MRI	magnetic resonance imaging
msec	millisecond
MV	mechanical ventilation
MVV	maximum voluntary ventilation

NaBr	sodium bromide
NaCl	sodium chloride
NAVA	neurally adjusted ventilatory assist
NBRC	National Board of Respiratory Care
NEEP	negative end expiratory pressure
nHFOV	nasal high-frequency oscillatory ventilation
NICU	neonatal intensive care unit
NIF	negative inspiratory force (also see MIP and MIF)
NIH	National Institutes of Health
NIV	noninvasive ventilation
nM	nanomole
nm	nanometer
NMBA	neuromuscular blocking agent
nM/L	nanomole per liter
NO	nitric oxide
NO_2	nitrous oxide
NP	nasopharyngeal
NPO	nothing by mouth
NPPV	noninvasive positive pressure ventilation
NPV	negative pressure ventilation
NSAIDs	nonsteroidal antiinflammatory drugs
nSIMV	nasal synchronized intermittent mandatory ventilation
N-SiPAP	nasal positive airway pressure with periodic (sigh) bilevel positive airway pressure breaths or bilevel nasal continuous positive airway pressure
NTE	neutral thermal environment
O_2	oxygen
O_2Hb	oxygenated hemoglobin
OH^-	hydroxide ions
OHDC	oxyhemoglobin dissociation curve
OSA	obstructive sleep apnea
OSHA	Occupational Safety and Health Administration
ΔP	change in pressure
P	pressure
P_{50}	PO_2 at which 50% saturation of hemoglobin occurs
P_{100}	pressure on inspiration measured at 100 msec
Pa	arterial pressure
PA	pulmonary artery
$P(A\text{-}a)O_2$	alveolar-to-arterial partial pressure of oxygen
P(A-awo)	pressure gradient from alveolus to airway opening
$PACO_2$	partial pressure of carbon dioxide in the alveoli
$PaCO_2$	partial pressure of carbon dioxide in the arteries
$P(a\text{-}et)CO_2$	arterial-to-end-tidal partial pressure of carbon dioxide
PAGE	perfluorocarbon associated gas exchange
PAH	pulmonary arterial hypertension
P_{al}	alveolar pressure
PAO_2	partial pressure of oxygen in the alveoli
PaO_2	partial pressure of oxygen in the arteries
PaO_2/FiO_2	ratio of arterial PO_2 to FiO_2
PaO_2/PAO_2	ratio of arterial PO_2 to alveolar PO_2
PAOP	pulmonary artery occlusion pressure (Also known as pulmonary capillary wedge pressure [PCWP])
PAP	mean pulmonary artery pressure
$\underline{PAP}$	pulmonary artery pressure
P_{aug}	pressure augmentation
PAV	proportional assist ventilation
P_{aw}	airway pressure
$\overline{P}_{aw}$	mean airway pressure
P_{awo}	airway opening pressure
PAWP	pulmonary artery wedge pressure
PB	barometric pressure
PBW	predicted body weight
P_{bs}	pressure at the body's surface
PC-CMV	pressure-controlled continuous mandatory ventilation
PCEF	peak cough expiratory flow
PC-IMV	pressure-controlled intermittent mandatory ventilation
PCIRV	pressure control inverse ratio ventilation
PCO_2	partial pressure of carbon dioxide
PC-SIMV	pressure-controlled synchronized intermittent mandatory ventilation
PCV	pressure-controlled ventilation
PCWP	pulmonary capillary wedge pressure
$PCWP_{tm}$	transmural pulmonary capillary wedge pressure
PDA	patent ductus arteriosus
PE	pulmonary embolism
PE_{max}	maximal expiratory pressure
PEA	pulseless electrical activity
P_ECO_2	partial pressure of mixed expired carbon dioxide
PEEP	positive end expiratory pressure
$PEEP_E$	extrinsic PEEP (set-PEEP)
$PEEP_I$	intrinsic PEEP (auto-PEEP)
$PEEP_{total}$	total PEEP (sum of intrinsic and extrinsic PEEP)
PEFR	peak expiratory flow rate
P_{es}	esophageal pressure
PET	positron emission tomography
$PetCO_2$	partial pressure of end-tidal carbon dioxide
P_{flex}	pressure at the inflection point of a pressure/volume curve
PFT	pulmonary function test(ing)
P_{ga}	gastric pressure
pH	relative acidity or alkalinity of a solution
P_{high}	high pressure during APRV
PHY	permissive hypercapnia
PIE	pulmonary interstitial edema
PIF	pulmonary interstitial fibrosis
PI_{max}	maximum inspiratory pressure (also MIP, MIF, NIF)
P_{inside}	inside pressure
$P_{intrapleural}$	intrapleural pressure (also Ppl)
PiO_2	partial pressure of inspired oxygen
PIP	peak inspiratory pressure (also P_{peak})
PISS	pin-indexed safety system
P_L	transpulmonary pressure
P_{low}	low pressure during APRV
PLV	partial liquid ventilation
P_M	mouth pressure
pMDI	pressurized metered dose inhaler
P_{mus}	muscle pressure
PO_2	partial pressure of oxygen
POCT	point of care testing
$P_{outside}$	pressure outside
PPACA	Patient Protection and Affordable Care Act
P_{peak}	peak inspiratory pressure (also PIP)
PPHN	primary pulmonary hypertension of the neonate
P_{pl}	intrapleural pressure
$P_{plateau}$	plateau pressure
ppm	parts per million
PPST	premature pressure support termination
PPV	positive pressure ventilation
PRA	plasma renin activity
PRVC	pressure regulated volume control
PS	pressure support
PSB	protected specimen brush
P_{set}	set pressure
psi	pounds per square inch
psig	pounds per square inch gauge

PS_{max}	maximum pressure support
P_{st}	static transpulmonary pressure at a specified lung volume
PSV	pressure support ventilation
P_{TA}	transairway pressure
$PtcCO_2$	transcutaneous PCO_2
$PtcO_2$	transcutaneous PO_2
P_{tm}	transmural pressure
P_{TR}	transrespiratory pressure
PTSD	posttraumatic stress disorder
P_{TT}	transthoracic pressure (also Pw)
P-V	pressure-volume
PV	pressure ventilation
PVC(s)	premature ventricular contraction(s)
$P\bar{v}O_2$	partial pressure of oxygen in mixed venous blood
PVR	pulmonary vascular resistance
PVS	partial ventilatory support
P_w	transthoracic pressure (also P_{TT})
Q	blood volume
$\dot{Q}$	blood flow
$\dot{Q}_{c'}$	pulmonary capillary blood flow
q2h	every 2 hours
$\dot{Q}_T$	cardiac output
$\frac{\dot{Q}_s}{\dot{Q}_t}$	shunt
$\dot{Q}sp$	physiologic shunt flow (total venous admixture)
R	resistance (i.e., pressure per unit flow)
$\bar{R}$	mean total resistance
RAM	random access memory
RAP	right atrial pressure
R_{aw}	airway resistance
rb	rebreathing
RCP	respiratory care practitioner
RDS	respiratory distress syndrome
Re	Reynolds number
R_E	total expiratory resistance
REE	resting energy expenditure
RH	relative humidity
R_I	total inspiratory resistance
RICU	respiratory intensive care unit
R_L	total pulmonary resistance
RM	lung recruitment maneuver
ROM	read-only memory
ROP	retinopathy of prematurity
RQ	respiratory quotient
RSS	really simple syndication
RSV	respiratory syncytial virus
RT	respiratory therapist
Rti	tissue resistance
RV	residual volume
RV/TLC%	ratio of residual volume to total lung capacity
RVEDP	right ventricular end-diastolic pressure
RVEDV	right ventricular end-diastolic volume
RVP	right ventricular pressure
RVSW	right ventricular stroke work
S	saturation in the blood phase
SA	sinoatrial
SaO_2	arterial oxygen saturation
$SBCO_2$	single breath carbon dioxide curve
SCCM	Society for Critical Care Medicine
SFIM	sporadic fatal infectious mononucleosis
S.I.	Système International d'Unités
SI	stroke index
SIDS	sudden infant death syndrome
SIMV	synchronized intermittent mandatory ventilation
Sine	sinusoidal
SNF	skilled nursing facility
sp.	species
sPEEP	spontaneous positive end expiratory pressure
SpO_2	oxygen saturation measured by pulse oximeter
STPD	standard temperature, pressure saturated; 0° Celsius, 760 mm Hg, dry
SV	stroke volume
SVC	slow vital capacity
$S\bar{v}O_2$	mixed venous oxygen saturation
SVN	small volume nebulizer
SVR	systemic vascular resistance
t	time
T	temperature
TAAA	thoracoabdominal aortic aneurysm
Tc	time constant
$tcCO_2$	transcutaneous CO_2
TCPL	time-cycled, pressure-limited ventilation
TCPL/IMV	time-cycled, pressure-limited intermittent mandatory ventilation
TCT	total cycle time
T_E	expiratory time
TGI	tracheal gas insufflation
TGV	thoracic gas volume
T_{high}	time for high-pressure delivery in APRV
T_I	inspiratory time
T_I%	inspiratory time percent
tid	three times per day
TI/TCT	duty cycle
TJC	The Joint Commission (formerly The Joint Commission on Accreditation of Healthcare Organizations [JCAHO])
TLC	total lung capacity
T_{low}	time for low-pressure delivery in APRV
TLV	total liquid ventilation
TOF	tetralogy of Fallot
torr	measurement of pressure that is equivalent to mm Hg
TTN	transient tachypnea of the neonate
TTOT	transtracheal oxygen therapy
TV	tidal volume
U	unit
UN	urinary nitrogen
USN	ultrasonic nebulizer
V	gas volume
v	venous
$\bar{v}$	mixed venous
$\dot{V}$	flow
$\dot{V}_E$	expired minute ventilation
$\dot{V}_A$	alveolar ventilation per minute
V_A	alveolar gas volume
VAI	ventilator-assisted individual
VALI	ventilator-associated lung injury
VAP	ventilator-associated pneumonia
VAPS	volume-assured pressure support
VBP	value-based purchasing
VC	vital capacity
V_C	volume lost to tubing compressibility
VC-CMV	volume-controlled continuous mandatory ventilation
VC-IMV	volume-controlled intermittent mandatory ventilation

VCIRV	volume-controlled inverse ratio ventilation
$\dot{V}CO_2$	carbon dioxide production per minute
V_D	volume of dead space
$\dot{V}_D$	physiologic dead space ventilation per minute
V_{Dalv}	alveolar dead space
$\dot{V}_{Dan}$	anatomic dead space ventilation per minute
V_{DAN}	volume of anatomic dead space
V_{Dmech}	mechanical dead space
V_D/V_T	dead space-to-tidal volume ratio
V_{Dbr}	rebreathing volume
$\dot{V}_{Dbr}$	rebreathing ventilation per minute
$\dot{V}_E$	expired volume per minute
VEDV	ventricular end-diastolic volume
VF	ventricular fibrillation
$\dot{V}_I$	inspired volume per minute
VILI	ventilator-induced lung injury
$\dot{V}_L$	actual lung volume (including conducting airways)
VLBW	very low birth weight
VM	vestibular membrane
$\dot{V}O_2$	oxygen consumption per minute
VS	volume support
VT	ventricular tachycardia
V_T	tidal volume
V_TA	alveolar tidal volume
V_{Texp}	expired tiadal volume
V_{Tinsp}	inspired tidal volume
vol%	volume per 100 ml of blood
$\frac{\dot{V}}{\bar{Q}}$	ventilation/perfusion ratio
VSV	volume support ventilation
VV	venovenous
W	work
WOB	work of breathing
WOBi	imposed work of breathing
wye	"wye" or Y connector
X	any variable
$\bar{X}$	mean value
Y	connects patient endotracheal tube to patient circuit
yr	year
ZEEP	zero end expiratory pressure