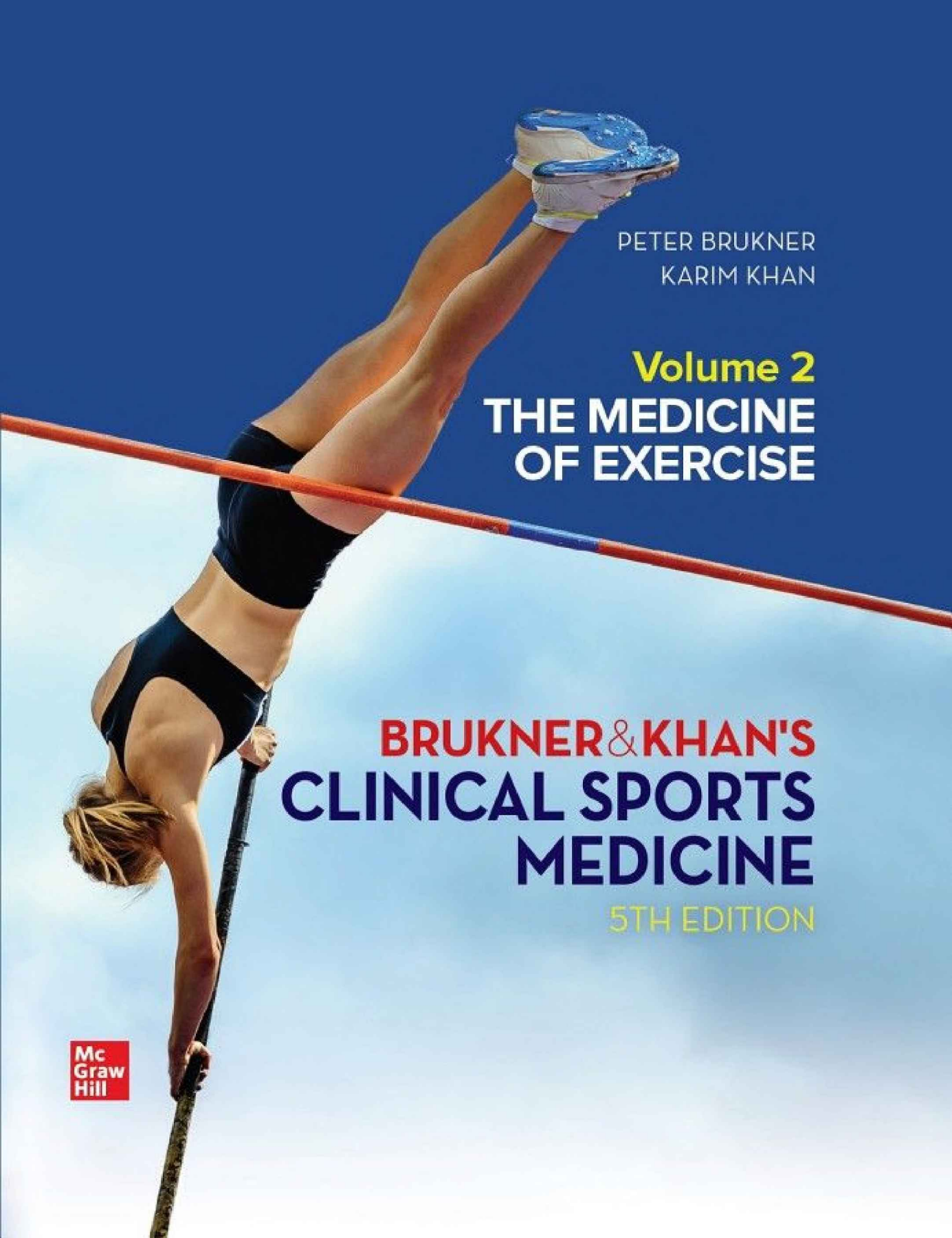


PETER BRUKNER
KARIM KHAN

Volume 2
THE MEDICINE OF EXERCISE

BRUKNER & KHAN'S CLINICAL SPORTS MEDICINE

5TH EDITION

Mc Graw Hill

CLINICAL SPORTS MEDICINE

We dedicate this fifth edition to the Clinical Sports Medicine community.
We are proud to be in a family of clinicians who deliver quality patient care with passion.

BRUKNER & KHAN'S

CLINICAL SPORTS MEDICINE

Volume 2
THE MEDICINE OF EXERCISE

5TH EDITION

Peter Brukner
Karim Khan

Mc
Graw
Hill

Notice
Medicine is an ever-changing science. As new research and clinical experience broaden our knowledge, changes in treatment and drug therapy are required. The editors and the publisher of this work have checked with sources believed to be reliable in their efforts to provide information that is complete and generally in accord with the standards accepted at the time of publication. However, in view of the possibility of human error or changes in medical sciences, neither the editors, nor the publisher, nor any other party who has been involved in the preparation or publication of this work warrants that the information contained herein is in every respect accurate or complete. Readers are encouraged to confirm the information contained herein with other sources. For example, and in particular, readers are advised to check the product information sheet included in the package of each drug they plan to administer to be certain that the information contained in this book is accurate and that changes have not been made in the recommended dose or in the contraindications for administration. This recommendation is of particular importance in connection with new or infrequently used drugs.

Reprinted 2019

Text and illustrations © 2019 McGraw-Hill Education (Australia) Pty Ltd
Additional owners of copyright are acknowledged in on-page credits.

Every effort has been made to trace and acknowledge copyrighted material. The authors and publisher tender their apologies should any infringement have occurred.

Reproduction and communication for educational purposes
The Australian Copyright Act 1968 (the Act) allows a maximum of one chapter or 10% of the pages of this work, whichever is the greater, to be reproduced and/or communicated by any educational institution for its educational purposes provided that the institution (or the body that administers it) has sent a Statutory Educational notice to Copyright Agency and been granted a licence. For details of statutory educational and other copyright licences contact: Copyright Agency, 66 Goulburn Street, Sydney NSW 2000. Telephone: (02) 9394 7600. Website: www.copyright.com.au

Reproduction and communication for other purposes
Apart from any fair dealing for the purposes of study, research, criticism or review, as permitted under the Act, no part of this publication may be reproduced, distributed or transmitted in any form or by any means, or stored in a database or retrieval system, without the written permission of McGraw-Hill Education (Australia) Pty Ltd, including, but not limited to, any network or other electronic storage.

Enquiries should be made to the publisher via www.mheducation.com.au or marked for the attention of the permissions editor at the address below.

National Library of Australia Cataloguing-in-Publication entry: (hardback)
Brukner & Khan's Clinical Sports Medicine
Volume 2: The Medicine of Exercise
Print ISBN: 9781760420512
eBook ISBN: 9781743767528

A catalogue record for this book is available from the National Library of Australia

---

Published in Australia by
McGraw-Hill Education (Australia) Pty Ltd
Level 33, 680 George Street, Sydney NSW 2000
Portfolio leads, Medical: Michael Weitz, Diane Gee-Clough
Senior content producer: Claire Linsdell
Custom and digital producer: Bethany Ng
Copy editor: Paul Leslie
Proofreader: Anne Savage
Cover design: Simon Rattray
Typeset in 9/11.5 That-Book by SPi Global, India

Foreword to the first edition (1993)

Sport in Australia is ingrained in the national consciousness more widely, deeply and indelibly than almost anywhere else in the world. When a prominent sportsperson sustains a sporting injury, either traumatically or from overuse, becomes excessively fatigued, or fails to live up to expectations, this assumes national importance. It is even more relevant nowadays with greater individual participation in sporting activities. The same type of problems occur for recreational athletes, middle-aged people wanting to become fit, or older people wishing to sustain a higher level of activity in their later years.

In *Clinical Sports Medicine* the authors take sport and exercise medicine out of the realm of the elite athlete and place it fairly and squarely where it belongs—as a subspecialty to serve everyone in the community who wishes to be active.

The book is organised in a manner that is sensible and usable. The chapters are arranged according to the anatomical region of the symptom rather than diagnostic categories. This results in a very usable text for the sports physician, general/family practitioner, physiotherapist, masseur, or athletic trainer whose practice contains many active individuals.

Practical aspects of sports medicine are well covered—care of the sporting team and concerns that a clinician might have when travelling with a team. In all, this is an eminently usable text which will find an important place among clinicians involved in the care of active individuals.

JOHN R SUTTON MD, FRACP
Professor of Medicine, Exercise Physiology and Sports Medicine
Faculty of Health Sciences
University of Sydney
Past President, American College of Sports Medicine

This foreword was written by the late Professor John Sutton before his untimely death in 1996; we honour the memory of this champion of the integration of science, physical activity promotion and multidisciplinary patient care.

Foreword

To study the phenomenon of disease without books is to sail an uncharted sea, while to study books without patients is not to go to sea at all.

—Sir William Osler

One of the pleasures of my professional life has been observing *Clinical Sports Medicine's* birth, adolescence and maturity over almost 30 years. In January of 1993, I held up high a copy of the first print-run, first edition, 697-page plain red book to the audience at the South African Sports Medicine Association (SASMA) Congress in Cape Town's Convention Centre.

I said that it was a revolutionary red book because it was very practical (symptom-oriented rather than pathology-based) and that with its five sections and 48 chapters, it propelled sports medicine beyond a narrow focus on athlete injury treatment (largely orthopaedic at that time). This red book defined what is now recognised as sport and exercise medicine—our specialty that provides comprehensive care (including prevention) for a much more inclusive constituency— any person who is active or who wants to be active. It was, as I already knew then, the book that would take an emerging yet immature discipline, across uncharted seas, to a land of hard science and clinical wisdom. Sport and exercise medicine could provide a beacon of all that is the very best in a patient-centred medical care, focusing on providing optimum health.

Fast forward to 2019, where Volume 2 of the fifth edition will again be waved aloft as a gold standard for clinicians who attend this year's South African Sports Medicine Association Congress. Each edition of *Clinical Sports Medicine* has clearly raised the educational bar in our specialty—each has provided substantially more value for the user, a word I use deliberately over 'reader'. Copies of this book are in tatters the world over because it is used! Now our field demands a two-volume fifth edition to do justice to the high quality science that now underpins our field. No more 'Mickey Mouse medicine'—a term one of my professors reserved for *sports medicine* in the 1980s.

Volume 2: The Medicine of Exercise provides some solutions for the global epidemic of non-communicable diseases (NCDs). It responds to *The Lancet's* 2012 and 2016 challenges in our field. As Richard Horton, the Editor, wrote: *We urge all sectors of government and society to take immediate, bold actions that help make active living a more desired, affordable, and accessible choice for all population groups.*

This dedicated volume of 40 chapters in six logical sections provides both the blueprint and the

step-by-step instructions for clinicians to take 'immediate bold action'. Clinicians have a wonderful opportunity to limit—dare I say reverse—some of the noncommunicable diseases from which their patients now suffer in ever-increasing numbers. The reality is that the advice is fairly straightforward; it is hardly rocket science. Yet it is based on the best available scientific evidence for promoting active living and rational eating.

I don't apologise for my challenging this belief—that as physicians we have not done all that we can to advance the health of our patients. The 'why' we need to do this is clear to clinicians —we know we should encourage exercise and healthy eating—but it is the 'how' that has been difficult. This volume will help the clinician clear that barrier. Type 2 diabetes mellitus is just one condition that, we now know, can be reversed in the majority. And the 'how' is outlined in this volume.

It has been my privilege to be an author of *Clinical Sports Medicine* since the second edition (2001) and I have appreciated that opportunity to reach young clinicians the world over. Congratulations to my very dear friends, Professors Peter Brukner and Karim Khan, for their leadership in what was once a nascent field but one which through their passion, commitment, dedication, wisdom and scholarship they have raised to a level that none of us could have ever imagined when the first edition was launched in Melbourne in December of 1992.

Comparisons are of course odious but it is my opinion, and I do not offer it glibly, that future generations will conclude that what Sir William Osler's *Principles and Practices of Medicine* did for medicine in the 1890s, Brukner and Khan's *Clinical Sports Medicine* fifth edition will do for the practice of the profession of sport and exercise medicine globally.

That is how highly I rate the contributions of these two uniquely gifted and visionary sports physicians who have written what will always be, like Osler's *Principles and Practices,* an utterly iconic text. A statement for the ages.

Following their lead, the challenge for the rest of us is to implement and promote what we now know is society's best buy for public health—more physical activity and the replacement of 'the diet of modern commerce' with the consumption of the real foods that humans had always eaten before we were mistakenly told to change 40 years ago.

Volume 2 of *Clinical Sports Medicine* is an evidence-based compendium of how we, as clinicians interested in the perfectly functioning human, can help direct the world's populations toward states of greatly improved health.

That is the opportunity that this epic work of meticulous scholarship delivers.

PROFESSOR TIMOTHY D NOAKES
OMS, MBChB, MD, DSc, PhD (hc), FACSM), (Hon), FFSEM (UK), (Hon), FFSEM (Ire)
Sports Physician and Exercise Physiologist
Former Discovery Health Professor of Exercise and Sports Science, University of Cape Town and Sports Science Institute of South Africa

Brief contents

PART A EXERCISE AND HEALTH

1 Physical inactivity: a global public health problem
2 Benefits and risks of physical activity
3 Prescribing physical activity: the clinical assessment
4 Prescribing physical activity: the written prescription
5 Prescribing physical activity: motivational interviewing
6 Nutrition for health

PART B MANAGING MEDICAL PROBLEMS

7 Obesity
8 Diabetes mellitus
9 Sudden cardiac death in sport
10 Cardiovascular symptoms
11 Respiratory symptoms during exercise
12 Gastrointestinal symptoms
13 Haematuria and other urinary symptoms
14 Neurological conditions
15 Rheumatological conditions
16 Osteoarthritis
17 Osteoporosis—physical activity for bone health
18 Infections
19 The tired athlete
20 Cancer
21 Physical activity in the prevention and treatment of depression

22 Anxiety disorders

PART C ENVIRONMENT

23 Heat
24 Cold
25 Altitude
26 Underwater
27 Physical activity and the built environment

PART D SPECIFIC GROUPS

28 Childhood and adolescence
29 Female-specific considerations: anatomy, physiology, injuries and performance
30 Transgender and intersex
31 Older people
32 The person with disability

PART E PERFORMANCE AND ETHICS

33 Nutrition for performance
34 Drugs and the athlete
35 Genetics in exercise and sport
36 Medico-legal issues
37 Harassment and abuse

PART F PRACTICAL SPORTS MEDICINE

38 Emergencies
39 Medical coverage of endurance events
40 Multisport endurance events

Contents

Foreword to the first edition

Foreword

Preface

About the authors

Editors

Co-authors

Acknowledgments

Guided tour of your book

PART A EXERCISE AND HEALTH

1 Physical inactivity: a global public health problem
with Daniel Friedman

Physical inactivity trends

The costs of physical inactivity

- Healthcare costs
- Productivity costs
- Quality of life

The way forward

2 Benefits and risks of physical activity
with Daniel Friedman

Physiology of physical activity: a clinician's primer

Maintaining homeostasis—a fancy word for survival
Adaptive protein changes
Benefits
Brain function and mental health
Cancer prevention
Cardiometabolic health
Pain reduction
Musculoskeletal health
Weight management
Healthy ageing
Longevity
Social wellbeing
Risks
Musculoskeletal risks
Cardiac risks
Respiratory risks
Dehydration and heat stroke

3 Prescribing physical activity: the clinical assessment
with Daniel Friedman

Why assess and counsel?
Evidence base and guidelines
A clinician's responsibility
A primary and secondary prevention opportunity
Who should do it?
Who should receive it?
When and where to do it?
What should be included in counselling?
Where else can the clinician turn for counselling resources?
The 5As model of behaviour change
A1: Assess
A2: Advise
A3: Agree
A4: Assist

A5: Arrange
What to do when time is limited
Enabling factors—what else can be done?

4 Prescribing physical activity: the written prescription
with Daniel Friedman

Why a written prescription?
Components of a written prescription: the FITT principle
Type
Time (duration)
Intensity
Frequency
Total volume
Progression
Minimising sedentary behaviour
Specific groups

5 Prescribing physical activity: motivational interviewing
with Daniel Friedman and Dane Vishnubala

Behaviour change theories
Classic learning theories
Social cognitive theory
Reasoned action approach
Fogg behaviour model
Transtheoretical stages of change
Motivational interviewing
Practical tips for successful motivational interviewing
Maintaining behaviour change

6 Nutrition for health
with Paul Mason and Daniel Friedman

Dietary guidelines
Macronutrients
Carbohydrates

Protein
Fats
Fluids
Alcohol
Micronutrients
Vitamins
Minerals
Types of diet
Low-calorie
Low-fat
Mediterranean
DASH
Low-carb
Paleo
Gluten-free
Low-FODMAP
Vegetarian and vegan
Intermittent fasting
Summary

PART B MANAGING MEDICAL PROBLEMS

7 Obesity

What is obesity?
Extent of the problem
Is obesity a disease?
What causes obesity?
Genetic factors
Socioeconomic disadvantage
Ethnicity
Energy balance: calories in = calories out
Lack of exercise
Sedentary lifestyle
Diet

Insulin resistance
The cost of food—is 'real food' more expensive?
Medical illnesses
Medications
Stress and mental illness
Poor sleep
Other factors
The obesogenic environment
The association between obesity and illness
Global burden of disease
Cardiovascular disease
Diabetes mellitus
Cancer
Musculoskeletal conditions
Sleep apnoea
Gallstone disease
Mental illness
Stigma
Management of the patient with obesity
Lifestyle interventions
Medical management
Solving the obesity problem
Policy interventions
Policies supporting more-informed choice
Policies aimed at changing the market environment
Childhood obesity
Summary

8 Diabetes mellitus
with Sandy Hoffmann and Matt Hislop
Types of diabetes
Type 1 diabetes
Type 2 diabetes
Clinical perspective

Pre-exercise screening and clearance for people with diabetes
Complications
Treatment
Pharmacotherapy in diabetes
Dietary management
Physical activity and diabetes
Benefits of physical activity
Exercise and type 1 diabetes
Exercise and type 2 diabetes
Diabetes and competition
Diabetes and travel
High-risk sports
Exercise and the complications of diabetes
Complications of physical activity in the diabetic athlete
Hypoglycaemia
Diabetic ketoacidosis in the athlete
Musculoskeletal manifestations of diabetes
Summary

9 Sudden cardiac death in sport
with Jonathan Drezner, Hamish MacLachlan and Sanjay Sharma

Incidence of sudden cardiac death
Sex, race and age as risk factors
Which sports carry the highest risk?
Aetiology of sudden cardiac death in athletes
SCD due to congenital or genetic structural heart disease
The cardiomyopathies
Disorders of the coronary arteries and aorta
Valvular heart disease
SCD due to congenital or genetic abnormalities predisposing to primary electrical disorders of the heart
Congenital long QT syndromes
Wolff–Parkinson–White syndrome
Brugada syndrome
Catecholaminergic polymorphic ventricular tachycardia

SCD due to acquired cardiac abnormalities
Myocarditis
Commotio cordis
Purpose of screening
Primary prevention of SCD in athletes—pre-participation cardiovascular screening
Secondary prevention—responding when an athlete has collapsed
Recognition of sudden cardiac arrest
Management of sudden cardiac arrest
Cardiopulmonary resuscitation
Early defibrillation
Summary

10 Cardiovascular symptoms
with André La Gerche and Jonathan Drezner

Putting things into perspective: sudden death and the prevalence of life threatening conditions
Cardiovascular symptoms: potentially life or death decisions
Clinical approach to symptoms that may be associated with important cardiac pathology
Syncope/near-syncope
Neurally mediated syncope (vasovagal syncope)
Post-exertional syncope
Exertional syncope
Syncope mimics—seizures and collapse
Exertional chest pain
Palpitations
Excessive fatigue or dyspnoea with exertion
Physical examination findings in sports cardiology—guide to the clinical approach
Specific physical examination findings
Hypertension
Heart murmur
Marfan syndrome
Non-invasive cardiovascular testing
Electrocardiogram
Echocardiography and associated tests for structural disease (cardiac CT, CMR)

Genetic testing when there is a family history of early sudden cardiac death
Temporary and permanent disqualification from sports
Summary

11 Respiratory symptoms during exercise
with Karen Holzer

Common respiratory symptoms
Shortness of breath and wheeze
Cough
Chest pain or tightness
Asthma
Epidemiology
Clinical features
Types of asthma
Pathophysiology of asthma
Risk factors
Asthma management
Exercise-induced bronchospasm
Epidemiology
Pathophysiology
Aetiology
Clinical features
Diagnosis
Treatment
Conditions that may mimic exercise-induced bronchospasm
Vocal cord dysfunction
Exercise-induced hyperventilation
Sinus-related symptoms
Investigations
Management of sinusitis
Other exercise-related conditions
Exercise-induced anaphylaxis
Cholinergic urticaria
Exercise-induced angioedema

12 Gastrointestinal symptoms

with Chris Milne and Paul Blazey

Upper gastrointestinal symptoms

Peptic ulcer disease

Lower gastrointestinal symptoms

Gastrointestinal bleeding

Treatment

Abdominal pain

Diarrhoea

Gastrointestinal Pathologies

Lactose intolerance

Coeliac disease

Crohn's disease and ulcerative colitis (inflammatory bowel disease—IBD)

FODMAPs

Irritable bowel syndrome

Small intestinal bacterial overgrowth

Constipation

Diagnostic pathway for athletes with potential gastrointestinal disease

Non-steroidal anti-inflammatory drugs and the gastrointestinal tract

Prevention of gastrointestinal symptoms that occur with exercise

Dietary fibre intake prior to competition

Solid foods prior to the race

Select the pre-event meal carefully

Dehydration

Fat and protein intake during exercise

Sports psychology

Ongoing symptom management

13 Haematuria and other urinary symptoms

with Chris Milne and Paul Blazey

Clinical anatomy and physiology

Exercise-related renal impairment

Rhabdomyolysis and myoglobinuria

Other exercise-related renal impairment concerns

Footstrike haemolysis
Athletic pseudonephritis
Abrasions of the bladder wall in long-distance runners
Renal trauma
Clinical approach to the athlete presenting with haematuria
Clinical approach to the athlete presenting with proteinuria
Exercise and the patient with renal impairment
Exercise for patients with renal transplantation
Prevention of renal complications of exercise
Summary

14 Neurological conditions
with James O'Donovan, Silke Appel-Cresswell and Paul Blazey
Cerebrovascular disease (stroke)
Effects of physical activity on stroke mortality
Effect of physical activity in the treatment of stroke
Considerations in prescribing physical activity for stroke patients
Parkinson's disease
Effect of physical activity in Parkinson's disease: prevention, disease modification and symptomatic benefit
Treatment approaches specific to Parkinson's disease
Considerations in planning a physical activity program for Parkinson's disease patients
Risks of adverse events in prescribing physical activity to those with Parkinson's disease
Multiple sclerosis
Does physical activity prevent the onset of multiple sclerosis or cause exacerbations?
Physical activity for the management of multiple sclerosis
Considerations in planning a physical activity program for those with multiple sclerosis
Epilepsy
Effects of physical activity on the management of epilepsy
Management of a seizure in the sport setting
Planning a physical activity program for patients with a neurological condition
Physical activity prescription for neurological conditions
Summary

15 Rheumatological conditions

with Christa Janse Van Rensburg

Age
Sex: mars versus venus
Anatomical site
Clinical history
Physical examination
The single swollen joint (monoarthritis)
Multiple swollen joints (polyarthritis or polyarthralgia)
Low back pain and stiffness
Joint pain and 'pain all over'
Diagnosis
Management
Non-pharmacological management
Pharmacological management
Summary

16 Osteoarthritis
with David Hunter and Pria Krishnasamy

Epidemiology
Pathophysiology
Clinical history and diagnosis
Hip osteoarthritis
Knee osteoarthritis
Ankle osteoarthritis
Foot osteoarthritis
Spine osteoarthritis
Shoulder osteoarthritis
Hand osteoarthritis
Prevention
Education
Prevention of disease through diet and exercise
Joint injury prevention
Management
Weight management in osteoarthritis

Exercise in the management of osteoarthritis
Biomechanical interventions
Psychological factors
Pharmacological management in osteoarthritis
When to refer for surgical intervention
Summary

17 Osteoporosis—physical activity for bone health
with Heather M Macdonald, Leigh Gabel and Heather A McKay
Key evidence—how bone adapts to physical activity and exercise
Maximising bone health during adolescence and early adulthood
A case for caution
Exercise prescription for bone health in middle-aged and older adults—stratified by fracture risk
Exercise prescription for low-risk individuals
Exercise prescription in moderate-risk individuals
Exercise prescription for high-risk individuals
Can physical activity reduce fractures?
Masters athletes: special bone health considerations
Masters runners
Masters cyclists
Summary

18 Infections
with Zafar Iqbal and Hasan Tahir
Exercise and infection
Exercise and the immune system
Exercise and clinical infections
Infection and athletic performance
Common infections in athletes
Skin infections
Respiratory and ear, nose and throat infections
Gastrointestinal and liver infections
Other infections

Preventive measures and reducing risk of infections

19 The tired athlete

Sandra Mejak

Assessment of the tired athlete

History

Other biopsychosocial stressors

Examination

Investigations

Common non-medical causes

Poor sleep

Non-functional overreaching and overtraining syndrome

Relative energy deficiency in sport

Common undiagnosed, untreated or undertreated medical causes

Infective causes of fatigue

Non-infective causes of fatigue

Endocrine causes of fatigue

Less common medical causes

Hypothyroidism

Diabetes mellitus

Myalgic encephalomyelitis/chronic fatigue syndrome

Coeliac disease

Eating disorders

Summary

20 Cancer

with Daniel Friedman, Marcos Agostinho, Kristin Campbell and Kathryn H Schmitz

A brief overview of cancer

How does cancer present?

How is cancer diagnosed?

How is cancer treated?

Physical activity for the primary prevention of cancer

How does physical activity prevent cancer?

Physical activity as an adjunct treatment for cancer

Physical activity decreases the adverse effects of anti-cancer therapy
Physical activity enhances anti-cancer therapy drug tolerance
Physical activity promotes overall survival
Physical activity benefits patients with advanced cancer
Physical activity's role in survivorship
Exercise prescription for cancer survivors

21 Physical activity in the prevention and treatment of depression
with Guy Faulkner, Mark Duncan and Paul Blazey

Forms of depression
Major or unipolar depression
Bipolar depression or dysthymia
Diagnosis
Management
Physical activity and depression
Physical activity—a preventive role?
Efficacy of using physical activity to treat depression
Exercise prescription—what is the dose?
Interactions of exercise with drug therapy
Contraindications to exercise
Psychological therapies
Pharmacological management
Summary

22 Anxiety disorders
with Saul Marks and Paul Blazey

Epidemiology
The anxiety disorders
Generalised anxiety disorder
Panic disorder or panic attack
Obsessive compulsive disorder or obsessional neurosis
Post-traumatic stress disorder
Agoraphobia, social anxiety and simple phobia
Debilitating performance anxiety

Clinical practice and management
Screening
Approaching an athlete about a potential mental health and wellbeing concern
Physical activity as a management strategy for mental health
Cognitive behavioural therapy
Pharmacotherapy
Summary

PART C ENVIRONMENT

23 Heat
with Sébastien Racinais

Biophysics of heat exchange
Beneficial acute responses to heat production
Detrimental responses to heat stress
Hyperthermia
Exertional heat illness
Adaptations to chronic or repeated exposures
Sweat rate
Changes in blood volume
Cardiovascular adaptations
Kinetics of acclimatisation: short and long-term adaptations
Hydration, dehydration and hyponatraemia
Hydration
Fluid quantity and composition
Guidelines for medical coverage of competitive events in the heat
Facilities and equipment recommendations
Medical team training
Medical management
Exercise-associated muscle cramps
Heat syncope and exercise-associated collapse
Exercise-associated hyponatraemia
Summary

24 Cold

with Mike Tipton

Thermoregulation in the cold

Effect of cold environments on the cardiovascular and respiratory systems

Other effects

Measuring environmental and body temperatures in the cold

Impact of cold on performance

Cold air and water: medical risks, mitigation and treatment

Hypothermia

Rewarming

Cold injuries

Frostbite

Non-freezing cold injury

Preventing cold injuries

Treatment of cold injuries and screening

Frostbite

Non-freezing cold injury

Cold immersion

Treatment of immersion casualties

Health screening

Summary

25 Altitude

with Michael Koehle and Yorck Olaf Schumacher

Medical concerns at altitude

High-altitude illness

Determinants of risk

General preventive measures

Chemoprophylaxis for particular conditions

Altitude training

The clinical physiology of adaptation at altitude

Putting altitude training into practice

26 Underwater

with James O'Donovan and Michael Koehle

Methods of diving
The physiology of diving
The pathophysiology of diving
The squeezes
Pulmonary barotrauma
Decompression sickness
Immersion pulmonary oedema
Internal carotid artery dissection
Medical certification of fitness to dive
Coronary artery disease
Respiratory
Diabetes
Other conditions for consideration in the medical exam
Other considerations for the diving athlete
Summary

27 Physical activity and the built environment
with Hamish Reid and Karen Milton

Community design
Mixed land use
Residential density
Connected streets
Footpaths
Safe crossings
Speed limits
Cycling infrastructure
Public transport
Parks and open public spaces
Building design
The workplace
Schools
Clinical practice
Clinical encounters

Active travel
Role modelling
Advocacy

PART D SPECIFIC GROUPS

28 Childhood and adolescence
with Carolyn Broderick and Paul Blazey

Characteristics of the younger athlete
Changes in sports performance with age and maturation
Determinants of peak performance
Aerobic capacity
Strength
Anaerobic capacity (power)
Creating a level playing field in adolescent sport
Weight-for-age competitions
Paediatric exercise medicine
Dyspnoea on exertion in the younger athlete—what is the diagnosis?
Poor exercise tolerance and fatigue in the younger athlete
Exercise prescription for children with established chronic disease
Type 1 diabetes
Childhood cancer
Cystic fibrosis
Haemophilia
Mitochondrial myopathies
McArdle disease
Juvenile idiopathic arthritis
Joint hypermobility syndrome and other connective tissue diseases
Congenital coronary artery abnormalities
Concussion in the younger athlete
Management of concussion in the younger athlete
Summary

29 Female-specific considerations: anatomy, physiology, injuries and performa

nce
with Genevra L Stone, Margo Mountjoy and Kathryn E Ackerman

Physical differences head to toe
Breast issues
Gynaecological injuries
Pelvic floor complications
Hypermobility
Patellofemoral syndrome
Anterior cruciate ligament injuries
Anaemia
Menstrual cycle
- Abnormal menstruation
- Menstrual cycle manipulation and contraception

Female athlete triad
- Energy availability
- Menstrual function
- Bone health

Relative energy deficiency in sport
- Endocrine
- Metabolic
- Haematological
- Growth and development
- Psychological
- Cardiovascular
- Gastrointestinal
- Immunological
- Potential performance effects of relative energy deficiency in sport
- Screening and return to play for female athlete triad and relative energy deficiency in sport

Pregnancy
Summary

30 Transgender and intersex
with Liesel Geertsema, Siobhan Statuta and Silvia Camporesi

Biology of normal sexual development

Basic concepts of genetics and sex
Sex versus gender
Chromosomal variants
Gene variants
Androgens and their receptors
Defining intersex
Sex is a spectrum
Defining transgender
Sex testing in sport
Visual inspection
Chromosome testing
DNA testing
On-demand multidisciplinary testing
Testosterone levels
Rationale for sex testing in sport
Women in sport
Fair play
An issue of human rights
The participation of transgender athletes in sport
The future of sex testing in sport
Clinical implications of sex testing in sport
Medical issues
Trust and sensitivity
The ethics of testing
Education

31 Older people
with Daniel Friedman and Ken Madden

What defines an older person?
What is healthy ageing?
A word on frailty
Benefits of physical activity in older people
The cardiovascular system
The respiratory system

Diabetes mellitus
Osteoarthritis
Osteoporosis and prevention of fall-related fractures
Functional independence
Cognitive and psychological function
Risks for physical activity in older people
Contraindications to physical activity in older people
Exercise prescription in older people
The inactive older adult
The generally active older adult
Special considerations for the active older adult
How do medication and physical activity interact in older people?
Medications affecting the renin-angiotensin system
Beta blockers
Diuretics
Other cardiac drugs
Non-steroidal anti-inflammatory drugs
Medications affecting the central nervous system
Insulin and oral hypoglycaemic drugs

32 The person with disability
with Nick Webborn and Cheri Blauwet

Sports participation among people with disability
Physical activity for people with disability
Prescribing exercise for people with disability
Classification to determine eligibility for participation
Medical issues in summer sport for para athletes
Common summer sport injuries
Common summer sport illnesses
Medical issues in winter sport for para athletes
Common winter sport injuries
Common winter sport illnesses
Anti-doping issues
Travel with teams

PART E PERFORMANCE AND ETHICS

33 Nutrition for performance

by James Morton and Graeme Close

Overview of exercise metabolism

Assessing the athlete

- Assessment of energy intake
- Assessment of energy expenditure
- Body composition

Macronutrient and micronutrient requirements for performance

- Carbohydrate
- Protein
- Fat
- Fluid
- Micronutrients

Supplements for performance

Special considerations

Nutrition periodisation

- CHO periodisation
- Energy periodisation
- Wider periodisation

Summary

34 Drugs and the athlete

Substances and methods prohibited at all times (in and out of competition)

- Non-approved substances
- Anabolic agents
- Peptide hormones, growth factors, related substances and mimetics
- Beta-2 agonists
- Hormone and metabolic modulators
- Diuretics and other masking agents

Prohibited methods

- Blood doping

Artificial oxygen carriers
Chemical and physical manipulation
Gene doping
Substances and methods prohibited in-competition
Stimulants
Narcotics
Cannabinoids
Glucocorticosteroids
Substances prohibited in particular sports
Beta blockers
Positive tests
Therapeutic use of a prohibited substance
Permitted substances
Deleted drugs
Caffeine
Alcohol
Non-intentional doping in sports
Drug testing
Testing procedure
The analytical procedure
Results management
Athlete's rights
Athlete's responsibilities
The role of the team clinician

35 Genetics in exercise and sport
with William Gibson and Daniel Gamu

Introductory genetics: important concepts and terminology
Genome
Genes
Genotype versus phenotype
Single nucleotide polymorphisms
Mendelian traits
Complex traits

Genetic mapping
Identifying risk using candidate gene and genome-wide approaches
Candidate gene approach
Genome-wide approach
Implications of genomics in sport: cautions and considerations
Services that provide genetic testing
Gene doping in sports

36 Medico-legal issues
by Hayden Opie
The practice of sports medicine
Legal and regulatory systems
The sports clinician/athlete relationship
Creation
Implications
The sports team clinician
Providing medical care and managing conflict of interest
Trust and confidence
Vicarious liability
Other roles
Managing risky sports
Neck injuries
Head injuries—concussion
Drugs in sport
Medico-legal aspects of human rights in sport
Sex, gender and pregnancy
Disability
Summary

37 Harassment and abuse
with Margo Mountjoy and Jenny Shute
What is harassment and abuse in sport?
Types of harassment and abuse (non-accidental violence)
Psychological abuse and harassment

Physical abuse
Sexual harassment and abuse
Neglect
Delivery mechanisms of harassment and abuse
Psychological harassment and abuse
Sexual harassment and abuse
Physical abuse
Neglect
Consequences of harassment and abuse
Impacts on the athlete
Impacts on sport
Prevention of harassment and abuse in sport
Role of the sport physician in prevention of harassment and abuse
Identification
Clinical management of allegations of harassment and abuse
Summary

PART F PRACTICAL SPORTS MEDICINE

38 Emergencies
with Shane Brun

The role of the physiotherapist in emergency care
The sequence of events in emergency care
Preparation
Triage
Primary survey
Resuscitate and stabilise
Focused history
Secondary survey
Frequent reassessment
Definitive care
The primary survey in detail
Basic life support
Airway with cervical spine control

Breathing and ventilation
Circulation and haemorrhage control
Appropriate use of analgesia in trauma
Recommended general and emergency medical equipment

39 Medical coverage of endurance events
with Timothy Noakes

Race organisation
The medical team
First-aid stations
Medical facility at the race finish
Summary

40 Multisport endurance events
by Allen Chang and Paul Auerbach

Injury prevalence in multisport endurance events
General approach to physiology as it relates to safety
Carbohydrates and sugars
Hydration and electrolytes
Rhabdomyolysis and renal injury
Management of injuries and additional safety concerns
What criteria should be used to determine if a competitor can complete?
Musculoskeletal injuries and improvised splints
Soft tissue injuries and infections
Medical evacuation
Summary

Preface

Helping clinicians to help patients has been the clear focus of *Clinical Sports Medicine* from its inception. In this volume we bring you more authors, more practical tips and more evidence of the work we do as sport and exercise medicine clinicians. If you are a loyal member of the *Clinical Sports Medicine* community you will already know that we completed *Volume 1: Injuries* and then dedicated a fresh year of our lives to *Volume 2: The Medicine of Exercise.* It was a boon for us to be able to concentrate on Volume 2 because historically (pre-2000) the focus of sports medicine had been injuries, and the first four editions of *Clinical Sports Medicine* really reflected that bias.

As governments began to wrestle with the crippling cost of non-communicable diseases (NCDs) they found there was no magic medication or operation to turn to. Suddenly, sport and exercise clinicians—those erstwhile medical 'extras', who had been fighting for specialty status in the 1980s—moved to centre stage, working with the World Health Organization, national and state or provincial governments, and health insurers. Research funding agencies supported various studies of exercise for heart disease, diabetes, cancer and cognitive function. National sports medicine bodies, such as those in Britain, Canada and Australia (BASM, CASM, ACSP), all added an 'E' for Exercise in their titles (BASEM, CASEM, ACSEP). It is telling that the shorter versions now seem very dated. Sports Medicine without 'Exercise'? Weird!

What's new?

Clinical Sports Medicine clearly needed a dedicated *Medicine of Exercise* volume to capture a decade of advances. So what's new in this Volume 2 of the fifth edition?

- *Our most comprehensive overview of exercise and physical activity medicine.*
- *19 totally new topics.* (See new content below.)
- *A practical focus and more detail.* The focus is one the practical elements of exercise prescription, with more tips, more practical tables and more illustrations.
- *Illustrated real-life patient stories.* We share lessons from the world's best athletes—their voices, their challenges and their clinicians' actions and tips.
- *More than 3000 references*—the solid foundation. Our chapter authors' clinical perspective is key, but what they share is founded on increasingly solid science.

Chapter authors

Volume 2: The Medicine of Exercise reflects the generosity of the 53 chapter authors and contributors from seven countries. Exercise medicine is arguably more diverse than injury medicine and we are grateful for their expert and enthusiastic contributions throughout chapters 1 to 40.

New content

We feel this is the first true contribution to the field of sport and exercise medicine. The following new authors have shared their clinical experience, anchored in new evidence and gained over many years:

Part A–Exercise for health does precisely what it says on the tin! World Health Organization technical advisor and remarkable medical student (at time of publication) Daniel Friedman takes the helm, steering the reader on a journey from the problem of physical inactivity—and why clinicians need to address non-communicable diseases (Chapter 1), to the clear physiological benefits of activity at the cellular level (Chapter 2), through the how of assessing the patient (Chapt er 3) and on to prescribing activity for him or her (Chapter 4). Keeping with our clinical focus, the part closes with tips for the clinician to complement training on motivational interviewing (Chapte r 5). The final chapter (Chapter 6, Nutrition for health) reflects the fact that nutrition is now recognised as a vital key to health (in particular with respect to NCDs). Nutrition papers are now published in *The Lancet, The BMJ* and JAMA—and that was not the case when we launched the first edition of *Clinical Sports Medicine.*

Part B–Managing medical problems. Six completely new chapters and ten that have been totally revised from the fourth edition are included. There are new chapters on management of obesity (C hapter 7), osteoarthritis (Chapter 16), osteoporosis (Chapter 17), cancer (Chapter 20), depression (C hapter 21) and anxiety (Chapter 22). The other chapters in this part describe and illustrate how to manage critical conditions found in ten other medical specialty areas: diabetes, sports cardiology (two chapters), sports respirology, gastrointestinal, renal and urinary, neurological, rheumatological, infection, and the tired athlete.

Part C–Environment. World leaders, including Professors Mike Tipton and Michael Koehle as well as Drs Sébastien Racinais and Olaf Schumacher, share decades of experience in this domain. Heat (C hapter 23), Cold (Chapter 24), Altitude (Chapter 25) and Underwater (Chapter 26) are substantial upgrades on their fourth edition counterparts. Physical activity and the built environment (Chapte r 27) is a completely new chapter; the built environment is one of the World Health Organization's Seven Investments for Better Health.

Part D–Specific groups. These five chapters focus on the very young (Chapter 28, Associate Professor Carolyn Broderick), girls and women (Chapter 29), older people (Chapter 31) and The person with disability (Chapter 32). Completely new too is the complex issue of transgender and

intersex. What endocrine pathways underpin the biology? When is it fair for a transgender athlete to compete? Does hyperandrogenism confer an unfair advantage? Dr Liesel Geertsema provides a very balanced view, as there are no easy answers (Chapter 30).

Part E: Performance and ethics. Four new chapters among five potentially contentious ones: nutrition for performance (new, Chapter 33), drugs in sport (Chapter 34), genetics in sport including genetic testing (new, Chapter 35), legal issues (new, Chapter 36), and harassment and abuse (new, Chapter 37) by Canadian professor and IOC Medical Commission member Dr Margo Mountjoy.

Part F–Practical sports medicine. The new chapter here is on multisport endurance events (Chap ter 40), by veteran and international leader Professor Paul Auerbach. Emergency medicine for the sideline clinician is covered in detail and helpfully illustrated (Chapter 38). Professor Timothy Noakes provides the latest from his four-decade experience of endurance event medicine (Chapter 39).

We are delighted with how Volume 2: The Medicine of Exercise *has turned out and for that we thank the champion team of multidisciplinary authors who so generously committed to sharing their expertise. They have provided an invaluable resource for our community.*

About the authors

Peter Brukner (OAM)

MBBS, DRCOG, FACSEP, FASMF, FACSM, FFSEM (Ireland, Hon), FFSEM (UK, Hon)

Sport and Exercise Medicine physician

Professor of Sports Medicine, La Trobe University, Melbourne, Australia

Chair, SugarByHalf

Founding Partner, Olympic Park Sports Medicine Centre, Melbourne, Australia

Associate Professor, Centre for Health, Exercise and Sports Medicine, The University of Melbourne, Australia

Honorary Fellow, Faculty of Law, The University of Melbourne, Australia

Adjunct Professor, School of Human Movement Studies, The University of Queensland, Australia

Adjunct Professor, Liverpool John Moores University, UK

Visiting Professor, Lee Kong Chian School of Medicine, Singapore

Visiting Associate Professor, Stanford University, USA 1997

Executive Member, Australian College of Sports Physicians 1985–2000

President, Australian College of Sports Physicians 1991–92, 1999–2000

Board of Trustees, American College of Sports Medicine 2000–02

State and Federal Council Member, Sports Medicine Australia 1984–90

Team physician

Team Doctor, Australian cricket team, 2012–17

Head, Sports Medicine and Sports Science, Liverpool Football Club, UK 2010–12

Socceroos 2007–10, Asian Cup Finals 2007, World Cup Finals 2010

Australian Olympic Team, Atlanta 1996, Sydney 2000

Australian Commonwealth Games team, Edinburgh 1986, Kuala Lumpur 1998

Australian team, World Student Games, Edmonton 1983, Kobe 1985, Zagreb 1987

Australian Athletics team 1990–2000, World Championships Tokyo 1991, Gothenburg 1995, Seville 1999

Australian team, World Cup Athletics, Havana 1992

Australian Men's Hockey team 1995–96

Australian team, World Swimming Championships, Madrid 1986

Melbourne Football Club (AFL) 1987–90

Collingwood Football Club (AFL) 1996

Books (co-author)

Food for Sport 1987

Stress Fractures 1999

Drugs in Sport—What the GP Needs to Know 1996, 2000

The Encyclopedia of Exercise, Sport and Health 2004

Essential Sports Medicine 2005

Clinical Sports Anatomy 2010

A Fat Lot of Good 2018

Editorial boards

British Journal of Sports Medicine
Clinical Journal of Sport Medicine
Current Sports Medicine Reports
The Physician and Sportsmedicine

Editor

Sport Health 1990–95

Awards

Inaugural Honour Award, Australian College of Sports Physicians 1996
Citation Award, American College of Sports Medicine 2000
Honorary Fellowship, Faculty of Sports and Exercise Medicine (Ireland) 2012
Medal of the Order of Australia 2006

Karim Khan Karim Khan (AO)

MD, PhD, MBA, FACSEP, FSMA, DipSportMed (CASEM), FACSM, FFSEM (Ireland,

Hon), FFSEM (UK, Hon)

Sport and Exercise Medicine physician

Professor, University of British Columbia (Department of Family Practice and School of Kinesiology), Vancouver, Canada

Scientific Director, Canadian Institutes of Health Research (CIHR)—Institute of Musculoskeletal Health and Arthritis (IMHA).

Adjunct Professor: Professor, School of Allied Health, College of Science, Health and Engineering, La Trobe University, Melbourne, Australia

Visiting Professor, School of Human Movement Studies, The University of Queensland, Brisbane, Australia

Clinical Professor, Centre for Musculoskeletal Studies, School of Surgery, University of Western Australia, Perth, Australia

Co-Director, Centre for Hip Health and Mobility, University of British Columbia, Vancouver, Canada, 2016–17

Medical Education Committee, American College of Sports Medicine 2002–04

Research Evaluation Committee, American College of Sports Medicine 2005–07

Exercise is Medicine Committee, American College of Sports Medicine 2009–11

Advisory Board to the International Olympic Committee 2015–

Director of Research and Education, Aspetar Orthopaedic and Sports Medicine Hospital, Qatar 2013–15

Team physician

Olympic Games Sydney 2000, Basketball Venue

Australian Women's Basketball (The Opals) 1991–96

The Australian Ballet Company 1991–96

The Australian Ballet School 1991–96

Australian team, World Student Games 1993

Australian team, Junior World Cup Hockey 1993

Editor-in-chief

British Journal of Sports Medicine 2008–20

BMJ Open Sport and Exercise Medicine 2015–18

Sport Health 1995–97

Books (co-author)

Physical Activity and Bone Health 2001

The Encyclopedia of Exercise, Sport and Health 2004

Editorial boards

The BMJ (International Advisory Board) 2008–14

Scandinavian Journal of Medicine and Science in Sport 2007–10

British Journal of Sports Medicine (North American Editor) 2005–07

Journal of Science and Medicine in Sport 1997–2001

Year Book of Sports Medicine 2008–10

Clinical Journal of Sport Medicine 2003–06

Selected awards

Prime Minister's Medal for Service to Australian Sport 2000

Sports Medicine Australia Fellows' Citation for Service 2005

Honorary Fellowship, Faculty of Sports and Exercise Medicine (Ireland) 2011

Honorary Fellowship, Faculty of Sport and Exercise Medicine (UK) 2014

Honorary Doctorate, NIH, Oslo (Norway) 2018

Honorary Doctorate, University of Edinburgh (UK) 2019

Officer of the Order of Australia 2019

Editors

In the writing of this Volume 2 of our fifth edition, we were very fortunate to have the assistance of two outstanding young writers, Daniel Friedman and Paul Blazey. Their contribution has been massive and we could not have done it without them. Heartfelt thanks!

Daniel Friedman MBBS (Hons) (2019e)

Daniel Friedman is a final year medical student from Monash University in Melbourne, Australia, with a keen interest in sport and exercise medicine. Daniel has completed medical training across rural Victoria and undertook an unusually high volume of shadowing leading sports medicine physicians in the clinic. After completing an internship for the World Health Organization (WHO) in 2017 in the non-communicable disease prevention program, Daniel served as a technical advisor to the WHO on physical activity, and assisted with development of the *Global Action Plan on Physical Activity 2018-30* and *ACTIVE Technical Package.*

Daniel is currently leading the development of the WHO's physical activity counselling toolkit, which aims to provide global best practice solutions to integrate

physical activity into routine clinical practice. Daniel is also an Associate Editor and Podcast Editor for the *British Journal of Sports Medicine* (BJSM). He has covered conferences around the world for the BJSM, and is a regular contributor to the journal's blog. Daniel loves most sporting activities—running, swimming and, cycling, basketball and tennis.

Paul Blazey BSc (Hons) Physiotherapy, PGCert Healthcare Education

Paul worked as a specialist musculoskeletal physiotherapist with the National Health Service (UK) and in sports-specific roles with Crystal Palace and Arsenal FC academy. He owned Freeflex Physio, a clinic run in conjunction with the University of East Anglia, that provided specialist sports physiotherapy services to students and athletes. He is an experienced teacher who worked at both the University of East Anglia and Health Education England. As well as teaching specific clinical physiotherapy courses, he was responsible for education governance and quality.

Paul moved to Vancouver, Canada, in 2017 to take up a role with the University of British Columbia and works clinically with athletes out of the Restore Physiotherapy Clinic with Dr Chris Napier. He is also part of the editorial team for the *British Journal of Sports Medicine.* Paul is an accomplished distance runner with a personal best of 2 hours 39 minutes over the marathon distance and he is interested in health promotion, injury prevention and the use of wearable technology within sport and everyday physical activity.

Co-authors

Kathryn E Ackerman MD, MPH, FACSM

Sports Medicine Physician and Endocrinologist; Medical Director, Female Athlete Program, Boston Children's Hospital; Associate Director, Sports Endocrine Research Lab, Massachusetts General Hospital; Assistant Professor of Medicine, Harvard Medical School, Boston, MA; Team Physician, USA Rowing

Marcos Agostinho MD, PGDipSEM, BASc

Primary Care Sports Physician, CUF Torres Vedras Hospital, Portugal; Team Physician SCU Torreense, Portugal

Paul S Auerbach MD, MS, FACEP, MFAWM, FAAEM

Redlich Family Professor Emeritus, Department of Emergency Medicine, Stanford University School of Medicine, Stanford, California; Adjunct Professor of Military/Emergency Medicine, Uniformed Services, University of the Health Sciences, Bethesda, Maryland, USA

Cheri Blauwet MD, FAAPMR

Sports Medicine Physician; Assistant Professor of Physical Medicine and Rehabilitation, Harvard University, Boston, USA; Spaulding Rehabilitation Hospital/Brigham and Women's Hospital, Boston, USA

Carolyn Broderick MBBS, FACSEP, PhD

Associate Professor, School of Medical Sciences, UNSW Sydney; Staff Specialist, Sport and Exercise Medicine, The Children's Hospital at Westmead, Sydney, Australia; Chief Medical Officer, Tennis Australia and Australian Open Tennis

Shane P Brun MBBS, FFSEM (UK), FASMF, FACRRM, FRACGP, FARGP, MTrauma (Dist), MSpMed, MEd, BAppSc, DCH

Associate Professor, James Cook University, Australia; Visiting Professor, University Malaya, Malaysia

Kristin Campbell PT, MSc, PhD

Associate Professor, Dept of Physical Therapy, University of British Columbia, Vancouver, Canada

Silvia Camporesi PhD, PhD

Senior Lecturer in Bioethics & Society; Director, MSc in Bioethics and Society, King's College London, UK

Allen 'Dig' Chang MD

Resident Physician, Department of Emergency Medicine, Stanford University Hospital and Kaiser Permanente, Santa Clara Medical Center, Palo Alto, CA, USA; Special Operations Physician, San Mateo County Tactical EMS

Graeme Close PhD, ASCC, rSEN, fBASES, fECSS

Professor of Human Physiology, Liverpool John Moores University, Liverpool, UK; Expert Nutrition Consultant, Rugby, UK

Silke Appel Cresswell MD

Associate Professor, Department of Medicine/ Neurology, University of British Columbia, Vancouver, Canada

Jonathan Drezner MD

Director, UW Medicine Center for Sports Cardiology; Professor, Department of Family Medicine, University of Washington, USA; Team Physician, Seattle Seahawks, Seattle Reign, and UW Huskies

Markus J Duncan MSc

PhD Candidate, School of Kinesiology, University of British Columbia, Canada

Guy Faulkner PhD

Professor, School of Kinesiology, University of British Columbia, Canada

Leigh Gabel BSc, PhD

Post-doctoral Research Fellow, Department of Radiology, McCaig Institute for Bone and Joint Health, University of Calgary, Calgary, Canada

Daniel Gamu MSc, PhD

Post-doctoral Research Fellow, BC Children's Hospital Research Institute, University of British Columbia, Vancouver, Canada

Liesel Geertsema MBChB, FACSEP

Sport and Exercise Medicine Physician, Aspetar Orthopaedic & Sports Medicine

Hospital, Doha, Qatar

William Gibson MD, PhD, FRCPC

Associate Professor, Department of Medical Genetics and Genomics, University of British Columbia; Senior Clinician Scientist, BC Children's Hospital, Vancouver, Canada

Matthew Hislop MBBS, MSc, FACSEP

Sport and Exercise Medicine Physician, Brisbane Sport and Exercise Medicine Specialists, Brisbane, Australia; Team Physician, Queensland State of Origin, Brisbane International Tennis Tournament, Queensland Ballet

Sandy Hoffmann MD, FACP, FACSM

Associate Clinical Professor, Idaho State University, Pocatello, Idaho, USA

Karen Holzer MBBS, FACSP, PhD

Sport and Exercise Medicine Physician, South Yarra Spine & Sports Medicine, Melbourne, Australia; Australian Team Doctor, Olympic Games, Beijing 2008

David Hunter MBBS, MSc (Clin Epi), MSpMed, PhD, FRACP (Rheum)

Florance and Cope Chair of Rheumatology, Professor of Medicine; Chair, Institute of Bone and Joint Research, Kolling Institute, University of Sydney; Rheumatologist, Royal North Shore Hospital, Sydney, Australia

Zafar Iqbal BSc, MBBS, MSc, MFSEM (UK), FRCP (UK)

Consultant in Sports and Exercise Medicine; Head of Sports Medicine, Crystal Palace FC; Medical Officer, Kent Cricket Club, UK

Christa Janse Van Rensburg MBChB, MSc, MMed, MD, FACSM

Rheumatologist and Associate Professor; Head, Section Sports Medicine and Associate, Sport, Exercise Medicine & Lifestyle Institute (SEMLI), Faculty of Health Sciences, University of Pretoria, South Africa

Michael Koehle MD, PhD, CCFP (SEM)

Director, Division of Sports Medicine, University of British Columbia; Professor, School of Kinesiology, University of British Columbia, Canada

Priathashini Krishnasamy MB BCh, BAO, MRCP, MSc SEM, FFSEM (UK)

Sport and Exercise Medicine Physician (UK); Institute of Bone and Joint Research, Kolling Institute of Medical Research, Northern Clinical School, Faculty of Medicine, University of Sydney; Department of Rheumatology, Royal North Shore Hospital, Sydney, Australia

André La Gerche MBBS, PhD, FRACP, FESC

Director, National Centre for Sports Cardiology; Consultant Cardiologist, St Vincent's Hospital, Melbourne; Head, Clinical Research Domain, Baker Heart and Diabetes Institute, Melbourne, Australia

Heather Macdonald BSc, PhD

Research Associate, Department of Family Practice, University of British Columbia, Vancouver, Canada; and Centre for Hip Health and Mobility, Vancouver, Canada

Hamish MacLachlan MRCP, MSc

Specialist Registrar in Cardiology, Cardiology Clinical Academic Group, St George's, University of London, UK

Kenneth Madden MSc, MD, FRCPC

Allan M McGavin Chair in Geriatric Medicine, Division Head (Geriatric Medicine, Vancouver General Hospital), University of British Columbia, Vancouver, Canada

Saul Marks BSch, MD, FRCPC

Sports Psychiatrist; Assistant Professor, Department of Psychiatry, Faculty of Medicine, University of Toronto, Toronto, Canada

Paul Mason MBBS, BPhysio, MOH, FACSEP

Sport and Exercise Medicine Physician, Sydney, Australia

Heather McKay PhD, FCAHS

Professor, Departments of Family Practice and Orthopaedics, University of British Columbia, Vancouver, Canada; and Centre for Hip Health and Mobility, Vancouver, Canada

Sandra Mejak MBBS, BMedSc (Hons), FACSEP

Sport and Exercise Medicine Physician, Active Sports Medicine, Perth, Australia; Australian Commonwealth Games Medical Team 2010–14

Chris Milne QSM, BHB, MBChB, Dip Obst, Dip Sports Med, FRNZCGP, FASCP

Sports Physician, Anglesea Sports Medicine, Hamilton, New Zealand; Medical Director, Rowing NZ; Olympic Team Physician 1996 to present, New Zealand; Chair Medical Commission, Oceania National Olympic Committees

Karen Milton BSc (Hons), MSc, PhD

Lecturer in Public Health, Norwich Medical School, University of East Anglia, Norwich, UK

James Morton PhD

Professor of Exercise Metabolism, Research Institute for Sport and Exercise Sciences, Liverpool John Moores University, UK; Head of Nutrition, Team Sky

Margo Mountjoy MD, PhD

International Olympic Committee Medical Commission-Games Group; Association of Summer Olympic International Federations (ASOIF) Medical + Scientific Consultative Group Chair; FINA Bureau-Sport Medicine; Associate Clinical Professor, McMaster University, Canada

Timothy Noakes OMS, MBChB, MD, DSc, FACSM (Hon), FFSEM (UK), OMS, MBChB, MD, DSc, PhD (hc), FACSM) (Hon), FFSEM (UK) (Hon), FFSEM (Ire)

Sports Physician and Exercise Physiologist; Former Discovery Health Professor of Exercise and Sports Science, University of Cape Town and Sports Science Institute of South Africa, Cape Town, South Africa

James O'Donovan MB BCh, BaO, MICGP, FFSEM (Ire), MSc (SEM)

Sports Medicine Fellow, Division of Sports Medicine, University of British Columbia, Vancouver, Canada

Hayden Opie AM, BCom, LLB (Hons), LLM

Senior Fellow, Melbourne Law School, The University of Melbourne, Australia; Arbitrator, Court of Arbitration for Sport, Switzerland; Past President, Australian and New Zealand Sports Law Association

Sébastien Racinais PhD, FECSS

Head of Athlete Health and Performance Research Centre, Aspetar Orthopaedic and Sports Medicine Hospital, Doha, Qatar

Hamish Reid MBChB, BSc, DiMM, DMCC, DipSEM, MRCEM, MRCS (Ed), FFSEM

Sport and Exercise Medicine Physician, Centre for Sport and Orthopaedic Medicine, Bermuda; Moving Medicine Design and Development lead, Faculty of Sport and Exercise Medicine, UK

Kathryn H Schmitz PhD, MPH, FACSM, FTOS

Professor, Departments of Public Health Science, Kinesiology, and Physical Medicine & Rehabilitation, Penn State University, Pennsylvania, USA

Yorck Olaf Schumacher MD

Aspetar Qatar Orthopaedic and Sports Medicine Hospital, Doha, Qatar

Sanjay Sharma BSAc, MD, FRCP, FESC

Head of Research, Cardiology Clinical and Academic Group, St George's, University of London; Medical Director, Virgin Money London Marathon; Chairman of the Football Association Expert Cardiac Committee, UK

Jenny Shute MBE, MA, BM, BCh

General Medical Practitioner; Medical Commission, Fédération Internationale de Ski (FIS); Lead Welfare Officer, FIS

Siobhan M Statuta MD

Associate Professor, Family Medicine and Physical Medicine & Rehabilitation; Team Physician, University of Virginia Sports Medicine, Charlottesville, Virginia, USA

Genevra L Stone MD

Emergency Medicine Resident, Beth Israel Deaconess Hospital, Harvard Medical School, Boston, MA, USA; Dual Olympian (rowing), silver medal single scull 2016

Hasan Tahir BSc, MBBS, MSc, MFSEM (UK), FRCP (UK)

Consultant Physician in Rheumatology and Acute Medicine, Clinical Lead for Rheumatology, Biological Therapies and Research, Hon. Reader in Investigational Clinical Rheumatology, University of London, UK; Professor of Clinical Sciences with St Matthew's University

Mike Tipton MBE, BEd (Hons), MSc, PhD, FPhysiol

Professor of Human & Applied Physiology, Extreme Environments Laboratory, Department of Sport & Exercise Science, University of Portsmouth, UK

Dane Vishnubala MBBS, PGCME, MRCGP, PGDipSEM, MFSEM, DipSEM (UK & I), FHEA

NHS Sport and Exercise Medicine Doctor; Public Health England, Lead Physical Activity Champion, University of Leeds, Yorkshire, UK

Nick Webborn OBE, MBBS, FFSEM, FACSM

Clinical Professor (SEM), University of Brighton; Honorary Clinical Professor in the School of Sport, Exercise and Health Sciences, Loughborough University, UK; International Paralympic Committee Medical Committee

Acknowledgements

If you want to go fast, go alone. If you want to go far, go together.
—African proverb

How long is a generation? As we two authors are about to shut our laptops on Edition 5, Volume 2, we reflect on the longer arc of the privilege and opportunity this book has afforded us. *Clinical Sports Medicine* was conceived in 1991 (OK Peter, I admit it was your idea. I have never denied that and yes, now it's in print—K2). In 2019, we have 28 years of thanks to give to over 500 contributors to five editions and what is essentially six books now. That's a generation of sport and exercise medicine clinicians and scientists; a female generation is currently 25.5 years. Note that we have become more evidence-based as we have aged—*lifelong learners!* The first edition of *Clinical Sports Medicine* had zero references and the authors had three publications between them (3 and 0, respectively).

We thank those who went far with us on what we hope has been a worthwhile journey over the 28 years. Some have been part of the *Clinical Sports Medicine* convoy from day 0 — a dinner at Sukhothai Restaurant in Johnston Street, Collingwood, Melbourne. Others joined later and provided one or more of those pearls that are so valued by the clinicians we speak to the world over. We thank every contributor on behalf of every clinician who has flicked through the pages of *Clinical Sports Medicine* to help the patient either in front of them or just out of sight.

For this fifth edition, *Volume 2:The Medicine of Exercise,* specific thanks go to the 53 chapter co-authors listed, with their affiliations, on pages xxix–xxxi. Because we wanted the world expert in every area to contribute to that chapter, very few authors contributed more than one chapter. That is a strength of this book—many subspecialist authors had their work woven together. The beauty of writing Volume 1 and Volume 2 across two years meant that we two authors could focus on the 'medicine of exercise' in a way that was impossible in a one-volume book. That's a compelling case for going far more slowly but ultimately with more support—more co-authors— than in the four single-volume editions. This two-volume edition brings you 48 and 40 chapters (88 in total) with 200 chapter authors—almost twice the number that built the 4th edition.

When one goes far together there is scope for all generations to contribute. The young bring curiosity, passion, vigour and stamina as well as innovation and facility with technology and platforms. We thank and applaud clinicians Paul Blazey (sports physiotherapy) and Daniel

Friedman (medicine) for being editors across all chapters in Volume 2. You made 2018 not only productive but also a rich year in our lives. We often hear emerging talents thanking 'mentors'—here we spell out the reciprocity of our relationship. We learned many things from you, and you introduced us to scintillating people who enliven our community. We will follow your bright trajectories with joy.

Find a job you enjoy doing, and you will never have to work a day in your life.
—Mark Twain

Taking the long view of gratitude again, we authors have been privileged to work in our vocation. Being a clinician is a gift, and being researchers and teachers as well means we are triply fortunate. We thank those who trusted us to be so privileged in university, college (e.g. Australasian College of Sport and Exercise Physicians), journal, media and sport team/federation settings. We hope we have lived up to the expectations of those who punted on us.

One closing paragraph on our first and very special *Volume 2: The Medicine of Exercise.* We thank all of you who had the vision that exercise and physical activity truly is the polypill. You kept working to test your hypothesis—that exercise is medicine—with equipoise. You are unsung heroes who demonstrated the benefits of exercise across organ systems (cardiovascular, respiratory, neurological) and in various populations (older people and kids, those living with diseases/disorders, those with disabilities, those who are marginalised). You are working in knowledge translation, implementation and scale-up. You provided the bedrock for this volume.

We are grateful to all those who have trusted us—patients and athletes, coaches, colleagues, trainees, readers. We are grateful to have been entrusted with leadership positions with their privileges and responsibility. Our simple hope is that we have added value to our remarkable community that goes far to help patients and athletes 24/7 and 365. A community that allows the world to benefit from physical activity, exercise and sport.

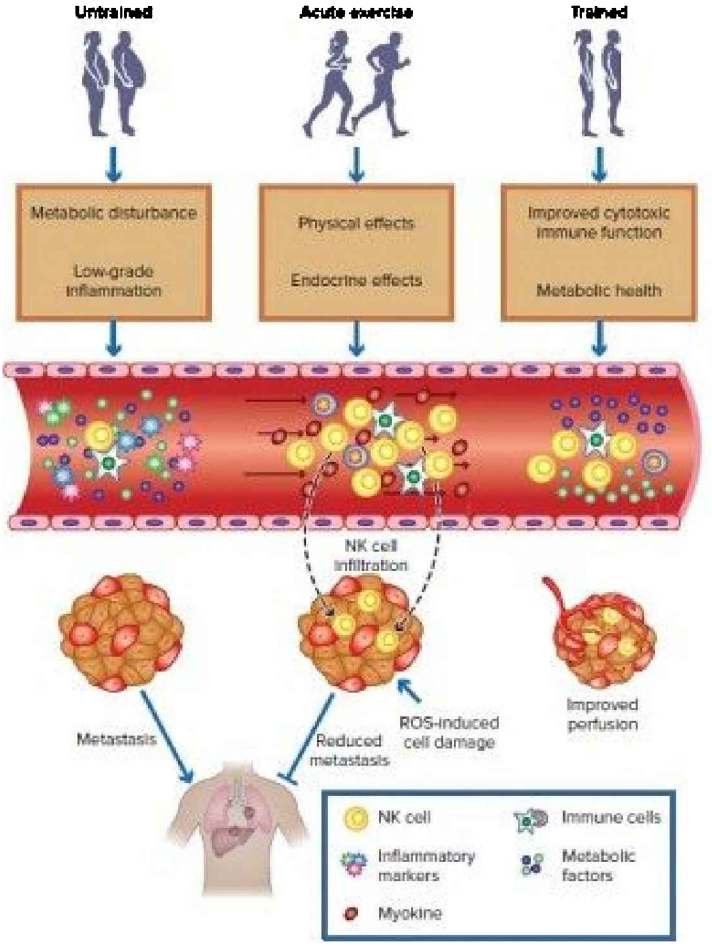
Guided tour of your book

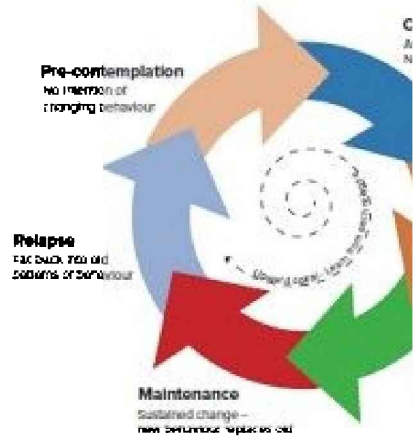
The principal text in its field, this second volume of the fifth edition of *Clinical Sports Medicine* continues to provide readers with quality up-to-date content. The engaging material has been contributed by leading experts from around the world. Look out for these key features, which are designed to enhance your learning.

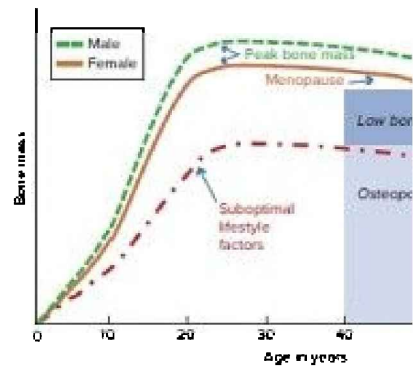
Premium, up-to-date content

PART A EXERCISE AND HEALTH discusses the global public health problem of physical inactivity and includes a chapter on nutrition. PART B MANAGING MEDICAL PROBLEMS considers the effect of activity levels on the most common medical issues, such as obesity, diabetes and cancer, as well as others. PART C ENVIRONMENT focuses on the effects of heat, cold, altitude and being underwater on the athlete and includes a chapter on the built environment and its influence on activity levels. PART D SPECIFIC GROUPS includes issues relating to treating children, older people and people with disability and discusses female-specific and transgender and intersex issues in sport. PART E PERFORMANCE AND ETHIC S discusses nutrition for performance, legal issues, genetics, harassment and abuse, and drugs and the athlete. PART F PRACTICAL SPORTS MEDICINE provides best practice medical advice regarding emergencies and endurance events, including multisport endurance events.

These topics are discussed via clear text, abundant clinical and other photos and relevant imaging. New data is obtained from research published in peer-reviewed journal articles and the reader is directed to the online references for further information. Tables and diagrams throughout illustrate the key concepts.







Tables

Page xxxv

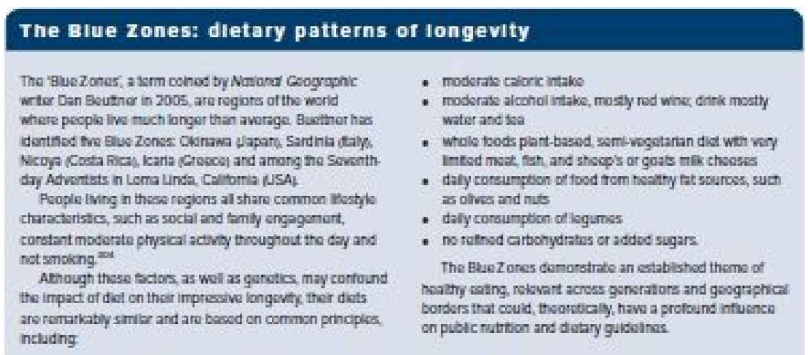
New tables summarise vast amounts of evidence to provide take-home messages. Primary sources are readily available.

Table 6.1 Types of amino acids

Essential	Conditionally essential	Non-essential
Histidine	Arginine	Alanine
Isoleucine	Cysteine	Aspartic acid
Leucine	Glutamine	Asparagine
Lysine	Glycine	Glutamic acid
Methionine	Proline	Serine
Phenylalanine	Tyrosine	
Threonine		
Tryptophan		
Valine		

Boxes

Boxes throughout the chapiters focus on specific topics.



The Blue Zones: dietary patterns of longevity

The 'Blue Zones', a term coined by *National Geographic* writer Dan Buettner in 2005, are regions of the world where people live much longer than average. Buettner has identified five Blue Zones: Okinawa (Japan), Sardinia (Italy), Nicoya (Costa Rica), Icaria (Greece) and among the Seventh-day Adventists in Loma Linda, California (USA).

People living in these regions all share common lifestyle characteristics, such as social and family engagement, constant moderate physical activity throughout the day and not smoking.[304]

Although these factors, as well as genetics, may confound the impact of diet on their impressive longevity, their diets are remarkably similar and are based on common principles, including:

- moderate caloric intake
- moderate alcohol intake, mostly red wine; drink mostly water and tea
- whole foods plant-based, semi-vegetarian diet with very limited meat, fish, and sheep's or goats milk cheeses
- daily consumption of food from healthy fat sources, such as olives and nuts
- daily consumption of legumes
- no refined carbohydrates or added sugars.

The Blue Zones demonstrate an established theme of healthy eating, relevant across generations and geographical borders that could, theoretically, have a profound influence on public nutrition and dietary guidelines.

Co-authors

The 53 **world-renowned co-authors** bring a truly global perspective to the book.

Co-authors

Kathryn E Ackerman MD, MPH, FACSM
Sports Medicine Physician and Endocrinologist; Medical Director, Female Athlete Program, Boston Children's Hospital; Associate Director, Sports Endocrine Research Lab, Massachusetts General Hospital; Assistant Professor of Medicine, Harvard Medical School, Boston, MA; Team Physician, USA Rowing

Marcos Agostinho MD, PGDipSEM, BASc
Primary Care Sports Physician, CUF Torres Vedras Hospital, Portugal; Team Physician SCU Torreense, Portugal

Permanente, Santa Clara Medical Center, Palo Alto, CA, USA; Special Operations Physician, San Mateo County Tactical EMS

Graeme Close PhD, ASCC, rSEN, fBASES, fECSS
Professor of Human Physiology, Liverpool John Moores University, Liverpool, UK; Expert Nutrition Consultant, Rugby, UK

Jonathan Drezner MD
Director, UW Medicine Center for Sports Cardiology; Professor, Department of Family Medicine, University of Washington, USA; Team Physician, Seattle

Case studies

Case studies provide real-world examples of issues discussed in the chapter.

CASE STUDY

Rob Waddell, rower—atrial fibrillation

Competing at the highest level of sport is hard enough without throwing a whole other variable into the mix. I used to be really scared every single race that I would have an episode of AF.

Rob Waddell (Fig. 10.4) was an elite-level rower for New Zealand, winning the world single sculls titles in 1998 and 1999, before capturing Olympic gold in the same discipline at the Sydney Olympics in 2000. He also held the world record for indoor rowing at both 2000 and 5000 metres.

Diagnosis

In the 1990s Waddell experienced a significant loss in power output, breathlessness and extreme fatigue both during training and racing.

A Holter monitor was used to assess his heart rhythm over an extended period of time, however the results were inconclusive. Waddell was sent to Auckland for electrophysiologic testing (See Need to Know box below) He was subsequently diagnosed with paroxysmal atrial fibrillation (AF).

Management

Despite treatment with high dose flecainide in an attempt to control his AF, the condition persisted, becoming increasingly more severe and intrusive throughout his career, particularly in the lead-up to the 2000 Olympics in Sydney.

Following his victory at the Sydney Olympics, Waddell decided to change sports and shift his focus to sailing, given the ongoing difficulty of managing his AF. The change in sports necessitated a 20 kg weight gain and, due to the more intermittent nature of the activity, Waddell was able to compete relatively asymptomatically and even stop taking flecainide.

In 2008, Waddell decided to return to rowing. During the deciding race of a best-of-three series that determined qualification for the Beijing Olympics, Waddell suffered a recurrence of his AF. He vividly described the experience as 'feeling like rowing through mud'. Waddell went on to qualify for the Beijing Olympics and placed fourth in the double sculls.

Waddell would later undergo radiofrequency ablation which dramatically improved his AF and enabled him to continue sailing competitively at the international level.

Figure 10.4 Rob Waddell on the podium at the 2000 Sydney Olympics
GETTY IMAGES/PHIL WALTER

Conclusion

Waddell's story provides a good example of a common problem faced by elite competitors with AF. With appropriate and careful management, athletes with AF may still be able to compete in their sport at the highest level.

Practice pearls and Need to know

Practice pearls are a valuable feature that provide clinical tips and important information

to keep in the forefront of your mind.

PRACTICE PEARL

Warning symptoms such as exercise-related syncope must be carefully evaluated to rule out potentially lethal cardiac disorders.

NEED TO KNOW

Those involved in sports where making weight is important, such as power lifting, boxing and wrestling, may consider omitting insulin, to support a reduced weight at weigh-in.[25] Education should always be the primary concern of the medical professional involved with these athletes, including the implications for their health and potentially performance.[26]

References

Over 3000 carefully chosen references. A comprehensive list of references for each chapter can be found here: **www.mhhe.com/au/CSM5e.**

PART A

Exercise and health

Chapter 1

Physical inactivity: a global public health problem

with Daniel Friedman

I believe that evidence supports the conclusion that physical inactivity is one of the most important public health problems of the 21st century, and may even be the most important.

Professor Steven N Blair, Arnold School of Public Health, University of South Carolina, USA

Read any blog, newspaper, journal article or social media feed and you will find they are all telling you the same thing: physical inactivity is a problem—a big one. Physical inactivity causes alarming levels of chronic disease now; and the future predictions of societal costs and decimated quality of life are dire.

This is not new information. There have been calls to address the problem for decades. Global action plans and national strategies declared war on physical inactivity long ago, yet it seems many countries are still struggling to mobilise the troops. How many more times do we need to be reminded that physical inactivity is one of the leading risk factors for global mortality and is estimated to cause 3.2 million deaths annually,[1] before we finally decide to get off the couch?

The four previous editions of *Clinical Sports Medicine* shone a spotlight on the burden of physical inactivity and sedentary behaviour, but clinicians also appreciate the importance of other pressing behavioural contributors to health. As the World Health Organization (WHO) reminds us, unhealthy eating habits, tobacco consumption and harmful use of alcohol contribute to the tsunami of non-communicable disease (NCD). The concern, as Professor Steven Blair underlined so clearly in 2009, is that 'the crucial importance of physical activity is undervalued and underappreciated by many individuals in public health and clinical medicine'.[2]

To raise awareness and provide the clinician with even more motivation to promote physical activity to their patients, family and friends, this chapter records the economic and health costs of physical inactivity. We outline some of the key policies and actions that could reverse downward

trends. A global health problem of this magnitude demands a calculated, methodical and consistent plan of attack. To make progress we must first understand the problem.

PHYSICAL INACTIVITY TRENDS

The WHO Global Recommendations on Physical Activity advise that adults should do at least 150 minutes of moderate-intensity or 75 minutes of vigorous-intensity aerobic physical activity throughout the week. Additionally, muscle-strengthening activities should be done at least twice weekly.[3] While there are no global recommendations on sedentary behaviour, emerging consensus indicates it should be limited whenever possible.[4]

From an evolutionary perspective, humans are primed to move; daily hunting and gathering for survival necessitated continual movement and exertion. However, today, many in the wealthy West no longer need to run, climb or even walk to procure food and water (Fig. 1.1). Everything is available at the touch of a button.

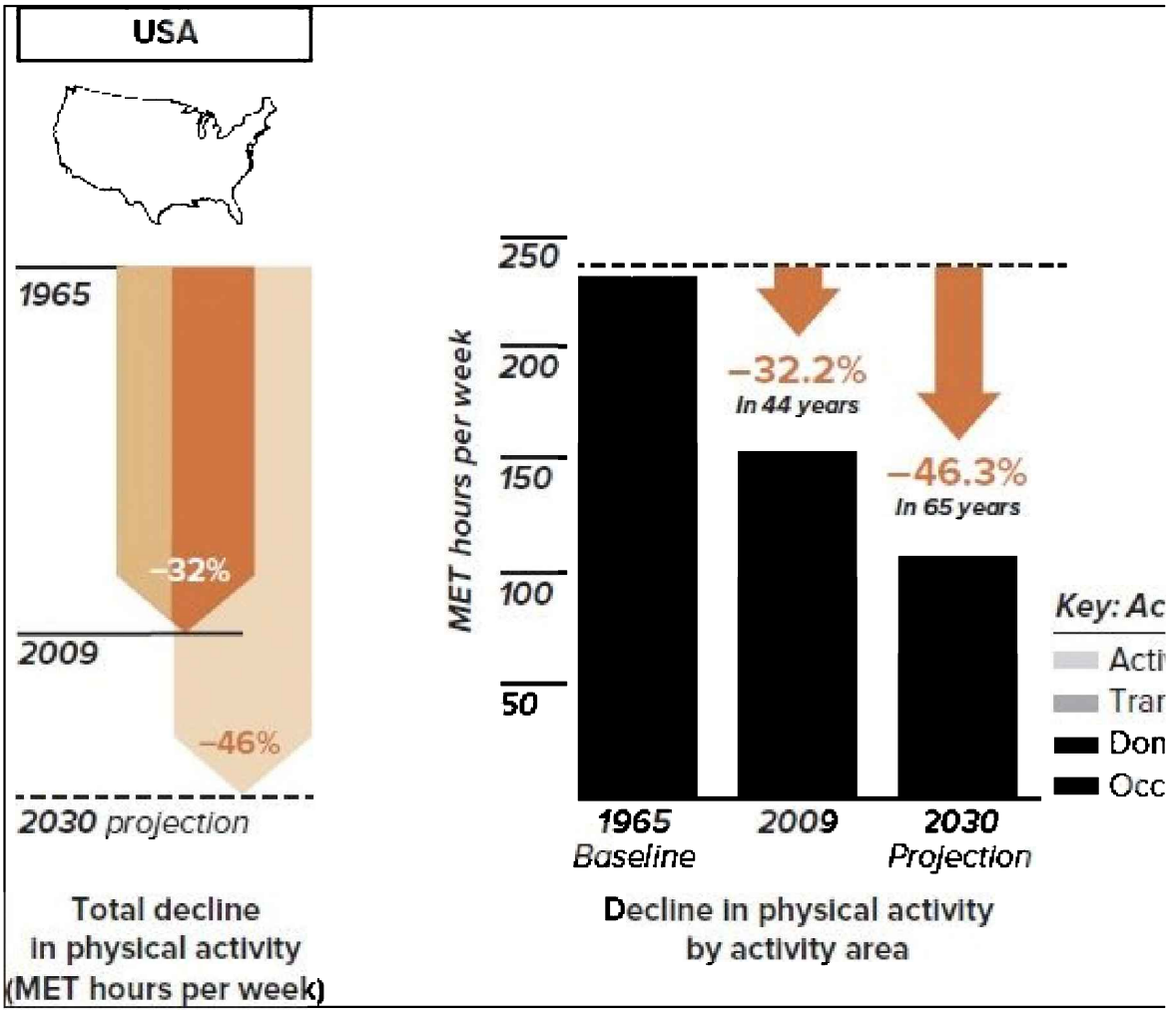


Figure 1.1 Figure 1.1 Historic and projected physical activity levels: the dramatic reduction in physical activity in the United States. One metabolic equivalent (MET) is defined as 1 kcal/bodyweight kg/hour and is roughly equivalent to the energy cost of sitting quietly
ADAPTED FROM 'DESIGNED TO MOVE' (P.3), ACSM/NIKE WWW.RACKCDN.COM/RESOURCES/PDF/EN/FULL-REPORT.PDF

The rapid development of technology has engineered physical labour out of most of our lives. In the 1960s, almost half of private industry occupations in the USA required at least moderate intensity physical activity and now fewer than 20% demand this level of activity.[5]

Global estimates[6] indicate that:

- 31% of adults are physically inactive; 34% of women and 28% of men

- 80% of 13–15 year olds are physically inactive; girls are less active than boys
- physical inactivity is more common in countries of high income than in those of low income
- physical inactivity increases with age
- the proportion of adults spending four or more hours per day sitting is 42%.

THE COSTS OF PHYSICAL INACTIVITY

Direct healthcare costs of physical inactivity combine with indirect costs (productivity losses due to morbidity and premature mortality etc.) to contribute to a hefty physical inactivity price tag that affects society and ultimately individuals through poor health.

Healthcare costs

Physical inactivity is responsible for approximately 30% of cardiovascular disease, 27% of diabetes, and 21–25% of breast and colon cancer.[7] The overall direct healthcare costs of physical inactivity can be calculated by estimating the proportions of diseases that can be directly attributable to physical inactivity, multiplying those by the relative risks for different diseases associated with physical inactivity and applying economic cost estimates from the healthcare system for treating the associated chronic diseases.

In 2013, the total direct healthcare cost of physical inactivity attributable to five major NCDs was US$53.8 billion:[8]

- $5 billion was spent on coronary heart disease
- $6 billion on stroke
- $37.6 billion on type 2 diabetes
- $2.7 billion on breast cancer
- $2.5 billion on colon cancer.

This estimate does not include costs attributable to musculoskeletal conditions, falls or depression and anxiety, and is limited by availability of country data. All of these costs (Tabl Page 4 e 1.1) are shared among governments, through public and private healthcare, and by patients who are forced to make out-of-pocket payments.

Table 1.1 Costs attributable to physical inactivity by country in 2013 (US$ million)

https://www.sciencedirect.com. Due to rights and permissions restrictions, this content cannot be reproduced in a digital format. The content is available in the print edition at page 3.

REPRINTED FROM *THE LANCET*, 388(1005), DING D, LAWSON KD, KOLBE-ALEXANDER TL ET AL. THE ECONOMIC BURDEN OF PHYSICAL INACTIVITY: A GLOBAL ANALYSIS OF MAJOR NON-COMMUNICABLE DISEASES. *LANCET* 1311–24, 2016, WITH PERMISSION FROM ELSEVIER.

According to 2017 data, if all Australians did an extra 15 minutes of brisk walking for at least five days each week, Australia's physical inactivity disease burden would be reduced by 13%.[9] In other words, Australians could save nearly A$60 million in healthcare dollars every year by simply going for a stroll!

NEED TO KNOW

If physical inactivity were not eliminated, but could be decreased instead by 10% or 25%, more than 533 000 or 1.3 million deaths, respectively, would be avoided each year.[10]

Productivity costs

The burden of physical inactivity extends well beyond healthcare dollars (Table 1.2). Indirect costs (Fig. 1.2) that are not often considered include productivity losses due to premature mortality, disability, absenteeism, presenteeism (employees who come in to work but have compromised productivity due to ill health), as well as informal care and other non-medical costs.

Table 1.2 Counting the cost of inactivity in Australia in 2013 (in A$)

https://www.sciencedirect.com. Due to rights and permissions restrictions, this content cannot be reproduced in a digital format. The content is available in the print edition at page 4.

REPRINTED FROM *THE LANCET*, 388(1005), DING D, LAWSON KD, KOLBE-ALEXANDER TL ET AL. THE ECONOMIC BURDEN OF PHYSICAL INACTIVITY: A GLOBAL ANALYSIS OF MAJOR NON-COMMUNICABLE DISEASES. *LANCET* 1311–24, 2016, WITH PERMISSION FROM ELSEVIER.

	Total spend (US$) in 2008	2008 Direct costs	2008 Indirect costs	2030 Direct costs projection	% Ir dire 200
USA	$147.0b — OR — ~2× the federal budget for the Department of Education (based on US$77.4b 2012 budget)	$90.1b	$56.5b	$191.7b	
UK	$33.0b — OR — Close to the National Health Service's annual efficiency target (based on £20b of annual efficiency savings over the next four years)	$16.1b	$16.7b	$26.0b	

Figure 1.2 Direct and indirect costs of physical inactivity in the past and as predicted for the future (US$)
ADAPTED FROM 'DESIGNED TO MOVE' (P. 9), ACSM/NIKE

- In Canada, osteoarthritis is projected to cost C$18 billion a year in lost productivity by 2031, as the condition causes substantial long-term absenteeism and disability, reduced employment and early retirement.[11]
- In Australia, the national impact of diabetes through lost labour-force participation of people aged 45–64 years is projected to reach A$807 million in lost income, $350 million in extra welfare payments, $166 million in lost taxation revenue and $3 billion in lost gross domestic product (GDP) by 2030.[12]
- In the USA, obesity-attributable absenteeism among employees costs over US$8.5 billion per year.[13]

In 2013, the total cost of productivity losses from physical inactivity-related deaths worldwide was US$13.7 billion. Of this, $3.2 billion was in North America and $3.8 billion was in Europe. When these indirect costs are combined with the direct healthcare costs, physical inactivity is estimated to be responsible for $67.5 billion in costs worldwide (Table 1.3).[8]

Page 5

Table 1.3 Total economic cost of physical inactivity attributable to five major NCDs in 2013 (US$ billion)

https://www.sciencedirect.com. Due to rights and permissions restrictions, this content cannot be reproduced in a digital format. The content is available in the print edition at page 5.

REPRINTED FROM THE LANCET, 388(10051), DING D, LAWSON KD, KOLBE-ALEXANDER TL ET AL. THE ECONOMIC BURDEN OF PHYSICAL INACTIVITY: A GLOBAL ANALYSIS OF MAJOR NON-COMMUNICABLE DISEASES. 1311–24, 2016, WITH PERMISSION FROM ELSEVIER.

The costs of physical inactivity versus smoking

Yes, physical inactivity is extremely costly. But how does it compare with other risk factors for poor health, such as smoking? In 2012, the total healthcare expenditure due to smoking was US$467 billion, or 5.7% of global health expenditure. When including indirect productivity costs, the total economic cost of smoking totalled US$1.9 trillion.[15] This seems like it is exponentially greater than the cost of physical inactivity, until you crunch the numbers.

Let's use Canada as an example. In 2013, the total economic burden attributable to smoking in Canada was C$18.7 billion.[16] For each of the 5.7 million smokers in Canada in 2013,[17] these costs represent approximately $3280 in total expenditure per smoker.

Compare this to the total economic burden attributable to physical inactivity in Canada in 2013, which was $10.8 billion.[16] In 2013, four out of five Canadians did not meet the recommended physical activity guidelines,[18] which is 28.13 million out of 35.16 million people. Therefore, the per person cost of physical inactivity in Canada in 2013 was $10.8 billion divided by 28.13 million, or $384—an amount equivalent to roughly one ninth of the attributable cost per smoker.

Now consider that the average smoker in Canada consumes 14 cigarettes per day,[19] or 98 per week. If we assume a linear relationship, the attributable cost per inactive Canadian mirrors the total economic burden of smoking 11 cigarettes per week. Therefore, according to our assumptive back-of-the-envelope calculations, the cost of physical inactivity in Canada is approximately that of smoking about half a pack of 20 cigarettes per week.

These costs are distributed unequally and disproportionately throughout the world. High-income countries carry a larger proportion of the economic burden and low- and middle-income countries suffer a larger proportion of the disease burden.[8]

Quality of life

Physical inactivity and subsequent ill health limits the degree to which we can enjoy the important possibilities of our lives. This subjective concept can be quantified using disability-adjusted life years (DALYs) (Fig. 1.3). One DALY can be thought of as one lost year of 'healthy' life. Page 6 Therefore, the sum of DALYs, or burden of disease, across the population can be thought of as a measure of the gap between current health status and an ideal health situation, where the entire population lives to an advanced age, free of disease and disability.[14]

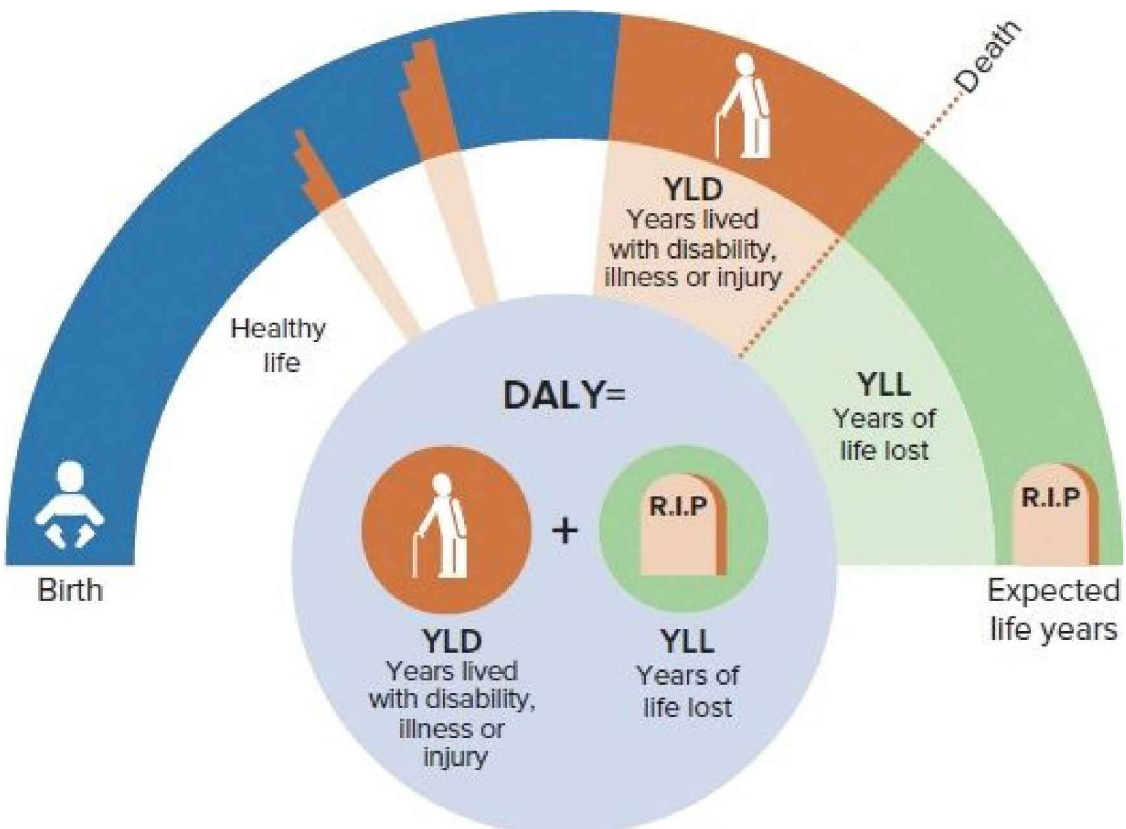


Figure 1.3 The concept of disability-adjusted life years (DALYs) and its components
© CROWN COPYRIGHT HTTPS://WWW.GOV.UK/GOVERNMENT/PUBLICATIONS/BURDEN-OF-DISEASE-STUDY-FOR-ENGLAND

In 2013, the lifetime disease burden associated with physical inactivity for the major NCDs was 13.4 million DALYs worldwide.[8]

THE WAY FORWARD

If we continue to remain on the couch, the global burden of physical inactivity will continue to gain weight, particularly in low- and middle-income countries. There are obviously economic and health arguments for solving the physical inactivity pandemic, but what exactly needs to be done?

Given the diversity of ways to be active and the multiple settings in which we must look to increase participation, the solution to physical inactivity lies beyond the scope of any single agency. As the WHO's Global Action Plan on Physical Activity 2018–2030 (GAPPA)[20] emphasises, a major reduction in the burden of physical inactivity and subsequent NCDs will come from a whole-of-system approach which implements effective population-wide interventions that address both upstream and downstream factors of participation.

NEED TO KNOW

WHO's Global Action Plan on Physical Activity 2018–2030: proposed targets for 2025

25% reduction of premature mortality from NCDs

+

10% relative reduction in the prevalence of insufficient physical activity

The '7 Best Investments for Physical Activity' from the International Society for Physical Activity and Health, in 2011,[21] captured this multidimensional approach, which has been revitalised in the most recent GAPPA. Both promote common key action areas, including:

- the built environment and transport (Chapter 27)
- schools and other educational institutions
- community and grassroots-based initiatives
- sports systems and programs
- public education
- healthcare
- advocacy and leadership
- monitoring and surveillance.

Every one of us must do our part to increase physical activity in all areas of society. We must

find ways to integrate physical activity back into our daily lives through implementation of effective evidence-based policy actions that make the healthier choices easier.

Physical inactivity's costs, whether human or economic, direct or indirect, are entirely preventable. Armed with an understanding of the size and consequences of the problem, it is clear that the time for action is now.

REFERENCES

1. World Health Organization (WHO). Physical inactivity: a global public health problem. Geneva, 2018. http://www.who.int/dietphysicalactivity/factsheet_inactivity/en/.
2. Blair SN. Physical inactivity: the biggest public health problem of the 21st century. *Br J Sports Med* 2009; 43(1):1–2.
3. World Heath Organization (WHO). Global Recommendations on physical activity for health. Geneva, 2010.
4. Katzmarzyk PT, Lee IM. Sedentary behaviour and life expectancy in the USA: a cause-deleted life table analysis. *BMJ Open* 2012; 2(4).
5. Church TS, Thomas DM, Tudor-Locke C et al. Trends over 5 decades in U.S. occupation-related physical activity and their associations with obesity. *PLoS ONE* 2011; 6(5).
6. Hallal PC, Andersen LB, Bull FC et al. Global physical activity levels: surveillance progress, pitfalls, and prospects. *Lancet* 2012; 380(9838):247–57.
7. World Health Organization (WHO) Global health risks: mortality and burden of disease attributable to selected major risks. Geneva, 2009.
8. Ding D, Lawson KD, Kolbe-Alexander TL et al. The economic burden of physical inactivity: a global analysis of major non-communicable diseases. *Lancet* 2016; 388(10051):1311–24.
9. Australian Institute of Health and Welfare (AIHW). Impact of physical inactivity as a risk factor for chronic conditions: Australian Burden of Disease. Canberra, Australia: 2017.
10. Lee IM, Shiroma EJ, Lobelo F et al. Impact of physical inactivity on the world's major non-communicable diseases. *Lancet* 2012; 380(9838):219–29.
11. Sharif B, Garner R, Hennessy D et al. Productivity costs of work loss associated with osteoarthritis in Canada from 2010 to 2031. *Osteoarthritis Cartilage* 2017; 25(2):249–58.
12. Schofield D, Shrestha RN, Cunich MM et al. The costs of diabetes among Australians aged 45–64 years from 2015 to 2030: projections of lost productive life years (PLYs), lost personal income, lost taxation revenue, extra welfare payments and lost gross

domestic product from Health&WealthMOD2030. *BMJ Open* 2017;7(1).

13. Andreyeva T, Luedicke J, Wang YC. State-level estimates of obesity-attributable costs of absenteeism. *J Occup Environ Med* 2014; 56(11):1120–7.
14. World Health Organization (WHO). Metrics: disability-adjusted life year (DALY). 2018, http://www.who.int/healthinfo/global_burden_disease/metrics_daly/en/.
15. Goodchild M, Nargis N, Tursan d'Espaignet E. Global economic cost of smoking-attributable diseases. *Tob Control* 2018; 27(1): 58–64.
16. Krueger H, Krueger J, Koot J. Variation across Canada in the economic burden attributable to excess weight, tobacco smoking and physical inactivity. *Can J Public Health* 2015 May 1; 106(4):e171–7.
17. Statistics Canada. Smoking, 2013. 2015, http://www.statcan.gc.ca/pub/82-625-x/2014001/article/14025-eng.htm.
18. Statistics Canada. Directly measured physical activity of adults, 2012 and 2013. 2015, http://www.statcan.gc.ca/pub/82-625-x/2015001/article/14135-eng.htm.
19. Reid J. *Tobacco Use in Canada: Patterns and Trends*, 2017 edition. Waterloo, ON: Propel Centre for Population Health Impact, University of Waterloo, 2017.
20. World Health Organization (WHO). Global action plan on physical activity 2018–2030: more active people for a healthier world. Geneva, 2018.
21. Global Advocacy for Physical Activity (GAPA), the Advocacy Council of the International Society for Physical Activity and Health (ISPAH). NCD Prevention: Investments that Work for Physical Activity, 2011.

Chapter 2

Benefits and risks of physical activity

with DANIEL FRIEDMAN

Eating alone will not keep a man [or woman] well; he [or she] must also take exercise.
Hippocrates (460–370 BCE)

Physical activity is good for us. Well before the age of double-blind randomised placebo-controlled trials and peer-reviewed journals, Hippocrates and others espoused the benefits of exercise on the body and mind. Herodicus (400 BCE), a former teacher of Hippocrates and regarded as the pioneer of sport and exercise medicine, devoted his time to recommending exercise to help recovery from athletic and gymnastic injuries. Later, Galen (131–201 BCE), a Greek physician to the gladiators, proclaimed that 'the form of exercise deserving our attention is therefore that which has the capacity to provide health of the body, harmony of the part and virtue in the soul and these things are true of the exercise with the small ball'.

Fast forward a few thousand years and we have proof of many benefits of physical activity and reduced sedentary behaviour. Empirical evidence that physical activity was associated with health came in the 1950s. Dr Jerry Morris, a Scottish epidemiologist credited as 'the man who invented exercise', established the importance of physical activity in preventing cardiovascular disease after noticing that sedentary drivers of London's double-decker buses had higher rates of cardiovascular diseases than did the conductors who climbed the stairs. 'Is this chance a phenomenon?' asked Morris in his 1953 *Lancet* paper.[1] He answered his own question by reproducing similar findings when extending the study to London postmen and less active postal clerks.

Today, systematic reviews conclude that physical inactivity is a key risk factor for the leading non-communicable diseases and, conversely, that regular physical activity has a fundamental role in the primary and secondary prevention of many diseases and injuries. We have an incontrovertible evidence base for the millennia-old conclusion: *physical activity is medicine.*

Simon Sinek, a successful British-American author and motivational speaker, encourages everybody to 'start with why',[2] and this is relevant if we expect people to undertake physical activity. Epidemiological data provide part of a compelling reason to exercise; the mechanistic 'why'—asking what does exercise do at the cellular/tissue level?—complements the epidemiological data. Why does physical activity confer so many health benefits unmatched by any medication?

Galen believed that physical activity 'thins the body, hardens and strengthens muscles, increases flesh, and elevates blood volume'.[3] Was he wrong? Here we explore Galen's hypothesis by delving into the physiological mechanisms whereby physical activity influences many (perhaps all) tissues and organ systems for health.

PHYSIOLOGY OF PHYSICAL ACTIVITY: A CLINICIAN'S PRIMER

The following describes the basic physiology of physical activity, one of the most extreme stresses to which the body can be exposed (Fig. 2.1).

https://www.sciencedirect.com. Due to rights and permissions restrictions, this content cannot be reproduced in a digital format. The content is available in the print edition at page 8.

Figure 2.1 A summary of the physiological response to physical activity
ADAPTED FROM *CELL*, 159, HAWLEY JA, HARGREAVES M, JOYNER MJ ET AL. INTEGRATIVE BIOLOGY OF EXERCISE, 738–49, FIGURE 1, 2014, WITH PERMISSION FROM ELSEVIER[5]

Maintaining homeostasis—a fancy word for survival

Physical activity provokes widespread changes in numerous cells, tissues and organs as a response to, or consequence of, the increased metabolic activity of contracting skeletal muscle. This preserves cellular oxygenation and acid-base homeostasis—both of which are critical for life. The physiological response depends on duration, intensity and frequency of the activity, as well as environmental conditions.

If we take a muscle-centric view, nearly all bodily systems support contracting skeletal muscle. The cardiovascular and respiratory systems instantly increase oxygen availability, release glycogen and fat for energy in the muscle and remove metabolic waste products and carbon dioxide. Page 8 Free fatty acids are released from adipose tissue, and the liver generates glucose. The nervous system is activated as are numerous endocrine signals to help regulate all of these functions. The subsequent forces generated by skeletal muscle contractions and gravity then put stress on bone, ligaments and tendons.[4]

Adaptive protein changes

Most of physical activity's long-term health benefits result from adaptations in the activity and abundance of proteins involved in specific metabolic, physiological and biomechanical processes—such as mitochondrial respiratory function, calcium cycling and contractile efficiency. These changes are accomplished via shifts in gene transcription and protein translation as well as post-

translational modifications.

The energetic and mechanical challenges imposed by physical activity are transient, as are the adaptive cellular responses which occur during the hours following physical activity. Therefore, the adaptive increase in any protein as the result of regular physical activity is a function of:[6]

- the half-life of the protein
- the transient increase in expression that occurs during recovery in between physical activity bouts
- the decrease in expression that occurs between bouts.

That explains why one cannot exercise for 5 minutes and be 'vaccinated' against the ails of physical inactivity for life. Use is or lose it. On the other hand, the good news is that every step counts!

BENEFITS

Which mechanisms underlie physical activity's force for preventing disease and improving health? Here we outline some of the physiological and mechanistic evidence for physical activity's benefits for different organs and systems (summarised in Table 2.1). We direct you to the relevant chapters for further reading.

Table 2.1 Summary of benefits of regular physical activity

Health benefit	Strength of evidence
Reduced risk of:	
• premature death	Strong
• cardiovascular disease	Strong
• stroke	Strong
• high blood pressure	Strong
• adverse blood lipid profile	Strong
• type 2 diabetes mellitus	Strong
• gestational diabetes mellitus	Strong
• metabolic syndrome	Strong
• bladder, breast, colon, endometrial, oesophageal adenocarcinoma, renal and gastric cancers	Strong
• depression	Strong
• anxiety	Strong
Prevention of weight gain	Strong
Weight loss in conjunction with reduced calorie intake	Strong
Decreased pain and improved physical function in adults with osteoarthritis of the knee and hip	Strong
Prevention of falls	Strong
Improved cognitive function in older adults	Strong
Improved physical function for older adults with frailty	Strong
Improved sleep quality	Strong
Lower risk of:	

• hip fracture	Moderate
• lung cancer	Moderate
Increased bone density	Moderate

ADAPTED FROM PHYSICAL ACTIVITY GUIDELINES ADVISORY COMMITTEE SCIENTIFIC REPORT 2018, DEPARTMENT OF HEALTH AND HUMAN SERVICES USA[14]

Brain function and mental health

Physical activity epidemiology began with studies that evaluated cardiac function as an outcome, as mentioned previously. Dramatic advances in neuroscience in the 2000s made it clear that physical activity has benefits above the neck as well as below it.

Cognitive decline

Physical activity is associated with a reduced risk of cognitive decline and risk of dementia, including Alzheimer's disease. In a meta-analysis of 15 prospective studies of 1–12 years duration with more than 33 000 participants, greater amounts of physical activity were associated with a 40% reduced risk of cognitive decline.[7]

One explanation is that regular aerobic physical activity blunts increases in cerebral choline, a metabolite that increases with neural loss, which is characteristic in Alzheimer's dementia and dementia with Lewy bodies.[8] Physical activity promotes brain health via its well-known attenuating influences on atherosclerotic cerebrovascular disease.[9] Neurotrophic factors, such as brain-derived neurotrophic factor (BDNF) and insulin-like growth factor 1 (IGF-1), are also implicated in age-related brain atrophy and neurodegenerative disease (see Chapter 31).

Anxiety and depression

Physical activity reduces both state and trait anxiety in adults and older adults. Physical activity reduces the risk of experiencing depressive symptoms and frank depression across the lifespan. Performing more than 30 minutes of physical activity per day reduces the odds of experiencing depression by 50%.[10]

One explanation is the 'endorphins hypothesis' that physical activity augments endorphin secretion. These endogenous brain opioid peptides reduce pain and cause general euphoria.[11] Regular aerobic activity is also associated with lower sympathetic nervous system and hypothalamic-pituitary-adrenal axis reactivity, which plays a critical role in developing adaptive responses to physical and psychological stressors (Chapters 21 and 22).[12]

Sleep

Acute bouts of physical activity and regular physical activity improve sleep. In a meta-analysis of 66 controlled intervention studies involving over 1200 adults, physical activity improved total sleep time, sleep efficiency, sleep onset latency and overall sleep quality.[13] However, the underlying mechanisms are currently being investigated.

Cancer prevention

Physical activity likely improves quality of life and reduces risk of recurrence in cancer patients. Physical activity is also linked with reduced risks of bladder, breast, colon, endometrial and oesophageal adenocarcinoma, renal and gastric cancers, with risk reductions ranging from 10–20%. Sedentary behaviour increases the risk of endometrial, colon and lung cancers by 20–35%.[14]

Evidence from mouse studies shows that physical activity:[15]

- controls cancer progression through direct effects on tumour intrinsic factors, such as growth rate, metastasis, tumour metabolism and immunogenicity of the tumour (Fig. 2.2)
- regulates tumour growth through interplay with systemic factors

https://www.sciencedirect.com. Due to rights and permissions restrictions, this content cannot be reproduced in a digital format. The content is available in the print edition at page 10.

Figure 2.2 Molecular mechanisms linking physical activity to cancer protection. Physical activity consists of acute sessions leading to physical regulation (increased blood flow, shear stress on the vascular bed, temperature increases, sympathetic activation) and endocrine regulation (release of catecholamines and exercise hormones, myokine secretion) that results in increased tumour perfusion, oxygen delivery, intratumoral metabolic stress, cellular damage and reactive oxygen species (ROS) production. These acute changes are able to elicit signalling pathways that prevent metastasis
FROM CELL METABOLISM, 27(1), HOJMAN P, GEHL J, CHRISTENSEN JF ET AL. MOLECULAR MECHANISMS LINKING EXERCISE TO CANCER PREVENTION AND TREATMENT, 10–21, FIGURE 1, 2018, WITH PERMISSION FROM ELSEVIER

- alleviates adverse events related to cancer and its treatment
- improves cancer treatment efficacy. (Chapter 20.)

Cardiometabolic health

Cardiovascular disease

There is very strong evidence of a significant relationship between greater amounts of physical activity and decreased incidence of cardiovascular disease, stroke and heart failure.[14] A meta-analysis of 21 prospective cohort studies with more than 650 000 participants found that physical activity is associated with a 10–30% reduced risk of cardiovascular disease.[16]

One important underlying mechanism of action is physical activity's ability to increase vascular nitric oxide (NO) concentration. Nitric oxide is responsible for vasodilation, which lowers peripheral resistance and increases vessel perfusion. Endothelial nitric oxide synthase, the main source of NO, is upregulated by an increase in flow-mediated shear stress associated with physical activity, due to a complex pattern of intracellular regulation like acetylation and phosphorylation.[17] (Chapter 10.)

Diabetes mellitus

The benefits of physical activity in people with type 1 diabetes include improved insulin sensitivity, improved blood lipid profiles, decreased resting heart rate and blood pressure, decreased body weight and decreased risk of coronary heart disease.[19]

Physical activity reduces the risk of developing type 2 diabetes and provides considerable benefits for people who have type 2 diabetes. Regular aerobic and resistance activity can reverse many of the defects in metabolism of both fat and glucose in people with type 2 diabetes and improve their haemoglobin A1c (HbA1c).[20] A systematic review including 20 cohort studies reported an inverse relationship between volume of moderate-to-vigorous physical activity and risk of type 2 diabetes, finding an average risk reduction of over 40% when comparing the most active with the least active participants.[21]

Physical activity or pharmacotherapy—comparative effectiveness

Physical activity prescription is about as effective as drug interventions in terms of its mortality benefits in the secondary prevention of coronary heart disease and diabetes, stroke rehabilitation and heart failure treatment. In the case of stroke rehabilitation, in particular, physical activity is more effective than drug interventions.[18]

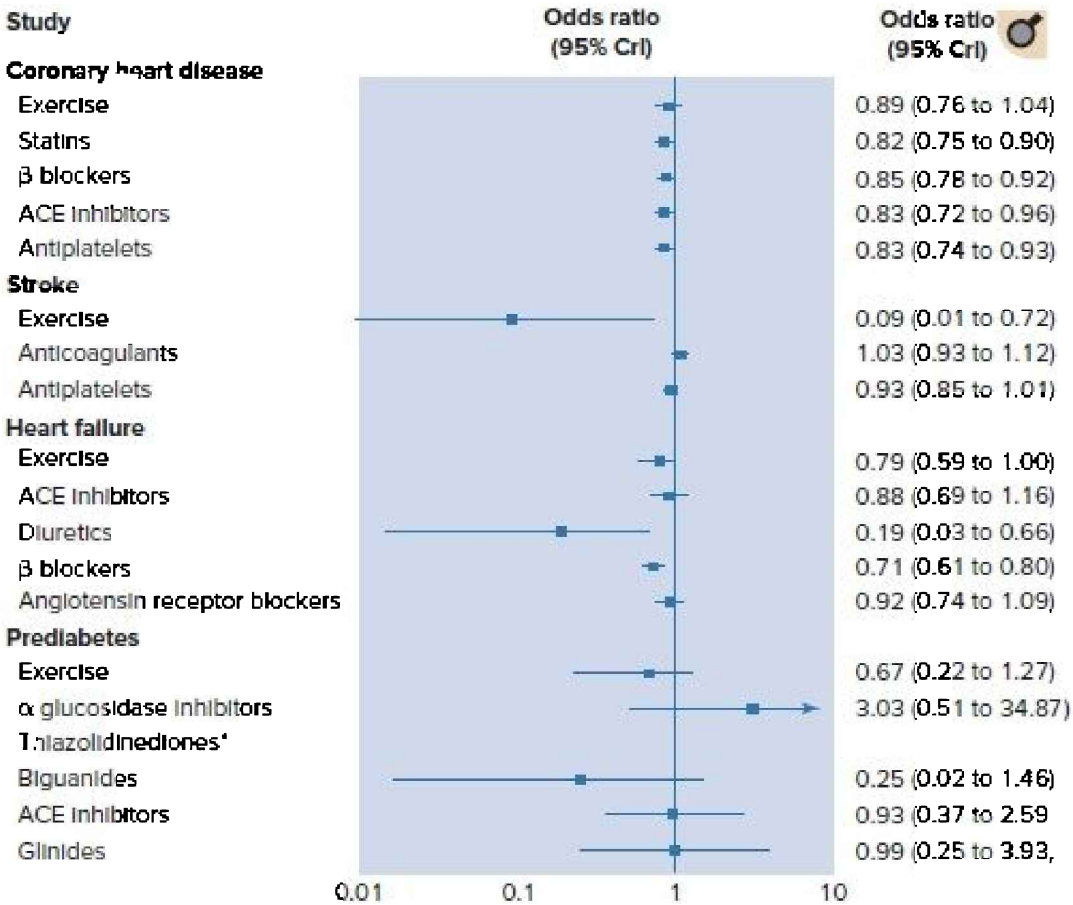


Figure 2.3 Comparative effectiveness of exercise and drugs. Findings of network meta-analysis: effects of exercise and drug interventions compared with control on mortality outcomes in coronary heart disease, stroke, heart failure and prediabetes. Results shown are odds ratios and 95% credible intervals. Odds ratios lower than 1.00 favour intervention compared with control

ACE=angiotensin converting enzyme

*Number of data points for thiazolidinediones was insufficient to obtain an estimate of odds ratio compared with control

ADAPTED WITH PERMISSION FROM *BR J SPORTS MED.* 2015 NOV; 49(21): 1414-1422.DOI: [10.1136/BJSPORTS-2015-F5577REP]

One of the most well-established mechanisms through which people with type 2 diabetes improve metabolic health with physical activity is through adaptations to skeletal muscle. Physical activity enhances muscle membrane glucose transport capacity by recruiting GLUT-4, a critical transport protein, to the sarcolemma and T tubules, where the protein can be active. Increasing the expression of GLUT-4 in skeletal muscle serves to 'mop up' glucose from the bloodstream and move it into muscle, thereby reducing the overall demand for insulin.[22] (Chapter 8.)

Hypertension

Physical activity reduces blood pressure among adults with prehypertension and normal blood pressure.[14] A narrative review of 27 randomised controlled trials showed that regular medium- to high-intensity aerobic activity reduces blood pressure by a mean of 11/5 mmHg.[23]

The antihypertensive effects of physical activity are mediated through enhanced baroreceptor sensitivity, decreased norepinephrine levels, reduced peripheral vascular resistance, improved insulin sensitivity, and alterations in the expression of vasodilator and vasoconstrictor factors. Aerobic activity decreases left ventricular mass and wall thickness, upregulates central antioxidant concentrations, reduces pro-oxidant levels and arterial stiffness, and increases central nitric oxide synthase activity. All of these adaptations contribute to superior endothelial function.[24] (Chapter 10.)

Pain reduction

When performed regularly, aerobic activity may be as effective as non-steroidal anti-inflammatory medication for reducing pain.[25, 26]

As in depression, elevated serum beta-endorphin concentrations induced by physical activity promote several psychological and physiological changes, including altered pain perception and responses to numerous stress hormones such as catecholamines and cortisol.[27]

Combining physical activity with other non-pharmacologic therapies such as cognitive behavioural therapy and self-management education may be an effective treatment strategy for pain reduction.[28, 29] (See Chapters 5 and 6, *Clinical Sports Medicine, Volume 1: Injuries.*)

Musculoskeletal health

Osteoarthritis

Vigorous physical activity does not accelerate osteoarthritis in normal joints.[30] On the contrary, aerobic and resistance activity reduce pain and improve physical function and quality of life for both osteoarthritis of the knee and hip.[14]

In an osteoarthritic knee, interleukin-1 beta induces the release of prostaglandins and NO, which ultimately results in reduced proteoglycan synthesis and reduced extracellular cartilage matrix. Dynamic compression of chondrocytes counteracts this release of prostaglandins and NO.[31] Thus, dynamic mechanical compression of an osteoarthritic knee through physical activity may inhibit the underlying inflammatory process, thereby reducing pain and permitting superior physical function (Chapter 16).

Osteoporosis

Physical activity is an important stimulus for the prevention and treatment of osteoporosis. Mechanical loading of physical activity improves bone microarchitecture, increases bone density and bone strength via the process of mechanotransduction (Fig 2.4). It also increases patients' strength and balance which reduces fall risk. During resistance activity (training or activities of daily living) muscle forces applied to bone at points of tendon attachments generate stimuli that

promote an osteogenic response (Chapter 17).

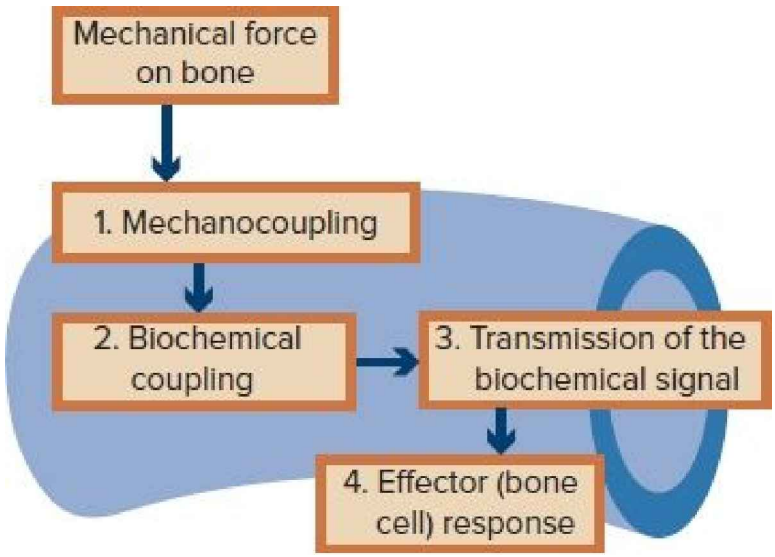


Figure 2.4 The four elements of mechanotransduction— how physical activity promotes bone health

Weight management

Although physical activity is not a primary independent solution to weight loss,[32] it does help attenuate weight gain. Prospective studies demonstrate an inverse association between physical activity and both weight gain and incidence of obesity, and a positive association between physical activity and maintenance of a BMI within the healthy range of 18.5 to 25 kg/m^2.[14]

Page 13

Substantial increases in physical activity can create energy deficits through increased energy expenditure, due to an increase in energy metabolism and requirements. Physical activity's stimulus also provides valuable metabolic adaptations that improve energy and macronutrient balance regulation. At high levels of physical activity, there is tight coupling between energy intake and energy expenditure, suggesting that physical activity also improves appetite control.[33] (Chapter 7.)

Healthy ageing

Physical activity slows or reverses declines in intrinsic capacity, and can help older adults compensate in ways that maximise their functional ability and independence. Regular aerobic and resistance activity in older adults has been shown to help improve musculoskeletal function and mobility, prevent cognitive impairment, delay the onset of dementia, reduce the risk of falls, and maintain sensory capacity to realise healthy ageing.[34–36]

Musculoskeletal function and mobility can be maintained thanks to physical activity's role in protecting against sarcopenia. After 50 years of age, muscle mass decreases at an annual rate of 1–2%. Muscle strength declines by 1.5% between the ages of 50 and 60 and by 3% thereafter, due to

denervation of motor units and a net conversion of fast type II muscle fibres into slow type I fibres (Chapter 31).[37]

Longevity

Physical activity reduces many major mortality risk factors including hypertension, type 2 diabetes mellitus, coronary heart disease, stroke and cancer. There is a clear inverse dose-response relationship between the amount of moderate-to-vigorous physical activity and all-cause mortality, with risk reduction per unit of time greater for more vigorous activity.[38] All-cause mortality is decreased by up to 35% in physically active people compared to inactive people.[39] Meeting the recommended physical activity guidelines of 30 minutes of moderate-intensity physical activity on 5 days a week compared with doing no activity is associated with a reduction in mortality risk of 19%.[40]

From the opposite perspective, regular physical activity is associated with an increase in life expectancy of up to 7 years.[39] Looking down the microscope, higher levels of physical activity are associated with longer telomeres, which are recognised as the caps at the end of each strand of DNA that protect our chromosomes, akin to the plastic tips at the end of shoelaces. Telomere length of leukocytes and skeletal muscle cells may be positively associated with healthy ageing and inversely correlated with the risk of cancer, cardiovascular disease, obesity, diabetes, chronic pain and stress.[41]

Social wellbeing

Many psychosocial benefits come from physical activity. Being active has the potential to improve mood, reduce stress, improve self-esteem, improve body image, improve confidence and build positive attitudes and habits (Table 2.1).

Being physically active provides opportunities to meet people and socialise, learn cooperation, foster healthy competition, challenge personal limits and achieve goals. The values and skills learnt on the sporting field can also translate to other areas of life, enabling personal development and wider success in multiple domains.

RISKS

Physical activity's benefits do not come without some risk, particularly when vigorous activity is undertaken suddenly by untrained or previously sedentary individuals. And although physical activity's health benefits far outweigh its risks, each and every risk must still be considered whenever prescribing to a patient population.[42]

Musculoskeletal injury is the most common risk. More serious but much less common risks include cardiac risks such as sudden cardiac arrest and myocardial infarction. The following is not intended to represent a comprehensive list of physical activity's risks. Rather, it provides a general overview of systems-based considerations and aims to prompt further reading.

Musculoskeletal risks

As *Clinical Sports Medicine Volume 1: Injuries* explores, injuries from physical activity can affect any type of musculoskeletal connective tissue. Injury to these tissues may be categorised as being either acute or due to overuse, based on the mechanism of injury and rapidity of symptom onset. Musculoskeletal injuries include those such as acute strains and tears, chronic strain, stress fractures, traumatic fractures, cartilage tears, tendinopathies, joint dislocations and bursitis. Although individuals who engage in physical activity have a higher risk of incurring minor injury, people who do not regularly participate in physical activity are more likely to incur more severe injuries when engaging in such activity.[43]

After intense physical activity for an extended period of time, such as in marathon running, skeletal muscle can break down rapidly causing rhabdomyolysis. However, exertional rhabdomyolysis is relatively uncommon, with an incidence of approximately 30 per 100 000 patient years.[44]

Cardiac risks

Although the most common risk of physical activity is musculoskeletal injury, vigorous physical activity in unaccustomed individuals can also trigger adverse cardiac responses, including acute myocardial infarction, malignant arrhythmias and sudden cardiac death. Importantly, while intense physical activity can influence the occurrence of sudden cardiac death, regular physical activity is associated with an overall reduction in the risk of the event and so may still be appropriately recommended in most patients (Chapters 9 and 10).[45]

Respiratory risks

Physical activity does not cause asthma; however, it can trigger exercise-induced bronchoconstriction. The underlying pathogenesis is poorly understood, and it is commonly misdiagnosed due to neither sensitive nor specific symptoms such as dyspnoea, chest tightness, wheezing and cough (Chapter 11).[46]

Dehydration and heat stroke

The incidence of heat stroke has increased in past decades, and it accounts for more deaths than all other natural disasters combined.[47] It is the second highest cause of death in sport after cardiac conditions.[48] Yet, given the number of persons exercising in heat, such cases remain rare, suggesting a natural protection from heat stroke in most athletes.

During prolonged physical activity, particularly in the heat, body water is lost via sweating. The fluid loss decreases circulatory blood volume, blood pressure and sweat production, which is often accompanied by weakness, fatigue, vomiting and diarrhoea.[49]

Physical activity performed in the heat can cause several physiological responses within the body that limit the performance capability of the individual, thereby protecting from exertional heat illness. When the person exercising in the heat is allowed to stop voluntarily, these inbuilt safety mechanisms come to the fore, preventing the development of heat stroke. When heat stroke does occur there are usually associated factors—recent illness, drug use, genetic predisposition—to

explain these rare events (Chapter 23).

REFERENCES

1. Morris JN, Heady JA, Raffle PA et al. Coronary heart-disease and physical activity of work. *Lancet* 1953; 265(6796):1111–20; concl.2.
2. Sinek S. *Start with why: how great leaders inspire everyone to take action*. Penguin Books, 2009.
3. Tipton CM. The history of 'Exercise Is Medicine' in ancient civilizations. *Adv Physiol Educ* 2014; 38(2):109–17.
4. Hamilton M, Owen N, Sedentary behaviour and inactivity physiology. In: Bouchard C, Blair SN, Haskell W. eds. *Physical Activity and Health*. 2nd edn. Illinois: Human Kinetics, 2012; 59–61.
5. Hawley JA, Hargreaves M, Joyner MJ et al. Integrative biology of exercise. *Cell* 2014; 159:738–49.
6. Neufer PD, Bamman MM, Muoio DM et al. Understanding the cellular and molecular mechanisms of physical activity-induced health benefits. *Cell Metabolism* 2015; 22:4–11.
7. Sofi F, Valecchi D, Bacci D et al. Physical activity and risk of cognitive decline: a meta-analysis of prospective studies. *J Intern Med* 2011; 269(1):107–17.
8. Matura S, Fleckenstein J, Deichmann R et al. Effects of aerobic exercise on brain metabolism and grey matter volume in older adults: results of the randomised controlled SMART trial. *Transl Psychiatry* 2017; 7(7):e1172.
9. Ahlskog JE, Geda YE, Graff-Radford NR et al. Physical exercise as a preventive or disease-modifying treatment of dementia and brain aging. *Mayo Clin Proc* 2011; 86:876–84.
10. Mammen G, Faulkner G. Physical activity and the prevention of depression: a systematic review of prospective studies. *Am J Prev Med* 2013; 45(5):649–57.
11. Dishman RK, O'Connor PJ. Lessons in exercise neurobiology: the case of endorphins. *Ment Health Phys Act* 2009; 2(1):4–9.
12. Anderson E, Shivakumar G. Effects of exercise and physical activity on anxiety. *Front Psychiatry* 2013; 4(Apr):27.
13. Kredlow MA, Capozzoli MC, Hearon BA et al. The effects of physical activity on sleep: a meta-analytic review. *J Behav Med* 2015; 38:427–49.
14. US Department of Health and Human Services. 2018 Physical Activity Guidelines Advisory Committee Scientific Report. Washington, DC: 2018. https://health.gov/paguidelines/second-edition/report/pdf/PAG_Advisory_Committee_Report.pdf.

15. Hojman P, Gehl J, Christensen JF et al. Molecular mechanisms linking exercise to cancer prevention and treatment. *Cell Metab* 2018; 27(1):10–21.
16. Li J, Siegrist J. Physical activity and risk of cardiovascular disease—a meta-analysis of prospective cohort studies. *Int J Environ Res Public Health* 2012; 9:391–407.
17. Schuler G, Adams V, Goto Y. Role of exercise in the prevention of cardiovascular disease: results, mechanisms, and new perspectives. *Eur Heart J* 2013; 34:1790–9.
18. Naci H, Ioannidis JPA. Comparative effectiveness of exercise and drug interventions on mortality outcomes: metaepidemiological study. *Br J Sports Med* 2015; 49(21):1414–22.
19. Yardley JE, Hay J, Abou-Setta AM et al. A systematic review and meta-analysis of exercise interventions in adults with type 1 diabetes. *Diabetes Res Clin Pract* 2014; 106(3):393–400.
20. Church TS, Blair SN, Cocreham S et al. Effects of aerobic and resistance training on hemoglobin A1c levels in patients with type 2 diabetes: a randomized controlled trial. *JAMA* 2010; 304(20):2253–62.
21. Warburton DE, Charlesworth S, Ivey A et al. A systematic review of the evidence for Canada's Physical Activity Guidelines for Adults. *Int J Behav Nutr Phys Act* 2010; 7:39.
22. Stanford KI, Goodyear LJ. Exercise and type 2 diabetes: molecular mechanisms regulating glucose uptake in skeletal muscle. *Adv Physiol Educ* 2014; 38(4):308–14.
23. Borjesson M, Onerup A, Lundqvist S et al. Physical activity and exercise lower blood pressure in individuals with hypertension: narrative review of 27 RCTs. *Br J Sports Med* 2016; 50:356–61.
24. Ghadieh AS, Saab B. Evidence for exercise training in the management of hypertension in adults. *Can Fam Physician* 2015; 61(3):233–9.
25. Kelley GA, Kelley KS, Hootman JM et al. Effects of community-deliverable exercise on pain and physical function in adults with arthritis and other rheumatic diseases: a meta-analysis. *Arthritis Care Res* 2011; 63(1):79–93.
26. Giannotti E, Koutsikos K, Pigatto M et al. Medium-/long-term effects of a specific exercise protocol combined with patient education on spine mobility, chronic fatigue, pain, aerobic fitness and level of disability in fibromyalgia. *Biomed Res Int* 2014; 2014:474029.
27. Harber VJ, Sutton JR. Endorphins and exercise. *Sports Med* 1984; 1:154–71.
28. Gonzalez Gonzalez J, del Teso Rubio M del M, Waliño Paniagua CN et al. Symptomatic pain and fibromyalgia treatment through multidisciplinary approach for primary care. *Reumatol Clin* 2015; 11(1):22–6.
29. Koele R, Volker G, van Vree F et al. Multidisciplinary rehabilitation for chronic widespread musculoskeletal pain: results from daily practice. *Musculoskeletal Care* 2014; 12(4):210–20.
30. Hunter DJ, Eckstein F. Exercise and osteoarthritis. *J Anat* 2009; 214:197–207.

31. Chowdhury TT, Bader DL, Lee DA. Dynamic compression counteracts IL- β induced INOS and COX-2 activity by human chondrocytes cultured in agarose constructs. *Eur Cells Mater* 2005; 10(Suppl 2):63.
32. Malhotra A, Noakes T, Phinney S. It is time to bust the myth of physical inactivity and obesity: you cannot outrun a bad diet. *Br J Sports Med* 2015 Aug 1; 49(15):967–8.
33. Chaput J-P, Klingenberg L, Rosenkilde M et al. Physical activity plays an important role in body weight regulation. *J Obes* 2011; 2011:1–11.
34. Livingston G, Sommerlad A, Orgeta V et al. Dementia prevention, intervention, and care. *Lancet* 2017; 390:2673–734.
35. World Health Organization (WHO). WHO Guidelines on Integrated Care for Older People (ICOPE). Geneva, 2017. http://www.who.int/ageing/publications/guidelines-icope/en/.
36. Northey JM, Cherbuin N, Pumpa KL et al. Exercise interventions for cognitive function in adults older than 50: a systematic review with meta-analysis. *Br J Sports Med* 2018 Feb; 52(3):154–60.
37. von Haehling S, Morley JE, Anker SD. An overview of sarcopenia: facts and numbers on prevalence and clinical impact. *J Cachexia Sarcopenia Muscle* 2010; 1(2):129–33.
38. Samitz G, Egger M, Zwahlen M. Domains of physical activity and all-cause mortality: systematic review and dose-response meta-analysis of cohort studies. *Int J Epidemiol* 2011; 40(5):1382–400.
39. Reimers CD, Knapp G, Reimers AK. Does physical activity increase life expectancy? A review of the literature. *J Aging Res* 2012; 2012:243958.
40. Woodcock J, Franco OH, Orsini N et al. Non-vigorous physical activity and all-cause mortality: systematic review and meta-analysis of cohort studies. *Int J Epidemiol* 2011; 40:121–38.
41. Arsenis NC, You T, Ogawa EF et al. Physical activity and telomere length: impact of aging and potential mechanisms of action. *Oncotarget* 2017; 8(27):45008–19.
42. Melzer K, Kayser B, Pichard C. Physical activity: the health benefits outweigh the risks. *Curr Opin Clin Nutr Metab Care* 2004; 7:641–7.
43. Diener-Martin E, Bruegger O, Martin BW. Physical activity promotion and safety prevention: what is the relationship in different population groups? *Br J Sports Med* 2011; 45(4):332–3.
44. Tietze DC, Borchers J. Exertional rhabdomyolysis in the athlete: a clinical review. *Sports Health* 2014; 6(4):336–9.
45. Corrado D, Migliore F, Basso C et al. Exercise and the risk of sudden cardiac death. *Herz* 2006; 31(6):553–8.
46. Smoliga JM, Weiss P, Rundell KW. Exercise induced bronchoconstriction in adults: evidence based diagnosis and management. *BMJ* 2016; 352:h6951.
47. Leon LR, Bouchama A. Heat stroke. *Compr Physiol* 2015; 5(2):611–47.

48. Casa DJ, Armstrong LE, Kenny GP et al. Exertional heat stroke: new concepts regarding cause and care. *Curr Sports Med Rep* 2012; 11:115–23.
49. Von Duvillard SP, Braun WA, Markofski M et al. Fluids and hydration in prolonged endurance performance. *Nutrition* 2004; 20:651–6.

Chapter 3

Prescribing physical activity: the clinical assessment

with DANIEL FRIEDMAN

Hippocrates said 'Walking is man's best medicine'—and this may have some personal challenges for you if you're very busy with work, or kids, or both, or you may be in pain or have other priorities . . . but my question for you is: Can you limit your sitting and sleeping to just 23 and 1/2 hours a day?

Dr Mike Evans, physician, Canada

More than 6 million YouTube viewers around the world are aware of this chapter's opening quote. Canadian physician Dr Mike Evans literally 'went viral' with his whiteboard animation of stories that illustrate the enormous potential of regular physical activity and limiting sedentary behaviour in the primary and secondary prevention of many diseases. However, this potential still remains largely untapped and only partially realised in day-to-day clinical practice. Despite the many calls for adoption of physical activity as a vital sign,[1–3] only a third to half of primary care physicians regularly counsel their patients on physical activity.[4, 5]

Many national action plans on physical activity recommend that clinicians should counsel on physical activity,[6] yet progress to meet targets has been slow and inconsistent.[7] The lack of physical activity training in medical and allied health school curricula, as well as in continuing professional development, means that clinicians often lack experience, knowledge and confidence to counsel their patients on physical activity.[8, 9] Many clinicians meet physical activity counselling outcomes with scepticism and distrust,[10] and instead reach for the familiar default—the prescription pad—even when a medication has limited evidence or a large number needed to treat (NNT), as well as the ever-present risk of adverse events. Failing to counsel on physical activity represents a missed opportunity—one that would enable clinicians to improve the health of patients, and with minimal cost.[11, 12]

Here we summarise the need for regular physical activity counselling in clinical practice. We share a straightforward framework for counselling that can be used easily in a variety of settings. This precedes Chapter 4, where we explore the different principles and elements of exercise prescription.

Establishing the optimum template for physical activity counselling takes time and practice, and can be achieved by considering the following questions in turn:

- Why perform routine physical activity counselling?
- Who should be performing the counselling? And who should be receiving it?
- When and where should counselling be performed?
- What should be included in the counselling?
- Where else can the clinician turn to find counselling resources?
- What should the clinician do if their time with a patient is limited?
- What else can be done to support routine counselling?

WHY ASSESS AND COUNSEL?

As emphasised in Chapter 1, physical inactivity has reached pandemic proportions. It is a global-scale problem that demands effective, scalable and low-cost solutions. One such solution is physical activity counselling.

Evidence base and guidelines

Despite mixed evidence regarding effective actions in health systems for increasing physical activity, face-to-face interventions delivered in primary care or community settings have been shown to increase physical activity over 12–24 months.[13] In 2017, the World Health Organization (WHO) identified physical activity counselling and referral as part of routine primary healthcare services as a cost-effective 'best buy' for tackling non-communicable diseases (NCDs),[14] Page 16 formalising the notion that they can increase self-reported physical activity at a reasonable cost.[15] This best buy is a pillar of the WHO's Global Action Plan on Physical Activity 2018–2030.[7]

Similarly, the UK National Institute for Health and Care Excellence (NICE) recommends that primary care practitioners deliver tailored, brief physical activity advice to patients and follow this up at subsequent appointments. In its recommendation, NICE defines brief advice as verbal advice, discussion, negotiation or encouragement, with or without written or other support or follow-up. Physical activity interventions can vary from basic advice to a more extended, individually focused discussion, often referred to as a brief intervention[16] (see 'Motivational interviewing' in Chapter 5).

What does the evidence suggest?

The number needed to treat (NNT) with an intervention of physical activity promotion, compared with any control, for one additional sedentary adult to report meeting recommended levels of physical

activity at 12 months is 12.[17] Compare this to another brief intervention, such as providing a smoker with tobacco cessation advice, which has an NNT between 50 and 120.[18]

A clinician's responsibility

Clinicians have a central role and responsibility in enabling all patients to live healthy lives. They should be well poised to promote comprehensive lifestyle interventions for the prevention and management of chronic diseases, and to provide the necessary guidance and support for patients to change their unhealthy behaviours. In a survey of 7238 people in Sweden, 76% of respondents thought healthcare professionals have a responsibility to promote physical activity to their patients.[19] However, this responsibility for patients' physical activity levels should be shared with other healthcare professionals, patients and society as a whole.[10]

Given that the clinician's voice is widely trusted and has considerable influence on public and individual opinion, routine patient encounters in all settings offer frequent and meaningful opportunities for supporting behaviour change. Clinicians have the potential to reach a large proportion of the population regularly and are therefore well placed to promote physical activity, especially to the least active, at-risk individuals. In developed countries, for example, 70–80% of adults visit their general practitioner at least once a year.[20]

A primary and secondary prevention opportunity

Frequent patient encounters offer many opportunities for primary and secondary prevention, such as advising on smoking cessation, diet and nutrition, stress management and other lifestyle interventions. Provision of effective advice on physical activity is less common, yet given physical activity's contributions to health, clinicians should regularly implement evidence-based interventions that solely target physical activity, as well as those delivered in combination with other risk factors such as diet, smoking and alcohol.

This shift of focus to prevention activities will reduce the incidence of chronic diseases and ultimately lessen physical inactivity's current health and economic burden, as discussed in Chapter 1.

WHO SHOULD DO IT?

Physical activity counselling should not be limited to sport and exercise medicine physicians. All clinicians should be trained in performing basic assessment and providing brief advice. This particularly applies to allied health professionals, who often have more time with patients than do primary care physicians.

Further, do not neglect the role clinic staff can play in assisting with assessment, which may be performed in the waiting room prior to consultation.

WHO SHOULD RECEIVE IT?

Physical activity counselling is beneficial for everyone. All individuals, of all ages and abilities, should be

encouraged to be active and gradually increase their activity levels to experience the health benefits. At-risk, sedentary individuals with chronic diseases in particular should be advised to view physical activity as medicine, alongside other aforementioned lifestyle interventions.

WHEN AND WHERE TO DO IT?

Physical activity counselling should ideally be performed during every clinical encounter, and should be routinely assessed as a vital sign alongside blood pressure and heart rate.[21, 22] All forms of counselling should be tailored to meet the needs and ability of the patient, as well as the time constraints of the consultation.

It can be useful conceptually to separate physical activity counselling opportunities into three separate occasions:

- upon first meeting a patient, when taking a complete medical history
- during every following clinical encounter, in brief, alongside other lifestyle counselling such as diet (Chapter 6)
- during separate follow-up consultations booked solely for physical activity counselling, offering more time for extensive discussion and detailed prescription.

The NICE categorises these opportunities into more concrete terms, as illustrated in Fig. 3.1.

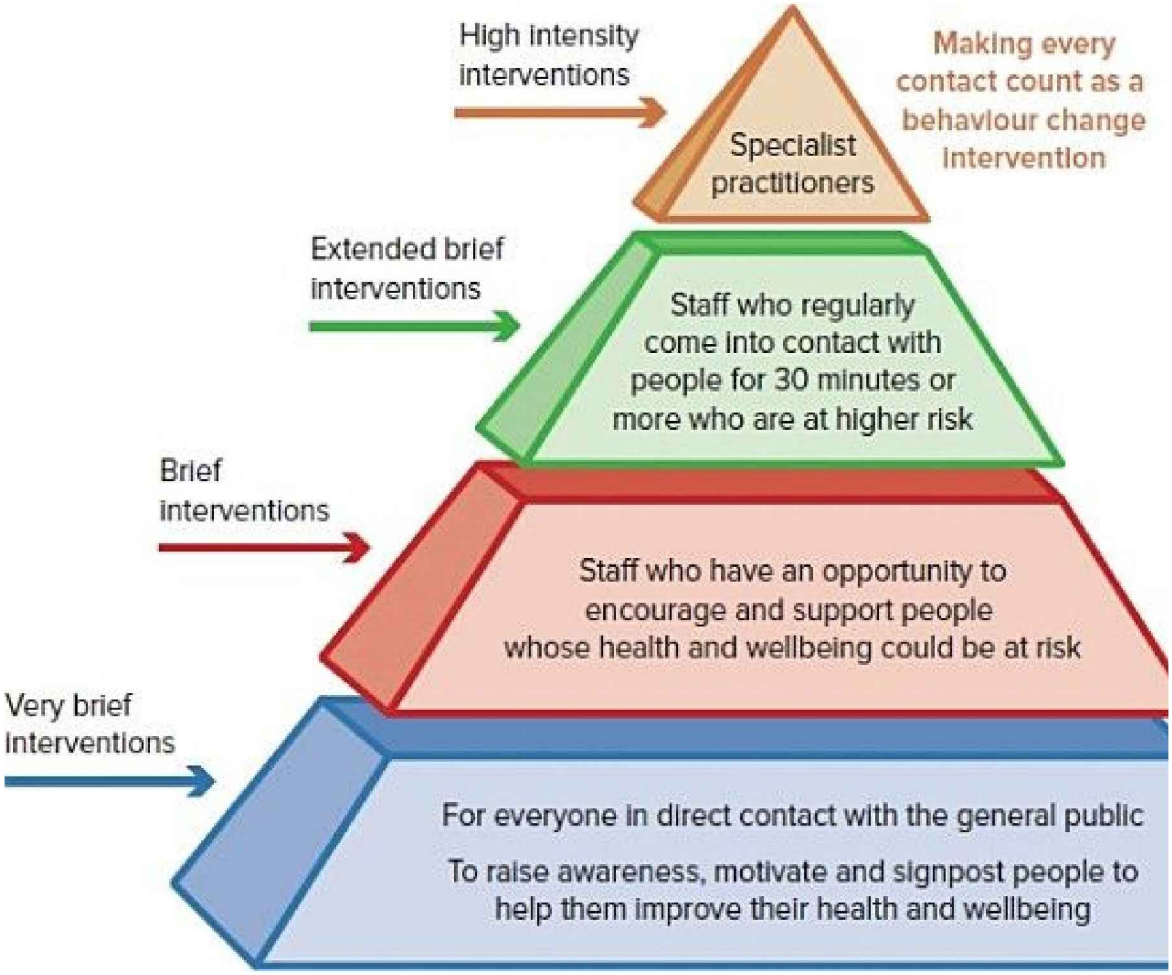


Figure 3.1 Behaviour change interventions mapped to NICE Behaviour change: individual approaches
© CROWN COPYRIGHT 2016

However, counselling should not only take place in the clinician's rooms. Some of the assessment may be performed prior to the consultation, for example in the waiting room beforehand through patient questionnaires. Each clinic should identify a method that is both feasible and efficient amid busy schedules.

WHAT SHOULD BE INCLUDED IN COUNSELLING?

The common elements of counselling are shown in Fig. 3.2 and are expanded in the section below ('The 5As model of behaviour change').

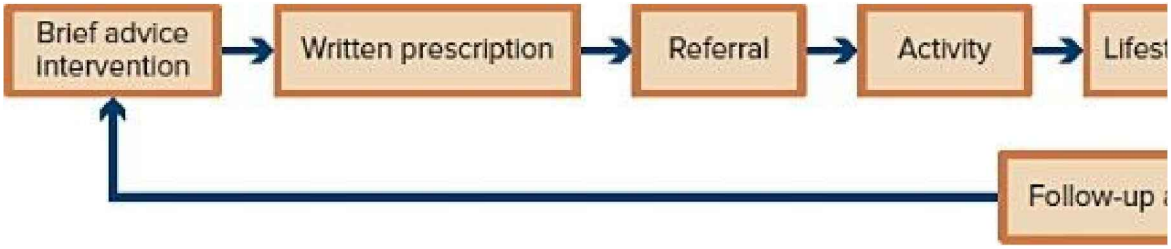


Figure 3.2 A common clinical pathway for physical activity counselling

WHERE ELSE CAN THE CLINICIAN TURN FOR COUNSELLING RESOURCES?

A number of health departments, medical colleges and independent organisations offer their clinicians how-to guides or manuals for physical activity counselling (Table 3.1). There are diverse resources available, differing in length, level of detail and supplementary tools used.

Table 3.1 Physical activity counselling manuals for clinicians around the world

Country	Source	Resource
Australia	Royal Australian College of General Practitioners (RACGP)	Guidelines for preventive activities in general practice (Red Book)
Canada	Alberta Centre for Active Living	Physical Activity Counselling Toolkit
South Africa	The Chronic Disease Initiative for Africa (CDIA)—iChange4Health	Helping People Change
Sweden	Swedish Professional Associations for Physical Activity (YFA)	Physical Activity in the Prevention and Treatment of Disease (FYSS)
Switzerland	Swiss College of Primary Care Medicine (and others)	Physical Activity Promotion in Primary Care (PAPRICA)—Handbook for Doctors
UK	NHS Health Scotland	Physical Activity Pathway Practitioners Guide
USA	American College of Sports Medicine (ACSM)	Guidelines for Exercise Testing and Prescription

Despite the number of apparently different manuals, they are based on the same fundamental principles and have been adapted from a common template or structure: the 5As model of behaviour change.

THE 5As MODEL OF BEHAVIOUR CHANGE

The 5As model of behaviour change is a stepwise, evidence-based approach to physical activity counselling that is used worldwide in a range of healthcare settings (Fig. 3.3).[22, 23] The model, originally developed for counselling in tobacco cessation,[24] has been adapted for other lifestyle interventions to much success.

Page 18

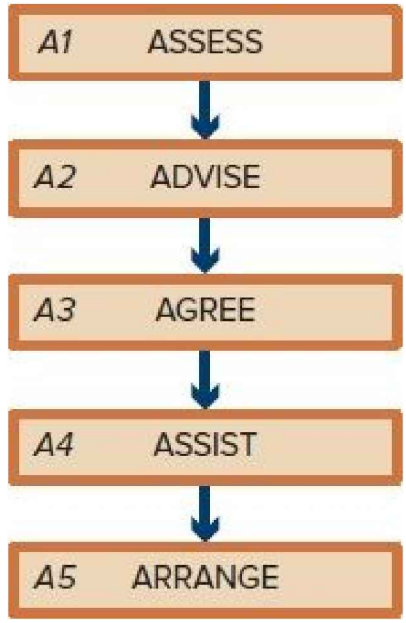


Figure 3.3 The 5As model of behaviour change

The 5As have a strong foundation in behaviour change theory and they are practical for busy patient-care settings. The approach is supported by evidence for increases in healthy behaviours, positive influence on mediators of behaviour change, and increased healthcare provider communication skills about behaviour change.[25]

We explore each of the key actions of the 5As that the clinician may follow to support patients to initiate behaviour change and sustain it. It is not intended to represent the only way to counsel, but rather aims to provide a tasting plate of different counselling components.

A1: Assess

Assess the patient's current physical activity level and readiness for physical activity.

A patient's physical activity and sedentary behaviour levels should be assessed on initial consultation, and at every subsequent clinical contact.

Clinicians may perform the assessment in person during the consultation, or it may be completed by the patient independently prior to the appointment to save time (for example, by completing a questionnaire while in the waiting room).

In general, it is important to assess:

- current levels of **physical activity** in all domains (recreation, transport, work, school etc.), including:
  - *type*—aerobic, strength, flexibility or balance
  - *frequency*—How often? How many days per week?

    - *intensity*—How hard are you working during the activity? During activity is it difficult to breathe or speak?
    - *duration*—For how long? At least 10 minutes at a time?
- current levels of **sedentary behaviour** (sitting or lying down) in all domains
- risks and contraindications.

There are many different questionnaires for physical activity assessment. The Canadian Society for Exercise Physiology (CSEP) 'Get Active Questionnaire',[26] which will be familiar to some readers as the PAR-Q, was designed to allow patients to independently pre-assess their readiness for physical activity, and decide whether it is necessary for them to seek advice from a clinician before becoming more physically active.

If the advice of a clinician is required, the patient should be assessed through a medical history and physical examination that specifically focus on contraindications to physical activity. (See 'Screening', in Chapter 46 of *Clinical Sports Medicine Volume 1: Injuries.*) Risk stratification hurdles do not necessarily need to be completed for all patients prior to physical activity counselling. Most people can begin exercising without first visiting a clinician.

Page 19

CSEP Get Active Questionnaire

The following questions will help to ensure that you have a safe physical activity experience. Please answer YES or NO to each question before you become more physically active. If you are unsure about any question, answer YES.

1. Have you experienced ANY of the following (a to f) within the past six months?
    a. A diagnosis of/treatment for heart disease or stroke, or pain/discomfort/pressure in your chest during activities of daily living or during physical activity?
    b. A diagnosis of/treatment for high blood pressure (BP), or a resting BP of 160/90 mmHg or higher?
    c. Dizziness or light-headedness during physical activity?
    d. Shortness of breath at rest?
    e. Loss of consciousness/fainting for any reason?
    f. Concussion?
2. Do you currently have pain or swelling in any part of your body (such as from an injury, acute flare up of arthritis, or back pain) that affects your ability to be physically active?
3. Has a health care provider told you that you should avoid or modify certain types of physical activity?
4. Do you have any other medical or physical condition (such as diabetes, cancer, osteoporosis, asthma, spinal cord injury) that may affect your ability to be physically active?

HTTP://WWW.CSEP.CA/CMFILES/GAQ_CSEPPATHREADINESSFORM_2PAGES.PDF

Once the patient is deemed medically ready for physical activity, other questionnaires can be used to assess his or her physical activity levels, such as the Global Physical Activity Questionnaire (GPAQ)[27]—which has further been adapted into various forms, such as the popular Scottish Physical Activity Screening Question (Scot-PASQ)[28] (see box below). The most simple questionnaires ask about a patient's exercise habits in brief, while more advanced questionnaires assess type of physical activity, frequency, intensity and duration, as well as consider how data are reported and their quality. Given the time constraints in primary care, even more succinct forms of assessment may be used, such as the Physical Activity Vital Sign Questions.[29]

Scottish Physical Activity Screening Question (Scot-PASQ)

1. In the past week, on how many days have you been physically active for a total of 30 minutes or more?
2. If four days or less, have you been physically active for at least two and a half hours (150 minutes) over the course of the past week?
3. If not, are you interested in being more physically active?

SCOT-PASQ, NHS HEALTH SCOTLAND

Potential disadvantages of these questionnaires are:

(a) they may not be accurate in measuring light or moderate activity and energy expenditure
(b) they depend on written language and question complexity
(c) they have not been validated in different patient populations.

Depending on feasibility, patients can be asked to keep a physical activity diary, or use wearable activity trackers such as pedometers, accelerometers, GPS systems or heart rate monitors, for more accurate measures of their physical activity levels. Accelerometers in particular have gained popularity due to their accuracy, ability to capture large amounts of data and ease of operation.[30] Many mobile phones and wearable fitness trackers are now capable of tracking physical activity data automatically, such as step count, and require little configuration.

All forms of assessment and relevant data should be consistent and recorded at every patient contact, to be submitted into the patient's paper or electronic records, to monitor progress and guide future practice.[2]

A2: Advise

Advise about the recommended amount of physical activity and highlight the associated health benefits that may interest the patient.

Brief advice is a short and structured conversation used to raise the patient's awareness and

plant the seeds for behaviour change. When delivering brief advice, it is important to use positive, simple language that delivers a straightforward message. It should be tailored to the patient's: Page 20

- age
- current level of activity and ability
- motivations and goals
- circumstances, preferences and barriers to being physically active
- health status—consider medical conditions or disabilities.

The overall aim should be to increase the patient's awareness of the direct causal link between physical activity and improved physical health and mental wellbeing. With time, the clinician will develop his or her own approach to delivering brief advice for different patient populations. (For an example see the box below.)

Although muscle strengthening activity is listed as a separate recommendation from aerobic activity in most physical activity guidelines, the two are often performed concurrently, such as in cross training, and do not necessarily need to be isolated.

Even if patients cannot feasibly meet the recommended levels of physical activity, remind them that *any physical activity is better than none at all.* Patients who perform even small amounts of physical activity throughout the week (75–90 minutes) still achieve dramatic reductions (up to 15%) in mortality risk.[31] In general, symptom-limited, moderate physical activity can be safely recommended unless patients are unstable or have certain uncontrolled medical conditions. For the balance of the adult population, the guidelines recommend that each of us should accumulate 150 minutes of moderate to vigorous physical activity per week[32]—that's only 22 minutes of walking per day!

A3: Agree

Agree on a realistic physical activity goal by exploring activities that the patient enjoys.

The patient's response to the advice provided can illustrate their psychological readiness or stage of change[33] for increasing their physical activity levels. At this point, the clinician should try to elicit whether the patient is open to increasing their activity levels or whether they are uninterested or ambivalent, and how important the change is for them. For information about behaviour change and assessing a patient's readiness for change, see Chapter 5.

When patients are not ready to increase their physical activity levels, the clinician should respect their decision and offer support if they change their minds in the future. The clinician should not argue the patient's decision, as this will likely create resistance and break rapport.

However, if the patient is ready to increase their physical activity levels, the clinician should discuss:

- what activities interest the patient
- what will motivate them to perform those activities; what has motivated them in the past

- what the foreseeable barriers are to performing those activities; what has stopped them in the past.

One popular method used for patient lifestyle change counselling is 'motivational interviewing', an approach that employs a non-judgmental, non-confrontational patient-centred style for eliciting behaviour change. It was originally developed for counselling within addiction medicine, and has since been found effective for other lifestyle interventions.[35, 36] We expand on motivational interviewing in Chapter 5.

Providing brief advice—a suggested structure

1. Highlight the benefits of physical activity:
   a. improves mood, sleep, weight, chronic inflammation, pain etc.
   b. reduces risk of cardiovascular disease, diabetes, depression, dementia etc.
   c. improves quality of life and extends life expectancy.
2. Explain the physical activity guidelines relevant to the patient's age group:
   a. 150 (75) minutes of moderate (vigorous) aerobic activity weekly—that is, 30 minutes of moderate physical activity on most days of the week
   b. muscle strengthening activity twice weekly (in combination with aerobic activity)
   c. consider balance training if patient is 65 years or older
   d. limit sedentary behaviour in all settings whenever possible.
3. Summarise the key takeaway points for the patient:
   a. The goal is at least 150 minutes of moderate intensity or 75 minutes of vigorous physical activity weekly.
   b. To achieve this, aim for 30 minutes of moderate physical activity on most days of the week. Start slowly and gradually build up duration and intensity.
   c. Walking is an easy way to get started.
   d. Limit sedentary behaviour whenever possible.

PRACTICE PEARL

When exploring the potential activities that interest the patient, the clinician should *always consider recommending that the patient walks.* Walking is convenient, requires no special skills or equipment, it is free, may be accommodated in occupational and domestic routines, is self-regulated, has a low ground impact and is inherently safe.[34]

Having explored potential activities that interest the patient, the clinician should implement patient-centred techniques to discuss realistic physical activity goals and agree on a physical

activity plan (Table 3.2).

Table 3.2 Setting *SMART* goals

Specific	Identify a specific physical activity goal	*Walk for 30 minutes per day before work*
Measurable	How will the physical activity be measured?	*Time the walk, track distance covered*
Achievable/**A**ttainable	How realistic is the goal? How can it be accomplished?	*Walk with a friend or family member* *Start by walking for 10 minutes non-stop every morning, and build up by 5 minutes each week.*
Relevant	Does the goal seem worthwhile? Does it match the patient's needs?	*Yes, there are many health benefits of walking.* *Yes, it matches the patient's needs.*
Time-based	Does the goal have a time-bound completion date?	*Reach the goal of walking for 30 minutes daily by the fourth week*

BOVEND'EERDT TJ, BOTELL RE, WADE DT. CLINICAL REHABILITATION (23(4)), WRITING SMART REHABILITATION GOALS AND ACHIEVING GOAL ATTAINMENT SCALING: A PRACTICAL GUIDE. PP.352–61. COPYRIGHT © 2009 REPRINTED BY PERMISSION OF SAGE PUBLICATIONS, INC.[37]

Each patient will have a different and constantly varying level of physical activity, and so the goal or message should be for a gradual and progressive increase, if not contraindicated—*start low, go slow.* Small changes to daily routine, such as taking the stairs and watching less television can be good starting points. Every minute adds up over the course of the day.

PRACTICE PEARL

To increase commitment, the clinician may also ask the patient to identify a friend or family member who could join them and support them in their efforts to become more active.

A4: Assist

Assist the patient in overcoming barriers by providing support as well as a written prescription.

The clinician may begin by discussing strategies to overcome the patient's barriers to meeting physical activity goals.

Common complaints

- I don't have the time.
  - *It's up to you how you spend your time, and if you set this as a goal, it can help you use your time more effectively.*
  - *Sometimes it isn't convenient to exercise, but 10-minute walks through active travel all add up at the end of a day.*
- The weather is always bad.

  - *All you need is a waterproof jacket and suitable footwear.*
  - *If you have access to indoor facilities, weather is no longer an excuse.*
- I am embarrassed that I look fat and awkward when I exercise.
  - *Wear comfortable, loose-fitting clothing.*
  - *Choose an appropriate exercise class with other people just like you, trying to improve the way they look.*
- I don't like feeling sore afterwards.
  - *Muscle soreness is only temporary; don't do too much too soon.*
- I can't afford all of the equipment.
  - *For everyday activities, you don't need any special equipment or clothing.*
  - *Walking is free.*

ADAPTED FROM PHYSICAL ACTIVITY PATHWAY PRACTITIONERS GUIDE SCOTLAND: NHS HEALTH SCOTLAND, 2013[38]

In addition to verbal instruction, the clinician should provide the patient with a written prescription for physical activity. For patients with stable conditions, clinicians can provide customised physical activity prescriptions that are tailored to the patient's preferences. The prescription can comprise as little instruction as a simple written suggestion of an activity, or a comprehensive solution with a supportive structure put in place by the provider or supporting system, if available. For further explanation about exercise prescription, refer to Chapter 4 for general principles, and Part B of this volume for prescription in specific conditions.

Page 22

To supplement the prescription, the patient should be provided with printed or internet-based support materials and resources relevant to their stage of change, as well as self-monitoring tools (e.g. physical activity diary, pedometer) if available.

A5: Arrange

Arrange and plan the follow-up visit

Patients should be reviewed every 3–6 months,[16] or sooner if necessary. If possible, a patient should ideally be followed up by the same clinician who assessed and counselled them originally.

Before a patient leaves the consultation, he or she should be provided with a safety net—an explanation of the red flags to look out for, and how to seek help when they do occur. Ongoing patient support may be achieved through telephone, email or online-based reminders, as well as mobile phone apps.[39]

All pertinent details of the consultation, including the patient's decisions and the materials distributed, should be consistently documented in order to support continuity of care.

Similar to other lifestyle interventions, patient adherence to physical activity tends to decrease after 12 months, but can be sustained when the physical activity is repeated[40] or combined with community supports.[41] Patients should be referred to other healthcare and social service providers, and community-based supports, as appropriate. Some examples include:

- specialists—sports and exercise medicine physicians, cardiologists etc.
- allied health—physiotherapists, occupational therapists, dietitians etc.
- community centres—recreation centres
- community-based programs—sports clubs, walking or running groups etc.

Clinicians should feel confident to prescribe physical activity to the majority of patients without referral, assuming that gradual increases in activity level are recommended.[42] In any case, clinicians should identify partners and supports within the local community, such as local recreation centres, sports programs and walking groups, to build extensive and reliable networks for patient referral.

Referral to a sport and exercise medicine specialist is indicated for patients with conditions classified as high risk, as well as patient populations that would benefit from physical activity but have difficulty engaging due to medical-related safety concerns. The role of the physical activity professional is to ensure safety and adaptation to the ability level of the patient, while providing support and ensuring accountability to maximise treatment efficacy.

During the follow-up consultation, the patient's physical activity and sedentary behaviour levels should be reassessed, and any changes since their last visit should be identified. Agreed physical activity plans and prescriptions can be adjusted according to patient progress, with a particular focus on barriers encountered and on the patient's successes, to encourage persistence.

WHAT TO DO WHEN TIME IS LIMITED

Completing the entire 5As counselling protocol can seem like a colossal task for every clinical encounter, given patients usually do not present seeking physical activity advice. In reality, clinicians have limited time with patients, and so counselling must be adapted based on these constraints.

Physical activity counselling can be addressed even in the last 30 seconds of a consultation; it does not have to distract from the purpose of the visit. And remember that referral is fine. The clinician's role is to emphasise physical activity's importance by measuring it at every visit and to make the diagnosis of physical inactivity where it exists.

ENABLING FACTORS—WHAT ELSE CAN BE DONE?

Unfortunately, simply having the information and tools needed for physical activity counselling is not enough. As is emphasised in the WHO's Global Action Plan on Physical Activity 2018–2030,[7] a multisectoral and multidisciplinary effort is needed from healthcare and social service providers, leaders of medical associations, of government agencies and of the community, to develop a system that enables implementation and sustainability. Clinicians must use their platform to advocate for a paradigm shift and lobby for the following enabling factors of physical activity counselling:

What to do if you have 5 minutes

1. **Assess**
   - Evaluate whether the patient is medically ready for physical activity.
   - Ask about the patient's physical activity and sedentary behaviour levels—this can be performed through a brief history or with the aid of a questionnaire, such as the Physical Activity Vital Sign Questions:[27]
     - *On average, how many days per week do you engage in moderate to strenuous exercise (like a brisk walk)?*
     - *On average, how many minutes do you engage in exercise at this level?*
2. **Advise**
   - Discuss the many health benefits of becoming more active, focusing on those that are likely to interest that specific patient.
   - Compare the patient's current activity levels with the recommended guidelines and encourage a gradual increase of activity to reach and surpass the target.
3. **Agree**
   - Discuss opportunities to increase incidental physical activity and limit sedentary behaviour. Emphasise that every minute adds up over the course of the day.
   - Set a physical activity goal and agree on a plan based on the patient's interests. Walking is always a good place to start.
4. **Assist**
   - Ask the patient about barriers they are facing or are likely to face, and plan how to overcome them.
   - Provide the patient with a written physical activity prescription (Chapter 4).
5. **Arrange**
   - Refer the patient to allied health professionals or community programs for ongoing support.
   - Schedule and plan the follow-up visit to track progress and adjust the agreed physical activity plan.

What to do if you have 3 minutes

1. **Assess**
   - Ask about the patient's physical activity levels:
     - *On average, how many days per week do you engage in moderate to strenuous exercise (like a brisk walk)?*
     - *On average, how many minutes do you engage in exercise at this level?*
2. **Advise**
   - Discuss the many health benefits of becoming more active, focusing on those that are likely to interest that specific patient.
   - Compare the patient's current physical activity levels with the recommended guidelines and

encourage a gradual increase of activity to reach and surpass the target.

3. **Arrange**
   - Schedule a follow-up visit.
   - Signpost a future discussion about physical activity and ask the patient to identify personal barriers to physical activity to discuss during the next visit.

What to do if you have 30 seconds

1. **Assess**
   - Ask about the patient's physical activity levels:
     - *On average, how many days per week do you engage in moderate to strenuous exercise (like a brisk walk)?*
     - *On average, how many minutes do you engage in exercise at this level?*
2. **Arrange**
   - Invite the patient to schedule another visit for physical activity counselling, which offers more time to discuss what they can do to improve their health.

- pre-service training—integration of physical activity training in medical and allied health curricula, to better equip tomorrow's clinicians
- in-service training—integration of physical activity training in continuing professional development (continued medical education) to educate current clinicians and clinic staff
- team-care—sharing patient care and physical activity counselling responsibilities among multiple clinicians to allow for expansion of counselling capacity
- patient records—strengthening patient records systems to accommodate physical activity assessment and other relevant data.

Tips for integrating physical activity assessment and counselling into your daily practice

- Display posters with the physical activity guidelines prominently in your consultation room and waiting room
- Ask about physical activity and sedentary behaviour at every consultation; consider physical activity a vital sign
- Apply the 5As to guide counselling—Assess, Advise, Agree, Assist, Arrange
- Ensure the patient leaves with a written physical activity prescription (Chapter 4)
- Remember that walking is free and can be recommended to nearly all patients
- Do not be afraid to refer on. In the care of your patient, always consider other physicians, physiotherapists, clinical exercise physiologists and certified fitness instructors

- Be aware of and have links with local resources for physical activity, such as community programs and local sporting facilities
- Follow up the patient every 3–6 months to chart progress, readjust physical activity plans and goals, solve problems, and identify and use social support

ADAPTED FROM KHAN KM, WEILER R, BLAIR SN. PRESCRIBING EXERCISE IN PRIMARY CARE. BMJ 2011;343:D4141[43]

REFERENCES

1. Sallis RE. Exercise is medicine and physicians need to prescribe it! *Br J Sports Med* 2009; 43(1):3–4.
2. Sallis R. Developing healthcare systems to support exercise: exercise as the fifth vital sign. *Br J Sports Med* 2011; 45(6):473–4.
3. Joy E, Blair SN, McBride P et al. Physical activity counselling in sports medicine: a call to action. *Br J Sports Med* 2013; 47(1):49–53.
4. Barnes PM, Schoenborn CA. Trends in adults receiving a recommendation for exercise or other physical activity from a physician or other health professional. *NCHS Data Brief* 2012(86):1–8.
5. Mindell J, Biddulph JP, Hirani V et al. Cohort profile: the health survey for England. *Int J Epidemiol* 2012; 41(6):1585–93.
6. National Physical Activity Plan. USA: 2016. http://physicalactivityplan.org/docs/2016NPAP_Finalforwebsite.pdf.
7. World Health Organization (WHO). Global action plan on physical activity 2018–2030: more active people for a healthier world. Geneva 2018.
8. Weiler R, Chew S, Coombs N et al. Physical activity education in the undergraduate curricula of all UK medical schools. Are tomorrows doctors equipped to follow clinical guidelines? *Br J Sports Med* 2012; 46(14):1024–6.
9. Courtney-Long EA, Stevens AC, Carroll D. Primary care providers' level of preparedness for recommending physical activity to adults with disabilities. *Prev Chronic Dis* 2017; 14:170328.
10. Persson G, Brorsson A, Ekvall Hansson E et al. Physical activity on prescription (PAP) from the general practitioner's perspective—a qualitative study. *BMC Fam Pract* 2013; 14:128.
11. Elley R, Kerse N, Arroll B et al. Cost-effectiveness of physical activity counselling in general practice. *N Z Med J* 2004; 117(1207):U1216.
12. Berra K, Rippe J, Manson JE. Making physical activity counseling a priority in

clinical practice: the time for action is now. *JAMA* 2015; 314(24):2617–18.

13. Müller-Riemenschneider F, Reinhold T, Nocon M et al. Long-term effectiveness of interventions promoting physical activity: a systematic review. *Prev Med* 2008; 47(4):354–68.
14. World Health Organization (WHO). Tackling NCDs: Best buys and other recommended interventions for the prevention and control of noncommunicable disease. Geneva, Switzerland: 2016.
15. Müller-Riemenschneider F, Reinhold T, Willich SN. Cost-effectiveness of interventions promoting physical activity. *Br J Sports Med* 2009; 43(1):70–6.
16. National Institute for Health and Care Excellence (NICE). Physical activity: brief advice for adults in primary care—Public health guideline [PH44]. NICE, 2013. https://www.nice.org.uk/guidance/ph44/chapter/1-Recommendations.
17. Orrow G, Kinmonth AL, Sanderson S et al. Effectiveness of physical activity promotion based in primary care: systematic review and meta-analysis of randomised controlled trials. *BMJ* 2012; 344:e1389.
18. Vuori IM, Lavie CJ, Blair SN. Physical activity promotion in the health care system. *Mayo Clin Proc* 2013; 88(12):1446–61.
19. Leijon ME, Stark-Ekman D, Nilsen P et al. Is there a demand for physical activity interventions provided by the health care sector? Findings from a population survey. *BMC Public Health* 2010; 10:34.
20. van Doorslaer E, Masseria C, Koolman X. Inequalities in access to medical care by income in developed countries. *CMAJ* 2006; 174(2):177–83.
21. Sallis RE, Baggish AL, Franklin BA et al. The call for a physical activity vital sign in clinical practice. *Am J Med* 2016; 129(9):903–5.
22. Eakin EG, Smith BJ, Bauman AE. Evaluating the population health impact of physical activity interventions in primary care—Are we asking the right questions? *J Phys Act Health* 2005; 2(2):197–215.
23. Whitlock EP, Orleans CT, Pender N et al. Evaluating primary care behavioral counseling interventions: an evidence-based approach. *Am J Prev Med* 2002; 22(4):267–84.
24. Fiore MC, Jaén CR, Baker TB et al. Treating Tobacco Use and Dependence: 2008 Update. Rockville, MD: US Department of Health and Human Services, 2008. https://www.ncbi.nlm.nih.gov/books/NBK63952/.
25. Carroll JK, Fiscella K, Epstein RM et al. A 5As communication intervention to promote physical activity in underserved populations. *BMC Health Serv Res* 2012; 12:374.
26. Get Active Questionnaire. Canada: Canadian Society for Exercise Physiology, 2017.
27. Global Physical Activity Questionnaire (GPAQ) analysis guide. Surveillance and Population-Based Prevention, Prevention of Noncommunicable Diseases

Department (PoNDD), eds. Geneva, Switzerland: WHO.

28. Scottish Physical Activity Screening Question (Scot-PASQ). NHS Health Scotland, eds. 2012.
29. Ball TJ, Joy EA, Gren LH et al. Concurrent validity of a self-reported physical activity 'vital sign' questionnaire with adult primary care patients. *Prev Chronic Dis* 2016; 13:E16.
30. Westerterp KR. Assessment of physical activity: a critical appraisal. *Eur J Appl Physiol* 2009; 105(6):823–8.
31. Wen CP, Wai JP, Tsai MK et al. Minimum amount of physical activity for reduced mortality and extended life expectancy: a prospective cohort study. *Lancet* 2011; 378(9798):1244–53.
32. World Health Organization (WHO). Global Recommendations on Physical Activity for Health. Geneva, Switzerland: 2010.
33. Prochaska JO, Velicer WF. The transtheoretical model of health behavior change. *Am J Health Promot* 1997; 12(1):38–48.
34. Morris JN, Hardman AE. Walking to health. *Sports Med* 1997; 23(5):306–32.
35. Rollnick S, Butler CC, Kinnersley P et al. Motivational interviewing. *BMJ* 2010; 340:c1900.
36. Enhancing Motivation for Change in Substance Abuse Treatment. Rockland, MD: Center for Substance Abuse Treatment, 1999.
37. Bovend'Eerdt TJ, Botell RE, Wade DT. Writing SMART rehabilitation goals and achieving goal attainment scaling: a practical guide. *Clin Rehabil* 2009; 23(4):352–61.
38. Physical Activity Pathway Practitioners Guide. Scotland: NHS Health Scotland, 2013.
39. Marcus BH, Ciccolo JT, Sciamanna CN. Using electronic/computer interventions to promote physical activity. *Br J Sports Med* 2009; 43(2):102–5.
40. Gagliardi AR, Abdallah F, Faulkner G et al. Factors contributing to the effectiveness of physical activity counselling in primary care: a realist systematic review. *Patient Educ Couns* 2015; 98(4):412–19.
41. Kahn EB, Ramsey LT, Brownson RC et al. The effectiveness of interventions to increase physical activity. A systematic review. *Am J Prev Med* 2002; 22(4 Suppl):73–107.
42. Thornton JS, Fremont P, Khan K et al. Physical activity prescription: a critical opportunity to address a modifiable risk factor for the prevention and management of chronic disease: a position statement by the Canadian Academy of Sport and Exercise Medicine. *Br J Sports Med* 2016; 50(18):1109–14.
43. Khan KM, Weiler R, Blair SN. Prescribing exercise in primary care. *BMJ* 2011; 343:d4141.

Chapter 4

Prescribing physical activity: the written prescription

with DANIEL FRIEDMAN

If exercise could be packed into a pill, it would be the single most widely prescribed and beneficial medicine in the nation.

Dr Robert Butler, world-renowned gerontologist, psychiatrist and author (1927–2010)

Over 30 years have passed since Robert Butler, the founder of the US National Institute on Aging, made what seemed like an audacious claim—that the benefits of exercise (physical activity, in fact) outweighed the products produced by the multibillion dollar pharmaceutical giants. Our level 5 evidence belief is that clinicians today still underappreciate physical activity's prodigious effects on health and quality of life. Too often, clinicians turn to their prescription pads to prescribe medication when physical activity may be as, or more, effective for many conditions,[1, 2] at less cost and with fewer adverse effects.

Writing an appropriate exercise prescription (R_X) can and should be simple. Like a drug prescription, it has a type and dose, a dosing frequency, a duration of treatment and a therapeutic goal.[3] This is true whether the exercise is walking for increased aerobic fitness, or whether it consists of several functional resistance exercises designed to emulate activities of daily living.

The exercise R_X should be individualised and tailored to each patient, based on the clinical assessment (Chapter 3) and common prescription principles. Exploring each patient's physical activity goals should be central to the exercise R_X, as personalising the exercise R_X substantially increases the likelihood that it will lead to action and sustainable change.

WHY A WRITTEN PRESCRIPTION?

Many clinicians argue that they already prescribe their patients physical activity. However, what

exactly is a patient to do with the throwaway recommendation 'You should do more exercise' and nothing else? In reality, too few clinicians are counselling their patients effectively. Out of over 13 000 Canadian primary care physicians, only 16% reported regularly using written physical activity prescriptions.[4]

To complete effective physical activity counselling using the 5As model of behaviour change (Chapter 3), it is essential to provide patients with a written prescription they can take away with them from the consultation (Fig. 4.1). A tangible prescription conveys to the patient that exercise is therapeutic, and it should be considered medicinal in its preventive and curative properties.[5] It formalises the notion that the lifestyle change advised by a clinician is necessary and that a patient should not rely on drugs for results.[6]

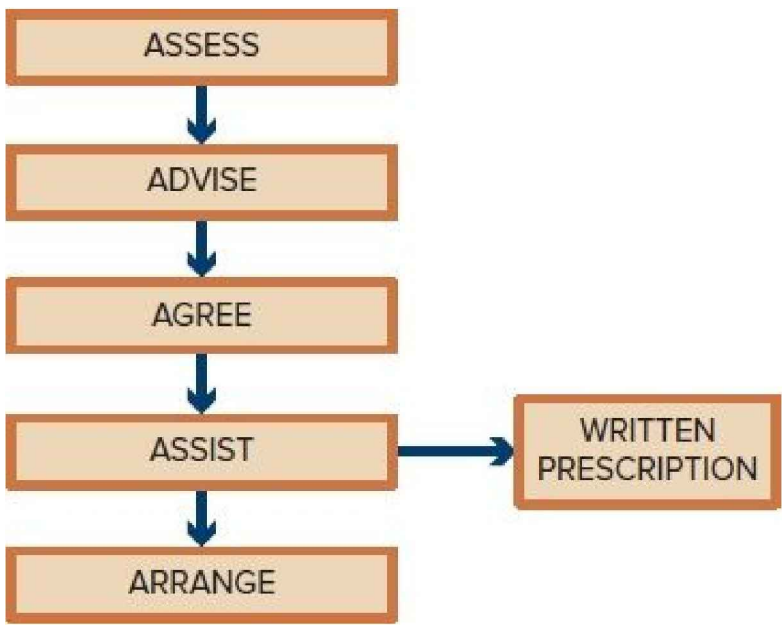


Figure 4.1 Written exercise prescription: an essential component of the 5As

It is increasingly common to find physicians providing personalised written physical activity prescriptions. Following the lead of New Zealand and Sweden, many countries have adopted exercise R_X as part of their 'physical activity on prescription' schemes—national physical activity promotion programs delivered through primary healthcare.[7]

The Green Prescription—New Zealand

Since 1998, New Zealand's Green Prescription (Green R_x) initiative has enabled clinicians to provide written advice to patients and their families to support them becoming more physically active and eat a healthier diet, as part of a total health plan.[8]

General practitioners or nurses provide written exercise prescriptions and refer the patient's details on to a patient support network, such as a regional sports trust, which then supports the patient to become more active, through Green R_x providers. A Green R_x support person then encourages the patient to become more active through monthly telephone calls, face-to-face meetings or group support sessions for up to 6 months. All the while, the patient's progress is reported back to the prescribing clinician.

Results of the Green R_x initiative indicate that it helps patients increase physical activity levels by as much as an additional hour each week, and patients maintain these increases over the longer term (2–3 years).[9] It is a cost-effective way of increasing activity in sedentary people, and also has the potential to have substantial economic impact through reduction of disease burden.[10] For more information about the initiative, see 'How the Green Prescription works' on the New Zealand Ministry of Health website, www.health.govt.nz.

Physical activity on prescription—Sweden

Written prescriptions are one of the five cornerstones of the Swedish Physical Activity on Prescription (PAP) (Fysisk aktivitet på recept, FaR) program, which enables clinicians to prescribe exercise that is individualised to their patients' circumstances. The adherence to PAP is comparable to other long-term treatments,[11, 12] and it is an effective method in primary care to increase patients' physical activity levels for at least 12 months.[13–16]

The Swedish written prescription includes type and dose of physical activity, the patient's current physical activity level, reason for prescription and personal goals. To ensure that the prescription is evidence-based, clinicians use the Swedish *Physical Activity in the Prevention and Treatment of Disease* (FYSS) book (Fig. 4.2).[17] In addition to written prescriptions, patients also receive physical activity diaries.

Figure 4.2 Sweden's Physical Activity on Prescription program provides patients with written prescriptions to increase their activity levels. Clinicians use the book that is available in every primary care doctor's office in Sweden, *Physical Activity in the Prevention and Treatment of Disease*
SHUTTERSTOCK.COM/JENS OTTOSON

Since 2007, there has been a yearly increase of 30–75% in the total number of PAPs prescribed in Sweden. In 2010, approximately 50 000 prescriptions were issued—equivalent to five PAPs for every 1000 people in Sweden.[18]

COMPONENTS OF A WRITTEN PRESCRIPTION: THE FITT PRINCIPLE

The classic exercise R_x has four components, which can be abbreviated by the acronym FITT:

- frequency
- intensity
- time
- type.

We credit the American College of Sports Medicine's, *ACSM's Guidelines for Exercise Testing and Prescription,* and extend this with two additional components:

- volume
- progression.

FITT-VP is a useful memory aid; however, it may not be the most effective order to follow in the actual exercise R_x process. The following subheadings follow the pragmatic order that enables a logical prescription for the patient.

Type

To provide the patient with an exercise program that provides a wide range of health benefits, an exercise R_x should include one or more types of physical activity. Specifically, aerobic, resistance, flexibility and balance training must all be considered. As emphasised in Chapter 3, it is essential to explore activities that interest the patient and prompt him or her to buy into behaviour change. If the decision to change behaviour does not come from the patient, ultimately it will not happen. The examples for various types of exercise provided here are merely illustrative. There is overlap—for example, hiking (aerobic training) can provide resistance training for the lower limb muscles, particularly if the hiking is in a mountainous region. Some commercial exercise programs, such as CrossFit®, aim to provide various types of exercise within one workout.

Page 27

- aerobic—walking, running, hiking, cycling, swimming, dancing
- resistance—climbing stairs, carrying objects, weight training with bodyweight/free weights (Table 4.1)/weight machines/resistance bands/suspension trainer, Pilates
- flexibility—stretching, Pilates, yoga, tai chi
- balance—yoga, tai chi, specific balance exercises.

Table 4.1 Resistance exercises classified by body region

Chest and shoulders	Upper and lower back	Abdomen/core	Arms	Lower body
• Push-up • Bench press • Seated overhead press	• Pull- or chin-up • Latissimus pull-down • Bent-over row	• Plank • Side plank • Bicycle crunch	• Arm curl • Triceps pull-down or extension	• Squats • Deadlifts • Seated leg press • Step-up • Side leg raise • Calf raise

For more information about types of exercise, see Chapter 10 of *Clinical Sports Medicine Volume 1: Injuries.*

PRACTICE PEARL

Ultimately, the best type of exercise is one the patient actually enjoys and will do.

Time (duration)

For a patient to receive the many health benefits of physical activity, it must be performed for a

sufficient duration. To meet the daily World Health Organization (WHO) recommendations for physical activity (Fig. 4.3),[19] adults should accumulate at least 22 minutes of moderate-intensity physical activity, or 11 minutes of vigorous physical activity, or a combination of moderate and vigorous physical activity every day. Ideally, individuals should be performing more than just the minimum requirements to achieve further health benefits. The ACSM recommends 20–60 minutes of continuous aerobic activity daily.[20]

Dogma has been that aerobic activity should be performed in bouts of at least 10 minutes duration to meet the guidelines.[19] If the patient cannot complete 10 minutes of continuous activity, break up the 10 minutes into smaller sessions and work towards increasing the duration. Performing physical activity in short bouts of 10–15 minutes can make it easier and more attractive for patients, allowing them to meet a realistic and achievable goal before increasing the 'dosage'. Some authors have challenged this dose limit;[21] some studies find that every step counts. The most recent physical activity guidelines in the UK reflect this encouragement for even small bouts of physical activity (e.g. such as climbing a flight of stairs or turning what would be a seated meeting into a short walking meeting).

PRACTICE PEARL

When patients are planning to engage in physical activity for the first time after a period of inactivity, encourage them to *start low, and go slow.* Recommend patients gradually build their daily physical activity, starting with light intensity activities, such as casual walking, which can then be increased in duration and intensity over time.

No specific amount of time is recommended for resistance training. 'Repetitions' and 'sets' are standard ways of referring to the quantity of resistance exercise, where a single repetition is one performance of a specific exercise (e.g. doing one squat) and a set comprises multiple repetitions performed without stopping (e.g. one set of 12 squats).

The ACSM recommends performing one set of 8–12 repetitions for 8–10 separate exercises that train the major muscle groups.[20] Resistance exercises should generally be repeated until it would be difficult to do another repetition with good form and technique, which is referred to as the 'repetition maximum'. Muscle mass and strength increase in response to stimuli, so the weight being lifted should be increased to maintain an 8–12 repetition maximum. For more information about resistance training, see *Clinical Sports Medicine Volume 1: Injuries.*

World Health Organization's global recommendations on physical activity for adults 18 years or older

1. Adults should do at least 150 minutes of moderate-intensity aerobic physical activity throughout the week, or do at least 75 minutes of vigorous-intensity aerobic physical activity throughout the week, or an equivalent combination of moderate- and vigorous-intensity activity.
2. Aerobic activity should be performed in bouts of at least 10 minutes duration.
3. For additional health benefits, adults should increase their moderate-intensity aerobic physical activity to 300 minutes per week, or engage in 150 minutes of vigorous-intensity aerobic physical activity per week, or an equivalent combination of moderate- and vigorous-intensity activity.
4. Muscle-strengthening activities, involving major muscle groups, should be done on two or more days a week.
5. Adults aged 65 and over with poor mobility should perform physical activity on three or more days per week to enhance balance and prevent falls.

Figure 4.3 WHO headquarters in Geneva, Switzerland
MARTIN GOOD/SHUTTERSTOCK.COM, MEMODJI/SHUTTERSTOCK

Resistance training apps

When prescribing resistance training to patients, clinicians should consider mobile apps that can assist with creating customised basic training programs. 'StrongLifts 5 × 5', for example, is a free mobile app that provides instructional videos on how to perform fundamental compound movements, such as the squat, deadlift, bench press, overhead press and bent-over row (Fig. 4.4). The app creates a varied 3-day program based on the user's subjective maximum lifting capacity, and can be used as a simple support tool for patients in their weekly physical activity routine.[22]

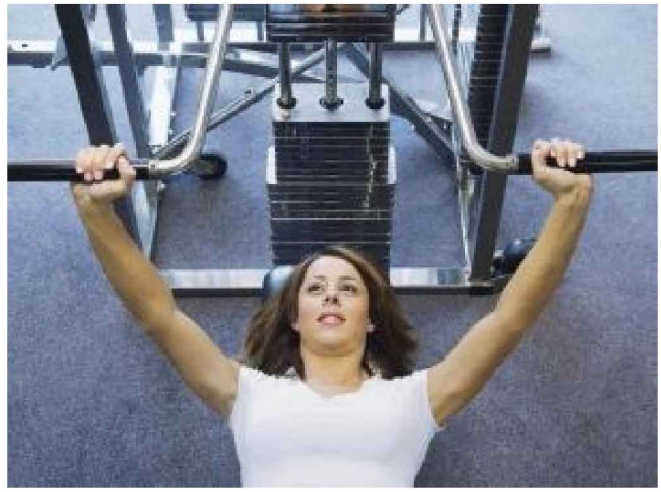


Figure 4.4 It is now easy for clinicians to support patients with a wide range of mobile apps. Although use of apps themselves is not proven to improve exercise adherence or contribute to health benefits, many individuals find them useful for at least a period of time
DESIGN PICS/KELLY REDINGER

Intensity

Physical activity can be carried out at different levels of intensity, from light to moderate to vigorous. Intensity refers to the rate at which the activity is being performed or the magnitude of the effort required to perform it. It can be thought of as 'how hard a person must work to do the activity'.

The WHO recommends that everyone should aim for at least moderate-intensity physical activity throughout the week, and can balance it with more vigorous activity for additional health benefits.[19] However, rather than using the same absolute workload for everyone, exercise R_x should be individualised according to relative intensity, in an attempt to provide a similar exercise stress for patients of differing physiological and functional capacities.[23]

Intensity can be measured subjectively or objectively by:

- rating of perceived exertion (RPE)
- heart rate (HR)
- oxygen consumption (VO_2).

Rating of perceived exertion

Using RPE, individuals subjectively rate how hard they are working using the Borg scale, ranging from 6 to 20, where 20 is maximal exertion (Table 4.2).[24] On the Borg scale, moderate exercise is rated 12–14. Other commonly used scales employ a simple 1–10 rating system. Rating of perceived exertion may be used with certain patients where heart rate is not an appropriate marker for intensity, for example in patients who take beta blockers.

Table 4.2 Borg's original rating of perceived exertion scale

Number Rating	Verbal Rating	Example
6		No effort at all. Sitting and doing nothing.
7	Very, very light	Your effort is just noticeable.
8		
9	Very light	Walking slowly at your own pace.
10		Light effort.
11	Fairly light	Still feels like you have enough energy to continue exercising.
12		
13	Somewhat hard	
14		Strong effort needed.
15	Hard	
16		Very strong effort needed.
17	Very hard	You can still go on but you really have to push yourself. It feels very heavy and you're very tired.
18		
19	Very, very hard	For most people, this is the most strenuous exercise they have ever done. Almost maximal effort.
20		Absolute maximal effort (highest possible). Exhaustion.

COPYRIGHT © 2016 PROVINCE OF BRITISH COLUMBIA. ALL RIGHTS RESERVED. REPRODUCED WITH PERMISSION OF THE PROVINCE OF BRITISH COLUMBIA. HTTPS://WWW.HEALTHLINKBC.CA/PHYSICAL-ACTIVITY/BORG-RATING-PERCEIVED-EXERTION-SCALE

Heart rate

Heart rate is a useful measure of intensity, assuming that it has a linear relationship with oxygen consumption in aerobic exercise. An individual's maximum heart rate was traditionally estimated as HR_{max} = 220 – age. However, a more accurate measure of a healthy adult's maximum heart rate can be calculated using the formula HR_{max} = 208 – (0.7 × age).[25] Training heart rate is often considered to be in the range of 50–85% of HR_{max}.

Oxygen consumption

The formula VO_2 refers to volume of oxygen uptake and it is usually measured in litres/min/kg. Oxygen uptake is a measure of exercise intensity; more intense exercise requires more oxygen uptake. Oxygen uptake has been precisely quantified for many physical activities but to simplify communication about oxygen uptake, activity intensity (or 'working metabolic rate') can be expressed in a ratio against oxygen uptake at rest. This ratio is referred to as metabolic equivalents (METs) (see Table 4.3 for examples). One MET is defined as the energy cost of sitting idly and is

equivalent to a caloric consumption of 1 kcal/kg/hour. One MET is considered to be the average resting energy expenditure of a typical person. Therefore, an exercise equivalent to 3 METs suggests that a particular exercise is three times more intense than sitting quietly.[26]

Table 4.3 Approximate metabolic costs of common activities

Sedentary <1.6 METs <40% max HR	Light 1.6–3.0 METs 40–55% max HR	Moderate 3–6 METs 55–70% max HR	Vigorous >6 METs 70–90% max HR
• Driving a car • Sitting, watching television or reading • Using a computer	• Walking casually (shopping, walking around the office) • Eating and preparing food • Playing an instrument	• Walking briskly (=4.8 km/h) on level terrain • Walking downstairs or down a hill • Cycling <16 km/h on level terrain • General gardening or home chores • Dancing—low impact • Resistance training—light	• Jogging or running • Walking or climbing briskly up a hill • Cycling >16 km/h or cycling on steep uphill terrain • Dancing—high impact • Most competitive sports—football, basketball, rugby, hockey etc.

ADAPTED FROM CDC'S 'GENERAL PHYSICAL ACTIVITIES DEFINED BY LEVEL OF INTENSITY'[27]

Intensity can also be expressed in absolute or relative terms, as two individuals can perform an activity at the same absolute intensity (e.g. walking at 3 km/h) but at a different relative intensity (as measured by %VO^2max). Therefore, the quantity and quality of physical activity Page 30 required to perform an exercise can vary considerably between individuals.

For a more complete list of the intensities of physical activities, see the US Centers for Disease Control and Prevention (CDC)'s 'General Physical Activities Defined by Level of Intensity'[27] or Jette et al.[26] which are both freely accessible online.

A simple and practical method for measuring the intensity of a physical activity is the 'talk test' (Table 4.4)—a person who is performing an activity at a moderate intensity level should still be able to comfortably talk during the activity, while a person who is performing an activity at a vigorous intensity should be breathing heavily and not be able to talk comfortably.

Table 4.4 The talk test

Intensity	What can be done during the activity?
Light	Sing
Moderate	Converse normally
Vigorous	Unable to converse; breathing heavily

ADAPTED FROM ENERGISING LIVES: A GUIDE TO PROMOTING PHYSICAL ACTIVITY IN PRIMARY CARE, NHS HEALTH SCOTLAND[28]

PRACTICE PEARL

As a general rule, a person who is performing an activity at a moderate intensity usually experiences an increase in breathing rate, an increase in heart rate and a feeling of increased warmth, which may be accompanied by perspiration.

High-intensity interval training

High-intensity interval training (HIIT) involves alternate bursts of short, intense physical activity interspersed with recovery periods.[29] These short bursts may last from 5 seconds to 10 minutes or longer, and are performed at approximately 70–95% of a person's maximum heart rate. The recovery periods may last equally as long, and are performed at 30–50% of maximum heart rate. For example, 30 seconds of hard sprinting followed by 30 seconds of jogging, repeated as many times as desired. There is no set formula for prescribing HIIT—the specific exercise and its intensity can be varied to meet the needs of the individual. For an example of a HIIT program for walking, see Table 4.5. Consistent with any exercise R_x, always consider FITT—the duration, intensity and frequency of the work intervals and the alternating recovery intervals.

Page 31

Table 4.5 HIIT for walking

1.	**Warm-up**	3 min	Walk briskly—you should still be able to breathe and talk easily
2.	**Repeat the following as many times as desired:**		
	a. High-intensity interval	1 min	Walk as quickly as possible—you should be breathing heavily and not be able to talk
	b. Recovery interval	1 min	Walk at a comfortable pace and catch your breath
3.	**Cool-down**	3 min	Continue to walk at a comfortable pace until completion

HIIT is popular due to its similar health benefits to more traditional endurance training, which can be achieved in shorter periods of time. While HIIT and endurance training both lead to improved cardiovascular fitness, HIIT leads to greater improvement in VO_2max.[30] HIIT is also more effective than moderate-intensity exercise at improving vascular function and markers of vascular health, perhaps due to its positive effects on cardiorespiratory fitness, cardiovascular disease risk factors, oxidative stress, inflammation and insulin sensitivity.[31]

HIIT can be easily modified and prescribed to patients of all abilities and with different medical conditions. Importantly, HIIT appears to be safe for rehabilitation of patients with cardiovascular disease and heart failure;[32] however, stress testing is advised in patients with higher risk.[29]

If a patient is looking to increase his or her physical activity levels and is new to HIIT, consider recommending mobile apps as a support. There are many HIIT apps available, such as the '7 Minute Workout', which provides users with videos of exercises and guided HIIT workouts (Fig. 4.5). Workouts can be customised based on desired goals and levels of ability.

Figure 4.5 One reason for the popularity of high-intensity interval training is that an effective workout takes much less time than what many considered was needed to 'get a sweat up' (and therefore be of value)

Frequency

Frequency refers to the number of times per day or week that an exercise should be performed. It is usually expressed in sessions, episodes or bouts.

Frequency depends on intensity and duration of the exercise. Long and intense exercise sessions cannot be completed as frequently as shorter and less demanding sessions. The number of recommended exercise sessions per week will vary based on patient abilities, preferences and goals.

The ACSM recommends *minimal* thresholds of 300 kcal per exercise session performed 3 days per week or 200 kcal per session performed 4 days per week. Patients with a low level of fitness can

benefit from multiple, short daily exercise sessions, while patients of moderate to higher levels of fitness can benefit from longer, more intense sessions.[21]

Resistance training is recommended at least twice weekly,[19] with at least 48 hours separating the exercise training sessions for the same muscle group.[21] Training different muscle groups on separate days of the week may improve adherence to an exercise R_x, as it leads to a more flexible and varied program.

Total volume

Volume is the product of frequency, intensity and time. Total volume refers to quantity and quality of weekly physical activity.

The weekly volume of exercise can be expressed as MET minutes (METs × total minutes), which adds the intensity dimension to time alone. The ACSM recommends 500–1000 MET minutes per week,[21] which is consistent with the WHO's recommendation for at least 150 minutes of moderate-intensity aerobic physical activity throughout the week.[19]

There is a clear, graded dose response of the volume of physical activity with all-cause mortality, stroke and cardiovascular disease risk factors, with risk reduction per unit time being the greatest for vigorous activity.[33, 34] A higher total volume is strongly associated with a lower risk of breast cancer, colon cancer, diabetes, ischaemic heart disease and ischaemic stroke, with most health gains occurring at a total activity level of 3000–4000 MET minutes per week,[35] which is notably well above the global recommendations.

Combined daily activities to accumulate 3000 MET minutes per week include:

- stair climbing—10 minutes
- walking or cycling for transportation—25 minutes
- vacuuming—15 minutes
- gardening—20 minutes
- running—20 minutes.

Even if a patient is unable to achieve this volume of physical activity, remember that *every minute still counts.* Patients who perform even small amounts of physical activity throughout the week, from 10–15 minutes daily, still achieve substantial reductions in mortality risk, up to 15%.[36] Increasing this to 30 minutes of physical activity per six days a week is associated with a 40% mortality risk reduction, irrespective of whether the activity is light or vigorous.[37]

Progression

Progression refers to increasing the dosage of physical activity. As the patient adapts to a given physical activity dose, one or more components of FITT can be increased as tolerated.

Increasing duration before frequency and intensity is a logical first step. The ACSM recommends

graded increases by 5–10 minutes every 1–2 weeks over the first 4–6 weeks. After a month or more, frequency and intensity may be gradually adjusted until recommended physical activity levels are met and can then be exceeded.[21]

The patient should be continuously assessed throughout exercise progression for any adverse effects of the increased total volume of exercise. Any element of FITT can be reduced at any time if the exercise is not being well tolerated.

Page 33

Stepping your way to 10 000

Step count has become a common indicator of overall physical activity volume thanks to the proliferation of wearable pedometers and accelerometers built into mobile phones. Ever since Japanese walking clubs embraced a pedometer manufacturer's device called 'Manpo-kei'—which translates as '10 000 step meter'—in the 1960s, 10 000 steps has become universally accepted as a benchmark for daily physical activity.[38] Should we still follow this recommendation?

Healthy adults take between 4000 and 18 000 steps/day.[39]

- US adults average 5100 steps/day.
- Japanese adults average 7200 steps/day.
- Australian adults average 7400 steps/day.[40]

Public health physical activity guidelines recommend at least 150 minutes of moderate-intensity aerobic physical activity throughout the week, which translates to 15 000 steps/week, or 2150 steps/day. These 15 000 steps should be of at least moderate intensity (≥ 100 steps/min) and, most importantly, be taken over and above steps taken during habitual and incidental physical activity (Fig. 4. 6).

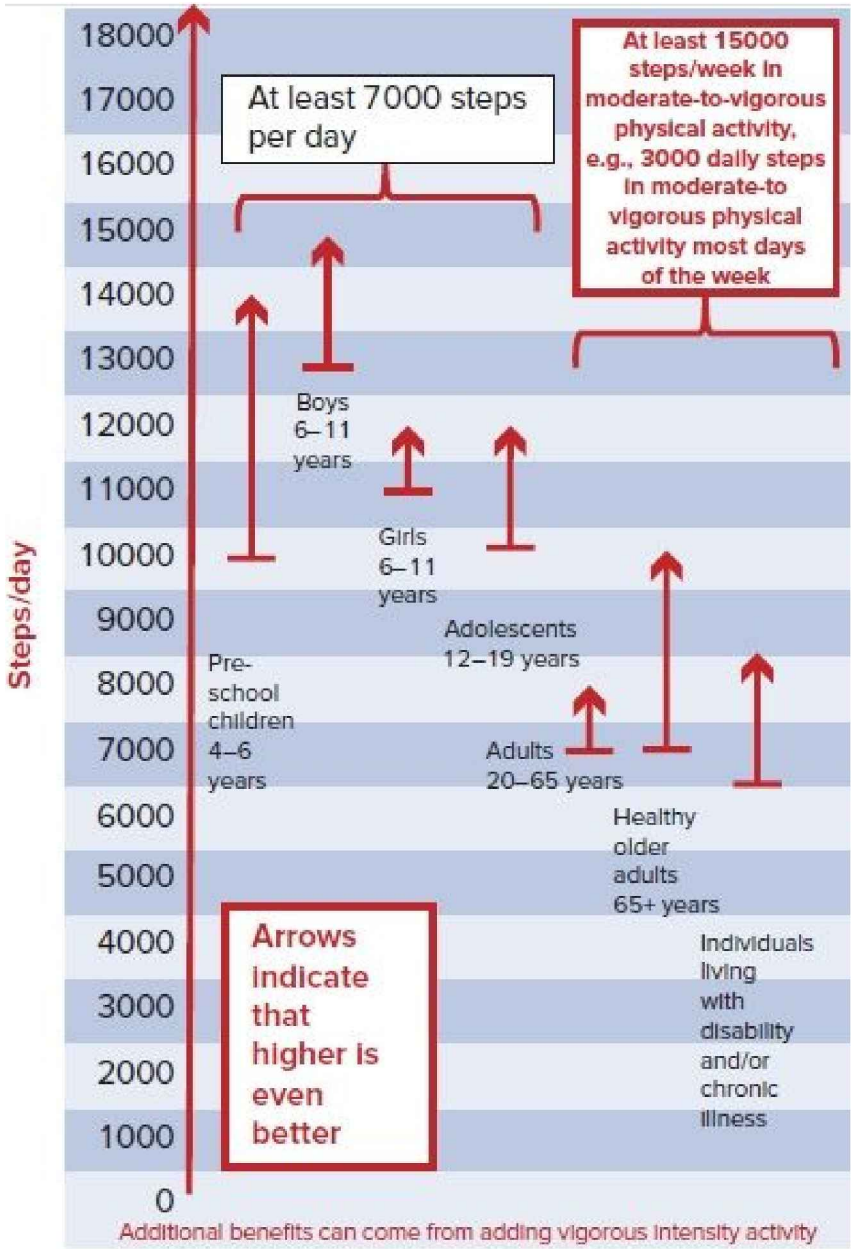


Figure 4.6 A guide for clinicians when discussing step counts with patients. Personal experience of the various elements of exercise prescription also adds authenticity to the patient encounter. For example, the authors of this chapter find it takes them 70–80 minutes to walk for 10 000 steps and about 60 minutes to get those steps when running

ADAPTED FROM BIOMED CENTRA / INT J BEHAV NUTR PHYS ACT. 2011[43]

Taking all of this into account, a recent review concludes that we should aim to accumulate at least 7000 steps/day, which suggests 10 000 can continue to be a reasonable target for all healthy adults.

But that does not mean 10 000 should be the upper limit. A 2017 study that equipped over 100 postal workers in the UK with activity trackers found that those who took ≥ 15 000 steps/day had zero cardiovascular disease risk factors.[41]

For patients who cannot achieve 10 000 steps/day due to limited mobility or medical conditions, the message should still be that 'any is better than none at all'. In contrast, for children and adolescents, 10 000 steps/day is probably too few. Sixty minutes of moderate- to vigorous-intensity physical activity in primary school children appears to be achieved with a total volume of 13 000–15 000 steps/day in boys and 11 000–12 000 steps/day in girls.[42]

An example of a progression of exercise prescription in the case of a patient with low back pain

The Swedish book *Physical Activity in the Prevention and Treatment of Disease* (FYSS) recommends that an exercise prescription that combines aerobic, resistance and flexibility training is beneficial for rehabilitation of non-specific chronic low back pain (Table 4.6). Patients with back pain should be advised to 'return to normal physical activity as best as possible'.[17]

Table 4.6 Applying FITT to exercise prescription for back pain

Type	Time	Intensity	Frequency
Aerobic			
• Walking • Swimming • Cycling	≥ 30 min	11–16/20 RPE, 60–80% HR_{max}	5–7 times/week
Resistance			
• Abdominal and back strengthening	8–15 reps/day, involving 8–10 muscle groups	As tolerated	Daily
Flexibility			
• Yoga	2 min/muscle group, 3 reps	To level of tension, before discomfort	Daily

ADAPTED FROM ACSM'S GUIDELINES FOR EXERCISE TESTING AND PRESCRIPTION,[20] ACSM'S EXERCISE MANAGEMENT FOR PERSONS WITH CHRONIC DISEASES AND DISABILITIES[44], ACSM'S RESOURCES FOR CLINICAL EXERCISE PHYSIOLOGY: MUSCULOSKELETAL, NEUROMUSCULAR, NEOPLASTIC, IMMUNOLOGIC, AND HEMATOLOGIC CONDITIONS[45]

Physical inactivity that can result from back pain has not been shown to improve back pain or function. A return to normal physical activity must be gradual, and alleviate a patient's fears of movement. Once symptoms improve, focused resistance training to increase abdominal and back strength should be recommended. For specific aetiology, such as spinal stenosis or disc herniation, the activity level must be adapted to the presence of symptoms.

The updated UK National Institute for Health and Care Excellence (NICE) guidelines on back pain recommend group exercise programs that include 'biomechanical, aerobic, and or mind-body approaches'.[46]

MINIMISING SEDENTARY BEHAVIOUR

Sedentary behaviour is defined as 'any waking behaviour characterized by an energy expenditure ≤1.5 metabolic equivalents (METs), such as sitting, reclining or lying down'.[47]

High levels of continuous sedentary behaviour, such as sitting for long periods of time, are associated with abnormal glucose metabolism and cardiometabolic morbidity, as well as overall mortality.[48]

There are currently no global recommendations on sedentary behaviour; however, emerging consensus reflected in some countries' guidelines recommends that sedentary behaviour in adolescents should be limited to two hours per day, and long periods of sitting should be broken up as often as possible.[49]

When prescribing exercise, clinicians should always consider advising patients to minimise sedentary behaviour. Simple recommendations include:

- Reduce all forms of screen time, including using the computer or phone and watching television.
- When watching television, using the computer or reading, schedule 5-minute breaks every 45 minutes to go for a quick walk.
- During television commercial breaks, perform calisthenics such as push-ups, squats and lunges.
- Save your television watching for the gym, when using a stationary bike or treadmill. This is a form of 'temptation bundling'—a way of combining 'want behaviours', such as watching television, with 'should behaviours', such as exercise, to ultimately encourage patients to increase should behaviours and develop healthy habits.[50]

Brukner & Khan's CSM

Patient Details Date

Patient goal:

	TYPE	TIME	INTENSITY	FREQUENCY	PROGRESSION
1.	*Walk*	*30 mins*	*"Conversational"*	*3 × week*	*Increase by 5 mins weekly up to 60 mins*
2.	*Sit to stand*	*30 secs*	*As many reps as possible*	*3 sets × 2 daily (b.d)*	*Increase by 5 secs daily until 60 secs*
3.					

*Disclaimer – red flags/adverse effects + who/how to seek help

Minimise sedentary behaviour

Sit less - fact

Use stairs - fact

Limit screen time - fact

☑ Referral needed Physio/OT/Cardio/Ortho/Rheum/Dietitian

Follow up date:

Person to review

Designation: GP/Physio/etc. Name + Signature:

Figure 4.7 Prescription pad

- Stand up and walk when talking on the phone.
- Take the stairs instead of an escalator or elevator.
- Try a sit-stand desk.
- Swap the car for the bike and cycle to work.
- Instead of trying to park the car close to your destination, aim to park as far away as you can

and walk the extra distance.

SPECIFIC GROUPS

Refer to Part D, Specific groups, for guidance on medical management in specific clinical contexts. The principles of careful evaluation, listening to the patient and making shared decisions apply as outlined above. In addition, special medical issues such as loss of autonomic function in some people with disability, or severe arthritis in others, add a level of complexity to clinical care.

REFERENCES

1. Naci H, Ioannidis JP. Comparative effectiveness of exercise and drug interventions on mortality outcomes: metaepidemiological study. *BMJ* 2013; 347:f5577.
2. Vina J, Sanchis-Gomar F, Martinez-Bello V et al. Exercise acts as a drug; the pharmacological benefits of exercise. *Br J Pharmacol* 2012; 167(1):1–12.
3. Moore GE. The role of exercise prescription in chronic disease. *Br J Sports Med* 2004; 38(1):6–7.
4. Petrella RJ, Lattanzio CN, Overend TJ. Physical activity counseling and prescription among Canadian primary care physicians. *Arch Intern Med* 2007; 167(16):1774–81.
5. Handcock P, Jenkins C. The Green Prescription: a field of dreams? *N Z Med J* 2003; 116(1187):U713.
6. Swinburn BA, Walter LG, Arroll B et al. Green prescriptions: attitudes and perceptions of general practitioners towards prescribing exercise. *Br J Gen Pract* 1997; 47(422):567–9.
7. Arsenijevic J, Groot W. Physical activity on prescription schemes (PARS): do programme characteristics influence effectiveness? Results of a systematic review and meta-analyses. *BMJ Open* 2017; 7(2):e012156.
8. New Zealand Ministry of Health. How the Green Prescription works. 2017. https://www.health.govt.nz/our-work/preventative-health-wellness/physical-activity/green-prescriptions/how-green-prescription-works.
9. Hamlin MJ, Yule E, Elliot CA et al. Long-term effectiveness of the New Zealand Green Prescription primary health care exercise initiative. *Public Health* 2016; 140:102–8.
10. Elley R, Kerse N, Arroll B et al. Cost-effectiveness of physical activity counselling in general practice. *N Z Med J* 2004; 117(1207):U1216.
11. Kallings LV, Leijon ME, Kowalski J et al. Self-reported adherence: a method for evaluating prescribed physical activity in primary health care patients. *J Phys Act Health* 2009; 6(4):483–92.

12. Leijon ME, Bendtsen P, Stahle A et al. Factors associated with patients self-reported adherence to prescribed physical activity in routine primary health care. *BMC Fam Pract* 2010; 11:38.
13. Kallings LV, Leijon M, Hellenius ML et al. Physical activity on prescription in primary health care: a follow-up of physical activity level and quality of life. *Scand J Med Sci Sports* 2008; 18(2):154–61.
14. Leijon ME, Bendtsen P, Nilsen P et al. Does a physical activity referral scheme improve the physical activity among routine primary health care patients? *Scand J Med Sci Sports* 2009; 19(5):627–36.
15. Rome A, Persson U, Ekdahl C et al. Physical activity on prescription (PAP): costs and consequences of a randomized, controlled trial in primary healthcare. *Scand J Prim Health Care* 2009; 27(4):216–22.
16. Sjoling M, Lundberg K, Englund E et al. Effectiveness of motivational interviewing and physical activity on prescription on leisure exercise time in subjects suffering from mild to moderate hypertension. *BMC Res Notes* 2011; 4:352.
17. *Physical activity in the prevention and treatment of disease*. 2nd ed. Sweden: Professional Associations for Physical Activity, 2010.
18. Swedish National Institute of Public Health. Professional Associations for Physical Activity, 2010. YFA, ed. Physical Activity in the Prevention and Treatment of Disease. Report 2010:14. http://www.fyss.se/fyss-in-english
19. World Health Organization (WHO). Global Recommendations on Physical Activity for Health. Geneva, 2010.
20. American College of Sports Medicine (ACSM). Riebe D, Ehrman JK, Liguori G et al. eds. *ACSM's guidelines for exercise testing and prescription*. 10th ed. Philadelphia: Wolters Kluwer, 2018.
21. Glazer NL, Lyass A, Esliger DW et al. Sustained and shorter bouts of physical activity are related to cardiovascular health. *Med Sci Sports Exerc* 2013 Jan; 45(1):109–15.
22. Anderson N, Stevenson S, Brozena J. StrongLifts 5 × 5 workout: mobile app user guide. *Br J Sports Med* 2018; 52:e3.
23. Mann T, Lamberts RP, Lambert MI. Methods of prescribing relative exercise intensity: physiological and practical considerations. *Sports Med* 2013; 43(7):613–25.
24. US Centers for Disease Control and Prevention (CDC). Perceived exertion (Borg rating of perceived exertion scale). August 2015. https://www.cdc.gov/physicalactivity/basics/measuring/exertion.htm.
25. Tanaka H, Monahan KD, Seals DR. Age-predicted maximal heart rate revisited. *J Am Coll Cardiol* 2001; 37(1):153–6.
26. Jette M, Sidney K, Blumchen G. Metabolic equivalents (METS) in exercise testing, exercise prescription, and evaluation of functional capacity. *Clin Cardiol* 1990; 13(8):555–65.

27. US Centers for Disease Control and Prevention. General Physical Activities Defined by Level of Intensity. https://www.cdc.gov/nccdphp/dnpa/physical/pdf/PA_Intensity_table_2_1.pdf
28. Energising Lives: A Guide to Promoting Physical Activity in Primary Care. NHS Health Scotland, 2008.
29. Thornton JS, Fremont P, Khan K et al. Physical activity prescription: a critical opportunity to address a modifiable risk factor for the prevention and management of chronic disease: a position statement by the Canadian Academy of Sport and Exercise Medicine. *Br J Sports Med* 2016; 50(18): 1109–14.
30. Milanovic Z, Sporis G, Weston M. Effectiveness of high-intensity interval training (HIT) and continuous endurance training for VO_2max improvements: a systematic review and meta-analysis of controlled trials. *Sports Med* 2015; 45(10):1469–81.
31. Ramos JS, Dalleck LC, Tjonna AE et al. The impact of high-intensity interval training versus moderate-intensity continuous training on vascular function: a systematic review and meta-analysis. *Sports Med* 2015; 45(5):679–92.
32. Rognmo O, Moholdt T, Bakken H et al. Cardiovascular risk of high-versus moderate-intensity aerobic exercise in coronary heart disease patients. *Circulation* 2012; 126(12):1436–40.
33. Oja P. Dose response between total volume of physical activity and health and fitness. *Med Sci Sports Exerc* 2001; 33(6 Suppl):S428–37; discussion S452–3.
34. Samitz G, Egger M, Zwahlen M. Domains of physical activity and all-cause mortality: systematic review and dose-response meta-analysis of cohort studies. *Int J Epidemiol* 2011; 40(5):1382–400.
35. Kyu HH, Bachman VF, Alexander LT et al. Physical activity and risk of breast cancer, colon cancer, diabetes, ischemic heart disease, and ischemic stroke events: systematic review and dose-response meta-analysis for the Global Burden of Disease Study 2013. *BMJ* 2016; 354:i3857.
36. Wen CP, Wai JP, Tsai MK et al. Minimum amount of physical activity for reduced mortality and extended life expectancy: a prospective cohort study. *Lancet* 2011; 378(9798): 1244–53.
37. Holme I, Anderssen SA. Increases in physical activity is as important as smoking cessation for reduction in total mortality in elderly men: 12 years of follow-up of the Oslo II study. *Br J Sports Med* 2015; 49(11):743–8.
38. Tudor-Locke C, Hatano Y, Pangrazi RP et al. Revisiting 'how many steps are enough?'. *Med Sci Sports Exerc* 2008; 40(7 Suppl):S537–43.
39. Tudor-Locke C, Craig CL, Brown WJ et al. How many steps/day are enough? For adults. *Int J Behav Nutr Phys Act* 2011; 8:79.
40. Australian Bureau of Statistics (ABS). Australian Health Survey: Physical Activity, 2011–12. Cat. no. 4364.0.55.004. Canberra: ABS, 2013. http://www.abs.gov.au/ausstat

s/abs@.nsf/Lookup/4364.0.55.004Chapter5002011-12.

41. Tigbe WW, Granat MH, Sattar N et al. Time spent in sedentary posture is associated with waist circumference and cardiovascular risk. *Int J Obes* 2017; 41:689.
42. *Int J Behav Nutr Phys Act*. 2011; 8: 79. Published online 2011 Jul 28. doi: 10.1186/1479-5868-8-79
43. Moore G, Durstine JL, Painter PL, eds. *ACSM's Exercise Management for Persons With Chronic Diseases and Disabilities*. 4th ed. Champaign, IL: Human Kinetics, 2016.
44. ACSM. *ACSM's Resources for Clinical Exercise Physiology: Musculoskeletal, Neuromuscular, Neoplastic, Immunologic, and Hematologic Conditions*. 2nd ed. Philadelphia: Wolters Kluwer, 2009.
45. Tudor-Locke C, Craig CL, Beets MW et al. How many steps/day are enough? for children and adolescents. *Int J Behav Nutr Phys Act* 2011; 8:78.
46. National Institute for Health and Care Excellence (NICE). Low back pain and sciatica in over 16s: assessment and management. NICE, 2016. https://www.nice.org.uk/guidance/ng59/chapter/Recommendations.
47. Australian Government: Department of Health. Australia's Physical Activity and Sedentary Behaviour Guidelines 2017 [updated 21 November 201725 August 2018]. Available from: http://www.health.gov.au/internet/main/publishing.nsf/content/health-pubhlth-strateg-phys-act-guidelines#apaadult
48. Owen N, Healy GN, Matthews CE et al. Too much sitting: the population health science of sedentary behavior. *Exerc Sport Sci Rev* 2010; 38(3):105–13.
49. Anderson G. Hip assessment: a comparison of nine different methods. *J Bone Joint Surg Br* 1972; 54B:621–5.
50. Milkman KL, Minson JA, Volpp KGM. Holding The Hunger Games hostage at the gym: an evaluation of temptation bundling. *Manage Sci* 2014; 60(2):283–99.

Chapter 5

Prescribing physical activity: motivational interviewing

with DANIEL FRIEDMAN and DANE VISHNUBALA

Obstacles don't have to stop you. If you run into a wall, don't turn around and give up. Figure out how to climb it, go through it, or work around it.

Michael Jordan, American professional basketball player

Facilitating positive behaviour change in patients is one of the biggest challenges facing clinicians on a daily basis. Why are some patients resistant to change, even if the change is in their best interests, such as exercising regularly or following a nutritious diet? Why don't patients act rationally and do what they know is logical, after a critical appraisal of the facts? And why can't they find a level of motivation for change that matches that of basketball great Michael Jordan?

The underlying psychology of behaviour change is complex, and can be difficult to navigate among different, constantly changing sociocultural contexts. As Nutbeam et al. explain,[1] an individual's desire to change is determined by a fluid interplay between their knowledge and understanding of health and disease, the personal meaning and relevance of that knowledge, their confidence in their ability to make changes, and a range of other factors acting as facilitators and barriers to change.

Building on Chapters 3 and 4, if clinicians are to join the global efforts on the war against physical inactivity, they must be equipped with the essential skills and tools for motivating and supporting behaviour change in all patients, from professional athletes to sedentary office workers. It is not enough to have the knowledge and simply pass on information. Clinicians must learn how to counsel patients effectively, implementing evidence-based practices that drive change from within and empower patients to take more control over their own health and over their environments.

In this chapter we explore:

- behaviour change theories that offer keys to supporting patients in adopting healthier lifestyles
- motivational interviewing as an effective counselling method for behaviour change
- supporting patients to maintain their healthy lifestyle habits.

BEHAVIOUR CHANGE THEORIES

When patients receive advice to adopt healthier lifestyle habits, it can be frustrating for clinicians when their advice is seemingly ignored or even contested. A clinician who encounters such resistance may try to reiterate their advice with greater authority, or perhaps adopt a more paternalistic and coercive style of counselling. When these methods do not succeed, clinicians label patients as 'unmotivated' and often lose motivation themselves to persist with lifestyle counselling.

Motivation can be defined as 'the internal state that activates behaviour and gives it direction'.[2] It is a dynamic state that changes frequently and can fluctuate as a result of a clinician's counselling style. What motivates one individual may not motivate another, and what motivates someone today may not motivate them tomorrow.

Behaviour change theories attempt to explain these complexities, providing a rationale for the irrationality of human behaviour. The following provides a brief overview of the most prevalent behaviour change theories. For a more comprehensive resource, readers can refer to *ABC of Behaviour Change Theories,* by Michie et al.[3]

Classic learning theories

Classic learning theories suggest that learning a new complex behaviour, such as changing from a sedentary to more active lifestyle, requires altering many of the small behaviours that make up a larger complex behaviour.[4] Behaviour modification principles propose that a patterned behaviour (e.g. walking for 30 minutes every day) can be learned by first breaking it up into smaller parts—also known as 'chunking'. Gradual incremental increases (e.g. increasing daily walking by 5 minutes each week) are then attempted, as the complex patterned behaviour contributes towards achieving the overall goal.

Classic learning theories also propose that whether or not behaviours such as physical activity are learned and maintained is dependent on reinforcement and anticipated future rewards (e.g. experiencing a feeling of accomplishment or receiving praise). This is known as 'operant conditioning'.

Social cognitive theory

Social cognitive theory suggests that behaviour change is affected by environmental influences, personal factors and attributes of the behaviour itself.[5] These elements must be viewed as a system, as each may be affected by the other two.

A central component of social cognitive theory is the concept of self-efficacy. An individual must possess self-efficacy and believe in their ability to perform the behaviour, as well as perceive an incentive to do so. The theory proposes that an individual must value the short- or long-term outcomes of the behaviour, viewing the action as a means to immediate benefit or as an investment

for long-term gain.[6]

Reasoned action approach

The reasoned action approach suggests that an individual's intentions are influenced by their attitude towards the behaviour, perceived societal norms about the behaviour and an individual's perceived control over the behaviour.[7] Attitude, perceived norms and behavioural control are all based on the individual's beliefs, which are shaped by diverse sociocultural and environmental factors.

For example, if an individual views cycling as a fun mode of transport (*attitude*), all of their colleagues cycle to work (*perceived norm*), and the individual has a bike that they are able to ride (*perceived control*), then the individual will likely choose to cycle to work.

Fogg behaviour model

The Fogg behaviour model[8] suggests that levels of ability and motivation determine whether triggers for behaviour change will succeed or fail. In other words, if an individual is to succeed at changing behaviour, they need to be motivated, have the ability to perform the behaviour, and require a trigger or catalyst to prompt action.

Nudging to get healthy

A 'nudge' refers to a small change in the environment that makes specific behaviours more likely. As behavioural economist Richard Thaler and co-author Cass Sunstein explain in their book *Nudge*[9] it can be thought of as 'any aspect of the choice architecture that alters people's behaviour in a predictable way without forbidding any options or significantly changing their economic incentives'. Some examples of nudges for healthy eating include putting nuts and seeds instead of confectionery at eye level in stores, making salad the default side option instead of chips, and adding calorie counts on menus.

A recent recipient of the Nobel Prize, Thaler explains that health behaviours are driven far less by conscious and cognitive processes than is acknowledged, and much of human behaviour is driven by automatic responses requiring little cognitive engagement. The setting in which we make decisions is never neutral, and external cues influence our choices.

A commonly researched nudge that promotes physical activity is 'point-of-decision prompts'—simple motivational signs placed on or near stairwells, elevators and escalators to encourage individuals to instead use the stairs (Fig. 5.1). Point-of-decision prompts are effective in increasing the use of stairs,[10] and are being increasingly used in workplaces around the world. While it may not be realistic for a sedentary individual to become a marathon runner overnight, taking the stairs is a practical and attainable first step towards improving his or her health.

Figure 5.1 Point-of-decision prompts for increasing physical activity include signs placed near elevators, escalators and stairwells that encourage individuals to take the more active option
© PHOTOALTO

According to this model, the underlying motivator for behaviour change is seeking pleasure and avoiding pain. Ability refers to an individual's belief in their self-efficacy. Page 37

Transtheoretical stages of change

Prochaska and DiClemente's transtheoretical stages of change posits that there are five stages in behaviour change: precontemplation, contemplation, preparation, action and maintenance (Fig. 5.2). In brief, an individual must first become aware of the problem before they begin to think about changing their behaviour, plan to change and then perform the action. Successful progression through the stages leads to action, and hopefully maintenance. Relapse is often cited as the sixth stage, and is a regression from the five stages, as the individual fails to maintain the behaviour and reverts to old habits.[11]

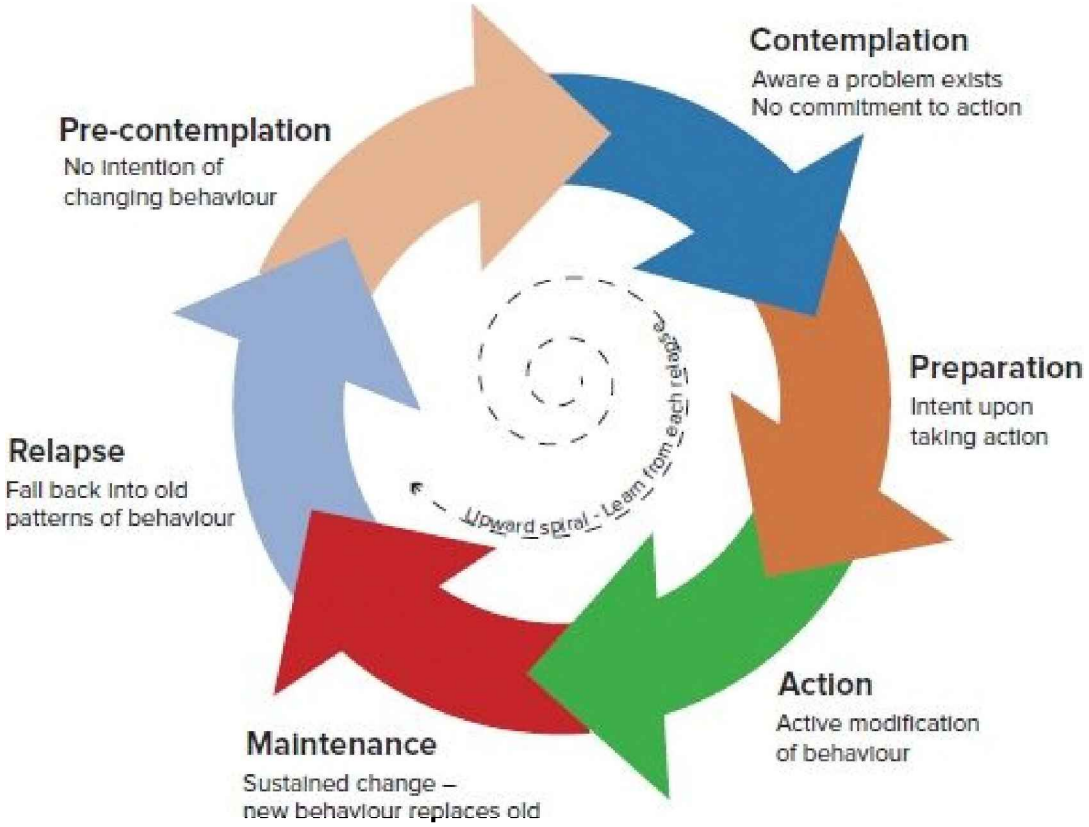


Figure 5.2 Prochaska and DiClemente's transtheoretical stages of change
PROCHASKA JO, VELICER WF. AMERICAN JOURNAL OF HEALTH PROMOTION (12(1)) THE TRANSTHEORETICAL MODEL OF HEALTH BEHAVIOR CHANGE, PP.38–48 COPYRIGHT © 1997 REPRINTED BY PERMISSION OF SAGE PUBLICATIONS, INC.

The stages of change can be conceptualised as a cyclical model and can be used to assess a patient's readiness for change (Table 5.1), as discussed in Chapter 3. Readiness to change is considered a dynamic process, in which the perceived advantages and disadvantages of change generate ambivalence, a conflicted state in which opposing attitudes coexist.

Table 5.1 Counselling for physical activity using the transtheoretical stages of change

Stage	Patient state	Tasks for clinician
Precontemplation	Not thinking about becoming more active	Increase the patient's perception of the benefits of physical activity through brief advice, and signpost a future discussion about physical activity
Contemplation	Thinking about becoming more active in the near future, but is still not yet ready	Help the patient weigh up advantages and disadvantages of change, by exploring ambivalence
Preparation	Beginning to plan to become more active and intends to initiate change in the near future	Develop an agreed physical activity plan by setting *SMART* goals (Chapter 3)
Action	Performing the change	Congratulate the patient and affirm change

Maintenance	Sustaining increased physical activity levels and making lifestyle modifications to reduce the chance of relapse	Help the patient to develop strategies to prevent relapse
Relapse	Returning to old behaviours and abandoning the change	Identify relapse as a learning opportunity and help the patient recommence the process of contemplation

MOTIVATIONAL INTERVIEWING

Motivational interviewing (MI) is a patient-centric counselling method that aims to increase patient motivation by helping them resolve their ambivalence. Originally developed for counselling for alcohol addiction, MI employs a non-judgmental and non-confrontational counselling style, in which the clinician listens, attempts to understand the patient's perspective, and emphasises that the patient should contemplate their own values to promote behaviour change. Ultimately, the clinician's goal is to guide the patient and bring out the patient's own desire for change.[12]

Formal MI training is needed to achieve optimal results, particularly when clinicians do not have a background in behaviour change counselling. There are many resources available to help clinicians wanting to learn more about MI, including the website www.motivationalinterviewing.org, the Swedish book *Physical Activity in the Prevention and Treatment of Disease* (FYSS)[13] (Fig. 5.3), which is freely available in English online, and the latest edition of Miller and Rollnick's book *Motivational Interviewing: Helping People Change.*[14]

Figure 5.3 Empathy is important in all aspects of clinical practice
©ERPRODUCTIONS LTD/BLEND IMAGES LLC

Practical tips for successful motivational interviewing

In the earlier edition of their book *Motivational Interviewing: Preparing People To Change Addictive Behavior,* Miller and Rollnick state that 'the strategies of motivational interviewing are more persuasive than coercive, more supportive than argumentative. The motivational interviewer must proceed with a strong sense of purpose, clear strategies and skills for pursuing that purpose, and a sense of timing to intervene in particular ways at incisive moments'.[12] Later, they also describe MI as 'collaborative, evocative and honouring of patient autonomy',[15] and capture its essence by outlining four key guiding principles.

Express empathy

Empathy is important in all aspects of clinical practice. Once a patient is aware that their clinician is attempting to understand their perspective, thoughts and feelings, the patient is more likely to elaborate on their situation. An empathic clinician uses reflective listening skills and communicates respect for and acceptance of their patients. In a study that analysed conversations between 40 primary care physicians and 320 of their patients, patients whose physicians were rated as more empathic had higher rates of satisfaction,[16] which can help build rapport and potentially improve patient outcomes.

PRACTICE PEARL

In a motivational interview, a clinician should spend equal amounts of time listening and talking. Allowing the patient to elaborate empowers the patient, provides specific examples with which the clinician can engage and leads to truly shared decision making.

Examples of non-empathic responses include:[17]

- ordering or directing
- warning or threatening
- providing solutions prematurely or when unsolicited
- persuading by arguing or lecturing
- preaching about what patients ought to do
- judging, criticising, disagreeing or blaming
- shaming or labelling.

Support the patient's self-efficacy

Many patients do not have a strong sense of self-efficacy and find it hard to envision change.

Patients that may have attempted behaviour change to improve their health, such as attending a gym or sustaining a diet, and have previously failed may perceive further efforts to change as futile. The clinician's role is to identify the patient's strengths and highlight these whenever possible to promote self-efficacy, even if unrelated to physical activity.

Self-efficacy is particularly influential in increasing physical activity levels,[18] and its positive effects on physical activity engagement is consistent across all ages and populations.[19]

Develop discrepancy

A patient's motivation for behaviour change can be enhanced when they perceive discrepancies between their current situation and their hopes for the future. The role of the clinician is to help their patient focus their attention on how their current behaviour is not consistent with the desired behaviour. The goal is to enable the patient to understand how the potential consequences of their current behaviour conflict with their personal values and limit the patient's future potential for health and wellbeing.

One method of developing discrepancy is exploring the advantages and disadvantages of behaviour change, which can be aided by the use of 'decisional balance exercises' (Table 5.2). It can be helpful to separate the behaviour from the patient, which may enable the patient to identify how their personal goals are being restricted by their current actions.

Table 5.2 Example of a decisional balance quadrant to help develop discrepancy in patients trying to become more active

Advantages of becoming more active • *I would be fitter and have more energy* • *I would improve my long-term health*	**Advantages of remaining sedentary** • *I can use the time to do other things, like watching television* • *I will not fail if I don't try*
Disadvantages of becoming more active • *I will probably be sore for the rest of the day and the day after* • *I might injure myself*	**Disadvantages of remaining sedentary** • *My health will continue to deteriorate* • *I will not be able to do physically demanding activities, such a*

PRACTICE PEARL

Clinicians should resist the 'righting reflex'. That is, they should resist the tendency to advise patients about the 'correct' path for good health, as this can often have a paradoxical effect and inadvertently push patients in the other direction.

Roll with resistance

Resistance can be described as a patient interrupting or arguing with a clinician, discounting the clinician's advice, shifting the blame to others for their behaviour, or generally being unwilling to change. These actions can be summarised as:[12]

- arguing

- interrupting
- denying
- ignoring.

In MI, rolling with resistance involves approaching a patient's resistance without judgment and recognising that the patient currently holds an opposing view to the one a clinician wishes to promote. It offers the clinician an opportunity to respond using techniques such as reflection, shifting the focus of the conversation, reframing or 'siding with the negative'[20]—all of which can be used to prevent resistance from affecting patient or clinician engagement in the interview.

Fundamental skills of motivational interviewing—OARS

Open-ended questions, **a**ffirmations, **r**eflections and **s**ummaries are all fundamental skills of MI, which together can be remembered by the acronym 'OARS'. As with all communications skills, simulation can be a great way to practise and improve. The use of these skills in practice is demonstrated in the example of a motivational interview below.

Open-ended questions

Open-ended questions are those that allow for a much broader answer and not a binary 'yes' or 'no'. They enable patients to drive the consultation and encourage them to provide information that the clinician may not have been able to obtain through narrower closed questioning. Open questions are particularly important at the beginning of a consultation, and should be used as appropriate throughout the balance of the interview.

Page 40

Example: *I understand you have some concerns about your fitness levels. Can you tell me about them?*

Affirmations

When expressed sincerely, affirming a patient's attitudes and efforts can help promote self-efficacy. Affirmations can take the form of compliments or statements of appreciation and understanding, and can help patients feel more confident about their ability to initiate and sustain behaviour change. It is particularly important to affirm a patient's past experiences that showcase their strengths and demonstrate that they have succeeded in behaviour change previously.

Example: *I think it's great that you want to be more active during the week and I appreciate you coming in to speak with me.*

Reflections

Reflective or active listening is a challenging skill in which the clinician should demonstrate that they have heard and understood a patient by restating their understanding of what has been said. It involves paying complete attention to what the patient is saying and listening carefully to the content, intent and feeling of the conversation, without interrupting or hurrying the patient.[21]

Miller and Rollnick describe reflective listening as 'a way of checking rather than assuming that you know what is meant'.[12] By checking what the patient means, the clinician can continue to build rapport and strengthen the empathic relationship. Reflections reduce the likelihood of resistance and encourage the patient to further explore their ambivalence, hopefully amplifying their desire for change.

Example: *You are beginning to worry about the impact your lack of exercise is having on your health.*

And now you want to find out about ways you can become active again.

Summaries

Summarising consists of briefly reviewing what the patient has said, and communicating it back to them. The difference between a summary and a reflection lies in how much is included. In a reflection, the clinician should echo one or two elements of what the patient has said, while in a summary many elements can be included. The objective of summarising what a patient has said is to convey to them that they are being heard and what they are saying is important.

Summaries are useful to periodically segment conversation, and link a patient's positive and negative feelings about physical activity to facilitate an understanding of ambivalence. In presenting a summary, the clinician can strategically select what information should be included, and invite correction by the patient to drive further discussion and mutual understanding. It can also be a productive way to begin and end each consultation, to provide a bridge when the patient is transitioning between stages of change.

Example: *If it is okay with you, let me check that I understand everything we have been discussing so far.....*

Recognising change talk

The ultimate goal of MI is to help patients find their own desire for change by guiding them throughout the process. Through the principles discussed above, clinicians can strengthen their patients' confidence by showing faith in patients' self-efficacy and emphasising that the decision to become more active ultimately lies with them. When conducting a motivational interview, clinicians can recognise patients who are likely to change behaviour by the way they speak. These patients express motivation, self-belief and commitment to and ideas about behaviour change.

'Change talk' comprises statements that indicate the patient is actively working on change. Patients talk about what they want to do (*desire*), why they should change (*reason*), how they could do it (*ability*) and how important it is for them (*need*), in no particular order. The final type of change talk is *commitment,* which is when a patient communicates their concrete intentions and plans for behaviour change. The clinician's task is to elicit and recognise change talk, rather than evoking resistance, so they can affirm and reinforce positive attitudes. Indicators of change talk statements include:

- desire—*I want/would like to . . .*
- reason—*I would probably feel better if . . .*
- ability—*I can/could/might be able to . . .*
- need—*I have/ought to . . .*
- commitment—*I will/intend to . . .*

Example of a motivational interview about increasing levels of exercise, demonstrating decisional balance

Clinician: So, a disadvantage of changing is that you don't enjoy exercise. *(reflective statement)* Can you tell me more about that? *(open exploratory question)*

Patient: Yes. I've never enjoyed exercise. It's too hard. When I have tried I've always found it really hard work and got breathless. I just don't think I'm the exercising type.

Clinician: So, you have always become breathless when you have exercised in the past and that's what you don't enjoy about exercise. *(reflective statement)*

Patient: That's right. When I've done an exercise class or gone running, no one else seems to go so red or get as out of breath as I do. They seem to enjoy it, but I guess that's because it's easy for them.

Clinician: You've tried different activities in the past. That's a really positive start. *(affirmation)* Could you tell me about any times that you've done physical activity in the past at a lower intensity where you haven't become breathless? *(open-ended question)*

Patient: Well, I do walk sometimes. That doesn't really feel like exercise though. I guess I could walk a bit faster without getting out of breath. *(change talk)*

Clinician: That's great. *(affirmation)* So, you recognise that walking can be a great form of exercise and that you could increase the intensity of walking by increasing your speed. *(reflection)* Are there any other activities where you could exercise without working at too high an intensity?

Patient: Well, I like the idea of being able to run. I saw an advert a few months ago for a beginners running group that combined walking and running. I don't think I'd be able to do that now, but I might try that in the future. *(change talk)*

Clinician: So, if I ask you to assess how confident you would be currently to join a beginners running group, on a scale of 1–10, where would you be?

Patient: Probably a 3. Even if I did make it to a session, I don't think I'd be able to keep up with everyone else and I wouldn't enjoy it.

Clinician: Okay. So, it's great that you rated your confidence to change as a 3 rather than a 1. Why was that?

Patient: Well. I know that I can walk without getting out of breath. I guess other people that are less fit than me have improved their fitness, so I think it is something I could possibly do. *(change talk)*

Clinician: What would need to change to take you from a 3 to a 7 or higher?

Patient: If I was already walking more briskly I'd probably feel more confident. Also, I could maybe go along to a session and see what other people do. If they aren't all really fit I might feel more confident to join in.

Clinician: So, you feel that you could be fitter and have more energy by increasing activity levels. Activities you've tried in the past have left you breathless which has meant that you haven't enjoyed them. You already do some walking, which is great, and you feel that if you could do more brisk walking and also go and observe a beginners' running session it might increase your confidence to join the group. Is all of that correct? *(summary)*

MAINTAINING BEHAVIOUR CHANGE

Once a patient successfully changes his or her behaviour, the next challenge for the clinician is to help the patient maintain it. It is not enough for an individual to increase physical activity or eat

healthy food for a single day; the change must be enduring for it to make a meaningful difference. Initial behaviour change may be motivated by expectations of uncertain long-term outcomes, such as walking more to reduce cardiovascular event risk; however, clinicians must recognise that maintenance motives are often different.

Individuals need at least one sustained motivator to maintain behaviour, which may include behaviour enjoyment, satisfaction with behavioural outcomes, self-determination or an experience of behavioural congruence with personal beliefs and values.[22] Building on Fogg's behaviour model (discussed above), it is particularly important that a patient is able to obtain pleasure from performing the new behaviour, rather than just from the experience of changing.

Human behaviour, whether under conscious control or occurring with little cognitive engagement (in the words of Thaler), occurs within a socioenvironmental context, with influences that either hinder or support behaviour change maintenance.[9] It is paramount that clinicians are aware of these barriers (Table 5.3) and facilitators, particularly when trying to anticipate and plan for potential hiccups for each patient. By doing so, a clinician can help reduce the patient's risk of relapse and transform their behaviour change into the status quo.

Table 5.3 Barriers to the uptake and maintenance of physical activity

	Barriers
Health and quality of life	• Physical ailments or chronic conditions • Fear of becoming injured
Sociocultural factors	• Lack of time • Lack of knowledge • Self-consciousness • Low socioeconomic factors
Physical environment	• Low neighbourhood safety • Poor weather • Lack of connected walking and cycling networks • Lack of open public green spaces
Access to facilities and resources	• Financial costs • Transport • Lack of availability or access to community physical activity programs
Psychological factors	• Lack of motivation • Low self-efficacy

ADAPTED FROM KELLY S, MARTIN S, KUHN I, COWAN A, BRAYNE C, ET AL. (2016) BARRIERS AND FACILITATORS TO THE UPTAKE AND MAINTENANCE OF HEALTHY BEHAVIOURS BY PEOPLE AT MID-LIFE: A RAPID SYSTEMATIC REVIEW. PLOS ONE 11(1): E0145074. HTTPS://DOI.ORG/10.1371/JOURNAL.PONE.014507 4[23]

REFERENCES

1. Nutbeam D, Harris E, Wise W. *Theory in a nutshell: a practical guide to health promotion theories*. McGraw-Hill, Sydney, 2010.
2. Kleinginna PR, Kleinginna AM. A categorized list of emotion definitions, with suggestions for a consensual definition. *Motiv Emot* 1981; 5(4):345–79.
3. Michie S, West R, Campbell R et al. *ABC of behaviour change theories*. 1st ed. Sutton, Surrey, UK: Silverback Publishing, 2014.
4. Skinner BF. *Science and human behavior*. New York: Macmillan, 1953.
5. Bandura A. *Social learning theory*. Englewood Cliffs, NJ: Prentice-Hall, 1977.
6. Bandura A. *Social foundations of thought and action: a social cognitive theory*. Englewood Cliffs, NJ: Prentice-Hall, 1986.
7. Fishbein M, Ajzen I. *Predicting and changing behaviour: the reasoned action approach*. New York: Psychology Press, 2010.
8. Fogg B. A behavior model for persuasive design. In: Proceedings of the 4th International Conference on Persuasive Technology— Persuasive'09. 2009. p. 1.
9. Thaler RH, Sunstein CR. *Nudge*. Penguin Random House UK, 2009.
10. Soler RE, Leeks KD, Buchanan LR et al. Point-of-decision prompts to increase stair use: a systematic review update. *Am J Prev Med* 2010; 38(2 Suppl):S292–300.
11. Prochaska J, DiClemente C. Stages and processes of self-change in smoking: toward an integrative model of change. *J Consult Clin Psych* 1983; 51(3):390–5.
12. Miller W, Rollnick S. *Motivational interviewing: preparing people to change addictive behavior*. New York, NY: Guilford Press, 1991.
13. Professional Associations for Physical Activity (Sweden). *Physical activity in the prevention and treatment of disease*. 2nd ed. Stockholm: Swedish National Institute of Public Health, 2010.
14. Miller WR, Rollnick S. *Motivational interviewing: helping people change*. 3rd ed. 2013.
15. Rollnick S, Miller WR, Butler CC. *Motivational interviewing in health care*. New York: The Guilford Press; 2008.
16. Pollak KI, Alexander SC, Tulsky JA et al. Physician empathy and listening: associations with patient satisfaction and autonomy. *J Am Board Fam Med* 2011; 24(6):665–72.
17. Gordon T. *Parent effectiveness training: the no-loss program for raising responsible children*. New York: Peter H Wyden, 1970.
18. McAuley E, Blissmer B. Self-efficacy determinants and consequences of physical activity. *Exerc Sport Sci Rev* 2000; 28:85–8.
19. De Bourdeaudhuij I, Sallis J. Relative contribution of psychosocial variables to the explanation of physical activity in three population-based adult samples. *Prev Med* 2002; 34(2):279–88.
20. Center for Substance Abuse Treatment. Chapter 3—Motivational interviewing as a

counseling style. In: *Enhancing motivation for change in substance abuse treatment*. Rockville, MD: US Department of Health and Human Services, Substance Abuse and Mental Health Services Administration, 1999. pp. 39–55.

21. Jahromi V, Tabatabaee S, Abdar Z et al. Active listening: the key of successful communication in hospital managers. *Electron Physician* 2015; 7(1):971–6.
22. Kwasnicka D, Dombrowski SU, White M et al. Theoretical explanations for maintenance of behaviour change: a systematic review of behaviour theories. *Health Psychol Rev* 2016; 10:277–96.
23. Kelly S, Martin S, Kuhn I et al. Barriers and facilitators to the uptake and maintenance of healthy behaviours by people at mid-life: a rapid systematic review. *PLoS ONE* 2016; 11(1):e0145074.

Chapter 6

Nutrition for health

with PAUL MASON and DANIEL FRIEDMAN

Let food be thy medicine and medicine be thy food
Hippocrates (460–370 BCE)

A healthy diet is one that optimises health by providing all essential nutrition while also maintaining an appropriate weight. The composition of such a diet, however, is subject to vigorous debate among both experts and lay people. Even in the 21st century, folklore and conventional wisdom continue to shape mainstream nutrition beliefs in the absence of convincing evidence. This is in part due to the difficulties and expense of performing suitable interventional research, with nutrition science historically based on less robust epidemiological research. Findings from these observational studies are often demonstrated to be erroneous when tested in randomised controlled trials.[1–3]

In recent years there has been growing interest in nutrition research thanks to increased funding and improved research methodologies. Combined with advancements in molecular biology and biochemistry, this has resulted in an improved understanding of healthy diets and underlying physiological mechanisms. These new understandings however, often contrast with existing orthodoxy and are not universally accepted.

Optimal dietary macronutrient composition is perhaps most contentious. Sugar has received much attention, many arguing it has increased potential for causing metabolic harms compared to other carbohydrates. The importance of sodium restriction, benefits of dietary fibre and required water intake are other longstanding beliefs that are being increasingly questioned. The gut microbiome is an exciting new area of nutrition science; however, many claims regarding prebiotics and probiotics are being made in advance of definitive evidence.

A significant amount of conventional thinking about nutrition is not well supported by evidence. In this chapter, we will examine the evidence base for current nutrition recommendations by exploring the current understanding of macronutrients, micronutrients, fluids and different

dietary patterns.

DIETARY GUIDELINES

Dietary goals for the American people were first recommended by the US Senate in 1977,[4] followed by the first edition of the Dietary Guidelines for Americans in 1980.[5] These were in turn used as a template for the Australian dietary guidelines that were introduced in 1980.[6] However, a recent systematic review and meta-analysis concluded that when introduced, the US guidelines were not consistent with best available scientific evidence.[7]

Since their inception, both the Australian and US dietary guidelines have evolved through regular revisions. Recent changes include removal of the recommended upper limit for individual sodium consumption from the Australian Dietary Guidelines[8] in September 2017, and the removal of the recommendation to limit both dietary cholesterol and total fat in the most recent edition of the Dietary Guidelines for Americans (8th edition, 2015–2020).[9] Many features of current dietary guidelines remain identical or very similar to their initial versions. The current Dietary Guidelines for Americans continues to advise that saturated fats should represent no more than 10% of total energy intake. Similarly, the current Australian Dietary Guidelines advise restricting intake of saturated fats, and current UK guidelines recommend not more than 35% of energy intake be derived from fat, with no more than 11% of this from saturated fat.[10]

Complementary with this view of fat, most guidelines recommend that carbohydrates should provide a significant proportion of total energy.[11, 12]

Nutrient terminology

Nutrient reference values (NRVs) in Australia and New Zealand are based on current knowledge regarding the level of intake required to prevent deficiency states in an otherwise healthy population. These reference values apply to macronutrients, micronutrients and vitamins.

The **recommended dietary intake** (RDI) for a group reflects the average daily intake to meet the requirements of 98% of individuals within that group. The RDI exceeds the nutrient requirements of most healthy people and should not be confused with requirements.

Estimated average requirement (EAR) is the daily intake of a nutrient thought to be sufficient for 50% of individuals within a group. By definition, 50% of individuals consuming the EAR will not be meeting their daily requirements.

If there is insufficient data to determine RDI and EAR for a given nutrient, requirements can be expressed as an **adequate intake** (AI), an estimation of the nutrient intake necessary to maintain a healthy state. Adequate intake is often based on observational data.

The **upper limit** (UL) is the maximum daily intake of a nutrient that is likely to pose no risk of adverse effects. Intake of nutrients far exceeding the UL is considered to be 'pharmacologic' dosing, and in Australia requires a medical prescription.

It is important to note that these recommendations exclude groups such as children, adolescents and

pregnant women.

Despite macronutrient intake recommendations on fat and carbohydrate forming a central tenet of most dietary guidelines, they are not supported by the balance of available evidence. A recent analysis of the methodology used to formulate the current edition of Dietary Guidelines for Americans found that sound scientific methodology was lacking. More than 70 relevant randomised controlled trials published after 2000 were excluded from the evidence base used.[13] Similar criticisms of improper methodology have been made regarding the current Australian Dietary Guidelines and Public Health England's Eatwell Guide.[14]

MACRONUTRIENTS

Macronutrients are the chemical compounds which provide the bulk of dietary energy. The three primary macronutrients are carbohydrates, protein and fat. Some also consider fibre to be a macronutrient. Fat provides 37 kJ/g (9 kcal/g) of energy compared to 17 kJ/g (4 kcal/g) for both carbohydrates and protein. More recent dietary guidelines have increased focus on patterns of eating, and reduced emphasis on individual nutrient intake. This approach may improve public adherence to dietary guidelines through easier comprehension and practical translation. Scientific understanding of the physiological and health effects of nutrients may be enhanced by considering nutrients individually, potentially improving our understanding of the associations between overall eating patterns and chronic diseases.

The benefit of understanding the physiology of individual nutrients is illustrated by considering the energy balance hypothesis of obesity. In the late 19th and early 20th centuries, the energy balance model of obesity was promoted, largely based on the technology of calorimetry available at the time.[15, 16] This model, while correctly based on the premise that weight gain occurs in the setting of positive energy balance, neglected the hormonal influences of different macronutrients. While our understanding of hormonal and biochemical impacts of varying macronutrient composition is still incomplete, it is now well understood that different macronutrients can have varying impacts on fat storage, even for iso-caloric intakes (Chapter 7). Macronutrients must therefore be considered not solely as a source of energy, but also as substances that have biochemical and hormonal impacts.

Carbohydrates

Carbohydrates are biological molecules consisting of carbon, hydrogen and oxygen atoms, that serve as a source of energy. The simplest form of carbohydrates are the monosaccharides—also known as simple sugars—which include glucose, fructose and galactose. Disaccharides are composed of two monosaccharides and include sucrose (glucose and fructose), lactose (glucose and galactose) and maltose (two molecules of glucose).

Complex carbohydrates are linear chains of glucose molecules called polysaccharides and are commonly referred to as starch. The term 'complex carbohydrate' was first introduced to

distinguish sugars from other carbohydrates that were thought to be nutritionally superior.[17]

The relative impact of carbohydrates on blood glucose levels can assessed by glycaemic index (GI). A standardised amount of carbohydrate is ingested followed by measurement of blood glucose levels usually two hours later. The increase in blood glucose level is then compared relative to pure glucose, the reference food which has a GI of 100. A GI less than 55 is considered low, while 70 or above is high. Glycaemic load (GL) is an extension of GI that considers the potential impact of carbohydrates on blood glucose levels, taking into account the total amount of absorbable glucose contained within a carbohydrate source.

Recommended carbohydrate intake

The current Dietary Guidelines for Americans[9] and Australian Dietary Guidelines[8] recommend that carbohydrates should constitute 45—65% of total energy intake. The UK dietary reference values also indicate that carbohydrates should constitute about 50% of energy intake.[10] These recommendations for high carbohydrate diets largely stem from a perceived need to limit dietary fat while ensuring adequate energy intake.

The need for glucose by red blood cells[18, 19] is often misinterpreted as meaning that humans have an obligate need for dietary carbohydrate. However, this need for glucose can be met from gluconeogenesis, where glucose is formed from non-carbohydrate precursors, including glycerol, lactate and some amino acids.[20]

Optimal functioning of the central nervous system is commonly thought to be dependent on dietary carbohydrates. However, it is now well understood that the brain can utilise ketones as a source of energy in the absence of glucose.[21–23] In a prolonged fasted state, ketones from fat oxidation can provide most of the energy needs of the brain,[24] with gluconeogenesis able to provide the balance of required energy.

Carbohydrates are therefore not an essential nutrient. In other words, the theoretical minimal level of carbohydrate intake consistent with good health is zero. This has been demonstrated over many years in those on strict ketogenic diets for the management of epilepsy.[25]

Despite evidence that carbohydrates are not an essential nutrient, current Dietary Guidelines for Americans recommend a minimum carbohydrate intake of at least 130 g per day to support neurological functioning. The recommendation to consume at least 130 g of carbohydrates per day stems from an Institute of Medicine report estimating the brain to have a capacity to metabolise 100 g of glucose per day in the absence of other energy substrate. The recommended intake of 130 g was thought to provide a margin of error over the 100 g usage identified.[26, 27] Despite compelling evidence to the contrary, this recommendation has persisted through revisions of the Dietary Guidelines for Americans.

In contrast, the Australian Dietary Guidelines and UK dietary reference values reflect the current understanding that carbohydrate is not an essential nutrient for adults. Neither guidelines set values for recommended daily intake (RDI), estimated average requirement (EAR) or adequate intake (AI). The Australian Dietary Guidelines recommend a minimum carbohydrate intake for

infants due to uncertainty as to whether gluconeogenesis can provide all the glucose needs of this population.

Sugar

Monosaccharides, or single sugars, are the simplest form of carbohydrate, and include glucose, fructose and galactose. Disaccharides are composed of two monosaccharides and include sucrose (glucose and fructose), lactose (glucose and galactose) and maltose (two molecules of glucose). Sucrose is arguably the most significant sugar in the Western diet, with a fructose content of 50% which is comparable to high fructose corn syrup (typically 42–55% fructose)—a sweetener made from corn starch that has been processed to convert its glucose into fructose.

Fructose is found in fruits, vegetables, and honey. It has been strongly implicated in the development and progression of non-alcoholic fatty liver disease (NAFLD), in both animal and human studies.[28] Following digestion, fructose enters the portal circulation and is almost completely extracted at first pass and converted to lactate and glucose. When glycogen stores are full, these products stimulate de novo lipogenesis, contributing to fatty liver.[29] This is consistent with large cohort studies demonstrating significantly increased risk of NAFLD with sugar-sweetened beverage intake.[30] NAFLD has been shown to be causally associated with insulin resistance, playing a significant role in the pathophysiology of diabetes, and fructose has been shown to be significantly more potent than glucose in contributing to hepatic steatosis and insulin resistance.[31]

PURE carbohydrates?

Recent research has shed light upon the efficacy of high and reduced carbohydrate diets.

The PURE (Prospective Urban Rural Epidemiology) study (2017)[12], which examined the dietary intake of over 135 000 individuals from 18 countries using validated food frequency questionnaires, found that over a median follow-up period of 7.4 years, high carbohydrate diets were associated with a higher risk of total mortality. In contrast, higher total fat intake, including saturated fat, was related to lower total mortality. Comparison of the highest and lowest quintiles of carbohydrate intake found a total mortality hazard ratio of 1.28 [1.12–1.46], reflecting a 28% increased chance of dying in those on the highest carbohydrate diets.

Despite its prospective nature, there were methodological limitations in this study which have been highlighted by critics. These include grouping of carbohydrate sources, the possibility that poverty may be associated with high carbohydrate diets and the use of food frequency questionnaires. The authors of this study stand by their findings however, having extensively controlled for covariates with the potential to confound results, and conclude that 'global dietary guidelines should be reconsidered'.

In 2015, the World Health Organization (WHO) recommended that no more than 10% of total daily energy intake should come from added sugars.[32] This recommendation is largely based on the relationship between added sugars and excess weight gain and dental caries. Additionally, high sugar diets have been shown to increase the risk of both type 2 diabetes[33–35] and cardiovascular

mortality.[36, 37] For an average adult intake of 8700 kJ (2080 kcal), 10% of daily energy intake is equivalent to 52 grams or 13 teaspoons of added sugar. Although this may seem like a considerable amount, more than half of Australians consume added sugar exceeding this level.[38] Fifty per cent of Australian children aged 12 years and older have evidence of tooth decay of their adult teeth.[39] The WHO conditionally recommends reducing energy intake from added sugar to less than 5% for improved dental health.[40] Further benefits in reducing added sugar intake to less than 5% of energy intake include improved intake of essential nutrients[41] and reduction in obesity and its biopsychosocial implications (Chapter 7).

Fibre

Fibre is the indigestible carbohydrate portion of food that is derived from plants. There are two types of fibre: soluble and insoluble. Both have different effects on the digestive system.

Soluble fibre dissolves in water and is readily fermented by bacteria in the colon, producing short-chain fatty acids (SCFAs) and gases. Ninety per cent of the SCFAs produced are either acetate, proprionate or butyrate.[42] The SCFAs are then metabolised by colonocytes that line the colon, producing ketones.

Artificial sweeteners

Each week, more than a quarter of Australians use sweeteners in both carbonated soft drinks and confectionery. In 2016, the market for food sweeteners was valued at US$85 billion. It is estimated to reach nearly US$118 billion by 2022.[43]

Unlike sugars, sweeteners generally do not contain any calories. Their use in beverages has been promoted as a means of reducing sugar consumption, providing a sweet taste without the energy of sugar to help promote weight loss.

Sweeteners, or sugar substitutes, can be divided into three groups:

1. sugar alcohols (erythritol, xylitol)
2. artificial sweeteners (aspartame, sucralose)
3. natural sweeteners (stevia).

Sweeteners have been linked with a number of health problems, however scientific data to support their safety and benefits are controversial. People who consume artificially sweetened soft drinks daily are about three times more likely than people who consume sugar-sweetened beverages to develop stroke or dementia.[44] Interestingly, type 2 diabetes is more prevalent in those who regularly consume artificially sweetened soft drinks.[45]

A 14-year French study that examined the risk of type 2 diabetes in 60 000 women, comparing those who consumed artificially sweetened drinks with those who drank sugar-sweetened beverages, found that the risk of developing type 2 diabetes was twice as high in the women drinking high levels of artificially sweetened beverages than those consuming similar amounts of sugar-sweetened beverages.[46]

Another study found a correlation between consuming artificially sweetened drinks and health

markers related to metabolic syndrome, such as weight, waist-to-hip ratio, fasting blood glucose, HbA1c and glucose tolerance test.[47] A US study found a similar correlation between daily consumption of diet soft drinks and the risk of metabolic syndrome (36% greater than non-drinker of diet soft drinks) and of type 2 diabetes (67% greater).[48] And finally, a review of 30 trials involving more than 400 000 subjects concluded that regularly drinking artificial sweeteners could be linked with a higher body mass index (BMI) and risk of diabetes, heart disease or stroke.[49] The same review also indicated that artificial sweeteners were not an effective tool in weight loss.

It is commonly believed that this supply of energy to the colonocytes may be of therapeutic benefit in the management of inflammatory bowel disease. However, this view is not strongly supported by evidence.[50] Further, the bacterial production of gases from fermentation of fibre can lead to bloating, abdominal pain and reflux.

The production of SCFAs from bacterial fermentation of fibre permits harvesting of energy that would otherwise be inaccessible. This is thought to contribute up to 5% of total energy derived in Western diets.[51] The ability of soluble fibre to nourish bacteria also gives rise to its classification as a 'prebiotic', promoting the proliferation of certain bacterial species. In contrast to soluble fibre, insoluble fibre is relatively resistant to fermentation by colonic bacteria and provides bulk to faeces.

While fibre is widely regarded as an effective means of preventing and treating constipation, there is a paucity of experimental data to support this. At the time of writing, there were no published randomised controlled trials on the effects of fibre on the symptoms of constipation. While insoluble fibre adds bulk to stool and decreases colonic transit time,[52] it does not increase stool moisture content.[53]

One 2012 experimental study in subjects with idiopathic constipation found that complete elimination of dietary fibre led to statistically significant reductions in constipation, bowel strain, bloating and anal bleeding. Further, several studies have found increased symptoms of constipation with higher intakes of insoluble fibre.[42, 54, 55] These findings bring into question the current paradigm of recommending fibre for treatment of constipation, with a clear need for further research.

Other proposed benefits of fibre include reduced all-cause mortality, improved blood sugar control and reduced risk of colorectal cancer.[56, 57] Despite the widespread acceptance of these claims, not all are supported by empirical evidence.[54, 57] High-fibre diets have been demonstrated in several observational studies to be associated with reduced risk of cardiovascular disease and all-cause mortality. This, however, is not a universal finding with regards to all sources of fibre, as fruit-associated fibre intake does not lead to a reduction in all-cause mortality.[58] This again highlights the limitations of epidemiological research.

Gut microbiota

The gut microbiota refers to the trillions of microbes (bacteria, fungi and viruses) that reside in our gastrointestinal tract. Healthy adult humans each typically harbour more than 2000 species of bacteria, mainly members of four phyla (Firmicutes, Bacteroidetes, Actinobacteria and Proteobacteria).[59] There is considerable variation in composition of gut bacteria between individuals. While some consider microbial diversity a sign of healthy gut function,[60] this has not yet been conclusively demonstrated.

In humans, the proximal colon is the site of highest bacterial numbers due to substrate availability.[61, 62] Gut microbiota can utilise non-digested food components such as fibre, protein and peptides to produce short-chain fatty acids (SCFAs). 90 per cent of the short-chain fatty acids produced are either acetate, proprionate or butyrate.[42] Fibre fermentation produces most SCFAs in diets containing plant foods, while amino acid fermentation is quantitatively more important in animal food-based diets.[63, 64]

Butyrate, a SCFA, is one of the few substrates able to provide energy to colonocytes. The others are glutamine and ketone bodies.[65] Following absorption, colonocytes oxidise butyrate to ketone bodies for energy. SCFAs may supply 60–70% of the energy needs of isolated colonocytes.[66] The production of SCFAs allows the salvage of energy mainly from dietary fibre that is not digested in the small intestine. It has been estimated that SCFAs can contribute to about 5–15% of the total caloric requirements of humans.[67]

Alterations in the gut microbiota have been associated with a growing number of diseases, including cardiovascular disease, obesity, type 2 diabetes, irritable bowel disease and inflammatory bowel and skin disease.[68] However, with the exception of *Clostridium difficile* infection, the role of these microbiota alterations in the pathogenesis of disease is still poorly understood and causality has not yet been proven.[69, 70]

Clostridium difficile infection is a symptomatic infection of the colon that results in watery diarrhoea, fever, nausea and abdominal pain. In the early 2000s, a previously rare ribotype of *C. difficile* causing severe and often fatal infections became more common. This has been associated with dietary trehalose, a manufactured sugar used to lower the freezing point of foods such as ice cream. Two epidemic ribotypes of *C. difficile* have been shown to uniquely metabolise trehalose leading to their proliferation. The introduction of trehalose as a food additive into the diet occurred shortly before the emergence of these two epidemic lineages.[71] In addition to antibiotics, faecal microbiota transplants have been shown to be effective in treating *C. difficile* infection.[72]

To date, most human studies that explore the gut microbiota are observational, and are therefore unable to demonstrate causality. The limitations of observational research in making conclusions regarding the health impacts of the microbiota can be seen with the association of certain microbiota with impaired metabolic health. Diets correlating with certain microbiota growth patterns and increased risk of type 2 diabetes have also been associated with reduced fasting glucose and HbA1c levels.[73] It is perhaps more likely that dietary changes lead to reduced metabolic risk, and alterations in the microbiota are merely a surrogate marker.

The Bacteroidetes and the Firmicutes phyla are the most plentiful of bacteria in the human gut.[74] The relative proportion of Firmicutes has been shown to be greater in obese persons, reducing with weight loss.[75] While this association has been demonstrated, mechanistic understanding is still relatively limited. The gut microbiota was famously associated with obesity in a study in which microbiota from lean and obese mice were transplanted into germ-free mice. The microbiota from obese mice produced a greater energy harvest through bacterial production of SCFAs from indigestible carbohydrate.[76] While interesting, this study has limitations in translating findings to humans. Existing microbe colonies are likely to limit the establishment of introduced microbes.[77, 78] Further, given that ketones have been shown to have an appetite suppressant effect,[79, 80] ketone production resulting from metabolism of SCFAs may lead to reduced food intake compensating for increased energy harvest.

High-intensity sweeteners are commonly used as sugar alternatives, being many times sweeter than sugar with minimal calories. Despite being 'generally recognised as safe' by regulatory agencies, some animal studies have shown that these sugar substitutes may have negative effects on the gut microbiota.[81] Sucralose, aspartame and saccharin have been shown to disrupt the balance and diversity of gut microbiota.[81] Sugar alcohols, which are commonly used as artificial sweeteners, are also FODMAPs and have been associated with osmotic diarrhoea in addition to having effects on the gut microbiota.[82]

Antibiotic use has been shown to cause long-term reductions in the diversity of the gut microbiota. A large proportion of worldwide antibiotic use is for animal agriculture, with low doses routinely given to livestock to increase their growth.[83] While several observational studies suggest that antibiotic use in humans may contribute to obesity, interventional studies have shown variable results, and further research is needed.[84]

Prebiotics and probiotics

Prebiotics are non-digestible food components, usually but not always carbohydrates such as fibre, that are able to selectively nourish specific bacteria.[80] Prebiotics lead to alterations in the microbiota and enhance the production of short-chain fatty acids.[85] Production of short-chain fatty acids is thought to provide health benefits, especially in the management of inflammatory bowel disease, however the evidence for this is limited.[86]

Probiotics are live microorganisms that lead to a transient alteration in the gut microbiota when ingested.[77] Probiotics-containing foods such as fermented milk and vegetable products (e.g. yoghurt and pickles) have formed a part of many traditional diets. Other fermented foods include: beer and wine, sourdough bread, sauerkraut, olives, cured meats, kefir (a fermented milk drink), lassi (Indian fermented yoghurt and milk), kombucha (a fizzy fermented tea), raw milk cheeses, kimchi (spicy Korean fermented cabbage), natto (Japanese fermented soya beans), Indonesian tempeh (tofu-like), chocolate, coffee and miso.

These fermented foods usually contain strains of either *Lactobacillus* or *Bifidobacterium* bacteria.[87] Supplementation with specific species of probiotics to improve health is increasingly common. Evidence to date suggests that probiotics in isolation assist in the management of antibiotic-associated diarrhoea,[88] and there is weaker evidence for their benefits in eczema[89] and mental health disorders[90] among other conditions. Given that most microbe supplements cannot establish themselves in the gut, they fail to lead to a sustained change in resident microbiota, and continued dosing may be necessary for sustained effect.[77, 78]

There is promising research on the benefits of probiotic supplementation combined with an energy substrate able to nourish the introduced species. This combination is termed a 'symbiotic', and there have been several studies with positive findings including reduced risk of neonatal sepsis[91] and necrotising enterocolitis.[92] This indicates the importance of appropriate substrate supply in permitting the persistence of introduced microbial species.

Proteins participate in virtually every cellular process and are essential to life. They perform a range of biological functions, including enzymatic catalysis of biochemical reactions, cell signalling, immune response, mechanical functions and structural support. Proteins may also serve as a fuel source under some circumstances, providing 17 kJ/g (4 kcal/g). They are composed of polymer chains of amino acids linked together by peptide bonds. Following digestion, consumed protein is broken down into its constituent amino acids, typically by denaturation through exposure to acid and the action of proteolytic enzymes.

There are 20 different amino acids found in humans (Table 6.1), nine of which cannot be synthesised de novo from other compounds. These nine are considered essential, meaning they must be obtained through diet.[93] Failure to obtain sufficient quantities of these essential amino acids can lead to protein-energy malnutrition and ultimately death. The essential amino acids are phenylalanine, valine, threonine, tryptophan, methionine, leucine, isoleucine, lysine, and histidine.[94] Additionally, six amino acids are conditionally essential, meaning that certain pathophysiological states, such as severe catabolic distress, can limit their synthesis.

Table 6.1 Types of amino acids

Essential	Conditionally essential	Non-essential
Histidine	Arginine	Alanine
Isoleucine	Cysteine	Aspartic acid
Leucine	Glutamine	Asparagine
Lysine	Glycine	Glutamic acid
Methionine	Proline	Serine
Phenylalanine	Tyrosine	
Threonine		
Tryptophan		
Valine		

Unlike fatty acids and glucose, which can be stored as triglyceride or glycogen respectively, amino acids cannot be stored. The total concentration of free amino acids in plasma is only about 2.5 mM.[95] Amino acids that are digested in amounts exceeding the need for biosynthesis are rapidly catabolised. All amino acids contain at least one nitrogen atom. While some nitrogen is used in biosynthesis, most is not needed and is eliminated as urea in the urine. The removal of nitrogen occurs early in the degradation of amino acids, leaving behind a carbon skeleton which may then be used for energy-producing glucose, ketone bodies, or both depending on the specific amino acid.

Recommended protein intake

There is ongoing debate regarding ideal protein intake. Many different factors determine protein requirements, such as stage of life, body weight, body composition, activity level, other macronutrient consumption and the presence of illness or injury.[93] The Australian Dietary Guidelines recommend different levels of protein intake based on age, sex and, for females, pregnancy and breast feeding status.[8] The Australian recommended daily intake (RDI) for adult

males aged 19–70 years is 0.84 g/kg, increasing to 1.07 g/kg for those over 70 years. The equivalent recommendation for females is 0.75 g/kg between 19 and 70 years, and 0.94 g/kg over 70 years. The recommended daily allowance provided for in the Dietary Guidelines for Americans is similar, recommending 0.8 g/kg for both males and females.[9]

Current dietary guidelines on protein intake were largely derived from nitrogen balance studies based on the structural requirement for protein. However, this approach neglects the role of protein in other metabolic processes.[96] Further, nitrogen balance studies to collect this data were usually performed on college-aged males, with findings extrapolated to female and elderly populations.[97, 98] Consequently, there are substantial questions regarding the validity of current dietary guideline recommendations regarding optimal protein intake.

One re-analysis of existing nitrogen balance data, based on an improved biological understanding of protein, found the mean requirement in adult males is 0.93 g/kg/day, 41% higher than the current American recommendation.[99]

Recommended protein intake for special populations

The elderly have an increased need for dietary protein due to a reduced anabolic response to dietary amino acids.[100] While current guidelines do recommend higher protein intakes in those over 70 years, this is still likely to be insufficient.[101] Available research suggests that 1.5 g protein/kg/day, or about 15–20% of total caloric intake, is a reasonable dietary protein target optimising health and function in the elderly.[98]

Participation in both endurance and strength exercise increases protein requirements compared to sedentary controls,[102] albeit for different reasons. Amino acids can serve as substrate for energy production in endurance athletes and serve a structural function in strength athletes. Experimental data from studies in strength and power athletes suggest that optimal protein intake may be up to 2.4 g/kg/day.[103] The rate of oxidation of amino acids during endurance exercise is largely dependent on exercise intensity.[102] A daily protein intake of 1.5 g/kg has been estimated as sufficient to meet the needs of most endurance distance runners (Chapter 33).[104]

Individuals following restrictive diets or who have digestive issues may find it more difficult to obtain sufficient dietary protein. In most cases however, protein supplementation is unnecessary, and sufficient quantities can be obtained from diet alone.

Too much or too little protein?

The optimal level of protein intake for good health probably exceeds the recommended intakes in dietary guidelines. Excess protein intake is often cited as leading to increased risk of osteoporosis,[105] with concerns arising from studies demonstrating a transient increase in calcium excretion with higher protein intakes.[106] There is no convincing evidence to support these concerns. The authors of a 2017 systematic review concluded that increased dietary protein was associated with improved bone mineral density,[107] while higher protein intakes have also been linked to a reduced risk of hip fracture in the elderly.[108]

Protein restriction is frequently advised in the setting of renal disease. However, again, this recommendation does not appear to be supported by the best available evidence. One long-term follow-up of 585 patients with renal disease demonstrated no beneficial effects of a low protein diet (0.58 g/kg/day) when compared to a high protein control group (1.3 g/kg/day).[109]

Additionally, there is no evidence that high protein diets are detrimental to renal function in those without renal disease, including in diabetics.[110] Multiple studies have failed to find association between high protein intake and renal impairment.[111] Further, a 2016 study evaluating very high protein intakes (3 g/kg/day) in resistance-trained men found no harmful effects on blood lipids, liver or kidney function.[112]

The Australian Dietary Guidelines recommend that protein ought to provide 15–25% of total energy intake to minimise the risk of chronic disease.[8] Adherence to this recommendation is likely to lead to a protein intake significantly exceeding the RDI. The upper limit of this recommendation, based on an average resting metabolic rate of 3.61 kJ/kg/hr,[113] represents a protein intake equivalent to 1.32 g/kg/day solely to meet basal energy needs. This contrasts with the Australian RDI for adult males and females of 0.84 g/kg and 0.75 g/kg respectively.

Protein sources

It is important to consider the source of dietary protein when assessing its impact on health. Animal sources of protein (e.g. meat, fish, eggs and dairy) provide a complete complement of all essential amino acids. Plant sources, with the exception of soy and certain seeds, generally lack one or more of the essential amino acids, and have a reduced content of essential amino acids in comparison to animal proteins.[114] Many health professionals hold concerns regarding the consumption of animal-sourced protein due to the concurrent consumption of saturated fat, however these concerns are yet to be substantiated.[115]

Multiple systems exist to rate proteins by their biological utility. Factors considered include the digestibility and subsequent absorption of the protein, as well as amino acid composition which is a major determinant of nutritional quality. The Protein Digestibility Corrected Amino Acids Score (PDCAAS) has been widely adopted as the standard method for determining the quality of dietary protein.[116] It does have several limitations however, such as failing to account for anti-nutrient factors like phytic acid and trypsin inhibitors, both found in plant foods, which limit the absorption of protein. Recently, the Digestible Indispensable Amino Acid Score (DIAAS) has been proposed as an alternative measure which addresses these shortcomings.[117]

Most measures of protein quality of foods rank whey protein isolate first. It has a complete complement of the 20 amino acids found in humans, is rapidly absorbed, and has a PDCAAS of 1.0, the highest score possible. It has a DIAAS score of 1.25 which is second only to that of whole milk with 1.32. Casein and egg proteins are also complete proteins, both obtaining a PCDAAS of 1.0. Plant- based sources of proteins are generally considered to be inferior to animal proteins due to incomplete amino acid profiles and reduced absorption profiles, often secondary to the previously mentioned anti-nutrient factors such as phytic acid and trypsin inhibitors.

Fats

Fats and oils are the most energy dense of the three main macronutrients, providing 37 kj/g. They are often referred to as lipids and serve both structural and metabolic functions. Triglycerides are the main constituents of both dietary and stored fat. Triglycerides are formed by combining glycerol with three fatty-acid molecules (Fig. 6.1). During digestion, triglycerides are broken down into these constituent parts, with glycerol able to be converted to glucose via the process of gluconeogenesis, and this can be an important source of glucose for red blood cells in states of reduced carbohydrate intake.

Page 51

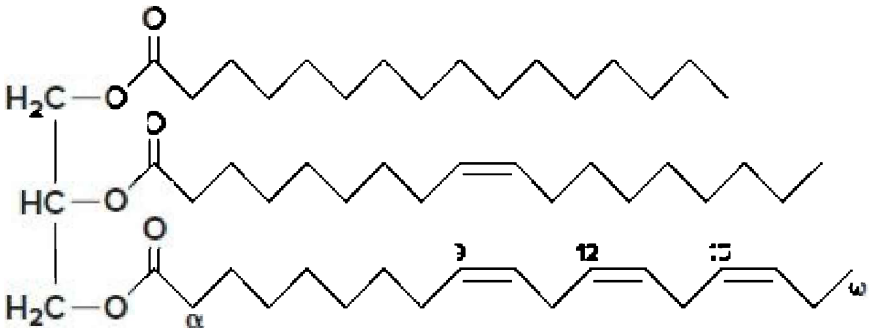


Figure 6.1 Example of an unsaturated fat triglyceride ($C_{55}H_{98}O_6$)

Types of fats

Fats may be classified according to their chemical structure. Fatty acids may be considered either saturated or unsaturated based on the presence or absence of double bonds between carbon atoms. Unsaturated fats may be further divided into monounsaturated or polyunsaturated fats (Fig. 6.2).

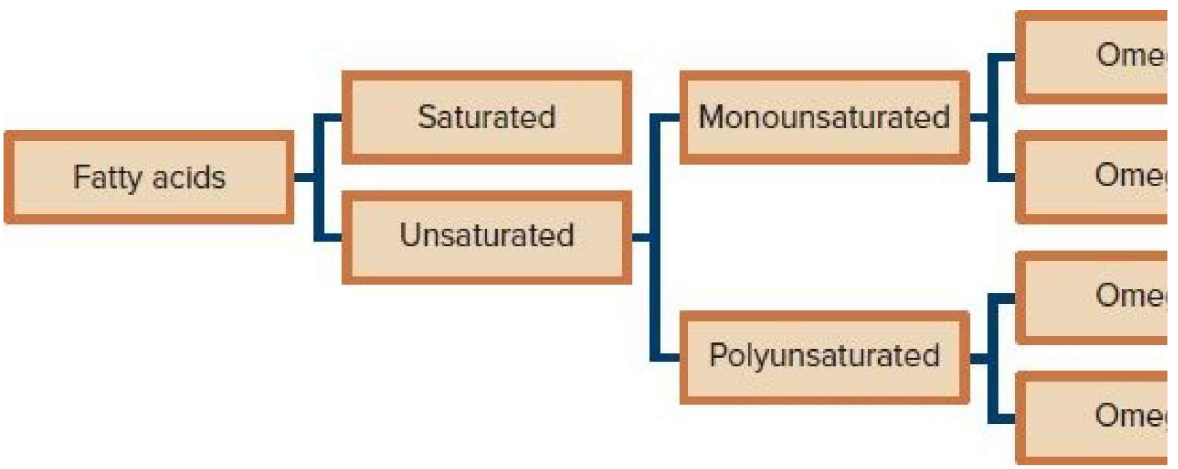


Figure 6.2 Different types of fatty acids

Saturated

Saturated fats have no double bonds between carbon atoms (Fig. 6.3). The term saturated refers to the inability to add further hydrogen atoms. Saturated fats tend to have a linear structure, allowing triglyceride molecules to pack closely together, which leads to saturated fats having higher melting points than unsaturated fats.

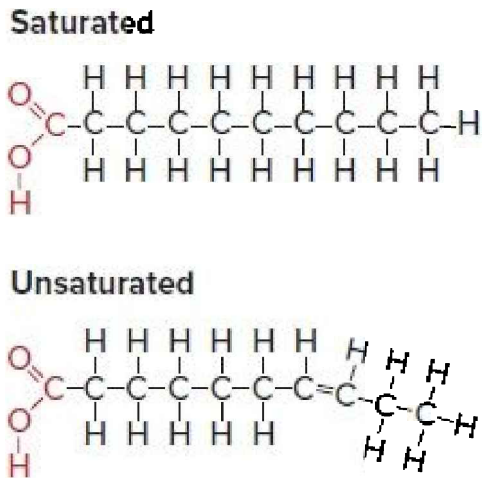


Figure 6.3 In contrast to unsaturated fats, saturated fats have no double bonds between carbon atoms

Unsaturated

Unsaturated fatty acids have one or more double bonds between carbon atoms (Fig. 6.3). These double bonds are prone to oxidation, with the risk of oxidation increasing with the number of double bonds. Subsequent oxidation products such as reactive aldehydes and alcohols are involved in various pathological states such as inflammation, atherosclerosis, neurodegenerative diseases and cancer.[118, 119]

Unsaturated fatty acids may be either monounsaturated (single carbon-to-carbon double bond) or polyunsaturated (two or more carbon-to-carbon double bonds). The location of the first double bond in relation to the methyl end of the fatty acid chain allows further classification of unsaturated fats. Polyunsaturated fats may have this first double bond after either the 3rd or 6th carbon atom from the methyl end and are denoted omega-3 and omega-6 fatty acids respectively. Monounsaturated fats may be either omega-7 or omega-9, with the first double bond after either the 7th or 9th carbon atom from the methyl end.

Unsaturated fatty acids may be either 'cis' or 'trans' isomers, which have different structures despite having the same molecular formula (Fig. 6.4).

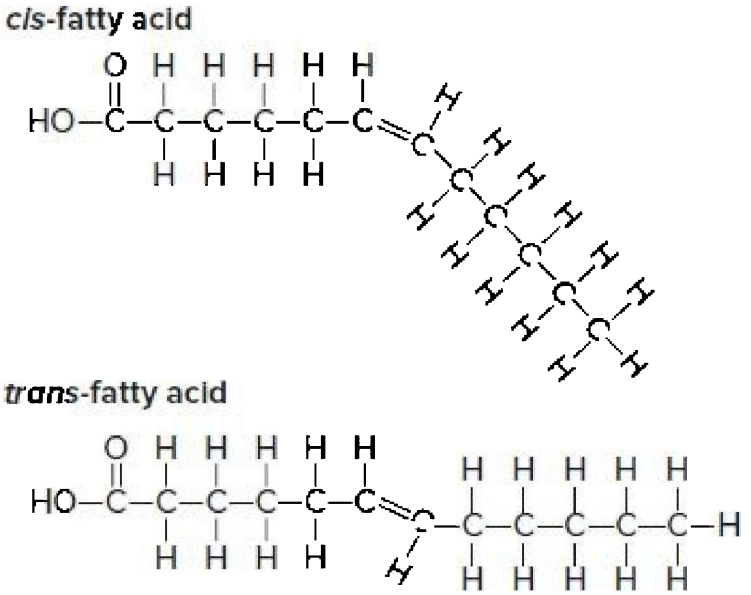


Figure 6.4 *Cis*-isomers contain a 'kink' within their structure which prevents them packing closely together. *Trans*-isomers are relatively straighter; they pack closer together and tend to be solid at room temperature like saturated fats.

Natural foods incorporate these three fat types in varying compositions, although one fat type often predominates. Notably, dairy is the only food group that contains more saturated than unsaturated fat (Fig. 6.5).

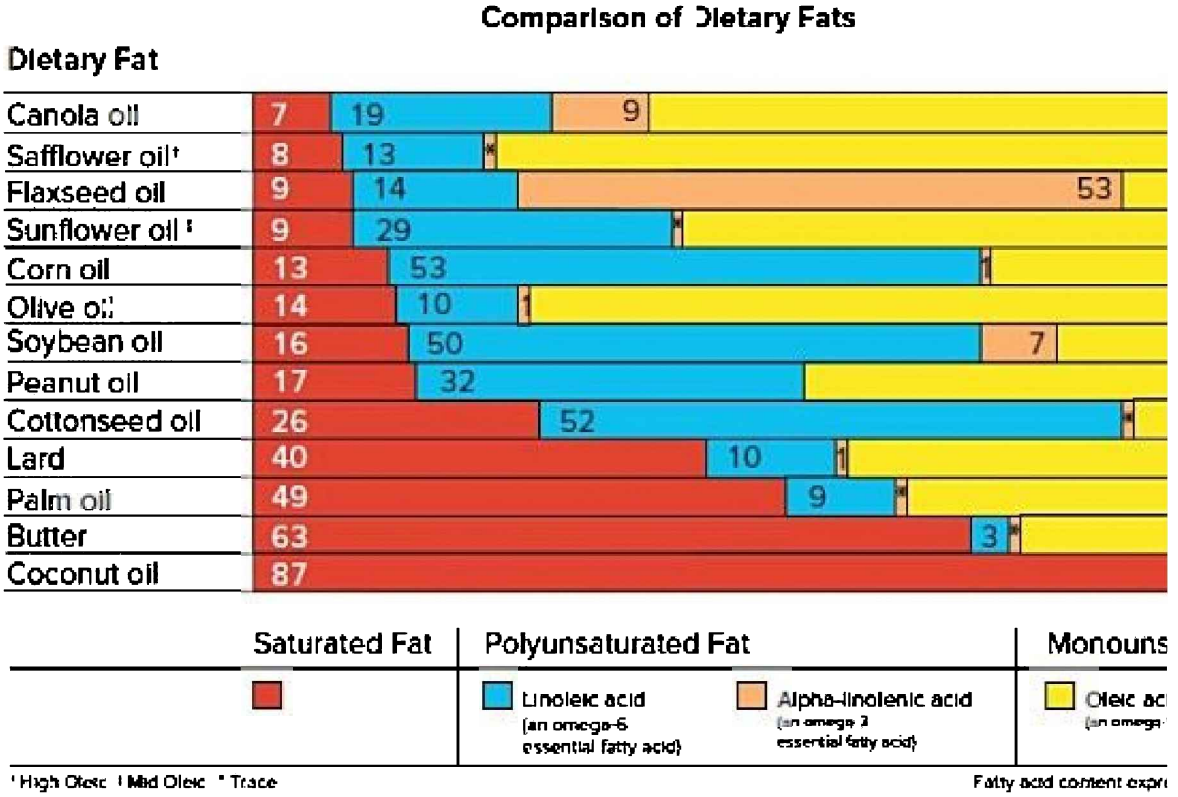


Figure 6.5 Foods contain all three fat types. Animal fats tend to contain mostly saturated fats, while seed (vegetable) oils contain mostly polyunsaturated fats.
CANOLA COUNCIL OF CANADA, HTTPS://WWW.CANOLAINFO.ORG/QUADRANT/MEDIA/FILES/DOWNLOADS/PDFS/DIETARYFATCHARTPRINT2016.PDF

Short-chain fatty acids

Fatty acids can also be categorised based on chain length determined by the number of carbon atoms in their tail. Short-chain fatty acids (SCFA), often known as volatile fats, contain fewer than six carbons. SCFAs may be found in small quantities in the diet, usually in the form of butyric acid found in milk, parmesan cheese and butter. Larger quantities of SCFAs may be produced by bacterial fermentation of incompletely digested food stuffs.[120] SCFAs are readily converted to ketones.

Medium-chain fatty acids

Medium-chain fatty acids (MCFA) have tails containing between 6 and 12 carbons. Passive absorption of MCFAs from the gastrointestinal tract directly into the portal circulation bypasses the need for transit through the lymphatic system with no need for bile salts.[121] Following absorption, MCFAs enter mitochondria independently of the carnitine transport system, undergoing preferential oxidation. Medium-chain triglycerides are therefore more ketogenic than

longer-chain fatty acids.

Long-chain fatty acids

Long-chain fatty acids (LCFA) contain between 13 and 21 carbons and require incorporation into chylomicrons and transportation through the lymphatic system for absorption. LCFAs tend to have higher melting points, as exemplified by tallow (rendered fat from ruminants) which has a chain length of 17 carbons. Very-long-chain fatty acids (VLCFA) have tails containing 22 or more carbons.

Cholesterol

Cholesterol is a misunderstood molecule that is essential for life. It is frequently confused with plasma lipoproteins, which are complex structures serving as a transport medium for triglyceride and cholesterol molecules within the circulation. A component of all animal cell membranes, cholesterol is necessary for both structural integrity and fluidity. Cholesterol also serves as a precursor for steroid hormones, bile acid and vitamin D. All animal cells produce cholesterol, with the amount produced within the body usually substantially more than that consumed. About 80% of total body cholesterol production occurs in the liver.

Ancel Keys, an American physiologist and epidemiologist, popularised the hypothesis that serum cholesterol (and saturated fat) were causally related to cardiovascular disease.[122] Acceptance of this theory led to the introduction of dietary guidelines recommending dietary restriction of both saturated fat and cholesterol. More than 50 years later, the balance of evidence no longer supports this hypothesis, yet changing the dietary guidelines to reflect the evidence has been a slow and contentious process.[123] The recommended limit on dietary cholesterol has been removed from the most recent editions of the Australian and American dietary guidelines.

The consumption of eggs has long been controversial given their cholesterol content. Observational studies examining egg consumption specifically, rather than dietary cholesterol overall, have not found it to be associated with cardiovascular disease, except maybe in people with diabetes.[124] However, randomised controlled trials are yet to find such an association.[125, 126] Current evidence suggests daily egg consumption may even be healthful. A 2018 large prospective cohort study of over 500 000 middle-aged Chinese adults found that daily egg consumption was associated with lower risk of cardiovascular disease, ischaemic heart disease, major coronary events, haemorrhagic stroke and ischaemic stroke. Daily egg consumption was found to be associated with an 18% reduced risk of death by cardiovascular disease and a 28% reduced risk of death by haemorrhagic stroke.[127]

Recommended fat intake: a brief history

Excess dietary fat, particularly saturated fat, has long been considered to increase the risk of coronary heart disease. This perspective gained prominence in the 1970s thanks to the influence of Ancel Keys who promoted his ‘diet–heart hypothesis’. This was based on the belief that total serum lipoprotein, and later more specifically low-density lipoprotein (LDL), were significant factors in the pathogenesis of coronary heart disease.[128] In making the case to support his hypothesis, Keys presented data from six countries demonstrating a relationship between mortality and dietary fat.[1]

[29] Four years after Keys' original paper, Yerushalmy and Hillebroe published a paper rebutting Keys' conclusion, presenting data from a further 15 countries.[130] By this time however, preliminary work on Keys' (in)famous Seven Countries Study was well underway and Keys' hypothesis proceeded to influence decades of future dietary policy and guidelines.

Most current dietary guidelines continue to stipulate that saturated fats should represent less than 10% of dietary energy (11% in the UK).[12] This concern regarding saturated fat may be 'the single most influential recommendation in conventional dietary advice', providing the basis to recommend low-fat dairy and lean meats over full-fat dairy and fattier cuts of meat, and to recommend margarine and vegetable/seed oils instead of butter and animal fats.[131]

The consequences of the original dietary guidelines

- Intake of animal fats, such as red meat, eggs and dairy, was reduced
- 'Low-fat' food products with added sugar products flooded the market
- Intake of ultra-processed foods increased
- Use of vegetable/seed oils increased

Despite the rapid acceptance of the 'diet–heart hypothesis', a systematic review and meta-analysis of studies available at the time of introduction of the first dietary guidelines demonstrates that the guidelines were not consistent with available scientific evidence.[7] It is now well understood that high-density lipoprotein (HDL) has a protective effect on cardiovascular disease, and the ratios between HDL and LDL, and triglycerides and HDL, are more predictive of cardiovascular risk than LDL in isolation.[132] Increasing dietary saturated fat intake has been shown to increase both HDL and LDL, potentially leading to more favourable ratios.[133]

Health implications of different types of fat

Not all dietary fats are created equal. Often, fats are referred to as 'good' fats or 'bad' fats. But what exactly makes a fat 'good' or 'bad'? Here we discuss the health implications of different types of fat.

Saturated fatty acids

Since the 1970s, dietary saturated fat has been widely considered to increase the risk of coronary heart disease based on the 'diet–heart hypothesis'. However, decades of research have failed to provide substantive support for this theory.

There have been multiple meta-analyses on this topic, with most finding no justification for recommending restricting saturated fat intake. The meta-analyses finding possible benefit from restricting saturated fats appear to have included inadequately controlled studies,[131] explaining this apparent heterogeneity. The balance of evidence indicates there is no mortality benefit from replacing saturated fat with polyunsaturated fat. This was illustrated by the PURE study,[12] featured

in an earlier box. Using standardised and validated country-specific food frequency questionnaires, the study's authors concluded that increased saturated fat consumption was associated with lower risk of mortality. There was no apparent upper limit of saturated fat intake beyond which this benefit was not noted. Covariates were extensively controlled for in this study, somewhat addressing concerns that the low-fat diets associated with higher mortality rates could be attributable to poverty. This has implications for existing dietary guidelines, which appear to not be consistent with the best available evidence.

Monounsaturated fatty acids

No significant association between either total or individual monounsaturated fatty acid intake with coronary heart disease has been identified.[134] While monounsaturated fats are generally regarded as 'healthy', contradictory findings exist between studies. One systematic review concluded that the replacement of dietary saturated fats with monounsaturated fats offered no benefit for secondary prevention of coronary heart disease,[135] while another concluded it is beneficial to replace dietary high-GI carbohydrates and saturated fats with monounsaturated fat.[136] This inconsistency of findings is replicated in mechanistic research which has failed to demonstrate a clear effect of monounsaturated fat on atherogenesis.[134, 137–139] More research with clinical end points is required to permit definitive conclusions on the health impacts of dietary monounsaturated fats.[136]

Polyunsaturated fatty acids: omega-3 and omega-6

Omega-6 (n-6) and omega-3 (n-3) are the two main series of polyunsaturated fatty acids (PUFAs).[140] Short-chain omega fats in the form of linoleic acid (LA) (n-6) and α-linolenic acid (ALA) (n-3) are unable to be synthesised in humans, and longer-chain variants require shorter-chain precursors. Omega fatty acids are therefore essential nutrients requiring a dietary source. Omega-3 fatty acids are generally considered to be anti-inflammatory relative to omega-6 fatty acids.[141]

Polyunsaturated fats have long been considered healthier than saturated fats. This is largely premised on the effects of saturated fat on serum lipids. On balance, evidence available from adequately controlled randomised controlled trials does not demonstrate that replacing dietary saturated fats with polyunsaturated fats confers any benefit with respect to coronary heart disease or total mortality.[131]

The standard Western diet provides approximately 10 times more linoleic fatty acid compared to α-linolenic fatty acid.[142] This intake is consistent with the Australian Dietary Guidelines which state that omega-6 consumption should be 10 times greater than omega-3 consumption.[8] It has been suggested however, that reducing the ratio of omega-6 fats to omega-3 fats closer to one is associated with reduced risk of many chronic diseases, including cardiovascular and inflammatory diseases.[143] Linoleic acid (n-6) and α-linolenic acid (n-3) can both be converted into longer-chain fatty acids within their respective series through desaturation and elongation reactions occurring mainly in the liver.

Conversion of the omega-3 series α-linolenic acid to the more biologically active eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) is limited, possibly in the order of 8%.[144, 145] Further, there is competition between the two series for metabolism. In diets where linoleic acid (n-6) is more prevalent than n-3 fatty acids, metabolism of n-6 fatty acids is favoured.[146]

While ALA is present in vegetable/seed oils such as flaxseed, soybean and canola oils, EPA and DHA are not. Given the low rate of conversion of ALA to more biologically active forms,[147, 148] consuming EPA and DHA directly from animal sources or supplementation is the only practical way to increase levels in the body.

Findings in epidemiologic studies based on red blood cell membrane levels of EPA and DHA demonstrate a 10-fold lower incidence of sudden cardiac death associated with high levels of n-3 fatty acids compared to lower levels.[149, 150] Large trials of EPA and DHA supplementation have failed to demonstrate any beneficial effects in terms of reductions of total mortality relating to cardiovascular disease.[151] This may be due to failure to adequately restrict n-6 fatty acid intake.

Polyunsaturated fats, including omega-3 and omega-6 fats, are susceptible to oxidation due to the presence of carbon-to-carbon double bonds which are sites where oxidation reactions can occur.[152] The two major oxidation reactions which may occur in polyunsaturated fats are auto-oxidation in the presence of oxygen and photo-oxidation due to exposure to UV radiation. Peroxides, aldehydes and several other compounds may be produced. These oxidation products have potential health implications due to their cytotoxic, mutagenic and neurotoxic actions.[119, 153]

PRACTICE PEARL

The rate of oxidation of polyunsaturated fats (e.g. vegetable oils) is increased with cooking, producing peroxides, aldehydes and other harmful substances. Cooking with monounsaturated and especially saturated fats is associated with less oxidation than is seen with polyunsaturated fats.

Trans fatty acids

There are two major types of trans fats present in the Western diet: industrial and ruminant. Trans fatty acids are characterised by the presence of a single carbon-to-carbon double bond. In contrast to monounsaturated fatty acids which also contain a single carbon-to-carbon double bond, trans fatty acids have a 'kink' in their structure and are relatively straighter (Fig. 6.4). Monounsaturated fats are classified as *cis*-isomers. The kink in the structure of trans fats allows them to pack closer together, improving their cooking qualities. Both industrial and ruminant trans fats may have their carbon-to-carbon double bond in a number of locations, however they appear to have distinct ratios of distribution.[154]

Industrial trans fats are produced by vegetable oil hydrogenation, which adds hydrogen atoms at the expense of carbon-to-carbon double bonds. This improves the cooking properties of vegetable oils so they are closer to that of solid saturated animal fats. While complete

hydrogenation converts vegetable oils to saturated fats, partial hydrogenation can result in the formation of a *trans*isomer of the fat. This occurs due to 'flipping' around a remaining carbon-to-carbon double bond, altering the structure. Most trans fats in the Western diet are derived from partially hydrogenated vegetable oils, with a small amount present in dairy and meat products from ruminant animals.[155]

A high consumption of trans fatty acids appears to significantly increase the risk of coronary heart disease mortality.[156] Interestingly, this may not extend to ruminant-derived trans fatty acid, despite their structural similarity.[157] Regulations have been introduced in many countries to limit the amount of trans fats in processed foods which appear to have been effective in reducing intake.[158–160]

FLUIDS

Misinterpretation of a 1945 recommendation from the US Food and Nutrition Board led to the long-established belief that drinking eight glasses of water per day is necessary for good health.[161] The original recommendation was '2.5 liters daily', with the understanding that most of this was contained in foods.[162] Subsequent interpretations of this advice neglected the water content of food, advising that this total should be derived solely from ingested fluids.

This misinterpretation is reflected in current guidelines. The Australian Nutrient Reference Values suggest that daily fluid intake from all drinks should be 2.6 L (10 cups) for men and 2.1 L (8 cups) for women.[163] It is also recommended that pregnant and lactating women consume an extra 200–500 mL per day. A specific value is not defined in the current Australian Dietary Guidelines, despite recommending the population to 'drink plenty of water'. The US Dietary Reference Intakes recommends a daily water intake from all beverages and foods of approximately 3.7 L for men, and 2.7 L for women.[164] The Eatwell Guide by Public Health England recommends 6–8 glasses of fluid intake daily, in addition to fluid provided by food.[14]

The Eatwell Guide also makes reference to thirst as a useful indication of increased fluid needs as might occur with hot weather or exercise.[165] This is useful advice as 2.5 L of water may be insufficient in some circumstances, such as when engaging in prolonged exercise in hot and humid conditions.

Advice to consume fluid in advance of thirst while exercising can cause hyponatraemia. This dilution of body fluids, which can also occur with consumption of electrolyte sports drinks, has led to multiple documented fatalities, and is termed 'exercise-associated hyponatraemia' (EAH). It is now accepted that drinking to thirst is the most effective means of preventing EAH.[166, 167]

PRACTICE PEARL

Patients should be advised to 'drink to thirst'. This will all but eliminate the risk of hyponatraemia while not posing any real risk of dehydration (in the presence of readily available fluid).

PRACTICE PEARL

For the recreational exerciser, it is likely that sports drinks offer no benefit over water, and are likely to be counterproductive, working against the achievement of exercise goals due to their substantial sugar content.

Alcohol

Alcohol is responsible for causing more than 30 conditions, including gout, infectious diseases, cancer, diabetes, neuropsychiatric diseases (including alcohol use disorders), cardiovascular disease, liver and pancreas disease, and unintentional and intentional injury.[168] While it is clear that excessive alcohol consumption causes substantial illness, disability and mortality, recommended intakes around the world vary significantly. Australian guidelines (2009) recommend drinking no more than two standard drinks per day to minimise lifetime risk of harm,[1 69] or no more than 140 g of alcohol per week. UK guidelines advise no more than 14 units of alcohol per week, or no more than 112 g per week. In the USA, an upper limit of 196 g per week is recommended for men, and an upper limit of 98 g per week is recommended for women.[170]

Caffeine

Caffeine is a central nervous system stimulant that mainly acts by reversibly blocking the action of adenosine at its receptor and consequently preventing the onset of adenosine-induced drowsiness. Caffeine can be found in drinks (coffee, tea, hot chocolate, soft drinks, energy drinks), in foods (chocolate) and in medications (analgesics, weight loss medications).

Consumption of up to 400 mg of caffeine (4 cups of coffee) per day in healthy adults is not associated with adverse cardiovascular, behavioural, reproductive or developmental effects. Evidence also supports consumption of up to 300 mg of caffeine (3 cups of coffee) per day in healthy pregnant women. There is limited safety data for children and adolescents, however the available evidence suggests that 2.5 mg caffeine/kg/day is an appropriate recommendation.[174]

Long-term coffee consumption, in particular, has beneficial effects for a number of chronic diseases, including cancer, cardiovascular, metabolic and neurological conditions.[175] Adverse outcomes associated with coffee consumption include increased risks of lung and gastric cancers, as well as increased serum lipids. However, the reported increased risk of lung and gastric cancers is likely confounded by smoking.[175]

Caffeine also has many positive cognitive effects, such as increasing alertness, improving concentration and mood, and limiting depression. It may disturb sleep and raise anxiety, but only in caffeine-sensitive individuals.[176] In non-randomised observational cohort studies, the lifelong consumption of caffeine has been associated with prevention of cognitive decline, and reduced risk of developing stroke, Parkinson's disease and Alzheimer's disease.[176]

This heterogeneity reflects a degree of uncertainty regarding the drinking risk thresholds associated with the lowest risk of mortality,[141] illustrated by recent studies which challenge the concept that moderate alcohol consumption is universally associated with lower cardiovascular disease risk.[141]

A 2018 combined analysis of data for 600 000 current drinkers in 83 prospective studies found that in high-income countries, the threshold for lowest risk of all-cause mortality is about 100 g of alcohol per week. This is slightly less than the UK recommendation, and approximately equal to the US recommendation for females. Those reporting an alcohol intake of over 350 g per week had a reduced life expectancy at age 40 years of 4–5 years.[170]

Interestingly, for the same amount of alcohol consumed per week, it may be more beneficial to drink smaller amounts more frequently than drinking the same amount on only 1–2 days per week. And for almost all associated diseases, the type of alcoholic beverage does not strongly modify the risk of the disease.[171]

Although alcohol is responsible for substantial morbidity and mortality, it has been suggested that red wine is beneficial for one's health. Specific components of red wine such as polyphenols (especially resveratrol) are thought to improve cardiovascular health due to their antioxidant properties.[172] Epidemiological studies do suggest red wine is beneficial for hypertension, dyslipidaemia, cardiovascular and metabolic diseases,[173] however in the absence of more robust randomised clinical controlled trials, many questions are still left unanswered.

MICRONUTRIENTS

Micronutrients are comprised of vitamins and minerals, which are essential elements required in small quantities to enable a wide variety of metabolic and physiologic processes.

Given the ubiquitous commercial claims for the nutritional essentiality of these substances, it is no surprise that nearly 50% of Australian and American adults report taking vitamin and mineral supplements.[177, 178] Despite massive yearly spending on all types of vitamins and minerals, current evidence does not demonstrate general benefits of supplements for the prevention of disease not related to nutritional deficiency.[178]

PRACTICE PEARL

Routine micronutrient supplementation is not recommended for the majority of the population, however targeted supplementation may be warranted for particular subgroups (e.g. pregnant women, vegans, people with osteoporosis) for whom nutrition requirements may be difficult to meet through diet alone.

Superfoods

Can we really prevent cancer and reverse ageing by sprinkling chia seeds on our porridge, adding acai berries to our smoothies, or substituting brown rice with quinoa for our kale salads? Probably not.

Although tasty (and often expensive!), 'superfoods' are not a panacea for good health. Rather, the label is used as a clever marketing device. Stories about superfoods sell magazines and make for good morning television, and industry often sponsors research to show that its foods or supplements are the elixir for optimal health and long life.

But what exactly is a superfood? The *Oxford Dictionary* defines superfood as 'a nutrient-rich food considered to be especially beneficial for health and well-being'.[180] If that's the case, shouldn't every real, whole, unprocessed food be considered super? In fact, there is no official definition of a superfood in nutrition science, and as of 2007, the European Union has banned superfood health claims on packaging, unless supported by scientific evidence.

Instead, some studies suggest that micronutrient supplementation in amounts that exceed the recommended dietary allowance (of, for example, beta-carotene, vitamin E, selenium, calcium) may have harmful effects, including increased risk of cancer, stroke and mortality.[179]

A well-balanced diet made up of real foods provides an adequate supply of all micronutrients. For most individuals, consuming extra vitamins and minerals does not generally offer any advantage–and instead is likely to make for expensive urine.

Vitamins

Vitamins are chemically unrelated families of organic substances that cannot be synthesised by humans and are essential for supporting normal metabolism. They have diverse biochemical functions, acting as enzyme cofactors, antioxidants and hormone-like regulators for the maintenance of cells, tissues and organs. Although most can be obtained from food alone, some require the help of bodily processes (e.g. vitamin D is synthesised in the skin with exposure to sunlight). They are sensitive to destruction by light, heat, chemical agents and food processing.

The 13 recognised vitamins can be divided into two classes based on their relative solubility in water and fat (Table 6.2). Each vitamin name (e.g. vitamin C) refers to a collection of chemical compounds with similar molecular structures and activities.

Table 6.2 Categories of vitamins

Fat-soluble vitamins	Water-soluble vitamins
Vitamin A	B vitamins[8]
Vitamin D	Vitamin C
Vitamin E	
Vitamin K	

Vitamin A

Vitamin A is a subclass of a family of fat-soluble compounds referred to as retinoic acids. There are two main forms of vitamin A:

- provitamin A carotenoids (e.g. beta-carotene)
- preformed vitamin A (e.g. retinol)

Vitamin A from animal sources or supplements is preformed (Table 6.3). Vitamin A toxicity, while rarely seen, is more likely to occur when it is derived from animal sources due to increased bioavailability.[181]

Table 6.3 Food sources of vitamin A

Preformed vitamin A	liver, kidney, egg yolk, butter
Provitamin A	green leafy vegetables, orange-fleshed sweet potatoes, pumpkins and carrots

Vitamin A from food is stored in the liver until required by the body to support a variety of biological processes, such as maintaining the integrity of epithelial surfaces and cellular differentiation in the eye, which is essential for vision.

Vitamin A deficiency can lead to xerophthalmia (pathologic dryness of the conjunctiva and cornea), night blindness, poor bone growth, non-specific dermatological problems, and impaired immune function.

Vitamin D

Vitamin D is a group of fat-soluble steroids responsible for increasing intestinal absorption of calcium, magnesium and phosphate. It plays an important role in muscle function, insulin resistance, immunity and parathyroid hormone regulation, as well as bone growth, density and remodelling.[182] Low levels of vitamin D increases bone turnover, which increases fracture risk. Additionally, unlike exogenous vitamin D supplementation, endogenously derived vitamin D (not from supplementation) is positively associated with reduced risk of all-cause mortality, cardiovascular mortality and cancer mortality[183] (Fig. 6.6).

Page 58

Figure 6.6 Foods rich in vitamin D such as those pictured above may support heightened levels of

endogenous vitamin D. Serum vitamin D has been associated with a decrease in both all-cause and cardiovascular-disease-related mortality rates.[183]

(A AND B) INGRAM PUBLISHING/ (C) OLEKSANDRA NAUMENKO/SHUTTERSTOCK (D) © EMILIO EREZA/AGE FOTOSTOCK

Vitamin D is found in a few naturally-occurring foods (Table 6.4), but some food products (e.g. milk, cereals, margarine, orange juice) have vitamin D added to them.

Table 6.4 Food sources of vitamin D

Portobello and crimini mushrooms	Sardines
Salmon	Egg yolk
Mackerel	Liver
Tuna	Dairy (e.g. milk, butter)

For most individuals, the predominant source of vitamin D is cholecalciferol (vitamin D^3), synthesised in the skin from cholesterol through a chemical reaction that is dependent on sunlight (UVB radiation) exposure. Vitamin D synthesis from sunlight is greatly influenced by season, time of day, latitude, altitude, air pollution, skin pigmentation, sunscreen use, glass and plastic filters, and ageing.[184] Whole body exposure of midday sun in summer for 10–15 minutes is comparable to taking 15 000 IU of vitamin D^3 orally.[185]

Vitamin D levels should be maintained above 80 nmol/L. The nutrient reference values (NRVs) for Australia and New Zealand are 200 IU (5 μg) a day for infants, children and adults below 50 years, 400 IU (10 μg) for those aged 50–70, and 600 IU (15 μg) for those over 70.[186] The US Institute of Medicine's recommended daily allowance (RDA) for vitamin D is 600 IU.[187] However, many experts contend that these amounts are far too low, and some even recommend as much as a 10-fold increase.

Vitamin D insufficiencies are estimated to affect over one billion people worldwide.[188] Insufficient vitamin D impairs bone metabolism and causes inadequate bone mineralisation, leading to osteomalacia (referred to as rickets when present in children) and increased risk of fracture. For individuals with low vitamin D levels, vitamin D^3 supplementation may be required. Notably, daily supplementation of 700 IU or greater has been shown to significantly reduce the risk of falls in the elderly and subsequent fracture rates.[189]

Vitamin E

Vitamin E refers to a group of fat-soluble antioxidant compounds that are found in naturally-occurring foods (Table 6.5). Vitamin E helps stop the production of reactive oxygen species when fat undergoes oxidation and aids immune function via regulation of gene expression and cell proliferation.[190]

Table 6.5 Food sources of vitamin E

Sunflower seeds	Squash
Almonds	Pine nuts
Hazelnuts	Peanuts
Spinach	Olive oil
Avocado	

Vitamin E deficiency is rare. Those at risk include individuals with Crohn's disease or cystic fibrosis.[191] Symptoms of deficiency include peripheral neuropathy, ataxia, skeletal myopathy, retinopathy and impaired immune response.

PRACTICE PEARL

High dose (≥400 IU/day) vitamin E supplements may increase all-cause mortality and should generally be avoided.[192]

Vitamin K

Vitamin K refers to a group of fat-soluble compounds that are essential for protein synthesis, blood coagulation and bone metabolism. These compounds include:

- phylloquinone (vitamin K_1)
- menaquinones (vitamin K_2)

Vitamin K_1 is found primarily in green leafy vegetables and is the main dietary form of vitamin K. Vitamin K_2, which is predominantly of intestinal bacterial origin, is present in small amounts in various animal-based and fermented foods (Table 6.6). Vitamin K_1 serves as a cofactor in the clotting cascade, helping to maintain blood homeostasis. Vitamin K_2 is involved in calcium transport, preventing calcium deposition in the lining of arterial walls,[193] and helps maintain the normal structure of bone.[193, 194]

Table 6.6 Food sources of vitamin K

Vitamin K1	Collards, spinach, kale, broccoli, soybeans, pumpkin, pine nuts, kiwi fruit, blueberries
Vitamin K2	Natto, sauerkraut, hard cheeses, egg yolk, butter, chicken, beef, bacon

It is postulated that phylloquinone can be converted to menaquinones in humans—a process

which has been found to occur in chimeric studies[195]—and it has been shown that menaquinones can be produced for nutrition requirements by human intestinal microflora.[196]

Vitamin K deficiency is rare. Newborns are at increased risk, as well as alcoholics and those with inflammatory bowel disease or cystic fibrosis. Deficiency results in coagulopathy, and common presenting symptoms include lethargy, easy bruising, nosebleeds and bleeding gums.

B vitamins

B vitamins are a class of water-soluble vitamins that play essential roles in cell metabolism. It is beyond the scope of this chapter to explore each of the eight B vitamins in depth. Rather, we will discuss the clinical relevance of several important B vitamins. Food sources of the common B vitamins are shown in Table 6.7.

Table 6.7 Food sources of B vitamins

Vitamin B_1	Yeast, legumes, pork, brown rice, cereals made from whole grains
Vitamin B_3	Turkey, chicken breast, liver, tuna, peanuts, mushrooms, green peas, sunflower seeds, avocado
Vitamin B_9	Dark leafy greens, liver, Brussels sprouts, asparagus, broccoli, citrus fruits, beans, peas, lentils, avocado, seeds and nut
Vitamin B_{12}	Liver, sardines, lamb, salmon, eggs, milk, cheese, nutritional yeast

Vitamin B_1 (thiamine)

Thiamine, along with necessary coenzymes, serves as a catalyst in the conversion of pyruvate to acetyl coenzyme A (CoA). It is involved in many cellular metabolic activities, including the tricarboxylic acid cycle, and participates in nerve impulse propagation.

Thiamine is primarily found in foods such as yeast, legumes, pork, brown rice, and cereals made from whole grains. White 'polished' rice or milled white cereals including wheat flour contain low amounts of thiamine. Cooking, baking, canning of some foods and pasteurisation can destroy thiamine, which is denatured at high pH and high temperatures. Dairy products, fruits and vegetables are poor sources of thiamine. Thiamine deficiency is most commonly reported in populations in which the diet consists mainly of polished rice or milled white cereals.

Thiamine's biologic half-life is approximately 10–20 days and continuous intake is required. Thiamine deficiency may cause either beriberi or Wernicke–Korsakoff syndrome. Beriberi may occur in infants, mainly in those breastfed by women with a thiamine-deficient diet. Clinical features may include cardiomegaly, tachycardia, cyanosis, dyspnoea and vomiting. Neurological symptoms may be seen in older infants. Beriberi in adults has two clinical phenotypes, classically described as 'dry' or 'wet'. Dry beriberi is characterised by a symmetrical peripheral neuropathy with both sensory and motor impairments. Wet beriberi includes signs of cardiac involvement with cardiomegaly, cardiomyopathy, heart failure, peripheral oedema and tachycardia. Adult beriberi is treated with thiamine replacement.

Wernicke–Korsakoff syndrome refers to two different syndromes representing a spectrum of neurological signs and symptoms. Wernicke's encephalopathy is an acute syndrome that without

urgent treatment may result in death or neurologic morbidity. Korsakoff syndrome is a chronic neurologic condition that may result from Wernicke's encephalopathy, characterised by short-term memory impairment and confabulation. Wernicke's encephalopathy classically occurs in alcoholics, however it is increasingly being seen following weight-loss surgery. Wernicke's encephalopathy is treated with large dose thiamine supplementation. Administration of dextrose to alcoholic patients is often delayed until after thiamine supplementation due to fears of precipitating Wernicke's encephalopathy. Thiamine toxicity has not been described, likely due to rapid renal clearance and lack of storage mechanisms.

Vitamin B_3 (niacin)

Vitamin B_3 is composed of nicotinic acid and nicotinamide, and plays an important role in energy transfer reactions in the metabolism of glucose, fat and alcohol. In other words, vitamin B_3 is required to help turn food into energy. Excessive vitamin B_3 from foods is not known to cause toxicity, however excessive supplemental vitamin B_3 has been associated with serious multisystem organ failure and fulminant hepatic failure.[197]

Vitamin B_3 deficiency, and/or deficiency of its precursor tryptophan (an essential amino acid), leads to pellagra, which is characterised by dermatitis, dementia and diarrhoea.[198]

Vitamin B_9 (folate)

Vitamin B_9, or as it is more commonly known, folate or folic acid, acts as a coenzyme or co-substrate in the synthesis of DNA and RNA, and in the metabolism of amino acids. It is essential for the production and maintenance of new cells and is particularly important during periods of cell division and growth (e.g. pregnancy).

Folate and folic acid are often used interchangeably when referring to vitamin B_9. Folate is the bioavailable, natural form of vitamin B_9 that is found in food, while folic acid is the synthetic form, primarily found in supplements and fortified food (e.g. bread, cereal, pasta).

Folic acid is substantially more bioavailable compared to naturally occurring food folates at equivalent intake levels.

As folate deficiency impairs nucleic acid synthesis and cell division, haematopoietic and cancer cells are particularly affected due to their greater frequency of cell division. Limited cell division leads to impaired production of erythrocytes, which results in megaloblastic anaemia (seen in conditions such as inflammatory bowel disease, coeliac disease and other malabsorption disorders).

Individuals with alcohol dependence are at high risk of deficiency, as chronic alcohol consumption impairs folate absorption[199] and these people are also likely to have poor quality diets that do not provide adequate amounts of folate. Importantly, folate deficiency during pregnancy leads to neural tube defects in the foetus,[200] and so supplementation, which has been shown to be preventive, is widely encouraged.[201]

Vitamin B_{12} (cobalamin)

Vitamin B_{12} is a water-soluble vitamin that functions as a co-factor in DNA synthesis, fatty acid and amino acid metabolism, myelin formation and maturation of erythrocytes. Vitamin B_{12} from ingested protein is cleaved from the amino acids through the action of digestive proteases in the stomach and small intestine. It is then bound to intrinsic factor, produced by gastric parietal cells, and absorbed in the terminal ileum. Given that absorption of vitamin B_{12} is dependent on intrinsic factor, conditions which decrease the secretion of intrinsic factor (e.g. pernicious anaemia, atrophic gastritis) or interrupt cleavage of the binding proteins (e.g. pancreatic insufficiency) can result in malabsorption and subsequent anaemia.

Vitamin B_{12} is not made by plants or animals, but by certain microbes, such as resident gut bacteria in ruminants. Animals store the vitamin in their livers and muscle tissue, and some pass the vitamin into their eggs and milk. Although most individuals obtain adequate dietary vitamin B_{12} by eating animal products, the vitamin can also be found in fortified foods and obtained through supplementation.

Individuals who eat a predominantly plant-based diet (e.g. vegetarians or vegans) are at high risk for deficiency, and so supplementation is critical for those who are not obtaining adequate amounts from fortified foods.

Although vitamin B_{12} deficiency can take years to develop, it can have severe consequences including paralysis, psychosis, blindness and death. Deficiency characteristically leads to megaloblastic anaemia, fatigue, weakness, constipation, weight loss and potentially irreversible nerve damage. Proton pump inhibitor (PPI) medication has been associated with an increased risk of vitamin B_{12} deficiency, as well impairing vitamin C, calcium, iron and magnesium metabolism.[202]

PRACTICE PEARL

When megaloblastic anaemia is detected, it is crucial to first rule out vitamin B_{12} deficiency before initiation of folic acid therapy, as folic acid may aggravate neurologic manifestations of underlying vitamin B_{12} deficiency. In severe megaloblastic anaemia, where therapy must be initiated immediately, concomitant folic acid and vitamin B_{12} should be given.

Vitamin C

Vitamin C, or ascorbic acid, is an essential water-soluble vitamin that functions as a cofactor in the synthesis of collagen, carnitine and some neurotransmitters. It is a naturally occurring micronutrient that is a potent antioxidant[203] and must be consumed for survival. Food sources of Vitamin C are shown in Table 6.8.

Table 6.8 Food sources of vitamin C

Guava	Orange

Black currant	Strawberry
Red capsicum (pepper)	Papaya
Kiwi fruit	Citrus fruits

Vitamin C deficiency leads to scurvy, which is characterised by lethargy, gum disease, painful limbs, bleeding from the skin and poor wound healing. More than 250 years since James Lind showed that citrus fruits were a cure for scurvy when testing his hypothesis on sailors in a prospective controlled therapeutic trial,[204] the disease is now most commonly found in individuals with mental health disorders and alcohol dependence.

Vitamin C for the prevention and treatment of the common cold has been the subject of much controversy in previous years. Vitamin C supplementation does not reduce the incidence of the common cold in the general population but may be beneficial for individuals engaging in intense physical activity. Supplementation may reduce the duration of the common cold, however further research is needed.[205]

PRACTICE PEARL

Vitamin C can help improve absorption of non-haeme iron, which is present in plant-based foods. However, its influence on absorption may be less substantial in meals of high iron availability, such as those containing haeme iron found in meat or fish.

Minerals

The word 'mineral' is in fact a misnomer, as dietary minerals are chemical elements required to carry out metabolic functions necessary for life. Like vitamins, they cannot be synthesised by humans and are essential nutrients that must be ingested. Some function as electrolytes, while others play a role in biological processes such as hormone synthesis, antioxidant activity, cell signalling and energy production.

The majority of chemical elements that are ingested by organisms are in the form of simple compounds. Plants absorb elements found in soil, which are subsequently ingested by animals that eat the plants, and again by animals that eat other animals (as well as plants). Minerals may also be obtained from the water we drink, which, like plants, varies based on location. The major (macro) minerals in humans are calcium, chloride, magnesium, phosphate, potassium, sodium and sulphur. The remaining elements found in humans are known as 'trace elements', all of which can be classified based on their estimated adult daily requirements (Table 6.9).

Table 6.9 Categories of minerals

Macro minerals (>100 mg/day)	Trace elements (1–100 mg/day)
Calcium	Chromium

Chloride	Cobalt
Magnesium	Copper
Phosphate	Fluoride
Potassium	Iodine
Sodium	Iron
Sulphur	Manganese
	Selenium
	Zinc

Calcium

As a major structural constituent of bones, calcium is the most abundant mineral found in the human body. Calcium concentration in blood and extracellular fluid must be tightly controlled to enable normal physiological function, so much so that the body will stimulate bone resorption when calcium intake is inadequate. Increased secretion of parathyroid hormone will also stimulate bone resorption. In addition to helping maintain a healthy skeleton, calcium plays an important role in mediating vasoconstriction and vasodilation, nerve impulse transmission, muscle contraction, coagulation and secretion of hormones.[206]

PRACTICE PEARL

Serum calcium levels are strictly regulated and do not necessarily reflect the calcium stores in bone.[207]

Although dairy may be the first thing that comes to mind when thinking about calcium, the mineral can be found in a variety of foods (Table 6.10), such as dark green leafy vegetables, legumes, nuts and seeds. Calcium is mostly absorbed in the jejunum and its absorption is favoured by a low pH. Cow's milk is the best-absorbed source of calcium, while other foods show high concentrations but varied bioavailability due to the actions of phytic acid and oxalates.[208]

Page 62

Table 6.10 Food sources of calcium

Sardines	Kale
Yoghurt	Okra
Cow's milk	Bok choy
Cheese	Almonds
Tofu	Broccoli
White beans	

Importantly, vitamin D increases calcium absorption in the intestine,[209] and helps maintain

serum calcium and phosphate concentrations to enable normal bone mineralisation (along with vitamin K_2).

Both hypercalcaemia and hypocalcaemia can have serious consequences. The most common cause of hypocalcaemia likely to seen by clinicians is vitamin D deficiency, although it may also be seen in people with reduced parathyroid hormone function or malabsorption disorders. Classic symptoms of hypocalcaemia are muscle twitching, spasms, paraesthesia and anaesthesia—and in severe cases, tetany, seizures and cardiac arrhythmias.[210] Hypercalcaemia, on the other hand, can lead to agitation, bone and/or abdominal pain, gastrointestinal disturbances, kidney stones and neurological dysfunction.[211]

Calcium (alongside vitamin D) is routinely supplemented to mitigate the risk of developing or slow the progression of osteoporosis, and for the subsequent prevention of fractures (Chapter 17). However, a 2015 meta-analysis found that calcium supplements have small, inconsistent benefits of fracture prevention and that dietary calcium intake is not associated with risk of fracture.[212] In fact, in a cohort study that examined milk consumption in over 100 000 people for over 20 years, high milk intake was associated with higher mortality in men and women, and with higher fracture incidence in women.[213] Of course, observational study designs make it difficult to control for confounding factors, yet it raises the question whether we should look at other methods or dietary sources for reducing risk of fractures.

Furthermore, isolated calcium supplementation may be associated with increased risk of cardiovascular events, as it may increase the risk of coronary artery calcification.[214]

Magnesium

Magnesium is a cofactor in over 300 enzymatic reactions, involved in physiological pathways that are responsible for nucleic acid and protein synthesis, ion transport, cell signalling and energy production among other processes.[215] Notably, magnesium is thought to play a role in insulin secretion, owing to the altered insulin secretion and sensitivity observed in magnesium-deficient animals.[216]

Magnesium is part of chlorophyll (the green pigment in plants), and so most green leafy vegetables are rich in magnesium. Other food sources are listed in Table 6.11.

Table 6.11 Food sources of magnesium

Spinach	Almonds
Brown rice	Black beans
Mackerel	Avocado
Dark chocolate	Yoghurt
Pumpkin seeds	

Magnesium deficiency is common in the Western world due to poor diet[217] and soil depletion.[218]

Modern agricultural methods have depleted soil of many nutrients, resulting in lower micronutrient content in the food we eat. Deficiency may impair vitamin D and calcium homeostasis,[219] raise blood pressure[220] and reduce insulin sensitivity.[221] Chronic latent magnesium deficiency has been associated with atherosclerosis, myocardial infarction, malignant tumours, kidney stones, premenstrual syndrome and psychiatric disorders.[222]

Supplementation is being explored in the management of hypertension, cardiovascular disease, type 2 diabetes, migraines and asthma. As magnesium plays a role in neuromuscular transmission and muscle cramps, it is hypothesised that deficiency may predispose to muscle cramps, however magnesium does not appear to be effective in the treatment of nocturnal leg cramps.[223] For women experiencing 'pregnancy-associated rest cramps', the literature is conflicting and further research in this population is needed.[224]

Potassium

Most people recognise potassium as an electrolyte that can be obtained from bananas (which surprisingly are not particularly rich in potassium relative to other foods (Table 6.12)). The term 'electrolyte' refers to a substance that dissociates into ions in solution, making it capable of conducting electricity. Potassium is the principal cation in intracellular fluid, while sodium is the principal cation in extracellular fluid. The concentration differences between potassium and sodium across cell membranes give rise to a membrane potential.

Page 63

Table 6.12 Food sources of potassium

Avocado	Tuna
Spinach	Dried apricot
Sweet potato, white potato and squash	Pomegranate
Tomato paste	White beans
Salmon	Banana

Potassium is required for the activation of sodium/potassium-ATPase and for the activity of pyruvate kinase, which is essential for carbohydrate metabolism. Evidence is also accumulating of the protective effect of dietary potassium on age-related bone loss and reduction of kidney stones.[225]

Modern Western diets have led to a decrease in potassium intake due to reduced consumption of fruits and vegetables, with a concomitant increased consumption of processed foods.[225] Acute potassium deficiency, which may present with fatigue, muscle cramps and/or intestinal paralysis, is most commonly seen with prolonged vomiting, diuretic use and kidney disease.

Some international organisations discourage the use of potassium supplements or potassium-rich salt replacers due to the risk of hyperkalaemia, particularly for people with kidney disease. However, recent data suggests a moderate increase in potassium intake using supplements could be

safe and void of risk of hazardous hyperkalaemia or renal deterioration in people with normal kidney function.[226]

Magnesium deficiency can exacerbate potassium deficiency and aggravate the adverse effects of hypokalaemia.[227] Recognition of concomitant magnesium deficiency and early treatment with magnesium are crucial for prevention and treatment of complications of hypokalaemia.

PRACTICE PEARL

Large doses of potassium, consumed in supplemental forms that can be rapidly absorbed, can cause hyperkalaemia and subsequent cardiac arrhythmias.

Sodium

Sodium and chloride are the major electrolytes present in extracellular fluid. They work in tandem to control extracellular volume and blood pressure. Various mechanisms (e.g. renin-angiotensin-aldosterone system) act on the kidneys to ensure that the amount of sodium lost via renal excretion compensates for the amount of sodium consumed to maintain homeostasis.

For decades, policy makers, organisations and clinicians have advised people to limit sodium consumption to reduce blood pressure and the subsequent risk of cardiovascular events. However, proposed benefits of dietary sodium restriction are generally based on extrapolation from anticipated reductions in blood pressure, in concert with other epidemiological data. Some observational studies and a meta-analysis have actually reported an increase in cardiovascular disease and mortality among those who consume the lowest levels of sodium, suggesting a U- or J-shaped curve of sodium and health outcomes.[228–230]

One large study that included over 100 000 participants in 17 countries found increased levels of all-cause mortality with daily urinary sodium excretions less than 3000 mg or greater than 6000 mg.[230] This is inconsistent with current Australian Dietary Guidelines which recommend a population target (suggested dietary target, or SDT) of 2000 mg of sodium daily, with the stated goal of reducing the average blood pressure of Australian adults by 2 mmHg. Interestingly however, the recommended upper limit of sodium intake for individuals has been removed, given an inability to identify a threshold level of sodium intake, below which represents reduced risk. These contradictory targets within the same dietary guideline are no doubt a source of confusion for those seeking guidance.

PRACTICE PEARL

Substantially lowering or restricting salt intake has not shown much benefit in clinical trials. Arguably, the majority of individuals would benefit more from consuming a diet that consists of unprocessed foods than they would from micromanaging their salt intake.

Iodine

Iodine is essential for the normal function of the thyroid gland. Iodine binds to tyrosine within the thyroid gland to form monoiodothyronine (MIT), diiodothyronine (DIT), triiodothyronine (T3) and thyroxine (T4). These thyroid hormones regulate the metabolic pattern of most cells and play a vital role in early growth and development of most organs (especially the brain).

Widespread food supply supplementation with iodine (e.g. table salt) has seen significant reduction of iodine deficiency in industrialised countries. However, deficiency still remains Page 64 a major public health problem in developing countries (and some developed countries) due to poor diet and the use of non-iodised salt. Iodine deficiency classically presents as an enlargement of the thyroid gland, known as a goitre, and can lead to hypothyroidism as well as stunting of physical growth and brain development in infants. Populations at particular risk of deficiency include pregnant women, lactating mothers and young infants.[231]

PRACTICE PEARL

Supplementation of high doses of iodine in otherwise healthy people generally does not offer any benefits, as iodine is readily excreted and normalised by the body.

Table 6.13 Food sources of iodine

Seaweed (and other sea vegetables)	Tuna
Cod	Lima beans
Yoghurt	Corn
Milk	Prunes
Eggs	

Iron

Iron is an essential structural and functional component of a multitude of proteins and enzymes that support essential biological processes such as oxygen transport, energy production and DNA synthesis. Although iron is essential, it can be harmful to cells because intracellular free iron can lead to the generation of free radicals which cause oxidative stress, and so concentrations must be tightly regulated. Hepcidin, a peptide hormone primarily synthesised by hepatocytes, is the primary regulator of systemic iron homeostasis and can be a helpful measure for diagnosing iron-refractory iron deficiency anaemia.[232]

Dietary iron is present in two main forms: haeme and non-haeme iron. Haeme iron is found in meat, poultry and fish, and is well absorbed. Non-haeme iron is found in vegetables and fruit (Table 6.14), as well as iron-fortified food products. Absorption and bioavailability of non-haeme iron is inferior to that of haeme, but can be improved with concurrent ingestion of vitamin C.[233] The poor bioavailability of plant-based sources of iron is thought to be due to the presence of phytate, which

chelates iron and prevents its absorption. Tannins present in tea and coffee can also impair absorption[234] acutely, and so it may be recommended to drink tea or coffee between meals, rather than during.

Table 6.14 Food sources of iron

Haeme iron	liver, grass-fed beef, sardines, turkey
Non-haeme iron	spirulina, lentils, tofu, beans, dark chocolate, spinach, pistachios, raisins, quinoa

Iron deficiency is the single most prevalent nutrition deficiency worldwide.[235] Insufficient iron intake or uptake, and iron loss through prolonged bleeding can cause iron deficiency anaemia, characterised by symptoms of fatigue, shortness of breath, dizziness, agitation, brittle nails and hair loss. Iron deficiency, or at least iron depletion, is common in women of all ages, particularly in pregnant women and in those who are menstruating. Iron deficiency anaemia in women is defined as a haemoglobin level of less than 120 g/L. Iron depletion is indicated by a normal haemoglobin level (>120 g/L) but serum ferritin level (an indicator of iron stores) of less than 30 µg/mL.

In cases of deficiency, increased oral intake, supplementation and/or transfusion may be required. Other than in deficiency states, iron supplementation is not generally recommended as it can instead lead to iron poisoning.

PRACTICE PEARL

An increased requirement for iron is seen in pregnancy, lactation and heavy menstruations, as well as in those who donate blood, perform strenuous exercise or follow a vegetarian or vegan diet.

Zinc

Zinc is an essential mineral that plays important roles in catalysing enzymatic reactions, providing structural support for proteins and cell membranes, and regulating gene expression. It is a key element that is required for growth and development, immunity, neurological function and reproduction.

Meat such as lamb, beef and chicken is rich in zinc, as are some nuts and legumes (Table 6.15). Zinc can also be found fortified in food products, such as breakfast cereals and bread.

Table 6.15 Food sources of zinc

Oysters	Cacao powder
Lamb	Cashews
Pumpkin seeds	Yoghurt
Grass-fed beef	Mushrooms

Lentils	Spinach
Chickpeas	Chicken

Mild dietary zinc deficiency has been shown to impair growth velocity, while severe deficiency has been found to cause growth retardation.[236] Other clinical manifestations of zinc deficiency include delayed sexual maturation, impotence, hypogonadism, oligospermia, alopecia, impaired taste, immune dysfunction, night blindness and impaired wound healing. In addition to malnutrition, causes of deficiency include alcoholism, pregnancy, prolonged parenteral nutrition, malabsorption disorders and extensive burns.[237]

Page 65

PRACTICE PEARL

Zinc is lost through sweat, and so supplementation may be important for athletes who do not obtain adequate amounts of zinc through diet alone.

Notably, taking large quantities of zinc over a period of weeks can interfere with copper bioavailability and cause copper deficiency.[238]

TYPES OF DIET

Countless diets have been described both for weight loss and promotion of good health. Expert opinion remains divided on the merits of various diets, as many have not been subject to rigorous scientific investigation. Much of the research in this field is plagued by the problems of assessment of dietary intake, confounding variables, follow-up of insufficient duration, and bias due to industry funding. And to compound these challenges, the mainstream media is often responsible for incomplete and incorrect reporting of the science, misinterpreting studies and often publicising hyperbolic and distorted content that makes for good headlines.

After the introduction of the dietary guidelines, low-fat and reduced calorie eating was widely accepted and endorsed as the ideal dietary pattern. However, in recent years this has been challenged, and we have seen a proliferation of other diets claiming to be the one true way to achieve weight loss and optimal health. Diets can be broadly categorised based on macronutrient composition and quantity, although some diets have elements common to more than one category (e.g. low-fat, low-carbohydrate):

- low-calorie—Weight Watchers, Jenny Craig, SlimFast®
- low-fat—Dr Oz, Zone
- low-fat whole foods—Mediterranean, DASH, Pritikin, Sonoma
- low-carbohydrate—Atkins, low-carb high-fat (LHCF/Banting), ketogenic, Protein Power, Sugar Busters

- low-GI—South Beach
- paleo—Paleo diet, Primal Blueprint, Paleo Solution, raw food
- food-sensitivity—gluten-free, low-FODMAPs
- vegetarian and vegan
- intermittent fasting—5:2, alternate day fasting

Low-calorie

The traditional approach to weight loss and management has been the prescription of diets that provide an energy intake below that of an individual's normal energy expenditure. Reducing the total energy content of the diet can be achieved by restricting protein, carbohydrate, fat or a combination of the three.

A low-calorie diet has been traditionally defined as a diet that provides an energy intake of 800–1500 kcal per day.[241] A *very* low-calorie diet further limits energy intake to less than 800 kcal per day.[242] However, these definitions are arbitrary. For example, a diet consisting of 700 kcal per day for a small, sedentary individual would induce only a modest energy deficit if the individual's resting energy expenditure is 1200 kcal per day. In contrast, a diet consisting of 1200 kcal per day for a tall, active individual would result in a substantial energy deficit if their daily energy requirement is 3000 kcal.

Low-calorie diets were initially developed to induce a near-fasting metabolic response without nutrient depletion, and were designed to produce rapid weight loss while preserving lean body mass.[242] They are often comprised solely of liquid formulations that are intended to completely replace other food intake for a specific period of time.

Although these diets may produce rapid weight loss and result in symptom improvement—such as reduced joint pain, improved sleep quality in obstructive sleep apnoea, reduced shortness of breath on exertion, reduced peripheral oedema and rapid improvement in metabolic control in diabetes[243]—there are concerns regarding subsequent weight maintenance as well as the diet's sustainability.

Do diets work?

Weight regain after weight loss is a common problem for all who have had a recent weight loss. Not only do they regain all the weight they have lost, but as many as two thirds of people regain more weight over the following 4–5 years than they lost.[239] For many people desperate to lose weight, dieting follows a cyclical pattern over many years: restrict, regain, gain extra, restrict again. The reasons for this are complex, including increased hunger and a slowing of metabolism in response to food deprivation.[240]

The body adjusts to reduced calorie intake by lowering its resting energy expenditure (REE)—the

energy that we use when at rest. When people find that they can no longer tolerate the deprivation/starvation involved in a calorie-deficit diet and return to eating as they did before, their total energy requirement (REE plus energy needed for activity) is lower and thus they regain weight.

Low-fat

Since the widespread introduction of the first dietary guidelines, low-fat diets have been promoted as a means of both improving cardiovascular health and losing weight. However, in recent years, there has been much critique of low-fat diets due to the failure of low-fat national dietary guidelines to prevent, or now improve, the obesity and diabetes pandemics.

As its name suggests, a low-fat diet is one that restricts fat, especially saturated fat and cholesterol. Typically, it promotes consumption of whole grains, lean meats, white fish, reduced fat dairy, legumes, vegetables and fruit, and discourages butter, whole eggs, and animal fat of any kind.

When compared with dietary interventions of similar intensity, evidence from randomised controlled trials does not support low-fat diets over other dietary interventions for long-term weight loss.[244] And when comparing low-fat to high-fat, there is no clear evidence that low-fat eating is superior with regards to health outcomes over the life span.

One particular concern with low-fat diets is the heavy reliance on carbohydrates, which are often processed grains (e.g. breads, cereal, and pasta). When the diet is consistently high in carbohydrate, such as processed grains or added sugars, the level of insulin in the blood remains elevated. This can lead to storage of the excess carbohydrate as fat through de novo lipogenesis when glycogen stores are full.[245–247] Additionally, high-carbohydrate diets can lead to an earlier return of appetite and hunger following meals,[248] which may facilitate weight gain over the long term.

Mediterranean

The Mediterranean diet has long been considered paradigm for healthy eating. There is no single definition of a Mediterranean diet, complicating research. The aim of the diet is to mimic the traditional dietary pattern that is prevalent throughout Mediterranean countries – including vegetables, fruits, whole grains, nuts, seeds, legumes, olive oil, selective dairy intake, moderate red wine intake during meals, moderate fish and limited meat consumption.

The Mediterranean diet is arguably the best-studied and most evidence-based diet to prevent cardiovascular disease[255] and reduce the risk of other chronic diseases such as cancer,[256, 257] depression,[258, 259] diabetes,[260, 261] obesity,[262] erectile dysfunction,[263] Parkinson's and Alzheimer's disease.[264] The diet is also known to improve features of cardiovascular disease, such as markers of inflammation,[265] as well as cardiovascular disease outcomes such as death and cardiovascular events.[264, 266]

Extra virgin olive oil, one representative component of this diet, is associated with reduced risks of cancer,[267] cardiovascular disease and mortality,[268] perhaps due to its anti-inflammatory,

antioxidant and vasodilatory effects.[269]

DASH

The 'dietary approaches to stop hypertension' (DASH) diet was originally tested for its effects on blood pressure,[270] from which the name derives, but has since been applied to both weight loss and general health promotion.

The diet is largely based on two studies, DASH[270] and DASH-Sodium,[271] which explored methods of reducing blood pressure through dietary changes. In the DASH study (1997) over 450 adults were fed a diet low in fruits, vegetables, and dairy products, with a fat content 'typical of the average diet in the United States'. They were then randomly assigned to receive for eight weeks either the control diet which is rich in fruits and vegetables; or a 'combination' diet which is rich in fruits, vegetables, and low-fat dairy products, and with reduced saturated and total fat. Sodium intake and body weight were maintained at constant levels. The researchers found that the combination diet significantly reduced systolic and diastolic blood pressure, respectively, by 5.5 and 3.0 mmHg more than the control diet, and that the fruits and vegetables diet reduced systolic blood pressure by 2.8 mmHg more and diastolic blood pressure by 1.1 mmHg more than the control diet.

Insulin resistance

Insulin is a peptide hormone produced by the beta islet cells of the pancreas that assists in the regulation of blood glucose levels by promoting the absorption of glucose into liver, fat and skeletal muscle cells and decreasing hepatic gluconeogenesis.

Glucose is stored in muscle as glycogen, in fat as triglycerides, and in the liver as both. The net effect of insulin is to remove glucose from the circulation by increasing tissue uptake and facilitating the conversion of glucose into glycogen or fat. Insulin resistance is a state in which liver, fat and skeletal muscle cells do not respond appropriately to insulin. Hyperinsulinaemia is a surrogate marker for insulin resistance.

Insulin resistance is considered a key aetiological factor in the development of metabolic syndrome, a condition associated with increased risk of cardiovascular disease, diabetes, chronic kidney disease and increased all-cause mortality.[249–252] Metabolic syndrome can be diagnosed in the presence of at least three of the five following medical conditions: abdominal obesity, high blood pressure, high blood sugar, high serum triglycerides and low high-density lipoprotein (HDL) levels.

The two dominant underlying causes of insulin resistance are thought to relate to hepatic production of diacylglycerol and inflammatory states.[253] Hepatic diacylglycerol production occurs in the state of excess carbohydrate consumption,[254] and thus reduced carbohydrate diets may be protective for the development of metabolic syndrome.

The DASH diet is now characterised by consumption of fruits, vegetables and low-fat dairy products; includes whole grains, poultry, fish and nuts; and attempts to reduce the intakes of red meat, sweets, sugar-containing beverages, total fat, saturated fat and cholesterol.[272] Since the

original trials, more recent data also suggest that the diet may be effective for improving blood pressure, as well as reducing total cholesterol and LDL concentrations. However, data suggest the diet does not significantly affect triglycerides, glucose or HDL.[273] Notably, simple substitution of low-fat for full-fat dairy foods in the DASH diet may lead to greater reduction of triglycerides and large and medium very-low density lipoprotein (VLDL) particle concentrations, while still reducing blood pressure to the same extent as the low-fat dairy DASH diet.[274]

In recent years, the US News & World Report[275] has consistently ranked DASH to be the best overall diet. This particular ranking system is based on the consensus opinion of a panel of expert judges who rate diets based on criteria including short- and long-term weight loss, diabetes and cardiovascular disease management, ease of compliance, 'nutritional completeness' and health risks. However, ignoring the fact that the ranking system is based on expert opinion, one could argue that data comparing DASH to other reasonable contenders are lacking.

Low-carb

There is no official agreed definition of a low-carbohydrate diet. As the name suggests, it is defined by restricting intake of total carbohydrate below a particular threshold. Given that the average Western diet consists of greater than 200 g of carbohydrate per day, it has been suggested that an intake of less than 150 g should be defined as low-carbohydrate. Many advocates of a low-carbohydrate diet would regard 50–100 g of carbohydrate as low-carbohydrate, while the extreme form of carbohydrate restriction, known as the ketogenic diet (see below), is less than 30–50 g per day.

All grains (whole or processed), legumes, starchy vegetables and most fruit are largely avoided, and are replaced with food containing a higher percentage of healthy fats and protein (e.g. meat, fish, eggs, dairy, nuts and seeds, olive oil). The percentage of fats and protein varies; one could follow a low-carbohydrate high-fat diet (with low to moderate protein), or a low-carbohydrate high-protein diet (with low to moderate fat). When discussing macronutrients, it becomes a balancing act.

Interest in low-carbohydrate diets is not a new phenomenon; they have been explored for diabetes management for decades. However, interest in low-carbohydrate eating has resurged in recent years.

There is a substantial and rapidly growing body of evidence indicating that low-carbohydrate diets are effective for weight loss and improving metabolic risk factors. The authors of a 2009 systematic review of randomised controlled trials of low-carbohydrate versus low-fat/low-calorie diets concluded that 'there were significant differences between the groups for weight, high-density lipoprotein cholesterol, triacylglycerols and systolic blood pressure, favouring the low-carbohydrate diet'.[276] Additionally, the authors found that there was a higher attrition rate in the low-fat compared with the low-carbohydrate groups.

Similarly, a 2012 meta-analysis of 23 randomised controlled clinical trials found that both low-carbohydrate and low-fat diets lowered weight and improved metabolic risk factors.[277] However, compared with individuals on low-fat diets, individuals on low-carbohydrate diets experienced a

significantly lower reduction in total cholesterol and LDL, as well as a greater increase in HDL cholesterol and a greater decrease in triglycerides.

High-protein

Since the boom of the Atkins diet in the early 2000s, different variations of low-carbohydrate high-protein diets have been increasingly popularised by the media as a promising strategy for weight loss and optimal health by improving satiety, decreasing fat mass and increasing lean body mass.

Long-term effects of high-protein diets depend on the population studied as well as the composition of their particular diet. In general, the diet has been shown to help weight loss and maintenance, as well as have beneficial effects on proposed metabolic risk factors. Lower triacylglycerol levels and fat mass loss, increased satiety (possibly mediated by increased leptin sensitivity), and fluid loss associated with reduced carbohydrate intake have all been discussed as potential underlying mechanisms.[278]

High fat—ketogenic

The ketogenic diet is a form of low-carbohydrate diet that reduces daily carbohydrate intake to approximately 20–30 g/day, although there is considerable variation in the amount of carbohydrate restriction required. A low carbohydrate intake forces the body to rely on fat as its primary fuel source—a state known as nutritional ketosis. The fuel source produced by the breakdown of fat is called 'ketone bodies' or simply 'ketones'.

In a ketogenic diet, the carbohydrate restriction is so severe that the only carbohydrates eaten come predominantly from green vegetables and nuts. It emphasises eating real foods high in fats and moderate protein, such as oily fish, eggs, butter, lard, liver and other organ meats, grass-fed beef and coconut and olive oils, and drinking bone broths, water and tea or coffee with cream.

The ketogenic diet continues to gain momentum in the sporting world, particularly in endurance events given the possibility of body fat being used as a primary energy source without the need to rely on limited glycogen stores. However, it is also increasingly being explored for general health and wellbeing, and for its application in particular conditions, such as diabetes. According to data from a 2018 online survey of over 300 people with type 1 diabetes who follow a very low-carbohydrate diet (36 ± 15 g of carbohydrates), a very low-carbohydrate diet can help people with type 1 diabetes maintain 'exceptional glycaemic control' with low rates of hypoglycaemia and other adverse events.[279]

Some people confuse nutritional ketosis with ketoacidosis. The latter is a serious medical emergency seen in type 1 diabetics, and is associated with blood ketone levels three to five times higher than those seen in nutritional ketosis—so it is not a concern for those on a ketogenic diet. Even in prolonged starvation ketosis, ketones do not typically rise beyond 6 mmol/L, which is well below the threshold of symptomatic ketoacidosis. Most people on low-carbohydrate diets will not produce ketone levels greater than 1.5 mmol/L.

Low-GI

The low-GI diet is similar to the above two diets, but perhaps not as severe as the ketogenic diet. In

simple terms, the diet promotes switching from high-GI carbohydrates (e.g. white bread and pasta) to lower-GI carbohydrates (e.g. whole grains, certain fruits and vegetables).

A low-GI diet may induce favourable metabolic effects—such as rapid weight loss, decrease of fasting glucose and insulin levels, reduction of circulating triglyceride levels and improvement of blood pressure.[280] However, there is a need for updated and better controlled studies testing these effects.

Paleo

Palaeolithic diets attempt to emulate the dietary patterns of our Stone Age ancestors with an emphasis on avoiding processed foods, while promoting the intake of vegetables, fruits, nuts, seeds, eggs and meats. Dairy and grains are avoided entirely.

A particular challenge in reaching conclusions about the Palaeolithic diet is the known variation in our ancestral dietary pattern and disagreement regarding its primary features. Many of the plant foods and nearly all of the animal foods consumed during the time of our hunter and gatherer ancestors are now extinct, and so replicating their diet may be easier said than done. Nonetheless, a number of trials using varying Palaeolithic diets have shown a range of health benefits, especially short-term improvements in metabolic syndrome components.[281]

Gluten-free

The avoidance of products containing wheat or gluten is a worldwide phenomenon that has given rise to a multibillion dollar industry that grows annually.[282] Gluten is a group of proteins found in wheat, barley, rye, oats and their derivatives. Gluten, which means 'glue' in Latin, gives elasticity to dough, enabling it to rise, and is responsible for the chewy texture of bread and other products.

Wheat contains hundreds of different proteins. Coeliac disease is characterised by an immune response to one specific protein and a specific enzyme, however it is not widely understood that individuals can and do react to several other components of wheat. There is increasing evidence that many individuals are sensitive to one of the wheat proteins,[283] a condition referred to as 'gluten sensitivity'.

Gluten sensitivity (and coeliac disease) does not necessarily present with gut symptoms, as it can affect nearly every tissue in the body.[284] Because of this and the inability to make a diagnosis on the basis of a simple test, a helpful way of determining if an individual has the condition is to trial a wheat-free diet.

The incidence of coeliac disease has increased over the past few decades, but it is still relatively uncommon, affecting 1% of Western populations.[283] Some individuals with coeliac-like symptoms, or sometimes non-bowel symptoms such as behaviour disturbances, test negative to coeliac disease yet respond very well to a gluten-free diet. This is referred to as 'non-coeliac gluten sensitivity', which may be induced by the consumption of fructans[285] (an oligosaccharide of the FODMAPs – see below).

Many individuals who are intolerant of gluten are also intolerant of other proteins found in foods such as dairy, eggs and coffee. Studies have shown that 50% of people with coeliac disease are

intolerant to casein, a protein found in milk.[286] This may explain why many individuals with coeliac disease continue to experience symptoms after adopting a gluten-free diet. For this reason, some recommend a completely grain- and dairy-free diet during the trial period.

Low-FODMAP

A proportion of people with irritable bowel syndrome (IBS), which causes symptoms such abdominal pain, bloating and diarrhoea, are sensitive to a group of carbohydrates known as FODMAPs[287]—an acronym that stands for:

- fermentable—meaning the carbohydrates are broken down (fermented) by bacteria in the large intestine
- oligosaccharides—'oligo' means 'few' and 'saccharide' means sugar. These are sugars longer than disaccharides and shorter than polysaccharides
- disaccharides—double sugars
- monosaccharides—single sugars
- polyols—sugar alcohols.

Due to poor absorption in the small intestine, FODMAPs transit to the distal small intestine and large bowel. Here they are osmotically active, attracting fluid and contributing to loose stool. FODMAPs may also be fermented by gut bacteria leading to gas production including hydrogen and methane, causing bloating.

Foods that contain FODMAPs include:

- vegetables—asparagus, onions, garlic, legumes, beetroot, celery, corn
- fruit—apples, pears, mangoes, watermelon, nectarines, peaches, plums
- dairy—cow's milk, yoghurt, soft cheese, cream, custard, ice cream
- grains—breads containing rye and wheat, wheat-based cereals with dried fruit, wheat pasta

As with gluten sensitivity, there is no one simple test to diagnose FODMAP sensitivity, so it may be recommended to trial the removal of all or particular FODMAPs from the diet.

Although removing these foods from one's diet is restrictive, a low-FODMAP diet is not designed to be permanent. It can be considered an elimination diet; it is highly restrictive for several weeks, and then foods are slowly reintroduced selectively to determine what, in particular, causes symptoms.

PRACTICE PEARL

The long-term health effects of adhering to a low-FODMAP diet, for relief of IBS symptoms or otherwise, are not known. Strict FODMAP avoidance is not recommended due to the risks of inadequate nutrient intake and potential adverse effects from altered gut microbiota.[290, 291]

Vegetarian and vegan

Vegetarian diets, also referred to as 'plant-based' diets, have exploded in popularity in recent years. As people continue to become more aware of the supposed health, ethical and environmental implications of their eating habits, they are increasingly turning away from animal products.

Page 70

The Blue Zones: dietary patterns of longevity

The 'Blue Zones', a term coined by *National Geographic* writer Dan Beuttner in 2005, are regions of the world where people live much longer than average. Buettner has identified five Blue Zones: Okinawa (Japan), Sardinia (Italy), Nicoya (Costa Rica), Icaria (Greece) and among the Seventh-day Adventists in Loma Linda, California (USA).

People living in these regions all share common lifestyle characteristics, such as social and family engagement, constant moderate physical activity throughout the day and not smoking.[304]

Although these factors, as well as genetics, may confound the impact of diet on their impressive longevity, their diets are remarkably similar and are based on common principles, including:

- moderate caloric intake
- moderate alcohol intake, mostly red wine; drink mostly water and tea
- whole foods plant-based, semi-vegetarian diet with very limited meat, fish, and sheep's or goats milk cheeses
- daily consumption of food from healthy fat sources, such as olives and nuts
- daily consumption of legumes
- no refined carbohydrates or added sugars.

The Blue Zones demonstrate an established theme of healthy eating, relevant across generations and geographical borders that could, theoretically, have a profound influence on public nutrition and dietary guidelines.

Vegetarian diets consist primarily of whole grains, vegetables, fruits, legumes, nuts and seeds. Variations include:

- lacto-ovo-vegetarian—includes dairy products and eggs
- lacto-vegetarian—includes dairy products but not eggs
- ovo-vegetarian—includes eggs but not dairy products
- vegan—does not include dairy products, eggs, or any other animal-derived products

Vegetarian diets have been associated with reductions in overall cardiovascular and cancer mortality;[290–292] long-term weight management;[293] glycaemic control;[294] decreased incidence and severity of high-risk conditions including obesity,[295] hypertension[296] and hyperlipidaemia;[297] and potential reversal of coronary artery disease[298, 299] and type 2 diabetes.[300]

However, it is often difficult to separate the observational effects of long-term vegetarian diets with other healthy lifestyle behaviours such regular exercise, avoidance of tobacco products and

moderation of alcohol intake. And importantly, eating only plant foods does not guarantee a nutritious diet, as sugar is of plant origin.

Although nutrient deficiency is a primary concern when considering a vegetarian diet, 'well-planned vegetarian diets are appropriate for individuals during all stages of the life cycle, including pregnancy, lactation, infancy, childhood, and adolescence, and for athletes'.[301] If ill-constructed however, vegetarian diets can combine the adverse effects of plant-based junk food with nutrient deficiencies.

PRACTICE PEARL

Vegans must ensure they obtain sufficient vitamin B_{12} from fortified food or supplements, and should consider supplementing their diet with algae-based omega-3 to obtain EPA and DHA, as the body is poor at converting α-linolenic acid (ALA) found in plant foods (e.g. flax seed, chia seeds and walnuts) to DHA.[147, 148]

Intermittent fasting

Also known as 'time-restricted feeding', intermittent fasting alternates periods of normal food intake with prolonged periods (usually 16–48 hours) of restricted or no food intake. Different variants of fasting diets include:

- 5:2 diet—calorie restriction for two non-consecutive days a week and unconstrained eating the other five days
- alternate-day fasting
- random meal skipping
- feeding window—eating only during a set 'window of time' every day (e.g. from 12 pm to 6 pm)

Although interest in fasting is increasing, due to reported benefits on metabolic health and physiological and molecular markers of health and longevity, clinical relevance remains low because of insufficient human data, lack of controlled trials and limited safety data.[303]

One interesting aspect associated with fasting diets is its proposed benefits on longevity, or 'delayed ageing'. Fasting catalyses regenerative processes in the body that reduce oxidative damage and inflammation, improve cellular protection and optimise energy metabolism.[304] Caloric restriction has been shown to extend lifespan in multiple animal models,[305] however it is not known whether fasting can extend human lifespan and, if it can, which variant of fasting is optimal.

Of course, the inability of most people to adhere to diets, especially restrictive diets such as fasting, somewhat limits fasting's feasibility. However, emerging evidence regarding 'fasting-mimicking' diets, characterised by consumption of a low-calorie diet for five days straight each month instead of completely fasting, suggests that periodic reduction of calorie intake can also

reduce markers and risk factors for ageing and age-related diseases.[306]

PRACTICE PEARL

Further clinical research in humans is needed before the use of fasting as a health intervention can be recommended to all patients.

SUMMARY

Different dietary approaches suit different people, and it is accepted that there is no one universal diet that is suitable for everyone. However, there is general agreement that a diet that is focused on real foods, and with minimal sugars, starches and ultra-processed foods, is most compatible with good health.

REFERENCES

1. Ioannidis JPA. Implausible results in human nutrition research. *BMJ* (Clinical research ed) 2013; 347:f6698.
2. Casazza K, Fontaine KR, Astrup A et al. Myths, presumptions, and facts about obesity. *N Engl J Med* 2013; 368:446–54.
3. Young SS, Karr A. Deming, data and observational studies. *Significance* 2011; 8:116–20.
4. Senate Select Committee on Nutrition and Human Needs. Dietary goals for the United States. 2nd ed. Washington D.C.: U.S. Government Printing Office, 1977.
5. USDA/HHS. Nutrition and your health: Dietary guidelines for Americans. 1st ed. Washington, DC: U.S: Goverment Printing Office, 1980.
6. Powles J, Wahlqvist ML, Robbins J et al. The development of food and nutrition policy in Australia, with special attention to the State of Victoria. *Asia Pac J Clin Nutr* 1992; 1(1):47–60.
7. Harcombe Z, Baker JS, Cooper SM et al. Evidence from randomised controlled trials did not support the introduction of dietary fat guidelines in 1977 and 1983: a systematic review and meta-analysis. *Open Heart* 2015; 2:e000196.
8. National Health and Medical Research Council (NHMRC). Australian Dietary Guidelines. Canberra, Australia 2013.
9. HHS/USDA. Dietary Guidelines for Americans 2015–2020. 8th ed. 2015.
10. British Nutrition Foundation. Nutrition Requirements 2016. Updated October 2016. https://www.nutrition.org.uk/attachments/article/234/Nutrition%20Requirements_Revised%20Oct%202016.pdf.
11. Hauber U, Bruce A, Neuhäuser-Berthold M. A comparison of dietary reference

values for energy of different countries. *Z. Ernahrungswissenschaft* 1997; 36:394–402.

12. Dehghan M, Mente A, Zhang X et al. Associations of fats and carbohydrate intake with cardiovascular disease and mortality in 18 countries from five continents (PURE): a prospective cohort study. *Lancet* 2017; 390(10107):2050–62.
13. Teicholz N. The scientific report guiding the US dietary guidelines: is it scientific? *BMJ* 2015; 351.
14. Harcombe Z. Designed by the food industry for wealth, not health: the 'Eatwell Guide'. *Br J Sports Med* 2017; 51:1730–1.
15. Schoffelen PFM, Plasqui G. Classical experiments in whole-body metabolism: open-circuit respirometry-diluted flow chamber, hood, or facemask systems. *Eur J Appl Physiol* 2018; 118(1):33–49.
16. Hargrove JL. History of the calorie in nutrition. *J Nutr* 2006; 136(12):2957–61.
17. World Health Organization (WHO). Food and Agriculture Organization of the United Nations (FAO). Carbohydrates in human nutrition. Rome, 1998.
18. Mather A, Pollock C. Glucose handling by the kidney. *Kidney Int* 2011; 79:S1–S6.
19. Gerich JE. Role of the kidney in normal glucose homeostasis and in the hyperglycaemia of diabetes mellitus: therapeutic implications. *Diabet Med* 2010; 27:136–42.
20. Westman EC, Feinman RD, Mavropoulos JC et al. Low-carbohydrate nutrition and metabolism. *Am J Clin Nutr* 2007; 86:276–84.
21. Mergenthaler P, Lindauer U, Dienel GA et al. Sugar for the brain: the role of glucose in physiological and pathological brain function. *Trends Neurosci* 2013; 36:587–97.
22. Falkowska A, Gutowska I, Goschorska M et al. Energy Metabolism of the Brain, Including the Cooperation between Astrocytes and Neurons, Especially in the Context of Glycogen Metabolism. *Int J Mol Sci* 2015; 16:25959–81.
23. Berg JM, Tymoczko JL, Stryer L. *Biochemistry* 5th ed. New York: WH Freeman, 2002; section 30.2.
24. Owen OE, Morgan AP, Kemp HG et al. Brain Metabolism during Fasting *J Clin Invest* 1967 Oct; 46(10): 1589–1595.
25. Martin K, Jackson CF, Levy RG et al. Ketogenic diet and other dietary treatments for epilepsy. *Cochrane Database Syst Rev* 2016; 2:Cd001903.
26. Institute of Medicine (US). *Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids*. Washington, DC: The National Academies Press; 2005.
27. Trumbo P, Schlicker S, Yates AA et al. Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein and Amino Acids. *J Am Diet Assoc* 2002; 102(11): 1621–30.
28. Leung C, Rivera L, Furness JB et al. The role of the gut microbiota in NAFLD. *Nat Rev Gastroenterol Hepatol* 2016; 13:412–25.

29. Payne AN, Chassard C, Lacroix C. Gut microbial adaptation to dietary consumption of fructose, artificial sweeteners and sugar alcohols: implications for host-microbe interactions contributing to obesity. *Obes Rev* 2012; 13:799–809.
30. Softic S, Cohen DE, Kahn CR. Role of Dietary Fructose and Hepatic De Novo Lipogenesis in Fatty Liver Disease. *Dig Dis Sci* 2016; 61:1282–93.
31. Stanhope KL, Schwarz JM, Keim NL et al. Consuming fructose-sweetened, not glucose-sweetened, beverages increases visceral adiposity and lipids and decreases insulin sensitivity in overweight/obese humans. *J Clin Invest* 2009; 119(5):1322–34.
32. WHO. Guideline: sugars intake for adults and children. Geneva, 2015.
33. Basu S, Yoffe P, Hills N et al. The relationship of sugar to population-level diabetes prevalence: an econometric analysis of repeated cross-sectional data. *PloS ONE* 2013; 8:e57873.
34. Malik VS, Popkin BM, Bray GA et al. Sugar-sweetened beverages and risk of metabolic syndrome and type 2 diabetes: a meta-analysis. *Diabetes Care* 2010; 33:2477–83.
35. Greenwood DC, Threapleton DE, Evans CEL et al. Association between sugar-sweetened and artificially sweetened soft drinks and type 2 diabetes: systematic review and dose-response meta-analysis of prospective studies. *Br J Nutr* 2014; 112:725–34.
36. Yang Q, Zhang Z, Gregg EW et al. Added sugar intake and cardiovascular diseases mortality among US adults. *JAMA Intern Med* 2014; 174:516–24.
37. Duffey KJ, Gordon-Larsen P, Steffen LM et al. Drinking caloric beverages increases the risk of adverse cardiometabolic outcomes in the Coronary Artery Risk Development in Young Adults (CARDIA) Study. *Am J Clin Nutr* 2010; 92:954–9.
38. Australian Bureau of Statistics. 4364.0.55.011 - Australian Health Survey: Consumption of added sugars, 2011–12 2016 [updated 27 April 2016. Available from: http://www.abs.gov.au/ausstats/abs@.nsf/mf/4364.0.55.011.
39. Australian Institute of Health and Welfare. 3.14 Oral health (Australia's health 2016). Canberra: AIHW; 2016.
40. Morenga LT, Mallard S, Mann J. Dietary sugars and body weight: systematic review and meta-analyses of randomised controlled trials and cohort studies. *BMJ* 2013; 346:e7492.
41. Marriott BP, Olsho L, Hadden L et al. Intake of added sugars and selected nutrients in the United States, National Health and Nutrition Examination Survey (NHANES) 2003–2006. *Crit Rev Food Sci Nutr* 2010; 50(3):228–58.
42. Mordor Intelligence. Food Sweetener Market—Growth, Trends, Forecast for the period (2018–2023). 2018.
43. Pase MP, Himali JJ, Beiser AS et al. Sugar- and artificially-sweetened beverages and the risks of incident stroke and dementia: A prospective cohort study. *Stroke* 2017;

48(5):1139–46.

44. Papier K, D'Este C, Bain C et al. Consumption of sugar-sweetened beverages and type 2 diabetes incidence in Thai adults: results from an 8-year prospective study. *Nutrition & Diabetes* 2017; 7:e283.
45. Fagherazzi G, Vilier A, Saes Sartorelli D et al. Consumption of artificially and sugar-sweetened beverages and incident type 2 diabetes in the Etude Epidemiologique aupres des femmes de la Mutuelle Generale de l'Education Nationale-European Prospective Investigation into Cancer and Nutrition cohort. *Am J Clin Nutr* 2013; 97(3):517–23.
46. Suez J, Korem T, Zeevi D et al. Artificial sweeteners induce glucose intolerance by altering the gut microbiota. *Nature* 2014; 514(7521):181–6.
47. Nettleton JA, Lutsey PL, Wang Y et al. Diet soda intake and risk of incident metabolic syndrome and type 2 diabetes in the Multi-Ethnic Study of Atherosclerosis (MESA). *Diabetes Care* 2009; 32(4):688–94.
48. Azad MB, Abou-Setta AM, Chauhan BF et al. Nonnutritive sweeteners and cardiometabolic health: a systematic review and meta-analysis of randomized controlled trials and prospective cohort studies. *CMAJ* 2017; 189(28):E929–e39.
49. Stewart ML, Nikhanj SD, Timm DA et al. Evaluation of the Effect of Four Fibers on Laxation, Gastrointestinal Tolerance and Serum Markers in Healthy Humans. *Ann Nutr Metab* 2010; 56:91–8.
50. Kaplan GG. Fiber and the Risk of Flaring in Patients With Inflammatory Bowel Diseases: Lessons From the Crohn's and Colitis Foundation of America Database. *Clin Gastroenterol Hepatol* 2016; 14:1137–9.
51. McNeil NI. The contribution of the large intestine to energy supplies in man. *Am J Clin Nutr* 1984; 39:338–42.
52. de Vries J, Miller PE, Verbeke K. Effects of cereal fiber on bowel function: A systematic review of intervention trials. *World J Gastroenterol* : WJG. 2015; 21:8952–63.
53. Eastwood MA, Robertson JA, Brydon WG et al. Measurement of water-holding properties of fibre and their faecal bulking ability in man. *Br J Nutr* 1983; 50:539–47.
54. Müller-Lissner SA, Kamm MA, Scarpignato C et al. Myths and misconceptions about chronic constipation. *Am J Gastroenterol* 2005; 100:232–42.
55. Markland AD, Palsson O, Goode PS et al. Association of low dietary intake of fiber and liquids with constipation: evidence from the National Health and Nutrition Examination Survey. *Am J Gastroenterol* 2013; 108:796–803.
56. Aune D, Chan DSM, Lau R et al. Dietary fibre, whole grains, and risk of colorectal cancer: systematic review and dose-response meta-analysis of prospective studies. *BMJ* 2011; 343.
57. Ho K-S, Tan CYM, Mohd Daud MA et al. Stopping or reducing dietary fiber intake reduces constipation and its associated symptoms. *World J Gastroenterol: WJG*. 2012;

18(33):4593–6.

58. Kim Y, Je Y. Dietary fiber intake and total mortality: a meta-analysis of prospective cohort studies. *Am J Epidemiol* 2014; 180:565–73.
59. Thursby E, Juge N. Introduction to the human gut microbiota. *Biochem J* 2017; 474(11):1823–36.
60. Mosca A, Leclerc M, Hugot JP. Gut microbiota diversity and human diseases: should we reintroduce key predators in our ecosystem? *Front Microbiol* 2016; 7.
61. Macfarlane GT, Gibson GR, Cummings JH. Comparison of fermentation reactions in different regions of the human colon. *J Appl Bacteriol* 1992; 72(1):57–64.
62. Rowland I, Gibson G, Heinken A et al. Gut microbiota functions: metabolism of nutrients and other food components. *Eur J Nutr* 2018; 57(1):1–24.
63. Neis EPJG, Dejong CHC, Rensen SS. The role of microbial amino acid metabolism in host metabolism. *Nutrients*. 2015; 7(4):2930–46.
64. David LA, Maurice CF, Carmody RN et al. Diet rapidly and reproducibly alters the human gut microbiome. *Nature* 2014; 505(7484):559–63.
65. Ardawi MS, Newsholme EA. Fuel utilization in colonocytes of the rat. *Biochem J* 1985; 231(3):713–9.
66. den Besten G, van Eunen K, Groen AK et al. The role of short-chain fatty acids in the interplay between diet, gut microbiota, and host energy metabolism. *J Lipid Res* 2013; 54(9):2325–40.
67. Hamer HM, Jonkers D, Venema K et al. Review article: the role of butyrate on colonic function. *Aliment Pharmacol Ther* 2008; Jan 15;27(2):104-19. DOI: 10.1111/j.1365-2036.2007.03562.x.
68. Singh RK, Chang H-W, Yan D et al. Influence of diet on the gut microbiome and implications for human health. *J Transl Med* 2017; 15:73.
69. Shreiner AB, Kao JY, Young VB. The gut microbiome in health and in disease. *Curr Opin Gastroenterol* 2015; 31(1):69–75.
70. Aydin Ö, Nieuwdorp M, Gerdes V. The Gut Microbiome as a Target for the Treatment of Type 2 Diabetes. *Curr Diab Rep* 2018; 18(8):55.
71. Collins J, Robinson C, Danhof H et al. Dietary trehalose enhances virulence of epidemic *Clostridium difficile*. *Nature* 2018; 553(7688):291–4.
72. van Beurden YH, Nieuwdorp M, van de Berg PJEJ et al. Current challenges in the treatment of severe Clostridium difficile infection: early treatment potential of fecal microbiota transplantation. Therapeutic Advances in Gastroenterology. 2017; 10(4):373–81.
73. Korem T, Zeevi D, Suez J et al. Growth dynamics of gut microbiota in health and disease inferred from single metagenomic samples. *Science* 2015; 349(6252):1101–6.
74. Zhang M, Yang X-J. Effects of a high fat diet on intestinal microbiota and gastrointestinal diseases. *World J Gastroenterol* 2016; 22(40):8905–9.

75. Ley RE, Turnbaugh PJ, Klein S et al. Microbial ecology: Human gut microbes associated with obesity. *Nature* 2006; 444(7122):1022–3.
76. Turnbaugh PJ, Ley RE, Mahowald MA et al. An obesity-associated gut microbiome with increased capacity for energy harvest. *Nature* 2006; 444(7122):1027–31.
77. Kristensen NB, Bryrup T, Allin KH et al. Alterations in fecal microbiota composition by probiotic supplementation in healthy adults: a systematic review of randomized controlled trials. *Genome Med* 2016; 8(1):52.
78. Walter J, Maldonado-Gómez MX, Martínez I. To engraft or not to engraft: an ecological framework for gut microbiome modulation with live microbes. *Curr Opin Biotechnol* 2018; 49:129–39.
79. Stubbs BJ, Cox PJ, Evans RD et al. A Ketone Ester Drink Lowers Human Ghrelin and Appetite. *Obesity* (Silver Spring, Md). 2018; 26(2):269–73.
80. Gibson AA, Seimon RV, Lee CMY et al. Do ketogenic diets really suppress appetite? A systematic review and meta-analysis. *Obes Rev* 2015; 16(1):64–76.
81. Nettleton JE, Reimer RA, Shearer J. Reshaping the gut microbiota: *Cell Metab* Impact of low calorie sweeteners and the link to insulin resistance? *Physiol Behav* 2016; 164:488–93.
82. Mäkinen KK. Gastrointestinal disturbances associated with the consumption of sugar alcohols with special consideration of xylitol: scientific review and instructions for dentists and other health-care professionals [Research article]. *Int J Dent* 2016. DOI: 10.1155/2016/5967907 2016
83. Blaser MJ. Antibiotic use and its consequences for the normal microbiome. *Science* (New York, NY). 2016; 352(6285):544–45.
84. Reijnders D, Goossens GH, Hermes GDA et al. Effects of gut microbiota manipulation by antibiotics on host metabolism in obese humans: a randomized double-blind placebo-controlled trial. 2016; 24(1):63–74.
85. Scheid MMA, Moreno YMF, Maróstica Junior MR et al. Effect of prebiotics on the health of the elderly. *Food Research International* 2013; 53(1):426–32.
86. Seksik P, Dray X, Sokol H et al. Is there any place for alimentary probiotics, prebiotics or synbiotics, for patients with inflammatory bowel disease? *Mol Nutr Food Res* 2008; 52(8):906–12.
87. Hemarajata P, Versalovic J. Effects of probiotics on gut microbiota: mechanisms of intestinal immunomodulation and neuromodulation. *Therap Adv Gastroenterol* 2013; 6(1):39–51.
88. Issa I, Moucari R. Probiotics for antibiotic-associated diarrhea: Do we have a verdict? *World J Gastroenterol* 2014; 20(47):17788–95.
89. Rather IA, Bajpai VK, Kumar S et al. Probiotics and atopic dermatitis: an overview. *Front Microbiol* 2016; 7:507.
90. Wallace CJK, Milev R. The effects of probiotics on depressive symptoms in humans: a

systematic review. *Ann Gen Psychiatry* 2017; 16:14.

91. Panigrahi P, Parida S, Nanda NC et al. A randomized synbiotic trial to prevent sepsis among infants in rural India. *Nature* 2017; 548(7668):407–12.
92. Feinberg M, Miller L, Engers B et al. Reduced necrotizing enterocolitis after an Initiative to promote breastfeeding and early human milk administration. *Pediatr Qual Saf* 2017; 2(2):e014.
93. Genton L, Melzer K, Pichard C. Energy and macronutrient requirements for physical fitness in exercising subjects. *Clin Nutr* 2010; 29:413–23.
94. Young VR. Adult amino acid requirements: the case for a major revision in current recommendations. *J Nutr* 1994; 124:1517S–23S.
95. Brosnan JT. Interorgan amino acid transport and its regulation. *J Nutr* 2003; 133:2068S-72S.
96. Bilsborough S, Mann N. A review of issues of dietary protein intake in humans. *Int J Sport Nutr Exerc Metab* 2006; 16:129–52.
97. Campbell WW, Crim MC, Dallal GE et al. Increased protein requirements in elderly people: new data and retrospective reassessments. *Am J Clin Nutr* 1994; 60:501–9.
98. Wolfe RR, Miller SL, Miller KB. Optimal protein intake in the elderly. *Clin Nutr* (Edinburgh, Scotland). 2008; 27: 675–84.
99. Elango R, Humayun MA, Ball RO et al. Evidence that protein requirements have been significantly underestimated. *Curr Opin Clin Nutr Metab Care* 2010; 13:52–7.
100. Baum JI, Kim I-Y, Wolfe RR. Protein consumption and the elderly: what is the optimal level of intake? *Nutrients* 2016; 8.
101. Volpi E, Campbell WW, Dwyer JT et al. Is the optimal level of protein intake for older adults greater than the recommended dietary allowance? *J Gerontol A Biol Sci Med Sci* 2013; 68:677–81.
102. Lemon PW. Beyond the zone: protein needs of active individuals. *J Am Coll Nutr* 2000; 19:513S–21S.
103. Tarnopolsky MA, Atkinson SA, MacDougall JD et al. Evaluation of protein requirements for trained strength athletes. *J Appl Physiol (1985)* 1992; 73:1986–95.
104. Schröder S, Fischer A, Vock C et al. Nutrition concepts for elite distance runners based on macronutrient and energy expenditure. *J Athl Train* 2008; 43:489–504.
105. Heaney RP. Protein intake and the calcium economy. *J Am Diet Assoc* 1993; 93:1259–60.
106. Cao JJ. High Dietary Protein Intake and Protein-Related Acid Load on Bone Health. *Curr Osteoporos Rep* 2017; 15:571–6.
107. Shams-White MM, Chung M, Du M et al. Dietary protein and bone health: a systematic review and meta-analysis from the National Osteoporosis Foundation. *Am J Clin Nutr* 2017; 105:1528–43.

108. Fung TT, Meyer HE, Willett WC et al. Protein intake and risk of hip fractures in postmenopausal women and men age 50 and older. *Osteoporos Int* 2017; 28:1401–11.
109. Levey AS, Greene T, Sarnak MJ et al. Effect of dietary protein restriction on the progression of kidney disease: long-term follow-up of the Modification of Diet in Renal Disease (MDRD) Study. *Am J Kidney Dis* 2006; 48:879–88.
110. Nuttall FQ, Gannon MC. Metabolic response of people with type 2 diabetes to a high protein diet. *Nutr Metab (Lond)* 2004; 1:6.
111. Martin WF, Armstrong LE, Rodriguez NR. Dietary protein intake and renal function. *Nutr Metab (Lond)* 2005; 2:25.
112. Antonio J, Ellerbroek A, Silver T et al. A High Protein Diet Has No *Harmful* Effects: A One-Year Crossover Study in Resistance-Trained Males. *J Nutr Metab* 2016; 2016:9104792.
113. McMurray RG, Soares J, Caspersen CJ et al. Examining variations of resting metabolic rate of adults: a public health perspective. *Med Sci Sports Exerc* 2014; 46:1352–8.
114. Hoffman JR, Falvo MJ. Protein—Which is Best? *J Sports Sci Med* 2004; 3:118–30.
115. Hamley S. The effect of replacing saturated fat with mostly n-6 polyunsaturated fat on coronary heart disease: a meta-analysis of randomised controlled trials. *Nutr J* 2017; 16(1):30.
116. Marinangeli CPF, House JD. Potential impact of the digestible indispensable amino acid score as a measure of protein quality on dietary regulations and health. *Nutr Rev* 2017; 75:658–67.
117. Mathai JK, Liu Y, Stein HH. Values for digestible indispensable amino acid scores (DIAAS) for some dairy and plant proteins may better describe protein quality than values calculated using the concept for protein digestibility-corrected amino acid scores (PDCAAS). *Br J Nutr* 2017; 117:490–9.
118. Guéraud F, Atalay M, Bresgen N et al. Chemistry and biochemistry of lipid peroxidation products. *Free Radic Res* 2010; 44:1098–124.
119. Uchida K. Role of reactive aldehyde in cardiovascular diseases. *Free Radic Biol Med* 2000; 28:1685–96.
120. Tsuji A. Small molecular drug transfer across the blood-brain barrier via carrier-mediated transport systems. *NeuroRx* 2005; 2:54–62.
121. Papamandjaris AA, MacDougall DE, Jones PJ. Medium chain fatty acid metabolism and energy expenditure: obesity treatment implications. *Life Sci* 1998; 62:1203–15.
122. VanItallie TB. Ancel Keys: a tribute. *Nutrition & Metabolism* 2005; 2:4.
123. McNamara DJ. Dietary cholesterol, heart disease risk and cognitive dissonance. *Proc Nutr Soc* 2014; 73(2):161–6.
124. Djousse L, Gaziano JM. Egg consumption in relation to cardiovascular disease and mortality: the Physicians' Health Study. *Am J Clin Nutr* 2008; 87(4):964–9.

125. Blesso CN, Andersen CJ, Barona J et al. Whole egg consumption improves lipoprotein profiles and insulin sensitivity to a greater extent than yolk-free egg substitute in individuals with metabolic syndrome. *Metabolism* 2013; 62(3):400–10.
126. Fuller NR, Caterson ID, Sainsbury A et al. The effect of a high-egg diet on cardiovascular risk factors in people with type 2 diabetes: the Diabetes and Egg (DIABEGG) study-a 3-mo randomized controlled trial. *Am J Clin Nutr* 2015; 101(4):705–13.
127. Qin C, Lv J, Guo Y et al. Associations of egg consumption with cardiovascular disease in a cohort study of 0.5 million Chinese adults. *Heart* 2018: heartjnl-2017–312651.
128. Ahrens EH. The diet-heart question in 1985: has it really been settled? *Lancet* (London, England). 1985; 1:1085–7.
129. Keys A. Atherosclerosis: a problem in newer public health. *J Mt Sinai Hosp N Y* 1953; 20:118–39.
130. Yerushalmy J, Hilleboe HE. Fat in the diet and mortality from heart disease; a methodologic note. *N Y State J Med* 1957; 57(14):2343–54.
131. Hamley S. The effect of replacing saturated fat with mostly n-6 polyunsaturated fat on coronary heart disease: a meta-analysis of randomised controlled trials. *Nutr J* 2017; 16:30.
132. Yusuf S, Hawken S, Ôunpuu S et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet* 2004; 364(9438):937–52.
133. Mensink RP, Zock PL, Kester AD et al. Effects of dietary fatty acids and carbohydrates on the ratio of serum total to HDL cholesterol and on serum lipids and apolipoproteins: a meta-analysis of 60 controlled trials. *Am J Clin Nutr* 2003; 77(5):1146–55.
134. Chowdhury R, Warnakula S, Kunutsor S et al. Association of dietary, circulating, and supplement fatty acids with coronary risk: a systematic review and meta-analysis. *Ann Intern Med* 2014; 160:398–406.
135. Schwingshackl L, Hoffmann G. Dietary fatty acids in the secondary prevention of coronary heart disease: a systematic review, meta-analysis and meta-regression. *BMJ Open* 2014; 4:e004487.
136. Joris PJ, Mensink RP. Role of cis-Monounsaturated Fatty Acids in the Prevention of Coronary Heart Disease. *Curr Atheroscler Rep* 2016; 18:38.
137. Degirolamo C, Shelness GS, Rudel LL. LDL cholesteryl oleate as a predictor for atherosclerosis: evidence from human and animal studies on dietary fat. *J Lipid Res* 2009; 50 Suppl:S434–9.
138. Gillingham LG, Harris-Janz S, Jones PJH. Dietary monounsaturated fatty acids are protective against metabolic syndrome and cardiovascular disease risk factors. *Lipids* 2011; 46:209–28.

139. Lucas L, Russell A, Keast R. Molecular mechanisms of inflammation. Anti-inflammatory benefits of virgin olive oil and the phenolic compound oleocanthal. *Curr Pharm Des* 2011; 17:754–68.
140. Burdge GC, Calder PC. Introduction to fatty acids and lipids. Intravenous lipid emulsions. *World Rev Nutr Diet* 2015; 112:1–16.
141. Calder PC. Omega-3 Fatty acids and inflammatory processes. *Nutrients* 2010; 2(3):355–74.
142. Baker EJ, Miles EA, Burdge GC et al. Metabolism and functional effects of plant-derived omega-3 fatty acids in humans. *Prog Lipid Res* 2016; 64:30–56.
143. Simopoulos AP. The importance of the omega-6/omega-3 fatty acid ratio in cardiovascular disease and other chronic diseases. *Exp Biol Med (Maywood)* 2008; 233(6):674–88.
144. Burdge GC, Wootton SA. Conversion of alpha-linolenic acid to eicosapentaenoic, docosapentaenoic and docosahexaenoic acids in young women. *Br J Nutr* 2002; 88(4):411–20.
145. Emken EA. Nutrition and biochemistry of trans and positional fatty acid isomers in hydrogenated oils. *Annu Rev Nutr* 1984; 4:339–76.
146. Calder PC. Omega-3 fatty acids and inflammatory processes: from molecules to man. *Biochem Soc Trans* 2017; 45:1105–15.
147. Brenna JT. Efficiency of conversion of alpha-linolenic acid to long chain n-3 fatty acids in man. *Curr Opin Clin Nutr Metab Care* 2002; 5(2):127–32.
148. Gerster H. Can adults adequately convert alpha-linolenic acid (18:3n-3) to eicosapentaenoic acid (20:5n-3) and docosahexaenoic acid (22:6n-3)? *Int J Vitam Nutr Res* 1998; 68(3):159–73.
149. Siscovick DS, Raghunathan TE, King I et al. Dietary intake and cell membrane levels of long-chain n-3 polyunsaturated fatty acids and the risk of primary cardiac arrest. *JAMA* 1995; 274:1363–7.
150. Albert CM, Campos H, Stampfer MJ et al. Blood levels of long-chain n-3 fatty acids and the risk of sudden death. *N Engl J Med* 2002; 346:1113–8.
151. von Schacky C. Omega-3 Index and Cardiovascular Health. *Nutrients* 2014; 6:799–814.
152. Ramana KV, Srivastava S, Singhal SS. Lipid peroxidation products in human health and disease [Research article]. 2013 Oxid Med Cell Longev 2014; :162414.
153. Shoeb M, Ansari NH, Srivastava SK et al. 4-hydroxynonenal in the pathogenesis and progression of human diseases. *Curr Med Chem* 2014; 21:230–7.
154. Stender S, Astrup A, Dyerberg J. Ruminant and industrially produced trans fatty acids: health aspects. *Food Nutr Res* 2008; 52.
155. Remig V, Franklin B, Margolis S et al. Trans fats in America: a review of their use, consumption, health implications, and regulation. *J Am Diet Assoc* 2010; 110:585–92.
156. Souza RJd, Mente A, Maroleanu A et al. Intake of saturated and trans unsaturated

fatty acids and risk of all cause mortality, cardiovascular disease, and type 2 diabetes: systematic review and meta-analysis of observational studies. *BMJ* 2015; 351:h3978.

157. Dawczynski C, Lorkowski S. Trans-fatty acids and cardiovascular risk: does origin matter? *Expert Rev Cardiovasc Ther* 2016; 14:1001–5.
158. Ratnayake WN, Swist E, Zoka R et al. Mandatory trans fat labeling regulations and nationwide product reformulations to reduce trans fatty acid content in foods contributed to lowered concentrations of trans fat in Canadian women's breast milk samples collected in 2009–2011. *Am J Clin Nutr* 2014; 100:1036–40.
159. Downs SM, Thow AM, Leeder SR. The effectiveness of policies for reducing dietary trans fat: a systematic review of the evidence. *Bull World Health Organ* 2013; 91:262–9H.
160. Wanders AJ, Zock PL, Brouwer IA. Trans Fat Intake and Its Dietary Sources in General Populations Worldwide: A Systematic Review. *Nutrients* 2017; 9.
161. Vreeman RC, Carroll AE. Medical myths. *BMJ* 2007; 335(7633):1288–9.
162. Valtin H. "Drink at least eight glasses of water a day." Really? Is there scientific evidence for "8 × 8"? *Am J Physiol Regul Integr Comp Physiol* 2002; 283(5):R993–1004.
163. NHMRC. Nutrient Reference Values for Australia and New Zealand: Water 2014 [updated 9 April 2014. Available from: https://www.nrv.gov.au/nutrients/water.
164. The Food and Nutrition Board. Dietary Reference Intakes: Water, Potassium, Sodium, Chloride, and Sulfate 2004 [Available from: http://www.nationalacademies.org/hmd/Reports/2004/Dietary-Reference-Intakes-Water-Potassium-Sodium-Chloride-and-Sulfate.aspx.
165. British Nutrition Foundation. Healthy hydration guide 2013 [updated January 2016. Available from: https://www.nutrition.org.uk/healthyliving/hydration/healthy-hydration-guide.html.
166. Hew-Butler T, Rosner MH, Fowkes-Godek S et al. Statement of the Third International Exercise-Associated Hyponatremia Consensus Development Conference, Carlsbad, California, 2015. *Clin J Sport Med* 2015; 25(4):303–20.
167. Noakes TD. Is drinking to thirst optimum? *Ann Nutr Metab* 2010; 57 Suppl 2:9–17.
168. Rehm J. The Risks Associated With Alcohol Use and Alcoholism. *Alcohol Res Health* 2011; 34(2):135–43.
169. NHMRC. Australian Guidelines to Reduce Health Risks from Drinking Alcohol. Canberra, Australia 2009.
170. Wood AM, Kaptoge S, Butterworth AS et al. Risk thresholds for alcohol consumption: combined analysis of individual-participant data for 599–912 current drinkers in 83 prospective studies. *Lancet* 2018; 391(10129):1513–23.
171. Mostofsky E, Mukamal KJ, Giovannucci EL et al. Key Findings on Alcohol Consumption and a Variety of Health Outcomes From the Nurses' Health Study. *Am J*

Public Health 2016; 106(9):1586–91.

172. Das DK, Mukherjee S, Ray D. Resveratrol and red wine, healthy heart and longevity. *Heart Fail Rev* 2010; 15(5):467–77.
173. Liberale L, Bonaventura A, Montecucco F et al. Impact of Red Wine Consumption on Cardiovascular Health. *Curr Med Chem* 2017.
174. Wikoff D, Welsh BT, Henderson R et al. Systematic review of the potential adverse effects of caffeine consumption in healthy adults, pregnant women, adolescents, and children. *Food Chem Toxicol* 2017; 109(Pt 1):585–648.
175. Grosso G, Godos J, Galvano F et al. Coffee, Caffeine, and Health Outcomes: An Umbrella Review. *Annu Rev Nutr* 2017; 37(1):131–56.
176. Nehlig A. Effects of coffee/caffeine on brain health and disease: What should I tell my patients? *Pract Neurol* 2016; 16(2):89–95.
177. Burnett AJ, Livingstone KM, Woods JL et al. Dietary Supplement Use among Australian Adults: Findings from the 2011–2012 National Nutrition and Physical Activity Survey. *Nutrients* 2017; 9(11):1248.
178. Manson JE, Bassuk SS. Vitamin and mineral supplements: What clinicians need to know. *JAMA* 2018; 319(9):859–60.
179. Rautiainen S, Manson JE, Lichtenstein AH et al. Dietary supplements and disease prevention—a global overview. *Nat Rev Endocrinol* 2016; 12(7):407–20.
180. Oxford English Dictionary, online edition. 2014.
181. Hathcock JN, Hattan DG, Jenkins MY et al. Evaluation of vitamin A toxicity. *Am J Clin Nutr* 1990; 52(2):183–202.
182. DeLuca HF. Overview of general physiologic features and functions of vitamin D. *Am J Clin Nutr* 2004; 80(6 Suppl):1689s-96s.
183. Schöttker B, Jorde R, Peasey A et al. Vitamin D and mortality: meta-analysis of individual participant data from a large consortium of cohort studies from Europe and the United States. *BMJ* 2014; 348.
184. Wacker M, Holick MF. Sunlight and Vitamin D: A global perspective for health. *Dermatoendocrinol* 2013; 5(1):51–108.
185. Holick MF. McCollum Award Lecture, 1994: vitamin D—new horizons for the 21st century. *Am J Clin Nutr* 1994; 60(4):619–30.
186. NHMRC. Nutrient Reference Values for Australia and New Zealand: Vitamin D 2014 [Available from: https://www.nrv.gov.au/nutrients/vitamin-d.]
187. Ross AC, Manson JE, Abrams SA et al. The 2011 Report on dietary reference intakes for calcium and vitamin D from the institute of medicine: what clinicians need to know. *J Clin Endocrinol Metab* 2011; 96(1):53–8.
188. Holick MF. Vitamin D: a D-Lightful health perspective. *Nutr Rev* 2008; 66(10 Suppl 2):S182–94.

189. Bischoff-Ferrari HA, Dawson-Hughes B, Staehelin HB et al. Fall prevention with supplemental and active forms of vitamin D: a meta-analysis of randomised controlled trials. *BMJ* 2009; 339:b3692.
190. Azzi A, Gysin R, Kempna P et al. Vitamin E mediates cell signaling and regulation of gene expression. *Ann N Y Acad Sci* 2004; 1031:86–95.
191. Farrell PM, Bieri JG, Fratantoni JF et al. The occurrence and effects of human vitamin E deficiency: a study in patients with cystic fibrosis. *J Clin Invest* 1977; 60(1):233–41.
192. Miller ER, 3rd, Pastor-Barriuso R, Dalal D et al. Meta-analysis: high-dosage vitamin E supplementation may increase all-cause mortality. *Ann Intern Med* 2005; 142(1):37–46.
193. Maresz K. Proper Calcium Use: Vitamin K(2) as a Promoter of Bone and Cardiovascular Health. *Integr Med (Encinitas)* 2015; 14(1):34–9.
194. Schwalfenberg GK. Vitamins K1 and K2: The Emerging Group of Vitamins Required for Human Health. *J Nutr Metab* 2017; 2017:6254836.
195. Okano T, Shimomura Y, Yamane M et al. Conversion of phylloquinone (Vitamin K1) into menaquinone-4 (Vitamin K2) in mice: two possible routes for menaquinone-4 accumulation in cerebra of mice. *J Biol Chem* 2008; 283(17):11270–9.
196. Conly JM, Stein K, Worobetz L et al. The contribution of vitamin K2 (menaquinones) produced by the intestinal microflora to human nutritional requirements for vitamin K. *Am J Gastroenterol* 1994; 89(6):915–23.
197. Ellsworth MA, Anderson KR, Hall DJ et al. Acute liver failure secondary to niacin toxicity. *Case Rep Pediatr* 2014; 2014:692530.
198. Hegyi J, Schwartz RA, Hegyi V. Pellagra: dermatitis, dementia, and diarrhea. *Int J Dermatol* 2004; 43(1):1–5.
199. Halsted CH, Villanueva JA, Devlin AM et al. Metabolic Interactions of Alcohol and Folate. *J Nutr* 2002; 132(8):2367S–72S.
200. Pitkin RM. Folate and neural tube defects. *Am J Clin Nutr* 2007; 85(1):285s-8s.
201. Folic acid for the prevention of neural tube defects: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med* 2009; 150(9):626–31.
202. Heidelbaugh JJ. Proton pump inhibitors and risk of vitamin and mineral deficiency: evidence and clinical implications. *Ther Adv Drug Saf* 2013; 4(3):125–33.
203. Padayatty SJ, Katz A, Wang Y et al. Vitamin C as an antioxidant: evaluation of its role in disease prevention. *J Am Coll Nutr* 2003; 22(1):18–35.
204. Baron JH. Sailors' scurvy before and after James Lind—a reassessment. *Nutr Rev* 2009; 67(6):315–32.
205. Hemila H, Chalker E. Vitamin C for preventing and treating the common cold. *Cochrane Database Syst Rev* 2013(1):Cd000980.
206. Beto JA. The Role of Calcium in Human Aging. *Clin Nutr Res* 2015; 4(1):1–8.

207. Burckhardt P. Calcium revisited: part I. *Bonekey Rep* 2013; 2:433.
208. Buzinaro EF, Almeida RN, Mazeto GM. [Bioavailability of dietary calcium]. *Arq Bras Endocrinol Metabol* 2006; 50(5):852–61.
209. Christakos S, Dhawan P, Porta A et al. Vitamin D and intestinal calcium absorption. *Mol Cell Endocrinol* 2011; 347(1–2):25–9.
210. Cooper MS, Gittoes NJL. Diagnosis and management of hypocalcaemia. *BMJ* 2008; 336(7656):1298–302.
211. Carroll R, Matfin G. Endocrine and metabolic emergencies: hypercalcaemia. *Ther Adv Endocrinol Metab* 2010; 1(5):225–34.
212. Bolland MJ, Leung W, Tai V et al. Calcium intake and risk of fracture: systematic review. *BMJ* 2015; 351.
213. Michaelsson K, Wolk A, Langenskiold S et al. Milk intake and risk of mortality and fractures in women and men: cohort studies. *BMJ* 2014; 349:g6015.
214. Anderson JJB, Kruszka B, Delaney JAC et al. Calcium intake from diet and supplements and the risk of coronary artery calcification and its progression among older adults: 10-year follow-up of the multi-ethnic study of atherosclerosis (MESA). *J Am Heart Assoc* 2016; 5(10).
215. Jahnen-Dechent W, Ketteler M. Magnesium basics. *Clin Kidney J* 2012; 5(Suppl 1):i3-i14.
216. Reis MA, Reyes FG, Saad MJ et al. Magnesium deficiency modulates the insulin signaling pathway in liver but not muscle of rats. *J Nutr* 2000; 130(2):133–8.
217. DiNicolantonio JJ, O'Keefe JH, Wilson W. Subclinical magnesium deficiency: a principal driver of cardiovascular disease and a public health crisis. *Open Heart* 2018; 5(1):e000668.
218. Guo W, Nazim H, Liang Z et al. Magnesium deficiency in plants: An urgent problem. *The Crop Journal* 2016; 4(2):83–91.
219. Rosanoff A, Dai Q, Shapses SA. Essential Nutrient Interactions: Does Low or Suboptimal Magnesium Status Interact with Vitamin D and/or Calcium Status? *Adv Nutr* 2016; 7(1):25–43.
220. Rosanoff A. [Magnesium and hypertension]. *Clin Calcium* 2005; 15(2):255–60.
221. Mooren FC, Kruger K, Volker K et al. Oral magnesium supplementation reduces insulin resistance in non-diabetic subjects - a double-blind, placebo-controlled, randomized trial. *Diabetes Obes Metab* 2011; 13(3):281–4.
222. Geiger H, Wanner C. Magnesium in disease. *Clin Kidney J* 2012; 5(Suppl 1):i25-i38.
223. Sebo P, Cerutti B, Haller DM. Effect of magnesium therapy on nocturnal leg cramps: a systematic review of randomized controlled trials with meta-analysis using simulations. *Fam Pract* 2014; 31(1):7–19.
224. Garrison SR, Allan GM, Sekhon RK et al. Magnesium for skeletal muscle cramps. *Cochrane Database Syst Rev* 2012(9):Cd009402.

225. Weaver CM. Potassium and health. *Adv Nutr* 2013; 4(3):368s-77s.
226. Cappuccio FP, Buchanan LA, Ji C et al. Systematic review and meta-analysis of randomised controlled trials on the effects of potassium supplements on serum potassium and creatinine. *BMJ Open* 2016; 6(8).
227. Chakraborti S, Chakraborti T, Mandal M et al. Protective role of magnesium in cardiovascular diseases: A review. *Mol Cell Biochem* 2002; 238(1):163–79.
228. Kalogeropoulos AP, Georgiopoulou VV, Murphy RA et al. Dietary sodium content, mortality, and risk for cardiovascular events in older adults: the Health, Aging, and Body Composition (Health ABC) Study. *JAMA Intern Med* 2015; 175(3):410–9.
229. Graudal N, Jurgens G, Baslund B et al. Compared with usual sodium intake, low- and excessive-sodium diets are associated with increased mortality: a meta-analysis. *Am J Hypertens* 2014; 27(9):1129–37.
230. O'Donnell M, Mente A, Rangarajan S et al. Urinary sodium and potassium excretion, mortality, and cardiovascular events. *N Engl J Med* 2014; 371(7):612–23.
231. Kapil U. Health consequences of iodine deficiency. *Sultan Qaboos Univ Med J* 2007; 7(3):267–72.
232. Girelli D, Nemeth E, Swinkels DW. Hepcidin in the diagnosis of iron disorders. *Blood* 2016; 127(23):2809–13.
233. Teucher B, Olivares M, Cori H. Enhancers of iron absorption: ascorbic acid and other organic acids. *Int J Vitam Nutr Res* 2004; 74(6):403–19.
234. Zijp IM, Korver O, Tijburg LB. Effect of tea and other dietary factors on iron absorption. *Crit Rev Food Sci Nutr* 2000; 40(5):371–98.
235. Johnson-Wimbley TD, Graham DY. Diagnosis and management of iron deficiency anemia in the 21st century. *Therap Adv Gastroenterol* 2011; 4(3):177–84.
236. Cole CR, Lifshitz F. Zinc nutrition and growth retardation. *Pediatr Endocrinol Rev* 2008; 5(4):889–96.
237. Prasad AS. Clinical manifestations of zinc deficiency. *Annu Rev Nutr* 1985; 5:341–63.
238. Duncan A, Yacoubian C, Watson N et al. The risk of copper deficiency in patients prescribed zinc supplements. *J Clin Pathol* 2015; 68(9):723–5.
239. Mann T, Tomiyama AJ, Westling E et al. Medicare's search for effective obesity treatments: diets are not the answer. *Am Psychol* 2007; 62(3):220–33.
240. Polidori D, Sanghvi A, Seeley RJ et al. How strongly does appetite counter weight loss? quantification of the feedback control of human energy intake. *Obesity (Silver Spring)* 2016; 24(11):2289–95.
241. Nicholas F. Low-calorie diets and sustained weight loss. *Obes Res* 2001; 9(S11):290S-4S.
242. Gilden TA, A. WT. The evolution of very-low-calorie diets: an update and meta-analysis. *Obesity (Silver Spring)* 2006; 14(8):1283–93.

243. Leeds AR. Formula food-reducing diets:A new evidence-based addition to the weight management tool box. *Nutr Bull* 2014; 39(3):238–46.
244. Tobias DK, Chen M, Manson JE et al. Effect of low-fat diet interventions versus other diet interventions on long-term weight change in adults: a systematic review and meta-analysis. *Lancet Diabetes Endocrinol* 2015; 3(12):968–79.
245. Acheson KJ, Schutz Y, Bessard T et al. Glycogen storage capacity and de novo lipogenesis during massive carbohydrate overfeeding in man. *Am J Clin Nutr* 1988; 48(2):240–7.
246. Schwarz JM, Clearfield M, Mulligan K. Conversion of sugar to fat: is hepatic de novo lipogenesis leading to metabolic syndrome and associated chronic diseases? *J Am Osteopath Assoc* 2017; 117(8):520–7.
247. Hellerstein MK. De novo lipogenesis in humans: metabolic and regulatory aspects. *Eur J Clin Nutr* 1999; 53 Suppl 1:S53–65.
248. Chandler-Laney PC, Morrison SA, Goree LLT et al. Return of hunger following a relatively high carbohydrate breakfast is associated with earlier recorded glucose peak and nadir. *Appetite* 2014; 80:236–41.
249. Huang PL. A comprehensive definition for metabolic syndrome. *Dis Model Mech* 2009; 2(5–6):231–7.
250. Ausk KJ, Boyko EJ, Ioannou GN. Insulin Resistance Predicts Mortality in Nondiabetic Individuals in the U.S. *Diabetes Care* 2010; 33(6):1179–85.
251. Mottillo S, Filion KB, Genest J et al. The metabolic syndrome and cardiovascular risk a systematic review and meta-analysis. *J Am Coll Cardiol* 2010; 56(14):1113–32.
252. Zimmet PZ, Alberti KG, Shaw JE. Mainstreaming the metabolic syndrome: a definitive definition. *Med J Aust* 2005; 183(4):175–6.
253. Erion DM, Shulman GI. Diacylglycerol-mediated insulin resistance. *Nat Med* 2010; 16(4):400–2.
254. Sanders FW, Griffin JL. De novo lipogenesis in the liver in health and disease: more than just a shunting yard for glucose. *Biol Rev Camb Philos Soc* 2016; 91(2):452–68.
255. Widmer RJ, Flammer AJ, Lerman LO et al. The mediterranean diet, its components, and cardiovascular disease. *Am J Med* 2015; 128(3):229–38.
256. Schwingshackl L, Hoffmann G. Adherence to Mediterranean diet and risk of cancer: a systematic review and meta-analysis of observational studies. *Int J Cancer* 2014; 135(8):1884–97.
257. Turati F, Carioli G, Bravi F et al. Mediterranean Diet and Breast Cancer Risk. *Nutrients* 2018; 10(3).
258. Sánchez-Villegas A, Martínez-González MA, Estruch R et al. Mediterranean dietary pattern and depression: the PREDIMED randomized trial. *BMC Medicine* 2013; 11:208-.
259. Sanchez-Villegas A, Henriquez P, Bes-Rastrollo M et al. Mediterranean diet and depression. *Public Health Nutr* 2006; 9(8a):1104–9.

260. Georgoulis M, Kontogianni MD, Yiannakouris N. Mediterranean Diet and Diabetes: Prevention and Treatment. *Nutrients* 2014; 6(4):1406–23.
261. Esposito K, Maiorino MI, Bellastella G et al. Mediterranean diet for type 2 diabetes: cardiometabolic benefits. *Endocrine* 2017; 56(1):27–32.
262. Bendall CL, Mayr HL, Opie RS et al. Central obesity and the Mediterranean diet: A systematic review of intervention trials. *Crit Rev Food Sci Nutr* 2017: 1–15.
263. Di Francesco S, Tenaglia RL. Mediterranean diet and erectile dysfunction: a current perspective. *Cent European J Urol* 2017; 70(2):185–7.
264. Sofi F, Cesari F, Abbate R et al. Adherence to Mediterranean diet and health status: meta-analysis. *BMJ* 2008; 337.
265. Schwingshackl L, Hoffmann G. Mediterranean dietary pattern, inflammation and endothelial function: a systematic review and meta-analysis of intervention trials. *Nutr Metab Cardiovasc Dis* 2014; 24(9):929–39.
266. Knoops KB, de Groot LM, Kromhout D et al. Mediterranean diet, lifestyle factors, and 10-year mortality in elderly european men and women: The hale project. *JAMA* 2004; 292(12):1433–9.
267. Psaltopoulou T, Kosti RI, Haidopoulos D et al. Olive oil intake is inversely related to cancer prevalence: a systematic review and a meta-analysis of 13800 patients and 23340 controls in 19 observational studies. *Lipids Health Dis* 2011; 10:127.
268. Guasch-Ferre M, Hu FB, Martinez-Gonzalez MA et al. Olive oil intake and risk of cardiovascular disease and mortality in the PREDIMED Study. *BMC Med* 2014; 12:78.
269. Nocella C, Cammisotto V, Fianchini L et al. Extra Virgin Olive Oil and Cardiovascular Diseases: Benefits for Human Health. *Endocr Metab Immune Disord Drug Targets* 2018; 18(1):4–13.
270. Appel LJ, Moore TJ, Obarzanek E et al. A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group. *N Engl J Med* 1997; 336(16):1117–24.
271. Sacks FM, Svetkey LP, Vollmer WM et al. Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. DASH-Sodium Collaborative Research Group. *N Engl J Med* 2001; 344(1):3–10.
272. Your guide to lowering your blood pressure with DASH : DASH eating plan: lower your blood pressure: Revised Apr. 2006. [Bethesda, Md U.S. Dept. of Health and Human Services, National Institutes of Health, National Heart, Lung, and Blood Institute, [2006]; 2006.
273. Siervo M, Lara J, Chowdhury S et al. Effects of the Dietary Approach to Stop Hypertension (DASH) diet on cardiovascular risk factors: a systematic review and meta-analysis. *Br J Nutr* 2015; 113(1):1–15.
274. Chiu S, Bergeron N, Williams PT et al. Comparison of the DASH (Dietary Approaches to Stop Hypertension) diet and a higher-fat DASH diet on blood pressure and lipids

and lipoproteins: a randomized controlled trial. *Am J Clin Nutr* 2016; 103(2):341–7.

275. https://health.usnews.com/best-diet/best-diets-overall
276. Hession M, Rolland C, Kulkarni U et al. Systematic review of randomized controlled trials of low-carbohydrate vs. low-fat/low-calorie diets in the management of obesity and its comorbidities. *Obes Rev* 2009; 10(1):36–50.
277. Hu T, Mills KT, Yao L et al. Effects of low-carbohydrate diets versus low-fat diets on metabolic risk factors: a meta-analysis of randomized controlled clinical trials. *Am J Epidemiol* 2012; 176(Suppl 7):S44–S54.
278. Pesta DH, Samuel VT. A high-protein diet for reducing body fat: mechanisms and possible caveats. *Nutr Metab (Lond)* 2014; 11:53.
279. Lennerz BS, Barton A, Bernstein RK et al. Management of type 1 diabetes with a very low–carbohydrate diet. *Pediatrics* 2018.
280. Radulian G, Rusu E, Dragomir A et al. Metabolic effects of low glycaemic index diets. *Nutrition Journal* 2009; 8:5-.
281. Manheimer EW, van Zuuren EJ, Fedorowicz Z et al. Paleolithic nutrition for metabolic syndrome: systematic review and meta-analysis. *Am J Clin Nutr* 2015; 102(4):922–32.
282. Jones AL. The Gluten-Free Diet: Fad or Necessity? *Diabetes Spectr* 2017; 30(2):118–23.
283. Biesiekierski JR, Iven J. Non-coeliac gluten sensitivity: piecing the puzzle together. *United European Gastroenterology J* 2015; 3(2):160–5.
284. Hadjivassiliou M, Sanders DS, Grunewald RA et al. Gluten sensitivity: from gut to brain. *Lancet Neurol* 2010; 9(3):318–30.
285. Skodje GI, Sarna VK, Minelle IH et al. Fructan, Rather Than Gluten, Induces Symptoms in Patients With Self-Reported Non-Celiac Gluten Sensitivity. *Gastroenterology* 2018; 154(3):529–39.e2.
286. Kristjánsson G, Venge P, Hällgren R. Mucosal reactivity to cow's milk protein in coeliac disease. *Clin Exp Immunol* 2007; 147(3):449–55.
287. Altobelli E, Del Negro V, Angeletti PM et al. Low-FODMAP Diet Improves Irritable Bowel Syndrome Symptoms: A Meta-Analysis. *Nutrients* 2017; 9(9):940.
288. Hill P, Muir JG, Gibson PR. Controversies and Recent Developments of the Low-FODMAP Diet. *Gastroenterol Hepatol (N Y)* 2017; 13(1):36–45.
289. Nanayakkara WS, Skidmore PM, O'Brien L et al. Efficacy of the low FODMAP diet for treating irritable bowel syndrome: the evidence to date. *Clin Exp Gastroenterol* 2016; 9:131–42.
290. Dinu M, Abbate R, Gensini GF et al. Vegetarian, vegan diets and multiple health outcomes: A systematic review with meta-analysis of observational studies. *Crit Rev Food Sci Nutr* 2017; 57(17):3640–9.
291. Huang T, Yang B, Zheng J et al. Cardiovascular disease mortality and cancer incidence in vegetarians: a meta-analysis and systematic review. *Ann Nutr Metab*

2012; 60(4):233–40.

292. Orlich MJ, Singh PN, Sabate J et al. Vegetarian dietary patterns and mortality in Adventist Health Study 2. *JAMA Intern Med* 2013; 173(13):1230–8.
293. Huang RY, Huang CC, Hu FB et al. Vegetarian diets and weight reduction: a meta-analysis of randomized controlled trials. *J Gen Intern Med* 2016; 31(1):109–16.
294. Lee YM, Kim SA, Lee IK et al. Effect of a brown rice based vegan diet and conventional diabetic diet on glycemic control of patients with type 2 diabetes: a 12-week randomized clinical trial. *PLoS ONE* 2016; 11(6):e0155918.
295. Tonstad S, Butler T, Yan R et al. Type of vegetarian diet, body weight, and prevalence of type 2 diabetes. *Diabetes Care* 2009; 32(5):791–6.
296. Appleby PN, Davey GK, Key TJ. Hypertension and blood pressure among meat eaters, fish eaters, vegetarians and vegans in EPIC-Oxford. *Public Health Nutr* 2002; 5(5):645–54.
297. Ferdowsian HR, Barnard ND. Effects of plant-based diets on plasma lipids. *Am J Cardiol* 2009; 104(7):947–56.
298. Ornish D, Brown SE, Billings JH et al. Can lifestyle changes reverse coronary heart disease? *Lancet* 1990; 336(8708):129–33.
299. Ornish D, Scherwitz LW, Billings JH et al. Intensive lifestyle changes for reversal of coronary heart disease. *JAMA* 1998; 280(23):2001–7.
300. McMacken M, Shah S. A plant-based diet for the prevention and treatment of type 2 diabetes. *J Geriatr Cardiol* 2017; 14(5):342–54.
301. Craig WJ, Mangels AR. Position of the American Dietetic Association: vegetarian diets. *J Am Diet Assoc* 2009; 109(7):1266–82.
302. Panagiotakos DB, Chrysohoou C, Siasos G et al. Sociodemographic and lifestyle statistics of oldest old people (>80 Years) living in Ikaria Island: The Ikaria Study. *Cardiol Res Pract* 2011; 2011:679187.
303. Horne BD, Muhlestein JB, Anderson JL. Health effects of intermittent fasting: hormesis or harm? A systematic review. *Am J Clin Nutr* 2015; 102(2):464–70.
304. Longo VD, Mattson MP. Fasting: molecular mechanisms and clinical applications. *Cell Metab* 2014; 19(2):181–92.
305. Masoro EJ. Overview of caloric restriction and ageing. *Mech Ageing Dev* 2005; 126(9):913–22.
306. Wei M, Brandhorst S, Shelehchi M et al. Fasting-mimicking diet and markers/risk factors for aging, diabetes, cancer, and cardiovascular disease. *Sci Transl Med* 2017; 9(377).

PART B

Managing medical problems

Chapter 7

Obesity

People are getting fatter in every Western country and also in the developing world. The World Health Organization (WHO) recognised obesity as a 'global epidemic' over 20 years ago.[1] In this chapter, we explore:

- definition and aetiology of obesity
- history of obesity
- managing obese patients
- policy interventions—as part of a whole-of-systems approach.

WHAT IS OBESITY?

In 2010, the Scottish Intercollegiate Guideline defined obesity as 'a disease process characterised by excessive body fat accumulation with multiple organ-specific consequences'.[2]

The medical definitions of 'overweight' and 'obesity' have been traditionally based on body mass index (BMI) results (Table 7.1). Body mass index is calculated using the following formula:

Table 7.1 BMI categories for adults

Weight category	BMI
Underweight	<18.5
Normal	18.5–24.9
Overweight	25.0–29.9
Obesity I	30.0–34.9
Obesity II	35.0–39.9
Extreme obesity III	>40.0

$$\text{BMI (kg/m}^2\text{)} = \text{weight (kg)/height}^2\text{ (m)}$$

So, if you weigh 80 kilograms and are 1.80 metres tall, your BMI is:

$$80/1.8^2 = 80/3.24 = 24.7$$

Body mass index levels are the most commonly used measure of obesity,[3] but they have their limitations, especially in men with large muscle mass and people with non-Caucasian ancestry. A number of other ways of measuring obesity are shown in the box.

More accurate measures of body fat

Body fat percentage is more precise than BMI. There are a number of methods of calculating body fat percentage.

DXA (dual-energy X-ray absorptiometry) scan

This total body scan is used more commonly to measure bone density, but also measures fat and muscle mass. It is the most accurate but also the most expensive method.

Body impedance analysis devices (BIA)

Bioelectrical impedance analysis (BIA) measures the body's resistance to a light electrical current. These are cheaper and quicker than DXA scans, but are not as accurate.

Skin callipers

Page 75

In skinfold testing, skin callipers are used to pinch the skin and the subcutaneous fat (fat underneath the skin), pull the skinfold away from the underlying muscle, and measure its thickness.

Skin callipers can be used at a single site or a sum of skinfolds can be performed. This is commonly used by fitness personnel working with sporting teams, and as long as the same person is doing the measuring, they are reasonably accurate at detecting changes in body fat.

Bathroom scales

Old-fashioned but still a good indication of progressive weight loss (or gain).

Waist measurement

Measure your waist circumference with a tape measure. Place the tape measure directly on your skin, halfway between your lowest rib and the top of your hip bone, roughly in line with your belly button. Breathe out normally and measure.

Waist measurement can be used in a number of ways:

Waist circumference

Refer to Table 7.2 for waist circumference thresholds for males and females. Measurements above these thresholds may indicate an increased risk of disease.

Table 7.2 Waist circumference thresholds indicating increased risk of disease

	Waist circumference for:	
Gender	Increased disease risk	High disease risk
Female	≥80 cm	≥88 cm

Male	≥94 cm	≥102 cm

Waist-to-hip ratio (WHR)

Measure waist circumference as above. Measure hip circumference at the widest point, usually at the top of the hip bone. Divide your waist measurement by your hip measurement or use an online calculator, such as www.mydr.com.au/tools/waist-to-hip-calculator.

Excess abdominal fat distribution is indicated by a WHR greater than 0.8 for women and 0.9 for men.

Waist-to-height (WH) ratio

A recent study suggested that the WH ratio is more accurate than BMI at predicting percentage body fat.[4] Divide your waist measurement by your height (make sure they are both in the same units, i.e. your height is in centimetres rather than metres) or use an online calculator, such as www.health-calc.com/body-composition/waist-to-height-ratio.

A ratio of more than 0.53 in men, and 0.54 in women, is a predictor of whole-body obesity. Greater than 0.59 in either sex is a predictor of abdominal obesity.

There are two different sites of fat accumulation: the relatively harmless subcutaneous fat, the fat found under the skin on arms, legs and buttocks, and the more dangerous visceral fat found wrapped around organs such as the liver, heart and bowel. Accumulation of visceral fat is strongly associated with obesity-related complications like type 2 diabetes and coronary artery disease, and is independent of age, overall obesity or the amount of subcutaneous fat.

Visceral adipose tissue and its adipose-tissue resident macrophages produce more pro-inflammatory cytokines, like tumour necrosis factor-alpha (TNF-alpha) and interleukin-6 (IL-6), and less adiponectin. These cytokine changes induce insulin resistance and play a major role in the pathogenesis of endothelial dysfunction and subsequent atherosclerosis.

The rate of visceral fat accumulation also differs according to the individual's sex and ethnic background; it is more prominent in Caucasian men, African-American women and Asian, Indian and Japanese men and women.

The term 'metabolic obesity', in reference to visceral fat accumulation in either lean or obese individuals, may identify those at risk for cardiovascular disease better than the currently used definitions of obesity.[5]

EXTENT OF THE PROBLEM

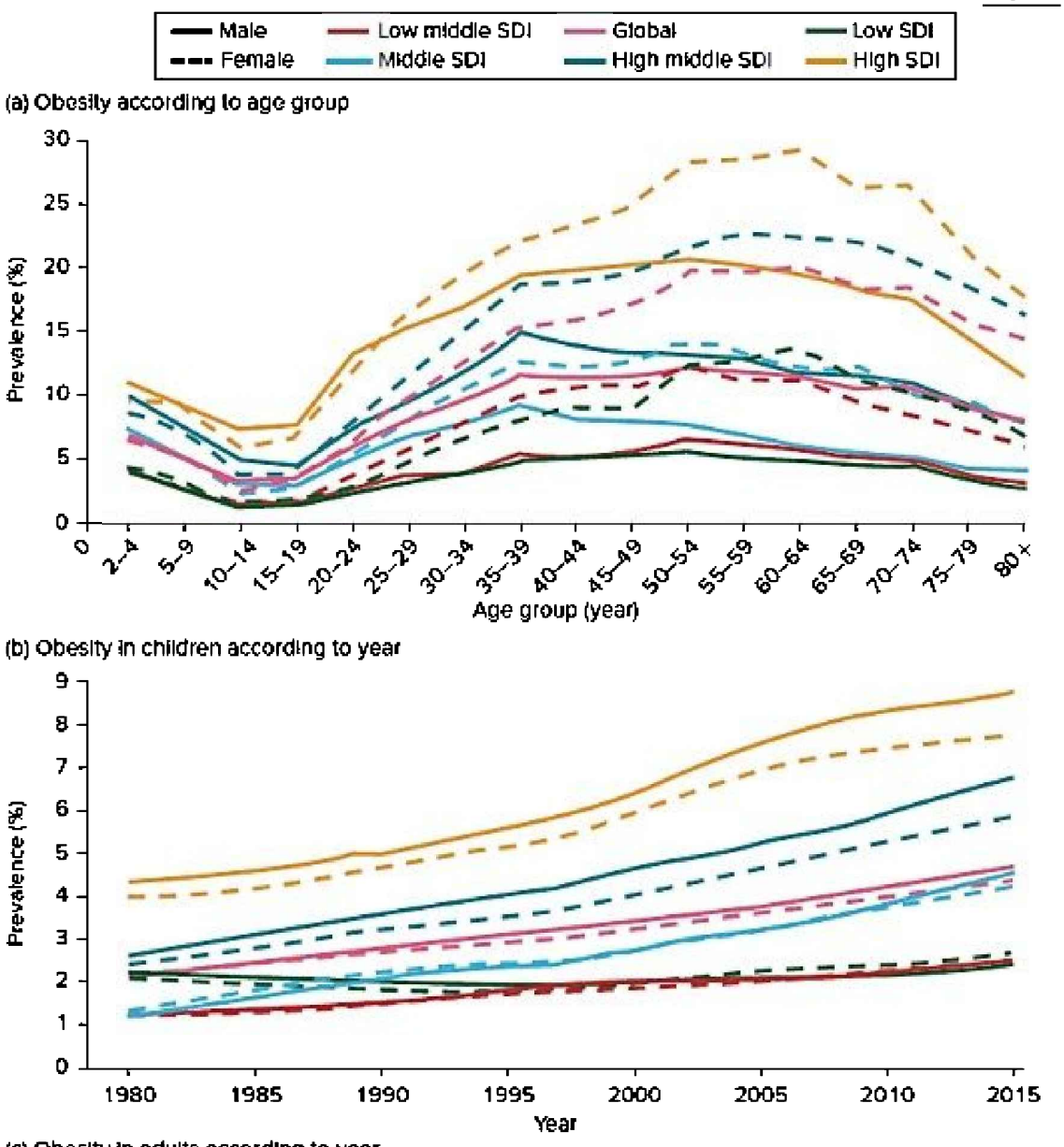
According to the WHO, in 2016 more than 1.9 billion adults 18 years and older were overweight. Of these, over 650 million were obese. Thirty-nine per cent of adults aged 18 years and over were overweight, and 13% were obese.[2]

Forty-one million children under the age of 5, and over 340 million children and adolescents aged 5–19, were overweight or obese in 2016.[6] The prevalence of overweight and obesity among children and adolescents aged 5–19 has risen dramatically from 4% in 1975 to over 18% in 2016. The rise has occurred similarly among both boys and girls—in 2016, 18% of girls and 19% of

boys were overweight.[2]

While just under 1% of children and adolescents aged 5–19 were obese in 1975, more than 124 million children and adolescents (6% of girls and 8% of boys) were obese in 2016.[2]

Most of the world's population live in countries where overweight and obesity now kills more people than underweight. Worldwide obesity has steadily increased over the past 40 years (Fig. 7.1) and has nearly tripled since 1975.



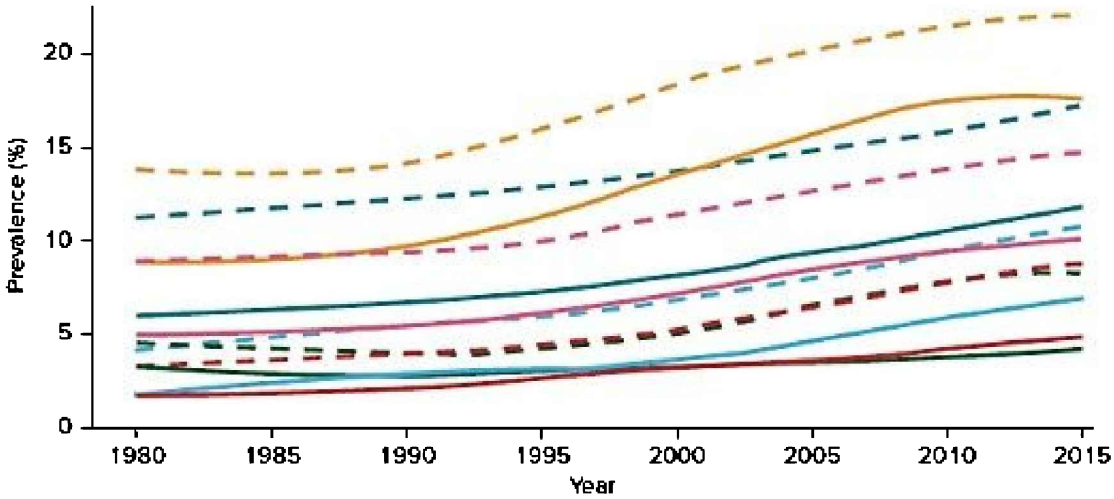


Figure 7.1 Prevalence of obesity at the global level, according to sociodemographic index (SDI). Shown is the age-specific prevalence of obesity at the global level and according to SDI quintile in 2015 (Panel A) and age-standardised prevalence trends at the global level and according to SDI quintile from 1980 to 2015 among children (Panel B) and adults (Panel C)

FROM THE NEW ENGLAND JOURNAL OF MEDICINE, GBD 2015 OBESITY COLLABORATORS. HEALTH EFFECTS OF OVERWEIGHT AND OBESITY IN 195 COUNTRIES OVER 25 YEARS. VOL 377, PAGES 13-27. COPYRIGHT © 2017 MASSACHUSETTS MEDICAL SOCIETY. REPRINTED WITH PERMISSION FROM MASSACHUSETTS MEDICAL SOCIETY

Among OECD countries, USA and Mexico have the highest rates of obesity (Fig. 7.2), followed by New Zealand, Hungary, Australia, UK and Canada.[7] More adults are obese than children, but the rate of increase is higher among children. In particular, there has been a tripling of obesity in youth and young adults in developing, middle-class countries, such as China, Brazil and Indonesia. This is a particularly worrisome trend because overweight children are at higher risk for the early onset of diseases such as type 2 diabetes, hypertension and chronic kidney disease.

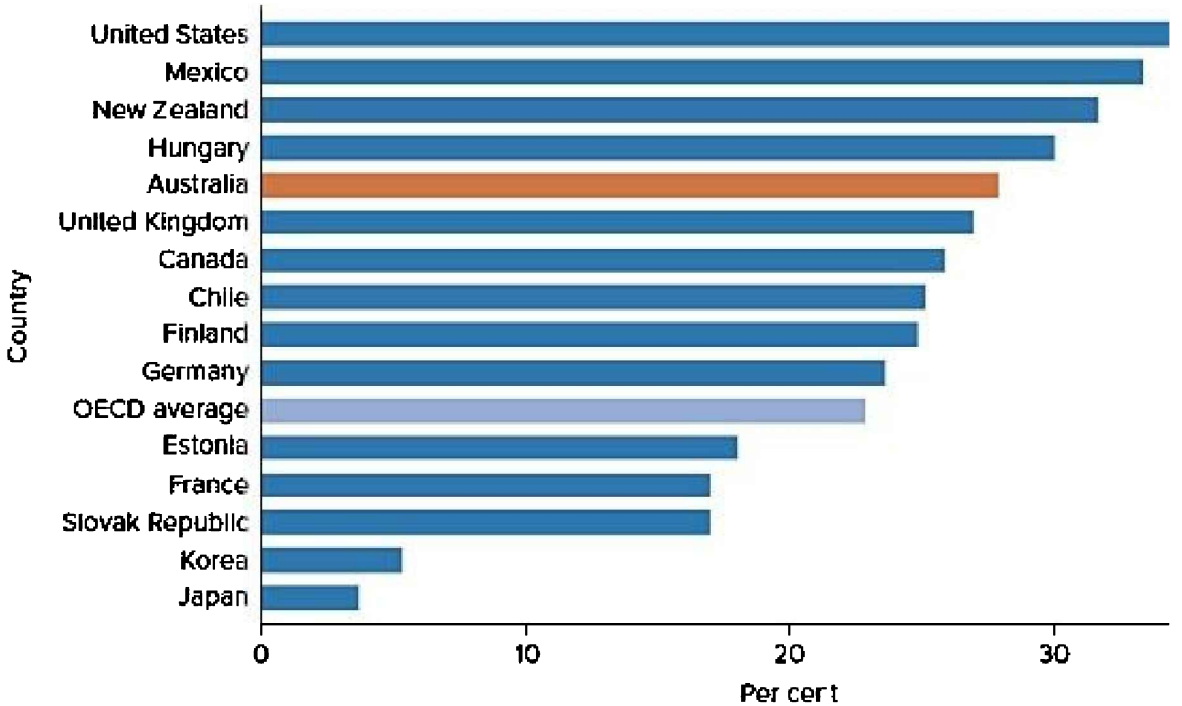


Figure 7.2 Proportion of obese people aged 15 and over, by selected OECD countries, 2016 or nearest year

ADAPTED AND REPUBLISHED WITH PERMISSION OF ORGANISATION FOR ECONOMIC COOPERATION AND DEVELOPMENT (OECD) FROM HEALTH AT A GLANCE 2015: OECD INDICATORS. PARIS: OECD. HTTP://WWW.OECD.ORG/HEALTH/HEALTH-SYSTEMS/HEALTH-AT-A-GLANCE-19991312.HTM, PERMISSION CONVEYED THROUGH COPYRIGHT CLEARANCE CENTER, INC

Obesity is responsible for about 5% of all deaths each year worldwide, and its global economic impact amounts to roughly US$2 trillion annually, or 2.8% of global GDP—nearly equivalent to the global impact of smoking or that of armed violence, war and terrorism.[8] Obesity rates are steadily increasing in most Western countries, as shown in Fig. 7.3.

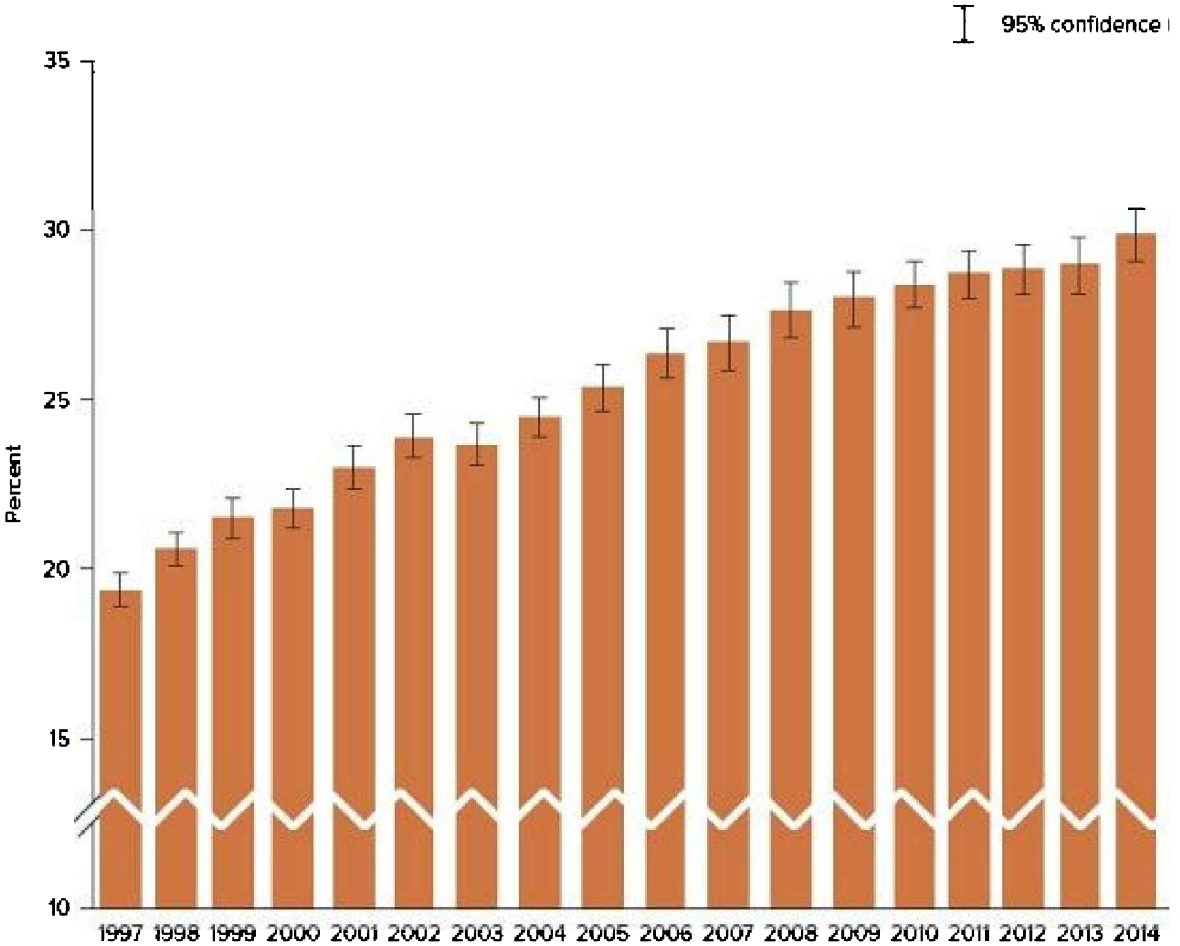


Figure 7.3 Prevalence of obesity among adults aged 20 and over, United States, 1997–September 2017
ADAPTED FROM NCHS, NATIONAL HEALTH INTERVIEW SURVEY 1997–SEPTEMBER 2017, SAMPLE ADULT CORE COMPONENT[9]

IS OBESITY A DISEASE?

The question of whether obesity should be called a 'disease' is a source of considerable controversy.[10] Over the past 40 years, various organisations, including the American Health Care Financing Administration (1977), Japanese Association for the Study of Obesity (2002) and Centers for Medicare and Medicaid Services in the USA (2004) have recognised obesity as a disease. The American Medical Association classified obesity as a disease in 2013, despite the opposition of its own Council on Science and Public Health (CSPH). The American Heart Association, American College of Cardiology and the Obesity Society released joint guidelines in 2013, stating that doctors should consider obesity a disease and more actively treat obese patients for weight loss.

Finally, in 2015, in the Nagoya Declaration, the Asia Oceania Association for the Study of Obesity

identified 'obesity disease' as a pathological state caused by obesity and requiring clinical intervention. In this document the association made the distinction between:

1. obesity disease—obesity accompanied by health problems, and
2. obesity—not accompanied by health problems; may subsequently be placed at risk of acquiring obesity disease due to progression of obesity, excessive visceral fat accumulation, ageing and other factors.[11]

WHAT CAUSES OBESITY?

Numerous factors are proposed as contributing to the obesity epidemic. These include socioeconomic factors, genetic factors, insulin resistance, poor diet, inadequate activity, insufficient sleep, associated medical illnesses, medications, smoking cessation and excess alcohol intake. The one thing that everyone agrees on is that obesity is a multifactorial problem. Let us consider some of these factors and their potential contribution to obesity.

Genetic factors

Not all people exposed to prevailing urban and rural environments become obese, which suggests the existence of underlying genetic mechanisms operating at the individual level. Although estimates vary, twin, family and adoption studies show that the rate of heritability of BMI is high, ranging from 40–70%.[12]

However, in light of the dramatic increase in obesity levels over the past four decades, which clearly cannot be related to genetic factors, this is likely to be an overestimation of the genetic component. Large genome-wide association studies to identify common single nucleotide polymorphisms (SNPs) associated with BMI have been unable to explain more than a small proportion (<2%) of BMI variability.[13, 14] Heritability is often misinterpreted as being the proportion of BMI variance caused by genetics; whereas heritability studies, rather than estimating cause, estimate the proportions of genetic variance and non-genetic variance that explain BMI variance in a given study population.

The study populations are usually based on twin cohorts which, even if reared apart, live within very narrow environmental variances, rather than the wide variance of environments across countries that results in high heritability estimates.[15] These estimates seriously understate the environmental effects and thus provide no indication of the potential to reduce obesity via environmental change.[16]

Socioeconomic disadvantage

There is a strong relationship between socioeconomic status (SES) and obesity, which varies depending on the country in which you live. In low-income countries, obesity mostly affects middle-aged adults (especially women) from wealthy, urban environments; whereas in high-income countries it affects both sexes and all ages, but is disproportionately greater in disadvantaged groups. These communities are characterised by insecure and erratic employment,

inadequate education, stress, depression and a lack of social cohesion.[17] The burden of obesity-related disease is inextricably linked to income inequality. Poverty predisposes individuals to obesity through multiple mechanisms and to chronic diseases, like diabetes, at any weight.[18]

A study of four British birth cohorts, with data spanning from 1953 to 2015, showed that socioeconomic inequalities in weight had reversed over time with lower socioeconomic position associated with lower weights in the 1946, 1958 and 1970 cohorts, but with higher weight in the 2001 cohort.[19] This inequality had persisted up until at least 2015 and was consistent with other UK studies.[20–22] Similar findings of increased obesity associated with lower socioeconomic status have been found in other countries.[23]

There is a strong but complex relationship between SES and childhood obesity. Low incomes directly constrain families' diet and exercise choices. Education levels, along with the cognitive burden of living under financial strain, are also associated with and contribute to the behaviours that lead to higher rates of childhood obesity.[24]

Those of lower SES are more likely to make poor food choices, such as consuming cheap, highly processed or takeaway foods of poor nutrient quality, and spend less time on food preparation. Children from low SES families are less likely to take part in organised sport or play. In addition to less infrastructure and support to participate in physical activity, children from low SES backgrounds are less likely to live in an environment conducive to physical activity, with fewer safe outdoor spaces and opportunities for active transport.[25]

Priya Fielding-Singh, a sociology researcher from Stanford University, interviewed 73 Californian families about food.[26] Families' SES affected not just their access to healthy food, but something even more fundamental: the meaning of food. She found that while both wealthy and poor kids asked for junk food, the parents responded differently to these pleas. An overwhelming majority of the wealthy parents told her that they routinely said 'no' to requests for junk food. In 96% of high-income families, at least one parent reported that they regularly decline such requests. Parents from poor families, however, almost always said 'yes' to junk food. Only 13% of low-income families had a parent that reported regularly declining their kids' requests. Poor parents honoured their kids' junk food requests to nourish them emotionally, not to harm their health. Similarly, wealthy parents who denied their kids processed foods did so to teach them healthy lifelong habits, not to deprive them.

Ethnicity

Significant variation is seen in ethnic groups, which is probably related to SES and cultural differences in food intake and physical activity. For example, in the UK, prevalence of obesity is higher among women of black Caribbean, black African and Pakistani ethnicities. For men, obesity prevalence is highest in black Caribbean, white and Irish ethnic groups (Fig. 7.4).[27]

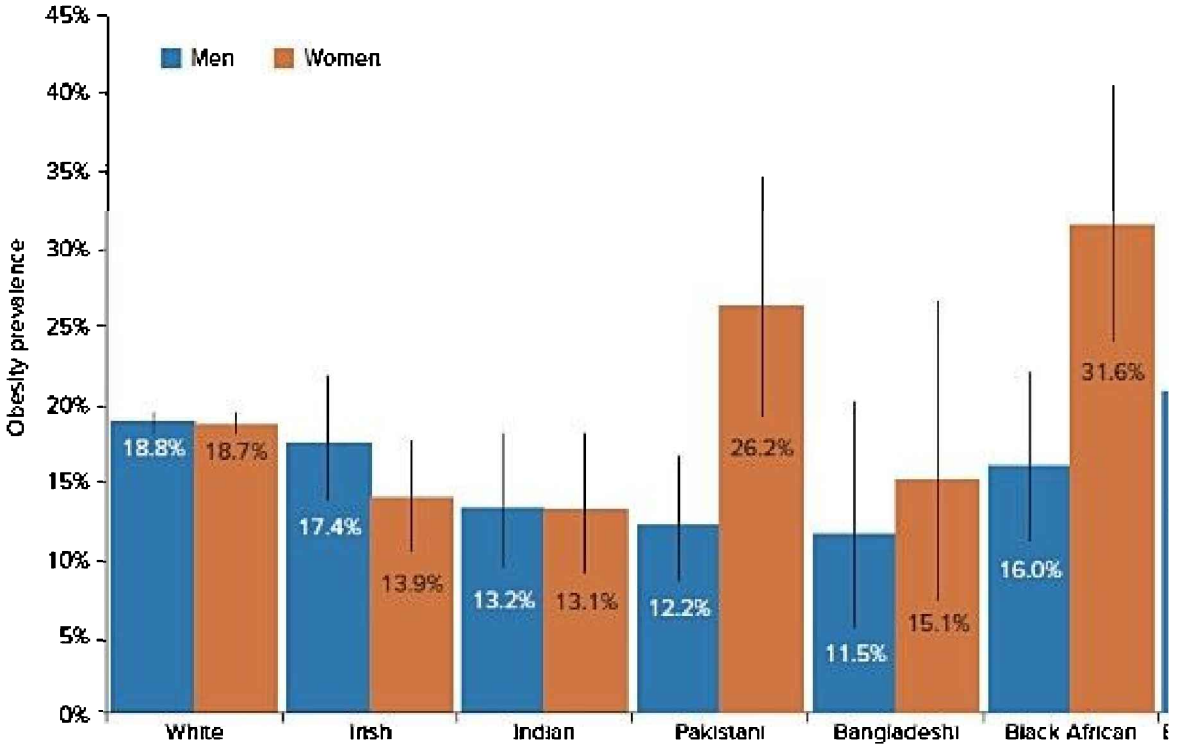


Figure 7.4 Adult obesity prevalence by ethnic group. Health Survey for England 2006 to 2010 (five-year average)

© CROWN COPYRIGHT 2016

In the US, non-Hispanic black women (48.9%) are most likely to be obese, compared with Hispanic women (34.2%) and non-Hispanic white women (29.4%). There is no significant difference in the prevalence of obesity by race and ethnicity groups among men (Fig. 7.5).

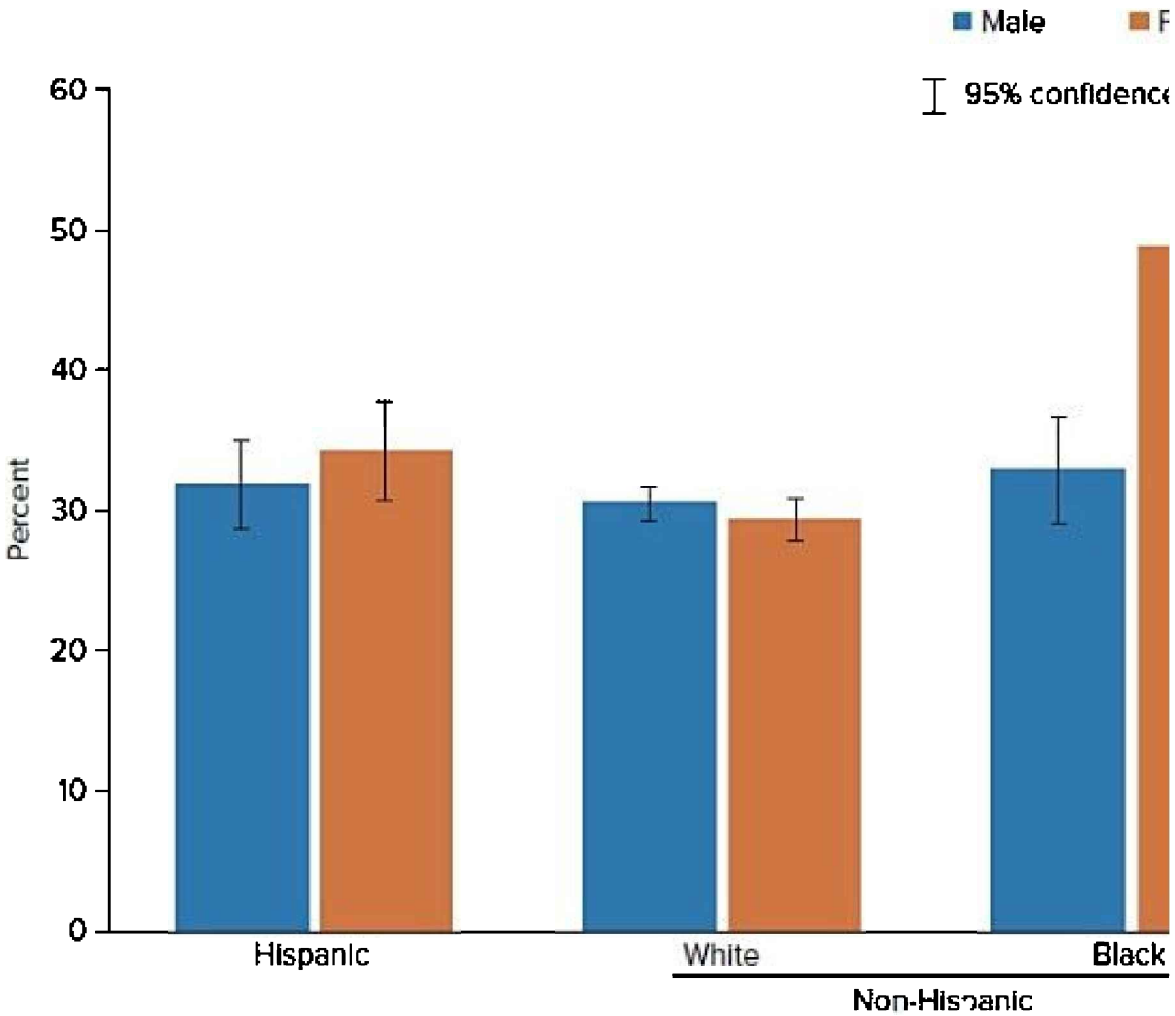


Figure 7.5 Age-adjusted prevalence of obesity among adults aged 20 and over by sex and race and ethnicity, United States, January–September 2017

ADAPTED FROM NCHS (US) NATIONAL HEALTH INTERVIEW SURVEY, JANUARY–SEPTEMBER 2017, SAMPLE ADULT CORE COMPONENT[9]

Energy balance: calories in = calories out

The first law of thermodynamics states that energy cannot be created or destroyed. In the nutrition and diet industry, this is expressed as 'energy in must equal energy out' and is called the energy balance equation:

Calories in = calories out

Or in other words:

Weight gain (energy balance) = energy in (food) - energy out (exercise)

This theory remains popular in spite of substantial evidence that losing weight as a result of either reducing caloric (food) intake or increasing energy output (exercise) is not effective in the medium- to long-term—due to the body's hormonal response to caloric restriction and weight loss.

Caloric restriction will result in short-term weight loss, but the body then responds to that weight loss in a number of different ways. The first effect is to stimulate appetite. Hormones that affect both hunger (ghrelin, leptin) and satiety (peptide YY, amylin, cholecystokinin) combine to increase appetite.

The other major response to caloric restriction and weight loss occurs in basal metabolic rate (BMR). The 'calories out' part of the equation consists of much more than merely the calories expended with exercise. More than 60% of energy expenditure is to maintain BMR—the energy expended on normal activities such as breathing, maintain circulation, body temperature, kidney function and so forth. The body's natural response is to conserve energy, so when caloric intake from food is reduced, the body compensates by reducing BMR.

These hormonally driven responses to reduced caloric intake and initial weight loss prevent further weight loss. When the dieting patient eventually gives up on his or her reduced-calorie diet regime, weight is slowly put back on. With the patient's BMR set at a lower rate, the patient is more likely to then not only regain all the initial weight lost, but gain additional weight once normal caloric intake is resumed.

What has happened in the past 40 years?

One popular theory about the cause of obesity is that we have become gluttonous and slothful over the past few decades, and this has led to overeating and obesity.[28, 29] However, it is hard to understand why this would suddenly have happened after thousands of years of eating.

As can be seen from Fig. 7.6 and 7.7, the rise in obesity commenced quite suddenly around 1980 and continued to increase steadily over the following 30 years. The speed and extent of weight gain varied somewhat by age, sex and ethnicity, but for all subgroups most people became heavier at about the same time.[30] It is implausible that each age, sex and ethnic group, with massive differences in life experience and attitudes, had a simultaneous decline in willpower related to healthy nutrition or exercise.[31] It is unlikely that any factor with a long induction period had a major role in precipitating the US obesity epidemic. Nor can quick-acting exposures have been important if they only affect certain subgroups of the population, because whole population distributions of bodyweight shifted to the right. Rather, the epidemic must have been caused by factors that led to rapid population-wide changes.[31]

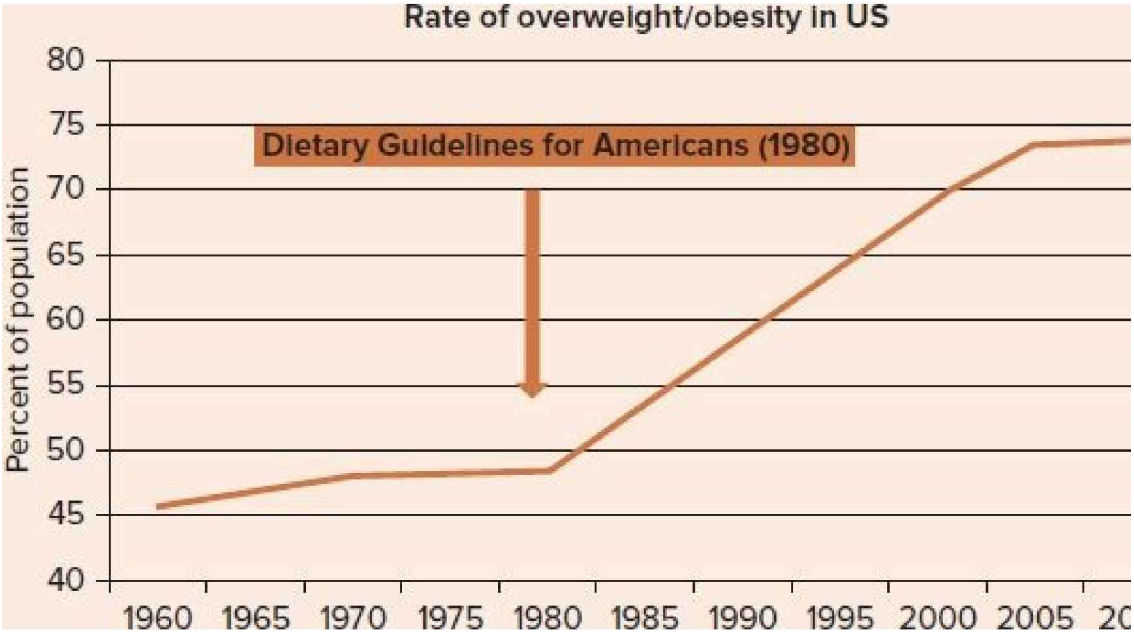


Figure 7.6 Rate of overweight/obesity in the US, 1960–2010

ADAPTED FROM NCHS (US), 2008 WITH SPECIAL FEATURE ON THE HEALTH OF YOUNG ADULTS HTTPS://WWW.CDC.GOV/NCHS/DATA/HUS/HUS08.PDF

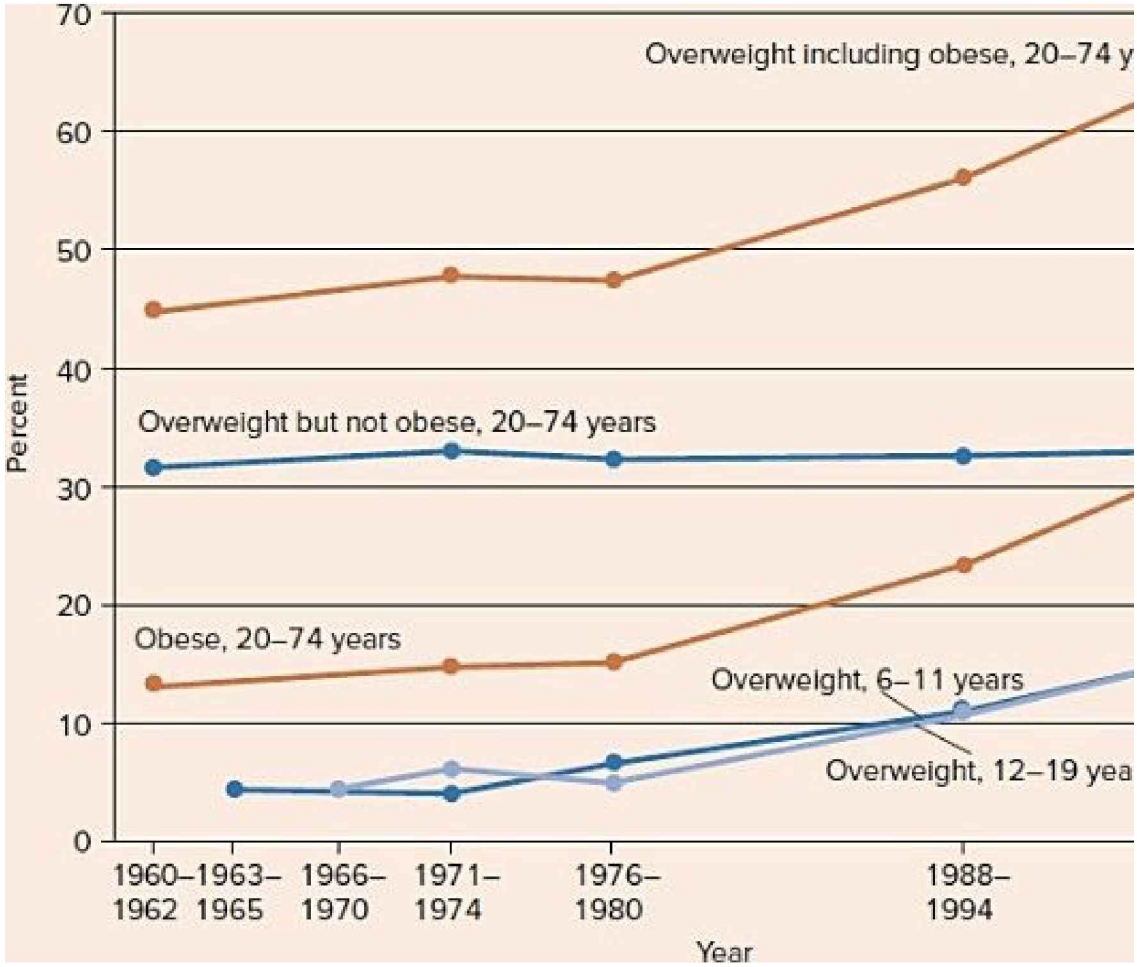


Figure 7.7 Overweight and obesity, by age: USA, 1960–2004
ADAPTED FROM NCHS (US) 2006, FIGURE 13, DATA FROM THE NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY (NHANES).

What happened around that time to cause such a dramatic increase?

The endorsement of the diet–heart hypothesis (that the serum cholesterol lowering effects of replacing saturated fat with vegetable oil rich in linoleic acid will diminish deposition of cholesterol in the arterial wall, slow progression of atherosclerosis, reduce coronary heart disease events, and improve survival[32]) and the demonisation of saturated fat greatly influenced the development of the Dietary Guidelines for the United States in 1977, followed by Australia in 1982 and many other countries in the English-speaking world. At the same time, the change to US Farm Bills led to a rapid increase in food production and thus an increase in food portion sizes;[33] accelerated marketing, availability and affordability of energy-dense foods;[34] and widespread introduction of cheap and potent sweetening agents, such as high-fructose corn syrup, which infiltrated the food system and affected the whole population simultaneously.[35]

The guidelines recommended a diet high in grains and low in fat, with vegetable oils taking the place

of most animal fats. Despite concerns at the time from a number of researchers, the guidelines were adopted and soon became the orthodox view, remaining more or less unchanged to this day. Recently, researcher Zoë Harcombe re-examined the evidence available at the time and found there was no scientific basis for the recommendations to cut fat from the US diet in the first place.[36]

The consequences of the Dietary Guidelines included:

1. **Intake of animal fats such as red meat, eggs and dairy was reduced.** Because of concerns about saturated fats, fatty meats were discouraged and lean meat promoted heavily. Eggs and dairy products, such as milk, butter, cream and cheese, were discouraged. Margarine was encouraged as a replacement for butter.
2. **'Low-fat' food products flooded the market.** The food industry responded to the dietary advice to reduce fat by producing a wide range of low-fat foods. Because removing the fat from food also removed much of the flavour, they replaced the fat with added sugar or sugar-like products.
3. **Intake of ultra-processed foods increased.** Ultra-processed foods are products that contain several manufactured ingredients not generally used when cooking from scratch, including natural and artificial flavours or colours, sweeteners, preservatives and other additives. Some examples of ultra-processed foods include mass-produced sugar-sweetened beverages, sweet or savoury packaged snacks, packaged baked goods, chicken or fish nuggets and other reconstituted meat products, and instant noodles and soups. A recent study showed that more than half of all calories consumed in the US come from ultra-processed foods. The authors imagine the Australian figures would be similar.
4. **Use of vegetable oils increased.** Instead of saturated fats, the use of polyunsaturated fats high in linoleic acid was encouraged as an alternative. Most prominently, the intake of so-called vegetable oils increased dramatically. These included corn, sunflower, peanut, safflower, cottonseed, rapeseed, canola and soybean oils.
5. **Takeaway food became more popular.** Fast foods—such as hamburgers, fish, chips and fried chicken—are cooked in vegetable oils because of their low cooking temperature and low cost.

Page 82

Following the introduction of the guidelines, consumption of sugar and vegetable (polyunsaturated fatty acid) oils increased, while animal fat consumption went down. It has been suggested that this combination of changes has led to the huge increases in the incidence of obesity and type 2 diabetes.

Page 83

Lack of exercise

If one accepts the calories in–calories out theory, then simply increasing the amount of exercise will lead to weight loss. Unfortunately, exercise plays a relatively minor role in weight loss. Studies of increased exercise at an individual, community or even country level show minimal, if any, long-term weight loss.

The Women's Health Study, the largest study ever to investigate diet and exercise, found no increased weight loss in the intense exercise group compared to low or medium levels of exercise.[37] A Cochrane review showed exercise resulted in only small weight losses across studies when compared with no treatment.[38]

Among the possible reasons for this lack of weight loss, a study from the Harvard School of Public Health found that appetite increases after exercise.[39] The effect of exercise on weight varies among individuals, and some people are quite sensitive to the effects of exercise, but for most of us, as Tim Noakes, Steve Phinney and Aseem Malhotra put it, 'you cannot outrun a bad diet'.[40]

Exercise may be helpful in maintaining weight loss (rather than generating weight loss). Among competitors from the television show 'The Biggest Loser',[41] the participants who were the most successful in maintaining weight loss were also those who had the greatest increase in physical activity after six years. The direction of causality is not known—it may be that losing weight facilitates being physically active. Also, high levels of exercise may be required to maintain weight loss, depending on food intake.[37, 42]

Sedentary lifestyle

Sedentary behaviour and physical activity occur relatively independently of each other, and various combinations of high or low sedentary behaviour and low or high physical activity levels exist.[43] Young people spend approximately 60% of their waking time sitting, which makes sedentary behaviour the most common behaviour (besides sleep) in children and adolescents.[44]

There is some evidence of a relationship between sedentary behaviour and cardiovascular disease;[45] however, a recent meta-analysis indicated that sedentary behaviour has little effect on body weight and obesity.[46]

Diet

As noted in the box, the current rise in rates of obesity in Western countries commenced around 1980, at the time of the introduction of Dietary Guidelines (initially in the US), which emphasised reduction of fat and cholesterol intake. There were a number of consequences of this policy change, including an increase in carbohydrate intake, especially of added sugar; increased intake of ultra-processed foods usually containing a combination of sugar, vegetable oils and refined grains; and increased use of vegetable oils in cooking replacing animal fats. Reducing the fat, especially the saturated fat, content of foods, resulted in a decrease in flavour and consequently the fat was replaced with sugars.

Sugar

There is a substantial body of evidence linking sugar intake and obesity.[47, 48] This link is particularly strong when the sugar is in liquid form—consumed in sugar-sweetened beverages (SSBs), colloquially known as 'soft drinks' or 'sodas'.[49–52]

In the last two decades of the twentieth century there was a large increase in the consumption of SSBs. In the UK, between 1975 and 2000, there was a five-fold increase in the amount of soft drink purchased for consumption in the home.[53] In the US, soft drink consumption increased by 61% between 1977 and 1997.[54] It also more than doubled in children and adolescents over the same period.[55]

In a survey of 75 countries, soft drink intake increased globally from 43 litres per capita per year in 1997 to 52 litres in 2010. A 1% rise in soft drink consumption was associated with an additional 48 overweight adults per 100 people, 2.3 obese adults per 100, and 0.3 adults with diabetes per 100.[5 6]

In a study of 50 000 nurses followed up for two 4-year periods (1991 to 1995 and 1995 to 1999), a higher consumption of SSBs was associated with a greater magnitude of weight gain. After adjustment for potential confounders, women who increased their SSB consumption from 1991 to 1995 and maintained a high level of intake gained on average 8.0 kg during the two periods.[57]

Similar results were reported by Palmer and colleagues in over 40 000 African-American women followed up for six years. Those whose SSB intake increased from less than one serving per week to greater than one serving per day gained the most weight, whereas those who decreased their intake gained the least weight (6.8 and 4.1 kg, respectively) after adjustment for potential confounders.[58]

Consumption of SSBs is associated with obesity in children. In one study, for each additional serving of SSB consumed, BMI and frequency of obesity increased, after adjustment for anthropometric, demographic, dietary and lifestyle variables. Baseline consumption of SSBs was also independently associated with change in BMI.[59] Dubois and colleagues found that in over 2000 children 2.5 years of age followed up for 3 years, regular consumers of SSBs between meals had a 2.4-fold greater odds of being overweight compared with non-consumers.[60]

Fats

As described in Chapter 6, there are different types of fat: saturated, monounsaturated and polyunsaturated. Polyunsaturated fats are further divided into omega-3 and omega-6 fats. Despite what is commonly believed, there is no evidence of a link between overall fat consumption and obesity. As Dr Walter Willett from the Harvard TH Chan School of Public Health stated in a 2002 review article entitled 'Dietary fat plays a major role in obesity: No', 'Diets high in fat do not account for the high prevalence of excess body fat in Western countries'.[61]

The most dramatic change in eating habits in the last century has been the increase in vegetable or seed oils. These polyunsaturated oils are high in omega-6 fats. As a result, the ratio of the pro-inflammatory omega-6 fats to the anti-inflammatory omega-3 has changed from the traditional 1:1 ratio to approximately 16:1 or even higher. High dietary intake of omega-6 fatty acids leads to increases in white adipose tissue and chronic inflammation, which are associated with obesity.[62]

Insulin resistance

It has long been recognised that insulin resistance is a common accompaniment of obesity.[63] Insulin resistance is likely to be both a cause and effect of obesity.

Biochemical studies have shown that insulin plays key roles in regulating white adipocyte lipid accumulation, by inhibiting lipolysis as well as promoting fatty acid uptake and triglyceride synthesis (lipogenesis), and by stimulating expression of genes involved in lipid uptake and

storage.[64, 65]

Clinical and experimental evidence indicates that hyperinsulinaemia could precede and promote obesity.[66–68] Studies demonstrating prevention of obesity in mice genetically incapable of sustained hyperinsulinaemia[69] strongly support the concept that excess insulin contributes to diet-induced obesity. Moreover, across multiple models, obesity and lipid homeostasis have been shown to be more sensitive to small changes in circulating insulin levels than glucose homeostasis. Collectively, these experiments also fit well with clinical and pre-clinical studies demonstrating that therapy with long-acting insulin analogues leads to weight gain, and with small trials showing weight loss with drugs that reduce insulin secretion.[70–72]

On the other hand, obesity, specifically visceral obesity, also known as 'central obesity', has been shown to increase the risk of insulin resistance. Each standard deviation (SD) increase in visceral adipose tissue mass increases the odds of insulin resistance by 80%, whereas an SD increase in subcutaneous adipose tissue mass decreases the odds of insulin resistance by 48%.[73] The propensity of visceral adipose tissue for increased inflammation, and the subsequent secretion of cytokines that impair insulin signalling, may significantly contribute to systemic insulin resistance in central obesity.[74]

The cost of food—is 'real food' more expensive?

It has been demonstrated in multiple countries that energy-dense foods composed of refined grains, added sugars, or fats are cheaper per calorie than are the recommended nutrient-dense foods,[75] and that cheaper and more energy-dense diets, often devoid of vegetables and fruit, tended to be selected across lower-income groups.[76] There may also be a link between low-cost calories and high obesity rates.[77]

Medical illnesses

Certain medical illnesses such as hypothyroidism, polycystic ovarian syndrome and Cushing's syndrome are associated with obesity.

Medications

Medications associated with weight gain include certain antidepressants, anticonvulsants (such as carbamazepine and valproate), some diabetes medications (insulin, sulfonylureas and thiazolidinediones), hormones (such as oral contraceptives) and most corticosteroids (such as prednisone). Weight gain may also be seen with some antihypertensive medications and antihistamines.

Stress and mental illness

For some people, emotions influence eating habits. Many people eat excessively in response to emotions such as boredom, sadness, stress or anger. While overweight people tend to have no more psychological disturbances than people of normal weight, those who seek treatment for serious weight problems may also have difficulties with binge eating.

Poor sleep

A majority of studies have demonstrated increased hunger or appetite, or increased caloric intake, especially from unhealthy food, in response to sleep restriction.[78, 79] Increase in hunger ratings by 14–30% have been reported. In studies providing *ad libitum* diet during 4–4.5 hours sleep restriction between 1 and 8 nights, caloric intake was found to be 20–30% greater after sleep restriction.[80]

Other factors

Other factors which may contribute to obesity include:

- quitting smoking—many who quit smoking gain weight in the first six months after quitting
- menopause—women may gain 5.5–7 kg during menopause
- pregnancy—women may not lose the weight they gained during pregnancy.

The obesogenic environment

The term 'obesogenic environment' was first used by Boyd Swinburn and refers to 'an environment that promotes gaining weight and one that is not conducive to weight loss' within the home or workplace,[81] and 'the sum of influences that the surroundings, opportunities or conditions of life have on promoting obesity in individuals or populations'.[82] Obesity is simply the result of people responding normally to the obesogenic environments in which they find themselves.

The obvious possible drivers of the epidemic are in the food system:[83] the increased supply of cheap, palatable, energy-dense foods; improved distribution systems to make food much more accessible and convenient; and more persuasive and pervasive food marketing.[84] Several studies have tested the hypothesis that increases in the food supply are the dominant drivers of the weight gain in populations.[84–86] Results from these investigations show that the rise in food energy supply was more than sufficient to explain the rise in obesity in the US from the 1970s,[85, 86] and most of the weight increase in the UK since the 1980s.[87] A related hypothesis is that the policies put in place in the US and other countries to increase the food supply from the 1970s led to a situation in which the abundance of food in these countries began to push up population energy intake.[87]

Looking at trends in high-, middle- and low-income countries, research has concluded that increases in the food energy supply, alongside increasing sedentary behaviour, explain the increases in population body weight, particularly in high-income countries.[88]

A distinction can be made between the obesogenic drivers within the food and physical activity environments, which are proximal determinants of behaviours, and more distal systemic drivers such as taxation regimes, regulation of the marketplace, and social and economic policies that set the conditions under which businesses and individuals operate. Many of these conditions can have distal effects on obesity.[89, 90]

Marketing of food and beverages is associated with increasing obesity rates[91] and is especially effective among children,[92, 93] and therefore a focus of policy strategies.[94] Other factors amplify or attenuate the effect of these causes and produce observed disparities in obesity prevalence across

and within populations. National wealth, government policy, cultural norms, the built environment,[80] genetic[95] and epigenetic mechanisms,[96] biological bases for food preferences,[97] and biological mechanisms that regulate motivation for physical activity[98] all influence growth of the epidemic.

The food environment is defined as any opportunity to obtain food. It includes physical, sociocultural, economic and policy influences at both micro and macro levels.[99] The broader food environment includes the home food environment, food policies and school food policies, in addition to the neighbourhood food environment.[100]

The neighbourhood food environment is a mixture of retail outlets (from small convenience stores to supermarkets), as well as restaurants and takeaway (fast-food) outlets, and is not limited to the residential neighbourhood. The neighbourhood food environment influences individual food choice and food intake through the concept of food access. For example, supermarket availability is negatively associated with obesity and fast-food availability positively associated.[101]

Cross-sectional research in Norfolk, England, reported that greater exposure to fast food and a lower education level is associated with greater fast-food consumption, BMI and odds of obesity.[102] Greater supermarket distance was found to be associated with higher BMI and odds of both overweight and obesity.[103] Exposure to takeaway food outlets in home, work and commuting environments combined was associated with marginally higher consumption of takeaway food, greater BMI and greater odds of obesity.[104]

The existing environments within a country (e.g. the built environment (Chapter 27),[105] transport systems, active recreation opportunities, cuisines and food culture, and culture around body size) can greatly moderate or modulate the effects of the global obesity drivers on population BMI.[68] These effects can be powerful and help to explain much of the differences in obesity prevalence between populations.[68] Other factors include the choice architecture of stores or food outlets,[106] the cost of food,[23] and the issues around food insecurity and austerity.[106]

The importance of the built environment in relation to obesity is debated. While mixed land use and urban sprawl are more consistently associated with overweight or obesity than other physical environmental factors, the evidence remains weak and the nature of associations between the physical environment and weight status needs further study.[107]

THE ASSOCIATION BETWEEN OBESITY AND ILLNESS

Obesity is a major risk factor for chronic and preventable conditions such as type 2 diabetes, heart disease, high blood pressure, stroke, musculoskeletal disorders and depression (Fig. 7.8). About 70% of people who are obese have at least one established medical condition,[108] resulting in medical costs about 30% higher than for people of the same age who are of healthy weight. Many more have serious health conditions of which they are unaware. For example, for every five known cases of type 2 diabetes, there are four undiagnosed cases.

	Associated with weight	Associated with metabolic consequences
Slightly increased	Varicose veins Musculoskeletal problems Back pain Stress incontinence Oedema/cellulitis	Cancer (breast, endometrial, colon) Reproductive abnormalities Impaired fertility Polycystic ovaries Skin complications Cataract
Moderately increased	Osteoarthritis Respiratory disease Hernia Psychological problems	Coronary heart disease Stroke Gout/hyperuricaemia
Greatly increased	Sleep apnoea Breathlessness Asthma Social isolation/depression Daytime sleepiness/fatigue	Type 2 diabetes Gall bladder disease Hypertension Dyslipidaemia Insulin resistance Atherosclerosis

Figure 7.8 Diseases associated with obesity

ADAPTED FROM BOOTH M, BAUR L & DENNY WILSON E, REPORT TO THE COMMONWEALTH ON AUSTRALIAN STANDARD DEFINITIONS FOR CHILD AND ADOLESCENT OVERWEIGHT AND OBESITY. WWW.HEALTH.GOV.AU

Global burden of disease

Obesity is associated with an increased risk of developing a number of chronic diseases and conditions, including type 2 diabetes, coronary heart disease, hypertension and stroke, asthma, depression, metabolic syndrome, dyslipidaemia, certain cancers, gastro-oesophageal reflux disease, gallbladder disease, reproductive problems, osteoarthritis and back pain, obstructive sleep apnoea, breathlessness, and psychological distress (Fig. 7.9). Most of the complications of obesity can be reduced by weight loss.[109]

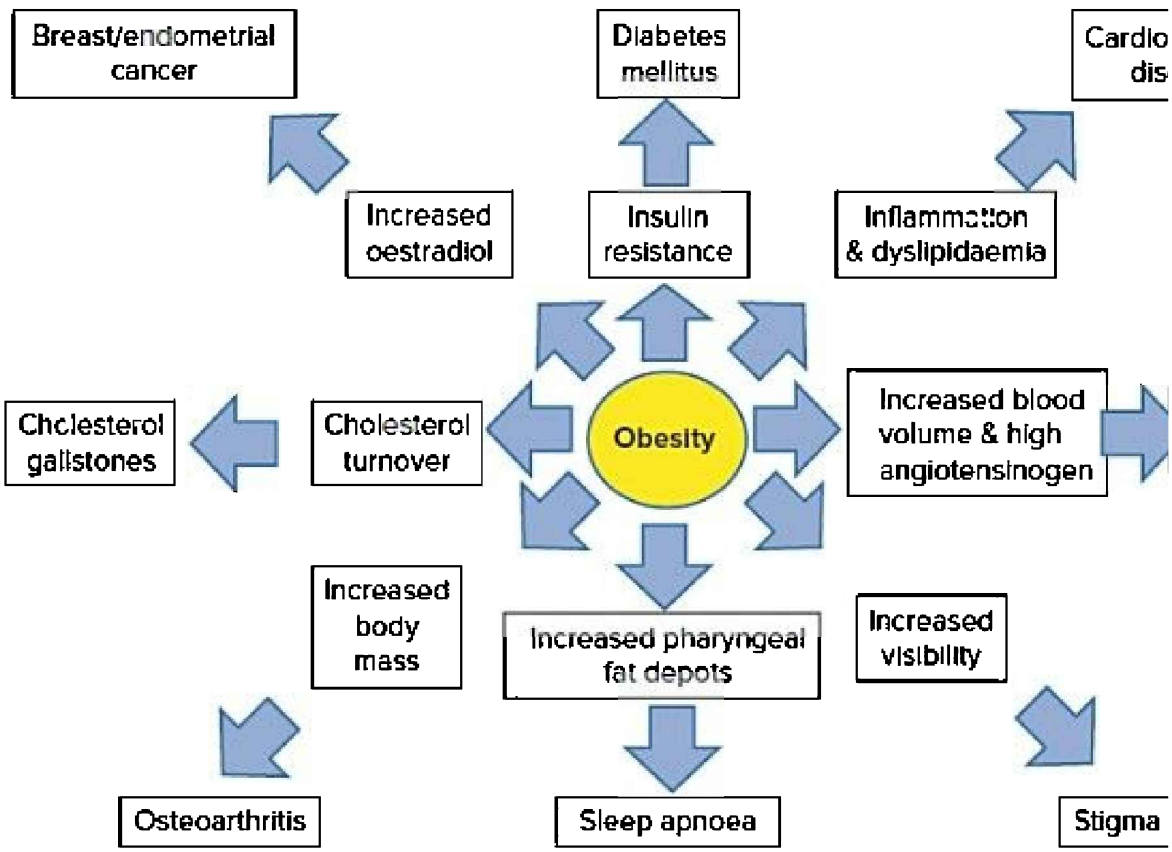


Figure 7.9 A model showing the relation between obesity and the disease with which it is associated
BRAY GA, KIM KK, WILDING JPH. OBESITY: A CHRONIC RELAPSING PROGRESSIVE DISEASE PROCESS. A POSITION STATEMENT OF THE WORLD OBESITY FEDERATION. OBES REV 2017;18(7):715–23. © WORLD OBESITY FEDERATION

Findings of large pooling studies used for the Global Burden of Disease (GBD) Study 2013 show consistent risks as BMI reached more than 23 kg/m^2, and especially for cardiovascular disease, cancer, diabetes, osteoarthritis and chronic kidney disease.[110] Above normal BMI, the relative risk of hospitalisation increases with even small increases in BMI.[111] Among women aged 50–84 in England, around one in eight hospital admissions are likely to be attributable to

overweight or obesity.[112]

A review of BMI and mortality, carried out by pooling many studies,[113] showed that the optimal BMI for lowest mortality was between 22.5 and 25 kg/m^2. For each increase of 5 BMI units, Page 87 total mortality rose by 30%, chronic kidney disease by 60% and diabetes mellitus by 120%. This relationship between BMI and risk for death has been confirmed repeatedly.[114, 115]

BMI is one predictor of risk and body fat another. When these two were examined together in a large Canadian population assembled from people who had undergone dual-energy X-ray absorptiometry to measure bone mineral density, low BMI and high body fat percentage were independently associated with increased mortality, and this may help explain the counterintuitive relationship between overweight and obesity.[116]

In a systematic evaluation of the health effects of high BMI, the GBD 2015 Obesity Collaborators found that excess body weight accounted for about 4 million deaths and 120 million disability-adjusted life years worldwide in 2015. Nearly 70% of the deaths that were related to high BMI were due to cardiovascular disease, and more than 60% of those deaths occurred among obese persons.[117]

Globally, 39% of deaths and 37% of disability-adjusted life years that were related to high BMI occurred among non-obese persons. Although some studies have suggested that overweight is associated with a lower risk of death from any cause than is a normal range of BMI (18–25),[118, 119] evidence from a meta-analysis[120] and a pooled analysis[121] of prospective observational studies showed a continuous increase in the risk of death associated with a BMI of more than 25.

Moderate obesity (BMI 30–35 kg/m^2) reduces life expectancy by an average of three years, while morbid obesity (BMI 40–50 kg/m^2) reduces life expectancy by 8–10 years. This 8–10 year loss of life is equivalent to the effects of lifelong smoking.[122]

A recent Australian analysis of 12 studies, involving 1.4 million people, found those with a BMI over 30 have a 40% higher risk of sudden death from heart attack than people of normal BMI.[123] The risk is highest among those who are obese from a young age. And most of those sudden deaths from heart attacks occurred in people with no other risk factors and seemingly normal hearts.

Some of the pathways by which obesity can lead to the development of chronic disease are shown in Fig. 7.10.

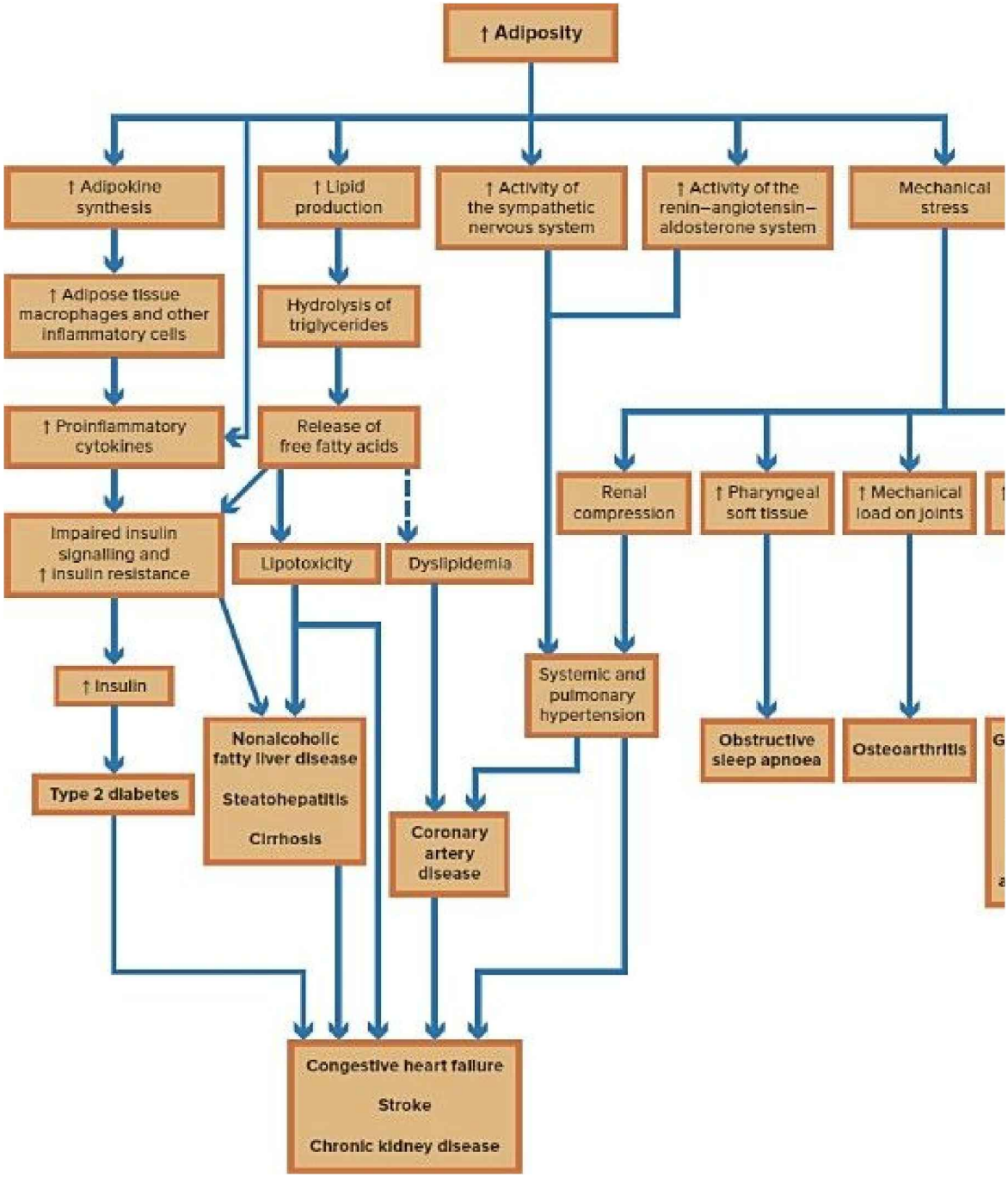


Figure 7.10 Pathways through which excess adiposity leads to major risk factors and common chronic diseases. Common chronic diseases are shown in red boxes. The dashed arrow denotes an indirect association

FROM THE NEW ENGLAND JOURNAL OF MEDICINE, EYMSFIELD & WADDEN, MECHANISMS, PATHOPHYSIOLOGY,

AND MANAGEMENT OF OBESITY, VOL 376, PAGES 254–66. COPYRIGHT © 2017 MASSACHUSETTS MEDICAL SOCIETY. REPRINTED WITH PERMISSION FROM MASSACHUSETTS MEDICAL SOCIETY

Cardiovascular disease

Cardiovascular disease (CVD) is the leading cause of death and disability-adjusted life years (DALYs) related to high BMI and accounts for 2.7 million deaths and 66.3 million disability-adjusted life years. Globally, 41% of BMI-related deaths and 34% of BMI-related DALYs are due to cardiovascular disease among obese persons.[104]

Numerous studies have shown a deleterious effect of high BMI on the risk of myocardial infarction.[124] In a recent study, obesity was associated with shorter longevity and a significantly increased risk of cardiovascular morbidity and mortality, compared with normal BMI. Despite similar longevity compared with normal BMI, overweight was also associated with significantly increased risk of developing CVD at an earlier age, resulting in a greater proportion of life lived with CVD morbidity.[125]

Diabetes mellitus

Diabetes was the second leading cause of BMI-related deaths in 2015 and contributed to 600 000 deaths and 30.4 million DALYs.[104] Obesity is one of the strongest predictors of diabetes.[126]

Cancer

The GBD Collaborators' evaluation of prospective observational studies showed sufficient evidence supporting a causal relationship between high BMI and cancers of the oesophagus, colon and rectum, liver, gallbladder and biliary tract, pancreas, breast, uterus, ovary, kidney and thyroid, along with leukaemia.[104] A review by the International Agency for Research on Cancer (IARC) came to similar conclusions, with the exception of leukaemia.[127]

Oestrogen production by adipose tissue and the associated risk of endometrial and breast cancer is well known. In post-menopausal women, adipose tissue is the major source of oestrogenic compounds, as the ovaries no longer produce oestrogens.[128]

Musculoskeletal conditions

Four per cent of the DALYs that are related to high BMI are from musculoskeletal disorders.[104] Osteoarthritis is more prevalent in people who are obese.[129] This can involve both weight-bearing and non-weight-bearing joints, suggesting that the pathophysiology must involve one or more of the increased body mass, circulating adipokines, inflammatory factors or other pathophysiologic mechanisms.[8]

Sleep apnoea

The prevalence of sleep apnoea is increased in the patient with obesity.[131] Accumulation of fat in the pharynx is a major risk factor for development of sleep apnoea.

Gallstone disease

Gallstone disease is more prevalent in the patient with obesity. Increasing body fat increases the turnover of cholesterol such that each kilogram of extra body fat produces an extra 20 mg of cholesterol each day, which must be secreted through the biliary tree.[132] In individuals with a tendency for gallstone formation, this extra load of cholesterol from increased fat may be the tipping point for the development of stone formation and gallbladder disease.[133]

Mental illness

Obesity is associated with an increased prevalence of mood, anxiety and other psychiatric disorders, particularly among persons with severe obesity.[134] Moreover, medications used Page 88 to treat bipolar disorder, major depression and some psychotic disorders can be accompanied by substantial weight gain.[124]

Stigma

Obese individuals face stigma and multiple forms of prejudice and discrimination. Weight bias remains persistent in settings of employment, healthcare, education, the media and in Page 89 close interpersonal relationships. Weight bias increases vulnerability to depression, low self-esteem, poor body image, maladaptive eating behaviours and exercise avoidance.[135]

The obesity paradox

There is a large body of evidence supporting the so-called 'obesity paradox', which posits that being overweight or even obese is protective against, or has no impact on CVD and overall mortality,[136] especially in elderly individuals or those with diagnosed coronary disease or other severe medical conditions.[137, 138]

To study the associations of body composition (assessed by five different measures) with incident CVD outcomes in healthy individuals, a British study looked at 296 535 participants (57.8% women) of white European descent without CVD at baseline from the UK Biobank.[139] The researchers found increasing adiposity has a detrimental association with cardiovascular health in middle-aged men and women. The risk of cardiovascular disease rose starting at a BMI of about 22[140] (Fig. 7.11). Other studies have found that a BMI of about 22 or even lower is the healthiest. Being underweight actually had a higher risk than being overweight/obese. The association of BMI with CVD appears more susceptible to confounding due to pre-existing comorbidities, when compared with other adiposity measures.

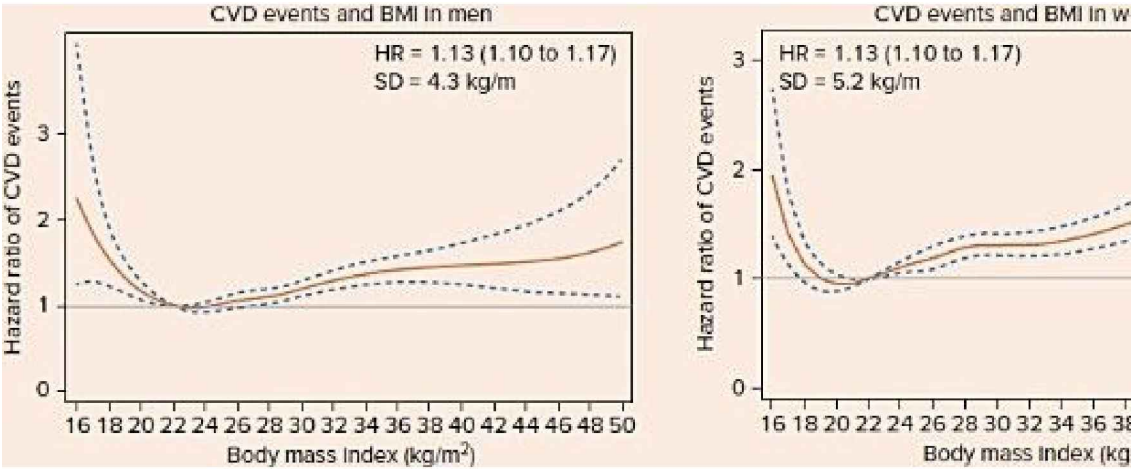


Figure 7.11 Cardiovascular events and BMI levels in men and women
EUROPEAN HEART JOURNAL, VOLUME 39, ISSUE 17, 1 MAY 2018, PAGES 1514–1520, HTTPS://DOI.ORG/10.1093/EURHEARTJ/EHY057[131]

MANAGEMENT OF THE PATIENT WITH OBESITY

No country has managed to reverse their obesity trends.[139] The management of the patient with obesity requires a multidimensional and multisectoral approach across and between all levels of society. Change must first be implemented upstream to see effects downstream that support lifestyle and medical interventions.

Lifestyle interventions

Lifestyle interventions are the first step in the management of the patient with obesity. These interventions include diet, exercise and behavioural therapy.

Diet

Diet is the single most important factor in the cause and management of obesity. There are two main classes of diets advocated: the calorie-restricted/low-fat diet or *caloric* approach, and the low-carb/high (healthy)-fat diet or *hormonal* approach. Both have been shown to be effective in producing short-term weight loss, but there are substantial differences in their sustainability.

Since the advent of the Dietary Guidelines in 1980 (see earlier box 'What has happened in the pas t 40 years?'), patients with obesity have been advised to both restrict calories and reduce their intake of fat, in particular saturated animal fats, such as those found in red meat and full-fat dairy. Calorie restriction is an effective short-term weight loss strategy, but as mentioned previously, the body responds to this weight loss in a number of ways, including increased hunger and reduced BMR. As a result, these diets are difficult to sustain and when the patient responds to their hunger by increasing calories, the weight is quickly regained and frequently the end result

is a net weight gain rather than a loss.

One consequence of the move to reduce the fat content of foods after the Dietary Guidelines was to replace the fat with additional carbohydrates, especially in the form of sugar, high-fructose corn syrup or other sugar equivalents. This is thought to be one of the primary explanations for the steady increase in levels of obesity since 1980.

As Dr Walter Willett stated in a 2002 review article, 'the emphasis on total fat reduction has been a serious distraction in efforts to control obesity and improve health in general'.[53]

Numerous randomised controlled trials (RCTs) have compared the weight loss associated with low-fat and low-carbohydrate diets. The Public Health Collaboration UK website keeps an ongoing tally of both RCTs[140] and meta-analyses[141] comparing low-carb diets with less than 130 g carbohydrate per day to low-fat diets with less than 35% of calories from fat. At the time of writing, there were 62 RCTs, of which 53 showed the low-carb diets to be more effective for weight loss.

A proven effective dietary approach to managing obesity is a low-carb, healthy-fat diet with:

- reduced sugar-sweetened beverages—soft drinks, fruit juices, fruit drinks, cordials, flavoured drinks (milks, coffees and teas)
- reduced starchy foods, which are broken down to sugar—pasta, rice, potatoes
- reduced processed grains—white bread and bread products (muffins, crumpets, biscuits etc.), breakfast cereals
- reduced foods with hidden sugars—flavoured yoghurts, muesli bars, sauces and dressings.

The emphasis should be on real food (grass-fed meat, dairy, fish, non-starchy vegetables, avocados, berries, nuts and olive oil).

By reducing glucose intake and subsequent insulin load, insulin resistance can be reversed, and the patient can benefit from weight loss as well as other health benefits. It is hoped that future Dietary Guidelines will be adjusted in line with the scientific evidence supporting this approach.

Low-calorie sweeteners and obesity

The role of low-calorie sweeteners (LCS) in weight management is controversial, with claims that LCS consumption may increase rather than decrease the risk of overweight and obesity.[142] Recent meta-analyses of acute and longer-term randomised controlled studies in human participants found clear evidence that consumption of LCS compared with sugar reduces energy intake and body weight.[143, 144] The one study (the CHOICE trial) that has looked at whether there is an advantage in switching from sugar-sweetened beverages to LCS-sweetened beverages versus switching to water found slightly, but not statistically significant, greater weight loss in the group switching to LCS.[145]

Another argument against the consumption of LCS is that exposure to sweetness encourages a sweet tooth and therefore increased intake of sweet, energy-containing foods and beverages. There is, though, little direct evidence to support these statements.[90]

Exercise

The benefits of exercise for health are proven (Chapters 1–5). It is undeniably the best buy for public health. The effect of exercise for weight loss, however, is relatively small and this applies particularly to the overweight or obese patient. A Cochrane review reported that when compared with no treatment, exercise resulted in small weight losses across studies.[38] Increasing exercise intensity increased the magnitude of weight loss.

Sedentary behaviour should be considered separately to exercise. A meta-analysis of data from prospective cohort studies also showed only small, inconsistent and non-significant associations between sedentary behaviour and body weight.[46]

Diet and exercise

A review of the evidence on long-term lifestyle programs in obese participants showed that a combination of diet and exercise was more effective in inducing moderate long-term weight loss and reducing blood lipids and blood pressure than either diet or exercise alone. The review also confirmed the moderate superiority of diet over exercise regarding anthropometric outcome parameters.[146] The Cochrane review mentioned above also concluded that a combination of diet and exercise resulted in a greater weight reduction than diet alone.[138]

Behavioural therapy

Behavioural therapy provides patients with techniques for adopting dietary and activity recommendations.[147] Foremost among these recommendations is regular recording of food intake, physical activity and weight. This task can be facilitated by smartphone apps, activity counters and cellular-connected scales.[147, 148] Ideally, patients review their progress approximately weekly with a trained interventionist, who provides encouragement and goal-setting and problem-solving instructions. Telephone-delivered lifestyle interventions result in approximately the same weight loss as in-person counselling.[149]

Web-based interventions that include personalised interventionist feedback can be prescribed, but typically result in only one-half to two-thirds of the weight loss achieved with in-person counselling.[126, 150] Web-based interventions, however, potentially have greater reach and convenience and lower costs than in-person counselling.[124]

Weight regain is common after a patient completes a lifestyle intervention program.[124] The most effective behavioural method for preventing weight regain is continued support on a fortnightly or monthly basis, whether in person or by telephone.[124, 151] Although long-term behavioural counselling is effective, it is not widely available. Moreover, when this approach fails to produce the additional weight loss that patients desire, it is challenging to persuade the patients to remain in counselling to maintain the smaller weight loss they have achieved.[124]

Other lifestyle choices

As previously mentioned, both sleep and stress play important roles in the management of obesity. Emerging evidence supports the benefits of behavioural, but not pharmacological, sleep extension

on appetite and glucose metabolism. Further research should focus on the feasibility and efficacy of strategies to optimise sleep duration and quality on obesity and diabetes risk in at-risk populations as well as those with established diseases.[75]

Why do lifestyle changes fail?

The majority of obese men, and more than two-thirds of obese women, report having attempted to lose weight in the past year.[152] Lifestyle intervention programs are effective in the management of obesity; however, the vast majority of weight-loss attempts fail.

Barriers to behaviour change include poor motivation; environmental, societal and social pressures; lack of time; health and physical limitations; negative thoughts or moods; socioeconomic constraints; gaps in knowledge or awareness; and lack of enjoyment of exercise. The most prominent predictors of adherence include early weight-loss success, lower baseline BMI, better baseline mood, being male and older age.[153]

Barriers to behaviour change need to be addressed early in treatment, with lifestyle intervention individualised accordingly. Predictors of adherence should also be taken into careful consideration, with negative moods and unrealistic weight loss expectations discussed at the outset. If adherence is improved, treatment effectiveness, health outcomes and the ultimate burden of chronic diseases could also be improved.[153]

Medical management

There are two main types of medical interventions in the management of the patient with obesity: pharmaceutical and surgical.

Medications

While lifestyle management is the mainstay of obesity treatment, a number of medications have proven useful and are in widespread use.[154] Various organisations advocate the use of weight-loss pharmacotherapy in patients with a BMI greater than 30 kg/m^2, or those with a BMI of 27–30 kg/m^2 with obesity-related complications.[155–157]

Phentermine (Duromine) has been the most commonly used drug in the treatment of obesity for a number of decades.[158] Phentermine is a sympathomimetic amine that acts as an appetite suppressant. It has been shown to be an effective weight-loss agent.[159] Given the effects of phentermine on the cardiovascular system, it should not be used in patients with a history of cardiovascular disease. Other contraindications include anxiety disorders, hyperthyroidism, history of drug or alcohol abuse or dependence, concomitant treatment with monoamine oxidase inhibitors, pregnancy and breastfeeding. It should be used with caution in patients with hypertension, history of cardiac arrhythmias or seizures.[160]

Orlistat (Xenical®) inhibits pancreatic and gastric lipases and thus reduces absorption of dietary fat. Taken with meals, approximately 30% of oral fat intake is excreted in the stool. Side effects are due to fat malabsorption and include steatorrhoea, oily spotting, flatulence with discharge, faecal

incontinence, fat-soluble vitamin deficiencies and calcium oxalate kidney stones.[154]

Liraglutide is a glucagon-like peptide-1 (GLP-1) agonist that was initially used to treat type 2 diabetes, and controls hyperglycaemia without causing hypoglycaemia or weight gain. Its side effect profile of decreased appetite, reduced energy intake and subsequent weight loss has led to its more recent approval as a weight management drug. It can be given independently of meals, as a subcutaneous injection into the abdomen, thigh or upper arms. Common side effects of liraglutide are gastrointestinal in nature, including nausea, vomiting, diarrhoea, constipation and dyspepsia, which can be mitigated by gradual dose escalation. Most gastrointestinal symptoms are mild to moderate, transient and diminish within days or weeks with continued treatment.[160] Liraglutide-induced weight loss is associated with an increased incidence of symptomatic gallstones.

Bariatric surgery

Bariatric surgery has become very popular in the past two decades and is one of the most effective means of weight reduction among the morbidly obese. A meta-analysis estimated that weight loss five years after bariatric surgery averages 12–17 units of BMI; the few studies with long follow-up have calculated that weight loss 10 years after bariatric surgery averages 6.5 to 7.1 BMI units.[161]

Three main types of bariatric surgery are currently performed.[162] Laparoscopic adjustable gastric banding, the least invasive and safest procedure, involves placing an inflatable Page 92 silicone band around the gastric fundus to create a small (approximately 30 mL) pouch. This restrictive procedure is reversible and does not cause anatomical gut changes.

Roux-en-Y gastric bypass restricts food intake by creating a small (<50 mL) pouch in the upper gastric fundus, which is anastomosed to a Roux limb of jejunum.[162] Food bypasses 95% of the stomach and duodenum and most of the jejunum. The recently introduced vertical-sleeve gastrectomy involves removal of approximately 70% of the stomach, with subsequent acceleration of gastric emptying.

Gastric banding results in a mean weight reduction of 15–20% at one year. Larger reductions can be achieved with vertical-sleeve gastrectomy and Roux-en-Y procedures—approximately 25% and 30%, respectively.[163–165] More than half of patients who undergo Roux-en-Y gastric bypass have weight loss of 25% or more at one year.[165]

Patients regain an average of 5–10% from their lowest weight at 10 years of follow-up,[166] with a higher frequency of full weight regain reported with gastric banding than with the other two operations. Concerns about efficacy and high re-operation rates have led to a decrease in the use of gastric banding. In addition to weight loss, pronounced clinical improvements are observed in most obesity-related health conditions, particularly type 2 diabetes, after Roux-en-Y gastric bypass, vertical-sleeve gastrectomy and, to a lesser extent, gastric banding.[124]

Owing to the increasing use of laparoscopic procedures, the 30-day mortality rates for all bariatric surgeries have decreased over the past decade. Gastric banding now has the lowest perioperative mortality rate (approximately 0.002%), with rates of 0.2% and 0.3% for Roux-en-Y gastric bypass and vertical sleeve gastrectomy, respectively.[162, 167]

Serious perioperative adverse events parallel these findings, with rates of approximately 1% for gastric banding and approximately 5% for vertical-sleeve gastrectomy and Roux-en-Y gastric bypass.[162, 167, 168] About one-fourth of patients treated with gastric banding or Roux-en-Y gastric bypass require surgical revisions at 10 or more years of follow-up; the data are limited for the more recently introduced vertical-sleeve gastrectomy.[162]

Limitations of current surgeries include high costs initially and, at one year, risks of short- and long-term complications, and weight regain in approximately 5–20% of patients.[166] However, Roux-en-Y gastric bypass and vertical-sleeve gastrectomy are effective long-term treatments for severe obesity.

SOLVING THE OBESITY PROBLEM

Attempts to change personal lifestyle choices have had limited impact on obesity. Overemphasis on individual-oriented solutions to reducing the obesity epidemic, which depend on high levels of personal agency in resisting or overcoming obesogenic environmental forces, is unrealistic and potentially widens health inequalities.[169] No single action will solve the obesity epidemic (Fig. 7.12).

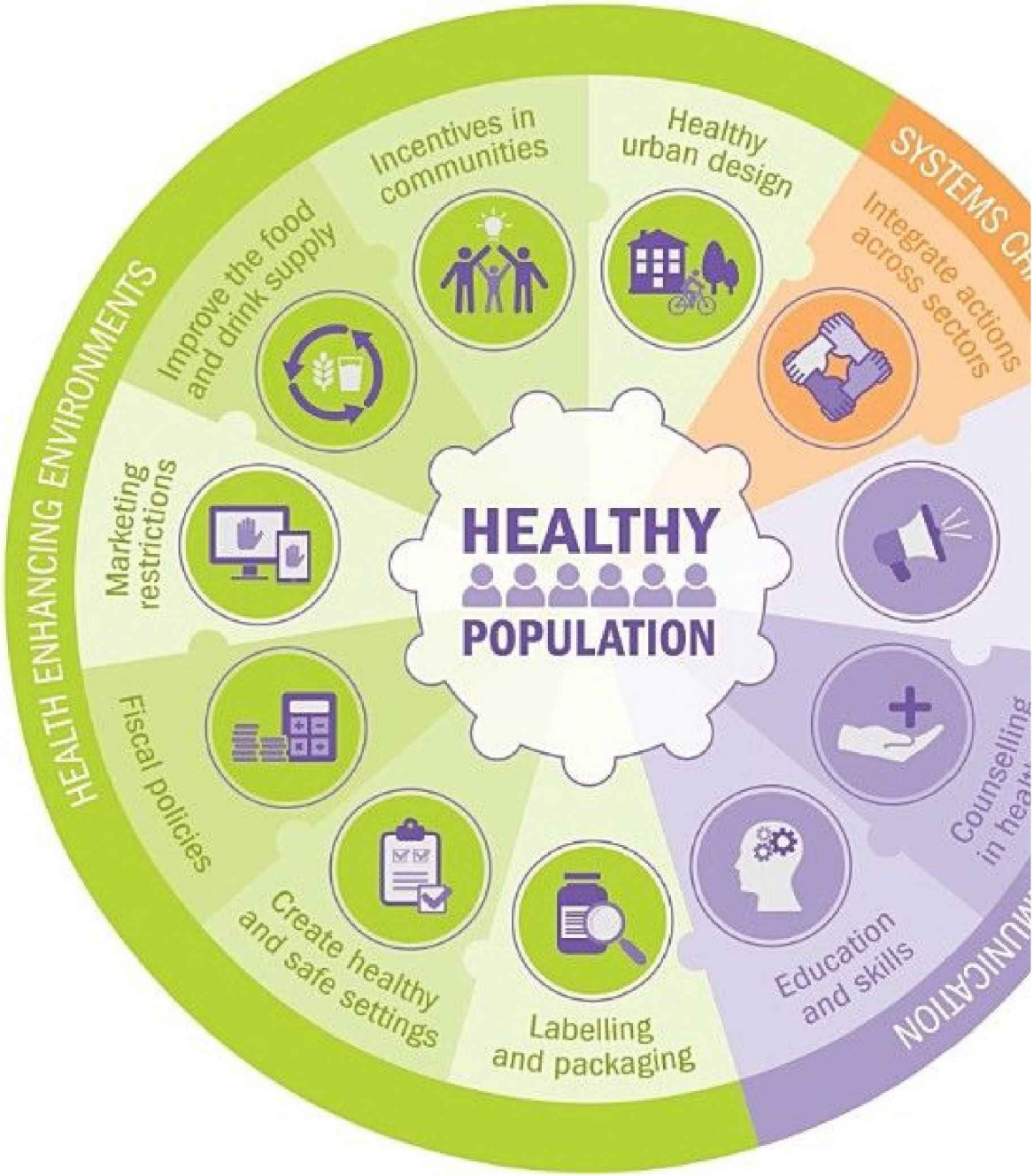


Figure 7.12 No single action will solve the obesity epidemic
THIS MATERIAL HAS BEEN REPRODUCED FROM THE WORLD CANCER RESEARCH FUND INTERNATIONAL DRIVING ACTION FRAMEWORK. WWW.WCRF.ORG/DRIVINGACTION

Clinicians' support for individuals to counteract obesogenic environments will continue to be

important, but the priority in the future will be for policies to reverse the obesogenic nature of these environments. Upstream (or macro-level) strategies are more likely to be successful. This can be achieved through whole-systems approaches to obesity,[170] using cross-sector and multi-agency working groups to consider the multiple factors involved in the aetiology of obesity that influence individual determinants. Examples of upstream approaches could be through use of planning laws[171] or through the taxation of unhealthy foods.[172] In the four years following the introduction, in Mexico in 2014, of the first significant nationwide tax on sugar-sweetened beverages, there has been a global increase in taxes on SSBs.[173]

During the past decade, researchers have proposed a range of interventions to reduce obesity. Among such interventions are restricting the advertising of unhealthy foods to children, improving school meals, using taxation to reduce consumption of unhealthy foods and providing subsidies to increase intake of healthy foods, and using supply-chain incentives to increase the production of healthy foods.[174]

Obesity is complex, multifactorial and challenging to address.[175] Our food environment is a sophisticated and complex system that requires a complex system approach.[176] The future of interventions in the food environment field is to adopt a systems approach, to encourage professionals in local and national governments to work together to develop policies and practices that are championed by the population and supported by all sectors including industry to enable healthier behaviours.

Although the empirical evidence for what could reduce population-level obesity and its inequality is scarce,[177] committed cross-government action is required on legislative changes that might help reverse the obesogenic environment, rather than voluntary suggestions. Examples include further legislative incentives for food manufacturers to reduce sugar content in food and drinks, as well as the advertising of such foods to children and parents, plus incentives for the sale of healthier alternatives.

POLICY INTERVENTIONS

Because health professionals are often in positions of influence in the community, we include a section on the evidence for policy intervention. To classify and assess the efficacy of the various interventions used in the management of obesity, we have used the classification of Mazzocchi and colleagues.[179] (Table 7.3). This classification divides the interventions into two broad categories—policies that support informed choice, and policies aimed at changing the market environment.

Table 7.3 Policy interventions in the management of obesity

Policies supporting more-informed choice:
Advertising controls
On advertising to children
On general advertising

Public information campaigns – social marketing
Nutrition education For children For adults
Nutrition labelling
Nutrition information on menus
Policies aimed at changing the market environment:
Fiscal measures
Taxes or subsidies on foods for the population at large
Subsidies to disadvantaged consumers
Regulation of meals
School meals
Workplace canteen meals
Nutrition-related standards
Government action to encourage private-sector action (e.g. reformulation):
Policy interventions not explicitly targeted at healthy eating but relevant (e.g. consumption tax rates, agricultural policy)

ADAPTED FROM ADOLESCENT OVERWEIGHT AND OBESITY. WWW.HEALTH.GOV.AU

Policies supporting more-informed choice

The policies evaluated under this heading aim to provide information to consumers and educate them to use it.

Advertising controls

Controls on advertising to children

There is widespread concern about the way food is marketed to children.[179] There is unequivocal evidence that the marketing of unhealthy foods and sugar-sweetened beverages is related to childhood obesity.[180] Following examination of the available evidence, the WHO found that advertising of unhealthy food influences children's food preferences, purchase requests and consumption patterns, such that there is a clear rationale for action to be taken by member countries.[181]

There is considerable variation between countries in the rules regarding television advertising of unhealthy foods. For example, in 2007 the UK moved from a voluntary agreement to the introduction of new rules restricting television advertising of products high in fat, salt or sugar (HFSS) during children's viewing hours. A 2010 review found that the HFSS regulations had reduced children's exposure to HFSS advertisements by 37% and had reduced children's exposure to advertisements featuring licensed characters and promotions.[182] There was also a significant shift in the content of food advertising towards non-HFSS products.

A number of reviews and empirical tests tend to provide evidence, albeit weak in some cases, that food advertising can influence the amount of unhealthy food being consumed by children.[183]

If we consider Australia as a case study, we note that the current approach to regulation is largely voluntary and self-regulatory, and has done little to reduce children's exposure to this

marketing. Over the course of a year, the average Australian child will see 35 hours of food advertising on television, of which over half will be for unhealthy foods. Children continue to be exposed to high volumes of unhealthy food marketing on television and, despite changes to the self-regulatory codes, there was no change in the rate of unhealthy food advertising on TV between 2011 and 2015.[184]

There has also been recent concern about advertising to children through social media. This is proving difficult to control.

Public information campaigns—social marketing

Social marketing is the process by which governments try to induce voluntary positive changes in the behaviour of individuals with the use of a wide range of commercial marketing techniques.[185] However, instead of focusing on profits, as in the private sector, social marketing focuses on the welfare of the individual and the society.

A number of social marketing campaigns have been implemented, primarily to increase fruit and vegetable consumption, such as Australia's *Go for 2&5* and the UK's *5 a Day* campaigns. A review of previous studies found evidence suggesting these types of interventions could increase consumption of fruit and vegetables. They indicated that the estimated yearly cost of this type of intervention could be around US$2.27 per target individual, with two-thirds of that amount being spent in broadcasting advertisements at the national level and the remaining amount being used to hire personnel to design and supervise the intervention.[178]

However, social marketing needs long periods of time to really achieve changes in attitudes among people and through society. Social marketing campaigns alone could take decades to have a real impact on healthy eating and weight outcomes, which would require constant and adequate funding from governments for a long period. It has been argued that short-lived social marketing campaigns are doomed to fail because of the nature of the environment in which individuals live nowadays, where a series of factors continuously encourages unhealthy behaviour.[186]

Generally public information campaigns have been relatively successful in raising awareness of unhealthy eating and its consequences, but less successful in translating the message into action.

Nutrition education

The main goal of nutrition education is to make people aware of what constitutes a healthy diet and of ways to improve their diets and lifestyles. This can be done through different channels, although in general it occurs within schools, targeting young children,[187] since food habits in early stages of life are said to determine practices and preferences in adulthood.[188]

Overall, the literature suggests that nutrition education can have an impact on healthy eating, but the impact is not homogeneous throughout the population.[183]

Education for children

At least moderately strong evidence supports the effectiveness of school-based interventions for preventing childhood obesity.[189] Most reviews summarising childhood obesity prevention

interventions focus on the school setting,[190] with fewer studies concentrating on preschool, community or home environments. One review from 2015 summarised findings across all settings in high-income countries.[189]

Evidence was strongest for school-based programs that included a home and community component and implemented either a physical activity-only or combined diet and physical activity intervention.

The introduction of health education programs, complemented by appropriate catering services within schools, increased fruit and vegetable intake, although dietary changes diminished after exposure to any program ended.[179]

There is a lack of consensus about the minimum duration needed to show an effect for school-based interventions, with estimates varying from between 6 weeks and 6–12 months; many school-based interventions are limited by the length of a school year (about 9 months) for practical scheduling reasons, whereas other interventions, such as environmental changes, can persist indefinitely.

The strength of evidence for obesity prevention in preschool and childcare settings is relatively weak because of the small number of studies published.[187] The authors of one review suggested that interventions grounded in social cognitive theory (e.g. education, skills building and goal-setting, to promote self-efficacy pertaining to target health behaviours) with parent involvement were most effective in the preschool setting.[191]

The evidence for the effectiveness of interventions in the community setting is moderate, particularly for combined diet and physical activity interventions that also include a school component;[192] however, considerable heterogeneity in study characteristics poses a challenge to the making of consistent recommendations.

The family and home environment is recognised as a strong influence on the health-related behaviours of children;[193] however, evidence for the effectiveness of primarily home-based interventions is mixed, with some studies reporting a favourable effect and others finding minimal evidence.[187]

All of the randomised controlled trials that report positive results in the school setting include a secondary home setting and use combined diet and physical activity intervention—including intervention elements such as enhanced or lengthened physical activity time, implementation of a nutrition education curriculum and improvement in participants' self-regulation and efficacy.[187]

Education for adults

A US study suggested that a 1% increase in state-level funding of nutrition education programs results in a 0.006% decrease in BMI per year. Therefore, in order to reach a normal range of BMI, funding for nutrition education should be increased by about 23 times (going from actual spending of some US$1.5 million to US$34 million).[194]

Food labelling

Food labelling legislation exists to inform the public about the ingredient and nutrient composition

of foods and to protect the public from misleading claims or claims not supported by sound scientific evidence.[195] A wealth of information is now provided on food packaging, including lists of ingredients and kilojoule/macronutrient content, which is broadly understood by those who use it, but is not as widely utilised to inform choice as it might be.

Research indicates that food labelling leads consumers to choose more healthful food options.[196] However, only a minority of consumers in Europe actually look at nutrition labels when shopping, and these consumers are limited to those with a particular interest in healthy eating.[197]

Most studies to date have found that the influence of nutrition labelling on food purchasing decisions is weak, especially when compared with taste, price, use-by date, brand, convenience and family preferences.[198, 199]

At present, in Australia it is mandatory for products to feature a nutrition information panel (NIP). The NIP provides the amount of energy and macronutrients per serve size (where serves vary greatly between products) and per 100 g. In this respect, the NIP fails to translate into simple and accessible information about the relative healthiness of products, and is particularly difficult to interpret for consumers from lower socioeconomic groups, non-English speaking backgrounds, those with low literacy, as well as children. The appearance of the industry's voluntary Daily Intake Guide, and a range of other health claims on some products, further contributes to consumer confusion.

Front-of-pack labelling schemes provide a judgment about the nutritional quality of products. The most common interpretive schemes are colour-coded (traffic-light) systems, such as that developed in 2006 by the UK Food Standards Agency, in which the amount of key negative nutrients (total sugar, total fat, saturated fat and salt) is ranked as high, medium or low (according to nutrient criteria per 100 g or per 100 mL of the product) and assigned a colour code of red, amber or green, respectively.[200] Since then, many retailers have used variants of the traffic-light labelling scheme on their products. In 2013, the UK government announced the introduction of a consistent traffic light-based front-of-pack labelling system, which has the support of major UK companies and all the major retailers.[201] The scheme remains voluntary.

In the US, the Institute of Medicine has proposed a system that allocates up to three stars to products meeting acceptable criteria for sodium, added sugars and saturated and trans fat.[202] Other interpretive schemes may provide an overall rating for a product based on its 'healthiness', such as the US Guiding Stars program,[203] or the Australian Health Star Rating System.[204] Since 2012, in Australia, government, industry and community (public health and consumer) groups have been working together on the Health Star Rating System, an overall healthiness indicator underpinned by a nutrient profile score.

In addition to the interpretive front-of-pack schemes, there are percentage daily intake (%DI) or guideline daily amount (%GDA) systems, which display the percentages of the major nutrients that a food provides, based on daily intake reference values for those nutrients. Percentage daily intake schemes are non-interpretive schemes, as only numerical information is provided.

Various schemes have been developed by food industry organisations based on percentage daily

intake, including the percentage guideline daily amount (%GDA) scheme in the UK[205] and Facts Up Front labelling system in the US.[206]

Nutrition information on menus

Another strategy to improve consumer information at the point of decision making is to require that restaurants list calorie counts on their menus. A randomised field experiment that provided customers with calorie information on menus found that the information reduced the average number of calories ordered by 60.7.[207] As with the nutrition facts panel on packaged foods, requiring the disclosure of calorie information seems to lead restaurants to reformulate their foods to improve their healthfulness.[208]

Policies aimed at changing the market environment

The following policies attempt to influence healthy eating by changing the market environment.

Fiscal measures

The introduction of fiscal measures (taxes or subsidies) aims to influence consumption by changing the relative prices of good and bad foods or nutrients, and by measures that influence the availability of foods for consumption.

However, regressive fiscal measures, including taxation, may also increase social inequalities in diet quality[209] and contribute to the already-widening gap in socioeconomic status-driven inequalities in health.[210–212]

Taxes or subsidies on foods for the population at large

The WHO has urged member governments to consider economic policies and measures that discourage the consumption of less-healthy food and drink options in order to reduce rates of obesity.[213]

Denmark began taxing soft drinks and juices in the 1930s, but repealed its sugar tax in 2014. Finland reintroduced an earlier soft drink tax in 2011, while Hungary taxes sugary drinks as part of its 2011 public health product tax, which covers all food products with unhealthy levels of sugar.

France introduced a targeted sugar tax on soft drinks in 2012. Sales of soft drinks declined in the year following the introduction of the tax, after several years of annual growth. A 2016 study by Mazzocchi et al. showed that the sugary drinks tax saw a 19 euro-cent per litre increase in price of non-pure fruit juices, a 16 euro-cent per litre increase for diet sodas, and little impact on prices of regular soft drinks.[214]

In January 2014, the Mexican government implemented an excise tax on sugar-sweetened beverages of approximately 10%, as an anti-obesity measure. A review of the first year found a 6.3% reduction in the observed purchases of SSBs in 2014, compared with the expected purchases in that same year based on trends from 2008 to 2012. These reductions were higher among lower-income households, residents living in urban areas and households with children. The study also found a 16.2% increase in water purchases.[215]

In 2016, the UK Government announced that it would implement a sugary drinks tax commencing in 2018. It was revealed that manufacturers of soft drinks will be taxed on the volume they produce or import. The levy has two bands: a tax of 18 pence per litre for drinks with total sugar content over 5 g per 100 mL, and 24 pence per litre for drinks with more than 8 g per 100 mL. Soft drink manufacturers reacted, even prior to the implementation of the tax, to reduce sugar content below the different bands (Fig. 7.13). It was estimated that the sugar content of between 645 and 861 million litres of drink per year was reduced sufficiently to no longer be subject to the tax—that is, about 3 billion servings with reduced sugar content.[216]

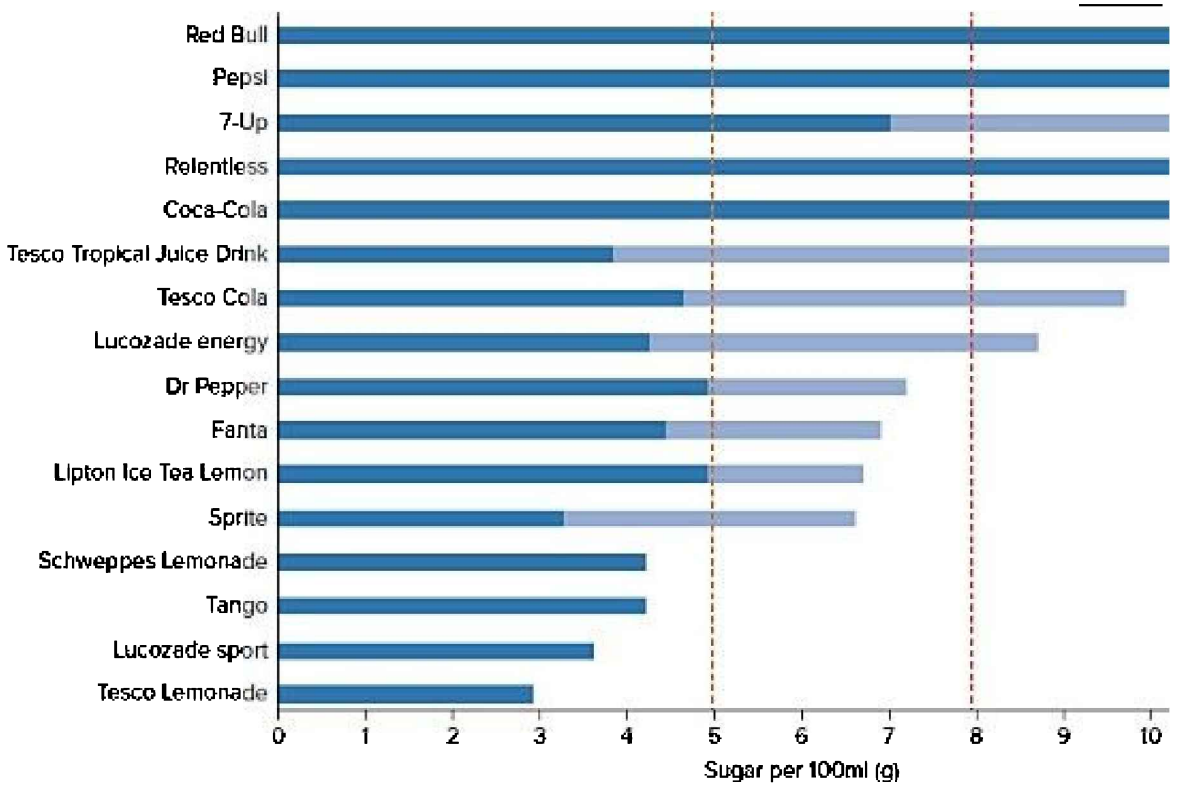


Figure 7.13 The introduction of the UK sugar tax has already led to extensive reformulation of sugary drinks (2016–2018)

ADAPTED FROM HTTP://WWW.BEHAVIOURALINSIGHTS.CO.UK/HEALTH/SUGARING-THE-BILL-WHY-LOWER-REVENUE-FROM-THE-SUGAR-TAX-IS-PROBABLY-A-GOOD-THING/

There has been criticism that the tax does not go far enough, as it does not include milk-based drinks, fruit juices, confectionery and sweets.

In November 2014, Berkeley, California, was the first city in the USA to pass a targeted tax on sugary drinks. The Measure D soda tax was approved by 76% of Berkeley voters on 4 November

2014, and took effect on 1 January 2015. The measure imposes a tax of one cent per ounce on the distributors of specified sugar-sweetened beverages such as soda, sports drinks, energy drinks and sweetened iced teas, but excludes milk-based beverages, meal replacement drinks, diet sodas, fruit juice and alcohol.

A study from 2016 compared the changing intake of SSBs and water in Berkeley versus San Francisco and Oakland (which did not have a sugary drink tax) before and after Berkeley passed its tax. This analysis showed a 26% decrease of soda consumption in Berkeley and 10% increase in San Francisco and Oakland, while water intake increased by 63% in Berkeley and 19% in the two neighbouring cities.[217]A 2017 before-and-after study concluded that one year after the tax was introduced in Berkeley, sugary drink sales decreased by 9.6%, when compared to a scenario where the tax was not in place.[218] This same study was also able to show that overall consumer spending did not increase.

An Australian study found that increasing the price of sugary drinks by 20% could reduce consumption by 12.6%.[219] It was calculated that this reduction in consumption had the potential to generate a decline in the prevalence of obesity of 2.7% among men and 1.2% among women, and could reduce the number of cases of type 2 diabetes by 800 per annum. The study also estimated that the levy could raise revenue in excess of $400 million per year, even when taking into account changes in consumption in response to the tax.

In New York City in 2012, Mayor Michael Bloomberg attempted to institute a ban on large-size sugary beverages—a portion control ban. The limit put a 16-ounce (475 mL) cap on sweetened bottled drinks and fountain beverages sold at city restaurants, delis, movie theatres, sports venues and street carts. The size limit applied to beverages with more than 25 calories per 8 ounces (235 mL). It did not include 100% juice drinks or beverages with more than 50% milk. The day before the ban was due to take effect, it was overturned by a judge, who ruled that the City Health Board did not have the authority to limit or ban a legal item under the guise of 'controlling a chronic disease.[220]

Subsidies to disadvantaged consumers

As mentioned previously, there is now at least a tacit understanding that nutrient-dense foods cost more, such that changing dietary behaviours may also require some economic interventions.[221, 222] The higher cost of vegetables and fruit may be a potential barrier to the adoption of healthier diets.[223, 224] The stated intent of pricing interventions[225, 226] and food assistance programs[227, 228] is to promote purchases of vegetables and fruit by lower socioeconomic status groups.[229–231]

Food vouchers to reduce the price of healthy foods, targeted to specific parts of the population (poor people, pregnant women, mothers of young children, and the elderly), may be viewed as a variant of a fiscal intervention. The rationale for food vouchers is that many vulnerable population groups have poorer diets because they cannot afford healthy food.[183]

The US Food Stamp Program, now SNAP, was originally designed to encourage the consumption

of surplus farm commodities by redirecting them to poor and ill-fed people, as well as acting as a welfare scheme for poor families unable to afford an adequate diet.

Zagorsky and Smith investigated the impact of the Food Stamp Program on participants' weight. Their findings suggest that female participants tended to gain weight (on average, 2.6 kg).[232]

Lin and colleagues examined the effectiveness of price subsidies to the poor and food stamps in the United States.[233] Their results suggest that a 10% fruit and vegetable price subsidy to low-income consumers would increase the consumption of fruits and vegetables by 4–7%, at an estimated cost of $734 million a year. If the same amount were used to finance food stamps, consumption of fruits and vegetables would increase by only 0.35–0.40%, suggesting that price subsidies are a much better alternative to the income subsidy of food stamps.

Overall, the literature suggests that vouchers for healthy foods targeted to low-income consumers are an effective way of increasing fruit and vegetable consumption. However, research into cost-effectiveness is still needed.

Regulation of meals

School meals

The school environment is thought to exert a significant influence on pupils' dietary habits. Most developed countries offer free or subsidised school meals, and food availability in schools is often complemented by vending machines offering a range of snacks and soft drinks high in sugar, unhealthy fat, and calories. The response by health authorities has varied among countries, including requiring improvements in the nutritional quality of school meals, increased availability of fruits and vegetables, banning vending machines and supplying healthier snacks.[183]

De Sa and Lock conducted a systematic review of the effectiveness of various interventions promoting fruit and vegetable consumption in schools. Their findings suggest that, in most cases, such schemes are effective in increasing intake and awareness, with both public health and agricultural benefits.[233]

Workplace canteen meals

The same is thought to be true for adults, where healthy meal provision in the workplace can be expected to have positive behavioural and health outcomes. One study found evidence that workplace interventions (e.g. group sessions with a nutritionist every two weeks for 20 months, reinforced by health-related activities and catering services offering healthy food) increase consumption of fruit and vegetables as well as physical activity, with corresponding decreases in unhealthy fat intakes.[178] Furthermore, those who were exposed to workplace interventions seemed to retain some of the benefits after retirement.

The Finnish government has influenced diets by providing healthy meals in the workplace; guidelines have been in place since the 1970s and are said to be closely followed, particularly in the public sector.[179] Indeed, those who eat at staff canteens are said to eat more vegetables, fish and boiled potatoes.

Nutrition-related standards

Nutrition-related standards could be applied to portion sizes as well as composition standards for trans fats, salt, saturated fats and sugar.

Many countries have acted to reduce trans fatty acid (TFA) intakes by a variety of methods, ranging from nutritional recommendations, programs to raise awareness of the adverse effects of TFAs, voluntary or mandatory labelling of the trans fat content in foods, and voluntary programs to encourage industry to reformulate food products to remove TFAs.[234]

Government action to encourage private-sector action

With rising trends of attention to health and nutrition around the globe, the food industry is under constant pressure to change and adapt. Therefore, reformulation is starting to gain a central role for health policy makers. The food industry, due to market forces and the determination to avert specific government regulation, has pre-emptively embarked on its own reformulation programs.

Although many governments have developed guidelines and strategic plans to improve dietary and physical activity patterns, the translation into action has been disappointing. Page 99
Almost all food policies recommended as priority actions, including front-of-pack traffic-light labelling, have been heavily contested by the food industry, so implementation is difficult politically. However, several of these direct actions are now well supported by cost-effectiveness evidence.[235, 236]

Reformulating processed food products to make them healthier has the potential to impact palatability, profits and the consumer expectations of a product. Therefore, food manufacturers are likely to face a conflict of interest when encouraged to make these changes.

Ideally, reformulation goals should be backed by government regulation or co-regulation, which will enable action to be taken where food manufacturers fail to meet the targets. It is important that reformulation targets are aligned with the Dietary Guidelines.

Active support from the food and beverage industries is needed to reduce obesogenic environments. They have the collective power to achieve this change, even though they have been criticised for their part in creating these surroundings. The food and beverage industries in particular have taken steps in recent years to respond to the obesity epidemic as individual companies and through representative organisations.[237]

A systematic review that assessed the impact of public health intervention on ready-to-eat meals sold by food outlets that are accessible to the general public suggests that it is the level of intrusiveness of an intervention, rather than the type of policy function, that determines the impact of the intervention. More intrusive interventions (e.g. restricting choice or manipulating price) appear more effective than less intrusive interventions that simply include providing information and enabling choice (e.g. calorie labelling laws).[238]

CHILDHOOD OBESITY

In most Western countries, the rate of childhood overweight/obesity is approximately one in four. We know that overweight and obese youth have an increased risk of becoming overweight adults.[239] Some of the adverse health outcomes of obesity in children are shown in Figure 7.14.

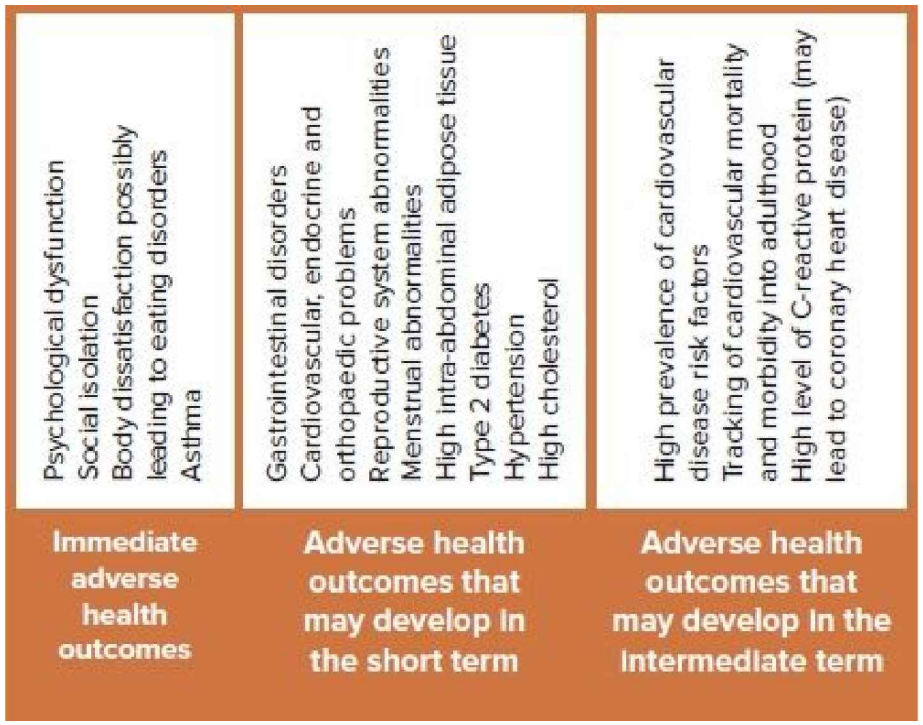


Figure 7.14 Adverse health outcomes of obesity in children
ADAPTED FROM: BOOTH M, BAUR L & DENNY WILSON E, REPORT TO THE COMMONWEALTH ON AUSTRALIAN STANDARD DEFINITIONS FOR CHILD AND ADOLESCENT OVERWEIGHT AND OBESITY.

Overweight and obesity in childhood and adolescence have adverse consequences on premature mortality and physical morbidity in adulthood.[240] A US study found that, compared with adolescents of normal weight, overweight and obese adolescents had over a third more sick days annually.[241] Childhood obesity was significantly associated with a lower general health score, more GP visits, more school absenteeism and more health-related limitations, in a Dutch cohort study.[242] Obese children experience breathing difficulties, increased risk of fractures, hypertension, early markers of cardiovascular disease, insulin resistance and psychological effects.[6, 243]

Childhood obesity may be associated with emotional and behavioural problems from a very young age.[244] Factors associated with mental health problems in obese children include lower levels of physical activity, low self-esteem, body dissatisfaction, eating disorders and weight-based teasing.[245] Children identify very overweight children as being less popular and see fat-related teasing and bullying as commonplace.[246]

Various Cochrane reviews have assessed the effects of diet, physical activity and behaviour-changing interventions for the treatment of overweight or obese children and adolescents at different ages.

In children aged 6–11 years, multicomponent interventions that incorporate diet, physical activity and behaviour change may be beneficial in achieving small, short-term reductions in BMI, BMI z-score and weight.[247] In adolescents aged 12–17, a review of 44 completed RCTs (4781 participants) found low quality evidence that multidisciplinary interventions involving a combination of diet, physical activity and behavioural components reduce measures of BMI, and moderate quality evidence that they reduce weight in overweight or obese adolescents, mainly when compared with no treatment or waiting list controls.[248]

SUMMARY

Obesity is a serious health problem that must be addressed using a multidimensional and crosscutting approach, both at the individual level with lifestyle interventions and at the community/government level with interventions that will improve the obesogenic environment. The unfortunate emphasis on restricting fat instead of sugar and processed foods over the past 40 years has been a significant factor in the current epidemic and needs to be addressed urgently by bringing the Dietary Guidelines into line with scientific evidence. The community needs to pressure governments into taking actions such as improved labelling, reduced advertising of unhealthy foods to children and, in those countries who have not already done so, the introduction of a sugar tax to combat this epidemic.

REFERENCES

1. World Health Organization (WHO). Obesity: preventing and managing the global epidemic. Report of a WHO consultation (WHO technical report series 894). Geneva, 2000.
2. Scottish Intercollegiate Guidelines Network (SIGN). Clinical management of obesity: a national clinical guideline. No. 15, February 2010.
3. Adab P, Pallan M. Is BMI the best measure of obesity? *BMJ* 2018; 360:k1274.
4. Swainson MG, Batterham AM, Tsakirides C et al. Prediction of whole-body fat percentage and visceral adipose tissue mass from five anthropometric variables. *PLoS ONE* 2017; 12(5):e0177175.
5. Hamdy O, Porramatikul S, Al-Ozairi E. Metabolic obesity: the paradox between visceral and subcutaneous fat. *Curr Diabetes Rev* 2006; 2(4):367–73.
6. WHO. Fact Sheets. Obesity and Overweight. 2018. http://www.who.int/mediacentre/factsheets/fs311/en/.
7. Organisation for Economic Co-operation and Development (OECD). Health at a glance 2015: OECD indicators. Paris: OECD, 2017.
8. Dobbs R, Sawers C, Thompson F et al. How the world could better fight obesity.

McKinsey Global Institute, November 2014. https://www.mckinsey.com/industries/healthcare-systems-and-services/our-insights/how-the-world-could-better-fight-obesity.

9. Schiller JS, Clarkje TC, Norris T. Early release of selected estimates based on data from January–September 2017 National Interview Survey. National Health Interview Survey Early Release Program. US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Health Statistics. Released March 2018.
10. Bray GA, Kim KK, Wilding JPH. Obesity: a chronic relapsing progressive disease process. A position statement of the World Obesity Federation. *Obes Rev* 2017; 18(7):715–23.
11. Nagoya Declaration 2015. The 8th Asia-Oceania Conference on Obesity (AOCO 2015). http://www.jasso.or.jp/data/data/pdf/nagoya2015.pdf.
12. Pigeyre M, Yazdi FT, Kaur Y et al. Recent progress in genetics, epigenetics and metagenomics unveils the pathophysiology of human obesity. *Clin Sci (Lond)* 2016; 130:943–86.
13. Bogardus C. Missing heritability and GWAS utility. *Obesity (Silver Spring)* 2009; 17:209–10.
14. Hebebrand J, Volckmar AL, Knoll N et al. Chipping away the 'missing heritability': GIANT steps forward in the molecular elucidation of obesity—but still lots to go. *Obes Facts* 2010; 3:294–303.
15. Swinburn BA, Sacks G, Hall KD et al. The global obesity pandemic: shaped by global drivers and local environments. *Lancet* 2011; 378:804–14.
16. Jencks C. Heredity, environment, and public policy reconsidered. *Am Sociol Rev* 1980; 45:723–36.
17. Cohen M. It's poverty, not individual choice, that is driving extraordinary obesity levels. The Conversation. 20 February 2018. https://theconversation.com/its-poverty-not-individual-choice-that-is-driving-extraordinary-obesity-levels-91447.
18. Ludwig DS, Pollack HA. Obesity and the economy: from crisis to opportunity. *JAMA* 2009; 301(5):533–5.
19. Bann D, Johnson W, Li L et al. Socioeconomic inequalities in childhood and adolescent body-mass index, weight, and height from 1953 to 2015: an analysis of four longitudinal, observational, British birth cohort studies. *Lancet Public Health* 2018; 3:e194–203.
20. White J, Rehkopf D, Mortensen LH. Trends in socioeconomic inequalities in body mass index, underweight and obesity among English children, 2007–2008 to 2011–2012. *PLoS ONE* 2016; 11:e0147614.
21. Stamatakis E, Wardle J, Cole TJ. Childhood obesity and overweight prevalence trends in England: evidence for growing socioeconomic disparities. *Int J Obes* 2010;

34:41–7.

22. Shackleton N, Hale D, Viner RM. Trends and socioeconomic disparities in preadolescent's health in the UK: evidence from two birth cohorts 32 years apart. *J Epidemiol Community Health* 2015; 70:140–6.
23. Darmon N, Drewnowski A. Contribution of food prices and diet cost to socioeconomic disparities in diet quality and health: a systematic review and analysis. *Nutr Rev* 2015; 73:643–60.
24. Guy's and St Thomas' Charity. Bite size: breaking down the challenge of inner-city childhood obesity. https://www.gsttcharity.org.uk/bitesize.
25. Murphy L, Demaio AR. Understanding and removing barriers to physical activity: one key in addressing child obesity. *Br J Sports Med* 2018 Jan 19. pii: bjsports-2017–098546. doi: 10.1136/bjsports-2017-098546. [Epub ahead of print]
26. Fielding-Singh P. A taste of inequality: food's symbolic value across the socioeconomic spectrum. *Sociol Sci* 2017 Aug 10. doi: 10.15195/v4.a17.
27. Public Health England. Adult slide set. 2013. Adult obesity prevalence by ethnic group. Health Survey for England 2006–2010.
28. Fineberg HV. Public health in a time of government austerity. *Am J Public Health* 2013; 103:47–9.
29. Ramos Salas X, Forhan M, Sharma AM. Diffusing obesity myths. *Clin Obes* 2014; 4:189–96.
30. Reither EN, Hauser RM, Yang Y. Do birth cohorts matter? Age-period-cohort analyses of the obesity epidemic in the United States. *Soc Sci Med* 2009; 69:1439–48.
31. Rodgers A, Woodward A, Swinburn B et al. Prevalence trends tell us what did not precipitate the US obesity epidemic. *Lancet Public Health* published online 28 February 2018. doi: 10.1016/S2468-2667(18)30021-5.
32. Ramsden CE, Zamora D, Majchrzak-Hong S et al. Re-evaluation of the traditional diet-heart hypothesis: analysis of recovered data from Minnesota Coronary Experiment (1968–73) *BMJ* 2016; 353:i1246.
33. Young LR, Nestle M. Expanding portion sizes in the US marketplace: implications for nutrition counseling. *J Am Diet Assoc* 2003; 103:231–40.
34. Bleich SN, Cutler D, Murray C et al. Why is the developed world obese? *Ann Rev Public Health* 2008; 29:273–95.
35. Bray GA, Nielsen SJ, Popkin BM. Consumption of high-fructose corn syrup in beverages may play a role in the epidemic of obesity. *Am J Clin Nutr* 2004; 79:537–43.
36. Harcombe Z. Dietary fat guidelines have no evidence base: where next for public health nutritional advice? *Br J Sports Med* 2017; 51:769–74.
37. Lee IM, Djoussé L, Sesso HD et al. Physical activity and weight gain prevention. *JAMA* 2010; 303(12):1173–9.
38. Shaw KA, Gennat HC, O'Rourke P et al. Exercise for overweight or obesity. *Cochrane*

Database Syst Rev 2006(4):CD003817. doi: 10.1002/14651858.CD003817.pub3.

39. Sonneville KR, Gortmaker SL. Total energy intake, adolescent discretionary behaviours and the energy gap. *Int J Obes* 2008; 32 Suppl 6:S19–37.
40. Malhotra A, Noakes T, Phinney S. It is time to bust the myth of physical inactivity and obesity: you cannot outrun a bad diet. *Br J Sports Med* 2015; 49(15):967–8.
41. Kerns JC, Guo J, Fothergill E et al. Increased physical activity associated with less weight regain six years after 'The Biggest Loser' competition. *Obesity (Silver Spring)* 2017; 25(11):1838–43.
42. Moholdt T, Wisløff U, Lydersen S et al. Current physical activity guidelines for health are insufficient to mitigate long-term weight gain: more data in the fitness versus fatness debate (the Hunt study, Norway). *Br J Sports Med* 2014; 48(20):1489–96.
43. Pearson N, Braithwaite RE, Biddle SJH et al. Associations between sedentary behaviour and physical activity in children and adolescents: a meta-analysis. *Obes Rev* 2014; 15(8):666–75.
44. Owen N, Salmon J, Koohsari MJ et al. Sedentary behaviour and health: mapping environmental and social contexts to underpin chronic disease prevention. *Br J Sports Med* 2014; 48(3):174–7.
45. Fletcher E, Leech R, McNaughton SA et al. Is the relationship between sedentary behaviour and cardiometabolic health in adolescents independent of dietary intake? A systematic review. *Obes Rev* 2015; 16(9):795–805.
46. Campbell SDI, Brosnan BJ, Chu AKY et al. Sedentary behavior and body weight and composition in adults: a systematic review and meta-analysis of prospective studies. *Sports Med* 2018; 48:585–95.
47. Te Morenga L, Mallard S, Mann J. Dietary sugars and body weight: systematic review and meta-analyses of randomised controlled trials and cohort studies. *BMJ* 2012; 346:e7492.
48. Siervo M, Montagnese C, Mathers JC et al. Sugar consumption and global prevalence of obesity and hypertension: an ecological analysis. *Public Health Nutr* 2013; 17:587–96.
49. Malik VS, Schulze MB, Hu FB. Intake of sugar-sweetened beverages and weight gain: a systematic review. *Am J Clin Nutr* 2006; 84:274–81.
50. Vartanian LR, Schwartz MB, Brownell KD. Effects of soft drink consumption on nutrition and health: a systematic review and meta-analysis. *Am J Public Health* 2007; 97:667–75.
51. Olsen NJ, Heitmann BL. Intake of calorically sweetened beverages and obesity. *Obes Rev* 2009; 10:68–75.
52. Hu FB. Resolved: there is sufficient scientific evidence that decreasing sugar-sweetened beverage consumption will reduce the prevalence of obesity and obesity-related diseases. *Obes Rev* 2013; 14:606–19.

53. Ministry of Agriculture, Fisheries and Food, Office for National Statistics. National Food Survey, 2000. [data collection]. 2nd ed. UK Data Service. SN: 4512, 2004. http://doi.org/10.5255/UKDA-SN-4512-1.
54. Putnam JJ, Allshouse JE. Food consumption, prices, and expenditures, 1970–97. Statistical Bulletin No. 965. Washington, DC: Food and Rural Economics Division, Economic Research Service, US Dept of Agriculture, 1999.
55. French SA, Lin BH, Guthrie JF. National trends in soft drink consumption among children and adolescents age 6 to 17 years: prevalence, amounts, and sources, 1977/1978 to 1994/1998. *J Am Diet Assoc* 2003; 103:1326–31.
56. Basu S, McKee M, Galea G et al. Relationship of soft drink consumption to global overweight, obesity, and diabetes: a cross-national analysis of 75 countries. *Am J Public Health* 2013; 103:2071–7.
57. Schulze MB, Manson JE, Ludwig DS et al. Sugar-sweetened beverages, weight gain, and incidence of type 2 diabetes in young and middle-aged women. *JAMA* 2004; 292:927–34.
58. Palmer JR, Boggs DA, Krishnan S et al. Sugar-sweetened beverages and incidence of type 2 diabetes mellitus in African American women. *Arch Intern Med* 2008; 168:1487–92.
59. Ludwig DS, Peterson KE, Gortmaker SL. Relation between consumption of sugar-sweetened drinks and childhood obesity: a prospective, observational analysis. *Lancet* 2001; 357(9255):505–8.
60. Dubois L, Farmer A, Girard M et al. Regular sugar-sweetened beverage consumption between meals increases risk of overweight among preschool-aged children. *J Am Diet Assoc* 2007; 107:924–34.
61. Willett WC. Dietary fat plays a major role in obesity: no. *Obes Rev* 2002; 3(2):59–68.
62. Simopoulos AP. An increase in the omega-6/omega-3 fatty acid ratio increases the risk for obesity. *Nutrients* 2016; 8(3):128.
63. Bonadonna RC, Groop L, Kraemer N et al. Obesity and insulin resistance in humans: a dose-response study. *Metabolism* 1990; 39(5):452–9.
64. Czech MP, Tencerova M, Pedersen DJ et al. Insulin signalling mechanisms for triacylglycerol storage. *Diabetologia* 2013; 56:949–64.
65. Kersten S. Mechanisms of nutritional and hormonal regulation of lipogenesis. *EMBO Rep* 2001; 2:282–6.
66. Corkey BE. Banting Lecture 2011: hyperinsulinemia: cause or consequence? *Diabetes* 2012; 61:4–13.
67. Genuth SM, Przybylski RJ, Rosenberg DM. Insulin resistance in genetically obese, hyperglycemic mice. *Endocrinology* 1971; 88:1230–8.
68. Odeleye OE, de Courten M, Pettitt DJ et al. Fasting hyperinsulinemia is a predictor of increased body weight gain and obesity in Pima Indian children. *Diabetes* 1997;

46:1341–5.

69. Templeman NM, Skoivsa S, Page MM et al. A causal role for hyperinsulinemia in obesity. *J Endocrinol* 2017; 232(3):R173–83.
70. Alemzadeh R, Langley G, Upchurch L et al. Beneficial effect of diazoxide in obese hyperinsulinemic adults. *J Clin Endocrinol Metab* 1998; 83:1911–15.
71. Lustig RH, Greenway F, Velasquez-Mieyer P et al. A multicenter, randomized, double-blind, placebo controlled, dose-finding trial of a long-acting formulation of octreotide in promoting weight loss in obese adults with insulin hypersecretion. *Int J Obes* 2006; 30:331–41.
72. Akovso S, Damgaard J, Fels JJ et al. Effects of insulin therapy on weight gain and fat distribution in the HF/HS-STZ rat model of type 2 diabetes. *Int J Obes* 2015; 39(10):1531–8.
73. McLaughlin T, Lamendola C, Liu A et al. Preferential fat deposition in subcutaneous versus visceral depots is associated with insulin sensitivity. *J Clin Endocrinol Metab* 2011; 96:E1756–60.
74. Hardy OT, Czech MP, Corvera S. What causes the insulin resistance underlying obesity? *Curr Opin Endocrinol Diabetes Obes* 2012; 19(2):81–7.
75. Maillot M, Darmon N, Darmon M et al. Nutrient-dense food groups have high energy costs: an econometric approach to nutrient profiling. *J Nutr* 2007; 137:1815–20.
76. Darmon N, Drewnowski A. Does social class predict diet quality? *Am J Clin Nutr* 2008; 87:1107–17.
77. Drewnowski A, Specter SE. Poverty and obesity: the role of energy density and energy costs. *Am J Clin Nutr* 2004; 79:6–16.
78. Reutrakul S, Van Cauter E. Sleep influences on obesity, insulin resistance, and risk of type 2 diabetes. *Metabolism* 2018 Mar 3. pii: S0026-0495(18)30063-5. doi: 10.1016/j.metabol.2018.02.010.
79. Chaput JP, Despres JP, Bouchard C et al. The association between sleep duration and weight gain in adults: a 6-year prospective study from the Quebec Family Study. *Sleep* 2008; 31:517–23.
80. Swinburn B, Egger G, Raza F. Dissecting obesogenic environments; the development and application of a framework for identifying and prioritizing environmental interventions for obesity. *Prev Med* 1999; 29(6):563–70.
81. Swinburn B, Egger G. Preventive strategies against weight gain and obesity. *Obes Rev* 2002; 3:289–301.
82. Cutler DM, Glaeser EL, Shapiro JM. Why have Americans become more obese? *J Econ Perspect* 2003; 17:93–118.
83. Kitchen P, Brignell J, Li T et al. The emergence of IMC: a theoretical perspective. *J Advertising Res* 2004; March:19–30.
84. Hall KD, Guo J, Dore M et al. The progressive increase of food waste in America and

its environmental impact. *PLoS ONE* 2009; 4:e7940.

85. Scarborough P, Burg MR, Foster C et al. Increased energy intake entirely accounts for increase in body weight in women but not in men in the UK between 1986 and 2000. *Br J Nutr* 2011; 105:1399–404.
86. Vandevijvere S, Chow CC, Hall KD et al. Increased food energy supply as a major driver of the obesity epidemic: a global analysis. *Bull World Health Organ* 2015; 93:446–56.
87. Swinburn B, Sacks G, Ravussin E. Increased food energy supply is more than sufficient to explain the US epidemic of obesity. *Am J Clin Nutr* 2009; 90:1453–6.
88. Egger G, Swinburn B. *Planet obesity: how we're eating ourselves and the planet to death*. Sydney: Allen & Unwin, 2010.
89. Sacks G, Swinburn B, Lawrence M. Obesity Policy Action framework and analysis grids for a comprehensive policy approach to reducing obesity. *Obes Rev* 2009; 10:76–86.
90. Goris JM, Petersen S, Stamatakis E et al. Television food advertising and the prevalence of childhood overweight and obesity: a multicountry comparison. *Public Health Nutr* 2010; 13:1003–12.
91. Committee on Food Marketing and the Diets of Children and Youth. *Food marketing to children and youth: threat or opportunity?* Washington, DC: National Academies Press, 2006.
92. Cairns G, Angus K, Hastings G. *The extent, nature and effects of food promotion to children: a review of the evidence to December 2008*. Geneva: WHO, 2009.
93. WHO. *Set of recommendations on the marketing of foods and non-alcoholic beverages to children*. Geneva: WHO, May 2010. http://whqlibdoc.who.int/publications/2010/9789241500210_eng.pdf, accessed 19 April 2011.
94. Bouchard C. Gene-environment interactions in the etiology of obesity: defining the fundamentals. *Obesity (Silver Spring)* 2008; 16(Suppl 3):S5–10.
95. Ahmed F. Epigenetics: tales of adversity. *Nature* 2010; 468(suppl):S20.
96. Kessler D. *The end of overeating: taking control of the insatiable American appetite*. Emmaus, PA: Rodale Books, 2009.
97. Sallis JF. Age-related decline in physical activity: a synthesis of human and animal studies. *Med Sci Sports Exerc* 2000; 32:1598–600.
98. Townshend TG, Lake AA. Obesogenic urban form: theory, policy and practice. *Health Place* 2009; 15:909–16.
99. Lake AA, Townshend TG, Burgoine T. Obesogenic neighbourhood food environments. In: Buttriss J, Welch A, Kearney J et al., eds. *Public health nutrition: the nutrition society textbook series*. Oxford: Wiley-Blackwell, 2017:327–38.
100. Cobb LK, Appel LJ, Franco M et al. The relationship of the local food environment with obesity: a systematic review of methods, study quality, and results. *Obesity*

(Silver Spring) 2015; 23:1331–44.

101. Burgoine T, Forouhi NG, Griffin SJ et al. Does neighborhood fast-food outlet exposure amplify inequalities in diet and obesity? A cross-sectional study. *Am J Clin Nutr* 2016; 103:1540–7.
102. Burgoine T, Mackenbach J, Lakerveld J et al. Interplay of socioeconomic status and supermarket distance is associated with excess obesity risk: a UK cross-sectional study. *Int J Environ Res Public Health* 2017; 14:1290.
103. Burgoine T, Forouhi NG, Griffin SJ et al. Associations between exposure to takeaway food outlets, takeaway food consumption, and body weight in Cambridgeshire, UK: population based, cross sectional study. *BMJ* 2014; 348:g1464.
104. Frank LD, Andresen MA, Schmid TL. Obesity relationships with community design, physical activity, and time spent in cars. *Am J Prev Med* 2004; 27:87–96.
105. Hollands GJ, Shemilt I, Marteau TM et al. Altering micro-environments to change population health behaviour: towards an evidence base for choice architecture interventions. *BMC Public Health* 2013; 13:1218.
106. Stuckler D, Reeves A, Loopstra R et al. Austerity and health: the impact in the UK and Europe. *Eur J Public Health* 2017; 27:18–21.
107. Mackenbach JD, Rutter H, Compernolle S et al. Obesogenic environments: a systematic review of the association between the physical environment and adult weight status, the SPOTLIGHT project. *BMC Public Health* 2014; 14:233.
108. Withrow D, Alter DA. The economic burden of obesity worldwide: a systematic review of the direct costs of obesity. *Obes Rev* 2011; 12(2):131–41.
109. National Institute for Health and Care Excellence (NICE). Obesity Clinical Knowledge Summary. London: NICE, 2012.
110. Ng M, Fleming T, Robinson M et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2014; 384(9945):766–81.
111. Korda R, Liu B, Clements M et al. Prospective cohort study of body mass index and the risk of hospitalisation: findings from 246 361 participants in the 45 and Up Study, *Int J Obes* 2013; 37(6):790–9.
112. Reeves G, Balkwill A, Cairns B et al., Million Women Study Collaborators. Hospital admissions in relation to body mass index in UK women: a prospective cohort study. *BMC Med* 2014; 12:45.
113. Whitlock G, Lewington S, Sherliker P et al., Prospective Studies Collaboration. Body-mass index and cause-specific mortality in 900,000 adults: collaborative analyses of 57 prospective studies. *Lancet* 2009; 373:1083–96.
114. Boggs DA, Rosenberg L, Cozier YC et al. General and abdominal obesity and risk of death among black women. *N Engl J Med* 2011; 365:901–8.
115. Berrington de Gonzalez A, Hartge P, Cerhan JR et al. Body-mass index and mortality

among 1.46 million white adults. *N Engl J Med* 2010; 363:2211–9.

116. Padwal R, Leslie WD, Lix LM et al. Relationship among body fat percentage, body mass index, and all-cause mortality: a cohort study. *Ann Intern Med* 2016; 164:532–41.
117. The GBD 2015 Obesity Collaborators. Health effects of overweight and obesity in 195 countries over 25 years. *N Engl J Med* 2017; 377:13–27.
118. Singh GM, Danaei G, Farzadfar F et al. The age-specific quantitative effects of metabolic risk factors on cardiovascular diseases and diabetes: a pooled analysis. *PLoS ONE* 2013; 8(7):e65174.
119. Flegal KM, Kit BK, Orpana H et al. Association of all-cause mortality with overweight and obesity using standard body mass index categories: a systematic review and meta-analysis. *JAMA* 2013; 309:71–82.
120. Xia X, Chen W, Li J et al. Body mass index and risk of breast cancer: a nonlinear dose-response meta-analysis of prospective studies. *Sci Rep* 2014 Dec 15;4:7480. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4265780/.
121. Di Angelantonio E, Bhupathiraju ShN, Wormser D et al. Body-mass index and all-cause mortality: individual-participant-data meta-analysis of 239 prospective studies in four continents. *Lancet* 2016; 388:776–86.
122. Dent M, Swanston D. Briefing note: obesity and life expectancy. Oxford: National Obesity Observatory, 2010.
123. How deadly is obesity, really? 6 minutes, Australian Doctor Group. 5 September 2017. https://www.6minutes.com.au/news/how-deadly-obesity-really.
124. Heymsfield SB, Wadden TA. Mechanisms, pathophysiology, and management of obesity. *N Engl J Med* 2017; 376:254–66.
125. Wormser D, Kaptoge S, Di Angelantonio E et al. Separate and combined associations of body-mass index and abdominal adiposity with cardiovascular disease: collaborative analysis of 58 prospective studies. *Lancet* 2011; 377:1085–95.
126. Khan SS, Ning H, Wilkins JT et al. Association of body mass index with lifetime risk of cardiovascular disease and compression of morbidity. *JAMA Cardiol* published online 28 February 2018. doi: 10.1001/jamacardio.2018.0022.
127. Menke A, Rust KF, Fradkin J et al. Associations between trends in race/ethnicity, aging, and body mass index with diabetes prevalence in the United States: a series of cross-sectional studies. *Ann Int Med* 2014; 161:328–35.
128. Lauby-Secretan B, Scoccianti C, Loomis D et al. Body fatness and cancer—viewpoint of the IARC Working Group. *N Engl J Med* 2016; 375:794–8.
129. Calle EE, Rodriguez C, Walker-Thurmond K et al. Overweight, obesity, and mortality from cancer in a prospectively studied cohort of US adults. *N Engl J Med* 2003; 348:1625–38.
130. Reyes C, Leyland KM, Peat G et al. Association between overweight and obesity and risk of clinically diagnosed knee, hip, and hand osteoarthritis: a population-based

cohort study. *Arthritis Rheumatol* 2016; 68:1869–75.

131. Li C, Ford ES, Zhao G et al. Prevalence of self-reported clinically diagnosed sleep apnea according to obesity status in men and women: National Health and Nutrition Examination Survey, 2005–2006. *Prev Med* 2010; 51:18–23.
132. Bray GA. The obese patient. *Major Prob Intern Med* 1976; 9:1–450.
133. Radmard AR, Merat S, Kooraki S et al. Gallstone disease and obesity: a population-based study on abdominal fat distribution and gender differences. *Ann Hepatol* 2015; 14:702–9.
134. Berkowitz RI, Fabricatore AN. Obesity, psychiatric status, and psychiatric medications. *Psychiatr Clin North Am* 2011; 34:747–64.
135. Puhl RM, Heuer CA. The stigma of obesity: a review and update. *Obesity (Silver Spring)* 2009; 17:941–64.
136. Doehner W, Clark A, Anker SD. The obesity paradox: weighing the benefit. *Eur Heart J* 2010; 31:146–8.
137. Hara M, Saikawa T, Kurokawa M et al. Leg fat percentage correlates negatively with coronary atherosclerosis. *Circ J* 2004; 68:1173–8.
138. Iliodromiti S, Celis-Morales CA, Lyall DM et al. The impact of confounding on the associations of different adiposity measures with the incidence of cardiovascular disease: a cohort study of 296 535 adults of white European descent. *Eur Heart J* 2018; 39(17):1514–20. doi: 10.1093/eurheartj/ehy057.
139. Roberto CA, Swinburn B, Hawkes C et al. Patchy progress on obesity prevention: emerging examples, entrenched barriers, and new thinking. *Lancet* 2015; 385:2400–9.
140. Public Health Collaboration. Randomised controlled trials comparing low-carb diets of less than 130g carbohydrate per day to low-fat diets of less than 35% fat of total calories. https://phcuk.org/rcts/.
141. Public Health Collaboration. Meta-analyses comparing low-carb diets of less than 130g carbohydrate per day to low-fat diets of less than 35% fat of total calories. https://phcuk.org/wp-content/uploads/2018/02/Meta-Analyses-Comparing-Low-Carb-To-Low-Fat-Diets-26.02.2018.pdf.
142. Rogers P. The role of low-calorie sweeteners in the prevention and management of overweight and obesity: evidence v. conjecture. *Proc Nutr Soc* 2017; 1–9. doi: 10.1017/S0029665117004049.
143. Miller PE, Perez V. Low-calorie sweeteners and body weight and composition: a meta-analysis of randomized controlled trials and prospective cohort studies. *Am J Clin Nutr* 2014; 100:765–77.
144. Rogers PJ, Hogenkamp PS, de Graaf C et al. Does low-energy sweetener consumption affect energy intake and body weight? A systematic review, including meta-analyses, of the evidence from human and animal studies. *Int J Obes* 2016; 40:381–94.

145. Tate DF, Turner-McGrievy G, Lyons E et al. Replacing caloric beverages with water or diet beverages for weight loss in adults: main results of the Choose Healthy Options Consciously Everyday (CHOICE) randomized clinical trial. *Am J Clin Nutr* 2012; 95:555–63.
146. Schwingshackl L, Dias S, Hoffmann G. Impact of long-term lifestyle programmes on weight loss and cardiovascular risk factors in overweight/obese participants: a systematic review and network meta-analysis. *Syst Rev* 2014; 3:130.
147. American College of Cardiology/American Heart Association Task Force on Practice Guidelines, Obesity Expert Panel, 2013. Expert Panel Report: guidelines (2013) for the management of overweight and obesity in adults. *Obesity (Silver Spring)* 2014; 22(Suppl 2):S5–39.
148. Steinberg DM, Tate DF, Bennett GG et al. The efficacy of a daily self-weighing weight loss intervention using smart scales and e-mail. *Obesity (Silver Spring)* 2013; 21:1789–97.
149. Appel LJ, Clark JM, Yeh H-C et al. Comparative effectiveness of weight-loss interventions in clinical practice. *N Engl J Med* 2011; 365:1959–68.
150. Harvey-Berino J, West D, Krukowski R et al. Internet delivered behavioral obesity treatment. *Prev Med* 2010; 51:123–8.
151. Perri MG, Limacher MC, Durning PE et al. Extended-care programs for weight management in rural communities: the Treatment of Obesity in Underserved Rural Settings (TOURS) randomized trial. *Arch Intern Med* 2008; 168:2347–54.
152. Ruhm CJ. Understanding overeating and obesity. *J Health Econ* 2012; 31:781–96.
153. Burgess E, Hassmen P, Pumpa KL. Determinants of adherence to lifestyle intervention in adults with obesity: a systematic review. *Clin Obes* 2017; 7(3):123–35.
154. Lee PC, Dixon J. Pharmacotherapy for obesity. *Aust Fam Physician* 2017; 46(7):472–7.
155. Jensen MD, Ryan DH, Apovian CM et al. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society. *Circulation* 2014; 129(25 Suppl 2):S102–38.
156. Apovian CM, Aronne LJ, Bessesen DH et al. Pharmacological management of obesity: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab* 2015; 100(2):342–62.
157. National Health and Medical Research Council (NHMRC). *Clinical practice guidelines for the management of overweight and obesity in adults, adolescents and children in Australia*. Melbourne: NHMRC, 2013. https://www.nhmrc.gov.au/guidelines/publications/n57.
158. Yanovski SZ, Yanovski JA. Long-term drug treatment for obesity: a systematic and clinical review. *JAMA* 2014; 311(1):74–86.
159. Li Z, Maglione M, Tu W et al. Meta-analysis: pharmacologic treatment of obesity.

Ann Intern Med 2005; 142(7):532–46.

160. Apovian CM, Garvey WT, Ryan DH. Challenging obesity: patient, provider, and expert perspectives on the roles of available and emerging nonsurgical therapies. *Obesity (Silver Spring)* 2015; 23(Suppl 2):S1–26.
161. Chang SH, Stoll CRT, Song JJ et al. The effectiveness and risks of bariatric surgery: an updated systematic review and meta-analysis, 2003–2012. *JAMA Surg* 2014; 149(3):275–87.
162. O'Brien P. Surgical treatment of obesity. In: De Groot LJ, Chrousos G, Dungan K et al., eds. *Endotext*. South Dartmouth, MA: MDText.com, 19 January 2016.
163. Sjostrom L, Narbro K, Sjostrom CD et al. Effects of bariatric surgery on mortality in Swedish obese subjects. *N Engl J Med* 2007; 357:741–52.
164. Schauer PR, Mingrone G, Ikramuddin S et al. Clinical outcomes of metabolic surgery: efficacy of glycemic control, weight loss, and remission of diabetes. *Diabetes Care* 2016; 39:902–11.
165. Ikramuddin S, Korner J, Lee WJ et al. Roux-en-Y gastric bypass vs intensive medical management for the control of type 2 diabetes, hypertension, and hyperlipidemia: the Diabetes Surgery Study randomized clinical trial. *JAMA* 2013; 309:2240–9.
166. Courcoulas AP, Belle SH, Neiberg RH et al. Three-year outcomes of bariatric surgery vs lifestyle intervention for type 2 diabetes mellitus treatment: a randomized clinical trial. *JAMA Surg* 2015; 150:931–40.
167. Longitudinal Assessment of Bariatric Surgery (LABS) Consortium. Perioperative safety in the longitudinal assessment of bariatric surgery. *N Engl J Med* 2009; 361:445–54.
168. Arterburn DE, Courcoulas AP. Bariatric surgery for obesity and metabolic conditions in adults. *BMJ* 2014; 349:g3961.
169. Rutter H, Bes-Rastrollo M, de Henauw S et al. Balancing upstream and downstream measures to tackle the obesity epidemic: a position statement from the European Association for the Study of Obesity. *Obes Facts* 2017; 10:61–3.
170. McKinnon RA, Orleans CT, Kumanyika SK et al. Considerations for an obesity policy research agenda. *Am J Prev Med* 2009; 36:351–7.
171. Lake AA, Henderson EJ, Townshend TG. Exploring planners and public health practitioners' views on addressing obesity: lessons from local government in England. *Cities Health* 2017;1–9.
172. Wright A, Smith KE, Hellowell M. Policy lessons from health taxes: a systematic review of empirical studies. *BMC Public Health* 2017; 17:583.
173. Backholer K, Blake M, Vandevijvere S. Sugar-sweetened beverage taxation: an update on the year that was 2017. *Public Health Nutr* 2017; 20(18):3219–24.
174. Hawkes C, Smith TG, Jewell J et al. Smart food policies for obesity prevention. *Lancet* 2015; 385:2410–21.

175. Townshend T, Lake A. Obesogenic environments: current evidence of the built and food environments. *Perspect Public Health* 2017; 137:38–44.
176. Rutter H, Savona N, Glonti K et al. The need for a complex systems model of evidence for public health. *Lancet* 2017; 390:2602–4.
177. Hillier-Brown FC, Bambra CL, Cairns J-M et al. A systematic review of the effectiveness of individual, community and societal level interventions at reducing socioeconomic inequalities in obesity amongst children. *BMC Public Health* 2014; 14:834.
178. Sassi F, Cecchini M, Lauer J et al. Improving lifestyles, tackling obesity: the health and economic impact of prevention strategies. OECD Health Working Paper No. 48. Paris: OECD, 2009.
179. Mazzocchi M, Traill WB, Shogren JF. *Fat economics: nutrition, health and economic policy*. New York: Oxford University Press, 2009.
180. World Health Organization (WHO) Regional Office for Europe. *Marketing of foods high in fat, salt and sugar to children: update 2012–13*. Copenhagen, 2013:1.
181. Worl Health Organization (WHO). *Set of recommendations on the marketing of foods and non-alcoholic beverages to children*. Geneva: WHO, May 2010:7. http://whqlibdoc.who.int/publications/2010/9789241500210_eng.pdf.
182. Ofcom (UK). *HFSS advertising restrictions—final review*. London, 2010.
183. Brambila-Macias J, Shankar B, Capacci S et al. Policy interventions to promote healthy eating: a review of what works, what does not, and what is promising. *Food Nutr Bull* 2011; 32(4):365–75.
184. King L, Hebden L, Grunseit A et al. Building the case for independent monitoring of food advertising on Australian television. *Public Health Nutr* 2013; 16(12):2249–54.
185. Halpern D, Bates C, Beales G et al. *Personal responsibility and changing behavior: the state of knowledge and its implications for public policy*. London: Cabinet Office, Prime Minister's Strategy Unit, 2004.
186. Wymer W. Rethinking the boundaries of social marketing: activism or advertising? *J Bus Res* 2009; 63:99–103.
187. Roos G, Lean M, Anderson A. Dietary interventions in Finland, Norway and Sweden: nutrition policies and strategies. *J Hum Nutr Diet* 2002; 15:99–110.
188. Oude Luttikhuis H, Baur L, Jansen H et al. Interventions for treating obesity in children. *Cochrane Database Syst Rev* 2009; 1:CD001872.
189. Wang Y, Cai L, Wu Y et al. What childhood obesity prevention programmes work? A systematic review and meta-analysis. *Obes Rev* 2015; 16:547–65.
190. Bleich SN, Vercammen KA, Zatz LY et al. Interventions to prevent global childhood overweight and obesity: a systematic review. *Lancet Diabetes Endocrinol* 2018; 6(4):332–46.
191. Ling J, Robbins LB, Wen F. Interventions to prevent and manage overweight or

obesity in preschool children: a systematic review. *Int J Nurs Stud* 2016; 53:270–89.

192. Bleich SN, Segal J, Wu Y et al. Systematic review of community-based childhood obesity prevention studies. *Pediatrics* 2013; 132:e201–10.
193. Novilla M, Barnes MD, De La Cruz NG et al. Public health perspectives on the family: an ecological approach to promoting health in the family and community. *Fam Community Health* 2006; 29:28–42.
194. McGeary KA. The impacts of state-level nutrition education program funding on BMI: evidence from the behavioural risk factor surveillance system. NBER Working Paper Series, WP 15001. Cambridge, MA: National Bureau of Economic Research, 2009.
195. Buttriss J. The role of nutritional labelling and signposting from a European perspective. *Proc Nutr Soc* 2018; Feb 13:1–10. doi: 10.1017/S0029665117004098.
196. Mathios AD. The impact of mandatory disclosure laws on product choices: an analysis of the salad dressing market. *J Law Econ* 2000; 43:651–77.
197. Wills JM, Grunert KG, Fernandez Celemin L et al. European consumers and nutrition labelling. *Food Eng Ingredients* 2009; 34(3):11–13.
198. Grunert KG, Wills JM. A review of European research on consumer response to nutrition information on food labels. *J Public Health* 2007; 15:385–99.
199. Grunert KG, Fernandez-Celemin L, Wills JM et al. Use and understanding of nutrition information on food labels in six European countries. *J Public Health* 2010; 18:261–77.
200. Food Standards Agency (FSA). Front-of-pack traffic light signpost labelling. Technical guidance, issue 2. FSA, 2007. http://www.food.gov.uk/multimedia/pdfs/frontofpackguidance2.pdf.
201. Department of Health. Final design of consistent nutritional labelling system given green light. London: UK Government, 19 June 2013. https://www.gov.uk/government/news/final-design-of-consistent-nutritional-labelling-system-given-green-light.
202. Institute of Medicine. *Front-of-package nutrition rating systems and symbols: promoting healthier choices*. Washington, DC: National Academies Press, 2012.
203. Sutherland LA, Kaley LA, Fischer L. Guiding stars: the effect of a nutrition navigation program on consumer purchases at the supermarket. *Am J Clin Nutr* 2010; 91(4):1090S–1094S.
204. Department of Health. Legislative and governance forum on food regulation, final communique. Canberra: Australian Government, 27 June 2014. http://www.health.gov.au/internet/main/publishing.nsf/Content/mr-yr14-dept-dept006.htm.
205. Food and Drink Federation (FDF). GDA labels: improving the food literacy of consumers. London: FDF, April 2010. http://www.fdf.org.uk/publicgeneral/GDA_Labelling_Apr2010.pdf.
206. Grocery Manufacturers Association, Food Marketing Institute. *Facts Up Front*. 2011. h

ttp://www.factsupfront.org/.

207. Wisdom J, Downs JS, Loewenstein G. Promoting healthy choices: information versus convenience. *Am Econ J Appl Econ* 2010; 2(2):164–78.
208. Bruemmer B, Krieger J, Saelens BE et al. Energy, saturated fat, and sodium were lower in entrees at chain restaurants at eighteen months compared with six months following the implementation of mandatory menu labeling regulation in King County, Washington. *J Acad Nutr Diet* 2012; 112(8):1169–76.
209. Darmon N, Lacroix A, Muller L et al. Food price policies improve diet quality while increasing socioeconomic inequalities in nutrition. *Int J Behav Nutr Phys Act* 2014; 11:66.
210. Mackenbach JP, Bos V, Andersen O et al. Widening socioeconomic inequalities in mortality in six Western European countries. *Int J Epidemiol* 2003; 32:830–7.
211. LeClerc A, Chastang JF, Menvielle G et al. Socioeconomic inequalities in premature mortality in France: have they widened in recent decades? *Soc Sci Med* 2006; 62:2035–45.
212. Singh GK, Siahpush M, Kogan MD. Rising social inequalities in US childhood obesity, 2003–2007. *Ann Epidemiol* 2010; 20:40–52.
213. World Health Organization. Global Action Plan for the Prevention and Control of Noncommunicable Diseases 2013–2020. World Health Assembly. Geneva: May 2013:32.
214. Mazzocchi M, Capacci S, Allais O et al. The impact of the French soda tax on prices, purchases and tastes: an ex post evaluation. Toulouse School of Economics, Food Economics and Policy Seminar, 28 April 2017. https://www.tse-fr.eu/seminars/2017-impact-french-soda-tax-prices-purchases-and-tastes-ex-post-evaluation.
215. Colchero MA, Molina M, Guerrero-Lopez CM. After Mexico implemented a tax, purchases of sugar-sweetened beverages decreased and water increased: difference by place of residence, household composition, and income level. *J Nutr* 2017; 147(8):1552–7.
216. Behavioural Insights Team in partnership with the Cabinet Office (UK). Sugaring the bill: why lower revenue from the sugar tax is probably a good thing. 6 April 2018. http://www.behaviouralinsights.co.uk/health/sugaring-the-bill-why-lower-revenue-from-the-sugar-tax-is-probably-a-good-thing/.
217. Falbe J, Thompson HR, Becker CM et al. Impact of the Berkeley Excise Tax on sugar-sweetened beverage consumption. *Am J Public Health* 2016; 106(10):1865–71.
218. Silver LD, Ng SW, Ryan-Ibarra S et al. Changes in prices, sales, consumer spending, and beverage consumption one year after a tax on sugar-sweetened beverages in Berkeley, California, US: a before-and-after study. *PLoS Med* 2017; 14(4):e1002283.
219. Veerman J, Sacks G, Antonopoulos N et al. The impact of a tax on sugar-sweetened beverages on health and health care costs: a modelling study. *PLoS ONE* 2016;

11(4):e0151460.

220. Ax, J, Bloomberg's ban on big sodas is unconstitutional: appeals court. Reuters, https ://www.reuters.com/article/us-sodaban-lawsuit/bloombergs-ban-on-big-sodas-is-unconstitutional-appeals-court-idUSBRE96T0UT20130730
221. Epstein LH, Jankowiak N, Nederkoorn C et al. Experimental research on the relation between food price changes and food-purchasing patterns: a targeted review. *Am J Clin Nutr* 2015; 95:789–809.
222. Waterlander WE, Steenhuis IH, de Boer MR et al. The effects of a 25% discount on fruits and vegetables: results of a randomized trial in a three-dimensional web-based supermarket. *Int J Behav Nutr Phys Act* 2012; 9:11.
223. Lennernas M, Fjellstrom C, Becker W et al. Influences on food choice perceived to be important by nationally-representative samples of adults in the European Union. *Eur J Clin Nutr* 1997; 51:S8–15.
224. Beydoun MA, Wang Y. How do socio-economic status, perceived economic barriers and nutritional benefits affect quality of dietary intake among US adults? *Eur J Clin Nutr* 2008; 62:303–13.
225. Waterlander WE, de Boer MR, Schuit AJ et al. Price discounts significantly enhance fruit and vegetable purchases when combined with nutrition education: a randomized controlled supermarket trial. *Am J Clin Nutr* 2013; 97:886–95.
226. Herman DR, Harrison GG, Afifi AA et al. Effect of a targeted subsidy on intake of fruits and vegetables among low-income women in the Special Supplemental Nutrition Program for Women, Infants, and Children. *Am J Public Health* 2008; 98:98–105.
227. Han E, Powell LM, Isgor Z. Supplemental nutrition assistance program and body weight outcomes: the role of economic contextual factors. *Soc Sci Med* 2012; 74:1874–81.
228. Anderson JV, Bybee DI, Brown RM et al. 5 a day fruit and vegetable intervention improves consumption in a low income population. *J Am Diet Assoc* 2001; 101:195–202.
229. Burr ML, Trembeth J, Jones KB et al. The effects of dietary advice and vouchers on the intake of fruit and fruit juice by pregnant women in a deprived area: a controlled trial. *Public Health Nutr* 2007; 10:559–65.
230. Herman DR, Harrison GG, Jenks E. Choices made by low-income women provided with an economic supplement for fresh fruit and vegetable purchase. *J Am Diet Assoc* 2006; 106:740–4.
231. Zagorsky J, Smith P. Does the US Food Stamp Program contribute to adult weight gain? *Econ Hum Biol* 2009; 7:246–58.
232. Lin B, Yen ST, Dong D et al. Economic incentives for dietary improvement among food stamp recipients. Presented at pre-conference workshop, Diet and obesity: role

of prices and policies. International Association of Agricultural Economists. 16 August 2009. http://ageconsearch.umn.edu/handle/53339.

233. de Sa J, Lock K. Will European agricultural policy for school fruit and vegetables improve public health? A review of school fruit and vegetable programmes. *Eur J Public Health* 2008; 18:558–68.
234. L'Abbe MR, Stender S, Skeaff M et al. Approaches to removing trans fats from the food supply in industrialized and developing countries. *Eur J Clin Nutr* 2009; 63:S50–67.
235. Haby MM, Vos T, Carter R et al. A new approach to assessing the health benefit from obesity interventions in children and adolescents: the Assessing Cost-Effectiveness in Obesity Project. *Int J Obes* 2006; 30:1463–75.
236. Vos T, Carter R, Barendregt J et al. Assessing cost-effectiveness in prevention (ACE–Prevention). Final report. September 2010. http://www.sph.uq.edu.au/docs/BODCE/ACE$$$P/ACE-Prevention_final_report.pdf.
237. Yach D, Khan M, Bradley D et al. The role and challenges of the food industry in addressing chronic disease. *Global Health* 2010; 6:10.
238. Hillier-Brown FC, Summerbell CD, Moore HJ et al. The impact of interventions to promote healthier ready-to-eat meals (to eat in, to take away or to be delivered) sold by specific food outlets open to the general public: a systematic review. *Obes Rev* 2017; 18(2):227–46.
239. Singh AS, Mulder C, Twisk JW et al. Tracking of childhood overweight into adulthood: a systematic review of the literature. *Obes Rev* 2008; 9(5):474–88.
240. Reilly JJ, Kelly J. Long-term impact of overweight and obesity in childhood and adolescence on morbidity and premature mortality in adulthood: systematic review. *Int J Obes* 2011; 35(7):891–8.
241. Pan L, Sherry B, Park S et al. The association of obesity and school absenteeism attributed to illness or injury among adolescents in the United States, 2009. *Adolesc Health* 2013; 52(1):64–9.
242. Wijga A, Scholtens S, Bemelmans W et al. Comorbidities of obesity in school children: a cross-sectional study in the PIAMA birth cohort. *BMC Public Health* 2010; 10:184.
243. Public Health England. Health risks. 2017. http://webarchive.nationalarchives.gov.uk/20170110171032/ https://www.noo.org.uk/NOO_about_obesity/child_obesity/Health_risks.
244. Griffiths LJ, Dezateux C, Hill A. Is obesity associated with emotional and behavioural problems in children? Findings from the Millennium Cohort Study. *Int J Ped Obes* 2011; 6(2–2):e423–32.
245. Gatineau M, Dent M. *Obesity and mental health*. Oxford: National Obesity Observatory, 2011.

246. Rees R, Oliver K, Woodman J et al. Children's views about obesity, body size, shape and weight: a systematic review. London: EPPI-Centre, Social Science Research Unit, Institute of Education, University of London, 2009.
247. Mead E, Brown T, Rees K et al. Diet, physical activity and behavioural interventions for the treatment of overweight or obese children from the age of 6 to 11 years. *Cochrane Database Syst Rev* 2017 Jun 22; 6:CD012651.
248. Al-Khudairy L, Loveman E, Colquitt JL et al. Diet, physical activity and behavioural interventions for the treatment of overweight or obese adolescents aged 12 to 17 years. *Cochrane Database Syst Rev* 2017 Jun 22; 6:CD012691.

Chapter 8

Diabetes mellitus

with SANDY HOFFMANN and MATT HISLOP*

When I was first diagnosed my biggest worry was that I may not be able to play football again. Injecting myself every day was demoralising. Fortunately, I can feel the support around me—not just from my team-mates and the fans, but also the coaches, physios and nutritionists who all help me bring my A-game.

Ben Coker, English professional soccer player

Many athletes have treated their type 1 or type 2 diabetes while having successful careers. British rower Sir Steven Redgrave provides just one remarkable story of sporting success while managing diabetes mellitus. Other athletes include Jay Cutler (NFL), Gary Hall (swimmer), Wasim Akram (cricket), Henry Slade (rugby union) and the all-diabetic men's professional cycling team Novo Nordisk, who compete with fully rostered type 1 and type 2 diabetic teams.

In this chapter we briefly review key clinically relevant pathophysiology of each type of diabetes. We then outline:

- how diabetes can be managed effectively during physical activity
- how physical activity can help patients control or reverse diabetic symptomology
- medical considerations for clinicians to consider when managing the diabetic athlete.

TYPES OF DIABETES

Most persons with diabetes fall into two broad categories: type 1 and type 2. There are other types of diabetes, but they are rare and will not be discussed in this chapter.

Type 1 diabetes

Type 1 diabetes, which was previously known as 'juvenile-onset' diabetes, is thought to be an inherited autoimmune disease, in which antibodies are produced against the beta cells of the pancreas, ultimately resulting in the absence of endogenous insulin production. The incidence of

type 1 diabetes varies throughout the world but represents approximately 10–15% of diabetic cases in the Western world.

The onset commonly occurs in childhood and adolescence but can become symptomatic at any age and is manifested by low or undetectable levels of plasma C-peptide. Insulin administration is essential to prevent ketosis, coma and death. The aims of treatment are tight control of blood glucose levels and prevention of microvascular and macrovascular complications.

Type 2 diabetes

Type 2 diabetes, previously known as 'maturity-onset' or 'adult-onset' diabetes, is typically a disease of later onset, although in developed countries it is increasingly seen in adolescents. It is linked to both genetic, environmental and lifestyle factors. It is characterised by diminished insulin secretion relative to serum glucose levels, in conjunction with peripheral insulin resistance, both of which result in chronic hyperglycaemia.

Approximately 90% of individuals with diabetes have type 2, and it is thought to affect 3–7% of people in Western countries. Some of the most recent World Health Organization (WHO) data for Europe suggests diabetes affects 10% of the European population of both men and women aged 25 and over.[1] The prevalence of type 2 diabetes increases with age. The definitive pathogenesis of type 2 diabetes remains unknown, but it is believed to be a heterogeneous disorder with a strong genetic factor. Approximately 80% of individuals with type 2 diabetes are obese, with sedentary lifestyle being a strong risk factor. This complication is only increasing, with developing countries exhibiting rapidly increasing rates of diabetes as their diets become westernised and reported exercise patterns reduce.[2]

Page 102

Type 2 diabetes is characterised by three major metabolic abnormalities:

- impairment in pancreatic beta cell insulin secretion in response to a glucose stimulus
- reduced sensitivity to the action of insulin in major organ systems, such as muscle, liver and adipose tissue ('insulin resistance')—this is the element that drives diabetes-related obesity (insulin is a fat-storing hormone)
- excessive hepatic glucose production in the basal state.

PRACTICE PEARL

C-peptide levels can help determine whether a person is making endogenous insulin.

CLINICAL PERSPECTIVE

Both type 1 and type 2 diabetes are diagnosed by detection of a fasting (>8 hours) plasma glucose level greater than or equal to 7 mmol/L (126 mg/dL), a plasma glucose level greater than or equal to 11.1 mmol/L (200 mg/dL) at 2 hours after an oral glucose challenge (oral glucose tolerance test), a glycosylated haemoglobin (HbA1c) level of 6.5% or higher, or by the appearance of other classic

symptoms of diabetes.[3]

Pre-exercise screening and clearance for people with diabetes

The American College of Sports Medicine (ACSM) recently updated its guidance on pre-participation screening, to encourage engagement in physical activity and prevent barriers within the diabetic population.[4] The American Diabetes Association (ADA) states that pre-exercise medical clearance is not necessary for asymptomatic individuals receiving diabetes care consistent with guidelines who start low- or moderate-intensity exercise programs such as brisk walking.[5] Due to the risk of silent ischaemia it is recommended that individuals intending to take part in high intensity activities still undergo screening tests.

Ideally patients should have reasonable diabetic control before considering vigorous or high-intensity exercise. Long-term diabetic control indicators such as HbA1c and fructosamine allow an objective measure. The HbA1c level allows assessment of the diabetes control in the preceding 2–3 months, and fructosamine in the preceding 3 weeks. The ideal HbA1c level for participating in competitive sports should be ≤7% for adults and ≤7.5% for adolescents. A blood glucose level diary should be kept, with measurements taken at variable times during the day.

The clinician undertaking a pre-participation evaluation (PPE) should focus on:

- *cardiovascular system*—blood pressure including postural drop, heart, presence of carotid or renal bruits, peripheral pulses
- *eyes*—retinopathy, glaucoma, cataracts
- *peripheral neuropathy*—with specific emphasis on examination of the feet.

Pre-exercise cardiac screening should be thorough. Ischaemic heart disease is present in up to 50% of patients with type 2 diabetes at the time of diagnosis. Chest pain is not always present in diabetic patients because silent ischaemia can occur secondary to autonomic neuropathy. The decision for laboratory screening and exercise stress testing is at the discretion of the healthcare professional performing the PPE.

Complications

Both type 1 and type 2 diabetes may result in complications that affect multiple end-organ systems. Fig. 8.1 demonstrates the association between diabetes and the incidence of acute myocardial infarction, believed to be linked with accelerated atherosclerotic plaque formation.[6–7] Peripheral arterial disease incidence is elevated dramatically and the risk of cerebral vascular incidents doubles.

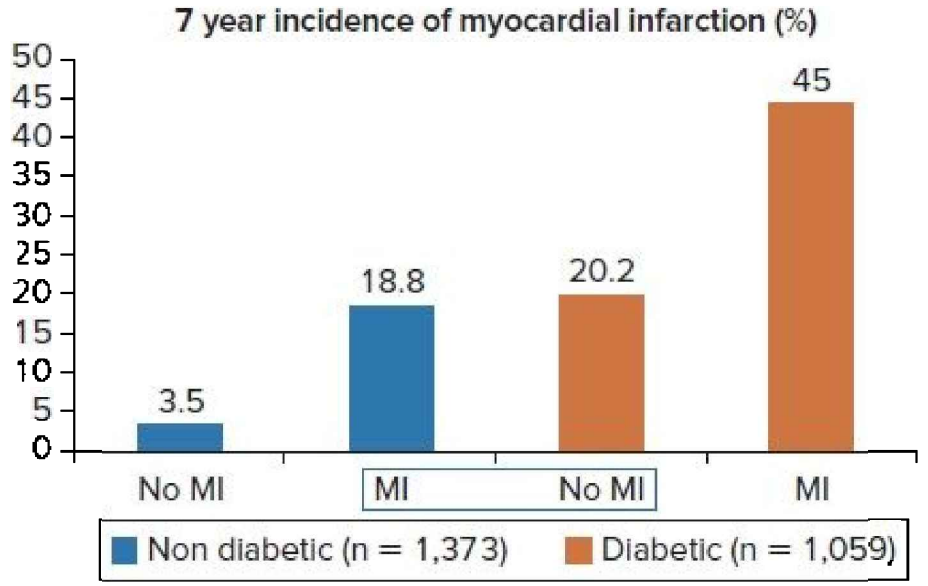


Figure 8.1 Risk of myocardial infarction (MI) for patients who had previously suffered an MI, in diabetic and non-diabetic patients

Based on data from Heffner et al, (1998) Mortality from Coronary Heart Disease in Subjects with Type 2 Diabetes and in Nondiabetic Subjects with and without Prior Myocardial Infarction (1998). DOI: 10.1056/NEJM199807233390404

Additionally, diabetes can cause retinopathy, nephropathy and autonomic neuropathy. This can lead to complications such as impaired gastric emptying, altered sweating and silent myocardial ischaemia. This can have serious implications for exercise. The risk of such complications is associated with both the duration of the diabetes and the diabetic control.

TREATMENT

The treatment of both type 1 and type 2 diabetes focuses on the maintenance of near normal blood glucose levels. This applies to both the general and the sporting population. For those patients with type 1 diabetes, exogenous insulin is essential. It is also imperative that type 1 diabetics maintain healthy eating and close monitoring of blood glucose levels, through self-monitoring or continuous glucose monitoring.

Many patients with type 2 diabetes can be managed with a combination of healthy eating, exercise and weight loss. However, if this is not adequate, a patient with type 2 diabetes may require the use of glucose-lowering agents (GLAs) (Table 8.1). These agents are used in preference to insulin—insulin being reserved only for patients in whom adequate control cannot be achieved.

Table 8.1 Examples of commonly used glucose-lowering agents

Class	Medication	Mechanism of action	Pros	Cons
Biguanides	Metformin	Lower hepatic glucose production	Lower CV events Hypoglycaemia rare Low cost	GI distress B12 deficiency Renal issues
Sulfonlyureas	Glyburide Glipizide Glimepiride	Increase insulin secretion	High efficacy Low cost	Hypoglycaemia Weight gain Frequent doses
GLP-1 receptor agonists	Exenatide Liraglutide Dulaglutide	Increase insulin secretion Decrease glucagon secretion Slows gastric emptying	Hypoglycaemia rare Lowers CV risk Weight loss	GI distress Tachycardia Injectible High cost
DPP-4 inhibitors	Sitagliptin Saxagliptin Linagliptin	Increase insulin secretion Decrease glucagon secretion	Hypoglycaemia rare Well tolerated	Angioedema High cost
SGLT2 inhibitors	Empagliflozin Dapaglifloxin Empagliflozin	Increase glusosuria	Hypoglycaemia rare Weight loss Lowers CV risk	GU infections Hypovolaemia DKA (rare) High cost
TZDs	Pioglitazone Rosiglitazone	Increase insulin sensitivity	Rare hypoglycaemia High A1c efficacy Low cost	Weight gain Bone fractures Oedema
Insulins	Multiple	Increase glucose uptake Decrease hepatic glucose production	Good response Lower microvascular complications	Hypoglycaemia Weight gain High cost

PRACTICE PEARL

All persons with type 2 diabetes can benefit from lifestyle interventions. Primary among the modifiable risk factors is the ability to engage in physical activity alongside nutritional management.

For people with either type 1 or type 2 diabetes, a low-fat, carbohydrate-controlled diet with an emphasis on an increased intake of complex carbohydrates and reduced simple carbohydrates is recommended. *For specific recommendations on nutrition for those with insulin resistance, refer to Chapter 6.*

Pharmacotherapy in diabetes

Four principal types of insulin are available for use in patients with diabetes:

- rapid-acting—very fast onset (within 5–15 minutes, with a peak of action 30–90 minutes) and short duration (4–6 hours).
- short-acting—rapid onset of action (30–60 minutes, with peak of action 2–3 hours) and longer duration (8–10 hours).
- intermediate-acting—slower onset (may take 2–4 hours, with peak of action 4–10 hours) and longer duration (12–18 hours).

- long-acting—slower onset (1–6 hours) and long duration (12–24 hours or longer), allowing a background level of insulin that is 'peakless' in most persons.

Patients with type 1 diabetes should be treated with multiple daily injections (MDI) of both prandial and basal insulin, or with continuous subcutaneous insulin infusion (CSII). Page 104

Education to teach athletes to match prandial insulin dosing to carbohydrate intake, pre-meal glucose levels and anticipated physical activity is imperative. Athletes should use rapid-acting insulin analogues for prandial doses, to reduce the risk of hypoglycaemia, and timing of administration should be individualised.[8, 9] Use of adjunctive agents commonly utilised for type 2 diabetics in athletes with type 1 diabetes, such as injectable amylin analogues (pramlintide), metformin, glucagon-like peptide-1 receptor agonists, dipeptidyl peptidase-4 inhibitors and sodium-glucose cotransporter 2 inhibitors, has not been studied in athletes with diabetes and should be used cautiously, under the supervision of a healthcare professional with expertise in diabetes management.

PRACTICE PEARL

Every athlete with type 1 diabetes needs to develop their own personalised insulin plan in relationship to variations in their physical activity.

The cornerstone of therapy in type 2 diabetes in the general population is lifestyle modification with weight loss, physical activity and healthy nutrition. If a trial of a healthy lifestyle for 2–3 months is unsuccessful in controlling the blood glucose level, pharmacologic agents are indicated. Several classes of agents are available, each with different pharmacologic properties, although metformin is the preferred initial agent.[8] If an HbA1c of less than 7% is not achieved after three months of monotherapy, combination therapy should be considered.

Dietary management

Individualised nutrition therapy, ideally in conjunction with a registered dietician, for optimal diabetic control is now well established and can assist in maximising athletic performance. Carbohydrate requirements for exercise vary considerably among individuals. People with diabetes should monitor their blood glucose levels to determine their carbohydrate needs before, during and after exercise (Table 8.2). *Any recommendations within this chapter are intended as a starting point only to guide athletes.*

Table 8.2 Suggested adjustment of carbohydrate intake to permit the person with diabetes to exercise

Activity	Duration of exercise	Blood glucose level mmol/L (mg/dL)	Adjustment
Low level	0.5 hour	<5.5 (<100)	10 g CHO*

		>5.5 (>100)	No extra food
Moderate intensity	1 hour	<5.5 (<100)	20–30 g CHO
		5.5–10 (100–180)	10 g CHO
		10–16.5 (180–300)	No extra food (*in most cases*)
		>16.5 (>300)	No extra food. Preferably do not exercise as blood glucose level may go up
Strenuous activity	1–2 hours	<5.5 (<100)	45–60 g CHO
		5.5–10 (100–180)	25–50 g CHO
		10–16.5 (180–300)	15 g CHO
		>16.5 (>300)	Preferably do not exercise as blood glucose level may go up
Varying intensity	Long duration		*Insulin may be decreased by as much as 50%*
	0.5–1 day		Increase carbohydrate before, during and after activity 10–50 g CHO per hour

* CHO = carbohydrate

Athletes involved in endurance events who are carbohydrate loading prior to competition may need to increase their insulin dosage to cope with the increased carbohydrate intake. It is then important that carbohydrate is ingested before, during and after the event.

Table 8.3 contains a summary of possible advice that can be provided to the physically active diabetic athlete. While it is advised that all insulin-dependent diabetic athletes seek individual counselling from appropriate clinicians to arrange a specific dietary and training program, there are some important points that all diabetic athletes should be aware of:

Page 105

Table 8.3 Dietary reminders for patients undertaking physical activity

Before exercise	During exercise	After exercise
• Know the effects of different types of physical activity and the environment on your blood glucose level. • Have quickly digested carbohydrates available (e.g. barley sugar, fruit juice). • Eat 1–2 hours prior to exercise to ensure ideal glucose levels. • Hydrate (dehydration can be confused with hypoglycaemia). • If insulin is injected prior to exercise, use a site away from the muscle group being exercised, so that it is not metabolised too quickly.	• When exercising intermittently, ingest carbohydrates during breaks, to control blood glucose levels. • Regular carbohydrate intake is usually necessary for long-duration exercise. • Hydrate.	• After vigorous exercise, blood glucose levels may continue to drop. Ingest carbohydrate when exercise is complete to replenish glycogen stores. • Alcohol consumption is discouraged after exercise as it dehydrates and lowers the blood glucose level. • Hydrate.

- Athletes need to learn the effects of different types of exercise, under different environmental conditions, on their blood glucose levels.

- It is important to always have carbohydrate-rich foods available, such as fruit, fruit juice, barley sugar or biscuits.
- Glucagon should be prescribed for all athletes who use insulin, and administration should not be limited to team physicians. Trainers, coaches and teammates should be instructed in the safe use of glucagon kits and where they are stored if needed.
- After vigorous exercise, blood glucose levels may continue to drop for many hours. It is important that carbohydrate is ingested when exercise is completed, to ensure replenishment of glycogen stores and to prevent hypoglycaemia.[10]
- Caffeine consumption 30 minutes prior to exercise has been shown to reduce the risk of post-exercise nocturnal hypoglycaemia, by producing a counter-regulatory hormonal response in those with type 1 diabetes.[11]
- Diabetic athletes have similar micronutrient needs to non-diabetic athletes. A sports nutritionist can assist in creating an eating plan that ensures a personalised program that addresses all the athlete's needs within their own sport.

PHYSICAL ACTIVITY AND DIABETES

All clinicians engaged with a patient with diabetes should work together closely when considering physical activity prescription for the patient. The target for an adult should be to achieve at least 30 minutes of continuous or intermittent moderate aerobic activity, equivalent to brisk walking, five or six days a week, for a total of 150 minutes of aerobic activity per week.[5] An alternative regimen for more physically fit athletes would be 75 minutes/week of vigorous-intensity or high-intensity interval training, especially for athletes with type 2 diabetes.[12–14] Additionally, resistance training should be included in the program as it works on alternative pathways to support the management of insulin resistance.[15, 16] Balance training should be considered 2–3 times per week for older adults, to reduce the risk of falls.[17] In long-standing diabetics, heart rate may be an unreliable indicator of exertion because of autonomic neuropathy. Utilising perceived exertion scales such as the Borg scale may be more useful.

PRACTICE PEARL

All diabetics can benefit from a balance and proprioception program in addition to aerobic and resistance training.

It is of extreme importance that athletes with diabetes, especially those using insulin, monitor their blood glucose levels before and after every work-out, as blood glucose responses to exercise are highly variable. If the work-out is prolonged or symptoms occur, the blood sugar level should also be taken during the exercise session. If no means exist to measure blood glucose levels before a work-out, then the work-out should be of short duration and low intensity, with a glucose supply

readily available.

All patients with diabetes should carry an identification card or bracelet identifying themselves as having diabetes. They should be educated to be alert to the early signs of hypoglycaemia for up to 24 hours after exercise. It is essential that they always carry glucose tablets or an alternative source of glucose. Dehydration during exercise should be prevented by adequate fluid consumption. It is also recommended that the diabetic athlete exercise with somebody else, if possible, in case of adverse reactions.

PRACTICE PEARL

Extreme ambient temperatures can reduce insulin action or change insulin absorption.

Benefits of physical activity

The benefits of exercise in type 1 diabetics include improved insulin sensitivity, improved blood lipids, decreased resting heart rate and blood pressure, decreased body weight and possibly decreased risk of coronary heart disease.[18]

It is well recognised that exercise reduces the risk of developing type 2 diabetes and provides considerable benefits for those with type 2 diabetes. A program of regular aerobic and resistance exercise can reverse many of the defects in metabolism of both fat and glucose that occur in people with type 2 diabetes and improve the HbA1c.[19] With the advent of 24-hour blood glucose monitors it has become much easier for individuals, especially those involved in sport, to monitor their resting levels, plan training accordingly and reduce the risk of nocturnal hypoglycaemia.[20] Evidence has suggested that those who adhere to exercise guidelines gain from improved glycaemic control for the 24-hour period immediately afterwards.[21]

Where contact sports are involved it is also key that the medical team take into account the potential effects of collisions and other injuries, which have been shown to increase the risk of hyperglycaemia. The medical team also has to consider the effects of regular sports therapies such as cryotherapy for the management of acute injuries where these may alter the insulin response of the injured athlete.

Exercise and type 1 diabetes

Control of blood glucose in a patient with type 1 diabetes is quite individualised and is achieved through a balance in carbohydrate intake, exercise and insulin dosage. The meal plan and insulin dosage should be adjusted according to the patient's response to exercise. A degree of trial and error is necessary for people with type 1 diabetes taking up new activities. Frequent self-monitoring should occur, at least until a balance is achieved among diet, exercise and insulin parameters. The ideal pre-exercise blood level is 6.6–10 mmol/L (120–180 mg/dL). Athletes who have blood glucose concentrations exceeding 13.9 mmol/L (250 mg/dL) and ketones in their urine, or a blood glucose level of more than 16.5 mmol/L (300 mg/dL) regardless of ketone status, should

postpone exercise and take supplemental insulin. Those with blood glucose levels less than 5.5 mmol/L (100 mg/dL) require a pre-exercise carbohydrate snack (e.g. fruit or another source well tolerated by the athlete prior to exercise).[5]

Exercise of 20–30 minutes at less than 70% VO_2max (e.g. walking, golf, table tennis) typically requires a rapidly absorbable carbohydrate (15 g fruit exchange or 60 calories) before exercise but needs minimal insulin dosing adjustments.

More vigorous activity of less than 1 hour (e.g. jogging, swimming, cycling, skiing, tennis) often requires a 25% reduction in pre-exercise insulin and 15–30 g of rapidly absorbed carbohydrate before, and every 30 minutes after, the onset of activity. Maintaining adequate hydration is important.

Strenuous activity of longer than 1 hour (e.g. marathon running, triathlon, cross-country skiing) may require a 30–80% reduction in pre-exercise insulin and ingestion of two fruit exchanges (30 g or 100–120 calories) every 30 minutes. It is also important to replace the fluid lost by sweating.

If early morning activity is to be performed, the basal insulin from the evening dose of intermediate-acting insulin may need to be reduced by 20–50%. The morning regular-acting insulin dose may also need to be reduced by 30–50% before breakfast, or even omitted if exercise is performed before food. Depending on the intensity and duration of the initial activity and likelihood of further activity, a reduction of 30–50% may be needed with each subsequent meal.

Athletes who use CSII (insulin-pump) therapy should reduce the basal pump rate by 50% one hour before high-intensity exercise and maintain the basal rate if performing low-intensity exercise. If eating a meal prior to competition, meal time bolus (insulin administration) should also be reduced by 50% for high-intensity activity, and a smaller reduction for low-intensity activity. Athletes participating in contact or collision sports should remove their pump 30 minutes before beginning of activity and use hourly boluses of insulin at 50% basal rate for activity lasting an hour or longer.[22] See box Subcutaneous insulin delivery for a brief overview of insulin-pump therapy.

Post-exercise hypoglycaemia can occur and can be immediate or delayed. Prevention of immediate hypoglycaemia can be accomplished by increasing carbohydrate during and immediately after exercise, careful glucose monitoring and avoidance of injecting insulin into exercising muscle.[10] Consuming 1.5 g CHO/kg body weight within 30 minutes of exhaustive, glycogen-depleting exercise allows for more efficient restoration of muscle glycogen. Intake of an additional 1.5 g CHO/kg 1–2 hours post exercise can help prevent late-onset post-exercise hypoglycaemia (LOPEH), which can occur up to 28 hours following such exercise.

PRACTICE PEARL

Late-onset post-exercise hypoglycaemia can present insidiously and be life threatening. It is important that after a bout of physical activity diabetics are encouraged to eat, to support recovery and prevent LOPEH from occurring.

If physical activity occurs spontaneously, then insulin adjustment may be impossible. Instead, supplementation with 20–30 g of carbohydrate, at the onset of exercise and every 30 minutes thereafter, may prevent hypoglycaemia. In elite athletes and with intense bouts of exercise, reductions in insulin dosage may be even higher than those listed above. During periods of inactivity (e.g. holidays, recovery from injury), increased insulin requirements are to be expected.

A practical guide to prescribing physical activity for patients with diabetes is shown in the box 'Practical tips for prescribing a physical activity program for a diabetic'.

Exercise and type 2 diabetes

All persons with type 2 diabetes should participate in a regular physical activity program. Patients taking GLAs may need to adjust their doses on days of prolonged exercise or withhold them altogether, depending on their blood glucose levels. They are also advised to carry some glucose with them and to be able to recognise the symptoms of hypoglycaemia. Hypoglycaemia is especially a risk in those people with diabetes taking sulfonylureas, due to their long half-lives and increased endogenous insulin production.

Diabetes and competition

Every diabetic athlete should develop an individual diabetes care plan for both training and competition.[22–24] As competition may require long-distance travel and necessitate altered eating patterns, the diabetic athlete should practise the match day routine at home and have snacks available as necessary. Good control of blood glucose levels may require regular access to carbohydrate-containing drinks, which can aid in rehydration during prolonged exercise.

NEED TO KNOW

Those involved in sports where making weight is important, such as power lifting, boxing and wrestling, may consider omitting insulin, to support a reduced weight at weigh-in.25 Education should always be the primary concern of the medical professional involved with these athletes, including the implications for their health and potentially performance.[26]

Diabetes and travel

A physician's letter should accompany diabetic travellers, stating that they carry insulin, needles and blood glucose testing equipment. Copies of prescriptions should be taken, and medications kept in their original packaging. Insulin should not be packed into checked luggage as there is a risk of it being misplaced, or freezing and thawing in the luggage hold. Insulin will generally keep for a month at room temperature. Additional supplies should include those needed to treat hypoglycaemia (including snacks), supplies for urine or blood ketone testing, a sharps container for used needles and spare parts for meters or pumps. General recommendations for travel can be reviewed at several websites, such as the American Diabetes Association (www.diabetes.org).

Travelling in a north–south direction generally requires no alteration to insulin doses. East-west travel of more than five hours generally requires athletes to adjust insulin doses. East-bound travel results in a shorter day and west-bound travel a longer one. Travellers should check blood glucose levels at least every six hours during travel. Continuous insulin pumps usually require no adjustment, as most pumps automatically reset to the destination time on arrival.

Subcutaneous insulin delivery

Continuous subcutaneous insulin infusions (CSII or pump therapy) are being used to tighten control and increase flexibility of treatment. Benefits include fewer erratic swings in blood glucose and decreased risk of hypoglycaemia, more appropriate matching of insulin to food intake, and improved targeting of the dawn phenomena.

There are two main components to insulin delivery in pump therapy:

- *Basal insulin* is delivered as a continuous infusion of small increments of rapidly acting insulin over 24 hours to meet requirements during fasting and sleep. This generally comprises 40-50% of total daily insulin use.
- *Bolus insulin* is patient-activated doses given with meals to correct hyperglycaemic excursions. Mealtime boluses can be delivered in one of two ways. The standard single wave bolus delivers the entire dose within 1-2 minutes, while a dual wave bolus gives part of the dose immediately with the remainder being infused slowly over a predetermined time. The infusion set is replaced every 2–3 days with a new subcutaneous infusion site. Some circulating insulin is required to maintain glycaemic control during exercise, which may be facilitated by an insulin pump.

High-risk sports

Diabetic patients are at increased risk of complications while participating in high-risk sports. Hypoglycaemic attacks, characterised by impaired concentration, in sports such as rock and mountain climbing and skydiving have the potential for serious if not fatal injury. This must also be taken into consideration from an athletic performance standpoint when the need to maintain peak performance over longer durations is necessary. A good clinical strategy with young otherwise healthy individuals is to support the development of an appropriate diabetic self-management program. This can be achieved by emphasising the additional benefits to their athletic performance alongside the benefits to their long-term health.

PRACTICE PEARL

Insulin pumps should be removed prior to participation in contact or collision sports.

Exercise and the complications of diabetes

Exercise is often neglected when the secondary complications of diabetes occur, but patients

should be encouraged to participate in physical activity throughout their lifespan. Some unique concerns for the patient with diabetes that warrant close scrutiny include autonomic and peripheral neuropathy, retinopathy and nephropathy.

Autonomic neuropathy

Abnormal autonomic function is common among those with diabetes of long duration. The risks of exercise when autonomic neuropathy is present include hypoglycaemia, abnormal heart rate and blood pressure responses (e.g. postural drop), impaired sympathetic and parasympathetic nervous system activity and abnormal thermoregulation.

Patients with autonomic neuropathy are at high risk of developing complications during exercise. Sudden death and myocardial infarction have been attributed to autonomic neuropathy and diabetes. In diabetic patients with autonomic neuropathy, high-intensity activity should be avoided, as should rapid changes in body position and extremes in temperature. Water activities and stationary cycling are recommended.

Peripheral neuropathy

Peripheral neuropathy (typically manifested as loss of sensation and of two-point discrimination) usually begins symmetrically in the lower and upper extremities and progresses proximally.

Podiatric review should occur on a regular basis and correct footwear can prevent the onset of foot ulcers. Regular close inspection of the feet and use of proper footwear are important. The patient should avoid exercise that may cause trauma to the feet. Feet and toes should be kept dry and clean, dry socks should be used.

Non weight-bearing activities, such as swimming, cycling and arm exercises, are recommended in those with insensitive feet. Activities that improve balance are also appropriate choices.

Diabetic retinopathy

The incidence of diabetic retinopathy is directly proportional to the severity and duration of the diabetes—98% of cases of type 1 and 78% of type 2 diabetes will progress to detectable retinopathy in 15 years from the diagnosis. Exercise that increases blood pressure may worsen retinopathy. Therefore, patients with proliferative retinopathy should avoid exercise that increases systolic blood pressure to 170 mmHg and prolonged Valsalva-like activities. Exercise that results in a large increase in systolic pressure (such as weightlifting) can cause retinal haemorrhage.

Exercise for these patients could include stationary cycling, walking and swimming. If possible, blood pressure should be monitored during the exercise program. Exercise is contraindicated if the individual has had recent photocoagulation treatment or surgery. Jarring of the head in contact sports may cause detachment of the retina.

Diabetic nephropathy

Nephropathy can be classified according to urinary albumin excretion rates:

- <20 μg/min—normoalbuminuria
- 20–200 μg/min—microalbuminuria

- >200 μg/min—overt nephropathy

Patients with microalbuminuria and overt renal disease should undertake light to moderate exercise only. Vigorous exercise that results in marked changes in haemodynamics should be avoided. This includes lifting heavy weights and high-intensity aerobic activities. Activities that are weight-bearing yet low impact are preferable.

Renal patients should be fully evaluated before commencing an exercise program. Fluid replacement is extremely important in these patients. Training programs for patients undergoing haemodialysis are encouraged, but should be developed in conjunction with a nephrologist.

Practical tips for prescribing a physical activity program for a diabetic

It is very important prior to starting a physical activity program that patients consult an appropriate healthcare professional, especially if undertaking a vigorous or high-intensity program, to identify potential risks associated with diabetes and increasing activity levels. Successfully increasing activity levels can support the achievement of health and lifestyle goals. Since every person will respond to exercise differently, special attention should be paid to understanding how the patient's blood glucose levels respond to different types of physical activity. Previously sedentary individuals are recommended to gradually build into an exercise regime.[5]

Nutrition

- Exercise 1–2 hours after eating a meal to ensure ideal glucose level during activity.
- Hydration before, during and after exercise is important, as dehydration can be confused with hypoglycaemia.
- Have fast-acting carbohydrates (food/fluid) accessible during and immediately after exercise.
- Generally, carbohydrates should be ingested following exercise, but depending on the intensity and duration, adjustments may be required. Table 8.2 outlines suggested carbohydrate intake pre/post activity. It is advised that individual blood glucose should always be tested before, during and after exercise to identify personal nutrition needs.

As a guideline:

- Short-burst high-intensity exercise—carbohydrate may not be necessary after exercise as glucose production may exceed uptake.
- Endurance or intermittent exercise—carbohydrate should be consumed before, during and after activity. Be sure to understand personal insulin requirements when ingesting more carbohydrate than usual (carb loading prior to an event).
- A small amount of caffeine 30 minutes prior to commencing exercise may help prevent hypoglycaemia if type 1 diabetes is present.

Insulin and blood glucose monitoring

- Individuals differ greatly in their insulin requirements. Duration and intensity of exercise, as well as type of diabetes, should all be considered. A personal protocol should be developed with a healthcare professional; this can be modified based on experience and consistency of exercise. If possible, avoid injecting insulin into the body part that will be exercised.
- Monitor blood glucose before, during and immediately after exercising.
- Additional blood glucose monitoring 4–6 hours after aerobic exercise should be performed to monitor for low blood sugar (hypoglycaemia).

Physical activity/exercise

A combination of aerobic and resistance exercises provides the most benefit to those with diabetes.[27] It has been observed that resistance training resulted in greater benefits for muscle glycogen uptake, with aerobic exercise contributing to greater benefits in insulin sensitivity. Pre-exercise health screening is not recommended for those persons who are going to start a low- to moderate-intensity walking program, but is recommended for those persons who are going to undertake high-intensity activities or are at high risk for cardiovascular disease.[4, 5]

A healthcare professional and exercise specialist will be able to tailor a program for each athlete, but following are general recommendations on physical activity dosages.

Aerobic

– 150 mins per week (spread over at least 3 days) of moderate to vigorous aerobic exercise. Exercise may be split into small time increments
  OR
– 75 mins per week of vigorous or high-intensity interval training

Intensity	Example
Moderate: 50–70% of maximum heart rate	Biking, walking, swimming, dancing, water aerobics
Vigorous: >70% of maximum heart rate	Jogging, aerobics, hockey, basketball, hiking

Resistance

– Resistance exercise 2–3 times per week on non-consecutive days has been proven to improve insulin sensitivity and glycaemic control (see below for examples of resistance exercise).
– Exercise prescription should target all major muscle groups to gain maximal effectiveness and overall health gains.
– Initial instruction and periodic supervision by an exercise specialist is recommended.
– Resistance training may prove more beneficial to those who find aerobic activities difficult due to comorbidities (e.g. upper limb resistance training for those with lower limb neuropathy).

Examples of resistance training exercises for diabetic patients, along with progressions, are included in the table below and Figure 8.2 a-c.

Exercises	Progression
Shoulder press	2–3 times per week
Bicep curls	• Start with 1 set, 10–12 reps, with moderate weight

Push-ups Lunge Squat Calf raise	• Progress to 2 sets, 10–12 reps • Progress to 3 sets, 8–10 reps, with heavier weight

Flexibility

– 2–3 times per week to increase range of motion around joints

Balance

– 2–3 times per week, especially in active older adults, to improve balance and reduce falls risk. This can be easily accomplished at home, with exercises such as single leg stands incorporated into an average day. In those who have additional complications such as neuropathy specific advice and an individualised program should be sought.
– *This can be easily accomplished at home, with exercises such as single leg stands incorporated into an average day—see fig. 8.2(d)*

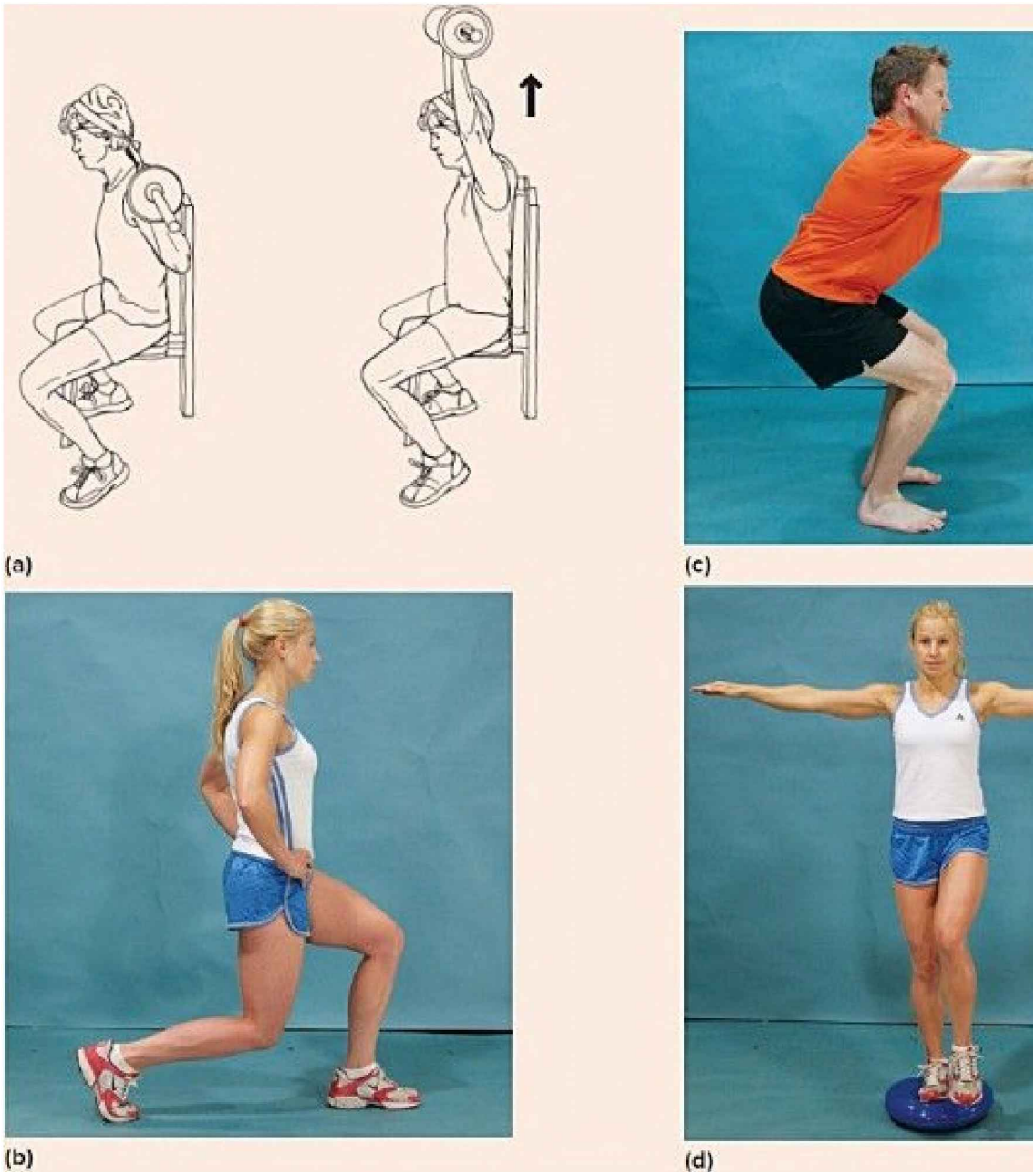


Figure 8.2 (a) Shoulder press (b) Lunge (c) Standard squat (d) Single leg balance on wobble cushion. All exercises can be progressed by increasing the number of sets/repetitions or adding weight/resistance

Things to bring/wear

- insulin medication

- quickly digested carbohydrates (e.g. fruit, barley sugar, biscuits, sport drinks)
- medical ID bracelet
- water
- glucose monitor
- comfortable shoes and socks

Sticking with it for health

Some people find it very difficult to incorporate exercise into their daily lives. The clinician is directed to Chapter 5 'Behaviour change', for a more detailed discussion. However, basic advice may include:

- exercise with a friend or partner
- educate yourself about diabetes and know the benefits associated with physical activity and proper nutrition
- search out community exercise programs or exercise counselling
- vary the activities to keep it interesting.

Beware! Signs of hypoglycaemia

Ensure your patients are aware of the following signs and understand what action to take:

- headache
- sweating
- hunger
- tremors
- nervousness
- confusion
- abnormal behaviour
- convulsions
- loss of consciousness.

Advice should be to focus on regular physical activity rather than intense exercise episodes, to avoid frustration.

Other things to consider

Be sure to take all factors into account when prescribing physical activity and adjust accordingly. This may include environment temperature, exercise duration and intensity of activity. Most important, advice should be given to monitor blood sugars frequently.

COMPLICATIONS OF PHYSICAL ACTIVITY IN THE DIABETIC ATHLETE

The diabetic athlete may suffer numerous complications associated with exercise, including hypoglycaemia and ketoacidosis.

Hypoglycaemia

Hypoglycaemia (blood glucose level <3.6 mmol/L [<65 mg/dL]) is the major concern among athletes with type 1 diabetes and has been shown to impair the performance of skilled tasks in athletes.[22] The use of excessive exogenous insulin will prevent hepatic glucose production leading to increased glucose uptake within skeletal muscle. This can create a subsequent risk of exercise-

induced hypoglycaemia.

Immediate post-exercise hypoglycaemia can occur up to 4 hours after exercise, and delayed-onset hypoglycaemia up to 24 hours after exercise. The effects are commonly nocturnal, with disturbed sleep patterns, altered recovery and impaired performance the following day.

The initial symptoms of hypoglycaemia include sweating, headache, nervousness, tremor and hunger. The symptoms of impending hypoglycaemia may be difficult to differentiate from symptoms experienced during vigorous exercise. If the hypoglycaemia is not corrected, confusion, abnormal behaviour, loss of consciousness and convulsions may occur.

At the first indication of hypoglycaemia, the athlete should ingest oral carbohydrate in solid or liquid form. Diabetic athletes should carry quickly digestible forms of carbohydrate (e.g. glucose tablets, barley sugar) or have a glucose–electrolyte solution available. The semiconscious or unconscious diabetic patient requires urgent intravenous glucose administration (50 mL of 50% solution) or glucagon injection.

Nocturnal hypoglycaemia may occur following late afternoon or evening training or competition. Symptoms may include night sweats, unpleasant dreams and early morning headaches.

Prevention of hypoglycaemia depends on adjustment of the carbohydrate intake and insulin dosage to meet the individual athlete's needs, as discussed above. A continual source of glucose must be available during exercise and, as a rule of thumb, athletes usually require 15–30 g of glucose per half hour of vigorous exercise. Nocturnal hypoglycaemia may be prevented by exercising earlier in the day, reducing the evening insulin dose or by consuming a complex carbohydrate prior to going to bed. For those providing medical cover at the end of endurance events or on the course of mass participation races, the onset of an acute episode of syncope because of hypoglycaemia should always be considered, even in the non-diabetic population.

PRACTICE PEARL

Carrying a small fast-acting source of glucose in your medical kit at events is always useful in the event of someone suffering a bout of hypoglycaemia.

Diabetic ketoacidosis in the athlete

Despite increased glucose uptake that occurs in exercise independent of insulin, a relative deficiency of insulin can lead to hyperglycaemia and possible diabetic ketoacidosis. Individuals with blood glucose levels of 20–25 mmol/L (364–455 mg/dL) and above are especially at risk of precipitating diabetic ketoacidosis if they exercise vigorously. This occurs because the counter-regulatory hormone response (glucagon, catecholamines, growth hormone and glucocorticoids) to exercise pushes the glucose levels higher and there is insufficient insulin to prevent ketosis. Therefore, an athlete must be aware of his or her glucose control before exercise. In addition, athletes with so-called 'brittle diabetes' must be very cautious in reducing their insulin dose before

exercise.

The presence of ketones in the urine confirms the presence of hypoinsulinaemia and thus increases the risk of hyperglycaemia and ketosis. Hyperglycaemia may manifest as poor concentration, dehydration or even under-performance, and athletes need to be aware of these signs. If the blood glucose level is >17 mmol/L (>309 mg/dL) or >14 mmol/L (>255 mg/dL) with the presence of ketones on urinalysis, then exercise should be avoided until insulin has been administered and metabolic control is re-established. Athletes should not exercise as a primary way to control high blood glucose levels.

Musculoskeletal manifestations of diabetes

Several musculoskeletal disorders are found in a higher prevalence in diabetic patients, compared with the normal population.[28, 29] The diagnosis of diabetes should always be considered in the patient presenting with the conditions listed below; the prevalence of these is summarised in Table 8.4.

Table 8.4 Prevalence of musculoskeletal disorders in patients with and without diabetes

Musculoskeletal disorder	With diabetes	Without diabetes
Osteoarthritis	18%	5%
Frozen shoulder (adhesive capsulitis)	11–30%	2–10%
Limited joint mobility	8–50%	0–26%
Dupuytren's contracture	20–63%	13%
Carpal tunnel syndrome	11–16%	0.125%
Flexor tenosynovitis	11%	<1%
Diffuse idiopathic skeletal hyperostosis	13–49%	1.6–13%

Osteoarthritis

There is growing evidence that metabolic derangements such as hyperglycaemia may contribute to development and worsening of osteoarthritis (see Chapter 16). Treatment consists of lifestyle modifications, especially weight loss and glucose control.[30]

Gout

All persons with gouty arthritis should be screened for the presence of diabetes. Treatment again consists of weight loss and glucose control as well as dietary avoidance of certain foods and alcohol.[31]

Fibrosing syndromes

Fibrosing syndromes include adhesive capsulitis of the shoulder, flexor tenosynovitis, Dupuytren's contracture, carpal tunnel syndrome and diabetic cheiroarthropathy. The common pathophysiology is collagen deposition and glycosylation in connective tissues. This leads to abnormal crosslinking, increased hydration, neuropathy, microangiopathy and disuse, causing

limited joint mobility. Management strategies include symptomatic relief and improvement in function with physiotherapy. Glycaemic control is important, but tight control has not been shown to prevent development or improve these conditions.

Frozen shoulder (adhesive capsulitis) appears at a younger age and is usually less painful in patients with diabetes.[32] It is associated with the duration of diabetes and with age. Physiotherapy can be helpful. The use of corticosteroid injections may increase blood sugar levels in people with diabetes for 24–48 hours after an injection.

Flexor tenosynovitis

Fibrous tissue proliferation in the tendon sheath leads to limitation of the normal movement of the tendon. It is associated with the duration of diabetes, but not age.[33, 34] A corticosteroid injection is often curative.

Dupuytren's contracture

Dupuytren's contracture is characterised by palmar or digital thickening, tethering or contracture of the hands. In diabetics the ring and middle finger are more commonly affected, compared with the fifth finger in non-diabetics.[33, 34] Treatment consists of optimising glycaemic control, physiotherapy and surgery if complications continue.

Carpal tunnel syndrome

Carpal tunnel syndrome has a prevalence of 11–16% in patients with diabetes. It is traditionally managed with education, activity modification, splinting and physiotherapy. If this is unsuccessful then surgery is a consideration.

PRACTICE PEARL

Consider testing for diabetes in any patient who presents with carpal tunnel syndrome.

Limited joint mobility

Limited joint mobility is also known as 'diabetic cheiroarthropathy'. It is characterised by thick, tight, waxy skin, mainly on the dorsal aspect of the hands, with flexion deformities of the metacarpophalangeal and interphalangeal joints. In the early stages paraesthesia and mild pain may develop, with symptoms increasing slowly. Treatment consists of splinting and individualised hand therapy.

Achilles tendinopathy

Structural changes in the Achilles tendon due to glycation may contribute to pain; they are also postulated to cause biomechanical changes that are a precursor to development of foot problems such as diabetic pressure ulcers.[35]

Diffuse idiopathic skeletal hyperostosis

Diffuse idiopathic skeletal hyperostosis (DISH) is characterised by new bone formation, particularly in the thoracolumbar spine. New bone appears to flow from one vertebra to the next and is more prominent on the right side of the thoracic vertebra. Ossification of ligaments and tendons can occur elsewhere, including the skull, pelvis, heels and elbows. Although DISH is commonly seen in persons with diabetes, a causal relationship is not definitive.[36] Management consists of education and physiotherapy. Short-term anti-inflammatories may be helpful during periods of exacerbation.

Diabetic neuropathic arthropathy (Charcot's joints)

Neuropathic (Charcot's) joints result from diabetic peripheral neuropathy and are seen usually in patients over 50 years of age who have had diabetes for many years.[29] The joints affected are weight-bearing joints. Management includes optimising glycaemic control, regular foot care and review. Total contact casting may be helpful in some cases; occasionally surgery is needed.

Diabetic muscle infarction

Diabetic muscle infarction is a spontaneous ischaemic necrosis of skeletal muscle that presents with acute or subacute pain, swelling and tenderness, typically in the thigh or calf. It is more common in persons with longstanding or poorly controlled diabetes. Although rare, it needs to be differentiated from deep vein thrombosis, intramuscular haematomas, infections and neoplasms.[37]

PRACTICE PEARL

Consider diabetic muscle infarction in an athlete with diabetes who presents with onset of swelling and tenderness of the thigh or calf without prior trauma.

Diabetic radiculoplexus neuropathies

Diabetic radiculoplexus neuropathy (DRPN), or diabetic amyotrophy, is distinct from other forms of diabetic neuropathy and is characterised by muscle weakness/wasting and by diffuse, proximal lower limb muscle pain and asymmetrical loss of tendon jerks. The shoulder girdle may be affected but less commonly. It occurs most often in older men with type 2 diabetes and is a diagnosis of exclusion (sinister causes must be sought). Management consists of stabilising glycaemic control and physiotherapy. Since the pathophysiology is thought to be mediated by an immuno-mediated pathway, immune system modulating therapy may be helpful.[38]

SUMMARY

The athlete with diabetes needs to have a good understanding of the effects of physical activity on blood glucose levels. With regular monitoring and appropriate adjustments to medications, insulin dosing and carbohydrate intake, the athlete with diabetes should be able to develop a diabetes care plan and participate fully in sporting activities. A physical activity prescription that combines aerobic and resistance

training produces greater benefits in managing diabetes and may offer the greatest benefits for supporting those with diabetes involved in sports outside the elite level. The recent advances in diabetic management should not preclude those with even the most severe forms of diabetes from competing at the highest level.

REFERENCES

1. World Health Organization (WHO) Regional Office for Europe. Data and statistics: the challenge of diabetes 2010 [accessed: 5th April 2018]. http://www.euro.who.int/en/health-topics/noncommunicable-diseases/diabetes/data-and-statistics.
2. Hossain P, Kawar B, El Nahas M. Obesity and diabetes in the developing world—a growing challenge. *N Engl J Med* 2007; 356(3): 213–15.
3. American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care* 2010; 33(Suppl 1): S62–9.
4. Riebe D, Franklin BA, Thompson PD et al. Updating ACSM's recommendations for exercise preparticipation health screening. *Med Sci Sports Exerc* 2015; 47(11): 2473–9.
5. Colberg SR, Sigal RJ, Yardley JE et al. Physical activity/exercise and diabetes: a position statement of the American Diabetes Association. *Diabetes Care* 2016; 39(11): 2065–79.
6. Stolar MW. Atherosclerosis in diabetes: the role of hyperinsulinemia. *Metabolism* 1988; 37(2 Suppl 1): 1–9.
7. Hernández MAL Hyperglycemia and diabetes in myocardial infarction. In: Oguntibeju OO, ed. *Diabetes mellitus—insights and perspectives*. Rijeka, Croatia: InTech, 2013: 169–92.
8. American Diabetes Association. Standards of Medical Care in Diabetes—2017: summary of revisions. *Diabetes Care* 2017; 40(Suppl 1): S4–5.
9. Chamberlain JJ, Kalyani R, Leal S et al. Treatment of type 1 diabetes: synopsis of the 2017 American Diabetes Association Standards of Medical Care in Diabetes. *Ann Intern Med* 2017; 167(7): 493–8.
10. Adolfsson P, Mattsson S, Jendle J. Evaluation of glucose control when a new strategy of increased carbohydrate supply is implemented during prolonged physical exercise in type 1 diabetes. *Eur J Appl Physiol* 2015; 115(12): 2599–607.
11. Richardson T, Thomas P, Ryder J et al. Influence of caffeine on frequency of hypoglycemia detected by continuous interstitial glucose monitoring system in patients with long-standing type 1 diabetes. *Diabetes Care* 2005; 28(6): 1316–20.
12. Snowling NJ, Hopkins WG. Effects of different modes of exercise training on glucose control and risk factors for complications in type 2 diabetic patients: a meta-analysis. *Diabetes Care* 2006; 29(11): 2518–27.

13. Jelleyman C, Yates T, O'Donovan G et al. The effects of high-intensity interval training on glucose regulation and insulin resistance: a meta-analysis. *Obes Rev* 2015; 16(11): 942–61.
14. Francois ME, Little JP. Effectiveness and safety of high-intensity interval training in patients with type 2 diabetes. *Diabetes Spectr* 2015; 28(1):39–44.
15. Dunstan DW, Daly RM, Owen N et al. High-intensity resistance training improves glycemic control in older patients with type 2 diabetes. *Diabetes Care* 2002; 25(10): 1729–36.
16. Herriott MT, Colberg SR, Parson HK et al. Effects of 8 weeks of flexibility and resistance training in older adults with type 2 diabetes. *Diabetes Care* 2004; 27(12): 2988–9.
17. Morrison S, Colberg SR, Mariano M et al. Balance training reduces falls risk in older individuals with type 2 diabetes. *Diabetes Care* 2010; 33(4): 748–50.
18. Kodama S, Tanaka S, Heianza Y et al. Association between physical activity and risk of all-cause mortality and cardiovascular disease in patients with diabetes. *Diabetes Care* 2013; 36(2): 471–9.
19. Pandey A, Swift DL, McGuire DK et al. Metabolic effects of exercise training among fitness-nonresponsive patients with type 2 diabetes: the HART-D study. *Diabetes Care* 2015; 38(8): 1494–501.
20. Iscoe KE, Corcoran M, Riddell MC. High rates of nocturnal hypoglycemia in a unique sports camp for athletes with type 1 diabetes: lessons learned from continuous glucose monitoring systems. *Can J Diabetes* 2008; 32(3): 182–9.
21. van Dijk J-W, van Loon LJC. Exercise strategies to optimise glycemic control in type 2 diabetes: a continuing glucose monitoring perspective. *Diabetes Spectr* 2015; 28(1): 24–31.
22. Horton WB, Subauste JS. Care of the athlete with type 1 diabetes mellitus: a clinical review. *Int J Endocrinol Metab* 2016; 14(2): e36091.
23. Jimenez CC, Corcoran MH, Crawley JT et al. National Athletic Trainers' Association position statement: management of the athlete with type 1 diabetes mellitus. *J Athl Train* 2007; 42(4): 536–45.
24. Harris GD, White RD. Diabetes in the competitive athlete. *Curr Sports Med Rep* 2012; 11(6): 309–15.
25. Hornsby WG, Chetlin RD. Management of competitive athletes with diabetes. *Diabetes Spectr* 2005; 18(2): 102–7.
26. MacKnight JM, Mistry DJ, Pastors JG et al. The daily management of athletes with diabetes. *Clin Sports Med* 2009; 28(3): 479–95.
27. Hansen E, Landstad BJ, Gundersen KT et al. Insulin sensitivity after maximal and endurance resistance training. *J Strength Cond Res* 2012; 26(2): 327–34.
28. Larkin ME, Barnie A, Braffett BH et al. Musculoskeletal complications in type 1

diabetes. *Diabetes Care* 2014; 37(7): 1863–9.

29. Merashli M, Chowdhury TA, Jawad AS. Musculoskeletal manifestations of diabetes mellitus. *QJM* 2015; 108(11): 853–7.
30. Velasquez MT, Katz JD. Osteoarthritis: another component of metabolic syndrome? *Metab Syndr Relat Disord* 2010; 8(4): 295–305.
31. Kim SC, Liu J, Solomon DH. Risk of incident diabetes in patients with gout: a cohort study. *Arthritis Rheumatol* 2015; 67(1): 273–80.
32. Huang YP, Fann CY, Chiu YH et al. Association of diabetes mellitus with the risk of developing adhesive capsulitis of the shoulder: a longitudinal population-based followup study. *Arthritis Care Res (Hoboken)* 2013; 65(7): 1197–202.
33. Fitzgibbons PG, Weiss AP. Hand manifestations of diabetes mellitus. *J Hand Surg Am* 2008; 33(5): 771–5.
34. Chammas M, Bousquet P, Renard E et al. Dupuytren's disease, carpal tunnel syndrome, trigger finger and diabetes mellitus. *J Hand Surg Am* 1995; 20(1): 109–14.
35. Batista F, Nery C, Pinzur M et al. Achilles tendinopathy in diabetes mellitus. *Foot Ankle Int* 2008; 29(5): 498–501.
36. Sencan D, Elden H, Nacitarhan V et al. The prevalence of diffuse idiopathic skeletal hyperostosis in patients with diabetes mellitus. *Rheumatol Int* 2005; 25(7): 518–21.
37. Horton WB, Taylor JS, Ragland TJ et al. Diabetic muscle infarction: a systematic review. *BMJ Open Diabetes Res Care* 2015; 3(1): e000082.
38. Laughlin RS, Dyck PJ. Diabetic radiculoplexus neuropathies. *Handb Clin Neurol* 2014; 126: 45–52.

* Thanks to Cam Stuart, who contributed to the 4th edition chapter.

Chapter 9

Sudden cardiac death in sport

with JONATHAN DREZNER, HAMISH MACLACHLAN and SANJAY SHARMA

Spanish footballer Nacho Barbera has died after suffering a cardiac arrest during a recent match. Barbera had been playing in the 13–14 year-old age group of Valencia-based side UD Alzira and was the captain of his team.

www.skysports.com, 4 February 2018

The sudden death of a young athlete on the playing field is a most devastating event. Sudden cardiac death (SCD) is the leading cause of mortality in young athletes during exercise and typically is the result of undiagnosed structural or electrical cardiovascular disease.[1–5] Sudden cardiac death is always tragic and it profoundly impacts the community, school and team where it occurs.

Athletes are viewed as the healthiest members of our society, and exercise and sport are widely encouraged to prevent illness and promote health. However, intense exercise and physical conditioning also may trigger an acute cardiovascular event or sudden cardiac arrest (SCA) in young individuals harbouring silent hereditary or congenital heart disease. This 'exercise paradox' is highlighted by the sudden death of a young athlete during training or competition.

Because of the importance of this topic and the large number of recent advances, SCD has a dedicated chapter. The clinical approach to other cardiac symptoms (such as chest pain, syncope, dyspnoea) is addressed in Chapter 10. The main goals of this chapter are to:

- review the incidence of SCD in young athletes—this is not a rare occurrence
- clarify the aetiology of SCD—sports physicians should have a detailed understanding of the various pathologies that underpin SCD, and all clinicians should be interested in the various ways the heart can fail:
  - structural

  - electrical
  - acquired
- outline how to evaluate an athlete for conditions that may cause SCD
- address three common diagnostic conundrums that need practical solutions
- briefly review the purpose of pre-participation cardiovascular screening (see also Chapter 46, 'Periodic medical assessment of athletes', in *Clinical Sports Medicine Volume 1: Injuries*)
- discuss the contemporary approach to primary and secondary prevention of SCD in sport.

INCIDENCE OF SUDDEN CARDIAC DEATH

The true incidence of SCD in young athletes is widely debated. Accurate calculation of the incidence of SCD in athletes requires a precise numerator (number of deaths per year) and an exact denominator (number of athlete participants per year) in the population studied. Variability in either of these accounts for unreliable estimates of incidence. The reported incidence of SCD in young competitive athletes (aged 12–35 years) varies widely, and it is challenging to compare studies with heterogeneous case identification methods that originate from different geographic regions (Table 9.1).

Table 9.1 Incidence of sudden cardiac death in young competitive athletes

Page 116

Study	Year	Country	Study design	Case identification	Denominator	Ages studied	SCD or SCA/SCD	Incidence
Van Camp[5]	1995	USA	Retrospective cohort	National Center for Catastrophic Sports Injury Research and media database	17 most popular sports. Athletes from NCAA, NAIA, NAJC, NFHS added together	17–24	SCD	1:300 000
Maron[7]	1998	USA	Retrospective cohort	Insurance claims	Minnesota State High School League	16–17	SCD	1:217 000
Corrado[9]	2003	Italy	Prospective cohort	Mandatory death reporting	Registered Italian athletes	12–35	SCD	1:47 000 athletes 1:143 000 young people
Eckart[10]	2004	USA	Retrospective cohort	Mandatory reporting of all deaths to Department of Defense	Numbers from Department of Defense	18–35	SCD	1:10 000
Drezner[11]	2005	USA	Retrospective survey	Survey answered by 244 Division I NCAA institutions	Number of athletes at surveyed schools	14–17	SCD	1:67 000
Atkins[12]	2009	USA/Canada	Prospective cohort	Emergency medical services reports	Population statistics	12–19	SCA/SCD	1:49 000

Chugh[13]	2009	USA	Prospective cohort	Emergency medical services reports	Population statistics	10–14	SCA/SCD	1:58 000
Drezner[14]	2009	USA	Cross-sectional survey	1710 high schools with AEDs surveyed for SCA/SCD	Number of student athletes reported by schools	14–17	SCA/SCD	1:46 000 SCD 1:23 000 SCA/SCD
Solberg[15]	2010	Norway	Retrospective cohort	Norwegian cause of death registry	Population statistics	15–34	SCD	1:111 000
Eckart[16]	2011	USA	Retrospective cohort	Mandatory reporting of all deaths to Department of Defense	Numbers from Department of Defense	18–34	SCD	<20 y 1:30 000 20–24 y 1:41 000 25–29 y 1:30 000 30–34 y 1:25 000
Harmon[3]	2011	USA	Retrospective cohort	NCAA/media/insurance claims database	Participation data from NCAA	18–26	SCD	1:43 000
Maron[17]	2013	USA	Retrospective cohort	US Registry of Sudden Death in Athletes	Minnesota State High School League	12–18	SCD	1:150 000
Roberts[18]	2013	USA	Retrospective cohort	Insurance claims	Minnesota State High School League	12–19	SCD	1:417 000
Maron[19]	2014	USA	Retrospective cohort	US Registry of Sudden Death in Athletes	Participation data from NCAA	17–26	SCD	1:83 000
Drezner[20]	2014	USA	Retrospective cohort	Media reports	National Federation of State High School Associations	14–18	SCA/SCD	1:154 000 SCD 1:71 000 SCA/SCD
Toresdahl[21]	2014	USA	Prospective observational	2149 schools reporting SCA/SCD on campus	Number of students at 2149 reporting schools	14–18	SCA/SCD	1:88 000
Harmon[8]	2015	USA	Retrospective cohort	Database of all NCAA deaths	Participation data from NCAA	17–24	SCD	1:54 000
Harmon[22]	2016	USA	Retrospective cohort	Media database of cases from 7 US states	National Federation of State High School Associations	14–18	SCA/SCD	1:67 000

Early estimates of SCD in the USA range from 1:160 000 to 1:300 000 deaths per year in young competitive athletes.[5–7] Passive collection methods, using retrospective review of media reports,

electronic databases and insurance claims, in these early landmark studies are limited by ascertainment and selection bias, which underestimate calculations of incidence and inhibit applicability to the modern era.[3, 8] Mandatory reporting systems of athlete deaths within good population demographics offer the most reliable method of case identification, although very few currently exist.

Corrado et al. prospectively studied a large well-defined population of non-athletes and athletes (aged 12–35 years) in the Veneto region of Italy over 25 years.[23] All cases of suspicious SCD were referred for a detailed post-mortem evaluation at a cardiac pathology centre. The unique pre-participation evaluation (PPE) program mandated by Italian law ensured athletes participating in organised sport were subject to annual medical follow-up. Corrado et al. estimated an incidence of 1:24 000 prior to the implementation of the PPE program.[23]

The US military is another well-defined target population that adopts a mandatory death reporting system with standardised autopsy protocols. Although military recruits do not meet the standard definition of competitive athletes, the regular, intense training involved in conjunction with a similar median age (19 years) makes this cohort a good comparator to the young athletic population. Over a 10-year period, a rate of SCD of 1:25 000 was demonstrated in recruits under the age of 35 years.[16]

Survival rates of SCA in athletes have significantly improved following widespread implementation of emergency service pathways and automated external defibrillators (AEDs).[14, 24] The increasing number of athletes surviving SCA may create the misconception of drastically falling rates of SCD. Primary preventive programs target both SCA and SCD; therefore it is prudent to incorporate survivors of SCA in estimates of incidence. A prospective population-based study conducted in 11 US and Canadian cities and utilising rigorous methodology, with all cases of SCA collected through the emergency medical services system, reported an incidence of SCA from cardiovascular disease of 1:27 000 in children and young adults (aged 14–24 years).[11]

A 10-year review was conducted on the aetiology and incidence of sudden death in National Collegiate Athletic Association (NCAA) athletes (aged 17–24 years) in the USA between 2003 to 2013.[8] Cases were identified primarily through the NCAA Resolutions database, a recommended system for institutions to report to the NCAA Director of Health and Safety on the death of any NCAA athlete. Additional information from autopsy reports was obtained when possible, before an expert panel adjudicated the cause of death. There were 4 242 519 athlete-years and 514 total deaths during this period. Seventy-nine (15%) of these were cardiovascular-related sudden deaths, resulting in an overall incidence of SCD of 1:53 703.[8] Most deaths from cardiovascular diseases occurred during exertion. Similar estimates of SCA/SCD incidence, ranging from 1:67 000 to 1:88 000, are reported in studies evaluating well-defined cohorts of US high school athletes.[21, 22]

Harmon et al. performed a comprehensive review of studies that have examined the incidence of SCD in athletes.[25] The objective of this review was to assess the methodological strengths and weaknesses used to arrive at estimates, compare studies with estimates of similar populations and

arrive at an approximation of incidence based on the best available evidence. The incidence of SCD across all 28 studies varied from 1:3000 to 1:917 000; however, studies with higher methodological quality yielded a higher estimate of incidence, ranging from 1:40 000 to 1:80 000.[25]

Sex, race and age as risk factors

Certain populations of athletes also seem to be at greater risk. Deaths are more common in males, with reports of male to female gender differences ranging from 5:1 to 9:1.[ref1" id="rr, ref2" id="rr, ref14" id="rr, ref26" id="rr, ref27" id="rr] Marijon et al. assessed characteristics and outcomes of SCA in middle-aged individuals (35–65 years) in a large, 12-year prospective study in a north-western US metropolitan region. They reported a significantly higher incidence of SCD in males, with a relative risk of almost 19.[28] Proposed explanations for these sex discrepancies include the higher male participation rates in more commonly played sports and sex-specific influences in phenotype expression. The incidence of SCD also seems to be disproportionately higher in black/African-American athletes. NCAA African-American athletes reveal a 3.2 times greater risk of SCD compared with white counterparts (1:21 000 versus 1:68 000).[8]

Some geographic areas have demonstrated a lower risk of SCD in young athletes, perhaps due to differences in the prevalence of certain inheritable cardiovascular disorders. In Norway, a retrospective study examined the rate of SCD in athletes aged 15–34 years, using a mandatory national forensic registry, and reported the incidence of SCD among physically active young men as 1:111 000.[15]

The prevalence of SCD increases with age. A 5-year prospective study of exercise-related SCD in the French general population aged 10–70 years[27] revealed that 94% of SCD occurred in recreational athletes, usually in the fifth decade.

Which sports carry the highest risk?

Although SCD can occur in any sport, deaths among young individuals occur most frequently in the most popular dynamic sports with a start–stop nature, notably in basketball in North America and soccer in Europe. In the NCAA, basketball is by far the highest risk sport, with an overall annual death rate of 1:15 000 (male and female), 1:9000 (male) and 1:4000 (male African-American).[8] Other groups at high risk of SCD include men's soccer (1:24 000) and men's American football (1:36 000).[8]

Additional questions exist regarding the relative risk of SCA/SCD in competitive athletes versus the general non-athletic population, and whether this risk justifies a separate, more advanced PPE program in athletes. Corrado et al. identified a 2.5 times relative risk for SCD due to sports activity in athletes versus an age-matched non-athletic population.[9] A prospective observational study of US high schools with over 4 million student-years demonstrated a relative risk of 3.6 for SCA on-campus in athletes versus non-athletes.[21] It is generally accepted that physical exertion through athletic participation triggers potentially fatal ventricular arrhythmias in predisposed individuals with quiescent cardiovascular disease. Data outlined above supports a targeted and more intensive screening program for the athletic community.

On the other hand, not all children are competitive athletes but most children are active and perform some form of exercise. According to statistics from the Centers for Disease Control (CDC), cardiovascular disease is second only to malignancy as the leading medical cause of death in individuals younger than 24 years old and accounts for over 2100 fatalities annually in the USA.[29] Thus, if specific preventive measures are valuable for children and young adults who participate in organised sports, is it time for these tests to be considered for all children?[30]

AETIOLOGY OF SUDDEN CARDIAC DEATH IN ATHLETES

Understanding both the aetiology and precipitating factors of SCD is paramount when devising preventive strategies such as PPE methods and the widespread availability of automated external defibrillators (AED). Most conditions predisposing to sudden death in athletes result in the same final common denominator (cardiac arrest) on presentation on the athletic field. Primary ventricular tachyarrhythmias are the predominant mechanisms of SCD in these inherited conditions, except in Marfan syndrome, where death is often from aortic rupture or dissection.

The age of an athlete is strongly associated with the aetiology of SCD. The cause of exercise-related SCD in masters athletes over the age of 50 years is overwhelmingly coronary artery disease (CAD), which accounts for over 80% of fatalities.[1" i, 1" i, 1" i] Sudden haemodynamic and metabolic changes leading to stress-related plaque rupture, in an exercise-mediated pro-thrombotic environment, may contribute to adverse outcomes. The athletes at greatest risk of this exercise paradox are those with little or no background in systemic training.[33–35] Approximately Page 119 50% of middle-aged athletes who die suddenly from atherosclerotic CAD have prodromal symptoms suggestive of myocardial ischaemia, and many have significant risk factors for CAD. Pathological findings in joggers and marathon runners dying suddenly reveal severe and extensive coronary atherosclerosis involving two or more large coronary arteries in over 70% of cases. Myocardial scarring is evident in approximately 40% and fresh infarcts are seen in 15% of cases.[36]

In contrast, SCD in younger athletes (<35 years old) is most commonly due to a variety of hereditary or congenital structural and electrical cardiac abnormalities, although a plethora of acquired conditions are also implicated (Table 9.2).[1–5, 7, 10, 23]

Table 9.2 Causes of sudden cardiac death in young athletes

Congenital/genetic pathology	
Disease of the myocardium	Hypertrophic cardiomyopathy Arrhythmogenic ventricular cardiomyopathy Dilated cardiomyopathy Left ventricular non-compaction cardiomyopathy
Coronary artery disease/anomalies	Congenital coronary artery anomalies Premature atheromatous coronary artery disease
Cardiac conduction tissue abnormalities	Wolff–Parkinson–White syndrome Right ventricular outflow tachycardia
Valvular heart disease and disorders of the aorta	Mitral valve prolapse Congenital aortic stenosis Marfan syndrome

Ion channelopathies	Congenital long QT syndrome Catecholaminergic polymorphic ventricular tachycardia
Acquired causes	
Infections (myocarditis)	
Drugs (cocaine, amphetamine)	
Electrolyte disturbances (hypokalaemia or hyperkalaemia)	
Hypothermia	
Hyperthermia	
Trauma (commotio cordis)	

Historical data reveal that the cardiomyopathies are the most common cause of death in young athletes, with hypertrophic cardiomyopathy (HCM) being the commonest cause in the USA and arrhythmogenic cardiomyopathy (AC) being the commonest cause in Italy. Regional discrepancies between studies reporting HCM[1, 17, 19, 37] or AC[9, 38] as the commonest cause of SCD may be explained by genetic variation, ascertainment bias of identified cases and different criteria for pathological diagnosis (Fig. 9.1). The difference between the US[1, 17, 19, 37] and Italian series[9, 38] may be partly explained by the fact that individuals with HCM are identified early in the mandatory Italian PPE program and are subsequently disqualified from sport.[39] Sudden cardiac death rates from HCM in Italian athletes had been significantly lower than in American athletes even prior to the development of the Italian screening program, suggesting that the lower HCM-related SCD rate is partly explained by the lower genetic cluster of HCM in the relatively homogeneous population of northern Italy.

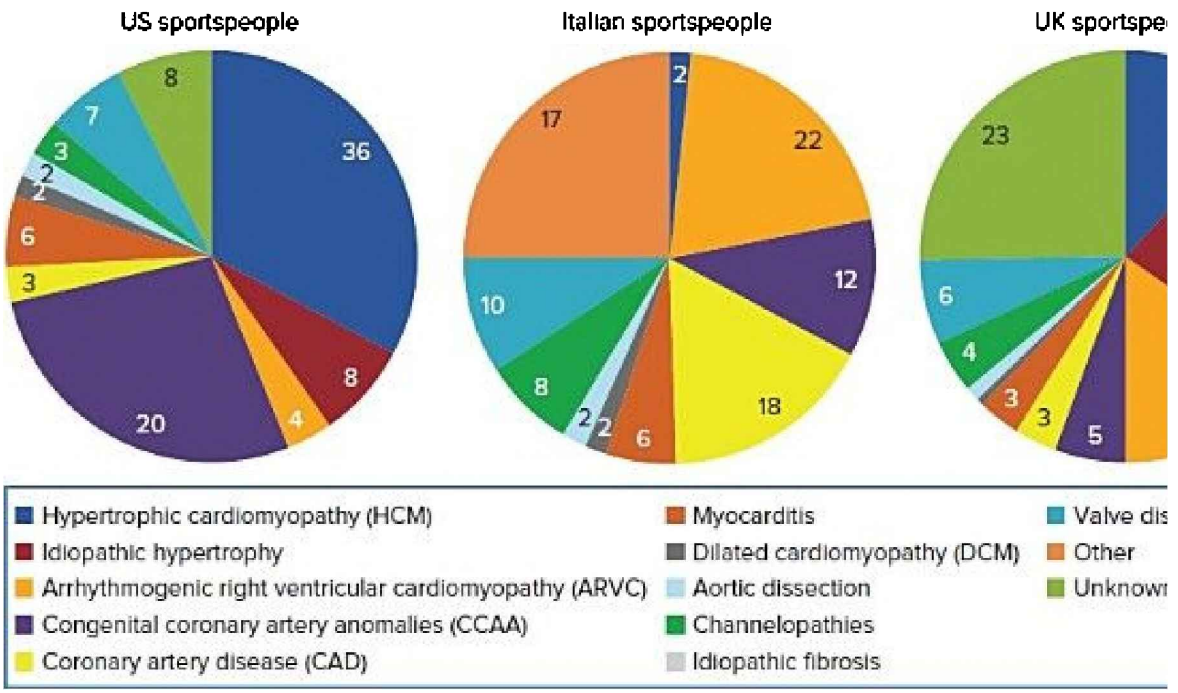


Figure 9.1 Geographical differences in the aetiology of sudden cardiac death in athletes in the USA,[1] Italy[9] and the UK[4] (<35 years). Numbers represent percentages.

Variation in expertise among pathologists also contributes to regional differences in the aetiology of SCD. A study of 720 consecutive cases of young individuals with SCD compared pathology reports between an expert cardiac pathologist and general pathologists and revealed a 41% disparity between the two groups. General pathologists were more likely to diagnose a structural abnormality in hearts considered normal by the expert pathologist.[4] Expert cardiac pathology and scrutiny of the precise cause of death in the young indicates that up to 40% of young athletes who suffered SCD had a structurally normal heart. When the toxicology screen is also normal, the term sudden arrhythmic death syndrome (SADS) is used to denote such deaths.[8, 40–42] Finocchiaro et al. investigated the causes of SCD in a large cohort of young sportspeople, of which 69% were competitive athletes.[42] A total of 357 consecutive cases of athletes who died suddenly underwent detailed post-mortem evaluation, including histological analysis by an expert cardiac pathologist. A structurally normal heart indicative of SADS was the most prevalent cause of death in 42% of cases. A structurally normal heart was the most common finding at autopsy in US collegiate athletes succumbing to SCD.[40]A meta-analysis of 34 studies that examined SCD aetiology in 4605 young individuals under the age of 35 years reported a structurally normal heart as the most common post-mortem finding (26.7% of cases).[43] This finding has now been demonstrated in children,[44] the general population,[45–47] non-athletes[48] and military recruits.[10, 16]

Sudden arrhythmic death syndrome is usually attributable to ion channelopathies, including congenital long QT syndrome (LQTS), Brugada syndrome and catecholaminergic polymorphic ventricular tachycardia (CPVT), as well as congenital accessory electrical pathways (Table 9.3). An accurate diagnosis of SADS is of vital importance when considering a diagnosis of an inherited ion channelopathy or cardiomyopathy as these exist in up to 50% of families later evaluated.[49]

Table 9.3 Causes of sudden cardiac deaths in structurally normal hearts

• Congenital long QT syndrome
• Brugada syndrome
• Catecholaminergic polymorphic ventricular tachycardia
• Short QT syndrome
• Wolff–Parkinson–White syndrome
• Right ventricular outflow tachycardia
• Coronary vasospasm
• Commotio cordis
• Electrolyte disturbances
• Hypothermia or hyperthermia
• Drugs (amphetamine or cocaine)

SCD DUE TO CONGENITAL OR GENETIC STRUCTURAL HEART DISEASE

The cardiomyopathies

Hypertrophic cardiomyopathy

Hypertrophic cardiomyopathy is a primary myocardial disorder, predominantly caused by mutations within genes encoding sarcomeric contractile proteins. The disorder is inherited as an autosomal dominant trait and characterised by left ventricular hypertrophy (LVH) (Fig. 9.2) in the absence of a cardiac or systemic cause and myocardial disarray on histology. Approximately 25% of affected individuals exhibit dynamic left ventricular outflow obstruction due to systolic anterior motion of the mitral valve leaflet against the interventricular septum, although this figure may rise to almost 70% during exercise.

Page 121

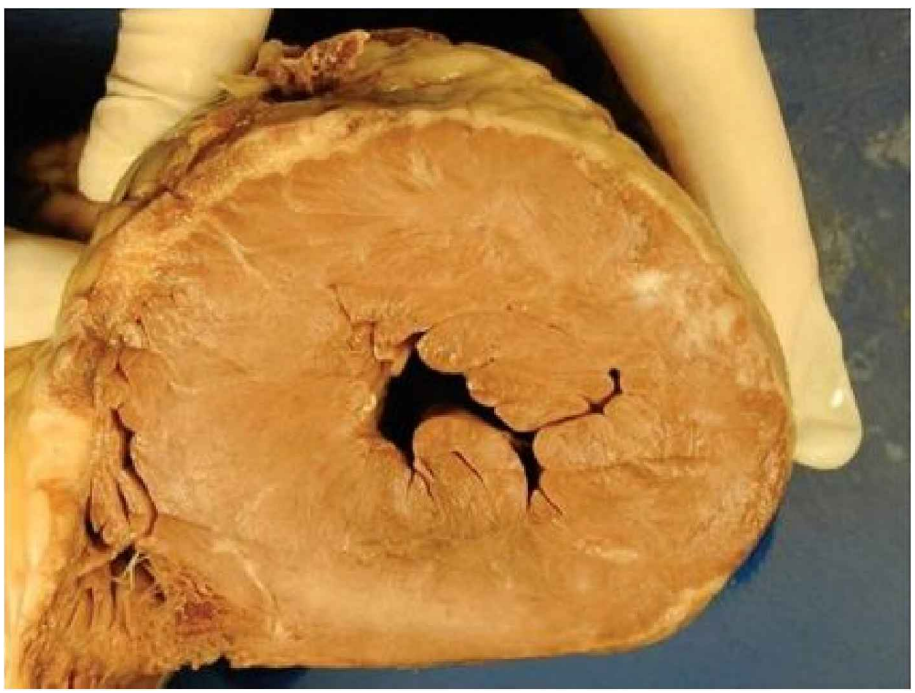


Figure 9.2 Macroscopic specimen of hypertrophic cardiomyopathy

The prevalence of HCM in the general population is 0.2%;[6] however, data in athletes reveal a significantly lower prevalence of 0.06–0.07%.[39, 40] Increased left ventricular mass, small left ventricular cavity size, impaired myocardial filling in diastole, dynamic left ventricular outflow obstruction in systole, myocardial ischaemia and cardiac arrhythmias are likely to preclude augmentation of stroke volume for prolonged periods and prevent most affected individuals from competing at the elite level, particularly in endurance sports such as long distance running, cycling and rowing. The same mechanisms may be associated with angina, dyspnoea that is disproportional

to the amount of exercise being performed, palpitations, exertional dizziness or syncope. (Management of cardiac symptoms other than sudden death is discussed in Chapter 10). HCM is renowned for its clinical and morphologic heterogeneity, and many affected individuals can compete at a national level without experiencing any symptoms.[50] In such athletes, sudden death is commonly the first presentation and usually occurs during or immediately after exercise.[51] Deaths are most commonly observed in male athletes in start–stop sports such as football and basketball, which rely heavily on skill and are predominantly confined to male athletes.[52]

Individuals with HCM who are capable of prolonged bouts of intensive exercise usually exhibit structurally mild disease. Sheikh et al.[53] reported structural and functional cardiac parameters in 106 young athletes with HCM compared with 101 sedentary HCM patients. Athletes with HCM exhibited mild hypertrophy of 15–16 mm or the apical variant of the disease. Athletes with HCM had a larger left ventricular cavity size compared with sedentary HCM patients. All athletes had normal indices of diastolic function and none revealed left ventricular outflow obstruction at rest.[53]

PRACTICE PEARL

The diagnosis of HCM is established primarily from transthoracic echocardiography or cardiac magnetic resonance imaging, but more than 90% of individuals with the condition also demonstrate an abnormal resting 12-lead electrocardiogram (ECG) (Fig. 9.8).[53, 54]

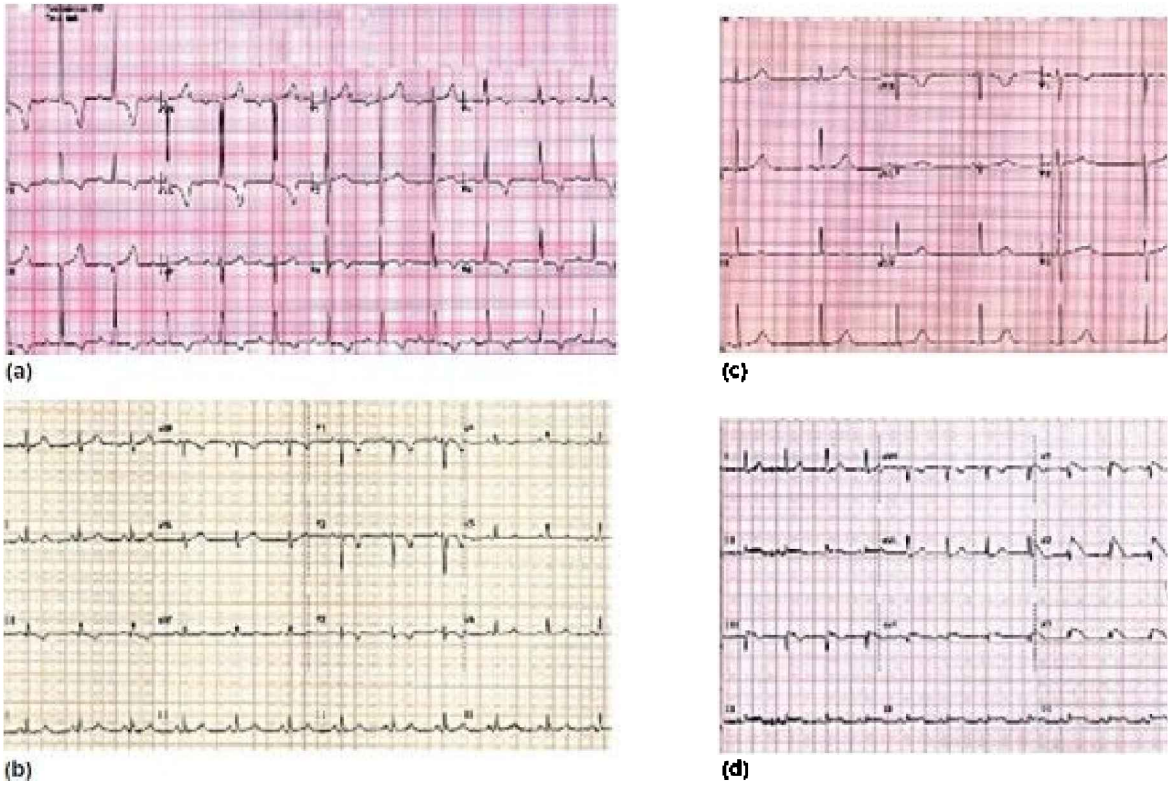


Figure 9.8 ECG changes in common structural and electrical cardiac abnormalities associated with sudden cardiac death (a) HCM—left ventricular hypertrophy associated with left axis deviation, ST-segment depression in leads I and aVL and deep T-wave inversion in leads I, aVL, V5 and V6 (b) Arrhythmogenic right ventricular cardiomyopathy (ARVC)—inverted T waves in V1–V4 (c) LQTS—a prolonged QT interval of >500 ms (d) Brugada syndrome—incomplete right bundle branch block with high take-off and coved pattern of downsloping ST-segment elevation in several leads but most marked in leads V1–V3

Imaging with echocardiography or cardiac magnetic resonance (CMR) is required for the diagnosis of HCM. Unexplained left ventricular hypertrophy (LVH) with a wall thickness of ≥ 13 mm in females or ≥ 15 mm in males, or >3 standard deviations from the individual's body surface area average is diagnostic.[55] Athletes with a maximum wall thickness of 12–15 mm represent a diagnostic dilemma to physicians. The clinical approach to those cases who fall within this grey zone is discussed later in this chapter.

Once a diagnosis is established, the risk of fatal arrhythmias during normal life activity can be predicted through a risk-stratification process that includes inquiring about symptoms and family history, exercise stress test and 24-hour Holter monitor.[56] Markers of high risk for SCD are shown in the box below.

The European Society of Cardiology HCM SCD risk calculator (http://www.doc2do.com/hcm/we

bHCM.html) aims to identify individuals at highest risk of SCD, who therefore would most benefit from having an implantable cardioverter defibrillator (ICD). Unfortunately, it is difficult to extrapolate the information derived from such a risk stratification algorithm derived in controlled laboratory conditions to the athletic arena, since intensive exercise for prolonged periods generates its own specific metabolic stresses that may trigger arrhythmias, even in individuals usually considered to be at low risk. The European and US guidelines recommend that all athletes with HCM should cease competitive sport, except those sports classified as low intensity class 1A.[57, 58] The guidelines concede that many affected athletes may not fall victim to SCD in the event of continued participation in high-dynamic and high-intensity sporting disciplines; however, the aim is to identify and ensure the safety of all individuals at risk of preventable premature death.

The notion that athletes with HCM protected with an ICD are safe to resume competitive sport[59] should be approached with caution, because exercise-induced shifts in metabolic and electrolyte states may reduce the efficacy of shock therapy.[60, 61] Exercise recommendations should therefore be based on the underlying disease process irrespective of ICD implantation, and an ICD should not be implanted solely to enable an affected athlete to continue to compete.

Markers of high risk for SCD

- Unheralded syncope
- History of SCA
- Family history of SCD (<40 years of age)
- Severe LVH (>30 mm)
- Non-sustained ventricular tachycardia
- Attenuated or decreased blood pressure response to exercise
- Late gadolinium enhancement on CMR

Idiopathic left ventricular hypertrophy

Idiopathic LVH is a term used to describe increased left ventricular mass of greater than 500 mg in the absence of myocyte disarray (the histological hallmark of HCM).[1] Most deaths from idiopathic LVH are described in athletes of African/Afro-Caribbean origin.[1, 2, 4]

The significance of LVH in the absence of myocardial disarray at post-mortem examination in cases of SCD is unknown. It remains unclear whether idiopathic LVH is a variant of HCM or whether it represents a situation whereby confounding genetic variables in black athletes result in the well-recognised exaggerated hypertrophic response,[62] which itself may become pathologic and predispose to arrhythmias. Conversely, the increased left ventricular mass identified in the athlete may represent a benign innocent bystander where the true cause of death from a potential ion channel disorder or accessory pathway has not been identified.[63]

Papadakis et al.[63] explored the hypothesis that such ambiguous findings at autopsy may

represent an innocent bystander in an athlete where the actual cause was an ion channel disorder. During comprehensive screening of first-degree relatives of decedents where idiopathic LVH was observed at autopsy, they diagnosed an ion channel disorder, primarily Brugada syndrome, in a significant proportion.[63] Although LVH is a well-recognised feature of cardiovascular adaptation to exercise, 60% of individuals exhibiting isolated LVH did not exercise regularly. A theory that LVH alters ion channel expression and function predisposing to malignant arrhythmia has been proposed.[63]

Arrhythmogenic cardiomyopathy

Arrhythmogenic cardiomyopathy (AC) is the commonest cause of SCD in young athletes in Italy.[38, 39] It is a familial disorder that is inherited as an autosomal dominant trait and mainly caused by mutations in genes encoding several cardiac desmosomal proteins. It is characterised histologically by progressive loss of myocardial cells with subsequent fibro-fatty replacement. The disorder was originally termed arrhythmogenic right ventricular cardiomyopathy—a misnomer, because it was predominantly thought to affect the right ventricle.[64] However, autopsy series show that over 70% of affected decedents also have left ventricular involvement. Left ventricular involvement is also recognised in isolation and invariably coexists with right ventricular involvement in advanced cases.[65] The condition usually manifests with arrhythmias of right ventricular origin and morphological changes affecting the right ventricle.

Most deaths in athletes occur during sport, particularly soccer, and predominantly affect males. In a large pathology series of 357 young athletes, AC accounted for 13% of cases and strongly predicted exercise-related SCD, which reinforces the importance of early detection and abstinence from sport.[42]

It is postulated that under conditions of mechanical stress, the inherent weakness of cell–cell junctions due to abnormal desmosomal proteins results in myocyte detachment and predisposes the athlete to fatal ventricular arrhythmias and SCD. The myocardium is subsequently repaired by fibro-fatty replacement, which forms further substrate for ventricular arrhythmias and subsequent heart failure.[66, 67] Most athletes are asymptomatic and SCD is usually the first presentation, although a small number present with palpitations, dizziness and exertional syncope.[38]

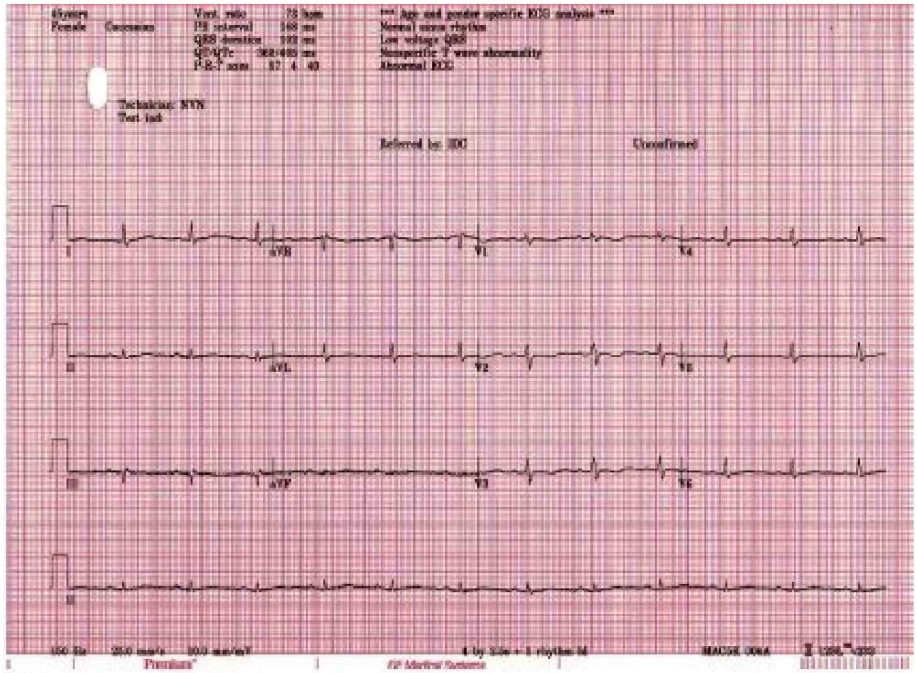
The prevalence of AC in the general population is between 1 in 1000 and 1 in 5000;[64] however, the prevalence of AC in athletes is unknown. There is some evidence that intensive ultra-endurance exercise may promote changes within the right ventricle that are identical to the classic description of the disease with right ventricular predominance, indicating that AC might be acquired through intensive exercise in a small proportion of athletes.[68–72]

The diagnosis of AC usually requires a combination of clinical suspicion from personal symptoms or family history together with a plethora of electrocardiographic and imaging studies. These include 12-lead ECG, signal average ECG where indicated, 24-hour Holter monitoring, exercise ECG, echocardiography with contrast to improve endocardial definition and CMR.[73] The diagnosis of AC can be difficult to make, especially in the concealed form of the disease, when the ECG may exhibit

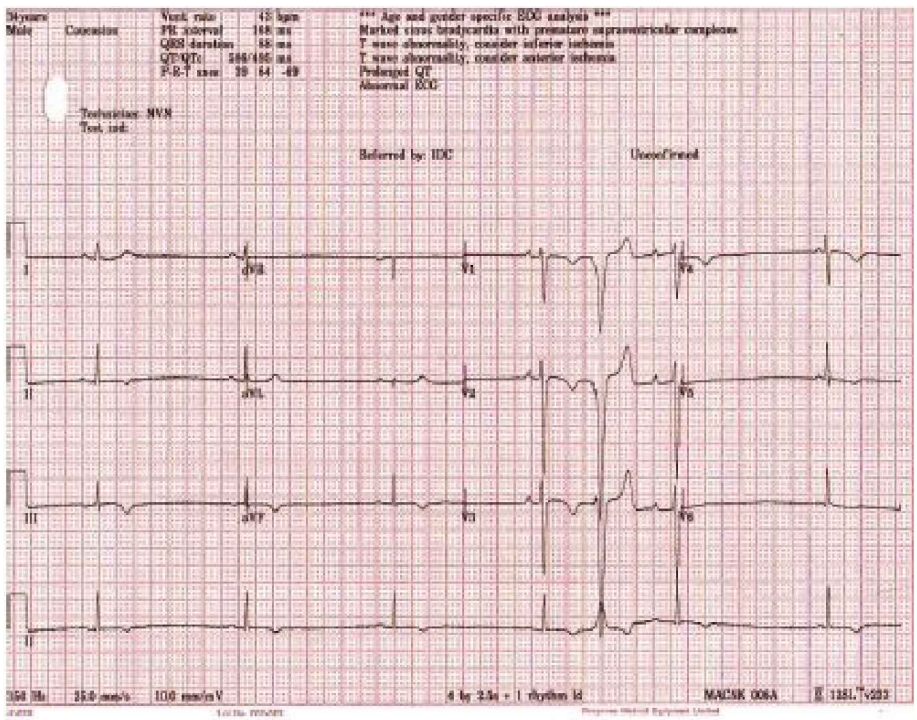
very subtle changes that overlap with electrical manifestations of athletic training and cardiac imaging tests appear normal.[64]

Although the right ventricle is amenable to endocardial biopsy, histological diagnosis of AC is rarely possible and is potentially dangerous for several reasons—the disease is patchy, characteristically affecting the thinnest portions of the right ventricle (notably the right ventricular inflow and outflow tract) and transmural tissue sampling is required for definitive diagnosis.

Phenotypic manifestations of AC on the 12-lead ECG include T-wave inversions and prolonged QRS duration in right ventricular leads (V1–V3), terminal S-wave duration >50 ms in V2, epsilon waves (delayed repolarisation) and ventricular extrasystoles of right ventricular origin (manifest with left bundle branch block morphology) (Fig. 9.3). Left ventricular involvement is characterised by T-wave inversion in the inferior and lateral leads and small (<0.6 mV) limb lead complexes. Holter monitoring and exercise testing are useful for identifying sustained or non-sustained ventricular arrhythmias with left bundle branch block morphology (Fig. 9.4).



(a)



(b)

Figure 9.3 ECG in two individuals with arrhythmogenic right ventricular cardiomyopathy demonstrating (a)

T-wave inversion in leads V1–V3 and a widespread T-wave inversion (more pronounced in V1–V4), and (b) a ventricular extrasystole of right ventricular origin (conducts with left bundle branch block morphology)

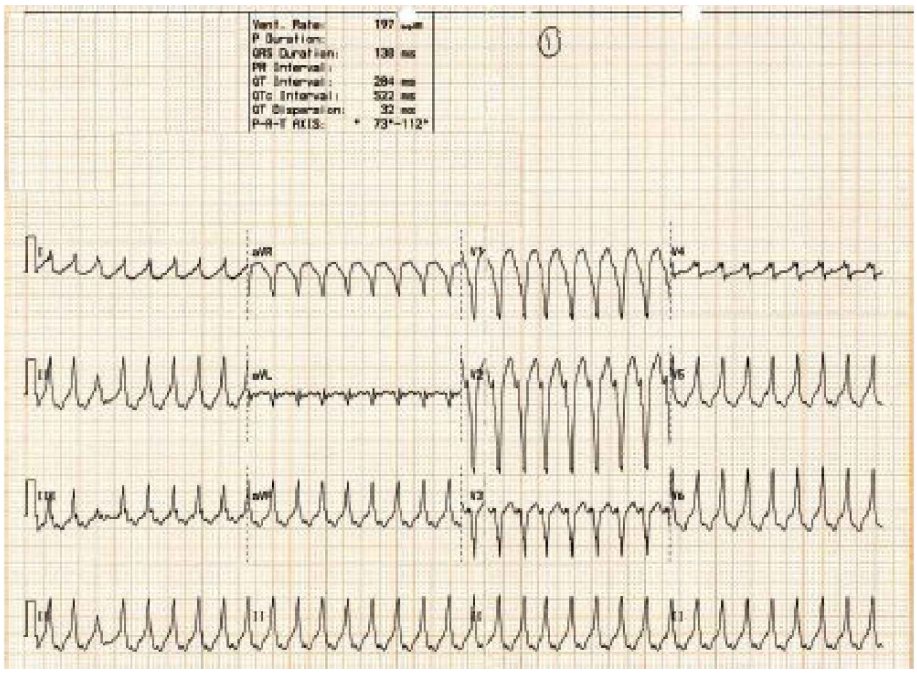


Figure 9.4 Ventricular tachycardia in an individual with arrhythmogenic right ventricular cardiomyopathy

Echocardiography reveals thinning of the akinetic and dyskinetic segments affecting the right ventricle or overt right ventricular dilatation and hypokinesia, but may be normal in the early phases of the disease. The sensitivity of echocardiographic diagnosis is improved with contrast agents. CMR may be more sensitive than echocardiography for the diagnosis of AC, particularly with concomitant left ventricular involvement, provided it is performed by an experienced operator.[64]

Athletes with AC should cease competitive sport, except those sports classified as 1A.[57, 58] Recent studies have demonstrated that endurance exercise accelerates the phenotype[68, 74] and increases the risk of arrhythmias[72] in genotype positive family members with AC, whereas moderate recreational exercise may be safe. For this reason, genotype positive/phenotype negative individuals follow the same recommendations for sports participation as those athletes with proven AC.

PRACTICE PEARL

The diagnosis of AC in an athlete is an indication for disqualification from all competitive sports

other than those of low intensity (class 1A).[57, 58]

Athletes at high risk of SCD even after abstinence from sport include those with a previous history of cardiac arrest, unheralded syncope, ventricular tachycardia with haemodynamic compromise and progressive deterioration of right ventricular function and left ventricular involvement. This small group should be offered an ICD to minimise the risk of SCD.[75]

Dilated cardiomyopathy

Dilated cardiomyopathy (DCM) is a rare cause of SCD in young athletes, accounting for approximately 4% of all SCDs.[1, 2, 4, 5, 23, 39] This is probably because most affected individuals have relatively low exercise capacity due to markedly impaired systolic function. The disorder can be either inherited or acquired secondary to infection, inflammation or toxic substances. A genetic aetiology should be considered in young individuals with a family history of DCM or SCD below 40 years of age.

The prevalence of DCM is reported as 1 in 2500, and it is characterised morphologically by left ventricular dilatation and impaired systolic function. A diagnosis of DCM is an indication for abstinence from competitive sports except those classified as 1A.[57, 58] However, gentle exercise for up to 30 minutes per day (moderately brisk walk or gentle cycling) may offer prognostic benefit. Pharmacological therapies, in the form of ACE inhibitors and beta blockers and also possibly aldosterone antagonists, are advised in all athletes with DCM.

Disorders of the coronary arteries and aorta

Congenital coronary artery anomalies

Congenital coronary artery anomalies (CCAA) are classified as anomalies of origin, course, destination and size or number of vessels. A main coronary artery arising from the anomalous sinus of the aortic root (Fig. 9.5) is identified in 0.5–1% of individuals.[76] A right coronary artery arising from the left coronary sinus is acknowledged as the most common variant; however, most deaths are linked with an anomalous left coronary artery origin.[76] The majority of patients remain asymptomatic and undiagnosed through life, while a minority present with SCD as first manifestation. Almost all cases of SCD from a CCAA occur in athletes aged <35 years and are linked with exercise. Sudden cardiac death has been predominantly attributed to mechanical compression of the anomalous coronary artery during exercise when it takes an interarterial course between the aorta and pulmonary artery or alternatively if the anomalous artery has an intramural course within the wall of the aorta.[77] Myocardial ischaemia precipitated by exercise may trigger electrical instability leading to ventricular fibrillation and SCD. Reports of CCAA causing SCD in athletes vary significantly between 1–33% of cases.[1–5, 8, 23, 42, 51]

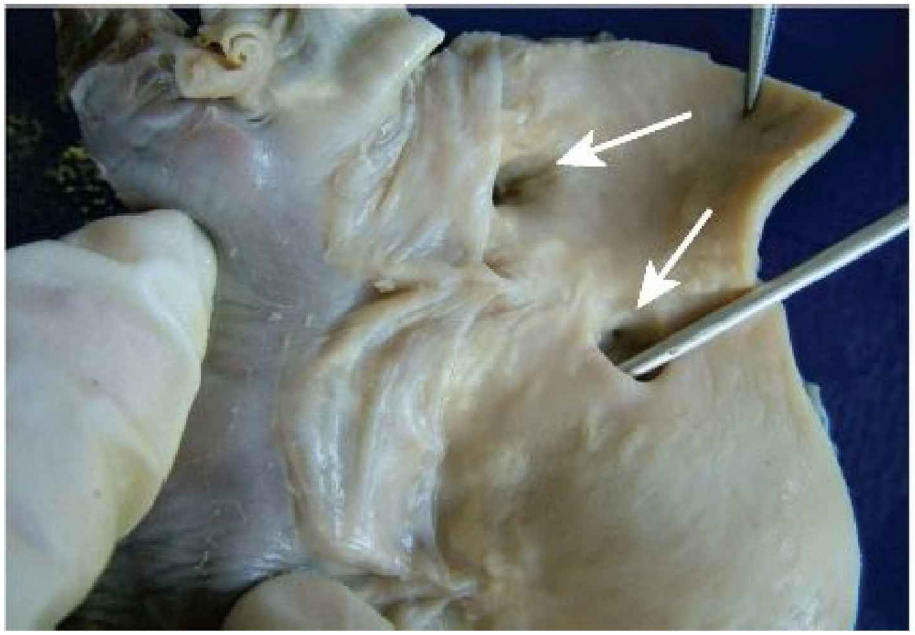


Figure 9.5 Origins of both main coronary arteries arising from the same sinus of Valsalva
WITH PERMISSION OF DR SANJAY SHARMA

The ECG is normal and most cases do not exhibit inducible myocardial ischaemia during exercise stress testing, even at high workloads. Echocardiography when performed by experienced ultrasonographers can often identify normal coronary origins;[78] however, the origin of the right coronary artery may not be accurately determined in up to 20% of athletes.

Computed tomography (CT) coronary angiography or magnetic resonance angiography (Fig. 10.2) are the imaging modalities of choice when clinical suspicion is raised.[79, 80] Although the former is associated with exposure to radiation, it is superior for providing better temporal relationships between the coronary artery and the main vessels compared with CMR.[81]

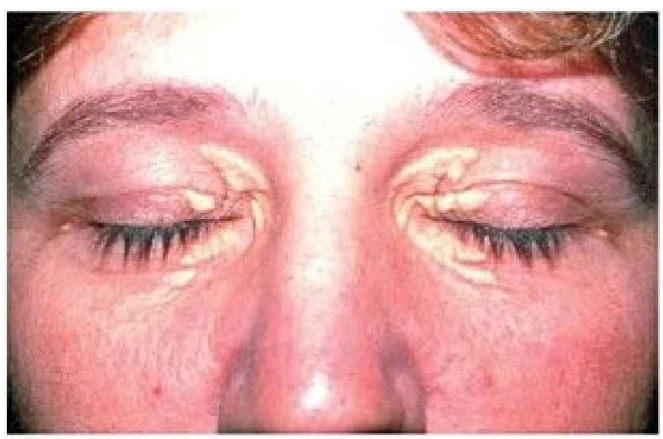
Recommendations for sport eligibility are determined by the individual's anatomy, symptoms, sequelae of disease (myocardial infarction) and outcome of non-invasive testing (exercise treadmill test). Participation three months after surgical correction is permitted in cases without prior myocardial infarction, left ventricular dysfunction or ventricular tachycardia during maximal exertion.[57, 58]

Premature coronary artery disease

Premature coronary artery disease accounts for 3–4% of all SCDs in young athletes, in large series from the USA and Italy;[1–5, 7, 9, 23] however, it has been reported more commonly in Japan, Australia and the UK.[4] The disorder is a common manifestation of familial hypercholesterolaemia, which has a prevalence of 1 in 250. Sudden death is almost always the first presentation in young athletes.

Prodromal symptoms of myocardial ischaemia may be absent; however, peripheral stigmata of hypercholesterolaemia, including xanthelasma, corneal arcus, palmar and eruptive xanthomata, are common and their presence should raise the suspicion of the disorder (Fig. 9.6).

(a)



(b)

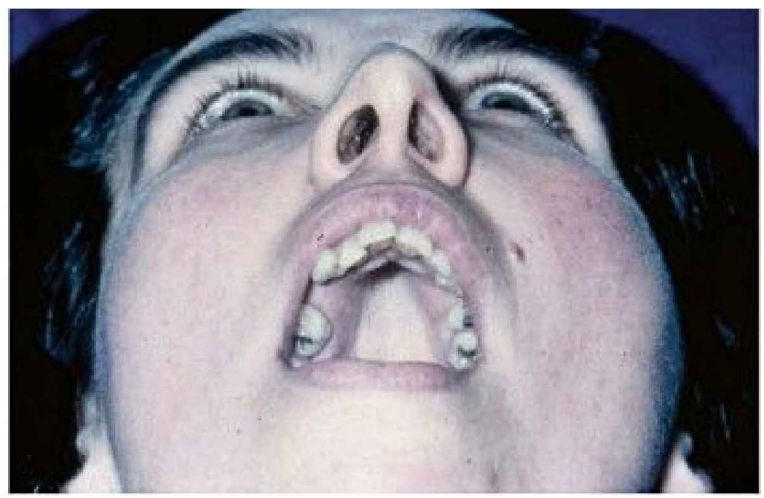
(c)

Figure 9.6 Peripheral stigmata of premature coronary artery disease (a)Eruptive xanthomata (b)Xanthelasma (c)Premature corneal arcus in a patient with familial hypercholesterolaemia

Marfan syndrome

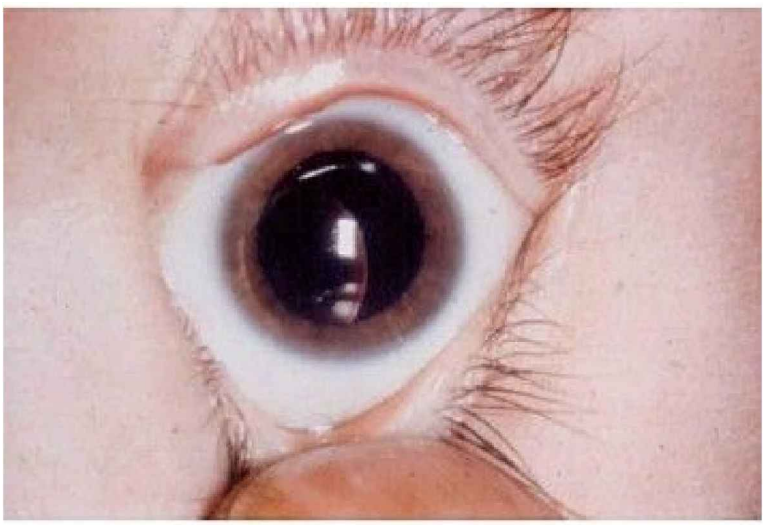
Marfan syndrome is a collagen disorder caused by mutations in the gene encoding fibrillin. It is inherited as an autosomal dominant trait and has a prevalence of 1 in 5000. The condition is characterised by skeletal, cardiac and ocular abnormalities (Fig. 9.7). Cystic medial necrosis in the tunica media of the aorta results in aortic dilatation and rupture or aortic dissection. The disorder accounts for approximately 3% of all exercise-related SCDs in young athletes.

Page 125



(a)

(b)



(c)

Figure 9.7 Features of Marfan syndrome (a)High-arched palate (b)Arachnodactyly (c)Lens dislocation

Affected patients are excessively tall and, by virtue of this trait, usually excel in basketball or volleyball. Exercise-related increases in aortic pressure may expedite aortic root dilatation, dissection and rupture, causing instantaneous death during sport.[82]

Page 126

PRACTICE PEARL

For athletes with Marfan syndrome, participation in sporting disciplines where isometric stress is a significant component is prohibited (e.g. powerlifting, wrestling, judo, sprinting, rowing and canoeing).[83]

Beta blockers were initially the therapy of choice for retarding progressive aortic dilatation although more recent studies have demonstrated at least non-inferiority with angiotensin receptor

blockers such as losartan.[84–86] Annual aortic surveillance is recommended and prophylactic aortic root replacement should be considered when the aortic root diameter exceeds 50 mm.

Marfan syndrome is discussed further in Chapter 10.

Valvular heart disease

Mitral valve prolapse

Mitral valve prolapse (MVP) is probably the commonest congenital valvular disorder; it affects 3–5% of the general population. Most individuals are asymptomatic, but in rare instances the condition is associated with ventricular tachycardia.[87] Autopsy studies[88, 89] and CMR assessment in survivors of aborted SCD with MVP have shown scarring in the posterior papillary muscle and the infero-basal left ventricular wall, suggesting that stretching forces from the flail leaflets provide a plausible explanation for the arrhythmogenic substrate.[88] Because of the relatively high frequency of MVP in the general population, it is not always possible to be certain whether the identification of MVP in a victim of SCD is causal or coincidental.

PRACTICE PEARL

An athlete with MVP is at low risk of SCD unless there is a history of syncope or documented ventricular arrhythmias, family history of premature SCD, disabling and protracted chest pain during sport or associated moderate to severe mitral regurgitation. The presence of T-wave inversion in the inferior leads, extrasystoles conducting with right bundle branch block morphology and infero-basal scar found on CMR appear to be additional risk factors for potentially fatal arrhythmias.

Aortic stenosis

Aortic stenosis due to a congenital bicuspid aortic valve (BAV) is a rare but recognised cause of SCD in young athletes, which can be identified through basic screening efforts involving cardiovascular physical examination. BAV may be associated with an aortopathy, which may result in aneurysm or rupture of the ascending thoracic aorta. Periodical assessment is recommended given the risk of disease progression and aortic root dilatation. Guidance on sports eligibility is determined by symptoms (aided by exercise testing) and echocardiographic parameters including pressure gradients, left ventricular size and function.[57, 58]

SCD DUE TO CONGENITAL OR GENETIC ABNORMALITIES PREDISPOSING TO PRIMARY ELECTRICAL DISORDERS OF THE HEART

Up to 40% of athletes who die suddenly have no identifiable cause at post-mortem examination. This phenomenon—autopsy negative sudden unexplained death—is referred to as sudden arrhythmic death syndrome (SADS).[90]

Experience from studies in first-degree relatives of victims of SADS indicates that at least 50% of these deaths are attributable to inherited ion channelopathies.[63] Fatal tachyarrhythmias due to undiagnosed accessory pathways comprise other potential causes (Table 9.3).

Congenital long QT syndromes

The congenital long QT syndromes (LQTS) are inherited as autosomal dominant or recessive traits and characterised by abnormalities in cardiac sodium or potassium ion channels. Abnormal shifts in electrical currents result in membrane instability during cardiac repolarisation and predispose to polymorphic ventricular tachycardia and ventricular fibrillation.

There are currently 15 different identified loci accounting for the disorder; these are termed LQTS-1 to LQTS-15, respectively. LQTS-1 (potassium ion channel), LQTS-2 (potassium ion channel) and LQTS-3 (sodium ion channel) account for approximately 95% of all known cases of the disorder.[91]

Adrenergic surges provoke ventricular arrhythmias, particularly in individuals with the LQTS-1 genotype.[92] Co-activation of the sympathetic and parasympathetic nervous systems during cold water immersion also may produce cardiac arrhythmias.[93] This stimulus may occur at a time when the QT interval does not match the underlying heart rate, further increasing the risk of cardiac arrhythmias.[93] Affected athletes may present with palpitations, dizziness and unheralded syncope secondary to polymorphic ventricular tachycardia. The latter may be associated with brief myoclonic movements, resulting in a misdiagnosis of epilepsy in recurrent cases.

Long QT syndrome is usually diagnosed on a resting ECG, which reveals a long QT interval (Fig. 9.8 panel C) in approximately 60% of cases (QTc >440 ms in males and QTc >460 ms in females). Exercise testing is recommended in all patients with suspected LQTS and often exhibits paradoxical prolongation of the QT interval during the recovery phase in LQTS-1 and occasionally LQTS-2.[94] Holter monitoring is also recommended to evaluate the possibility of associated episodes of polymorphic ventricular tachycardia.[92]

The prevalence of congenital LQTS in the general population is approximately 1 in 2500 (0.04%).[91] However, based on the findings from screening programs in athletes, a long QT interval is identified in 0.42% of elite athletes.[95] This discrepancy suggests that the vast number of athletes with a slightly prolonged QT interval probably do not harbour gene mutations for LQTS. Indeed, athletes demonstrate longer QT intervals than sedentary individuals, therefore the 99th percentile value from the general population is used to define a prolonged QT interval in athletes (>470 ms in males and >480 ms in females).[96] Even these values cannot be considered diagnostic of long QT syndrome for athletes in the absence of symptoms or a relevant family history. In our experience, a QTc ≥ 500 ms suggests long QT syndrome in athletes and is usually accompanied by other features of the condition such as paradoxical prolongation of the QT interval with exercise.[95] Calculation the QTc accurately in this group is difficult because of profound bradycardia, sinus arrhythmia, slightly wide QRS complexes and prominent U waves associated with athletic training. Automated

values of QTc must be checked manually using the tangent method.

Genetic testing is recommended in all cases where the diagnosis remains unclear; however, the diagnostic yield from genetic analysis is only 75%. In the context of uncertain cases with less obvious QT prolongation, a Schwartz score of >3 (combining age, symptoms, family history, T-wave morphology and history of torsades de pointes) is considered diagnostic.[9] [7] Athletes with LQTS should receive a non-selective beta blocker, such as nadolol or propranolol, although this may result in disqualification from certain sports (shooting, gymnastics, archery, golf). Special consideration should be given to athletes undertaking swimming events given the close association of SCD and LQTS-1. Those who wish to continue intense physical exercise should be counselled on precautionary measures such as: avoidance of hyperthermia, avoidance of QT-prolonging drugs (www.crediblemeds.org), hydration/electrolyte replenishment and an emergency service plan incorporating an AED.[98] Referral for ICD and restriction to class 1A sports should be considered for those who remain symptomatic despite beta blocker therapy, survive cardiac arrest or demonstrate ventricular tachycardia and ventricular fibrillation.[99] The US consensus states that asymptomatic athletes may return to competitive sport after 3 months of compliant beta blocker therapy.[57]

Page 128

Wolff–Parkinson–White syndrome

Wolff–Parkinson–White syndrome (WPW) is characterised by the presence of an accessory conduction pathway between the atria and ventricles with a predilection to re-entrant supraventricular tachyarrhythmias, which may degenerate to ventricular fibrillation.

The accessory pathway can be identified by the presence of a delta wave and a short PR interval on the 12-lead ECG (Fig. 9.9). The ECG pattern of ventricular pre-excitation is found in approximately 1 to 4.5 per 1000 individuals,[100, 101] although not all will report cardiovascular symptoms consistent with WPW. Those with symptoms or documented atrial fibrillation are considered at higher risk of SCD and should be investigated with an electrophysiological study. Risk of SCD is determined by the refractoriness of the accessory pathway and induction of AF at the shortest pre-excited RR interval.[102] A short pre-excited RR interval of <240 ms during induced atrial fibrillation and <220 ms during isoproterenol infusion, multiple accessory pathways and easy induction of atrial fibrillation are associated with increased risk of SCD. Athletes with any of these features should be offered catheter ablation.

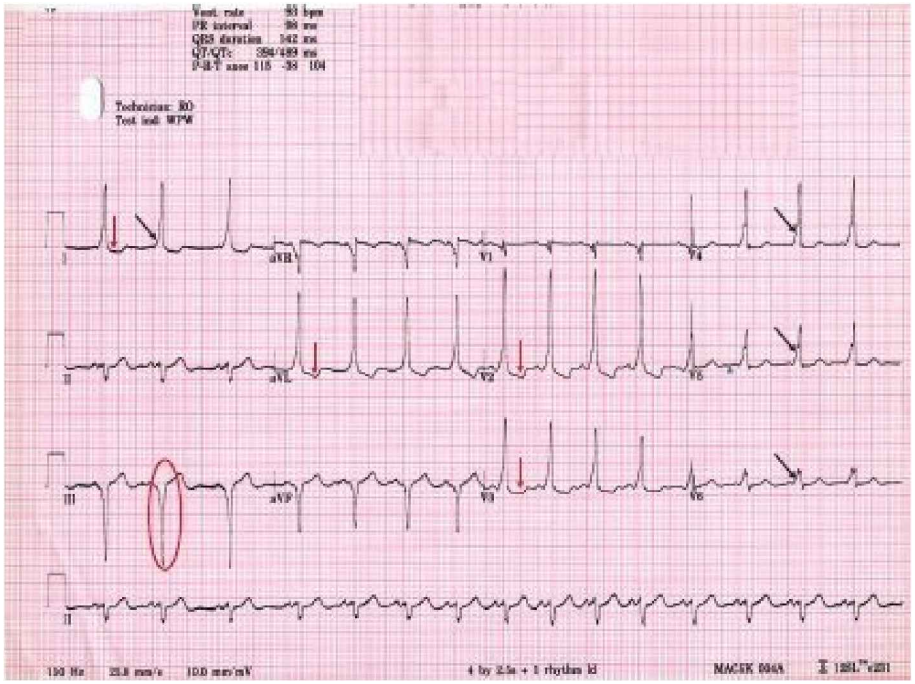


Figure 9.9 ECG demonstrating a short PR interval and slurred upstroke to the QRS complex or delta wave (black arrows) in Wolff–Parkinson–White syndrome. Other findings that suggest WPW include a large Q wave in lead III (red circle), absence of a Q wave in V6 (blue arrowhead) and ST-segment depression in V2-V3 and leads I and aVL (red arrows)

Radiofrequency ablation is the definitive treatment in athletes with high-risk pathways who wish to continue to participate in competitive sport. Return to sport after successful ablation is usually possible after 1–3 months.[57, 58]

Brugada syndrome

Brugada syndrome (BrS) is characterised by right bundle branch block, ST-segment elevation (Fig. 9.8 panel D) and a propensity to sudden death due to polymorphic tachycardia and/or ventricular fibrillation in the absence of other cardiomyopathies.[103] This inherited ion channelopathy follows an autosomal dominant pattern with variable penetrance and a prevalence ranging from 1 in 1000 (Asia) to 1 in 100 000 (Europe).[104]

Diagnosis is made through electrocardiographic identification of the type 1 Brugada pattern either spontaneously or through provocation with intravenous administration of a sodium channel blocker. Affected individuals may present with unheralded syncope or SCD. Mixed phenotypic expressions of the disease, ranging from distinct repolarisation abnormalities to subclinical cardiac conduction defects, also occur. Most deaths from Brugada syndrome occur at slow heart rates, with deaths typically occurring during sleep, and theoretically the condition should not preclude high-

intensity sport.[105] However, chronic intensive exercise promotes increased cardiac vagal tone with subsequent resting bradycardia. Furthermore, prolonged endurance exercise is associated with high core temperatures of >40° C (104°F), which is a recognised trigger in BrS.[106] Asymptomatic athletes with Brugada syndrome should be subjected to exercise testing to exhaustion. Those who do not demonstrate symptoms, ventricular arrhythmia or ST-segment elevation between 1 and 4 minutes into recovery should not be restricted from competitive sport. The same recommendations apply to those who are genotype positive but phenotype negative.[57]

The ICD is the only established treatment to prevent SCD and is reserved for survivors of aborted SCD, and those with sustained ventricular arrhythmias and unheralded syncope.

Catecholaminergic polymorphic ventricular tachycardia

Catecholaminergic polymorphic ventricular tachycardia (CPVT) is a hereditary ion channel disorder characterised by adrenergically mediated polymorphic ventricular tachycardia due to mutations within genes encoding the ryanodine receptor calsequestrin or the ankyrin-B proteins. Intensive physical exercise (e.g. swimming) or emotional stress are well-recognised triggers for SCD particularly in child and adolescent athletes.[107, 108] Stress-induced syncope is one clinically recognised manifestation.[108, 109]

Typically, the baseline ECG is normal; however, exercise stress testing may demonstrate multifocal ventricular premature beats, which, in the context of unheralded syncope, should raise clinical suspicion of the condition in individuals with a structurally normal heart. Ventricular tachycardia with a beat-to-beat 180° alternating QRS axis (bi-directional ventricular tachycardia) is considered to be highly characteristic of CPVT; however, this is an exceptionally rare manifestation of the disorder. Prevention of SCD includes medical therapy with beta blockers and/or flecainide and avoidance of moderate- to high-intensity exercise.[57, 109] Individuals with ongoing ventricular tachycardia or syncope despite pharmacological therapy and lifestyle modification should be offered an ICD.

SCD DUE TO ACQUIRED CARDIAC ABNORMALITIES

Myocarditis

Myocarditis is usually due to a viral illness. It accounts for 3–13% of all SCDs in athletes. The inflammation and subsequent focal necrosis of the myocardium is thought to be the substrate for malignant ventricular tachyarrhythmias causing sudden death.

Most affected individuals experience coryzal symptoms and a mild febrile illness; however, sudden death in a relatively asymptomatic athlete is the commonest presentation. Overt cardiac symptoms are rare and include chest pain, dyspnoea and palpitation.

The ECG usually reveals non-specific ST and T-wave abnormalities but may be normal. Echocardiography may also be normal in mild cases. A raised serum cardiac troponin is useful in confirming the diagnosis in an athlete with a febrile illness associated with chest pain, palpitation and non-specific ECG abnormalities.[110] The gold standard investigation for the diagnosis of

myocarditis remains endomyocardial biopsy (EMB). EMB is, however, limited by procedural risk and low sensitivity, given the patchy distribution of the inflammatory process, and thus is reserved for recurrent cases. Non-invasive myocardial evaluation with CMR can be extremely useful in making the diagnosis of myocarditis and for monitoring disease progression (Fig. 9.10).[111] Apart from revealing cardiac function, the scan may offer further information with regards to the extent of inflammation identified by late gadolinium enhancement (LGE). Previous studies have suggested several parameters that may be associated with poor outcome including clinical symptoms,[112] type of virus[113] and left ventricular size and function.[114] More recent data suggests the presence of LGE is superior to these parameters in predicting subsequent risk of sudden death.[115–117]

Page 130

https://www.sciencedirect.com. Due to rights and permissions restrictions, this content cannot be reproduced in a digital format. The content is available in the print edition at page 130.

Figure 9.10 The role of cardiac magnetic resonance in the assessment of cardiovascular disease in athletes[111]

REPRINTED FROM JACC: CARDIOVASCULAR IMAGING, 11(2), GATI S, SHARMA S, PENNELL D. THE ROLE OF CARDIOVASCULAR MAGNETIC RESONANCE IMAGING IN THE ASSESSMENT OF HIGHLY TRAINED ATHLETES, 247-59, 2018, WITH PERMISSION FROM ELSEVIER

Athletes with proven myocarditis should be assessed with an echocardiogram, CMR, 24-hour Holter monitor and exercise test no earlier than 6 months after initial presentation. Both US and European experts allow athletes to resume competitive sports when left ventricular function has returned to baseline, serum biomarkers for myocardial injury, inflammation and heart failure have normalised, and there are no clinically relevant arrhythmias on Holter monitoring and graded exercise.[57, 58] The precise role of LGE in determining return to play in an athlete with good left ventricular function and absence of complex ventricular arrhythmias is unknown; however, we recommend annual surveillance of such athletes.

Commotio cordis

Commotio cordis refers to SCD from ventricular fibrillation resulting from blunt trauma to the chest wall. The precise frequency of the problem is unknown but it has been reported with increasing frequency in the past decade. The incidence is higher in children and adolescents due to their relatively thin and compliant chest walls. Sports usually associated with commotio cordis include baseball, field hockey, lacrosse, ice hockey, karate and judo. The victim is often struck by an innocent-appearing blow or a projectile object regarded as a standard implement of the game. Collapse from sudden cardiac arrest due to ventricular fibrillation is usually instantaneous but also can be delayed several seconds.[118]

Animal experiments in a juvenile swine model have provided insights into the mechanism

responsible for ventricular fibrillation. Induction of ventricular fibrillation occurs following chest wall blows during a vulnerable window just before the peak of the T wave. A rapid rise in left ventricular pressure follows, which is thought to activate ion channels via mechano-electric coupling. The generation of an inward current via mechanosensitive ion channels results in augmentation of repolarisation and non-uniform myocardial activation and is the cause of premature ventricular depolarisations that trigger ventricular fibrillation in commotio cordis.

Survival after commotio cordis is approximately 15% and only possible with prompt cardiac defibrillation. The velocity and hardness of the projectile object are recognised determinants of ventricular fibrillation. Several measures to prevent commotio cordis have been suggested, which include use of softer 'safety' balls in field hockey and baseball and the use of chest barriers in sports vulnerable to commotio cordis.[119] Use of AEDs in young athletes vulnerable to such trauma has saved lives.

Evaluation of an athlete for conditions causing sudden cardiac death

History, examination and investigations help in the evaluation of an athlete at risk of SCD. The four common diagnostic conundrums facing the clinician are discussed later in this chapter, in the box 'Common diagnostic conundrums'.

History

Most athletes are evaluated as part of cardiovascular or PPE programs implemented by sporting organisations to exclude potentially lethal inherited or congenital cardiac disorders prior to clearance for competition. Rarely, cardiovascular evaluation may be triggered because of symptoms of cardiovascular disease or a family history of premature cardiovascular disease or SCD in a first-degree relative (parent, sibling). In many situations, athletes are investigated at centres with expertise in conditions capable of causing SCD in athletes (particularly cardiomyopathy) as well as knowledge regarding the impact of cardiovascular training on cardiac size, in order to enable the differentiation between physiological adaptation and cardiac pathology (see Chapter 10 for more information on the differentiation).

Sudden cardiac death is often the first clinical manifestation of a quiescent cardiovascular condition; with up to 80% of athletes with SCD reporting no history of cardiovascular symptoms.[51, 120] The presence of exertional chest pain, dyspnoea disproportionate to the exercise performed, palpitations, dizziness or syncope during exercise are ominous symptoms and warrant thorough evaluation (Chapter 10). It is prudent to ascertain any family history of premature cardiac disease or SCD in first-degree relatives, as most conditions discussed above are hereditary. Ventricular arrhythmias in family members may present as syncope, epilepsy or unexplained drowning, and inquiry into these circumstances may provide further important information regarding serious familial cardiac disease. Where possible, it is important to obtain post-mortem reports on first-degree relatives who suffered premature SCD as this may prove useful in differentiating death from a hereditary disorder (such as HCM) and a congenital disorder (such as CCAA).

Physical examination

General physical examination may prove useful in identifying signs of Marfan syndrome (Fig. 9.7) and peripheral stigmata of familial hypercholesterolaemia (Fig. 9.6). Cardiac auscultation may raise suspicion of aortic stenosis, mitral valve prolapse with regurgitation and HCM (of which approximately 25% have resting left ventricular outflow obstruction).

12-lead ECG

The majority of cardiac conditions associated with an increased risk of SCD are suggested or identified by abnormalities on a 12-lead ECG. Sensitivity of the ECG is limited by the inability to identify certain cardiovascular disorders associated with SCD, such as anomalous coronary arteries, premature coronary atherosclerosis, CPVT and aortopathies. Regular exercise is associated with enlarged cardiac chambers and increased vagal tone that manifests as specific electrical manifestations on the ECG (Fig . 9.11).

https://www.sciencedirect.com. Due to rights and permissions restrictions, this content cannot be reproduced in a digital format. The content is available in the print edition at page 132.

Figure 9.11 The 2017 International Consensus Standards for ECG Interpretation in Athletes
FROM JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY, 69(8), SHARMA S, DREZNER JA, BAGGISH A ET AL. INTERNATIONAL RECOMMENDATIONS FOR ELECTROCARDIOGRAPHIC INTERPRETATION IN ATHLETES, 1057-75, FIGURE 1, 2017, WITH PERMISSION FROM ELSEVIER

Ethnicity is a recognised determinant of cardiovascular adaption to exercise. Black athletes commonly demonstrate anterior T-wave inversion (V1–V4) preceded by J-point elevation and ST-segment elevation.[121] This is considered a normal variant and does not require secondary evaluation in the absence of symptoms or a family history of cardiac disease.[96] Similarly, T-wave inversion in the anterior precordial leads (V1–V3) may be considered a normal juvenile pattern in athletes under the age of 16 who have not reached physical maturity. This pattern is rare (0.1%) in white athletes over the age of 16 years and warrants secondary evaluation of underlying cardiac disease, specifically arrhythmogenic right ventricular cardiomyopathy (ARVC) (Fig. 9.8 panel B).[122]

Hypertrophic cardiomyopathy is associated with ECG anomalies in 90% of individuals. Evidence suggests that T-wave inversion in the inferolateral or lateral leads is associated with quiescent cardiomyopathy.[121] This pattern of T-wave inversion in association with ST-segment depression is common in HCM but rare in athletes; and these are the most sensitive markers of HCM during screening of athletes.[53]

Page 132

Echocardiography

Echocardiography is the most commonly used preliminary investigation for the diagnosis of HCM and valvular heart disease; however, it only proves diagnostic in relatively advanced cases of AC. The echocardiographic assessment of an athlete with chest pain or syncope should also involve identification of the origins of the coronary ostia to rule out the diagnosis of anomalous coronary origins, as exercise testing lacks sensitivity and is invariably normal in these conditions.

When to use further imaging investigations

Cardiac magnetic resonance (CMR) is the investigation of choice in athletes with cardiac dimensions or regional wall motion abnormalities consistent with a cardiomyopathy and athletes with uncommon T-wave inversion patterns, ST-segment depression and left bundle branch block (Fig. 9.10). CT coronary angiography is the investigation of choice for confirming the diagnosis of CCAA. Following the diagnosis of cardiomyopathy athletes are subject to exercise stress testing and prolonged ambulatory ECG monitoring for risk stratification purposes.

In the past two decades, there have been major advances in the molecular genetics of HCM, AC and LQTS. However, marked genetic heterogeneity and incomplete knowledge of causal mutations do not

currently allow timely diagnosis in the majority of affected individuals. Additionally, failure to identify a genetic abnormality when screening for known mutations for a particular disorder such as HCM cannot be regarded as exclusion of the disease, as many mutations are yet to be identified. Continuing advances in molecular genetics and refinement of genetic analytic techniques hold promise and may be useful in facilitating diagnoses in difficult clinical scenarios.

Common diagnostic conundrums

Athlete's heart versus hypertrophic cardiomyopathy

Regular participation in sport is associated with modest increases in ventricular wall thickness and cavity size as well as enhanced diastolic filling. This reversible physiological cardiac remodelling enables enhanced left ventricular filling and the augmentation of a large stroke volume even at rapid heart rates for sustained increases in cardiac output.[123]

A small proportion of male athletes, predominantly involved in endurance sports, demonstrate extreme physiological adaptation with left ventricular wall thickness measurements of 13–15 mm.[124] Although the majority of individuals with HCM have a mean left ventricular wall thickness of 18–20 mm, approximately 8% have morphologically mild hypertrophy in a lower range. Therefore a male athlete with a wall thickness of 13–15 mm falls into a grey zone where the differentiation between physiological and pathological LVH is crucial, since diagnostic errors have the potential for serious consequences.

In the majority of athletes, the differentiation between 'athlete's heart' and HCM is possible with echocardiography alone. Physiological LVH is homogeneous and associated with enlarged chamber size and normal indices of diastolic function. In contrast, individuals with HCM often show bizarre patterns of LVH, small chamber size and impaired diastolic function. End-diastolic LV dimensions (LVEDD) >55 mm are common in trained athletes but rare in HCM, where LV cavity size is most often <45 mm. In contrast, a diagnosis of HCM is favoured by abnormal pulsed and tissue Doppler indices of LV diastolic filling with impaired relaxation. With high spatial resolution, CMR can better define wall thickness and identify regions of hypertrophy in the left ventricular apex or the left ventricular free wall that may not be visualised with echocardiography.[125] Furthermore, CMR allows for detection of LGE and myocardial fibrosis. T1 mapping and extracellular volume assessment may provide quantitative assessment of myocardial composition for athletes with a wall thickness between 12 and 15 mm (Fig. 9 .10).[111]

A large study reporting electrocardiographic, echocardiographic and CMR data in over 100 athletes with HCM showed that most athletes with HCM have mild asymmetric LVH (= 16 mm); one third have hypertrophy confined to the apex and almost all athletes have normal diastolic parameters.[53] Furthermore, 15% have an LV cavity >55 mm. Over 95% of athletes, however, show markedly abnormal ECG patterns and 33% show LGE on CMR. These findings suggest that asymmetric patterns of LVH and an abnormal ECG are better discriminators of HCM compared to an enlarged LV cavity and normal diastolic function and underscore the importance of CMR in the investigation of an athlete with a wall thickness of 13–15 mm.[53]

In equivocal cases, the presence of a family history of HCM or SCD and low peak oxygen consumption (<50 mL/kg/min) on cardiopulmonary exercise testing favour HCM. Genetic analysis has a high positive-predictive accuracy but low negative-predictive accuracy and, despite the advances in molecular genetics of cardiomyopathy in the past decade, gene testing remains costly and time consuming. In rare cases re-evaluation with ECG and echocardiography following a period (8–12

weeks) of de-training may be the only practical method of differentiating between the two entities (Fig. 9.12).[126]

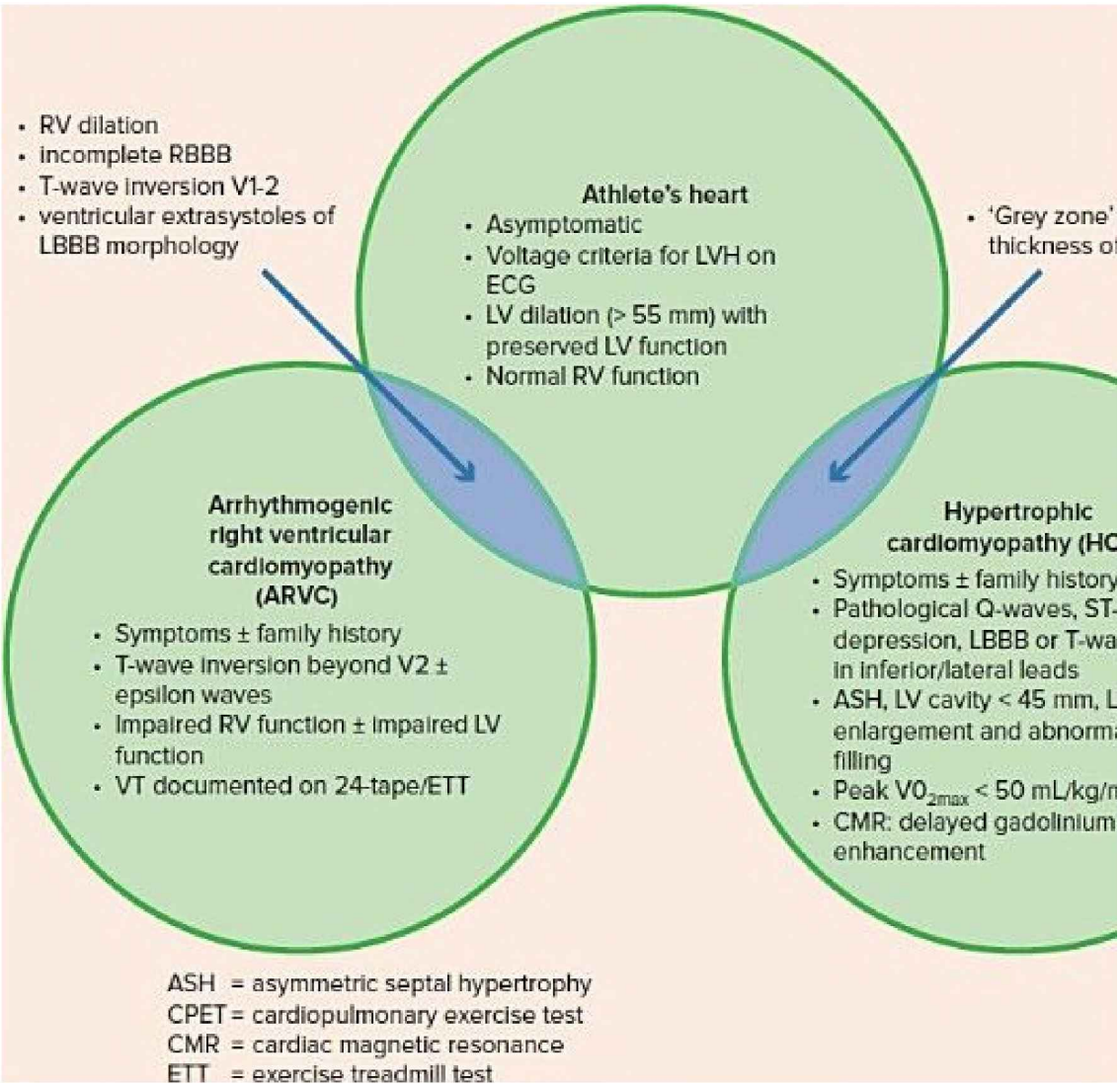


Figure 9.12 Differentiation of physiological changes in athlete's heart from those of pathology in hypertrophic cardiomyopathy (HCM) and arrhythmogenic right ventricular cardiomyopathy (ARVC)

Athlete's heart versus arrhythmogenic right ventricular cardiomyopathy

The diagnosis of ARVC in athletes is particularly challenging due to an early concealed phase of the disease and requires a high level of expertise (Fig. 9.12). Minor ECG abnormalities in right ventricular leads, infrequent ventricular extrasystoles of right ventricular origin, and subtle morphological changes of the right ventricle may be the only objective manifestations of the disorder and these may overlap with physiological adaptation of the right ventricle with regular exercise.[127]

Right ventricular size alone (both inflow and outflow measurements) cannot reliably differentiate between athlete's heart and ARVC, since almost 50% of endurance athletes exhibit enlarged right ventricular dimensions and 6% fulfil criteria for the diagnosis of ARVC according to the Task Force criteria.[128] Zaidi et al. assessed the accuracy of diagnostic criteria for AC by comparing characteristics of athletes with anterior T-wave inversion and well-characterised patients with AC and anterior T-wave inversion.[129] Indicators of AC included syncope, Q waves or precordial QRS amplitudes <1.8 mV, three abnormal signal-averaged ECG parameters, LGE, right ventricular ejection fraction ≤ 45%, wall motion abnormalities at CMR, >1000 ventricular extrasystoles (or >500 non-right ventricular outflow tract) per 24 hours, ventricular tachyarrhythmias or attenuated blood pressure response during exercise.[129]

Electrical repolarisation changes in athletes of African/Afro-Caribbean origin

The interpretation of repolarisation changes in athletes of African/Afro-Caribbean origin (black athletes) can be challenging and often results in a diagnostic dilemma. Experience in these athletes indicates a high prevalence of repolarisation changes including T-wave inversion,[130] which can be a marker of cardiac pathology (particularly cardiomyopathy) in white athletes and require further investigation to exclude pathology.

Studies in black British and French athletes suggest that 23% of black male athletes exhibit T-wave inversion. In many instances the T-wave inversion is deep and affects the inferior and lateral leads, which is a pattern common to HCM.[121, 131] The scenario is compounded by the fact that black athletes exhibit a greater magnitude of LVH compared with Caucasian athletes participating in similar sports,[132] and black males appear to be more prone to exercise-related SCD from HCM according to studies in the USA.[8]

Not surprisingly, the identification of deep T-wave inversion in a black athlete generates anxiety among sports physicians and cardiologists. However, the experience of the authors suggests that T-wave inversion in black athletes is most commonly confined to leads V1–V4 (12–13%) and is often preceded by J-point elevation and convex ST-segment elevation. The T waves in these leads may be asymmetrical or biphasic (Fig. 9.13) and are not associated with cardiac pathology (Fig. 9.14). Such T-wave patterns resolve rapidly (within six weeks of cessation of training) and follow-up of such athletes for over five years has not resulted in any fatalities.

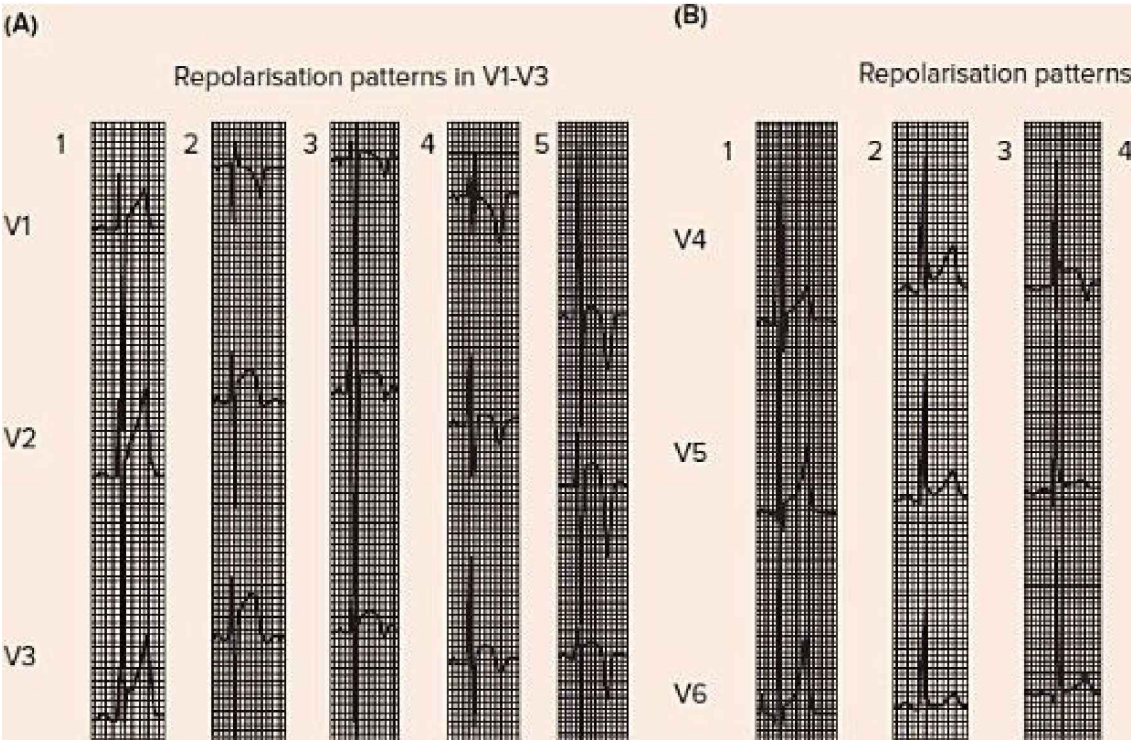


Figure 9.13 Patterns of repolarisation on 12-lead ECG. Variants of repolarisation and T-wave inversion are common in leads V1–V4 in black athletes as shown in panels 1–4. Panel 5 shows T-wave inversion extending to the lateral leads (V5–V6), which is abnormal and requires further evaluation with cardiac imaging to rule out hypertrophic cardiomyopathy

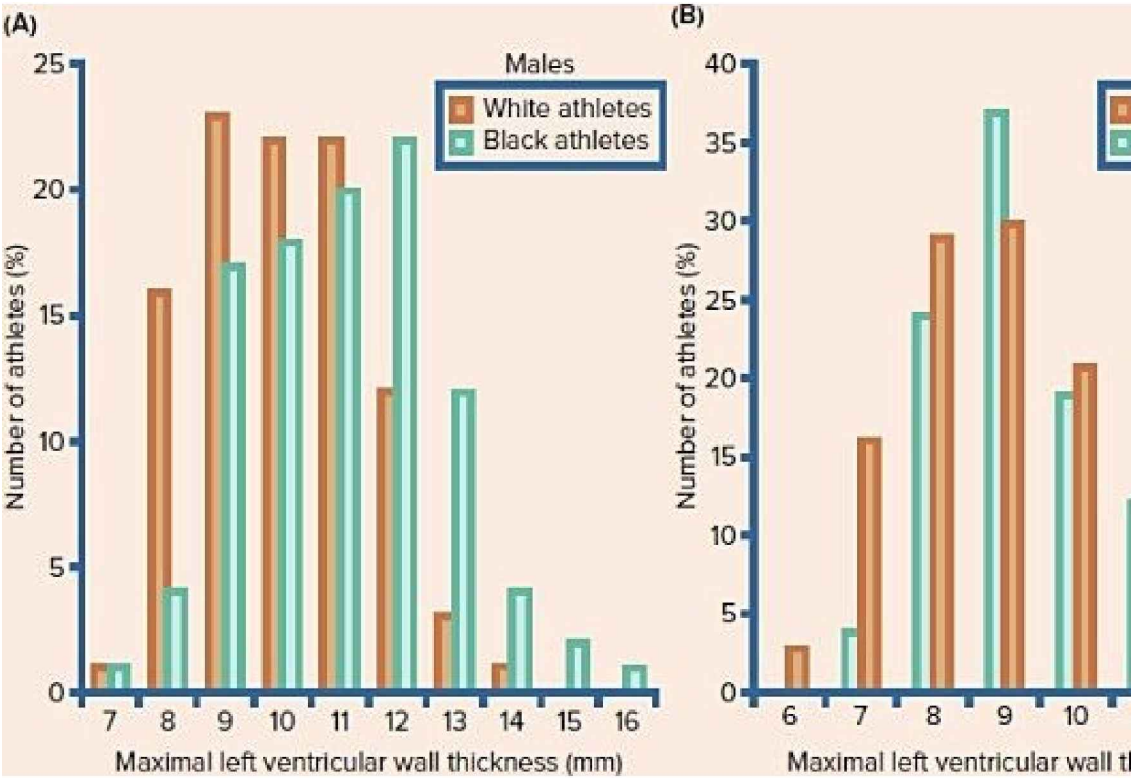


Figure 9.14 Comparison of maximal left ventricular wall thickness (mm) in male athletes (panel A62) and female athletes (panel B134). A small but important proportion of black athletes have ventricular thickness exceeding the upper limit of that seen among white athletes.

In contrast, HCM has been identified in athletes with contiguous T-wave inversion in the inferior and lateral leads.[121] Based on these findings we would consider T-wave inversion in leads V1–V4 as a normal variant in asymptomatic black athletes outside the context of familial cardiomyopathy. In contrast, investigation is recommended in all black athletes with T-wave inversion in contiguous inferior and/or lateral leads. The precise significance of T-wave inversion in the inferior leads in isolation is unknown and warrants further investigation with an echocardiogram at the very least. Index of suspicion and echocardiographic findings should guide further evaluation with CMR. This approach is supported by Schnell et al., who evaluated 155 athletes with pathological T-wave inversion (not including anterior T-wave inversion in black athletes).[133] Cardiac disease was identified in 44.5% of athletes, with HCM accounting for the most common pathology (81%). Almost all of these athletes had deep inferolateral T-wave inversion. Echocardiography was abnormal in approximately half (53.6%) of cases, with CMR identifying a further 24% of athletes with disease.[133] These results underscore the role of CMR in investigating an athlete's pathological T-wave inversion despite normal echocardiographic features (Fig. 9.10).

Black female athletes also exhibit a greater prevalence of T-wave inversion and LVH (Fig. 9.14 panel B) compared with Caucasian females; however, the differences between the two ethnicities are less marked than in male athletes (Fig. 9.14 panel A).[134]

Athlete's heart versus left ventricular non-compaction cardiomyopathy

The differentiation between athlete's heart and dilated cardiomyopathy or trabeculations of the myocardium suspicious for left ventricular non-compaction cardiomyopathy (LVNC) is a well-recognised diagnostic challenge in sports cardiology (Fig. 9.12). LVNC is a cardiomyopathy characterised by a thin, outer compacted myocardial layer, prominent myocardial trabeculations (non-compacted inner layer), impaired systolic function and predilection to fatal ventricular arrhythmias. Data suggests it is a clinically and morphologically heterogeneous disorder, with some individuals presenting with heart failure and malignant arrhythmia, while others remain asymptomatic. A prophylactic implantable cardioverter defibrillator is considered in those with severe symptoms or ventricular arrhythmia.

The diagnosis is based on imaging studies demonstrating a myocardial structure consisting of an outer (compacted) and inner (trabeculated) layer whereby the ratio of the thickness of the non-compacted to compacted layer is at least 2. The dilemma in differentiating benign myocardial trabeculations from a primary cardiomyopathy arises because the current echocardiographic[135–137] and more recently proposed CMR diagnostic criteria[138, 139] for LVNC are derived from small cohorts and lack specificity, particularly in asymptomatic low-risk populations.

Advances in tissue harmonics over the past two decades have unsurprisingly coincided with increased reports of features consistent with LVNC in patients with heart failure,[140] and in low-risk cohorts, including patients with sickle cell anaemia[141] and athletes,[142] particularly those of African/Afro-Caribbean origin. In a study of 1000 asymptomatic athletes, 18% exhibited increased left ventricular trabeculation and 8% fulfilled echocardiographic criteria for LVNC.[142] The majority of athletes meeting echocardiographic criteria demonstrated features of the athlete's ECG, such as sinus bradycardia, early repolarisation or voltage criterion for LVH. Echocardiography revealed normal or increased left ventricular size and normal systolic and diastolic function. A minority (0.9%) demonstrated T-wave inversion and reduced left ventricular systolic function. A comparison was made between athletes who shared features of LVNC and patients clinically diagnosed with the condition. The findings were used to design a multimodal diagnostic approach to low-risk athletes fulfilling criteria for LVNC. Gati et al. propose that, in athletes fulfilling echocardiographic criteria for LVNC, a pathological diagnosis is only considered in the presence of reduced LV function, lateral T-wave inversion on ECG, low-peak oxygen consumption, ventricular arrhythmias on an exercise test or Holter monitor, or the presence of fibrosis on CMR.[142]

The mechanism for the development of increased LV trabeculations in low-risk cohorts is unclear; however, the common factor appears to be an increased preload, which may lead to an exaggeration in myocardial trabeculations in response to increased wall stress (an epiphenomenon) rather than LVNC cardiomyopathy.[111, 143] The distinction between cardiac remodelling from athletic training (athlete's heart) and LVNC is important when one considers that primary cardiomyopathies are a recognised cause of exercise-related SCD in young athletes.

PURPOSE OF SCREENING

Is the purpose of pre-participation cardiovascular screening purely to prevent SCD, or is the goal of screening to identify young athletes with cardiovascular conditions at risk for SCD? The American Heart Association (AHA) states that the principal objective of screening is to reduce the cardiovascular risks associated with physical activity and enhance the safety of athletic participation.[144] The American College of Cardiology contends that the ultimate objective of pre-participation screening of athletes is the detection of 'silent' cardiovascular abnormalities that can lead to SCD;[145] and the Pre-participation Physical Evaluation monograph states the primary objective of screening is to detect potentially life-threatening or disabling conditions before

participation in competitive sports.[146]

Therefore, perhaps, it is the prevalence of cardiovascular conditions with the potential for sudden death, rather than the incidence of SCD itself, that should influence the rigour of pre-participation screening procedures. The goal of screening is early detection of occult cardiovascular disorders, as many of these conditions can be effectively managed through activity modification and disease-specific medical intervention (pharmacotherapy, radiofrequency ablation, ICD or even surgery) to reduce the risk of sudden death.

The AHA estimates the combined disease prevalence of all cardiovascular disorders that potentially predispose young athletes to SCD is 0.3%.[144] Several other screening studies from several countries reveal a similar prevalence of potentially lethal cardiovascular diseases in athletes, ranging 0.16–0.7% (Table 9.4);[23, 147–152] however, this is likely to be an underestimate because ECG screening will not detect aortopathy, CCAA, CAD or CPVT. In other words, at least 1 in 300 young athletes may harbour an occult cardiovascular condition that places them at risk for SCD.

Table 9.4 Prevalence of cardiovascular disorders with risk for sudden cardiac death

Study	Population	Prevalence
Maron (2007)[144]	Estimate in competitive athletes; age 12–35 (USA)	0.3%
Fuller (1997)[153]	5617 high school athletes (USA)	0.4%
Corrado (2006)[23]	42 386 athletes; age 12–35 (Italy)	0.2%
Wilson (2008)[147]	2720 athletes and children; age 10–17 (UK)	0.3%
Bessem (2009)[148]	428 athletes; age 12–35 (Netherlands)	0.7%
Carro Hevia (2009)[150]	1220 amateur athletes (Spain)	0.16%
Baggish (2010)[149]	510 college athletes (USA)	0.6%
Fudge (2014)[154]	1339 high school athletes (USA)	0.4%
Sheikh (2014)[151]	3210 athletes; age 14–35 (UK)	0.5%
Drezner (2015)[155]	790 college athletes (USA)	0.6%
Dhutia (2016)[152]	4925 athletes; age 14–35 (UK)	0.6%
Drezner (2016)[156]	5258 college athletes (USA)	0.25%

PRIMARY PREVENTION OF SCD IN ATHLETES—PRE-PARTICIPATION CARDIOVASCULAR SCREENING

The AHA[157] and European Society of Cardiology (ESC)[58] both advocate PPE on medical, ethical and legal grounds, although disagreement across the Atlantic remains with regards to the adopted screening protocol. Concerns relate to cultural differences, efficacy of individual screening modalities, limited availability of resources and expertise, and the potential downstream economic burden of evaluation on national healthcare systems.

American Heart Association

The AHA advocates a PPE protocol that consists of 10 elements for personal and family history and four elements for physical examination.[19] A positive response for any one of these 14 elements is considered sufficient for further evaluation. The effectiveness of this pragmatic model is limited, when considering up to 80% of athletes report no history of cardiovascular symptoms prior to SCD[5, 120] and history questionnaires yield a high false-positive response rate, up to 30–37%.[154–156] Furthermore, the majority of conditions associated with SCD are seldom identified on physical examination.[51]

European Society of Cardiology

In Italy, a mandatory state-sponsored screening program exists, incorporating the 12-lead ECG in conjunction with personal and family history as well as physical examination. Over a 25-year follow-up period a significant reduction (approximately 90%) in the incidence of SCD was demonstrated in screened athletes compared with unscreened non-athletic individuals.[23] Consequently, the ESC recommends a PPE with ECG as part of its screening protocol[54]—a recommendation also endorsed by the IOC[158] and FIFA.[159]

A recent meta-analysis of 15 studies comparing screening strategies revealed the ECG is five times more sensitive than history and 10 times more sensitive than physical examination for detecting athletes with potential serious cardiac diseases, while demonstrating a lower false-positive rate (6%, 8% and 10%, respectively).[157]

American Medical Society for Sports Medicine

The American Medical Society for Sports Medicine (AMSSM) addressed the complex topic of cardiovascular screening in athletes and the potential addition of an ECG to the standard pre-participation history and physical examination in a 2016 position statement.[160] The AMSSM affirmed that the primary goal of cardiovascular screening in competitive athletes is to identify cardiac disorders at elevated risk of SCD and to reduce morbidity and mortality through individualised and disease-specific management. The AMSSM recognised that the pre-participation history and physical examination, while pragmatic and widely practised, was limited in its ability to identify athletes with conditions at risk for SCD. ECG screening offers enhanced detection of cardiac disorders at potential risk of SCD, but it also may increase false-positive results and the associated downstream consequences. The AMSSM proposed a new framework to assist physicians in choosing a screening strategy (Fig. 9.15), underscored by considerations regarding the individual risk of the athlete as well as physician expertise and available cardiology resources for accurate ECG interpretation and the secondary evaluation of ECG abnormalities. More intensive screening with ECG of higher risk groups should therefore be thoughtfully considered. ECG screening often has been framed as a choice between universal, mandatory screening or no screening at all. In the absence of clear outcomes-based evidence, AMSSM respects physician autonomy to implement the most appropriate screening strategy based on their athlete population and community resources.

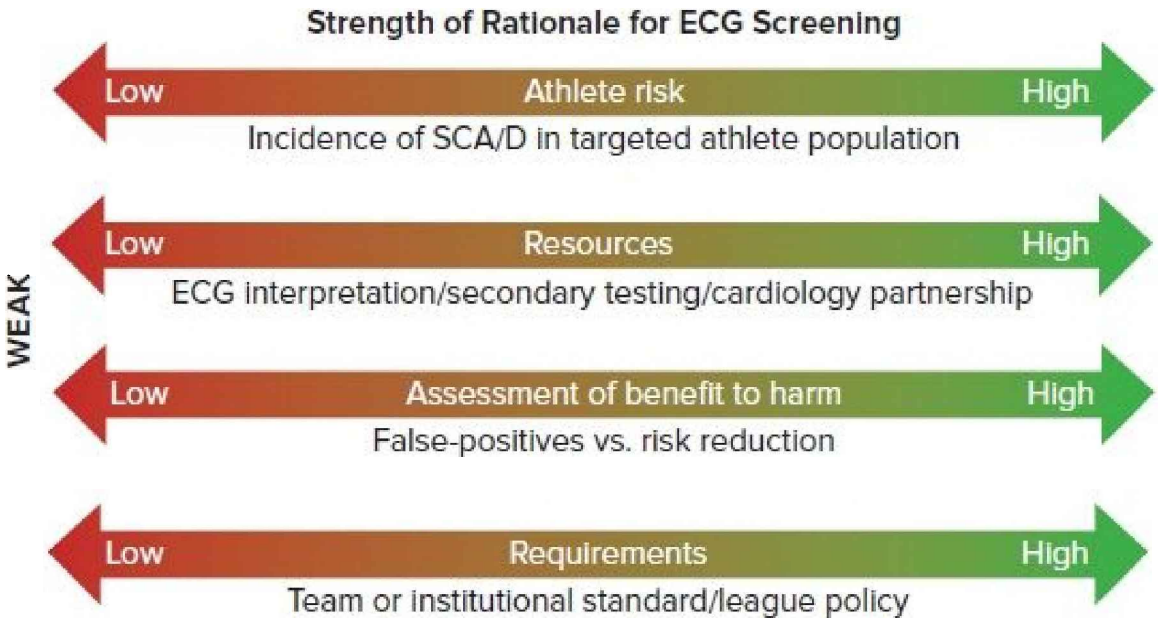


Figure 9.15 Major considerations and strength of rationale for electrocardiogram screening
DVORAK J, GRIMM K, SCHMIED C ET AL. DEVELOPMENT AND IMPLEMENTATION OF A STANDARDISED PRECOMPETITION MEDICAL ASSESSMENT OF INTERNATIONAL ELITE FOOTBALL PLAYERS—2006 FIFA WORLD CUP GERMANY. CLINICAL JOURNAL OF SPORT MEDICINE 2009;19(4):316–21. DOI: 10.1097/JSM.0B013E3181B21B6E. HTTPS ://JOURNALS.LWW.COM/CJSPORTSMED/FULLTEXT/2004/05000/THE_PREPARTICIPATION_EVALUATION__AN_OPPOR TUNITY.1.ASPX[160]

Cost-effectiveness and feasibility of PPE

The European recommendation for ECG screening remains controversial, as the majority of countries do not have the infrastructure to cope with such large-scale screening programs. There are also concerns regarding the cost-effectiveness, efficacy and impact of false-positive results.

Highly trained athletes may develop ECG changes that mimic those observed in patients with cardiomyopathy. This is particularly relevant to black male athletes, as described above, and some adult endurance athletes who reveal a relatively high prevalence of T-wave inversion.[130, 161] Misinterpretation of benign physiological ECG changes is not uncommon, particularly when performed by physicians without expertise in sports cardiology.[162] False-positive ECG findings can result in unnecessary, costly secondary investigations and disqualification from sport. Over the last decade, a plethora of studies[53, 128, 163–165] have greatly improved ECG criteria, progressing from the ESC 2009[166] recommendations, to the Seattle criteria in 2013[167] and, ultimately, the international recommendations for ECG interpretation in athletes in 2017.[96] These recommendations account for adolescent athletes, black ethnicity and some non-specific electrical anomalies, notably axis deviation and voltage criteria for atrial enlargement.[96] Application of these international recommendations to white athletes has reduced the false-positive rate to <3%,[168] but

is still associated with a relatively high false-positive rate in black athletes.[169]

Reliable assessments of cost-effectiveness are limited by the subjective criteria used for each screening modality and in turn the threshold for secondary evaluation. Caution must be taken when extrapolating cost figures to countries with varying demographic makeup and prevalence of disease. False-positive ECG results yield unnecessary downstream investigations that compromise favourable cost outcomes. Studies applying these contemporary ECG criteria have demonstrated an impressive reduction in false-positive rates.[164, 166, 170–172] More recently, Dhutia et al. investigated the financial implications of ECG screening in young athletes in the UK and evaluated the impact of modification of ECG interpretation criteria on cost. A total of 4925 previously unscreened athletes were prospectively evaluated with history, physical examination and ECG (interpreted with the 2010 ESC recommendations). Those with abnormal results were referred for secondary investigations. Application of contemporary ECG criteria decreased cost of de novo screening per athlete from US$110 to $80, and cost per serious diagnosis from $35 993 to $26 405.[168] The international recommendations were associated with a significantly lower number of abnormal ECGs and resulted in an impressive 27% reduction in cost of screening, without compromising the ability to detect athletes with serious cardiac disease.[168] Whether incurring these costs provides a solution for athletes nationwide remains a contentious issue. It is certainly arguable that with low event rates in a large athletic population, financially less-endowed organisations should invest saved costs in improving training and facilities for cardiopulmonary resuscitation (CPR) and access to AEDs.[14, 26, 27]

PPE in veteran athletes

Pre-participation screening of older athletes (aged over 40 years) to identify coronary disease, the commonest cause of SCD in this age group, is less straightforward, since a routine ECG would fail to identify almost all asymptomatic athletes and an exercise stress test is associated with low sensitivity in such individuals.[173] CT coronary angiography is more specific but it is expensive and associated with radiation. However, the usefulness of this modality for risk stratification has been questioned recently, following reports that lifelong male runners have a higher coronary calcium compared to sedentary individuals with the same Framingham risk score.[174]

Marijon et al. evaluated the characteristics of 1247 individuals (aged 35–65 years) who had suffered SCA during sport.[28] They reported pre-existing cardiac disease in 16%, ≥ 1 cardiovascular risk factor in 56%, and an overall 36% of cases that described typical cardiovascular symptoms during the week preceding the SCA.[28] This study highlights the importance of recognising cardiac symptoms, treating cardiovascular risk factors and taking careful attention to pre-existing cardiac disease. This suggests that public awareness and education may have an important role in a strategy of reducing the risk of SCA in sports, particularly in veteran athletes.

Both the AHA and the European Association of Cardiovascular Prevention and Rehabilitation (EACPR) have taken a pragmatic approach in this regard and recommended initial evaluation with a health questionnaire relating to symptoms of coronary disease and the presence of specific risk

factors.[175, 176] Only athletes with symptoms and recognised risk factors for coronary disease should be evaluated with an exercise test or CT coronary angiography, on the understanding that neither test can predict rupture of a small atheromatous plaque and subsequent myocardial infarction during exercise. Coronary artery calcification in the general population is associated with a greater risk of future cardiovascular events and clinicians may encourage lifestyle modifications or pharmacological adherence in an attempt to lower risk.[177, 178]

SECONDARY PREVENTION—RESPONDING WHEN AN ATHLETE HAS COLLAPSED

No screening program offers absolute prevention against SCA, and every school, club and organisation that sponsors athletic activities should be prepared to respond to a collapsed athlete with an acute cardiac emergency. Treatment of SCA begins with early recognition, early CPR and early defibrillation. A comprehensive emergency response plan for SCA, including access to an AED, increases the likelihood of bystander CPR, reduces the time to defibrillation and improves survival from SCA in the athletic setting.[11, 14] Successful programs require an organised and practised response, an established communication method to activate the emergency medical services (EMS) system, and rescuers trained and equipped to provide CPR and defibrillation.

Recognition of sudden cardiac arrest

Prompt recognition of SCA is the first step to an efficient emergency response. Sports medicine professionals and other anticipated first responders to SCA in an athlete, such as coaches and trainers, must maintain a high index of suspicion for SCA in any collapsed and unresponsive athlete. Delayed recognition of SCA by first responders can lead to critical delays or even failure to activate the EMS system, initiate CPR and provide early defibrillation.

Resuscitation can be delayed because SCA is commonly mistaken for a seizure. Brief seizure-like activity or involuntary myoclonic jerks have been reported in over 50% of young athletes with SCA.[14, 179] Another challenge to recognising SCA in athletes includes inaccurate rescuer assessment of respirations or pulse. Occasional or agonal gasping, often characterised by prominent abdominal movements, can occur in the first minutes after SCA and can be misinterpreted as normal breathing.[180] Occasional gasping does not represent adequate breathing and if present should not prevent rescuers from initiating CPR. Lay rescuers and even healthcare professionals also can be inaccurate in assessing signs of circulation and the presence of a pulse.

In studies, rescuers with basic CPR training failed to recognise the absence of a pulse in 10% of pulseless victims, failed to correctly identify a pulse in 45% of victims with a pulse and accurately identified pulselessness in only 2% of pulseless victims within 10 seconds.[181] In high school and college athletes with SCA, perceived ongoing respirations or a pulse after collapse were reported in approximately half the cases.[14, 179]

Management of sudden cardiac arrest

Public access to defibrillators and first-responder AED programs improve survival from SCA by

increasing the likelihood that SCA victims receive bystander CPR and early defibrillation. These programs require an organised and practised response plan, with rescuers trained and equipped to recognise SCA, activate the EMS system, provide CPR and use an AED.[182] The AHA emphasises the need for time-sensitive interventions for victims of SCA and has outlined four critical steps in a 'chain of survival' to save lives in the event of a cardiovascular emergency:[183]

1. early recognition of the emergency and activation of the local emergency response system
2. early cardiopulmonary resuscitation (CPR)
3. early defibrillation (AED)
4. early advanced life support and cardiovascular care (hospital).

Every school, club and organisation that sponsors athletic activities should have an emergency response plan for SCA, with written policies and procedures to ensure an efficient and structured response to a cardiac emergency.[184, 185] Essential elements of emergency planning include training of anticipated responders in CPR and AED use, establishing an effective communication system, ensuring access to early defibrillation, integrating on-site responder and AED programs with the local EMS system, and practising and reviewing the response plan (Table 9.5).[185]

Table 9.5 Key components of emergency planning for sudden cardiac arrest

• Develop a written emergency response plan for SCA.
• Establish an effective and efficient communication system.
• Identify and train likely responders in CPR and AED use.
• Access to early defibrillation through on-site AED(s).
• Integrate and register the AED with the local EMS system.
• Practise and review the response plan with potential first responders at least annually.

SCA = sudden cardiac arrest; AED = automated external defibrillator; CPR = cardiopulmonary resuscitation; EMS = emergency medical services

Consensus guidelines and several public access defibrillation studies uniformly support access to early defibrillation, targeting a time interval of less than 3 minutes from collapse to first shock.[185–188]

Cardiopulmonary resuscitation

Cardiopulmonary resuscitation (CPR) provides a small but critical amount of blood flow to the heart and brain and increases the likelihood that defibrillation will restore a normal rhythm in time to prevent neurological damage. Resuming CPR immediately after shock delivery is also critical. Many victims can have pulseless electric activity or asystole for several minutes after defibrillation and CPR is needed to provide perfusion.[189–191] Unfortunately, bystander CPR is initiated in less than one-third of cases of witnessed SCA[192, 193] and, if initiated, more than 40% of chest compressions are of insufficient quality.[194]

Efforts have focused on ways to simplify CPR recommendations and emphasise the fundamental importance of high-quality CPR. The recommended compression–ventilation ratio changed from 15:2 to 30:2 and the defibrillation sequence from 3 stacked shocks to 1 shock followed by immediate CPR to minimise interruptions in chest compressions. Minimising the interval between stopping chest compressions and delivering a shock (i.e. the pre-shock pause) also improves the chances of shock success and patient survival. For most adults with out-of-hospital cardiac arrest, bystander CPR with chest compression only (hands-only CPR) achieves outcomes similar to those of conventional CPR (compressions with rescue breathing).[195, 196]

Cardiopulmonary resuscitation recommendations were updated in the 2010 AHA Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care, and the 2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations.[196–198] These guidelines changed the basic life support sequence from A–B–C (Airway, Breathing, Chest compressions) to C–A–B (Chest compressions, Airway, Breathing). In the A–B–C sequence, chest compressions are often delayed while the responder opens the airway to give mouth-to-mouth breaths or retrieves a barrier device or other ventilation equipment.

By changing the sequence to C–A–B, chest compressions are initiated sooner and ventilation only minimally delayed until completion of the first cycle of chest compressions. Starting with chest compressions may ensure that more victims receive CPR and that rescuers who are unable or unwilling to provide ventilations will at least perform chest compressions.

Immediate activation of the emergency response system and chest compressions should be started in any unresponsive victim without normal breathing (i.e. only gasps). Hands-only (compression-only) CPR is encouraged for the untrained lay rescuer. Adequate chest compressions include:

- compressing to a depth of at least 5 cm (2 in.)
- allowing complete recoil of the chest after each compression
- minimising any pauses in compressions
- avoiding excessive ventilation.[197]

Early defibrillation

The single greatest factor affecting survival from SCA is the time interval from cardiac arrest to defibrillation.[183] In the USA, survival rates from out-of-hospital cardiac arrest are <10% when dependent on traditional EMS systems.[199–202] Drezner et al. reported a 7-year analysis of survival trends in the USA following exercise-related SCA in youth. During the 7-year period 2000–2006, a total of 486 cases of exercise-related SCA were identified in individuals aged 5–22, with an overall survival rate of 11% (range 4–21%) per year.[203] Survival following SCA has been greatly improved by lay rescuer and public access defibrillation programs designed to shorten the time interval from SCA to shock delivery.[11, 182, 204–210] These programs train lay rescuers and non-traditional first

responders in CPR and AED use and place AEDs in public locations where risk for SCA is high.

Rapid defibrillation in public settings such as casinos, airlines and airports has led to survival rates ranging from 41%–74% if bystander CPR is provided and defibrillation occurs within 3–5 minutes of collapse.[11, 182, 204–210] Once transported to a setting for advanced cardiac life support, rapid cooling (induced hypothermia) for victims with ventricular fibrillation arrest has been shown to improve survival and decrease neurological complications.[211]

Limited research is available regarding early defibrillation programs in the athletic setting. Questions also exist as to whether early defibrillation in young athletes who suffer SCA from a diverse aetiology of structural and electrical cardiac diseases can provide the same survival benefit as demonstrated in the older general population with a predominance of coronary artery disease as the cause of SCA. Initial research, including a retrospective survey on AED utilisation at college athletic venues, found an overall immediate resuscitation rate of 54% in older non-students but did not identify a survival benefit in a small number of intercollegiate athletes with SCA.[11, 179, 212]

Subsequent research using cross-sectional and prospective study designs has demonstrated an improved survival rate for young athletes with SCA if early defibrillation is achieved. Drezner et al.[14] reported on a cohort of 1710 US high schools with an on-site AED program. Thirty-six cases of SCA were described, including 14 cases of high school student athletes (mean age 16; range 14–17) and 22 cases of older non-students (mean age 57; range 42–71), such as employees and spectators. All but one case of SCA was witnessed, 94% received bystander CPR and an AED deployed a shock in 30 of 36 (83%) cases. Twenty-three of the 36 SCA victims (64%) survived to hospital discharge, including 9 of the 14 student athletes (64%) and 14 of the 22 older non-students (64%). Although this was a cross-sectional cohort study, this was the first study to suggest a survival benefit for early defibrillation in young athletes with SCA.

Drezner et al. later published a 2-year prospective study monitoring all SCA cases in 2149 US high schools.[24] School-based AED programs were present in 87% of participating schools. Each school was contacted quarterly to report cases of SCA on the school campus, and 95% of schools confirmed participation for the full 2-year study period. Fifty-nine cases of SCA were confirmed during the study period, including 26 (44%) cases in students (mean age 16 years; range 13–20) and 33 (56%) in adults (mean age 56 years; range 20–80). Ninety-three per cent of cases were witnessed and 92% received prompt CPR. A defibrillator was applied in 50 (85%) cases and a shock delivered on site in 39 (66%). Overall, 42 of 59 (71%) SCA victims survived to hospital discharge, including 22 of 26 (85%) students and 20 of 33 (61%) adults. Sixteen of 18 (89%) student athletes, and 8 of 9 (89%) adults, who arrested during physical activity survived to hospital discharge. Thus, witnessed, exercise-related SCA is largely a survivable event if prompt CPR and defibrillation are achieved.

A goal of less than 3 minutes from collapse to shock delivery (time it takes to recognise an emergency, notify designated responders, access the AED, reach the victim, apply the electrodes and deliver the first shock) is recommended.[185, 186, 188] If a facility has only one AED, it should be centrally located so it can be brought to the site of SCA through activation of the emergency response plan. Consideration should be given to the most populated areas and proximity to athletic

facilities. For larger venues and schools with distant or multiple athletic facilities, duplicate equipment is needed.

The AED should be highly visible and near a telephone or other means of activating the EMS system and on-site response team. All staff should be instructed on the location of the AED. The AED should be easily accessible during all hours the facility is open, including any sponsored event after usual working hours. The AED should be secured (i.e. an alarmed unlocked cabinet) but not placed in a locked box, cabinet or room that is inaccessible at the time of an emergency.

To avoid potentially fatal delays in resuscitation, a collapsed and unresponsive athlete should be treated as having had a cardiac arrest until a non-cardiac cause of collapse can be clearly determined or the athlete becomes responsive (Table 9.6). Brief seizure-like activity in a collapsed athlete should be assumed due to SCA. Agonal respirations or gasping with prominent abdominal movements may also be present but should not preclude the responder from initiating CPR and applying an AED as soon as possible. Young athletes who collapse shortly after being struck in the chest should be suspected of having commotio cordis and emergency procedures for SCA initiated.

Page 142

Table 9.6 Management of sudden cardiac arrest in athletes

https://www.sciencedirect.com. Due to rights and permissions restrictions, this content cannot be reproduced in a digital format. The content is available in the print edition at page 142.

SCA = sudden cardiac arrest; AED = automated external defibrillator; CPR = cardiopulmonary resuscitation; EMS = emergency medical services; VF = ventricular fibrillation

THE LANCET, 362(9394), BEHR E, WOOD DA, WRIGHT M ET AL. CARDIOLOGICAL ASSESSMENT OF FIRST-DEGREE RELATIVES IN SUDDEN ARRHYTHMIC DEATH SYNDROME, 1457-9, 2003, WITH PERMISSION FROM ELSEVIER

SUMMARY

- Sudden cardiac death is the leading cause of death in young athletes during sport and is usually caused by an inherited or congenital cardiac disorder.
- The incidence of SCD is substantially higher than initially recognised and the risk is appreciably higher in males and black/African athletes.
- The distinction of athlete's heart from cardiomyopathy requires a careful assessment of electrocardiographic findings and cardiac morphology and function on advanced imaging.
- More rigorous pre-participation screening is warranted in higher risk athlete groups. ECG screening substantially increases the sensitivity to detect conditions predisposing to SCD and can be performed with a low false-positive rate when contemporary criteria are used to guide ECG interpretation.

PRACTICE PEARL

A high suspicion of SCA must be maintained for any collapsed and unresponsive athlete and an AED applied as soon as possible for rhythm analysis and defibrillation if indicated.[203]

- Experienced cardiology resources are needed for the proper secondary investigation of ECG abnormalities.
- Emergency response planning for SCA and prompt availability of AEDs are recommended for all organised athletic settings.
- Early recognition of SCA is based on assessing responsiveness and the absence of normal breathing. Victims of SCA may initially have gasping respirations with periodic abdominal movements or even appear to be having a seizure. These atypical presentations may confuse a rescuer, causing a delay in calling for help or beginning CPR.
- All efforts should be made to minimise interruptions in chest compressions both before and after defibrillation.
- Sudden cardiac arrest in athletes can be effectively treated through prompt recognition of SCA, a coordinated emergency response, early CPR and early defibrillation.

REFERENCES

1. Maron BJ, Doerer JJ, Haas TS et al. Sudden deaths in young competitive athletes: analysis of 1866 deaths in the United States, 1980–2006. *Circulation* 2009; 119(8): 1085–92. doi: 10.1161/circulationaha.108.804617.
2. Maron BJ. Sudden death in young athletes. *N Engl J Med* 2003; 349(11): 1064–75. doi: 10.1056/NEJMra022783.
3. Harmon KG, Asif IM, Klossner D et al. Incidence of sudden cardiac death in National Collegiate Athletic Association athletes. *Circulation* 2011; 123(15): 1594–600. doi: 10.1161/circulationaha.110.004622.
4. De Noronha SV, Sharma S, Papadakis M et al. Aetiology of sudden cardiac death in athletes in the United Kingdom: a pathological study. *Heart* 2009; 95(17): 1409–14. doi: 10.1136/hrt.2009.168369.
5. Van Camp SP, Bloor CM, Mueller FO et al. Nontraumatic sports death in high school and college athletes. *Med Sci Sports Exerc* 1995; 27(5): 641–7. doi: 10.1249/00005768-199505000-00005.
6. Maron BJ, Gardin JM, Flack JM et al. Prevalence of hypertrophic cardiomyopathy in a general population of young adults: echocardiographic analysis of 4111 subjects in the CARDIA study. *Circulation* 1995; 92(4): 785–9. doi: 10.1161/01.CIR.92.4.785.
7. Maron BJ, Gohman TE, Aeppli D. Prevalence of sudden cardiac death during competitive sports activities in Minnesota high school athletes. *J Am Coll Cardiol* 1998; 32(7): 1881–4. doi: 10.1016/S0735-1097(98)00491-4.
8. Harmon KG, Asif IM, Maleszewski JJ et al. Incidence, cause and comparative frequency of sudden cardiac death in National Collegiate Athletic Association

athletes: a decade in review. *Circulation* 2015; 132(1): 10–19. doi: 10.1161/circulationaha.115.015431.

9. Corrado D, Basso C, Rizzoli G et al. Does sports activity enhance the risk of sudden death in adolescents and young adults? *J Am Coll Cardiol* 2003; 42(11): 1959–63. doi: 10.1016/j.jacc.2003.03.002.
10. Eckart RE, Scoville SL, Campbell CL et al. Sudden death in young adults: a 25-year review of autopsies in military recruits. *Ann Intern Med* 2004; 141(11): 829–34. doi: 10.7326/0003-4819-141-11-200412070-00005.
11. Drezner JA, Rogers KJ, Zimmer RR et al. Use of automated external defibrillators at NCAA Division I universities. *Med Sci Sports Exerc* 2005; 37(9): 1487–92. doi: 10.1249/01.mss.0000177591.30968.d4.
12. Atkins DL, Everson-Stewart S, Sears GK et al. Epidemiology and outcomes from out-of-hospital cardiac arrest in children: the Resuscitation Outcomes Consortium Epistry—Cardiac Arrest. *Circulation* 2009; 119(11): 1484–91. doi: 10.1161/circulationaha.108.802678.
13. Chugh SS, Reinier K, Balaji S et al. Population-based analysis of sudden death in children: the Oregon Sudden Unexpected Death Study. *Heart Rhythm* 2009; 6(11): 1618–22. doi: 10.1016/j.hrthm.2009.07.046.
14. Drezner JA, Rao AL, Heistand J et al. Effectiveness of emergency response planning for sudden cardiac arrest in United States high schools with automated external defibrillators. *Circulation* 2009; 120(6): 518–25. doi: 10.1161/circulationaha.109.855890.
15. Solberg EE, Gjertsen F, Haugstad E et al. Sudden death in sports among young adults in Norway. *Eur J Prev Cardiol* 2010; 17(3): 337–41. doi: 10.1097/HJR.0b013e328332f8f7.
16. Eckart RE, Shry EA, Burke AP et al. Sudden death in young adults: an autopsy-based series of a population undergoing active surveillance. *J Am Coll Cardiol* 2011; 58(12): 1254–61. doi: 10.1016/j.jacc.2011.01.049.
17. Maron BJ, Haas TS, Ahluwalia A et al. Incidence of cardiovascular sudden deaths in Minnesota high school athletes. *Heart Rhythm* 2013; 10(3): 374–7. doi: 10.1016/j.hrthm.2012.11.024.
18. Roberts WO, Stovitz SD. Incidence of sudden cardiac death in Minnesota high school athletes 1993–2012 screened with a standardised pre-participation evaluation. *J Am Coll Cardiol* 2013; 62(14): 1298–301. doi: 10.1016/j.jacc.2013.05.080.
19. Maron BJ, Haas TS, Murphy CJ et al. Incidence and causes of sudden death in US college athletes. *J Am Coll Cardiol* 2014; 63(16): 1636–43. doi: 10.1016/j.jacc.2014.01.041.
20. Drezner JA, Harmon KG, Marek JC. Incidence of sudden cardiac arrest in Minnesota high school student athletes: the limitations of catastrophic insurance claims. *J Am Coll Cardiol* 2014; 63(14): 1455–6. doi: 10.1016/j.jacc.2013.11.012.

21. Toresdahl BG, Rao AL, Harmon KG et al. Incidence of sudden cardiac arrest in high school student athletes on school campus. *Heart Rhythm* 2014; 11(7): 1190–4. doi: 10.1016/j.hrthm.2014.04.017.
22. Harmon KG, Asif IM, Maleszewski JJ et al. Incidence and aetiology of sudden cardiac arrest and death in high school athletes in the United States. *Mayo Clin Proc* 2016; 91(11): 1493–502. doi: 10.1016/j.mayocp.2016.07.021.
23. Corrado D, Basso C, Pavei A et al. Trends in sudden cardiovascular death in young competitive athletes after implementation of a preparticipation screening program. *JAMA* 2006; 296(13): 1593–601. doi: 10.1001/jama.296.13.1593.
24. Drezner JA, Toresdahl BG, Rao AL et al. Outcomes from sudden cardiac arrest in US high schools: a 2-year prospective study from the national registry for AED use in sports. *Br J Sports Med* 2013; 47(18): 1179–83. doi: 10.1136/bjsports-2013-092786.
25. Harmon KG, Drezner JA, Wilson MG et al. Incidence of sudden cardiac death in athletes: a state-of-the-art review. *Br J Sports Med* 2014; 48(15): 1185–92. doi: 10.1136/bjsports-2014-093872.
26. Berdowski J, De Beus MF, Blom M et al. Exercise-related out-of-hospital cardiac arrest in the general population: incidence and prognosis. *Eur Heart J* 2013; 34(47): 3616–23. doi: 10.1093/eurheartj/eht401.
27. Marijon E, Tafflet M, Celermajer DS et al. Sports-related sudden death in the general population. *Circulation* 2011; 124(6): 672–81. doi: 10.1161/circulationaha.110.008979.
28. Marijon E, Uy-Evanado A, Reinier K et al. Sudden cardiac arrest during sports activity in middle age. *Circulation* 2015; 131(16): 1384–91. doi: 10.1161/circulationaha.114.011988.
29. Murphy SL, Xu J, Kochanek KD. Deaths: preliminary data for 2010. *Natl Vital Stat Reports* 2012; 60(4): 1–51. https://www.cdc.gov/nchs/data/nvsr/nvsr60/nvsr60_04.pdf, accessed 18 April 2018.
30. Maron BJ, Friedman RA, Caplan A. Ethics of preparticipation cardiovascular screening for athletes. *Nat Rev Cardiol* 2015; 12(6): 375–8. doi: 10.1038/nrcardio.2015.21.
31. La Gerche A, Baggish AL, Knuuti J et al. Cardiac imaging and stress testing asymptomatic athletes to identify those at risk of sudden cardiac death. *JACC Cardiovasc Imaging* 2013; 6(9): 993–1007. doi: 10.1016/j.jcmg.2013.06.003.
32. Maron BJ, Epstein SE, Roberts WC. Causes of sudden death in competitive athletes. *J Am Coll Cardiol* 1986; 7(1): 204–14. doi: 10.1016/S0735-1097(86)80283-2.
33. Albert CM, Mittleman MA, Chae CU et al. Triggering of sudden death from cardiac causes by vigorous exertion. *N Engl J Med* 2000; 343(19): 1355–61. doi: 10.1056/NEJM200011093431902.
34. Mittleman MA, Maclure M, Tofler GH et al. Triggering of acute myocardial infarction by heavy physical exertion protection against triggering by regular

exertion. *N Engl J Med* 1993; 329(23): 1677–83. doi: 10.1056/NEJM199312023292301.

35. Siscovick DS, Weiss NS, Fletcher RH et al. The incidence of primary cardiac arrest during vigorous exercise. *N Engl J Med* 1984; 311(14): 874–7. doi: 10.1056/NEJM198410043111402.
36. Thompson PD, Funk EJ, Carleton RA et al. Incidence of death during jogging in Rhode Island from 1975 through 1980. *JAMA* 1982; 247(18): 2535–8. doi: 10.1001/jama.1982.03320430039028.
37. Maron BJ, Doerer JJ, Haas TS et al. Profile and frequency of sudden deaths in 1463 young competitive athletes: from a 25-year US national registry, 1980–2005. *Circulation* 2006; 114(Suppl 18). https://www.ahajournals.org/doi/10.1161/circ.114.suppl_18.II_830-c, accessed 23 January 2018.
38. Corrado D, Thiene G, Nava A et al. Sudden death in young competitive athletes: clinicopathologic correlations in 22 cases. *Am J Med* 1990; 89(5): 588–96. doi: 10.1016/0002-9343(90)90176-E.
39. Corrado D, Basso C, Schiavon M et al. Screening for hypertrophic cardiomyopathy in young athletes. *N Engl J Med* 1998; 339(6): 364–9. doi: 10.1056/NEJM199808063390602.
40. Harmon KG, Drezner JA, Maleszewski JJ et al. Pathogeneses of sudden cardiac death in National Collegiate Athletic Association athletes. *Circ Arrhythmia Electrophysiol* 2014; 7(2): 198–204. doi: 10.1161/CIRCEP.113.001376.
41. Holst AG, Winkel BG, Theilade J et al. Incidence and aetiology of sports-related sudden cardiac death in Denmark implications for preparticipation screening. *Heart Rhythm* 2010; 7(10): 1365–71. doi: 10.1016/j.hrthm.2010.05.021.
42. Finocchiaro G, Papadakis M, Robertus JL et al. Aetiology of sudden death in sports: insights from a United Kingdom regional registry. *J Am Coll Cardiol* 2016; 67(18): 2108–15. doi: 10.1016/j.jacc.2016.02.062.
43. Ullal AJ, Abdelfattah RS, Ashley EA et al. Hypertrophic cardiomyopathy as a cause of sudden cardiac death in the young: a meta-analysis. *Am J Med* 2016; 129(5): 486–96.e2. doi: 10.1016/j.amjmed.2015.12.027.
44. Bagnall RD, Weintraub RG, Ingles J et al. A prospective study of sudden cardiac death among children and young adults. *N Engl J Med* 2016; 374(25): 2441–52. doi: 10.1056/NEJMoa1510687.
45. Margey R, Roy A, Tobin S et al. Sudden cardiac death in 14-to 35-year olds in Ireland from 2005 to 2007: a retrospective registry. *Europace* 2011; 13(10): 1411–18. doi: 10.1093/europace/eur161.
46. Puranik R, Chow CK, Duflou JA et al. Sudden death in the young. *Heart Rhythm* 2005; 2(12): 1277–82. doi: 10.1016/j.hrthm.2005.09.008.
47. Papadakis M, Sharma S, Cox S et al. The magnitude of sudden cardiac death in the young: a death certificate-based review in England and Wales. *Europace* 2009; 11(10): 1353–8. doi: 10.1093/europace/eup229.

48. Meyer L, Stubbs B, Fahrenbruch C et al. Incidence, causes and survival trends from cardiovascular-related sudden cardiac arrest in children and young adults 0 to 35 years of age: a 30-year review. *Circulation* 2012; 126(11): 1363–72. doi: 10.1161/circulationaha.111.076810.
49. Behr ER, Dalageorgou C, Christiansen M et al. Sudden arrhythmic death syndrome: familial evaluation identifies inheritable heart disease in the majority of families. *Eur Heart J* 2008; 29(13): 1670–80. doi: 10.1093/eurheartj/ehn219.
50. Maron BJ, Klues HG. Surviving competitive athletics with hypertrophic cardiomyopathy. *Am J Cardiol* 1994; 73(15): 1098–104. doi: 10.1016/0002-9149(94)90290–9.
51. Maron BJ, Shirani J, Poliac LC et al. Sudden death in young competitive athletes: clinical, demographic and pathological profiles. *JAMA* 1996; 276(3): 199–204. doi: 10.1001/jama.276.3.199.
52. Maron BJ, Carney KP, Lever HM et al. Relationship of race to sudden cardiac death in competitive athletes with hypertrophic cardiomyopathy. *J Am Coll Cardiol* 2003; 41(6): 974–80. doi: 10.1016/S0735-1097(02)02976-5.
53. Sheikh N, Papadakis M, Schnell F et al. Clinical profile of athletes with hypertrophic cardiomyopathy. *Circ Cardiovasc Imaging* 2015; 8(7):e003454. doi: 10.1161/circimaging.114.003454.
54. Corrado D, Pelliccia A, Bjørnstad HH et al. Cardiovascular pre-participation screening of young competitive athletes for prevention of sudden death: proposal for a common European protocol Consensus Statement of the Study Group of Sport Cardiology of the Working Group of Cardiac Rehabilitation and Exercise Physiology and the Working Group of Myocardial and Pericardial Diseases of the European Society of Cardiology. *Eur Heart J* 2005; 26(5): 516–24. doi: 10.1093/eurheartj/ehi108.
55. Elliott PM, Anastasakis A, Borger MA et al. 2014 ESC Guidelines on diagnosis and management of hypertrophic cardiomyopathy. *Eur Heart J* 2014; 35(39): 2733–79. doi: 10.1093/eurheartj/ehu284.
56. Elliott PM, Poloniecki J, Dickie S et al. Sudden death in hypertrophic cardiomyopathy: identification of high risk patients. *J Am Coll Cardiol* 2000; 36(7): 2212–18. doi: 10.1016/S0735-1097(00)01003-2.
57. Maron BJ, Udelson JE, Bonow RO et al. Eligibility and disqualification recommendations for competitive athletes with cardiovascular abnormalities: Task Force 3: Hypertrophic cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy and other cardiomyopathies and myocarditis: a Scientific Statement from the American Heart Association and American College of Cardiology. *J Am Coll Cardiol* 2015; 66(21): 2362–71. doi: 10.1016/j.jacc.2015.09.035.
58. Pelliccia A, Fagard R, Bjørnstad HH et al. Recommendations for competitive sports participation in athletes with cardiovascular disease. *Med dello Sport* 2005; 58(3):

157–91. doi: 10.1093/eurheartj/ehi325.

59. Lampert R, Olshansky B, Heidbuchel H et al. Safety of sports for athletes with implantable cardioverter-defibrillators: results of a prospective, multinational registry. *Circulation* 2013; 127(20): 2021–30. doi: 10.1161/circulationaha.112.000447.
60. Kim J, Gremion G. Cardiac arrest during long-distance running races. *N Engl J Med* 2013; 61(1): 28–9. doi: 10.1056/NEJMoa1106468.
61. Elliott PM, Sharma S, Varnava A et al. Survival after cardiac arrest or sustained ventricular tachycardia in patients with hypertrophic cardiomyopathy. *J Am Coll Cardiol* 1999; 33(6): 1596–601. doi: 10.1016/S0735-1097(99)00056-X.
62. Basavarajaiah S, Wilson M, Whyte G et al. Prevalence of hypertrophic cardiomyopathy in highly trained athletes: relevance to pre-participation screening. *J Am Coll Cardiol* 2008; 51(10): 1033–9. doi: 10.1016/j.jacc.2007.10.055.
63. Papadakis M, Raju H, Behr ER et al. Sudden cardiac death with autopsy findings of uncertain significance: potential for erroneous interpretation. *Circ Arrhythmia Electrophysiol* 2013; 6(3): 588–96. doi: 10.1161/circep.113.000111.
64. Sen-Chowdhry S, Morgan RD, Chambers JC et al. Arrhythmogenic cardiomyopathy: aetiology, diagnosis and treatment. *Annu Rev Med* 2010; 61(1): 233–53. doi: 10.1146/annurev.med.052208.130419.
65. Norman M, Simpson M, Mogensen J et al. Novel mutation in desmoplakin causes arrhythmogenic left ventricular cardiomyopathy. *Circulation* 2005; 112(5): 636–42. doi: 10.1161/circulationaha.104.532234.
66. Delmar M, McKenna WJ. The cardiac desmosome and arrhythmogenic cardiomyopathies: from gene to disease. *Circ Res* 2010; 107(6): 700–14. doi: 10.1161/circresaha.110.223412.
67. Corrado D, Basso C, Pilichou K et al. Molecular biology and clinical management of arrhythmogenic right ventricular cardiomyopathy/dysplasia. *Heart* 2011; 97(7): 530–9. doi: 10.1136/hrt.2010.193276.
68. Heidbüchel H, Hoogsteen J, Fagard R et al. High prevalence of right ventricular involvement in endurance athletes with ventricular arrhythmias: role of an electrophysiologic study in risk stratification. *Eur Heart J* 2003; 24(16): 1473–80. doi: 10.1016/S0195-668X(03)00282-3.
69. Ector J, Ganame J, Van Der Merwe N et al. Reduced right ventricular ejection fraction in endurance athletes presenting with ventricular arrhythmias: a quantitative angiographic assessment. *Eur Heart J* 2007; 28(3): 345–53. doi: 10.1093/eurheartj/ehl468.
70. La Gerche A, Connelly KA, Mooney DJ et al. Biochemical and functional abnormalities of left and right ventricular function after ultra-endurance exercise. *Heart* 2008; 94(7): 860–6. doi: 10.1136/hrt.2006.101063.
71. Sharma S, Papadakis M, Whyte G. Chronic ultra-endurance exercise: implications in

arrhythmogenic substrates in previously normal hearts. *Heart* 2010; 96(16): 1255–6. doi: 10.1136/hrt.2010.195172.

72. La Gerche A, Claessen G, Dymarkowski S et al. Exercise-induced right ventricular dysfunction is associated with ventricular arrhythmias in endurance athletes. *Eur Heart J* 2015; 36(30): 1998–2010. doi: 10.1093/eurheartj/ehv202.
73. Marcus FI, McKenna WJ, Sherrill D et al. Diagnosis of arrhythmogenic right ventricular cardiomyopathy/dysplasia: proposed modification of the task force criteria. *Circulation* 2010; 121(13): 1533–41. doi: 10.1161/circulationaha.108.840827.
74. Heidbüchel H, La Gerche A. The right heart in athletes: evidence for exercise-induced arrhythmogenic right ventricular cardiomyopathy. *Herzschrittmacherther Elektrophysiol* 2012; 23(2): 82–6. doi: 10.1007/s00399-012-0180-3.
75. Corrado D, Calkins H, Link MS et al. Prophylactic implantable defibrillator in patients with arrhythmogenic right ventricular cardiomyopathy/dysplasia and no prior ventricular fibrillation or sustained ventricular tachycardia. *Circulation* 2010; 122(12): 1144–52. doi: 10.1161/circulationaha.109.913871.
76. Angelini P. Coronary artery anomalies: an entity in search of an identity. *Circulation* 2007; 115(10): 1296–305. doi: 10.1161/circulationaha.106.618082.
77. Cheezum MK, Liberthson RR, Shah NR et al. Anomalous aortic origin of a coronary artery from the inappropriate sinus of Valsalva. *J Am Coll Cardiol* 2017; 69(12): 1592–608. doi: 10.1016/j.jacc.2017.01.031.
78. Wyman RA, Chiu RY, Rahko PS. The 5-minute screening echocardiogram for athletes. *J Am Soc Echocardiogr* 2008; 21(7): 786–8. doi: 10.1016/j.echo.2007.11.013.
79. Prakken NH, Cramer MJ, Olimulder MA et al. Screening for proximal coronary artery anomalies with 3-dimensional MR coronary angiography. *Int J Cardiovasc Imaging* 2010; 26(6): 701–10. doi: 10.1007/s10554-010-9617-0.
80. Pelliccia A, Spataro A, Maron BJ. Prospective echocardiographic screening for coronary artery anomalies in 1360 elite competitive athletes. *Am J Cardiol* 1993; 72(12): 978–9. doi: 10.1016/0002-9149(93)91120-7.
81. Angelini P. Novel imaging of coronary artery anomalies to assess their prevalence, the causes of clinical symptoms and the risk of sudden cardiac death. *Circ Cardiovasc Imaging* 2014; 7(4): 747–54. doi: 10.1161/circimaging.113.000278.
82. Yetman AT, Bornemeier RA, McCrindle BW. Long-term outcome in patients with Marfan syndrome: is aortic dissection the only cause of sudden death? *J Am Coll Cardiol* 2003; 41(2): 329–32. doi: 10.1016/S0735-1097(02)02699-2.
83. Maron BJ, Ackerman MJ, Nishimura RA et al. Task Force 4: HCM and other cardiomyopathies, mitral valve prolapse, myocarditis and Marfan syndrome. *J Am Coll Cardiol* 2005; 45(8): 1340–5. doi: 10.1016/j.jacc.2005.02.011.
84. Brooke BS, Habashi JP, Judge DP et al. Angiotensin II blockade and aortic-root dilation in Marfan's syndrome. *N Engl J Med* 2008; 358(26): 2787–95. doi: 10.1056/NEJ

Moa0706585.

85. Groenink M, Den Hartog AW, Franken R et al. Losartan reduces aortic dilatation rate in adults with Marfan syndrome: a randomised controlled trial. *Eur Heart J* 2013; 34(45): 3491–500. doi: 10.1093/eurheartj/eht334.
86. Forteza A, Evangelista A, Sánchez V et al. Efficacy of losartan vs. atenolol for the prevention of aortic dilation in Marfan syndrome: a randomised clinical trial. *Eur Heart J* 2016; 37(12): 978–85. doi: 10.1093/eurheartj/ehv575.
87. Kligfield P, Levy D, Devereux RB et al. Arrhythmias and sudden death in mitral valve prolapse. *Am Heart J* 1987; 113(5): 1298–307. doi: 10.1016/0002-8703(87)90958-6.
88. Basso C, Marra MP, Rizzo S. Arrhythmic mitral valve prolapse and sudden cardiac death. *Circulation* 2015; 132: 556–66. doi: 10.1161/circulationaha.115.016291.
89. Steriotis A, Krexi L, Plonczak A et al. Histopathological study of 62 sudden cardiac death victims with isolated mitral valve prolapse. *Heart* 2016; 102(Suppl 6):A112.2-A112. doi: 10.1136/heartjnl-2016-309890.155.
90. Behr E, Wood DA, Wright M et al. Cardiological assessment of first-degree relatives in sudden arrhythmic death syndrome. *Lancet* 2003; 362(9394): 1457–9. doi: 10.1016/S0140-6736(03)14692-2.
91. Hedley PL, Jørgensen P, Schlamowitz S et al. The genetic basis of long QT and short QT syndromes: a mutation update. *Hum Mutat* 2009; 30(11): 1486–511. doi: 10.1002/humu.21106.
92. Schwartz PJ, Priori SG, Spazzolini C et al. Genotype-phenotype correlation in the long-QT syndrome: gene-specific triggers for life-threatening arrhythmias. *Circulation* 2001; 103(1): 89–95. doi: 10.1161/01.cir.103.1.89.
93. Shattock MJ, Tipton MJ. 'Autonomic conflict': a different way to die during cold water immersion? *J Physiol* 2012; 590(14): 3219–30. doi: 10.1113/jphysiol.2012.229864.
94. Takenaka K, Ai T, Shimizu W et al. Exercise stress test amplifies genotype-phenotype correlation in the LQT1 and LQT2 forms of the long-QT syndrome. *Circulation* 2003; 107(6): 838–44. doi: 10.1161/01.cir.0000048142.85076.A2.
95. Basavarajaiah S, Wilson M, Whyte G et al. Prevalence and significance of an isolated long QT interval in elite athletes. *Eur Heart J* 2007; 28(23): 2944–9. doi: 10.1093/eurheartj/ehm404.
96. Sharma S, Drezner JA, Baggish A et al. International Recommendations for Electrocardiographic Interpretation in Athletes. *J Am Coll Cardiol* 2017; 69(8): 1057–75. doi: 10.1016/j.jacc.2017.01.015.
97. Schwartz PJ, Moss AJ, Vincent GM et al. Diagnostic criteria for the long QT syndrome: an update. *Circulation* 1993; 88(2): 782–4. doi: 10.1161/01.CIR.88.2.782.
98. Johnson JN, Ackerman MJ. QTc: how long is too long? *Br J Sports Med* 2009; 43(9): 657–62. doi: 10.1136/bjsm.2008.054734.
99. Priori SG, Blomström-Lundqvist C, Mazzanti A et al. 2015 ESC Guidelines for the

management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. *Eur Heart J* 2015; 36(41): 2793–867. doi: 10.1093/eurheartj/ehv316.

100. Hiss RG, Lamb LE. Electrocardiographic findings in 122 043 individuals. *Circulation* 1962; 25(6): 947–61. doi: 10.1161/01.CIR.25.6.947.
101. Rao AL, Salerno JC, Asif IM et al. Evaluation and management of Wolff–Parkinson–White in athletes. *Sports Health* 2014; 6(4): 326–32. doi: 10.1177/1941738113509059.
102. Pappone C, Santinelli V, Rosanio S et al. Usefulness of invasive electrophysiologic testing to stratify the risk of arrhythmic events in asymptomatic patients with Wolff–Parkinson–White pattern: results from a large prospective long-term follow-up study. *J Am Coll Cardiol* 2003; 41(2): 239–44. doi: 10.1016/S0735-1097(02)02706-7.
103. Brugada P, Brugada J. Right bundle branch block, persistent ST segment elevation and sudden cardiac death: a distinct clinical and electrocardiographic syndrome: a multicenter report. *J Am Coll Cardiol* 1992; 20(6): 1391–6. doi: 10.1016/0735-1097(92)90253-J.
104. Mizusawa Y, Wilde AAM. Brugada syndrome. *Circ Arrhythmia Electrophysiol* 2012; 5(3): 606–16. doi: 10.1161/circep.111.964577.
105. Corrado D, Basso C, Buja G et al. Right bundle branch block, right precordial ST-segment elevation and sudden death in young people. *Circulation* 2001; 103(5): 710–17. doi: 10.1161/01.cir.103.5.710.
106. Antzelevitch C, Brugada P, Borggrefe M et al. Brugada syndrome: Report of the Second Consensus Conference. *Circulation* 2005; 111(5): 659–70. doi: 10.1161/01.CIR.0000152479.54298.51.
107. Priori SG, Napolitano C, Memmi M et al. Clinical and molecular characterisation of patients with catecholaminergic polymorphic ventricular tachycardia. *Circulation* 2002; 106(1): 69–74. doi: 10.1161/01.CIR.0000020013.73106.D8.
108. Choi G, Kopplin LJ, Tester DJ et al. Spectrum and frequency of cardiac channel defects in swimming-triggered arrhythmia syndromes. *Circulation* 2004; 110(15): 2119–24. doi: 10.1161/01.CIR.0000144471.98080.CA.
109. Haugaa KH, Leren IS, Berge KE et al. High prevalence of exercise-induced arrhythmias in catecholaminergic polymorphic ventricular tachycardia mutation-positive family members diagnosed by cascade genetic screening. *Europace* 2010; 12(3): 417–23. doi: 10.1093/europace/eup448.
110. Basso C, Corrado D, Thiene G. Arrhythmogenic right ventricular cardiomyopathy in athletes: diagnosis, management and recommendations for sport activity. *Cardiol Clin* 2007; 25(3): 415–22. doi: 10.1016/j.ccl.2007.08.009.
111. Gati S, Sharma S, Pennell D. The role of cardiovascular magnetic resonance imaging in the assessment of highly trained athletes. *JACC Cardiovasc Imaging* 2018; 11(2): 247–59. doi: 10.1016/j.jcmg.2017.11.016.

112. Kindermann I, Kindermann M, Kandolf R et al. Predictors of outcome in patients with suspected myocarditis. *Circulation* 2008; 118(6): 639–48. doi: 10.1161/circulationaha.108.769489.
113. Mahrholdt H, Wagner A, Deluigi CC et al. Presentation, patterns of myocardial damage and clinical course of viral myocarditis. *Circulation* 2006; 114(15): 1581–90. doi: 10.1161/circulationaha.105.606509.
114. Caforio ALP, Calabrese F, Angelini A et al. A prospective study of biopsy-proven myocarditis: prognostic relevance of clinical and aetiopathogenetic features at diagnosis. *Eur Heart J* 2007; 28(11): 1326–33. doi: 10.1093/eurheartj/ehm076.
115. Gräni C, Eichhorn C, Bière L et al. Prognostic value of cardiac magnetic resonance tissue characterisation in risk stratifying patients with suspected myocarditis. *J Am Coll Cardiol* 2017; 70(16): 1964–76. doi: 10.1016/j.jacc.2017.08.050.
116. Grün S, Schumm J, Greulich S et al. Long-term follow-up of biopsy-proven viral myocarditis: predictors of mortality and incomplete recovery. *J Am Coll Cardiol* 2012; 59(18): 1604–15. doi: 10.1016/j.jacc.2012.01.007.
117. Aquaro GD, Perfetti M, Camastra G et al. Cardiac MR with late gadolinium enhancement in acute myocarditis with preserved systolic function: ITAMY Study. *J Am Coll Cardiol* 2017; 70(16): 1977–87. doi: 10.1016/j.jacc.2017.08.044.
118. Madias C, Maron BJ, Weinstock J et al. Commotio cordis sudden cardiac death with chest wall impact. *J Cardiovasc Electrophysiol* 2007; 18(1): 115–22. doi: 10.1111/j.1540-8167.2006.00684.x.
119. Classie JA, Distel LM, Borchers JR. Safety baseballs and chest protectors: a systematic review on the prevention of commotio cordis. *Phys Sportsmed* 2010; 38(1): 83–90. doi: 10.3810/psm.2010.04.1765.
120. Corrado D, Schmied C, Basso C et al. Risk of sports: do we need a pre-participation screening for competitive and leisure athletes? *Eur Heart J* 2011; 32(8): 934–44. doi: 10.1093/eurheartj/ehq482.
121. Papadakis M, Carre F, Kervio G et al. The prevalence, distribution and clinical outcomes of electrocardiographic repolarization patterns in male athletes of African/Afro-Caribbean origin. *Eur Heart J* 2011; 32(18): 2304–13. doi: 10.1093/eurheartj/ehr140.
122. Papadakis M, Basavarajaiah S, Rawlins J et al. Prevalence and significance of T-wave inversions in predominantly Caucasian adolescent athletes. *Eur Heart J* 2009;30(14): 1728–35. doi: 10.1093/eurheartj/ehp164.
123. Sharma S, Whyte G, Elliott P et al. Electrocardiographic changes in 1000 highly trained junior elite athletes. *Br J Sports Med* 1999; 33(5): 319–24. doi: 10.1136/bjsm.33.5.319.
124. Pelliccia A, Maron BJ, Spataro A et al. The upper limit of physiologic cardiac hypertrophy in highly trained elite athletes. *N Engl J Med* 1991; 324(5): 295–301. doi:

10.1056/nejm199101313240504.

125. Chan RH, Maron BJ, Olivotto I et al. Prognostic value of quantitative contrast-enhanced cardiovascular magnetic resonance for the evaluation of sudden death risk in patients with hypertrophic cardiomyopathy. *Circulation* 2014; 130(6): 484–95. doi: 10.1161/circulationaha.113.007094.
126. Wilson MG, Chandra N, Papadakis M et al. Hypertrophic cardiomyopathy and ultra-endurance running two incompatible entities? *J Cardiovasc Magn Reson* 2011; 13(1): 77. doi: 10.1186/1532-429X-13-77.
127. Bauce B, Frigo G, Benini G et al. Differences and similarities between arrhythmogenic right ventricular cardiomyopathy and athlete's heart adaptations. *Br J Sports Med* 2010; 44(2): 148–54. doi: 10.1136/bjsm.2007.042853.
128. Zaidi A, Ghani S, Sheikh N et al. Clinical significance of electrocardiographic right ventricular hypertrophy in athletes: comparison with arrhythmogenic right ventricular cardiomyopathy and pulmonary hypertension. *Eur Heart J* 2013; 34(47): 3649–56. doi: 10.1093/eurheartj/eht391.
129. Zaidi A, Sheikh N, Jongman JK et al. Clinical differentiation between physiological remodelling and arrhythmogenic right ventricular cardiomyopathy in athletes with marked electrocardiographic repolarization anomalies. *J Am Coll Cardiol* 2015; 65(25): 2702–11. doi: 10.1016/j.jacc.2015.04.035.
130. Magalski A, Maron BJ, Main ML et al. Relation of race to electrocardiographic patterns in elite American football players. *J Am Coll Cardiol* 2008; 51(23): 2250–5. doi: 10.1016/j.jacc.2008.01.065.
131. Sharma S, Chandra N, Papadakis M. Cardiac adaptations to intense physical exercise in African/Afro-Caribbean athletes. *e-journal ESC Counc Cardiol Pract* 2010; 8(35). https://www.escardio.org/Journals/E-Journal-of-Cardiology-Practice/Volume-8/Cardiac-adaptations-to-intense-physical-exercise-in-African-Afro-Caribbean-athle, accessed 23 January 2018.
132. Basavarajaiah S, Boraita A, Whyte G et al. Ethnic differences in left ventricular remodelling in highly-trained athletes: relevance to differentiating physiologic left ventricular hypertrophy from hypertrophic cardiomyopathy. *J Am Coll Cardiol* 2008; 51(23): 2256–62. doi: 10.1016/j.jacc.2007.12.061.
133. Schnell F, Riding N, O'Hanlon R et al. Recognition and significance of pathological T-wave inversions in athletes. *Circulation* 2014; 131(2): 165–73. doi: 10.1161/circulationaha.114.011038.
134. Rawlins J, Carre F, Kervio G et al. Ethnic differences in physiological cardiac adaptation to intense physical exercise in highly trained female athletes. *Circulation* 2010; 121(9): 1078–85. doi: 10.1161/circulationaha.109.917211.
135. Ahmed MA, Yousuf M, Syed AU et al. Isolated non-compaction of left ventricular myocardium. *J Coll Physicians Surg Pakistan* 2005; 15(5): 302–3. doi: 10.1161/01.CIR.82.

2.507.

136. Stöllberger C, Winkler-Dworak M, Blazek G et al. Prognosis of left ventricular hypertrabeculation/noncompaction is dependent on cardiac and neuromuscular comorbidity. *Int J Cardiol* 2007; 121(2): 189–93. doi: 10.1016/j.ijcard.2006.11.007.
137. Jenni R. Echocardiographic and pathoanatomical characteristics of isolated left ventricular non-compaction: a step towards classification as a distinct cardiomyopathy. *Heart* 2001; 86(6): 666–71. doi: 10.1136/heart.86.6.666.
138. Petersen SE, Selvanayagam JB, Wiesmann F et al. Left ventricular non-compaction: insights from cardiovascular magnetic resonance imaging. *J Am Coll Cardiol* 2005; 46(1): 101–5. doi: 10.1016/j.jacc.2005.03.045.
139. Jacquier A, Thuny F, Jop B et al. Measurement of trabeculated left ventricular mass using cardiac magnetic resonance imaging in the diagnosis of left ventricular non-compaction. *Eur Heart J* 2010; 31(9): 1098–104. doi: 10.1093/eurheartj/ehp595.
140. Kohli SK, Pantazis AA, Shah JS et al. Diagnosis of left-ventricular non-compaction in patients with left-ventricular systolic dysfunction: time for a reappraisal of diagnostic criteria? *Eur Heart J* 2008; 29(1): 89–95. doi: 10.1093/eurheartj/ehm481.
141. Gati S, Papadakis M, Van Niekerk N et al. Increased left ventricular trabeculation in individuals with sickle cell anaemia: physiology or pathology? *Int J Cardiol* 2013; 168(2): 1658–60. doi: 10.1016/j.ijcard.2013.03.039.
142. Gati S, Chandra N, Bennett RL et al. Increased left ventricular trabeculation in highly trained athletes: do we need more stringent criteria for the diagnosis of left ventricular non-compaction in athletes? *Heart* 2013; 99(6): 401–8. doi: 10.1136/heartjnl-2012-303418.
143. Ghani S, Papadakis M, Kemp S et al. Results of a nationally implemented de novo cardiac screening programme in elite rugby players in England. *Br J Sports Med* 2016; 50(21): 1338–44. doi: 10.1136/bjsports-2015-095902.
144. Maron BJ, Thompson PD, Ackerman MJ et al. Recommendations and Considerations Related to Preparticipation Screening for Cardiovascular Abnormalities in Competitive Athletes: 2007 Update A Scientific Statement from the American Heart Association Council on Nutrition, Physical Activity and Metabolism: Endorsed by the American College of Cardiology Foundation. *Circulation* 2007; 115(12): 1643–55. doi: 10.1161/circulationaha.107.181423.
145. Maron BJ, Zipes DP. Eligibility Recommendations for Competitive Athletes With Cardiovascular Abnormalities: Bethesda Conference 36. *J Am Coll Cardiol* 2005; 45(8): 1318–73. doi: 10.1016/j.jacc.2005.02.002.
146. Bernhardt DT, Roberts WO. *PPE: preparticipation physical evaluation*. American Academy of Pediatrics, May 2010. https://books.google.com/books?id=yZ-eQQAACAAJ, accessed 23 January 2018.
147. Wilson MG, Basavarajaiah S, Whyte GP et al. Efficacy of personal symptom and

family history questionnaires when screening for inherited cardiac pathologies: the role of electrocardiography. *Br J Sports Med* 2008; 42(3): 207–11. doi: 10.1136/bjsm.2007.039420.

148. Bessem B, Groot FP, Nieuwland W. The Lausanne Recommendations: a Dutch experience. *Br J Sports Med* 2009; 43(9): 708–15. doi: 10.1136/bjsm.2008.056929.
149. Baggish AL, Hutter AM Jr., Wang F et al. Cardiovascular screening in college athletes with and without electrocardiography: a cross-sectional study. *Ann Intern Med* 2010; 152(5): 269–75. doi: 10.7326/0003-4819-152-5-201003020-00004.
150. Carro Hevia A, Fernández MM, Palacio JMA et al. ECG as a part of the preparticipation screening programme: an old and still present international dilemma. *Br J Sports Med* 2011; 45(10): 776–9. doi: 10.1136/bjsm.2009.063958.
151. Sheikh N, Papadakis M, Ghani S et al. Comparison of electrocardiographic criteria for the detection of cardiac abnormalities in elite black and white athletes. *Circulation* 2014; 129(16): 1637–49. doi: 10.1161/circulationaha.113.006179.
152. Dhutia H, Malhotra A, Gabus V et al. Cost implications of using different ECG criteria for screening young athletes in the United Kingdom. *J Am Coll Cardiol* 2016; 68(7): 702–11. doi: 10.1016/j.jacc.2016.05.076.
153. Fuller CM, McNulty CM, Spring DA et al. Prospective screening of 5615 high school athletes for risk of sudden cardiac death. *Med Sci Sports Exerc* 1997; 29(9): 1131–8. doi: 10.1097/00005768-199709000-00003.
154. Fudge J, Harmon KG, Owens DS et al. Cardiovascular screening in adolescents and young adults: a prospective study comparing the Pre-participation Physical Evaluation monograph 4th edition and ECG. *Br J Sports Med* 2014; 48(15): 1172–8. doi: 10.1136/bjsports-2014-093840.
155. Drezner JA, Prutkin JM, Harmon KG et al. Cardiovascular screening in college athletes. *J Am Coll Cardiol* 2015; 65(21): 2353–5. doi: 10.1016/j.jacc.2015.02.072.
156. Drezner JA, Owens DS, Prutkin JM et al. Electrocardiographic screening in National Collegiate Athletic Association athletes. *Am J Cardiol* 2016; 118(5): 754–9. doi: 10.1016/j.amjcard.2016.06.004.
157. Harmon KG, Zigman M, Drezner JA. The effectiveness of screening history, physical exam and ECG to detect potentially lethal cardiac disorders in athletes: a systematic review/meta-analysis. *J Electrocardiol* 2015; 48(3): 329–38. doi: 10.1016/j.jelectrocard.2015.02.001.
158. Bille K, Figueiras D, Schamasch P et al. Sudden cardiac death in athletes: the Lausanne Recommendations. *Eur J Cardiovasc Prev Rehabil* 2006; 13(6): 859–75. doi: 10.1097/01.hjr.0000238397.50341.4a.
159. Dvorak J, Grimm K, Schmied C et al. Development and implementation of a standardised precompetition medical assessment of international elite football players 2006 FIFA World Cup Germany. *Clin J Sport Med* 2009; 19(4): 316–21. doi: 10.10

97/JSM.0b013e3181b21b6e.

160. Drezner JA, O'Connor FG, Harmon KG et al. AMSSM Position Statement on Cardiovascular Preparticipation Screening in Athletes: current evidence, knowledge gaps, recommendations and future directions. *Br J Sports Med* 2017; 51(3): 153–67. doi : 10.1136/bjsports-2016-096781.
161. Pelliccia A, Maron BJ, Culasso F et al. Clinical significance of abnormal electrocardiographic patterns in trained athletes. *Circulation* 2000; 102(3): 278–84. do i: 10.1161/01.CIR.102.3.278.
162. Viskin S, Rosovski U, Sands AJ et al. Inaccurate electrocardiographic interpretation of long QT: the majority of physicians cannot recognise a long QT when they see one. *Heart Rhythm* 2005; 2(6): 569–74. doi: 10.1016/j.hrthm.2005.02.011.
163. Gati S, Sheikh N, Ghani S et al. Should axis deviation or atrial enlargement be categorised as abnormal in young athletes? The athlete's electrocardiogram: time for re-appraisal of markers of pathology. *Eur Heart J* 2013; 34(47): 3641–8. doi: 10.109 3/eurheartj/eht390.
164. Brosnan M, La Gerche A, Kalman J et al. The Seattle Criteria increase the specificity of preparticipation ECG screening among elite athletes. *Br J Sports Med* 2014; 48(15): 1144–50. doi: 10.1136/bjsports-2013-092420.
165. Malhotra A, Dhutia H, Gati S et al. Anterior T-wave inversion in young white athletes and nonathletes: prevalence and significance. *J Am Coll Cardiol* 2017; 69(1): 1–9. doi: 10.1016/j.jacc.2016.10.044.
166. Corrado D, Biffi A, Basso C et al. 12-lead ECG in the athlete: physiological versus pathological abnormalities. *Br J Sports Med* 2009; 43(9): 669–76.
167. Corrado D, Pelliccia A, Heidbuchel H et al. Recommendations for interpretation of 12-lead electrocardiogram in the athlete. *Eur Heart J* 2010; 31: 243–59.
168. Dhutia H, Malhotra A, Finocchiaro G et al. Impact of the International Recommendations for Electrocardiographic Interpretation on Cardiovascular Screening in Young Athletes. *J Am Coll Cardiol* 2017; 70(6): 805–7. doi: 10.1016/j.jacc.2 017.06.018.
169. Waase MP, Mutharasan RK, Whang W et al. Electrocardiographic findings in National Basketball Association athletes. *JAMA Cardiol* 2018; 3(1): 69–74. doi: 10.1001/ jamacardio.2017.4572.
170. Riding NR, Sheikh N, Adamuz C et al. Comparison of three current sets of electrocardiographic interpretation criteria for use in screening athletes. *Heart* 2015; 101(5): 384–90. doi: 10.1136/heartjnl-2014-306437.
171. Pickham D, Zarafshar S, Sani D et al. Comparison of three ECG criteria for athlete pre-participation screening. *J Electrocardiol* 2014; 47(6): 769–74. doi: 10.1016/j.jelectr ocard.2014.07.019.
172. Berge HM, Gjesdal K, Andersen TE et al. Prevalence of abnormal ECGs in male soccer

players decreases with the Seattle Criteria, but is still high. *Scand J Med Sci Sport* 2015; 25(4): 501–8. doi: 10.1111/sms.12274.

173. Lahav D, Leshno M, Brezis M. Is an exercise tolerance test indicated before beginning regular exercise? A decision analysis. *J Gen Intern Med* 2009; 24(8): 934–8. doi: 10.1007/s11606-009-1029-2.
174. Merghani A, Maestrini V, Rosmini S et al. Prevalence of subclinical coronary artery disease in masters endurance athletes with a low atherosclerotic risk profile. *Circulation* 2017; 136(2): 126–37. doi: 10.1161/circulationaha.116.026964.
175. Maron BJ, Araujo CGS, Thompson PD et al. Recommendations for Preparticipation Screening and the Assessment of Cardiovascular Disease in Masters Athletes: an Advisory for Healthcare Professionals from the Working Groups of the World Heart Federation, the International Federation of Sports Medicine, and the American Heart Association Committee on Exercise, Cardiac Rehabilitation, and Prevention. *Circulation* 2001; 103(2): 327–34.
176. Borjesson M, Urhausen A, Kouidi E et al. Cardiovascular evaluation of middle-aged/senior individuals engaged in leisure-time sport activities: Position Stand from the Sections of Exercise Physiology and Sports Cardiology of the European Association of Cardiovascular Prevention and Rehabilitation. *Eur J Cardiovasc Prev Rehabil* 2011; 18(3): 446–58. doi: 10.1097/HJR.0b013e32833bo969.
177. Hecht H, Blaha MJ, Berman DS et al. Clinical indications for coronary artery calcium scoring in asymptomatic patients: Expert Consensus Statement from the Society of Cardiovascular Computed Tomography. *J Cardiovasc Comput Tomogr* 2017; 11(2): 157–68. doi: 10.1016/j.jcct.2017.02.010.
178. Carr JJ, Jacobs DR, Terry JG et al. Association of coronary artery calcium in adults aged 32 to 46 years with incident coronary heart disease and death. *JAMA Cardiol* 2017; 2(4): 391–9. doi: 10.1001/jamacardio.2016.5493.
179. Drezner JA, Rogers KJ. Sudden cardiac arrest in intercollegiate athletes: detailed analysis and outcomes of resuscitation in nine cases. *Heart Rhythm* 2006; 3(7): 755–9. doi: 10.1016/j.hrthm.2006.03.023.
180. Ruppert M, Reith MW, Widmann JH et al. Checking for breathing: evaluation of the diagnostic capability of emergency medical services personnel, physicians, medical students and medical laypersons. *Ann Emerg Med* 1999; 34(6): 720–9. doi: 10.1016/S0196-0644(99)70097-1.
181. American Heart Association. Part 4: Adult Basic Life Support. *Circulation* 2005; 112(24 Suppl):IV-19–34. doi: 10.1161/circulationaha.105.166553.
182. Hallstrom AP, Ornato JP, Weisfeldt M et al. Public-access defibrillation and survival after out-of-hospital cardiac arrest. *N Engl J Med* 2004; 351(7): 637–46. doi: 10.1056/NEJMoa040566.
183. American Heart Association. Part 4: The Automated External Defibrillator: Key Link

in the Chain of Survival. *Resuscitation* 2000; 46(1–3):73–91. doi: 10.1016/S0300-9572(00)00272-0.

184. Andersen JC, Courson RW, Kleiner DM et al. National Athletic Trainers' Association Position Statement: Emergency Planning in Athletics. *J Athl Train* 2002; 37(1): 99–104.
185. Drezner JA, Courson RW, Roberts WO et al. Inter-Association Task Force Recommendations on Emergency Preparedness and Management of Sudden Cardiac Arrest in High School and College Athletic Programs: A Consensus Statement. *J Athl Train* 2007; 42: 143–58. doi: 10.1097/JSM.0b013e3180415466.
186. Hazinski MF, Markenson D, Neish S et al. Response to Cardiac Arrest and Selected Life-Threatening Medical Emergencies: the Medical Emergency Response Plan for Schools: A Statement for Healthcare Providers, Policymakers, School Administrators and Community Leaders. *Circulation* 2004; 109(2): 278–91. doi: 10.1161/01.CIR.0000109486.45545.AD.
187. Myerburg RJ, Estes NAM, Fontaine JM et al. Task Force 10: Automated External Defibrillators. *J Am Coll Cardiol* 2005; 45(8): 1369–71. doi: 10.1016/j.jacc.2005.02.017.
188. Casa DJ, Almquist J, Anderson SA et al. The Inter-Association Task Force for Preventing Sudden Death in Secondary School Athletics Programs: Best-Practices Recommendations. *J Athl Train* 2013; 48(4): 546–53. doi: 10.4085/1062-6050-48.4.12.
189. White RD, Russell JK. Refibrillation, resuscitation and survival in out-of-hospital sudden cardiac arrest victims treated with biphasic automated external defibrillators. *Resuscitation* 2002; 55(1): 17–23. doi: 10.1016/S0300-9572(02)00194-6.
190. Berg MD, Clark LL, Valenzuela TD et al. Post-shock chest compression delays with automated external defibrillator use. *Resuscitation* 2005; 64(3): 287–91. doi: 10.1016/j.resuscitation.2004.07.017.
191. Carpenter J, Rea TD, Murray JA et al. Defibrillation waveform and post-shock rhythm in out-of-hospital ventricular fibrillation cardiac arrest. *Resuscitation* 2003; 59(2): 189–96. doi: 10.1016/S0300-9572(03)00183-7.
192. Herlitz J, Ekström L, Wennerblom B et al. Effect of bystander initiated cardiopulmonary resuscitation on ventricular fibrillation and survival after witnessed cardiac arrest outside hospital. *Br Heart J* 1994; 72(5): 408–12.
193. Stiell IG, Nichol G, Wells G et al. Health-related quality of life is better for cardiac arrest survivors who received citizen cardiopulmonary resuscitation. *Circulation* 2003; 108(16): 1939–44. doi: 10.1161/01.CIR.0000095028.95929.B0.
194. Wik L. Quality of cardiopulmonary resuscitation during out-of-hospital cardiac arrest. *JAMA* 2005; 293(3): 299. doi: 10.1001/jama.293.3.299.
195. Rea TD, Fahrenbruch C, Culley L et al. CPR with chest compression alone or with rescue breathing. *N Engl J Med* 2010; 363(5): 423–33. doi: 10.1056/NEJMoa0908993.
196. Field JM, Hazinski MF, Sayre MR et al. Part 1: Executive Summary: 2010 American

Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation* 2010; 122(18 Suppl 3):S640–56. doi: 10.1161/circulationaha.110.970889.

197. Travers AH, Rea TD, Bobrow BJ et al. Part 4: CPR Overview: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation* 2010; 122(18 Suppl 3):S676–84. doi: 10.1161/circulationaha.110.970913.
198. Hazinski MF, Nolan JP, Billi JE et al. Part 1: Executive Summary: 2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations. *Circulation* 2010; 122(16 Suppl 2):S250–75. doi: 10.1161/circulationaha.110.970897.
199. Becker LB, Ostrander MP, Barrett J et al. Outcome of CPR in a large metropolitan area where are the survivors? *Ann Emerg Med* 1991; 20(4): 355–61. doi: 10.1016/S0196-0644(05)81654-3.
200. Gallagher EJ, Lombardi G, Gennis P. Effectiveness of bystander cardiopulmonary resuscitation and survival following out-of-hospital cardiac arrest. *JAMA* 1995; 274(24): 1922–5. doi: 10.1001/jama.1995.03530240032036.
201. Bobrow BJ. Minimally interrupted cardiac resuscitation by emergency medical services for out-of-hospital cardiac arrest. *JAMA* 2008; 299(10): 1158. doi: 10.1001/jama.299.10.1158.
202. Graham R, McCoy MA, Schultz AM. *Strategies to improve cardiac arrest survival: a time to act*. Washington, DC: National Academies Press, 2015. doi: 10.17226/21723.
203. Drezner JA, Chun JSDY, Harmon KG et al. Survival trends in the United States following exercise-related sudden cardiac arrest in the youth: 2000–2006. *Heart Rhythm* 2008; 5(6): 794–9. doi: 10.1016/j.hrthm.2008.03.001.
204. Caffrey SL, Willoughby PJ, Pepe PE et al. Public use of automated external defibrillators. *N Engl J Med* 2002; 347(16): 1242–7. doi: 10.1056/NEJMoa020932.
205. Page RL, Joglar JA, Kowal RC et al. Use of automated external defibrillators by a US airline. *N Engl J Med* 2000; 343(17): 1210–16. doi: 10.1056/NEJM200010263431702.
206. Valenzuela TD, Roe DJ, Nichol G et al. Outcomes of rapid defibrillation by security officers after cardiac arrest in casinos. *N Engl J Med* 2000; 343(17): 1206–9. doi: 10.1056/nejm200010263431701.
207. Weaver WD, Hill D, Fahrenbruch CE et al. Use of the automatic external defibrillator in the management of out-of-hospital cardiac arrest. *N Engl J Med* 1988; 319(11): 661–6. doi: 10.1056/NEJM198809153191101.
208. White RD, Asplin BR, Bugliosi TF et al. High discharge survival rate after out-of-hospital ventricular fibrillation with rapid defibrillation by police and paramedics. *Ann Emerg Med* 1996; 28(5): 480–5. doi: 10.1016/S0196-0644(96)70109-9.
209. Myerburg RJ, Fenster J, Velez M et al. Impact of community-wide police car

deployment of automated external defibrillators on survival from out-of-hospital cardiac arrest. *Circulation* 2002; 106(9): 1058–64. doi: 10.1161/01.cir.0000028147.92190.A7.

210. White RD, Bunch TJ, Hankins DG. Evolution of a community-wide early defibrillation programme: experience over 13 years using police/fire personnel and paramedics as responders. *Resuscitation* 2005; 65(3): 279–83. doi: 10.1016/j.resuscitation.2004.10.018.
211. Kim F, Carlbom D. Therapeutic hypothermia for cardiac arrest: yes, we can. *Rev Española Cardiol* (English ed.) 2009; 62(7): 726–8. doi: 10.1016/S1885-5857(09)72351-5.
212. Coris EE, Miller E, Sahebzamani F. Sudden cardiac death in Division I collegiate athletics: analysis of automated external defibrillator utilisation in National Collegiate Athletic Association Division I athletic programs. *Clin J Sport Med* 2005; 15(2): 87–91. doi: 10.1097/01.jsm.0000152715.12721.fa.

Chapter 10

Cardiovascular symptoms

with ANDRE LA GERCHE and JONATHAN DREZNER

Once you're into the race, your heart isn't in rhythm, oxygen is running out and you lose power and become weaker and weaker as the race goes on. It feels like you're dragging something behind the boat.
Nathan Cohen, Olympic double sculls rowing gold medallist, London 2012

As discussed in Chapter 9, sudden cardiac death is the leading cause of death in young athletes during sport and is typically the result of undiagnosed structural or electrical cardiovascular disease.[1–4] Some athletes present with symptoms that can alert the clinician to underlying cardiac pathologies. However, identifying the athlete with symptoms representing a sinister pathological condition can be extremely difficult. For example, syncope during exercise is an important 'red flag' symptom, yet for athletes suffering these events, a benign explanation is far more likely. This chapter will provide a logical framework for working through these difficult clinical scenarios. We will discuss symptoms and clinical signs that can indicate serious pathology, as well as commonly encountered symptoms that may not represent a serious disorder.

In this chapter we:

- discuss the management of five key symptoms:
  - syncope and exercise-related collapse
  - syncope mimics (e.g. seizure and exertional collapse)
  - exertional chest pain
  - palpitations
  - excessive fatigue/dyspnoea
- discuss physical examination findings that may be relevant to cardiovascular health
- provide an overview of contemporary investigations for cardiovascular disease, which include electrocardiography, cardiac imaging (echocardiography, cardiac magnetic resonance and CT coronary angiography) and, occasionally, specialised investigations such as electrophysiological

studies and genetic testing
- discuss the approach to temporary and permanent disqualification from sport because of cardiac diagnoses.

Abbreviations used in this chapter

ARVC	Arrhythmogenic right ventricular cardiomyopathy
CCAA	Congenital coronary artery anomaly
CPVT	Catecholaminergic polymorphic ventricular tachycardia
CT	Computed tomography
DCM	Dilated cardiomyopathy
ECG	Electrocardiogram
HCM	Hypertrophic cardiomyopathy
LQTS	Long QT syndrome
CMR	Cardiac magnetic resonance

PUTTING THINGS INTO PERSPECTIVE: SUDDEN DEATH AND THE PREVALENCE OF LIFE THREATENING CONDITIONS

The incidence of sudden death in young athletes (=35 years) is 0.6–3.6 per 100 000 athletes per year and the majority of deaths are due to cardiovascular causes.[1, 2, 5–8] For reasons that remain unexplained, the risk is approximately 3- to 10-fold greater among males than females and is higher among competitive athletes than non-athletes.[5, 7, 9] Although considerable attention has focused on young athletes, the risk of sudden cardiac death is considerably higher among athletes older than 35 years of age.[7, 10] In general, inherited cardiomyopathies are the most frequent identified cause of sudden cardiac death in young athletes, while acquired heart disease, principally coronary artery disease, is most frequent in athletes of middle age and older.[1, 5, 7, 11–13] However, there is considerable overlap, particularly among 30–50-year-old athletes, and it may also be that the incidence of inherited cardiomyopathies is underestimated in this group as autopsies are not common and coronary disease causation more frequently presumed. Each of the conditions predisposing to sudden cardiac death should be considered in potential screening strategies for a 36-year-old marathon runner evaluation (Fig. 10.1).

The causes of sudden cardiac death vary with age

It can be anticipated that three athletes per thousand will have an underlying cardiac condition that places them at risk of a life-threatening event.[15, 16] The most common inherited or congenital pathologies associated with sudden cardiac death in young people are hypertrophic cardiomyopathy (prevalence ~0.05–0.2%),[17–19] anomalous coronary arteries (~0.2%),[20] arrhythmogenic right ventricular cardiomyopathy (~0.1%)[21] and ion channel disorders (~0.007–0.2%),[19, 22] These

prevalence estimates, derived from unselected populations, may be higher than among athletes in which a 'healthy cohort' effect is likely. This term refers to the phenomenon that in the setting of competitive sport, many individuals with underlying cardiovascular disease have chosen to drop out because their performance is limited by the pathology. For acquired heart disease, approximately 0.5% of an asymptomatic population with a median age of 51 years was identified as having significant coronary artery disease,[23] but, again, this probably overstates the risk in asymptomatic athletes with well-controlled coronary risk factors.

https://www.sciencedirect.com. Due to rights and permissions restrictions, this content cannot be reproduced in a digital format. The content is available in the print edition at page 144.

Figure 10.1 Age-dependent changes in incidence and aetiology of sudden cardiac death. This figure summarises studies that assessed the causes of sudden cardiac death in athletes.1, 5–7, 11–14 The majority of deaths may be attributed to inherited cardiomyopathies and channelopathies in those aged <30 years but there is no absolute cut-off. Thus, athletes aged in their 30s and 40s (the median age in many competitive sports) are at greatest risk of sudden cardiac death caused by inherited and acquired causes.

ADAPTED FROM JACC: CARDIOVASCULAR IMAGING, 6, LA GERCHE A, BAGGISH AL, KNUUTI J ET AL. CARDIAC IMAGING AND STRESS TESTING ASYMPTOMATIC ATHLETES TO IDENTIFY THOSE AT RISK OF SUDDEN CARDIAC DEATH, 993-1007, 2013, WITH PERMISSION FROM ELSEVIER

CARDIOVASCULAR SYMPTOMS: POTENTIALLY LIFE OR DEATH DECISIONS

A critical part of the care of the athlete is being alert to symptoms that raise the possibility of cardiac pathology. However, symptoms are neither sensitive nor specific.[24] For example, in studies, only 21% of athletes who died from HCM[25] and 44% of athletes who died of a CCAA[26] had any signs or symptoms of cardiovascular disease prior to death. Similarly only 10–20% of autopsy-negative sudden unexplained deaths had previous symptoms.[27, 28] In some conditions, such as ARVC, CPVT and LQTS, symptoms are more likely to present prior to a catastrophic event. Note that these conditions may first present with symptoms that can be discovered during pre-participation screening. The absence of symptoms does not exclude these conditions, but it does influence diagnostic probabilities and subsequent management. Symptoms such as palpitations, near-syncope, syncope and unexplained seizure activity, especially when triggered by physical exertion, should be carefully investigated given they may signal a serious disorder and flag a life-threatening event (Table 10.1). However, it also must be recognised that even these warning symptoms are statistically more likely to represent a benign condition in the young athlete.[29]

Table 10.1 Symptoms associated with certain cardiac ion channel disorders

Disorder	Trigger	Clinical event
LQTS-1	Emotional stress, physical exercise, swimming and diving into water	Syncope, sudden death, seizure-like activity, drowning or near-drowning, motor vehicle accident
LQTS-2	Emotional stress, physical exercise, loud noises	Syncope, sudden death, seizure-like activity, motor vehicle accident
LQTS-3	Rest or sleep	Sudden death or sudden infant death
CPVT	Emotional stress, physical exercise	Syncope, sudden death, seizure-like activity, drowning or near-drowning

In the general athletic population, cardiovascular symptoms are uncommon. Although more frequent (up to 33%) when ascertained during a pre-participation screening questionnaire,[30–35] it is unclear whether symptoms provoked by a questionnaire are as predictive as an unprovoked self-report. It is evident that the sensitivity of cardiovascular symptoms identified during screening as a predictor of potentially lethal cardiovascular disease remains low (approximately 20%).[36] This inefficiency may be unavoidable given that serious cardiovascular disorders are relatively uncommon in athletes and cardiovascular symptoms overlap with the normal physical sensations experienced by individuals during intense exercise. However, it remains critical that symptoms are carefully explored and afforded due attention.

Cardiovascular symptoms in athletes also may be misinterpreted or disregarded by medical providers. A 1996 report summarised nine publications detailing 469 sudden deaths from cardiac causes in young persons.[37] These studies collectively reported preceding symptoms of dizziness, chest pain, syncope, palpitations, dyspnoea or a family history of sudden death from a cardiac cause in 25–61% of their study populations.[37] In a Swedish cohort of 15–35-year-olds having suffered sudden cardiac death, investigators reported that 92 of 162 (57%) individuals had preceding symptoms that were often misinterpreted.[38] In 20 of 21 patients found to have CPVT, syncope was found to be a presenting symptom, although the diagnosis of CPVT was generally delayed due to the misdiagnosis of epilepsy or vasovagal events.[39] Up to 20% of patients who have LQTS and present with syncope (but are not diagnosed and treated) will experience sudden death in the first year after their syncope and 50% will suffer sudden cardiac death by 5 years.[40]

PRACTICE PEARL

Warning symptoms such as exercise-related syncope must be carefully evaluated to rule out potentially lethal cardiac disorders.

CLINICAL APPROACH TO SYMPTOMS THAT MAY BE ASSOCIATED WITH IMPORTANT CARDIAC PATHOLOGY

Before addressing each of the critical cardiovascular symptoms that clinicians need to evaluate, we review which symptoms to ask about in the clinical assessment. Patients often fail to volunteer cardiac symptoms, so some symptoms need to be raised specifically.

Other questions regarding cardiovascular risks include current or past illicit drug use, ergogenic supplement use (i.e. anabolic steroids, human growth hormone and stimulants) and a recent acute viral syndrome (risk of myocarditis). In older patients (>35 years), risk factors for coronary artery atherosclerosis such as hypertension, diabetes, hyperlipidaemia, tobacco use or a family history of premature atherosclerotic disease should be investigated.

Page 146

Specific questions to ask during cardiovascular screening

Ask if there has been any:

- exertional chest pain/discomfort that makes you stop exercise
- passing out or nearly passing out during exercise (syncope/near-syncope)
- palpitations, heart racing or irregular pulse
- excessive exertional or unexplained shortness of breath (dyspnoea), or fatigue associated with exercise
- unexplained heart murmur
- history of elevated systemic blood pressure
- family history of sudden cardiac arrest or sudden cardiac death in a relative <40 years of age
- family history of a genetic heart condition, unexplained sudden death or collapse.

In the following sections we outline the clinical approach to common cardiovascular symptoms —syncope and exercise-related collapse, syncope mimics (seizures and collapse), exertional chest pain, palpitations and excessive fatigue/dyspnoea (Table 10.2). Later in the chapter we consider the red flag of family history of early sudden cardiac death.

Table 10.2 Associated disorders and recommended evaluation in athletes with cardiovascular symptoms

Symptom	Potential cardiac disorders	Evaluation and testing to consider
Syncope/near-syncope during exercise (including secondary seizure activity)	Cardiomyopathy (HCM, ARVC, DCM, LVNC)	ECG, echocardiography, consider CMR to evaluate cardiac morphology and presence of late gadolinium enhancement that indicates myocardial fibrosis
	Congenital coronary artery anomalies (CCAAs)	Echocardiography, consider cardiac CT or CMR if coronary artery origins not well visualised
	Ion channel disorders (LQTS, CPVT, Brugada syndrome)	ECG, stress ECG, ambulatory monitoring
Exertional chest pain	Coronary artery atherosclerosis	ECG, stress ECG

	Congenital coronary artery anomalies	Echocardiography, consider cardiac CT or CMR if coronary artery origins not well visualised
	Cardiomyopathy	ECG, echocardiography, consider CMR
Palpitations	Supraventricular tachyarrhythmias, ventricular arrhythmias, premature atrial and ventricular contractions, sinus tachycardia, ventricular pre-excitation, cardiomyopathies and ion channel disorders	ECG, echocardiography, stress ECG, ambulatory ECG monitoring, consultation with electrophysiologist
Excessive dyspnoea/fatigue during exercise	Cardiomyopathy, myocarditis	ECG, echocardiography, stress ECG, consider pulmonary function testing

ARVC = arrhythmogenic right ventricular cardiomyopathy; CPVT = catecholaminergic polymorphic ventricular tachycardia; ECG = electrocardiogram; HCM = hypertrophic cardiomyopathy; LQTS = long QT syndrome; LVNC = left ventricular non-compaction

Syncope/near-syncope

Syncope is common in young individuals, including athletes. The lifetime prevalence of syncope approaches 40–50%.[41, 42] In a cohort of 7568 young athletes undergoing screening, 474 athletes (6.2%) reported a syncopal episode in the preceding 5 years.[29] Of these 474 athletes, only 6 (1.3%) experienced syncope during exercise, and structural heart disease (hypertrophic cardiomyopathy) was diagnosed in one athlete. Neurally mediated syncope was diagnosed in all cases of non-exertional syncope and in 4 of the 6 athletes with exertional syncope. Thus, although syncope is frequently a frightening symptom for the athlete and observers, it is benign in the vast majority of cases. The athlete with syncope during exercise raises more concern and should be carefully investigated, *but the outcome is still more likely to be benign.*

The diagnostic work-up of exertional syncope is usually performed in consultation with a cardiologist and should include ECG, echocardiogram, stress ECG or exercise echocardiography and possibly advanced cardiac imaging, such as CMR or CT coronary angiography to rule out rare structural abnormalities (such as ARVC and CCAAs) that are associated with syncope. If all of these studies are normal, prolonged monitoring with an external ambulatory monitor should be considered. A small percentage of individuals may even require an implantable loop monitor. The specific cardiac causes of syncope and near-syncope (also called 'pre-syncope') are discussed below.

Neurally mediated syncope (vasovagal syncope)

The most common cause of syncope or near-syncope is neurally mediated syncope, also known as neurocardiogenic or vasovagal syncope.[43] Neurally mediated syncope is more common in female athletes and the incidence tends to peak in adolescence. Frequently symptoms usually lessen or resolve by age 30–40 years.

The diagnosis of neurally mediated syncope is based on the clinical history. Careful questioning is critical to avoid unnecessary testing and to provide important reassurance. Neurally mediated syncope is often triggered by certain events such as fear, pain, excitement, venepuncture or prolonged standing. It nearly always occurs while the patient is standing. It is unusual for this type

of syncope to occur with sitting and rarely occurs while lying down.

Premonitory symptoms are common and include lightheadedness, dizziness, flushing, nausea, tunnel vision and profuse sweating. The individual often slumps to the ground before completely losing consciousness and, therefore, is usually able to avoid injury. Onlookers often describe the person as appearing pale and clammy immediately prior to losing consciousness. Once the individual is on the ground, blood flow is restored to the brain, so typically the syncope episodes are short-lived, although brief seizure-like activity is not uncommon. Following the episode individuals often have a prolonged period of nausea and fatigue and occasionally individuals may feel ill until they have had some sleep.

Post-exertional syncope

Post-exertional syncope, occurring while standing in a huddle or at the finish line, is typically neurally mediated (see also Chapter 38 for more on the management of exercise-associated collapse).[44–47] Exercise-associated collapse, commonly observed at endurance events, refers to athletes who are unable to stand or walk unaided after exertion because of weakness, lightheadedness, faintness or dizziness.[48]

During exercise, increases in heart rate and stroke volume result in a substantial rise in cardiac output and offset the diminished systemic vascular resistance from vasodilatation to exercising muscles. After exercise, without the muscular activity (muscle pump) to maintain venous return, cardiac filling may reduce dramatically. It is postulated that forceful ventricular contractions against a diminished ventricular volume excessively stimulate ventricular mechanoreceptors, causing reflex vasodilatation and bradycardia, and subsequent hypotension and possibly syncope.[49]

Adverse effects from anti-hypertensive medications such as diuretics and beta blockers may also cause syncope in older individuals.

Exertional syncope

Syncope occurring during exercise is a red flag symptom and should raise concern. Exertional syncope can occur because of outflow obstruction (e.g. in HCM or aortic stenosis) or arrhythmias. Exercise can trigger arrhythmias in individuals with an underlying pathological substrate such as ARVC, HCM, CPVT and LQTS (conditions that were reviewed in Chapter 9). Syncope associated with exertional outflow obstruction invariably occurs during intense exercise. Typically, symptoms progress from a brief period of lightheadedness to syncope if exercise continues.

Syncope caused by arrhythmic disorders often occurs during exertion (not post exertion) with abrupt loss of consciousness or only a very brief period of lightheadedness prior to the syncope. Secondary injury is common as individuals are unconscious before they hit the ground and, therefore, cannot protect their heads.

Syncope due to a ventricular arrhythmia (such as ventricular tachycardia or ventricular fibrillation) is a life-threatening event. In approximately half of athletes with sudden cardiac arrest, syncope is followed by brief seizure-like activity.[50, 51] In some cases, the ventricular arrhythmia self-terminates and the individual regains consciousness, usually within seconds of

collapse.

Prolonged syncope should be treated as a sudden cardiac arrest.

PRACTICE PEARL

Syncope during exercise is frequently related to a cardiac condition and it should therefore be thoroughly investigated. Post-exertional syncope is usually benign.

Syncope mimics—seizures and collapse

Some common conditions mimic syncope and should be considered in the differential diagnosis.

Unexplained seizure activity

Seizures can be difficult to distinguish from syncope. Myoclonic movements caused by cerebral hypoperfusion can mimic true seizures. The clinical difference between the two is that if cerebral hypoperfusion is causing the myoclonic movements, the individual would faint first and seconds later the involuntary body movements would start, whereas with a true seizure the myoclonic movements would begin concurrently with the loss of postural tone and consciousness (see *Clinical Sports Medicine Volume 1: Injuries*—Chapter 20).[52] In addition, seizure patients may have an aura prior to the episode (not to be confused with tunnel vision, which is seen in cerebral hypoperfusion) and are postictal after the episodes.

The postictal state is characterised by prolonged confusion, whereas in syncope there may be only brief confusion about what occurred. Patients suffering neurally mediated syncope are often profoundly fatigued after the event. Tongue biting, incontinence and injury are not sufficiently specific to aid in the differential diagnosis of most patients.

Any patient with an unexplained seizure episode should also have a cardiovascular work-up, including at minimum a 12-lead ECG and an echocardiogram, and possibly an exercise ECG test. In individuals who have classic seizures and a confirmatory encephalogram, the cardiac work-up may be limited; however, if there is still any doubt, then long-term cardiac monitoring should be performed in order to ensure that arrhythmias are not triggering the seizure activity.

Exertional collapse

Collapse is an important differential diagnosis that can be confused with true syncope. It is characterised by a *more gradual onset* of an altered conscious state caused most commonly by heat-related illness or hyponatraemia. While beyond the scope of the current chapter, these are potentially life-threatening conditions when severe. Typically heat stroke is associated with progressive agitation and delirium, progressing quite rapidly to haemodynamic instability and multi-organ failure. It is diagnosed as a core temperature exceeding 104°F or 40°C in combination with neurocognitive changes, and should be treated with rapid cooling and supportive care. It is

reported as one of the major causes of death in sporting events.[53] Hyponatraemia is associated with ingestion of excessive amounts of water during endurance sporting events, resulting in fatigue, drowsiness and obtundation if sufficiently severe. Both conditions are considered in greater depth in Chapter 23.

Exertional chest pain

Chest pain, discomfort or tightness is common in exercising individuals of all ages and is often a normal sensation during intense exertion, but may be secondary to cardiac, pulmonary or musculoskeletal processes.

PRACTICE PEARL

Chest pain with exertion, particularly if it is severe enough to cause an individual to stop exercising, is an important symptom that may reflect an underlying cardiovascular disorder.

Diseases such as CCAA, myocarditis, HCM, DCM and atherosclerotic coronary disease often present with chest pain that is 'dull' or 'pressing' in nature and is usually exertional and relieved by rest.

Chest pain that is pleuritic (increases with deep inspiration) may be due to pericarditis, but this is not a typical finding. In most cases, pleuritic chest pain is secondary to musculoskeletal syndromes or pulmonary conditions such as pulmonary embolism or pneumonia, which are unusual in the young athlete.

Investigating exertional chest pain

Any young athlete with exertional chest pain should be evaluated for the presence of CCAA and HCM. An ECG and transthoracic echocardiogram (Table 10.3) are usually sufficient to rule out HCM, but in some cases cannot be relied on to rule out apical HCM or anomalous coronary arteries. Cardiac magnetic resonance has a high sensitivity and specificity for anomalous coronary arteries and should be undertaken when there is a question of anomalous coronary arteries.

Older athletes with exertional chest pain should undergo cardiac stress testing to evaluate for ischaemic heart disease.

Palpitations

Palpitations are common in young individuals and in many cases are secondary to sinus tachycardia or not related to a cardiac process at all. Palpitations also may be due to supraventricular tachycardias or ventricular tachycardias.

PRACTICE PEARL

Palpitations that come on suddenly, or that are associated with other symptoms such as light-headedness, chest pain or dyspnoea, require expert cardiac evaluation to exclude a potentially lethal cardiac disorder.

Investigating palpitations

The only method to truly diagnose the cause of palpitations is to capture an ECG while the patient is having symptoms. Typically, this requires ambulatory monitoring and a stress test. In general, ambulatory monitoring should be undertaken in individuals with palpitations unless they are so benign as to be barely noticeable.

Treatment of palpitations

Supraventricular tachycardias are not generally associated with sudden cardiac death, but usually need to be treated. Treatment may consist of abortive manoeuvres such as Valsalva, preventive measures such as beta blockers or calcium channel blockers, or curative measures such as radiofrequency ablation.

Referral to a cardiologist should be considered when symptoms interfere with the patient's quality of life.

Ventricular arrhythmias are more concerning and are associated with syncope, severe lightheadedness, and sudden death. Patients require referral to a cardiologist.

Excessive fatigue or dyspnoea with exertion

Fatigue is expected with sports, but excessive fatigue or dyspnoea on exertion is unusual. A helpful method to assess these symptoms is to compare current symptoms to an individual's previous energy level, or to compare the athlete to his or her peers of a similar conditioning level.

Fatigue is rarely a cardiac symptom but can be seen with dilated cardiomyopathies. Excessive fatigue or dyspnoea on exertion is especially troubling if of recent onset or worsening with time. Excessive fatigue following a viral syndrome may suggest myocarditis.

Dyspnoea on exertion can be seen with heart diseases such as HCM, aortic stenosis, subaortic membranes and dilated cardiomyopathies. It can also be seen in individuals with congenital heart block or acquired heart block such as that observed in Lyme disease.

Investigating exertional fatigue

The evaluation of patients with exertional fatigue and dyspnoea includes an ECG, echocardiography, and laboratory studies to exclude medical causes such as anaemia. In some circumstances, stress ECG, cardiopulmonary exercise testing or pulmonary function tests may be indicated.

PHYSICAL EXAMINATION FINDINGS IN SPORTS CARDIOLOGY—GUIDE TO THE CLINICAL APPROACH

The physical examination is rarely as illuminating as the history. Most cardiac diseases that place

the athlete at risk for sudden cardiac death are not associated with an abnormal physical examination. An exception is a systolic ejection murmur of the left ventricular outflow tract, which can be due to HCM, subaortic membranes or bicuspid aortic valve with stenosis. Murmurs are absent in the vast minority of individuals with HCM because at rest only one-quarter of individuals with HCM have outflow tract obstruction; however, with exertion about half may develop obstruction.[54]

Other important aspects of the physical examination include recognising the physical stigmata of Marfan syndrome (Chapter 9), such as a high-arched palate, arachnodactyly (long, slender fingers), hyperlaxity, tall height and a long arm/wing span.

Screening for hypertension and assessing for coarctation of the aorta with right and left blood pressure measurements and femoral artery palpation are also important aspects of the examination.

Patients with HCM, ARVC, DCM, LQTS, CPVT, ventricular pre-excitation, and Brugada syndrome generally have normal physical examinations. These conditions cannot be ruled out by physical examination alone.

See the box for an indication of which patients should be referred to a cardiologist.

When should patients be referred to a cardiologist?

Patients should be referred for concerning symptoms and findings on examination.

In patients with syncope, if the symptoms are classic for neurally mediated syncope (i.e. presence of prodromal symptoms prior to syncope) and a resting ECG is normal, the patient does not need referral to a specialist.

However, in patients with syncope that is unexplained or concerning (i.e. syncope during exercise), referral to a cardiologist is indicated.

Patients with exertional syncope require a comprehensive cardiac evaluation and typically should be referred, even if there are no findings on preliminary work-up.

Exertional chest pain that makes an athlete stop exercising or with features of ischaemic heart disease needs an extensive evaluation.

Palpitations can generally be diagnosed by prolonged ambulatory monitoring:

- If the prolonged ambulatory monitoring captures an event and shows that the symptoms are not associated with supraventricular or ventricular arrhythmias, then, in general, no referral is needed and reassurance is warranted.
- However, if palpitations are due to premature ventricular contractions, supraventricular tachycardias or ventricular tachycardias, referral to a cardiologist is warranted.
- Occasionally, even patients with atrial premature beats will require cardiology referral, even though atrial premature beats are typically benign.

Excessive fatigue or dyspnoea on exertion is equally likely to be non-cardiac in aetiology. A resting ECG and echocardiogram is reasonable to exclude HCM or DCM. Patients also may require a work-up for anaemia, asthma or other medical causes of fatigue and dyspnoea as indicated.

SPECIFIC PHYSICAL EXAMINATION FINDINGS

The physical examination may present some important clinical information, which is discussed in this section.

Hypertension

Hypertension is a common cardiovascular disorder encountered in the athletic population, with an elevated blood pressure found in approximately 6% of athletes presenting for routine pre-participation screening.[55, 56] Athletes with persistently elevated blood pressure should be questioned about a family history of hypertension and the use of stimulants (such as caffeine, nicotine and ephedrine) or anabolic steroids.

The American College of Cardiology and the American Heart Association published new guidelines in 2017 for the prevention, detection, evaluation and management of high blood pressure in adults.[57] Key updates to prior guidelines include the removal of 'prehypertension' as a diagnosis and classification of elevated blood pressure as a systolic blood pressure of 120–129 mmHg and diastolic blood pressure <80 mmHg, and the diagnosis of stage 1 hypertension as a systolic blood pressure of 130–139 mmHg or diastolic blood pressure 80–89 mmHg.[57] Stage 2 hypertension is defined as a systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg.[57]

The blood pressure guidance for children and adolescents was also reviewed in 2017 by the American Academy of Pediatrics.[58] The classification schema in children aged ≥ 13 years is similar to adult cut-offs (see box). In children aged < 13 years, due to the difficulty in measuring this age group, who grow at differing rates, clinicians are advised to refer to the tables produced by the academy to obtain normative values for age, height and gender. It is still unclear whether heightened values in younger athletes are indicative of future cardiovascular disease risk. To remain consistent with adult guidelines the category for prehypertension has been removed and the three remaining categories are: elevated BP (>90th percentile); stage 1 hypertension (=95th percentile); and stage 2 hypertension (=95th percentile +12 mmHg). The percentiles were produced from the age, height and gender characteristics of over 50 000 children and adolescents.

PRACTICE PEARL

Use of the American Academy of Pediatrics normative tables for age, height and gender are required to judge blood pressure in paediatric athletes under 13 years. Elevated values must be observed at three consecutive measurements to be considered clinically significant. All children and adolescents diagnosed with hypertension require a careful evaluation for secondary causes of hypertension and target end-organ disease.

Blood pressure classification for adults and children aged ≥ 13 years

Normal <120/80 mmHg
Elevated blood pressure 120–129 / <80 mmHg
Stage 1 hypertension 130–139 / 80–89 mmHg
Stage 2 hypertension ≥140 / >90 mmHg
Hypertensive crisis >180/120 mmHg

Evaluation includes blood chemistries (glucose, creatinine, electrolytes, lipid profile and thyroid function), haematocrit, urinalysis and ECG. A renal ultrasound is also recommended for all children with stage 1 or stage 2 hypertension.

Evaluation of target organ disease, including an echocardiogram, is recommended for Page 151 all young athletes diagnosed with stage 1 or stage 2 hypertension.[58]

Athletes found to have end-organ damage should not be allowed to participate in any competitive sport until their blood pressure is further evaluated, treated and under control, at which time eligibility for participation can be re-evaluated.[59]

Management of hypertension in athletes

Pharmacologic therapy may be required in some athletes with hypertension. The drugs of choice for the exercising individual are usually angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers. These drugs control blood pressure without an associated decrease in aerobic capacity. Occasionally, athletes may notice an exaggeration of a tendency to postural hypotension when they cease aerobic exercise; this is a good reason to gradually cool down. This allows sufficient blood return to the right side of the heart to maintain pressure while upright without fainting.

If ACE inhibitors or angiotensin receptor blockers are contraindicated or poorly tolerated, dihydropyridine calcium channel blockers should be considered in a competitive athlete as they do not cause any reduction in maximum aerobic capacity. For those athletes who exercise in cold conditions, the highly vascular selective calcium antagonist felodipine is a good choice as it enhances peripheral blood flow and may thereby reduce the tendency for frostbite.

Beta blockers and diuretics are commonly used to control blood pressure in the general population. However, both drugs reduce maximum exercise capacity, which is not desirable for most competitive athletes. Diuretics reduce plasma volume, which may make the athlete more prone to heat illness (Chapter 23). For the elite athlete with hypertension, both diuretics and beta blockers are banned drugs in various sports and therefore may be contraindicated.

Heart murmur

Auscultation of the heart should be performed in both the supine and standing positions (and with Valsalva manoeuvre), specifically to identify murmurs of dynamic left ventricular outflow tract obstruction. Standing is preferred to sitting because the diagnostic murmur of HCM (if present) becomes louder when the patient is standing due to decreased venous return. Only about 25% of patients with HCM have a murmur at rest.[60]

Significant murmurs that may indicate left ventricular outflow tract obstruction are typically

early systolic, harsh, heard best at the right upper sternal border, and increase with manoeuvres that decrease venous return, such as Valsalva or moving from squatting to standing. In contrast, the murmur of aortic stenosis typically diminishes with manoeuvres that decrease venous return and increases with manoeuvres that increase venous return (i.e. squatting). Both pathologic entities are important to recognise.

A pansystolic (holosystolic) murmur, heard best at the apex with radiation to the axilla, may indicate mitral valve regurgitation and could be related to a dilated cardiomyopathy. Systolic ejection or midsystolic clicks are typically abnormal at any age.

A diastolic murmur heard at the right upper sternal border may represent aortic regurgitation and indicate an incompetent aortic valve, such as that present in Marfan syndrome or sometimes present with a bicuspid aortic valve. If aortic regurgitation is suspected, it can be accentuated by hand grip, which increases systemic vascular resistance.

PRACTICE PEARL

Harsh systolic murmurs and any diastolic murmur should be considered pathologic. An echocardiogram should be requested to clarify the aetiology of any concerning murmur.

A common murmur in well-trained athletes is a hyperdynamic 'flow' murmur. These are characterised by a grade 1/6 or 2/6 soft early systolic murmur heard best at the upper sternal border. The murmur results from an overall increase in plasma volume and thus stroke volume that occurs as a physiologic adaptation to regular physical training. Often the murmur is only heard when the athlete is supine (increased venous return), and is absent when the athlete is standing or sitting; the murmur should diminish with the strain phase of a Valsalva manoeuvre. While distinguishing physiologic from pathologic murmurs can be difficult for even experienced examiners, in the absence of concerning symptoms or family history, innocent sounding murmurs typically require no further investigation.

Marfan syndrome

Cardiovascular complications are the major cause of morbidity and mortality in patients with Marfan syndrome. Marfan syndrome causes a progressive dilatation and weakness (cystic medial necrosis) of the proximal aorta that can lead to rupture and sudden death. Myxomatous degeneration of the mitral and aortic valves may also lead to valvular dysfunction. Marfan syndrome is caused by mutations in the fibrillin-1 (FBN-1) gene, with 75% of cases inherited through autosomal dominant transmission with variable expression and 25% of cases from de novo mutations.[61]

The risk of aortic rupture or dissection increases during adolescence and 50% of undiagnosed patients with Marfan syndrome die by 40 years of age.[61] Symptoms of aortic dissection typically include sudden excruciating chest or thoracic pain, often described as tearing or ripping. Heart failure also occurs secondary to aortic valve incompetence.

Physical examination findings include highly variable clinical features usually manifested in adolescence and young adulthood (see Chapter 9, Fig. 9.8). An international expert panel has established a revised Ghent nosology, which puts more weight on the cardiovascular manifestations and the presence of aortic root aneurysm and ectopia lentis as cardinal clinical features.[62] In the absence of any family history, the presence of these two manifestations is sufficient for the unequivocal diagnosis of Marfan syndrome. In the absence of either of these two, the presence of a bona fide FBN-1 mutation or a combination of systemic manifestations is required. For the latter a new scoring system has been designed.[62]

NON-INVASIVE CARDIOVASCULAR TESTING

Athletes with cardiovascular symptoms should undergo specific testing with the intent to rule out (or rule in) cardiac disorders known to cause sudden cardiac death. In this section we discuss ECGs, echocardiography, CMR and CT, as well as the genetic investigations that are appropriate when there is a family history of inherited conditions or early cardiac death. Table 10.3 shows a summary of non-invasive cardiovascular testing.

Table 10.3 Non-invasive cardiovascular testing

Test	What the test involves and what it measures
Electrocardiography (ECG)	ECG measures the electrical activity and function of the heart via surface electrode Characteristic ECG abnormalities may reflect underlying cardiac disease.
Ambulatory ECG monitoring	Ambulatory ECG monitoring is the prolonged (e.g. 24 hours or longer) ECG monito This technique may be useful in the diagnosis of arrhythmias or abnormal prematu
Stress electrocardiography	Stress or exercise ECG is performed by monitoring the patient electrocardiographic It is used to investigate ischaemic heart disease or coronary artery anomalies that It can also be useful in the work-up of exertional syncope or palpitations.
Echocardiography	Echocardiography is the clinical application of ultrasound to the diagnosis of heart
Cardiac magnetic resonance CMR	Cardiac magnetic resonance provides accurate assessment of cardiac morphology The additional value of late gadolinium enhancement (LGE) for the detection of my
Cardiac computed tomography (CT) angiography	Cardiac CT angiography provides an accurate assessment of the course of the pro Cardiac CT does involve radiation to the chest that should be considered when per

Electrocardiogram

Training-related ECG alterations are common physiologic adaptations to regular exercise and are considered normal variants in athletes.[63] These variants include:

- isolated QRS voltage criteria for right or left ventricular hypertrophy
- sinus bradycardia
- sinus arrhythmia
- first-degree atrioventricular (AV) block

- incomplete right bundle branch block
- early repolarisation/ST-segment elevation
- ST-segment elevation followed by T-wave inversion V1–V4 in black athletes
- T-wave inversion V1–V3 in athletes < 16 years of age
- ectopic atrial or junctional rhythm
- Mobitz type 1 (Wenckebach) second-degree atrioventricular block.

Isolated increases in QRS amplitude are common in trained athletes. However, QRS voltage criteria for left ventricular hypertrophy accompanied by any non-voltage criteria for pathologic left ventricular hypertrophy (such as a 'strain' pattern of repolarisation, ST-segment depression, T-wave inversion or pathologic Q waves) are abnormal and require further evaluation.

ECGs are readily accessible and should be performed for all cardiovascular symptoms; they can suggest structural cardiac disorders or diagnose primary electrical disease (Tables 10.4 and 10.5).

Table 10.4 ECG interpretation in athletes—abnormal findings

Abnormal ECG finding	Definition
T-wave inversion[a]	>1 mm in depth from baseline in two or more adjacent leads not including lea
ST-segment depression	≥0.5 mm in depth in two or more adjacent leads
Pathologic Q waves	Q/R ratio ≥ 0.25 or Q waves ≥ 40 ms in duration in two or more leads (exclud
Complete left bundle branch block	QRS >0.12 s, predominantly negative QRS complex in lead V1 (QS or rS), a
Profound non-specific intraventricular conduction delay	Any QRS >0.14 s
Mobitz type II second-degree AV block	Intermittently non-conducted P waves not preceded by PR prolongation and
Third-degree AV block	Complete heart block
Ventricular pre-excitation	PR interval <0.12 s with a delta wave (slurred upstroke in the QRS complex)
Long QT interval	QTc ≥0.47 s (99th% males) QTc ≥0.48 s (99th% females) QTc ≥0.50 s (unequivocal LQTS)
Brugada-like ECG pattern	Coved pattern: initial ST elevation ≥2 mm (high take-off) with downsloping S1
Epsilon wave	Small negative deflection just beyond the QRS in V1 or V2
Profound sinus bradycardia	<30 BPM or sinus pauses ≥3 s
Atrial tachyarrhythmias	Supraventricular tachycardia, atrioventricular nodal re-entrant tachycardia, at
Premature ventricular contractions	≥2 per tracing
Ventricular arrhythmias	Couplets, triplets, non-sustained ventricular tachycardia

*Any abnormal finding is considered training-unrelated and suggests the possibility of underlying pathologic cardiac disease, requiring further diagnostic work-up.*63

[a] Exception to T-wave inversion: J-point and ST-segment elevation with an upward ('domed') convexity, followed by a negative T wave in V2–V4 is a common pattern of early repolarisation seen in athletes of African-Caribbean descent and should be considered normal. This should not to be confused with the downsloping ST-segment elevation in V1–V3 found in a Brugada-like ECG pattern, which is abnormal. T-wave inversion in V1–V3 in athletes less than 16 years old represents the juvenile T-wave pattern and should be considered normal.

Table 10.5 ECG interpretation in athletes—borderline findings

Borderline ECG finding	Definition
Left axis deviation	–30° to –90°
Left atrial enlargement	Prolonged P-wave duration of >120 ms in leads I or II with negative portion of the P
Right axis deviation	>120°
Right atrial enlargement	P wave ≥2.5 mm in II, III or aVF
Complete right bundle branch block	rSR' pattern in lead V1 and an S wave wider than the R wave in lead V6 with QRS d

These ECG findings in isolation likely do not represent pathologic cardiovascular disease in athletes, but the presence of two or more borderline findings may warrant additional investigation until further data become available.[63]

ADAPTED FROM DREZNER ET AL.[63]

PRACTICE PEARL

ECGs in athletes should be interpreted using contemporary criteria, to assist in distinguishing physiologic changes commonly found in an athlete's heart from abnormalities suggesting a pathologic disorder.

An ECG is abnormal in up to 95% of patients with hypertrophic cardiomyopathy,[64, 65] often with prominent Q waves, deep negative T waves, and ST-segment depression or T-wave inversion in the lateral or inferolateral leads.

In ARVC, the ECG may show right precordial T-wave inversion (beyond V1), an epsilon wave (small positive deflection or notch seen between the end of the QRS complex and onset of the T wave in leads V1–V3), delayed S-wave upstroke ≥ 55 ms from the nadir of the S wave to the end of the QRS complex in V1–V3, prolongation of QRS duration (>120 ms) or a right bundle branch block pattern. Calculation of the QT interval corrected for heart rate (QTc) can be variable with some overlap of normal and abnormal values. The 99th percentile upper limit of normal is 0.47 seconds in men and 0.48 seconds in women.[66]

Patients with LQTS may also have bizarre, flat or peaked T-wave morphology, alternating T-wave polarity (T-wave alternans), or prominent U waves or T–U wave complexes.[67]

A QTc >0.5 seconds regardless of symptoms or family history distinguishes individuals most at risk for sudden cardiac death.[40]

Echocardiography and associated tests for structural disease (cardiac CT, CMR)

Echocardiography remains the standard test to evaluate for structural cardiac disease such as HCM. The diagnosis is suggested by pathologic, asymmetric left ventricular wall thickening (≈ 16 mm), usually involving the intraventricular septum, a non-dilated left ventricle and impaired diastolic

function. In cases where the diagnosis of HCM is uncertain (i.e. borderline left ventricular wall thickness of 13–15 mm), CMR (Fig. 10.2) can more accurately estimate left ventricular morphology and can be used with delayed gadolinium enhancement to identify myocardial fibrosis/scar. These features would support a diagnosis of HCM. Cardiac magnetic resonance also may be helpful in athletes with marked T-wave inversion in the lateral or inferolateral leads on ECG, to rule out apical-variant HCM that may not be identified by echocardiography.

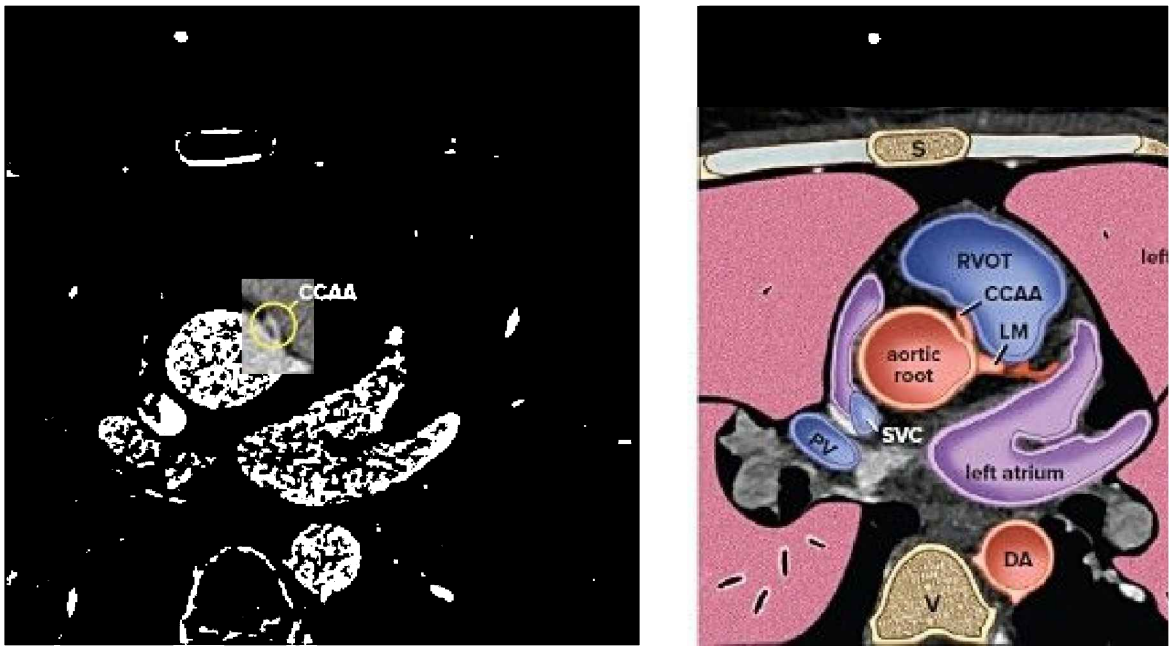


Figure 10.2 An example of cardiac magnetic resonance (CMR) showing a congenital coronary artery anomaly (CCAA), which can be a 'silent' presentation or may be associated with exertional syncope or chest pain. The panel on the right provides orientation (S = sternum, RVOT = right ventricular outflow tract, LM = left main coronary artery, SVC = superior vena cava, DA = descending aorta, V = thoracic vertebral body)
COURTESY OF JENNIFER ELLIS/JON LEIPSIC

Echocardiogram, CMR or CT may demonstrate right ventricular dilatation and wall thinning, reduced right ventricular ejection fraction, focal right ventricular wall motion abnormalities or right ventricular aneurysms suggestive of ARVC. Fibro-fatty infiltration of the right ventricle consistent with a diagnosis of ARVC is best seen on CMR.

In evaluation of the coronary artery origins, transthoracic echocardiography can reliably identify the coronary ostia in about 95% of patients. Advanced cardiac imaging such as CT angiography, CMR or coronary angiography may be needed in some cases to detect anomalous origins and can also identify other coronary anomalies such as an acute angled take-off, intramyocardial course and hypoplastic coronary arteries.

Genetic testing when there is a family history of early sudden cardiac death

Many of the diseases that put a patient at risk of sudden cardiac death have a genetic origin. Thus, a family history of sudden cardiac death, especially if the relative died when they were younger than 40 years, should heighten awareness about the potential for an inheritable cardiac disease. Most of the cardiac diseases that cause sudden cardiac death are autosomal dominant; thus, only one parent need be affected. These diseases, including HCM, ARVC, Brugada syndrome, CPVT and LQTS, have established mutations that can be identified through genetic testing, although the exact role of genetic testing in athletes remains to be determined.

Page 155

Approximately 65% of patients with HCM have an identified gene mutation and a small percentage have multiple mutations. Currently over 900 mutations have been identified including many on the myosin heavy chain and myosin binding protein C.[68] Less commonly, HCM is caused by abnormalities in troponin T, troponin I, tropomyosin, myosin light chains and actin genes. Multiple mutations are thought to put the individual at an increased risk of sudden death.[69]

Abnormalities in the desmosome, including plakoglobin, desmoplakin and plakophilin, are the cause of most cases of ARVC.[70] However, ARVC genetic testing is still primarily a test of specialised research centres.

Only about 20% of patients with Brugada syndrome carry an identified gene.[71] In LQTS, commercially available testing evaluates for several LQTS types; approximately 75% of genetic LQTS are type 1, 2 or 3.[72]

In CPVT, approximately one-half test positive for an abnormality in the ryanodine receptor gene, and this test is carried out by most commercial genetic testing services.[73]

Genetic screening can be expensive and the clinical significance of abnormalities found at screening is often unclear.

PRACTICE PEARL

Genetic screening in the athlete should be limited to those who have a borderline diagnosis or in whom there is a documented genetic disease in the family.

TEMPORARY AND PERMANENT DISQUALIFICATION FROM SPORTS

Careful activity recommendations involving temporary or permanent sports disqualification for athletes with identified cardiovascular disease should be made in consultation with a cardiologist. Exercise recommendations in athletes with underlying cardiovascular disease susceptible to sudden cardiac death are predicated on the likelihood that intense athletic training and competition act as a trigger to increase the risk of death or disease progression.[59]

The 2015 American Heart Association, American College of Cardiology and Heart Rhythm Society guidelines provide eligibility recommendations for competitive athletes with cardiovascular abnormalities.[74] These expert consensus recommendations provide a

Page 156

framework on which to base clearance decisions once a cardiovascular abnormality is identified, taking into account the severity of disease, potential for sudden death or disease progression, and the type and intensity of exercise involved in a particular sport (for a classification of intensity see Fig. 10.3). While the natural history and absolute risk of a life-threatening cardiovascular event is uncertain for many of the conditions predisposing to sudden cardiac death, it is generally accepted that withdrawal from intense athletic training and competition can reduce the exposure risk in athletes with a pathologic cardiovascular disorder.[75]

https://www.sciencedirect.com. Due to rights and permissions restrictions, this content cannot be reproduced in a digital format. The content is available in the print edition at page 156.

Figure 10.3 Intensity classification system for different sports—from the 2015 guidelines
FROM MITCHELL JH, HASKELL W, SNELL P, VAN CAMP SP. TASK FORCE 8: CLASSIFICATION OF SPORTS. J AM COLL CARDIOL. 2005;45:1364–1367. DOI: 10.1016/j.JACC.2005.02.015. WITH PERMISSION. COPYRIGHT © 2005, JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY, ELSEVIER

Individuals disqualified from competitive sports should be guided to engage in recreational exercise considered to be safe, in order to maintain general health. The American Heart Association provides recommendations for physical activity and recreational sports participation for young patients with genetic cardiovascular diseases, which is a useful starting point.[76] Many experts suggest that the level of exertion be guided by the ability to converse during the activity. If an individual is so dyspnoeic that they can no longer talk, the level of exertion is considered too intense.

CASE STUDY

Rob Waddell, rower—atrial fibrillation

Competing at the highest level of sport is hard enough without throwing a whole other variable into the mix. I used to be really scared every single race that I would have an episode of AF.

Rob Waddell (Fig. 10.4) was an elite-level rower for New Zealand, winning the world single sculls titles in 1998 and 1999, before capturing Olympic gold in the same discipline at the Sydney Olympics in 2000. He also held the world record for indoor rowing at both 2000 and 5000 metres.

Figure 10.4 Rob Waddell on the podium at the 2000 Sydney Olympics
GETTY IMAGES/PHIL WALTER

Diagnosis

In the 1990s Waddell experienced a significant loss in power output, breathlessness and extreme fatigue both during training and racing.

A Holter monitor was used to assess his heart rhythm over an extended period of time, however the results were inconclusive. Waddell was sent to Auckland for electrophysiologic testing (See Need to Know box below.) He was subsequently diagnosed with paroxysmal atrial fibrillation (AF).

Management

Despite treatment with high dose flecainide in an attempt to control his AF, the condition persisted, becoming increasingly more severe and intrusive throughout his career, particularly in the lead-up to the 2000 Olympics in Sydney.

Following his victory at the Sydney Olympics, Waddell decided to change sports and shift his focus to sailing, given the ongoing difficulty of managing his AF. The change in sports necessitated a 20 kg weight gain and, due to the more intermittent nature of the activity, Waddell was able to compete relatively asymptomatically and even stop taking flecainide.

In 2008, Waddell decided to return to rowing. During the deciding race of a best-of-three series that determined qualification for the Beijing Olympics, Waddell suffered a recurrence of his AF. He vividly described the experience as feeling 'like rowing through mud'. Waddell went on to qualify for the Beijing Olympics and placed fourth in the double sculls.

Waddell would later undergo radiofrequency ablation which dramatically improved his AF and enabled him to continue sailing competitively at the international level.

Conclusion

Waddell's story provides a good example of a common problem faced by elite competitors with AF. With appropriate and careful management, athletes with AF may still be able to compete in their sport at the highest level.

In some cases, early detection of clinically significant cardiovascular disease may permit timely therapeutic interventions, such as pharmacologic management or implantable cardioverter defibrillators (ICDs), that can alter the clinical course and significantly prolong life. For children diagnosed with LQTS, individualised management (i.e. with beta blockers and/or ICDs) and in-depth counselling were associated with low cardiac event rates and no deaths in two independent cohorts of young athletes.[77, 78] Although there is controversy about athletes with ICDs competing, data from the ICD Sports Safety Registry has described cardiovascular outcomes in a small cohort of competitive athletes with ICDs.[79] Over a median 31-month follow-up, there were no occurrences of death or resuscitated cardiac arrest or arrhythmia.[79] However, the implantation of an ICD should not allow a return to sport in those with underlying structural heart disease that would otherwise prohibit competition.

Page 158

NEED TO KNOW

Electrophysiologic testing—This method is valuable in provoking known (or suspected) but infrequent arrhythmias where previous tests have been inconclusive. Normally conducted under a local anaesthetic, a temporary electrode catheter is placed through peripheral veins (or arteries) into the heart using a fluoroscope. The catheter can be positioned in the atria, ventricles or both. The test records cardiac electrical signals and maps the spread of electrical impulses during each beat, thus showing the location of the heart block. It can diagnose the specific origin of an arrhythmia and is more specific than ECG.

SUMMARY

Cardiovascular symptoms in athletes warrant a comprehensive diagnostic evaluation to rule out conditions that predispose to sudden death. While not all athletes with underlying heart disease manifest symptoms, prodromal symptoms such as syncope, exertional chest pain and excessive dyspnoea/fatigue may occur in some athletes as warning events prior to sudden cardiac death. Careful evaluation of athletes with cardiovascular symptoms can detect potentially lethal cardiovascular disease and, through appropriate treatment, counselling and activity modification, reduce the risk for sudden death in sport.

REFERENCES

1. Maron BJ, Doerer JJ, Haas TS et al. Sudden deaths in young competitive athletes: analysis of 1866 deaths in the United States, 1980–2006. *Circulation* 2009; 119: 1085–

92.

2. Harmon KG, Asif IM, Maleszewski JJ et al. Incidence, cause and comparative frequency of sudden cardiac death in National Collegiate Athletic Association athletes: a decade in review. *Circulation* 2015; 132: 10–19.
3. Maron BJ. Sudden death in young athletes. *N Engl J Med* 2003; 349(11): 1064–75.
4. Harmon KG, Asif IM, Maleszewski JJ et al. Incidence and etiology of sudden cardiac arrest and death in high school athletes in the United States. *Mayo Clin Proc* 2016; 91: 1493–502.
5. Corrado D, Basso C, Rizzoli G et al. Does sports activity enhance the risk of sudden death in adolescents and young adults? *J Am Coll Cardiol* 2003; 42: 1959–63.
6. Corrado D, Basso C, Pavei A et al. Trends in sudden cardiovascular death in young competitive athletes after implementation of a preparticipation screening program. *JAMA* 2006; 296: 1593–601.
7. Marijon E, Tafflet M, Celermajer DS et al. Sports-related sudden death in the general population. *Circulation* 2011; 124: 672–81.
8. Harmon KG, Asif IM, Klossner D et al. Incidence of sudden cardiac death in National Collegiate Athletic Association athletes. *Circulation* 2011; 123: 1594–600.
9. Toresdahl BG, Rao AL, Harmon KG et al. Incidence of sudden cardiac arrest in high school student athletes on school campus. *Heart Rhythm* 2014; 11: 1190–4.
10. Eckart RE, Shry EA, Burke AP et al. Sudden death in young adults: an autopsy-based series of a population undergoing active surveillance. *J Am Coll Cardiol* 2011; 58: 1254–61.
11. Thompson PD, Funk EJ, Carleton RA et al. Incidence of death during jogging in Rhode Island from 1975 through 1980. *JAMA* 1982; 247: 2535–8.
12. de Noronha SV, Sharma S, Papadakis M et al. Aetiology of sudden cardiac death in athletes in the United Kingdom: a pathological study. *Heart* 2009; 95: 1409–14.
13. Van Camp SP, Bloor CM, Mueller FO et al. Nontraumatic sports death in high school and college athletes. *Med Sci Sports Exerc* 1995; 27: 641–7.
14. La Gerche A, Baggish AL, Knuuti J et al. Cardiac imaging and stress testing asymptomatic athletes to identify those at risk of sudden cardiac death. *JACC Cardiovasc Imaging* 2013; 6: 993–1007.
15. Drezner JA, O'Connor FG, Harmon KG et al. AMSSM Position Statement on Cardiovascular Preparticipation Screening in Athletes: current evidence, knowledge gaps, recommendations and future directions. *Br J Sports Med* 2017; 51(3): 153–67.
16. Maron BJ, Friedman RA, Kligfield P et al. Assessment of the 12-Lead Electrocardiogram as a Screening Test for Detection of Cardiovascular Disease in Healthy General Populations of Young People (12–25 Years of Age): A Scientific Statement From the American Heart Association and the American College of Cardiology. *J Am Coll Cardiol* 2014; 64: 1479–514.

17. Maron BJ, Gardin JM, Flack JM et al. Prevalence of hypertrophic cardiomyopathy in a general population of young adults: echocardiographic analysis of 4111 subjects in the CARDIA study: coronary artery risk development in (young) adults. *Circulation* 1995; 92(4): 785–9.
18. Maron BJ, Mathenge R, Casey SA et al. Clinical profile of hypertrophic cardiomyopathy identified de novo in rural communities. *J Am Coll Cardiol* 1999; 33: 1590–5.
19. Rodday AM, Triedman JK, Alexander ME et al. Electrocardiogram screening for disorders that cause sudden cardiac death in asymptomatic children: a meta-analysis. *Pediatrics* 2012; 129: e999–1010.
20. Davis JA, Cecchin F, Jones TK et al. Major coronary artery anomalies in a pediatric population: incidence and clinical importance. *J Am Coll Cardiol* 2001; 37: 593–7.
21. Gemayel C, Pelliccia A, Thompson PD. Arrhythmogenic right ventricular cardiomyopathy. *J Am Coll Cardiol* 2001; 38: 1773–81.
22. Cerrone M, Napolitano C, Priori SG. Genetics of ion-channel disorders. *Curr Opin Cardiol* 2012; 27: 242–52.
23. Pilote L, Pashkow F, Thomas JD et al. Clinical yield and cost of exercise treadmill testing to screen for coronary artery disease in asymptomatic adults. *Am J Cardiol* 1998; 81: 219–24.
24. Campbell RM, Berger S, Drezner J. Sudden cardiac arrest in children and young athletes: the importance of a detailed personal and family history in the pre-participation evaluation. *Br J Sports Med* 2009; 43: 336–41.
25. Maron BJ, Shirani J, Poliac LC et al. Sudden death in young competitive athletes: clinical, demographic and pathological profiles. *JAMA* 1996; 276: 199–204.
26. Basso C, Maron BJ, Corrado D et al. Clinical profile of congenital coronary artery anomalies with origin from the wrong aortic sinus leading to sudden death in young competitive athletes. *J Am Coll Cardiol* 2000; 35: 1493–501.
27. Tester DJ, Spoon DB, Valdivia HH et al. Targeted mutational analysis of the RyR2-encoded cardiac ryanodine receptor in sudden unexplained death: a molecular autopsy of 49 medical examiner/coroner's cases. *Mayo Clin Proc* 2004; 79: 1380–4.
28. Eckart RE, Scoville SL, Campbell CL et al. Sudden death in young adults: a 25-year review of autopsies in military recruits. *Ann Intern Med* 2004; 141(11): 829–34.
29. Colivicchi F, Ammirati F, Santini M. Epidemiology and prognostic implications of syncope in young competing athletes. *Eur Heart J* 2004; 25: 1749–53.
30. Fuller CM, McNulty CM, Spring DA et al. Prospective screening of 5615 high school athletes for risk of sudden cardiac death. *Med Sci Sports Exerc* 1997; 29: 1131–8.
31. Wilson MG, Basavarajaiah S, Whyte GP et al. Efficacy of personal symptom and family history questionnaires when screening for inherited cardiac pathologies: the role of electrocardiography. *Br J Sports Med* 2008; 42: 207–11.

32. Bessem B, Groot FP, Nieuwland W. The Lausanne Recommendations: a Dutch experience. *Br J Sports Med* 2009; 43(9): 708–15.
33. Carro Hevia A, Fernández MM, Palacio JMA et al. ECG as a part of the preparticipation screening programme: an old and still present international dilemma. *Br J Sports Med* 2011; 45(10): 776–9.
34. Baggish AL, Hutter AM Jr., Wang F et al. Cardiovascular screening in college athletes with and without electrocardiography: a cross-sectional study. *Ann Intern Med* 2010; 152(5): 269–75.
35. Drezner JA, Owens DS, Prutkin JM et al. Electrocardiographic screening in National Collegiate Athletic Association athletes. *Am J Cardiol* 2016; 118: 754–9.
36. Harmon KG, Zigman M, Drezner JA. The effectiveness of screening history, physical exam and ECG to detect potentially lethal cardiac disorders in athletes: a systematic review/meta-analysis. *J Electrocardiol* 2015; 48: 329–38.
37. Liberthson RR. Sudden death from cardiac causes in children and young adults. *N Engl J Med* 1996; 334: 1039–44.
38. Wisten A, Messner T. Symptoms preceding sudden cardiac death in the young are common but often misinterpreted. *Scand Cardiovasc J* 2005; 39: 143–9.
39. Leenhardt A, Lucet V, Denjoy I et al. Catecholaminergic polymorphic ventricular tachycardia in children. A 7-year follow-up of 21 patients. *Circulation* 1995; 91: 1512–19.
40. Hobbs JB, Peterson DR, Moss AJ et al. Risk of aborted cardiac arrest or sudden cardiac death during adolescence in the long-QT syndrome. *JAMA* 2006; 296: 1249–54.
41. Kapoor WN. Syncope. *N Engl J Med* 2000; 343: 1856–62.
42. Strickberger SA, Benson DW, Biaggioni I et al. AHA/ACCF Scientific Statement on the Evaluation of Syncope: from the American Heart Association Councils on Clinical Cardiology, Cardiovascular Nursing, Cardiovascular Disease in the Young and Stroke, and the Quality of Care and Outcomes Research Interdisciplinary Working Group; and the American College of Cardiology Foundation: in collaboration with the Heart Rhythm Society: endorsed by the American Autonomic Society. *Circulation* 2006; 113: 316–27.
43. Grubb BP. Clinical practice. Neurocardiogenic syncope. *N Engl J Med* 2005; 352: 1004–10.
44. Sneddon JF, Scalia G, Ward DE et al. Exercise induced vasodepressor syncope. *Br Heart J* 1994; 71: 554–7.
45. Sakaguchi S, Shultz JJ, Remole SC et al. Syncope associated with exercise, a manifestation of neurally mediated syncope. *Am J Cardiol* 1995; 75: 476–81.
46. Calkins H, Seifert M, Morady F. Clinical presentation and long-term follow-up of athletes with exercise-induced vasodepressor syncope. *Am Heart J* 1995; 129: 1159–

64.

47. Kosinski D, Grubb BP, Kip K et al. Exercise-induced neurocardiogenic syncope. *Am Heart J* 1996; 132: 451–2.
48. Roberts WO. Exercise-associated collapse care matrix in the marathon. *Sports Med* 2007; 37: 431–3.
49. O'Connor FG, Oriscello RG, Levine BD. Exercise-related syncope in the young athlete: reassurance, restriction or referral? *Am Fam Physician* 1999; 60: 2001–8.
50. Drezner JA, Rao AL, Heistand J et al. Effectiveness of emergency response planning for sudden cardiac arrest in United States high schools with automated external defibrillators. *Circulation* 2009; 120: 518–25.
51. Drezner JA, Toresdahl BG, Rao AL et al. Outcomes from sudden cardiac arrest in US high schools: a 2-year prospective study from the National Registry for AED Use in Sports. *Br J Sports Med* 2013; 47: 1179–83.
52. Link MS, Estes NAM, 3rd. How to manage athletes with syncope. *Cardiol Clin* 2007; 25: 457–66, vii.
53. Yankelson L, Sadeh B, Gershovitz L et al. Life-threatening events during endurance sports: is heat stroke more prevalent than arrhythmic death? *J Am Coll Cardiol* 2014; 64: 463–9.
54. Maron MS, Olivotto I, Zenovich AG et al. Hypertrophic cardiomyopathy is predominantly a disease of left ventricular outflow tract obstruction. *Circulation* 2006; 114: 2232–9.
55. Ljungqvist A, Jenoure P, Engebretsen L, et al. The International Olympic Committee (IOC) Consensus Statement on periodic health evaluation of elite athletes March 2009. *Br J Sports Med* 2009 Sep;43(9):631–43.
56. Berge HM, Isern CB, Berge E. Blood pressure and hypertension in athletes: a systematic review. *Br J Sports Med*. 2015 Jun;49(11):716–23.
57. Whelton PK, Carey RM, Aronow WS et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol* 2018; 71(19): e127–248.
58. Flynn JT, Kaelber DC, Baker-Smith CM et al. Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents. Subcommittee on Screening and Management of High Blood Pressure in Children. *Pediatrics* 2017; 140(3): e20171904. doi: 10.1542/peds.2017-1904.
59. Maron BJ and Zipes DP. *Introduction: eligibility recommendations for competitive athletes with cardiovascular abnormalities-general considerations*. J Am Coll Cardiol. 2005 Apr 19;45(8):1318–21.
60. Maron BJ. Hypertrophic cardiomyopathy. *Lancet* 1997; 350(9071): 127–33.

61. Ammash NM, Sundt TM, Connolly HM. Marfan syndrome: diagnosis and management. *Curr Probl Cardiol* 2008; 33: 7–39.
62. Loeys BL, Dietz HC, Braverman AC et al. The revised Ghent nosology for the Marfan syndrome. *J Med Genet* 2010; 47: 476–85.
63. Drezner JA, Sharma S, Baggish A et al. International criteria for electrocardiographic interpretation in athletes: Consensus statement. *Br J Sports Med* 2017; 51: 704–31.
64. Maron BJ, Roberts WC, Epstein SE. Sudden death in hypertrophic cardiomyopathy: a profile of 78 patients. *Circulation* 1982; 65: 1388–94.
65. Calore C, Zorzi A, Corrado D. Clinical meaning of isolated increase of QRS voltages in hypertrophic cardiomyopathy versus athlete's heart. *J Electrocardiol*. 2015 May-Jun;48(3):373–9.
66. Goldenberg I, Moss AJ, Zareba W. QT interval: how to measure it and what is 'normal'. *J Cardiovasc Electrophysiol* 2006; 17: 333–6.
67. Vetter VL. Clues or miscues? How to make the right interpretation and correctly diagnose long-QT syndrome. *Circulation* 2007; 115: 2595–8.
68. Landstrom AP, Ackerman MJ. Mutation type is not clinically useful in predicting prognosis in hypertrophic cardiomyopathy. *Circulation* 2010; 122: 2441–50.
69. Van Driest SL, Vasile VC, Ommen SR et al. Myosin binding protein C mutations and compound heterozygosity in hypertrophic cardiomyopathy. *J Am Coll Cardiol* 2004; 44: 1903–10.
70. Sen-Chowdhry S, Syrris P, McKenna WJ. Role of genetic analysis in the management of patients with arrhythmogenic right ventricular dysplasia/cardiomyopathy. *J Am Coll Cardiol* 2007; 50: 1813–21.
71. Antzelevitch C, Brugada P, Borggrefe M et al. Brugada Syndrome: Report of the Second Consensus Conference: endorsed by the Heart Rhythm Society and the European Heart Rhythm Association. *Circulation* 2005; 111: 659–70.
72. Goldenberg I, Moss AJ. Long QT syndrome. *J Am Coll Cardiol* 2008; 51: 2291–300.
73. Napolitano C, Priori SG. Diagnosis and treatment of catecholaminergic polymorphic ventricular tachycardia. *Heart Rhythm* 2007; 4: 675–8.
74. Maron BJ, Zipes DP, Kovacs RJ. Eligibility and Disqualification Recommendations for Competitive Athletes With Cardiovascular Abnormalities: Preamble, Principles, and General Considerations: A Scientific Statement From the American Heart Association and American College of Cardiology. *J Am Coll Cardiol* 2015; 66: 2343–9.
75. Corrado D, Basso C, Pavei A et al. Trends in sudden cardiovascular death in young competitive athletes after implementation of a preparticipation screening program. *JAMA* 2006; 296(13): 1593–601.
76. Maron BJ, Chaitman BR, Ackerman MJ et al. Recommendations for Physical Activity and Recreational Sports Participation for Young Patients With Genetic

Cardiovascular Diseases. *Circulation* 2004; 109: 2807–16.

77. Johnson JN, Ackerman MJ. Return to play? Athletes with congenital long QT syndrome. *Br J Sports Med* 2013; 47: 28–33.

78. Aziz PF, Sweeten T, Vogel RL et al. Sports participation in genotype positive children with long QT syndrome. *JACC Clin Electrophysiol* 2015; 1: 62–70.

79. Lampert R, Olshansky B, Heidbuchel H et al. Safety of sports for athletes with implantable cardioverter-defibrillators: results of a prospective, multinational registry. *Circulation* 2013; 127: 2021–30.

Chapter 11

Respiratory symptoms during exercise

with KAREN HOLZER

If you learn to manage your asthma and take the correct medication, there's no reason you shouldn't be the best.

Paul Radcliffe, marathon world record holder

The respiratory system is critical to athletic performance. The integrity of this system results in the delivery of oxygen to the blood (and subsequently to both the exercising muscles and organs important for exercise, such as the heart) and the elimination of waste products such as carbon dioxide. Any dysfunction of these processes results in impaired performance. A number of medical conditions (such as asthma and respiratory infections) may affect performance.

COMMON RESPIRATORY SYMPTOMS

There are a number of symptoms with which an athlete may present that indicate the presence of respiratory disease. These include:

- (dyspnoea) shortness of breath
- wheeze
- cough
- chest pain or tightness
- lightheadedness.

Shortness of breath and wheeze

Some degree of breathlessness is a normal physiological response to exercise. Dyspnoea occurring during intense exercise may represent the reaching of maximal exercise and ventilatory capacity;

however, particularly at lower-intensity exercise, it may represent an underlying respiratory or cardiac condition.

Breathlessness is a subjective symptom that can be defined as 'an increased difficulty in breathing'. Despite the frequency of this complaint, the exact physiological mechanism is unknown. The most important cause from an athletic point of view is asthma, more specifically exercise-induced asthma (EIA) or exercise-induced bronchospasm (EIB). In the older athlete, especially with a history of smoking, chronic obstructive pulmonary disease (COPD) and cardiac ischaemia should be considered. More recently, vocal cord dysfunction (VCD), a condition characterised by paradoxical laryngeal movement, has become increasingly recognised. Dyspnoea may be classified clinically as acute, chronic or intermittent (see box).

Although the clinical history combined with the examination of the patient may indicate the likely cause of the dyspnoea, it is important to remember that the examination at rest is often normal. This is particularly seen in patients who are troubled by EIB, vocal cord dysfunction and cardiac ischaemia.

A musculoskeletal examination should also be performed to assess for the presence of thoracic stiffness or costochondritis.

Investigations

Respiratory function tests (e.g. spirometry) are required to further assess dyspnoea. Spirometry pre- and post-bronchodilator should be performed. A bronchial provocation challenge test should be performed in the case of normal or mildly abnormal spirometry, to assess for both the presence and severity of EIA/EIB.

If a cardiac cause is suspected, an exercise ECG and echocardiogram are required, often combined in a stress echocardiogram. A chest X-ray may be required if clinical suspicions of a respiratory tract infection, cardiac failure, carcinoma, COPD or a pneumothorax arise.

Blood tests, in particular the haemoglobin level and iron studies, may be required to exclude anaemia or severe iron deficiency. Gastroscopy may be required to assess for gastro-oesophageal reflux.

Causes of dyspnoea in athletes

Acute

- Asthma: exercise-induced asthma (EIA), exercise-induced bronchospasm (EIB)
- Vocal cord dysfunction (also known as exercise-induced laryngeal obstruction)
- Cardiac causes
- Infections
- Spontaneous pneumothorax

Pulmonary embolism (rare)

Aspiration of foreign body (can occur in athletes with dental prosthesis or those who chew gum)

Chronic

Asthma

Chronic obstructive pulmonary disease (COPD)

Cardiac dysfunction—cardiac failure, ischaemia, valvular

Anaemia

Metabolic disorders (e.g. diabetes mellitus)

Pulmonary dysfunction

Obesity

Intermittent

Asthma: exercise-induced asthma and exercise-induced bronchospasm

Left ventricular dysfunction

Mitral stenosis

Psychological

Psychological factors, such as anxiety, are considered once other diagnoses are excluded and may require further assessment.

Cough

Coughing is such a common symptom that its presence and severity may be underestimated by both patients and clinicians.

From the clinical history it is important to determine the nature of the cough, and in particular whether the cough is acute or chronic, productive or non-productive. The timing of the cough is also important: whether it occurs during the day or night; and whether it occurs before or after exercise. Any associated disease such as sinusitis or gastro-oesophageal reflux should also be noted. It is important to establish whether the patient is or has been a smoker, exposed to passive smoking, worked with birds or worked in older buildings.

From this clinical history the aetiology of the cough may be established. A guide to the causes of acute and chronic cough is shown in Table 11.1.

Table 11.1 Causes of cough

Acute	Chronic
Upper respiratory tract infection	Post-nasal drip
Asthma	Asthma
Bronchitis	Chronic bronchitis
Bronchogenic carcinoma	Gastro-oesophageal reflux
Foreign body inhalation	Post-infective cough
Left ventricular failure	Psychogenic
	Carcinoma
	Interstitial lung disease

Benign tumours of the lung
Drugs (e.g. ACE inhibitors)

ACE = angiotensin-converting enzyme

The treatment of cough is more likely to succeed if a specific diagnosis is made. The treatment of asthma and respiratory tract infections is discussed below. Non-specific treatment for cough (e.g. pholcodine, 10 mg 6-hourly) may be helpful when the symptoms are distressing. Perhaps more effective than any medication is an adequate explanation and reassurance when appropriate.

Chest pain or tightness

When considering respiratory symptoms, chest pain and/or tightness is important. Many people with asthma may present with a subjective feeling of chest tightness alone. As well as the respiratory causes of chest tightness, there are other important and even life-threatening causes of chest tightness (such as cardiac ischaemia). Hence, this symptom must be investigated appropriately.

The causes of chest pain are outlined in Table 11.2. Successful treatment depends on the correct diagnosis being made. Prompt investigation of patients with this symptom is essential because of a number of potentially life-threatening causes.

Table 11.2 Causes of chest pain or tightness in the athlete

Common causes	Conditions not to be missed
Asthma	Cardiac ischaemia
Exercise-induced bronchoconstriction	Carcinoma
Infection	Interstitial lung disease
Chest wall injuries	Herpes zoster (shingles)
Referred pain from thoracic spine	

Investigation of the athlete with chest pain or tightness is very similar to that of the athlete with dyspnoea and may include chest X-ray, spirometry, bronchial provocation challenge tests, exercise ECG, echocardiogram, blood tests and/or gastroscopy. The investigations should be guided by the history and examination findings.

Page 161

ASTHMA

Asthma is a chronic inflammatory disorder of the airways in which many inflammatory cells and cellular elements play a role—in particular, mast cells, eosinophils, T lymphocytes, macrophages, neutrophils and epithelial cells. In susceptible individuals, this inflammation causes recurrent episodes of widespread but variable airflow obstruction that is usually reversible, either spontaneously or with treatment. The inflammation also causes an increase in existing bronchial hyperresponsiveness to a variety of stimuli. Common stimuli or triggers include upper respiratory

tract infections, cigarette smoke, exercise, inhaled allergens (e.g. dust mite, pollens), emotional triggers (e.g. stress, laughter), changes in temperature and weather, and environmental factors (e.g. dust, bushfires, pollution).

Epidemiology

The incidence and prevalence of asthma depends on the age of the population studied, the nature of the population and the criteria used for diagnosis. Asthma is more prevalent in developed countries and it is thought by some that the 'clean' lifestyle in these countries may contribute. Although asthma has a global distribution, the countries and regions with a relatively high burden of disease are: Australia, New Zealand, some countries in Africa, the Middle East, South America and north-western Europe.

The prevalence of asthma in Australia in 2014–15 was 11%.[1] Asthma is more common in children than adults, with over half the cases developing in childhood and another third before the age of 40. Genetic factors are thought to play a role.

Clinical features

The characteristic symptoms of asthma are:

- cough—dry, irritating and persistent, often worse in the early morning or late at night
- wheeze
- shortness of breath
- chest tightness.

However, since the degree of airway narrowing and obstruction varies with the condition and treatment, the symptoms can also vary from being not recognised, to low grade and occasional, through to severe and persistent. The symptoms are usually reversible, either spontaneously or with treatment.

Types of asthma

Historically, a distinction was made between intrinsic (non-allergic) and extrinsic (allergic) asthma in the International Disease Classification. This distinction is now rarely applied as it has been shown that the two types of asthma share many of the same pathological features.

Most existing guidelines classify patients with asthma as having intermittent or persistent asthma based on the severity of asthma, as determined by the patient's symptoms and spirometry before treatment is commenced. Importantly, the classification may change with time and a severe episode of asthma may occur in any of the groups.[2] The current classification of asthma is outlined below:

1. Mild intermittent asthma:
    - Symptoms of cough, chest tightness, shortness of breath and/or wheeze occur less than twice a week and are not present between asthma episodes.

- Asthma episodes are brief (a few hours to a few days) and may vary from mild to severe.
- Night-time symptoms occur less than twice a month.
- Spirometry when not having an asthma episode is 80% or greater than predicted and the peak expiratory flow rate (PEFR) has less than 20% variability.

2. Mild persistent asthma:
   - Symptoms of cough, chest tightness, shortness of breath and/or wheeze occur more than twice a week but less than once a day.
   - Asthma episodes interfere with daily activities.
   - Night-time symptoms occur 3–4 times a month.
   - Spirometry when not having an asthma episode is 80% or greater than predicted and the PEFR has less than 30% variability.
3. Moderate persistent asthma:
   - Symptoms of cough, chest tightness, shortness of breath and/or wheeze occur daily and inhaled short-acting asthma medications are used every day.
   - Episodes interfere with daily activities, occur more than twice a week and last for a few days.
   - Night-time symptoms occur five or more times a month.
   - Spirometry is abnormal: it is greater than 60% but less than 80% of predicted value; the PEFR has greater than 30% variability.
4. Severe persistent asthma:
   - Symptoms of cough, chest tightness, shortness of breath and/or wheeze are continuous.
   - Daily physical activities are limited.
   - Asthma episodes occur frequently.
   - Night-time symptoms are frequent.
   - Spirometry is abnormal and less than or equal to 60% of predicted value; the PEFR has less than 30% variability.

More recently, the 2016 Global Initiative for Asthma (GINA) guidelines[3] categorised asthma severity as mild, moderate or severe. Severity is assessed retrospectively from the level of treatment required to control symptoms and exacerbations, as follows: Page 162

- Mild asthma—well controlled with as-needed reliever medication alone or with low-intensity controller treatment such as low-dose inhaled corticosteroids (ICSs), leukotriene receptor antagonists or chromones
- Moderate asthma—well controlled with low-dose ICS/long-acting beta-2 agonists (LABA)
- Severe asthma—requires high-dose ICS/LABA to prevent it from becoming uncontrolled; or remains uncontrolled despite this treatment.

There does, however, need to be a clear distinction between severe and uncontrolled asthma. Prior to the diagnosis of severe asthma, the following factors need to be ensured:

1. correct inhaler technique
2. adherence to medication guidelines
3. correct diagnosis
4. exclusion of comorbidities (e.g. rhinosinusitis, gastro-oesophageal reflux, sleep apnoea)
5. limited/reduced exposure to sensitising or irritant agents.

Pathophysiology of asthma

The pathophysiology of asthma is complex and involves:

1. airway inflammation
2. intermittent airflow obstruction
3. bronchial hyperresponsiveness.

Airway inflammation

Airway inflammation appears to be an important factor leading to the development of increased airway reactivity. This inflammation may be acute, subacute or chronic. The principal inflammatory cells involved in asthma include mast cells, eosinophils, epithelial cells, macrophages and activated T lymphocytes. A series of immunological and cellular events occur in response to airway triggers. Exposure to specific and individualised triggers leads to the chemo-attraction of a number of inflammatory cells, in addition to the release of a number of inflammatory mediators such as histamine, prostaglandins, leukotrienes and cytokines, which result in a further influx of inflammatory cells into the airways.

Intermittent airway obstruction

As a consequence of acute airway inflammation, the following changes within the airways occur: mucosal oedema due to the increased permeability of the airway epithelium, increased mucus production and the contraction of the airway smooth muscle. The combined result is narrowing of the airways, which is the pathophysiological hallmark of asthma. Neurological factors, possibly mediated by the autonomic nervous system via the action of neuropeptides, have also been shown to play a role. This bronchial hyperreactivity may persist and become permanent.

Bronchial hyperresponsiveness

Bronchial hyperresponsiveness (also called bronchial hyperreactivity) may occur in response to specific stimuli, such as house dust mites (*Dermatophagoides pteronyssinus*) or fungal spores (e.g. *Aspergillus fumigatus*). It may also occur in response to non-specific stimuli such as cold, dust, smoke and exercise. The role of food allergy in asthma remains controversial. Food intolerance does not necessarily indicate an allergic mechanism. Skin prick tests and radioallergosorbent tests (RAST) may be helpful in confirming the patient's atopic status.

Drugs may be implicated in the production of asthma, especially beta-blocking agents and prostaglandin inhibitors, such as aspirin (ASA), and non-steroidal anti-inflammatory drugs (NSAIDs). Occasionally, drugs used to treat asthma (such as ipratropium bromide) have been responsible for provoking bronchoconstriction.

Psychological factors also can induce an exacerbation of asthma in those with an underlying airway hyperreactivity (AHR). Therefore, stress and emotional disturbance need to be taken into account in the overall management of asthmatic patients. It should be noted, however, that emotional disturbances can also cause breathing issues in those without underlying AHR, but this is not asthma.

Risk factors

The main risk factors for the development and worsening of asthma are:

1. *Genetic predisposition.* Atopy is characterised by the body's production of immunoglobulin E (IgE) after exposure to common environmental allergens. A person with high levels of IgE in the blood is more likely to have an allergic response when exposed to certain allergens in the environment. There is a strong association between the presence of atopic conditions such as allergic dermatitis and allergic rhinitis and the development of asthma. Studies have shown that approximately 75% of subjects with asthma report rhinitis, and subjects with rhinitis have an increased risk for asthma and lower airway hyperreactivity. Numerous studies have shown a genetic predisposition for the development of asthma. Although this relationship is stronger in the earlier years, it persists into the adult years, especially if both parents have asthma.[4]
2. *Environmental exposures.* Although allergic diseases have predisposing genetic factors, the interaction of environmental factors in the pathogenesis of allergic diseases is irrefutable. Environmental factors, either ingested or inhaled, have been suggested to play a major role in the pathogenesis of allergic asthma. Such environmental factors include air pollutants, respiratory viruses, tobacco smoke, endotoxins and environmental allergens both seasonal and perennial, such as house dust mites, spores, animal dander and pollens, to name a few.[5]

Asthma management

The general principles of asthma management are listed below:

1. Accurate diagnosis of asthma and severity: this is based on a combination of clinical history, examination and laboratory testing.
2. Asthma is an inflammatory disease and treatment should be primarily directed against this inflammatory component.
3. Bronchodilators should be used for the relief of symptoms only. Increased use of bronchodilators indicates the need for increased anti-inflammatory treatment.
4. Recognition of symptoms and objective assessment of airflow obstruction by regular PEFR measurements are essential for optimal asthma management.

5. The patient must take responsibility for the initial assessment and treatment of worsening asthma through the use of a predetermined self-management plan. This should be provided by the managing clinician.

Assessing the severity of an exacerbation of asthma may be impacted by the episode's speed of onset or by the setting in which it occurs. Severe episodes can occur within minutes, with little or no warning. All patients should be educated to always carry their bronchodilator with them so that it can be used immediately. At any time, if the patient fails to respond appropriately or if the PEFR falls significantly, urgent medical attention is required.

PRACTICE PEARL

All patients with asthma should always carry their bronchodilator with them

In a patient with chronic asthma, deterioration in PEFR indicates worsening asthma. Symptoms alone are a poor indicator of the severity of asthma, and thus regular PEFR measurements are essential to avoid a delay in diagnosis and consequently a delay in commencing appropriate treatment. Patients should assess their airway function on a regular basis with the use of a peak flow meter (Fig. 11.1).

Figure 11.1 Patients with asthma should regularly assess their airway function with a peak flow meter

While it is difficult to establish strict criteria for hospital admission, the severity of the attack and the previous history of response to treatment are the main guides. Continued observation is essential once admitted.

EXERCISE-INDUCED BRONCHOSPASM

Exercise-induced asthma (EIA) or exercise-induced bronchospasm (EIB) is described as a transitory increase in airway resistance that occurs following vigorous exercise.[6]

Epidemiology

Although EIB occurs mainly in those with clinically recognised asthma—in 80% of asthmatics not taking inhaled corticosteroids and in 50% of those who do—it has also been documented in healthy asymptomatic persons—schoolchildren, defence force recruits, highly trained athletes and skaters. One study reported that 10% of Australian schoolchildren with no suggestive history of asthma have EIB.[7] The prevalence of EIB in the total Australian population is thought to be 12%, with equal distribution in both sexes. In elite athletes, the prevalence has also been shown to be significantly higher, particularly in those participating in cold weather, endurance- or swimming pool-based sports.

The prevalence of EIB in elite athletes has progressively increased over the years. In the 1976 and 1980 Summer Olympic Games, 9.7% and 8.5%, respectively, of the Australian Olympic athletes reported asthma in a physical examination.[8] However, in the 2000 Australian Summer Olympic team, 21% of the athletes reported asthma or EIB.[9] Similarly, in the 1984 US Summer Olympic team, 11% reported on a medical history that they had asthma,[10] whereas in the 1996 Summer Olympic Games, 17% of the athletes had asthma, as defined by athlete-reported use of medication or previous diagnosis of asthma by a physician.[11]

A similar high prevalence of EIB was seen in the 1998 US Winter Olympic team; 22% had asthma defined as athlete-reported use of asthma medication or previous diagnosis of asthma by a physician.[12] With the advent of required formalised laboratory testing and stricter guidelines for the use of asthma medications in major sporting competitions, the prevalence of asthma/EIA was reduced in subsequent international competitions.

More recently, the prevalence of asthma/EIB in athletes competing in either the Summer or Winter Olympic Games between 2004 and 2010 was found to be approximately 8%; it was the most common chronic medical condition in the Olympic athletes.[13] Furthermore, it was shown that the prevalence of asthma and EIA/EIB in both summer and winter athletes, was:

- much higher in endurance compared to non-endurance athletes
- significantly higher in the older athletes.

This suggests that years of endurance training may provoke airway injury and inflammation with possible airway remodelling and the development of AHR and asthma.[13]

Pathophysiology

In most cases, bronchoconstriction does not occur during the first few minutes of exercise but rather begins during the first few minutes of recovery.

It is well accepted that the combination of heat and water loss during strenuous exercise, as air is conditioned for gas exchange in the alveoli, results in an increase in the osmolarity of the airway surface fluid.[14] This increase in osmolarity leads to mast cell degranulation and the release of a number of inflammatory mediators, including leukotrienes, cytokines, histamine and prostaglandins, which induce a transient bronchoconstriction occurring soon after exercise.

However, the actual mechanism responsible for the development over time of increased AHR and EIB in athletes is not known. It does appear that the combination of dehydration of the small airways, combined with the increased mechanical forces on the airways during the severe hyperpnoea of exercise, may result in injury to the airway epithelium. This may be further compounded by the inhalation of allergens, irritants, pollutants and cold air. The subsequent injury–repair process of the airway epithelium may contribute to the development of the AHR seen in the athletes.

Impact of the injury to the airway epithelium

1. Short-term:
   (a) The immediate impact of injury on the airway epithelium is a reduction in the integrity of the physical barrier of the epithelium. This results in an increased risk of the penetration of the airway epithelium by pathogens (bacteria and viruses), and pollutants and irritants (ozone, allergens, chlorine). Consequently, athletes are at increased risk of upper respiratory infections following intense endurance events.[15]
   (b) A reduction in the release of the bronchoprotective prostaglandins (PgE2) by epithelial cells. PgE2 functions to inhibit mast cell activation and thus the release of inflammatory mediators, as well as inducing the relaxation of airway smooth muscle. Consequently, post-exercise, an increase in airway narrowing and a reduction in mucociliary (sputum) clearance could occur. The short-term post-exercise insult on the airways has been shown to last less than 20 hours.
2. Long-term:
   Although the airway epithelium recovers rapidly following exercise, an important potential consequence is the activation of inflammatory mechanisms in both the recovering injured and surrounding uninjured cells. The injury–repair response is associated with many tissue responses including: hypersecretion, plasma exudation, the recruitment and activation of leucocytes, and the proliferation of fibroblasts and smooth muscle cells.

In endurance athletes who train daily, repeated injury to the airway with the associated injury–repair response and consequent changes in the subepithelial environment, may result in a change in the contractile properties of the airway smooth muscle, with a long-term risk of the development of AHR.

Importantly, both the seasonal variability observed in the AHR in elite athletes, combined with the resolution of the AHR in swimmers who are having a break from swimming, suggests that at least some of the changes that occur in the airways are transient.[16]

Aetiology

The aetiology of EIB in elite athletes appears to vary depending on the sporting discipline. Exercise-induced bronchospasm is thought to develop as a consequence of injury to the airways secondary to exposure of the airways to large volumes of cold air, allergens, pollens, pollutants, smoke or dust. Elite athletes may increase their ventilation during intense exercise to up to 200 L/min and thus the load of such substances delivered to the airways may be extremely large.

In summer sports, exposure to and inhalation of allergens play a major role in the development of EIB.[17–20] In winter sports, inhalation of cold air,[21] and in swimmers, inhalation of the gases of chlorine and its metabolites, which form a layer on the water surface of all pools, play a role.[22]

Clinical features

During exercise, flow rates and volumes actually improve in many subjects, in both those with and without EIB. When exercise is continued for 6–8 minutes, the flow rates begin to fall in those with EIB. The lowest rates are usually, observed 5–12 minutes following exercise cessation. It is the falling flow rates and volumes that are characteristic of the 'asthmatic response'.

Siblings of asthmatics, hay fever sufferers and patients with cystic fibrosis may also increase their flow rates during exercise, but only those with EIB show a reduction in excess of 10% after cessation of exercise.[23] When establishing a history of EIB, it is important to confirm that the patient had symptoms after exercise ceased, not only during exercise.

Most athletes with mild EIB recover spontaneously within minutes or soon after treatment with a bronchodilator; however, more severe bronchoconstriction may persist for up to an hour without treatment. In 50% of athletes who suffer from EIB, there is a period after an episode of bronchoconstriction where further exercise is followed by either less severe or no bronchoconstriction at all. This 'refractory period' may persist for up to four hours following the initial episode of EIB.

Diagnosis

A clinical suspicion of EIB may be indicated by symptoms of:

- dyspnoea
- chest tightness
- wheeze
- a dry cough post-exercise
- poor performance
- fatigue.

Often the symptoms are made worse when exercising during the pollen season, indoors or in cold air. A firm diagnosis of EIB, however, cannot be made based on symptoms alone as these have been shown to be poor indicators of EIB. A number of studies have shown that a diagnosis based purely on a history of exercise-related respiratory symptoms has a high level of misdiagnosis, both overdiagnosis and underdiagnosis.[24, 25]

Diagnosis depends on demonstrating a deterioration in lung function, in particular the forced expiratory volume in one second (FEV^1), measured by lung spirometry following a recognised bronchial provocation challenge test (Figs 11.2 and 11.3). Previously, reductions in PEFR or forced expiratory flow (FEF^{25-75}) were also accepted, but these are now discouraged due to problems with reliability and reproducibility.

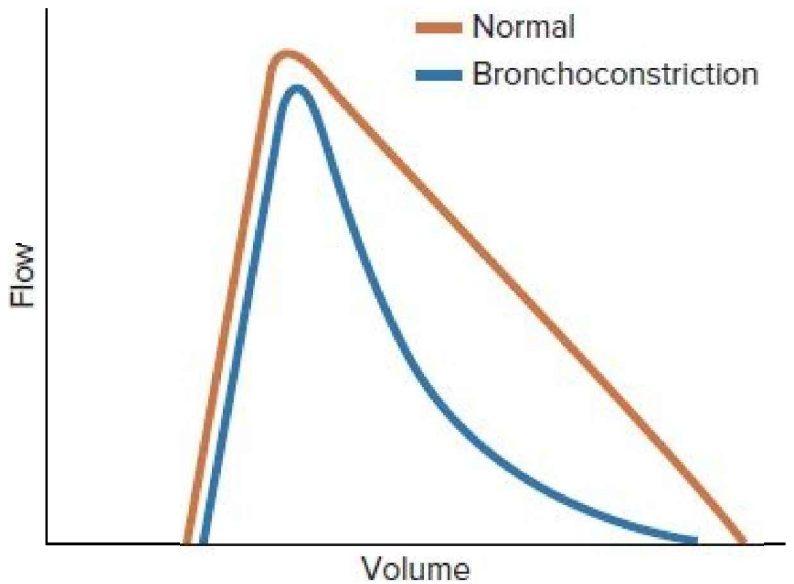


Figure 11.2 Flow volume graph showing normal and bronchoconstriction pattern

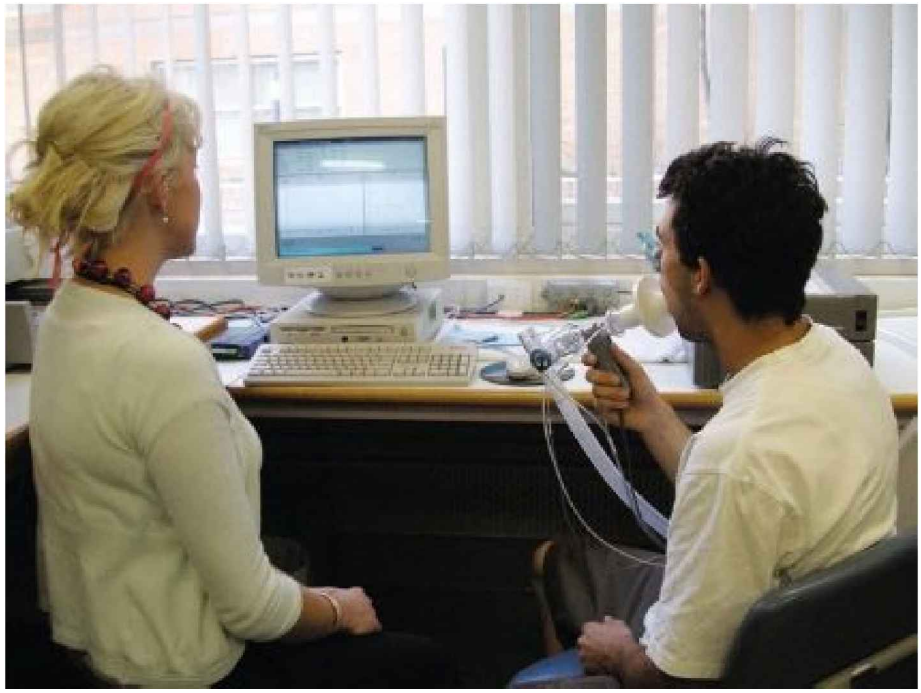


Figure 11.3 Lung spirometry

Until 2010, the International Olympic Committee Medical Commission (IOC-MC) and other major sporting bodies required objective evidence of asthma or EIB for athletes to be permitted to use certain permitted beta agonists. The use of these medications required submission of abbreviated therapeutic use exemption (aTUE) forms (see Chapter 34). However, this requirement was removed in 2010 for two of the more commonly used asthma medications—inhaled salbutamol and salmeterol—and now a simple declaration of use at the time of the drug test is sufficient. However, as of January 2018, restrictions were introduced on the maximum doses of inhaled salmeterol, inhaled formoterol and salbutamol, both in and out of competition (Chapter 34).[26]

Page 166

The World Anti-Doping Agency (WADA) still requires objective evidence of asthma or EIB for athletes to be permitted to use particular asthma medications (some types of short- and long-acting inhaled beta-2 agonists). Use of these medications requires submission of TUEs for all athletes at state level or above, as dictated by the WADA in January 2010.

Bronchial provocation challenge tests

The challenge tests are classified as being either direct or indirect.

Direct challenge tests

Direct challenge tests, otherwise known as pharmacological challenge tests, involve the administration of increasing doses of a drug, usually histamine or methacholine, that acts directly

on the airway smooth muscle receptors to elicit bronchoconstriction. The main problem with this type of challenge test is that although they have a high sensitivity for detecting bronchial hyperresponsiveness, they have a low specificity for EIB, as both healthy subjects and those with other lung diseases may also have a positive response. Another disadvantage is that direct challenge tests, in contrast to indirect challenge tests, cannot be used to assess the response of a patient to treatment.

Indirect challenge tests

Indirect challenge tests act indirectly by provoking mast cell degranulation and thus the release of mediators, which then act on the receptors to elicit narrowing of the airways (see box). They have been found to have both a high sensitivity and specificity for EIB.

Indirect challenge tests for exercise-induced bronchospasm

Exercise challenge test

The exercise challenge test involves exercising the patient on an exercise bike or treadmill for a minimum of 4 minutes, but preferably for up to 8 minutes, at an intensity sufficient to raise ventilation to approximately 50% of the predicted maximum voluntary ventilation for the duration of the exercise.

This test has the disadvantage that in elite athletes a sufficient level of ventilation cannot be achieved.[27]

Eucapnic voluntary hyperpnoea challenge test

The eucapnic voluntary hyperpnoea (EVH) challenge test (Fig. 11.4) requires the voluntary hyperventilation of dry air containing 4.9% carbon dioxide. One of two protocols may be used:

Figure 11.4 Eucapnic voluntary hyperpnoea (EVH) challenge test

- The progressive protocol involves the patient ventilating at each of 30%, 60% and 90% of his or her maximum voluntary ventilation for a period of 3 minutes.
- The steady state protocol involves the patient ventilating at 80% maximum voluntary ventilation for 6 minutes.

The progressive protocol is recommended for clinically recognised asthmatics, while the steady state protocol is recommended for asymptomatic subjects, elite athletes, defence force recruits and persons with no recent history of asthma or in those in whom no airway narrowing was elicited in the progressive protocol.

This challenge test is the current gold standard for the diagnosis of exercise-induced bronchospasm (EIB).[28, 29]

Hyperosmolar saline challenge test

The hyperosmolar saline challenge test requires the administration of increasing doses of inhaled 4.5% saline, which is thought to increase the osmolarity of the airways and, in susceptible individuals, leads to mast cell degranulation and release of mediators. These mediators then act to provoke airway narrowing. After each dose of saline, measurements of lung function are recorded. The test is aborted when the lung function falls by greater than 15% from pre-testing levels or when the full dose of 22 mL is reached. The response is said to be mild when the dose causing a fall of 15% is greater than 6 mL, moderate at 2.0–6.0 mL and severe at less than 2.0 mL.

This test is particularly valuable for assessing a subject's suitability for scuba diving.[29]

Mannitol challenge test

The mannitol challenge test is similar to the hyperosmolar challenge test. This test requires the administration of doubling doses of inhaled mannitol, which acts to increase the osmolarity of the airways, thus leading to mast cell degranulation and subsequent airway narrowing in those with bronchial hyperresponsiveness. Again, after each dose, airway function is measured. The test is continued until a greater than 15% fall in lung function occurs or a cumulative dose of 635 mg of mannitol is given.

This test has been shown to have a high sensitivity and specificity for the diagnosis of EIB in athletes.[29] This test has the advantages of not being laboratory dependent (unlike those above), or time consuming, and being safe and inexpensive.[30]

Diagnostic criteria

Each of the above challenge tests involves the measurement of lung function, in particular the FEV^1, PEFR or $FEF^{25–75}$ for up to 20 minutes following the challenge. The FEV^1 is the most sensitive and reliable measure of lung function and is universally accepted. The $FEF^{25–75}$, which measures the flow through the mid-portions of the vital capacity, was previously considered important in the diagnosis of EIB; however, similar to the PEFR, it has high variability and is dependent on the vital capacity, which can change from pre- to post-exercise. Thus, the diagnosis of EIB based on changes in the PEFR or $FEF^{25–75}$ is not recommended.

Depending on the type of challenge test, the accepted fall in the FEV^1 for a positive challenge varies from 10% to 20% and must occur within a specified period following the administration of the challenge dose or within a specific cumulative dose of administered agent. The IOC-MC accepts a fall of 10% in FEV^1 from baseline on two consecutive measurements for the eucapnic voluntary hyperpnoea challenge test and the exercise challenge test, both in the field and laboratory, of 15% for the hypertonic (also called hyperosmolar) saline challenge test and of 20% for the methacholine challenge test (Table 11.3).

Table 11.3 Diagnostic criteria for exercise-induced bronchospasm as guided by the IOC-MC

Bronchial provocation challenge test	Change in FEV^1 from baseline values
Post-bronchodilator	Increase by ≥ 12%
Eucapnic voluntary hyperpnoea challenge	Decrease by ≥ 10%
Laboratory exercise challenge	Decrease by ≥ 10%
Field exercise challenge	Decrease by ≥ 10%
Methacholine challenge	Decrease by ≥ 20%
Hypertonic saline challenge	Decrease by ≥ 15%

It is important that on the day of testing patients do not undertake any form of exercise prior to the challenge and that they withhold their usual asthmatic medication, for a duration (as instructed) depending on the type of medication.

The severity of the EIB can be assessed either by the percentage fall in the FEV^1 in response to a standard challenge (e.g. exercise or hyperventilation) (Table 11.4) or the dose of an agent required to induce a 15% fall in FEV^1 (e.g. hypertonic saline or mannitol) (Table 11.5).

Table 11.4 Severity of exercise-induced bronchospasm—exercise/hyperpnoea challenge test

Severity	Fall in FEV[1]
Mild	10–25%
Moderate	25.1–50%
Severe	50%

Table 11.5 Severity of exercise-induced bronchospasm—hypertonic saline challenge test

Severity	Saline (mg)
Mild	6
Moderate	2.0–6.0
Severe	<2.0

The factors influencing the severity of EIB are:[31]

1. type of exercise—endurance sports, cold weather sports and swimming (Table 11.6)
2. duration of exercise
3. intensity of exercise—in general, the more strenuous the exercise, the more likely EIB will occur
4. environmental factors:
   (a) cold more than warm
   (b) dry more than humid
   (c) air pollutants (e.g. sulphur dioxide and ozone)
5. interval since last episode of EIB (refractory period)
6. underlying bronchial hyperreactivity.

Table 11.6 Sports likely to be associated with exercise-induced bronchospasm

- Middle/long-distance running
- Cross-country skiing
- Figure skating
- Swimming
- Aerobics
- Cycling
- Dancing
- Basketball
- Soccer
- Rugby

Treatment

The treatment of EIB is summarised in the flow chart in Figure 11.5.

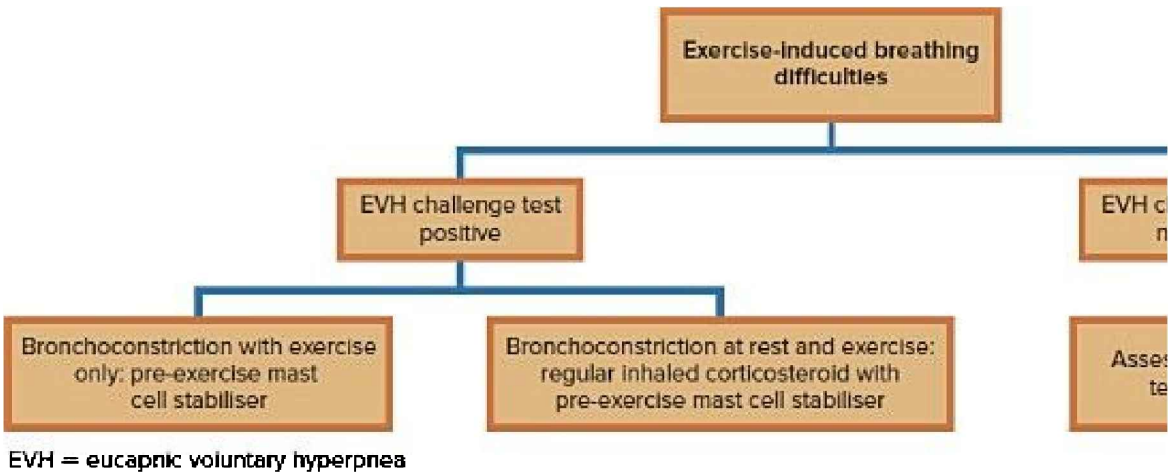


Figure 11.5 Management of exercise-induced bronchospasm

Non-pharmacological treatment

Most principles of non-pharmacological treatment are based on the theory that the primary stimulus for EIB is respiratory water loss.

Masks

Masks capture some of the heat and water on expiration so that it is inhaled in the next inspiration. They have been found to be successful in reducing the severity of EIB.[32]

Nose breathing

Nose breathing during exercise has a similar effect to that of wearing masks.[33] However, nose breathing is not effective in everyone or during vigorous exercise. In addition, in some athletes the nasal mucosa is as sensitive as the lower airways, leading to nasal stuffiness, increased secretions and sneezing.

Exercise training

The results of exercise training have been controversial. Training has been shown to increase the threshold at which EIB occurs.[34] There are a few reports of a reduced severity in EIB symptoms post-training, but the majority of studies demonstrate no change in the occurrence or degree of EIB.[35, 36]

Warm-up

Both submaximal work and short sprints have been shown to facilitate marked reductions in EIB

for subsequent exercise.[37–39] It is felt that such warm-ups increase bronchial blood flow and thus improve water delivery to the airways.

Refractory period

The refractory period occurs after exercise in more than 50% of subjects and may be used to lessen the severity of EIB.[40] The exact mechanism whereby a person becomes refractory is not known, but may be secondary to an improved delivery of water to the airways during the second episode of exercise. This effect is short-lived (a few hours) and can be inhibited by the use of NSAIDs.

Pharmacological treatment

Sodium cromoglycate (cromolyn sodium)

Sodium cromoglycate (cromolyn) is a prophylactic aerosol medication administered in a dose of 20–40 mg, 5–10 minutes prior to exercise. Its mode of action is thought to be that of stabilisation of the basement membrane of the mast cell, preventing the release of the mediators for EIB. It also acts to decrease vagal nerve afferent activity. It is most effective within two hours of administration and has been shown to prevent both the early- and late-phase asthmatic reactions. It has no bronchodilating effects so cannot be used in the treatment of acute symptoms. It has minimal adverse effects.[41]

Nedocromil sodium

Like sodium cromoglycate, nedocromil sodium has a membrane-stabilising effect, preventing the release of mediators from mast cells and other inflammatory cells. It is administered in an inhaled dose of 4 mg, 5–10 minutes prior to exercise, with a duration of action of up to four hours. It, too, is effective in preventing the early- and late-phase asthmatic reactions but it is ineffective when used to treat acute symptoms.[42–44] Although it has minimal adverse effects, some patients do complain of the taste of this medication.

Beta-2 agonists

Inhaled beta-2 agonists are the most effective drugs available for the relief of acute asthma symptoms. They induce bronchodilation, prevent the release of mediators from mast cells, and modify the effects of the mediators on both the contractility of smooth muscle and the permeability of mucosal cells. Although it is effective in providing rapid symptomatic improvement to EIB, regular use of beta-2 agonists leads to tolerance to the effects of these medications and may result in a reduction in baseline lung function, poor asthma control and increased bronchial hyperresponsiveness.[45] Two main types of beta-2 agonists are available:

- Short-acting agents (e.g. salbutamol/albuterol, terbutaline). These agents have a rapid onset of action, usually within 5 minutes, with peak bronchodilation occurring within 15 minutes. Duration of action varies but effectiveness against EIB usually lasts 3–6 hours. These agents are the gold standard for the treatment of symptoms of EIB but are not recommended for use in the prevention of EIB.

- Long-acting agents (e.g. salmeterol, formoterol). These agents have a slower onset of action and, as such, cannot be used in the treatment of symptoms of EIB. The onset of action usually occurs within 20 minutes and the duration of action is at least 12 hours. Formoterol has been shown to induce bronchodilation at both 15 minutes and 4 hours post-administration.[46] As well as the above complications associated with regular use of beta-2 agonists, salmeterol has the additional problem of a reduction in the acute bronchoprotection against EIB.[47]

Leukotriene antagonists

Leukotrienes are potent bronchoconstrictors that also act to stimulate bronchial secretion of mucus and increase venopermeability, leading to airway oedema. They are present in the airways of asthmatics but not normal subjects. Leukotriene antagonists (montelukast, zafirlukast) given orally prior to exercise attenuate the bronchoconstrictor and inflammatory response that would otherwise occur in response to the exercise.[48] One study showed that montelukasts provided superior protection compared with inhaled salmeterol (a long-acting beta-2 agonist).[49]

Inhaled corticosteroids

Inhaled corticosteroids improve asthma symptoms by reducing airway inflammation and bronchial hyperreactivity. They do not have an immediate bronchodilator effect and are not effective if used as prophylaxis just prior to exercise. The main role of corticosteroids is that of a maintenance therapy to help control asthma, but in doing so they also act to reduce bronchial responsiveness to exercise, thereby reducing the propensity for EIB. They are often used on a regular basis, with sodium cromoglycate (cromolyn) or nedocromil sodium given prior to exercise.

Inhaled corticosteroids have been shown to reduce the incidence and severity of EIB.[50, 51] The main adverse effects are oral candidiasis and dysphonia, both of which can be reduced by rinsing the mouth following administration.[49]

Theophylline

The role of theophylline in the management of asthma has changed profoundly over recent years, as research into the inflammatory aetiology of asthma has led to the development of medications aimed to minimise this inflammation. Theophylline should not be used as intermittent prophylaxis for EIB as it is not a potent bronchodilator. In addition, the intermittent use increases the likelihood of adverse effects such as headaches, nausea, vomiting, tachycardia and central nervous system stimulation. The use of theophylline is, therefore, now limited to those with moderate–severe chronic asthma not controlled by mainstream anti-asthmatic medications.

CASE STUDY

Exercise-induced asthma

A 22-year-old female world champion Olympic distance triathlete presented with a deterioration in

performance over a 6-month period. She had gone from constantly being on the podium at international events to being unable to win a medal at national events. She described a feeling of 'becoming lactic' through a race and, when more details were sought, she described feeling heavy and struggling to get enough air. She felt that her fitness was the issue. Post-race a nagging cough would be present. She otherwise had no problems at rest or with light exercise.

Examination at rest, and in particular her cardiorespiratory examination, was unremarkable. Spirometry at rest was normal for her age and sex; however, suboptimal for what would be expected for a triathlete. A bronchial provocation challenge test was positive. Post-bronchodilator administration, the respiratory function increased substantially above the pre-challenge values.

The tests thus confirmed the presence of exercise-induced asthma. This was successfully managed with individually tailored asthma medications. Within six weeks of starting the medications, she was back on the international podium and within two months had qualified for the upcoming Olympic Games.

Other agents

Recent studies have suggested that fish oil,[52] diets low in sodium,[53] and diets high in vitamin C[54] may all play a protective role in relation to EIB.

Treatment model

It is important to note that some drugs used to treat asthma are banned by the WADA (Chapter 34). In athletes subject to drug-testing procedures, clinicians are urged to check current banned drug listings. A treatment model for those athletes with EIB is shown in Table 11.7. In athletes who are prone to developing EIB, the regular use of medication prior to exercise is advised.

Table 11.7 Pharmacological treatment of exercise-induced bronchospasm

Severity	Pre-exercise treatment	Regular treatment	Symptom treatment
Mild	Sodium cromoglycate (cromolyn)/nedocromil sodium		Short-acting beta-2 agonist
Moderate	Sodium cromoglycate (cromolyn)/nedocromil sodium	Low-dose inhaled corticosteroids	Short-acting beta-2 agonist
Severe	Sodium cromoglycate (cromolyn) and/or nedocromil sodium	Higher dose inhaled corticosteroids	Short-acting beta-2 agonist

CONDITIONS THAT MAY MIMIC EXERCISE-INDUCED BRONCHOSPASM

Vocal cord dysfunction

Vocal cord dysfunction is defined as the involuntary adduction of the vocal cords during inspiration.[55] During normal breathing, the true vocal cords abduct during inspiration and expiration; however, during vocal cord dysfunction, the true vocal cords adduct inappropriately during inspiration, resulting in airflow obstruction. Less commonly, severe narrowing of the vocal cords may occur during expiration.

Christensen and colleagues,[56] on behalf of the European Respiratory Society, European

Laryngological Society and the American College of Chest Physicians, recommended that the term ' vocal cord dysfunction' be replaced by 'induced laryngeal obstruction', with that occurring during exercise to be called 'exercise-induced laryngeal obstruction'. In this chapter, however, we will continue to use the term 'vocal cord dysfunction'.

The actual prevalence of VCD has not been adequately investigated. However, in those with exercise-induced dyspnoea, studies have found that approximately 30% have VCD. Page 171 Furthermore, numerous studies have now shown that the prevalence of VCD is higher in patients with asthma than those without.

Previously, the condition was thought to occur more commonly in women; however, it has now been shown to occur more frequently in adolescents, but with a female predominance.

Clinical features

The classical presentation of VCD in response to exercise is that of recurrent episodes of respiratory distress with the classic symptoms of dyspnoea, wheeze and cough (Table 11.8). The episodes can be precipitated by emotional stress, intense exercise and both extrinsic (e.g. pollutants) and intrinsic (e.g. gastro-oesophageal reflux) factors. Classically, in contrast to asthma, the symptoms occur and peak during exercise and resolve within 5 minutes of stopping the exercise. On closer questioning or on witnessing an episode, there is usually marked throat tightness and the wheeze is actually an inspiratory stridor—the hallmark feature of vocal cord dysfunction. The symptoms are variable and not necessarily reproducible when exercising under identical conditions. Both acute or prophylactic treatment with inhaled beta-2 agonists is ineffective. The symptoms may be worse during times of stress or moderate to severe lethargy. The features of vocal cord dysfunction are shown in Table 11.8.

Table 11.8 Comparative features of exercise-induced bronchospasm, vocal cord dysfunction and exercise-induced hyperventilation

Feature	Exercise-induced bronchospasm	Vocal cord dysfunction	Hyperventilation
During or after exercise	Worse in first 12 minutes following cessation of exercise	Worse during exercise Resolves within 5 minutes of cessation	Worse during exercise Resolves within 5 minutes of cessation
Reproducibility under controlled situations	Reproducible	Often not reproducible	Often not reproducible
Classic symptoms	Chest tightness Dyspnoea Cough Expiratory wheeze	Throat tightness/choking Dyspnoea Inspiratory stridor	Throat tightness Dyspnoea
Site of tightness	Chest	Throat	Throat
Bronchial provocation challenge tests	Abnormal	Normal	Normal
Spirometry	May be abnormal at rest	Normal at rest; abnormal during episode	Normal at all times
Laryngoscopy	Normal	Abnormal	Normal
Effect of beta-2 agonists	Prophylactic—prevents episode Therapeutic—resolves symptoms	Prophylactic—nil effect Therapeutic—nil effect	Prophylactic—nil effect Therapeutic—nil effect
Symptoms outside exercise	May be present	Absent	Absent

PRACTICE PEARL

Vocal cord dysfunction should be considered in all athletes complaining of exercise-induced dyspnoea, especially when either a diagnosis of EIB has been excluded or, alternatively, made but the athlete has failed to respond to appropriate treatment.

Investigations

The diagnosis is often one of exclusion:

1. Spirometry—may occasionally show a truncated inspiratory loop, but at rest is usually unremarkable.
2. A bronchial provocation challenge test should be performed—this may reveal or exclude underlying asthma or airway hyperreactivity, in addition to the inspiratory loop often being truncated in those with VCD following the challenge.
3. Exercise challenge—reproduction of the symptoms during an exercise challenge allows the treating physician to witness the episode.
4. Laryngoscopy—this is the recommended procedure for the diagnosis of VCD. The typical finding is inspiratory adduction of the anterior two-thirds of the vocal cords, with a posterior diamond-shaped chink. However, in the absence of acute symptoms the laryngoscopy is often normal. It is thus recommended that the laryngoscopy be performed during or immediately after intense exercise. Newman et al.[55] found that the laryngoscopy was only positive in 60% of those patients with VCD when asymptomatic compared with 100% during an acute episode. Similarly Morris et al.[57] found that the majority of patients with exertional VCD only had positive laryngoscopies during or immediately after exercise, not at rest.
5. Continuous laryngoscope exercise test allows the constant visualisation of the larynx throughout exercise, thus allowing an accurate diagnosis of laryngeal dysfunction.

Treatment

Treatment should initially address an underlying associated cause present, including EIA, laryngeal polyps etc. The treatment of VCD usually revolves around speech and relaxation therapy. It is essential that the speech therapist has experience with patients with vocal cord dysfunction. The focus of speech therapy is on respiratory control and diaphragmatic breathing patterns. As the athlete gains control over breathing patterns, he or she may realise a sense of control of this condition and reduce the emotional stress associated with dyspnoea.

Consultation with a psychologist is recommended to help the athlete recognise and come to terms with stress. It is also important for the psychologist to assess for and manage any other underlying psychological conditions.

Speech therapy, alone or in combination with other treatment interventions, has proven to be successful in reducing or eliminating the paroxysms of wheezing, stridor and dyspnoea.[58] With appropriate treatment, nearly all athletes who have VCD should be able to exercise and compete unimpeded.[59]

Weinberger et al.[60] trialled the use of inhaled anticholinergics prior to exercise in those with exercise-induced VCD and found that this is a good prophylactic treatment, in their small study cohort; however, more formalised studies are needed.

Exercise-induced hyperventilation

Exercise-induced hyperventilation is a common condition occurring both in athletes with underlying EIB and those without. Often during intense exercise, the athlete loses control of his or her breathing, resulting in rapid shallow breaths—the abdominal muscles are not used. The patient typically presents with dyspnoea and throat tightness occurring while exercising and resolving immediately with rest. The features of exercise-induced hyperventilation are shown in Table 11.8.

Bronchial provocation challenge tests, preferably a eucapnic voluntary hyperpnoea challenge test, should be performed to exclude underlying EIB. In those with known EIB not responding to treatment, the challenge test should be performed while the athlete is on medication, to confirm adequate control. An exercise challenge test should be performed to allow the treating physician to assess the athlete while he or she is experiencing the symptoms. Laryngoscopy is required to exclude vocal cord dysfunction.

Page 173

CASE STUDY

Vocal cord dysfunction

An 18-year-old footballer presented with a few months history of worsening ‘asthma’. He described an exercise-related dyspnoea and, if he continued to run, a loud wheeze and, at times, light headedness.

Having consulted the team sports physician, he was started on a salbutamol (Ventolin) inhaler both prior to a game and when symptoms occurred. He was taking a minimum of eight puffs per game for little improvement. He had had no formal investigations.

Examination at rest, and in particular his cardiorespiratory examination, was essentially unremarkable. Spirometry was normal pre- and post-bronchodilator. A bronchial provocation challenge test was normal.

A field challenge test revealed issues with his breathing technique. He failed to use his diaphragm and abdominal muscles; however, he overused his upper respiratory accessory muscles. A stridor developed. As he continued to run, he became lightheaded and unsteady.

Respiratory examination at the time of his symptoms was unremarkable. A laryngoscopy excluded the presence of a laryngeal web or polyps.

A diagnosis of vocal cord dysfunction was made. He was encouraged to stop using the inhaler and underwent a formalised breathing retraining program. His symptoms resolved.

Treatment involves educating the athlete to breathe, especially during times of stress or intense

exercise. Consultation with a psychologist with experience in this area is essential. Training is required and appropriate exercises are given. Concentration on the use of abdominal muscles during breathing is required. Principles similar to the Buteyko method of breathing may be used.

SINUS-RELATED SYMPTOMS

Sinusitis is a common disorder in both athletes and non-athletes. While acute infections are easily diagnosed, chronic sinusitis may be far more subtle in its presentation. The paranasal sinuses are air-filled spaces within the skull that communicate with the nose. Most commonly, the maxillary sinus is affected.

Clinical features of acute sinusitis may include facial pain, headache, toothache, post-nasal drip, cough, rhinorrhea, nasal obstruction, pyrexia and epistaxis. It is important to establish whether these symptoms are evidence of infective sinusitis or, alternatively, inflammation that is causing pain in the absence of infection. Inflammatory sinus pain may accompany acute exacerbations of rhinitis and is often short-lived. Features of chronic sinusitis are vague facial pain, post-nasal drip, cough, nasal obstruction, dental pain, malaise and halitosis.

General and local factors may predispose towards sinusitis. General factors include diabetes, immune deficiency, mucus abnormalities and disturbances in cilia function. Specific or local factors that may predispose athletes to this condition include anatomical deformities, polyps, foreign bodies, dental infections, cigarette smoking, barotraumas and local tumours. Failure to respond to therapy or recurrent episodes should prompt the search for a complicating condition (e.g. fracture, tumour or other abnormality).

Investigations

A computed tomography (CT) scan is the diagnosis of choice for chronic sinusitis. It allows the visualisation of structural abnormalities predisposing to the development of sinusitis, in addition to the common changes occurring with sinusitis, including soft-tissue attenuation, air–fluid levels and polyp formation.

In the patient with infective sinusitis, microbiological culture of nasal pus may be useful; however, the presence of normal bacterial flora makes interpretation difficult. Approximately 50% of infections are due to Haemophilus *influenzae* or *Streptococcus pneumonia,* but there are a variety of other organisms that may play a role, including *Branhamella catarrhalis* (most common organism in children) and other mixed oral anaerobes.

Management of sinusitis

The principles of management of sinusitis are:

1. appropriate antibiotic therapy
2. the establishment of sinus drainage through the release of obstruction and the stimulation of mucus flow
3. the control of any predisposing factors.

Systemically administered decongestants, including pseudoephedrine, are of some value in the treatment of acute sinusitis. However, a topical decongestant is more effective and will have fewer systemic adverse effects.

Antihistamines usually slow mucociliary function, but may have a role, especially if sinusitis is the result of nasal allergy. The use of topical steroids is widely advocated in the acute situation, but there is often a latent period before these are effective. The maintenance of hydration in the treatment of these patients is critical.

There may well be a role for surgery in either the acute or chronic condition where there is an anatomical deformity, polyps or a failure to respond to medical treatment.

OTHER EXERCISE-RELATED CONDITIONS

Exercise-induced anaphylaxis

Approximately 500 cases of exercise-induced anaphylaxis have been reported, mostly occurring in athletes.[61, 62] Numerous attacks may occur before the diagnosis is correctly made.

The condition is characterised by a sensation of warmth, pruritis, cutaneous erythema, angioedema, urticaria (greater than 1 cm diameter), upper respiratory tract obstruction and, occasionally, vascular collapse. It is considered a distinct entity from other exertion-related phenomena.

Risk factors include:

- previous atopic history (50%)
- family atopic history (67%)
- food ingestion (e.g. shellfish, celery, nuts, alcohol)
- weather conditions (e.g. heat, high humidity)
- drug ingestion (e.g. aspirin [ASA], NSAIDs).

The management of this condition involves:

1. prevention through modification of the exercise program to:
   (a) decrease intensity
   (b) avoid exercise during warm and humid days
   (c) stop exercise at the earliest sign of itching
   (d) avoid meals 4 hours before exercise
2. drugs/therapy
   (a) antihistamines
   (b) cromoglycate (cromolyn)
   (c) adrenaline (epinephrine)—athlete should have an injection available during exercise
   (d) pre-treatment does not prevent onset.

Cholinergic urticaria

Cholinergic urticaria is an exaggerated cholinergic response to rapid elevation of the core body temperature through a mechanism such as exercise (most commonly), hot showers, fever or anxiety.[63] It is characterised by generalised flushing, urticarial rash and pruritus. Generally, the urticarial papules appear first, within 10 minutes of starting exercise, on the neck or upper thorax and spread to the limbs.[64] Systemic reactions such as syncope, abdominal pain and wheezing are rare. Cholinergic symptoms such as lacrimation, salivation and diarrhoea may be observed. Recovery usually occurs spontaneously in 2–4 hours provided there are no systemic symptoms.[63] Antihistamines are generally used in treatment (e.g. hydroxyzine, 250 mg/day or cyproheptadine, 4 mg/day).

Exercise-induced angioedema

Angioedema is a non-itchy swelling occurring in the deep dermis and subcutaneous tissue. Although angioedema can affect any body region, it tends to involve the face and oral region. Occasional visceral manifestations occur. Attacks may be life-threatening if the airway is involved. Frank asthmatic attacks rarely occur in the setting of exercise-induced angioedema.[65]

Prevention may be achieved with modification of the exercise program and/or the use of antihistamines (e.g. diphenhydramine). Selective histamine H^2-receptor blockers (e.g. cimetidine) have been used in the treatment of this condition.

REFERENCES

1. Australian Bureau of Statistics (ABS) 2016. National Health Survey: First Results, 2014–15. ABS Cat no. 4364.0.55.001. Canberra: ABS.
2. National Institutes of Health. Practical guide for the diagnosis and management of asthma. Bethesda, MD: NIH Publication, 1997.
3. Global Initiative for Asthma. Global strategy for asthma management and prevention, 2016. https://www.ginasthma.org.
4. Paaso EMS, Jaakkola MS, Lajunen TK et al. The importance of family history in asthma during the first 27 years of life. *Am J Respir Crit Care Med* 2013; 188: 624–6.
5. Mukherjee AB, Zhang Z. Allergic asthma: influence of genetic and environmental factors. *J Biol Chem* 2011; 286(38): 32883–9.
6. Anderson SD. Exercise-induced asthma. In: Middleton E, Reed C, Ellis E et al., eds. *Allergy: principles and practice*. 4th ed. St Louis, MO: CV Mosby, 1993: 1343–67.
7. Anderson S. Exercise-induced asthma. In: Carlsen K-H, Ibsen T, eds. *Exercise-induced asthma and sports in asthma*. Copenhagen: Munksgaard Press, 1999: 11–17.
8. Fitch KD. Management of allergic Olympic athletes. *J Allergy Clin Immunol* 1984; 73:

722–7.

9. Corrigan B, Kazlaukas R. Medication use in athletes selected for doping control at the Sydney Olympics (2000). *Clin J Sport Med* 2003; 13: 33–40.
10. Voy RO. The US Olympic Committee experience with exercise-induced bronchospasm, 1984. *Med Sci Sports Exerc* 1986; 18(3): 328–30.
11. Weiler JM, Layton T, Hunt M. Asthma in United States Olympic athletes who participated in the 1996 summer games. *J Allergy Clin Immunol* 1998; 102(5): 722–6.
12. Weiler JM, Ryan EJ, 3rd. Asthma in United States Olympic athletes who participated in the 1998 Olympic winter games. *J Allergy Clin Immunol* 2000; 106(2): 267–71.
13. Fitch KD. An overview of asthma and airway hyperresponsiveness in Olympic athletes. *Br J Sports Med* 2012; 46: 413–16.
14. Daviskas E, Gonda I, Anderson SD. Local airway heat and water vapour losses. *Respir Physiol* 1991; 84: 115–32.
15. Nieman DC. Is infection risk linked to exercise workload? *Med Sci Sports Exerc* 2000; 32: S406–11.
16. Kippelen P, Anderson SD. Airway injury during high-level exercise. *Br J Sports Med* 2012; 46(6): 385–90.
17. Boulet L-P, Turcotte H, Laprise C. Comparative degree and type of sensitisation to common indoor and outdoor allergens in subjects with allergic rhinitis and/or asthma. *Clin Exp Allergy* 1997; 27: 52–9.
18. Helenius IJ, Tikkanen HO, Haahtela T. Association between type of training and risk of asthma in elite athletes. *Thorax* 1997; 52: 157–60.
19. Holzer K, Anderson SD, Douglass J. Exercise in elite summer athletes: challenges for diagnosis. *J Allergy Clin Immunol* 2002; 110(3): 374–80.
20. Warner JO. Bronchial hyperresponsiveness, atopy, airway inflammation and asthma. *Pediatr Allergy Immunol* 1998; 9: 56–60.
21. Langdeau JB, Boulet LP. Prevalence and mechanisms of development of asthma and airway hyperresponsiveness in athletes. *Sports Med* 2001; 31(8): 601–16.
22. Drobnic F, Freixa A, Casan P et al. Assessment of chlorine exposure in swimmers during training. *Med Sci Sports Exerc* 1996; 28(2): 271–4.
23. Anderson SD, Silverman M, Konig P et al. Exercise-induced asthma: a review. *Br J Dis Chest* 1975; 69: 1–39.
24. Rundell KW, Im J, Mayers LB et al. Self-reported symptoms and exercise-induced asthma in the elite athlete. *Med Sci Sports Exerc* 2001; 33(2): 208–13.
25. Holzer K, Douglass J, Anderson SD. Methacholine has a low sensitivity to identify elite athletes with a positive response to eucapnic voluntary hyperpnea and should not be used to exclude potential exercise-induced bronchoconstriction. *Respirology* 2002; 7(suppl): A28.

26. World Anti-Doping Agency. Summary of major modifications and explanatory notes. 2018 Prohibited List. https://www.wada-ama.org/sites/default/files/prohibited_list_2018_summary_of_modifications_en.pdf
27. Anderson SD. Exercise-induced asthma. In: Kay AB, ed. *Allergy and allergic diseases*. Oxford: Blackwell Scientific Publications, 1997; 692–711.
28. Anderson SD, Argyros GJ, Magnussen H et al. Provocation by eucapnic voluntary hyperpnoea to identify exercise induced bronchoconstriction. *Br J Sports Med* 2001; 35: 344–7.
29. Holzer K, Anderson SD, Chan H-K et al. Mannitol as a challenge test to identify exercise-induced bronchoconstriction in elite athletes. *Am J Respir Crit Care Med* 2003; 167(4): 534–47.
30. Anderson SD, Brannan J, Spring J et al. A new method for bronchial-provocation testing in asthmatic subjects using a dry powder of mannitol. *Am J Respir Crit Care Med* 1997; 156: 758–65.
31. Mahler DA. Exercise-induced asthma. *Med Sci Sports Exerc* 1993; 25(5): 554–61.
32. Nisar M, Spence DPS, West D et al. A mask to modify inspired air temperature and humidity and its effect on exercise induced asthma. *Thorax* 1992; 47: 446–50.
33. Shturman-Ellstein R, Zeballos RJ, Buckley JM et al. The beneficial effect of nasal breathing on exercise-induced bronchoconstriction. *Am Rev Respir Dis* 1978; 118: 65–73.
34. Fitch KD, Blitvich JD, Morton AR. The effect of running training on exercise-induced asthma. *Ann Allergy Asthma Immunol* 1986; 7: 90–4.
35. Welsh L, Kemp JG, Roberts RG. Effects of physical conditioning on children and adolescents with asthma. *Sports Med* 2005; 35(2): 127–41.
36. Ram FS, Robinson SM, Black PN. Effects of physical training in asthma: a systematic review. *Br J Sports Med* 2000; 34(3): 162–7.
37. de Bisschop C, Guenard H, Desnot P et al. Reduction of exercise-induced asthma in children by short, repeated warm ups. *Br J Sports Med* 1999; 33: 100–4.
38. Schnall RP, Landau LI. Protective effects of repeated short sprints in exercise-induced asthma. *Thorax* 1980; 35: 828–32.
39. McKenzie DC, McLuckie SL, Stirling DR. The protective effects of continuous and interval exercise in athletes with exercise-induced asthma. *Med Sci Sports Exerc* 1994; 26(8): 951–6.
40. Edmunds A, Tooley M, Godfrey S. The refractory period after exercise-induced asthma: its duration and relation to the severity of exercise. *Am Rev Respir Dis* 1978; 117: 247–54.
41. Anderson SD. Exercise-induced asthma: stimulus, mechanism, and management. In: Barnes PJ, Rodger I, Thomson NC, eds. *Asthma: basic mechanisms and clinical management*. London: Academic Press, 1988: 503–22.

42. Speelberg B, Verhoeff NPLG, van den Berg NJ et al. Nedocromil sodium inhibits the early and late asthmatic response to exercise. *Eur Respir J* 1992; 5: 430–7.
43. Spooner C, Rowe BH, Saunders LD. Nedocromil sodium in the treatment of exercise-induced asthma: a meta-analysis. *Eur Respir J* 2000; 16(1): 30–7.
44. Spooner CH, Saunders LD, Rowe BH. Nedocromil sodium for preventing exercise-induced bronchoconstriction. *Cochrane Database Syst Rev* 2002; 1: CD001183.
45. Bhagat R, Kalra S, Swystun A. Rapid onset of tolerance to the bronchoprotective effect of salmeterol. *Chest* 1995; 108: 1235–9.
46. Ferrari M, Balestreri F, Baratieri S et al. Evidence of the rapid protective effect of formoterol dry-powder inhalation against exercise-induced bronchospasm in athletes with asthma. *Clin Invest Med* 2000; 67: 510–13.
47. Rupp NT. Diagnosis and management of exercise-induced asthma. *Phys Sportsmed* 1996; 24(1): 77–87.
48. Makker HK, Lau LC, Thomson HW et al. The protective effect of inhaled leukotriene D_4 receptor antagonist ICI 204,219 against exercise-induced asthma. *Am Rev Respir Dis* 1993; 147: 1413–18.
49. Ferrari M, Segattini C, Zanon R et al. Comparison of the protective effect of salmeterol against exercise-induced bronchospasm when given immediately before a cycloergometric test. *Respiration* 2002; 69(6): 509–12.
50. Henriksen JM, Dahl R. Effects of inhaled budesonide alone and in combination with low-dose terbutaline in children with exercise-induced asthma. *Am Rev Respir Dis* 1983; 128: 993–7.
51. Waalkans HJ, van Essen-Zandvliet EE, Gerritsen J et al. The effect of an inhaled corticosteroid (budesonide) on exercise-induced asthma in children. *Eur Respir J* 1993; 6: 652–6.
52. Mickleborough TD, Lindley MR, Ionescu AA et al. Protective effect of fish oil supplementation on exercise-induced bronchoconstriction in asthma. *Chest* 2006; 129(1): 39–49.
53. Mickleborough TD. Salt intake, asthma, and exercise-induced bronchoconstriction: a review. *Phys Sportsmed* 2010; 38(1): 118–31.
54. Tecklenburg SL, Mickleborough TD, Fly AD et al. Ascorbic acid supplementation attenuates exercise-induced bronchoconstriction in patients with asthma. *Respir Med* 2007; 101(8): 1770–8.
55. Newman KB, Mason UG, 3rd, Schmaling KB. Clinical features of vocal cord dysfunction. *Am J Respir Crit Care Med* 1995; 152(4 Pt 1): 1382–6.
56. Christensen PM, Heimdal JH, Christopher KL et al.; ERS/ELS/ACCP Task Force on Inducible Laryngeal Obstructions. ERS/ELS/ACCP 2013 International consensus conference nomenclature on inducible laryngeal obstructions. *Eur Respir Rev* 2015; 24(137): 445–50.

57. Morris MJ, Deal LE, Bean DR et al. Vocal cord dysfunction in patients with exertional dyspnoea. *Chest* 1999; 116 (6): 1676–82.
58. Sullivan MD, Heywood BM, Beukelman DR. A treatment for vocal cord dysfunction in female athletes: an outcome study. *Laryngoscope* 2001; 111(10): 1751–5.
59. Newshaun KR, Claben DK, Miller DJ et al. Paradoxical vocal cord dysfunction management in athletes. *J Athl Train* 2002; 37: 325–8.
60. Weinberger M, Doshi D. Vocal cord dysfunction: a functional cause of respiratory distress. *Breathe* 2017; 13(1): 15–21.
61. Castells MC, Horan RS, Sheffer AL. Exercise induced anaphylaxis. *Clin Rev Allergy Immunol* 1999; 17: 413–24.
62. Castells MC, Horan RS, Sheffer AL. Exercise induced anaphylaxis. *Curr Allergy Asthma Rep* 2003; 3: 15–21.
63. Volcheck GW, Li JT. Exercise-induced urticaria and anaphylaxis. *Mayo Clin Proc* 1997; 72(2): 140–7.
64. Sweeney TM, Dexter WW. Cholinergic urticaria in a jogger: ruling out exercise-induced anaphylaxis. *Phys Sportsmed* 2003; 31(6): 32–6.
65. Leung AKC, Hedge HR. Exercise-induced angioedema and asthma. *Am J Sports Med* 1989; 17(3): 442–3.

Chapter 12

Gastrointestinal symptoms

with CHRIS MILNE and PAUL BLAZEY

But there was something about me that was broken, unhealthy, unfit. Some called it allergies, some called it asthma, some just called it being out of shape. But no matter what we called it, no one knew how to fix it.

Novak Djokovic, 14-time Grand Slam winner, *Serve to Win*, 2013

The gut is not an athletic organ. During exercise, blood is directed away from the splanchnic vessels and to the exercising muscles. The gut therefore becomes relatively ischaemic causing many of the gastrointestinal symptoms associated with exercise. These symptoms may be divided into those relating to the upper gut and those relating to the lower gut (Table 12.1). Bleeding is another important clinical presentation, as discussed below.

Table 12.1 Gastrointestinal symptoms associated with exercise

Upper gastrointestinal tract	Lower gastrointestinal tract
Heartburn	Cramping
Reflux	Urge to defecate
Nausea	Diarrhoea
Vomiting	Rectal bleeding
Bloating	Flatulence
Epigastric pain	

Physiological changes that alter gastrointestinal function during exercise include reduced blood flow to the abdominal viscera, gastrointestinal hormone change and alterations to gastric emptying rates alongside intestinal motility. Vigorous diaphragmatic movements, abdominal contractions and intestinal jarring can all cause mechanically induced abdominal symptoms.[1]

Although the incidence of gastrointestinal symptoms is increased with exercise, the presence of symptoms in an athlete should not automatically be assumed to be solely related to exercise.

Athletes as well as non-athletes suffer from common conditions such as hiatus hernia and peptic ulceration, inflammatory bowel disease, polyps and cancer. Physical activity confers a 25% reduction in colon cancer risk.[2] Clinical judgment is required to appreciate when these conditions must be considered in the athlete with gastrointestinal symptoms.

A summary of the management of common gastrointestinal symptoms is shown in Table 12.2.

Table 12.2 Treatment of common gastrointestinal problems

Symptoms	Treatment
Heartburn, reflux, epigastric pain	Avoid solid foods prior to exercise Antacid medication Histamine H_2-receptor antagonist (rarely necessary)
Gastrointestinal bleeding	Ensure adequate hydration Reduce jarring (e.g. food, shoes, soft surfaces)
Abdominal stitch	Reassurance Avoid pre-exercise meal
Runner's diarrhoea	Reduce fibre content of food 24 hours prior to run Antidiarrhoeal medication (e.g. loperamide)

UPPER GASTROINTESTINAL SYMPTOMS

Heartburn, reflux, nausea, vomiting and upper abdominal pain are the most common upper gastrointestinal (GI) tract symptoms related to exercise. Upper GI symptoms can affect anywhere from 30 to 70% of athletes.[3, 4] Gastro-oesophageal reflux is a common complaint among athletes and can even cause asthma-like symptoms.[5] Twenty per cent of patients with established reflux consider exercise to be the major contributor to their symptoms.

Page 176

The mechanism by which exercise causes reflux is not well understood, as reflux is normally associated with relaxation of the lower oesophageal sphincter. This has not been described with exercise. Reflux appears to be more common when exercise is performed after a meal. Importantly, exercise does not appear to have any effect on gastric acid secretion.

PRACTICE PEARL

Distinguishing between chest pain due to gastro-oesophageal reflux or oesophageal muscular spasm and chest pain due to causes of chest wall or cardiac origin can be difficult. Any athlete presenting with chest pain on exertion must be thoroughly assessed to exclude cardiac causes.

Much attention has been paid to the factors that may affect the gastric emptying rate. Exercise at a very high intensity reduces the gastric emptying rate. However, as this level of exercise intensity cannot be maintained for long periods, its effect on the gastric emptying rate may be insignificant. Increased volume in the stomach results in an initial rapid emptying, followed by a

phase of reduced emptying once the volume of the stomach has decreased to about 30% of its initial content.

Until recently, it was thought that osmolality was an important factor in the rate of gastric emptying. While it is true that liquids empty more quickly than solids, there does not appear to be significant differences in the gastric emptying rate for liquids of different osmolality.[6, 7] Other factors that may be involved include gastrointestinal hormone levels, particle size, meal volume, dietary fibre, gastric acidity and the athlete's anxiety level.

Treatment

The treatment of upper gastrointestinal symptoms associated with exercise is aimed at reducing the contents of the stomach during exercise. This is achieved by avoiding solid foods for at least three hours before intense exercise. The pre-exercise meal should be high in carbohydrate and low in fat and protein.

If additional measures are required, the use of antacid medication, in either tablet or liquid form, may reduce the incidence of heartburn and upper abdominal pain. Antacids usually remain in the stomach for 30 minutes. If this is not sufficient, the use of histamine H^2-receptor antagonists (such as ranitidine and cimetidine) may occasionally be necessary. Domperidone 10–20 mg, 1 hour before meals, may also be effective.

Athletes in prolonged endurance events (over 4 hours duration), who need to consume food while exercising, are particularly susceptible to upper gastrointestinal symptoms. Chewing gum is a mechanical means of stimulating gastric emptying and avoids possible complications of medications. Always trial any chosen intervention before 'race day'.

Peptic ulcer disease

Initially believed to be the result of stress or acid in the stomach, peptic ulcer disease was discovered to be bacterial in nature, largely thanks to Australian doctors, Robin Warren and Barry Marshall. They were awarded the Nobel Prize in 2005 for discovering that *Helicobacter pylori* (H pylori) bacteria is the main cause of peptic ulcer disease.

In 1984, in frustration at their findings not being accepted in the medical mainstream, Dr Marshall deliberately infected himself by drinking a solution of the bacterium. He demonstrated the efficacy of antibiotics by curing himself but it was not until the mid 1990s that antibiotic treatment was included in peptic ulcer management guidelines.

Due to increasing antibiotic resistance H pylori infection-related peptic ulcers remain a concern.[8] NSAIDs and aspirin may also disrupt the protective mucus lining of the stomach leading to an increased susceptibility to bacterial infiltration (e.g. H pylori).[9] Therefore, those taking either NSAIDs or aspirin are at increased risk of both peptic and duodenal ulceration. For further discussion of NSAIDs see later section of this chapter, Non-steroidal anti-inflammatory drugs and the gastrointestinal tract. Only a small number of people with H pylori infection or who take NSAIDs develop peptic ulcer disease, suggesting that individual susceptibility to bacterial virulence and drug toxicity is essential to the initiation of pathophysiological changes.

Athletes are known to have a high rate of NSAID use increasing their risk of suffering peptic ulcer disease.[10] As H pylori remains the main cause of peptic ulcers, a patient with dyspepsia can undergo a test-and-treat strategy with non-invasive measures (e.g. urea breath and stool antigen tests). Endoscopy remains the gold standard for diagnosis.

Treatment

Standard therapy for peptic ulcers involves the administration of two antibiotics simultaneously, alongside medication to inhibit acid production in the stomach (proton pump inhibitor [PPI]); this combination is called 'triple therapy'. If the H Pylori can be eliminated, the patient will be cured. Ideally, antimicrobial susceptibility tests should support appropriate antibiotic selection. Where this is not possible, first-line therapy should be based on the local prevalence of antibiotic resistance. Table 12.3 outlines possible strategies for eliminating the bacteria and reducing the risk of future morbidity.

Page 177

Table 12.3. Possible pharmacological management strategies for *Helicobacter pylori* induced peptic ulcer.

https://www.sciencedirect.com. Due to rights and permissions restrictions, this content cannot be reproduced in a digital format. The content is available in the print edition at page 177.

Other regimens used in the treatment of *Helicobacter pylori* combine different antibiotics with similar results (eg, triple therapy could combine a proton pump inhibitor [PPI] plus amoxicillin plus metronidazole or PPI plus metronidazole plus clarithromycin). Sequential quadruple therapy consists of a 5-day dual therapy with a PPI and amoxicillin followed by a 5-day triple therapy with a PPI plus clarithromycin plus tinidazole or metronidazole. Hybrid quadruple therapies combine 10-14 days of dual therapy with PPI and amoxicillin with 7 days of treatment with clarithromycin and metronidazole at the end (or start, for reverse therapy). *Use metronidazole if patients have penicillin allergy. †Double doses: omeprazole 40 mg, lansoprazole 60 mg, rabeprazole 40 mg, esomeprazole 40 mg. ‡Used as rescue regimen, bismuth-based therapy can be added to these drugs (for fluoroquinolone-based quadruple therapy). §To be used when at least three recommended options have failed and if *H pylori* susceptibility testing is not available.

FROM THE LANCET, 390, ANGEL LANAS, FRANCIS K L CHAN, PEPTIC ULCER DISEASE, 613–24, 2017, WITH PERMISSION FROM ELSEVIER

LOWER GASTROINTESTINAL SYMPTOMS

Although bleeding can occur in both upper and lower GI illness/injury we consider it more commonly part of lower GI disease. The following three concerns are among the most common presentations for a sports medicine practitioner.

Gastrointestinal bleeding

An occasional bloody stool is frequently noted by runners,[11] and the incidence of occult bleeding is high.[12] As the amount of bleeding in most cases is small, most athletes are not affected clinically; however, occasionally iron-deficiency anaemia may occur. Reduced iron stores are denoted by a low serum ferritin level.

The most frequently reported site of exercise-associated gastrointestinal haemorrhage is the fundus of the stomach. The mechanism underpinning this transitory haemorrhagic gastritis is uncertain. Ischaemia may play a role, as may direct trauma from the diaphragm. In susceptible individuals, the gastritis may result in part from the general stress of competition along with the associated rise in key stress hormones such as adrenalin (epinephrine) and cortisol. Non-steroidal anti-inflammatory drugs (NSAIDs) contribute to gastrointestinal bleeding in runners.[11, 12].A Mallory–Weiss tear secondary to forceful vomiting may present with signs of upper gastrointestinal bleeding.

No examples of bleeding from the small intestine have been reported. However, colonic bleeding has been observed, particularly from the proximal colon.

The aetiology of gastrointestinal bleeding associated with exercise is uncertain and is likely to be multifactorial. During exercise, blood flow is diverted from the splanchnic bed to the exercising muscles. Blood flow to the gastrointestinal tract may be reduced by as much as 75% during intense exercise.[13] A number of other factors may contribute to a reduction of blood flow. Such factors include exercise in the fasted state, as the absence of nutrients within the intestine reduces the blood flow to that area. Also, high thermal stress, dehydration and high exercise intensity play a role.

It must be remembered that gastrointestinal bleeding in an athlete is not necessarily associated with exercise and the athlete with obvious gastrointestinal bleeding should be fully investigated to determine the source of the bleeding.

Treatment

If no obvious cause of the bleeding is established, ensure adequate hydration to prevent aggravation of the relative ischaemia. As the mechanical effect of jarring while running is thought by some to be a contributory factor to gastrointestinal bleeding, the amount of jarring should be reduced by using appropriate footwear and avoiding running on hard surfaces.

Those athletes with a known tendency for gastrointestinal bleeding and those who complain of fatigue should have the state of their iron stores assessed by measurement of their serum ferritin levels. Serum ferritin levels of less than 30 ng/mL in women and 50 ng/mL in men indicate reduced iron stores.

Abdominal pain

Many athletes complain of a sharp, colicky pain in the left or right upper quadrant during strenuous exercise. This is commonly referred to as a ‘stitch’. The exact cause of this common phenomenon is unknown, but it may be due to muscle spasm of the diaphragm or trapping of gas in the hepatic or splenic flexure of the colon. This condition has often been thought to be associated with exercise undertaken soon after eating a solid meal. There is no proof of this; however, avoiding a solid meal prior to exercise may be an appropriate treatment. Exhaling on foot-strike on the opposite side to the pain may be helpful.

Occasionally, athletes get a ‘claudication-type’ abdominal pain. This occurs in association with intense endurance exercise and is thought to occur as a consequence of relative ischaemia due to

shunting of blood away from the gastrointestinal tract to the exercising muscles.[11, 13] This effect is aggravated by dehydration. A separate rare cause of abdominal pain is 'caecal slap' on the right psoas muscle.

The possibility of abdominal pain being referred from the thoracic spine should always be considered. A thorough examination of the thoracic spine should be performed in any athlete who complains of abdominal pain. Hypomobility detected in one or more intervertebral segments should be corrected by manual therapy techniques, and the effect on the athlete's symptoms noted.

Waterman and Kapur (2012)[3] reported that in many cases continued training is the best way to address the abdominal pain, which appears to reduce in those who have greater experience in their athletic discipline.

Diarrhoea

Diarrhoea appears to be more frequent with exercise,[14] especially with long-distance running—as a result the terms 'runner's trots' and 'runner's diarrhoea' have been coined to describe the condition. Athletes may complain of an urge to defecate while running, and approximately half of those who experience this urge to defecate complain of episodes of diarrhoea during running.

The incidence of diarrhoea seems to be related to the intensity of the exercise and occurs more commonly in competition than in training. The anxiety associated with competition may be a contributory factor.

The exact cause of diarrhoea is uncertain. Relative intestinal ischaemia, described previously, may be a contributory factor. Studies of the relationship between intestinal transit time and exercise have shown conflicting results; however, intestinal motility seems to increase with intense exercise. This increase in gut motility and changes in intestinal secretion and absorption may be related to the increased level of endorphins associated with exercise.

When faced with a patient with diarrhoea, the clinician should also seek a history of vitamin and mineral supplementation, or ingestion of caffeine or artificial sweeteners prior to exercise. Each of these may contribute to diarrhoea.

PRACTICE PEARL

Acute diarrhoea is usually due to an infective cause and may be viral or bacterial.

Acute diarrhoea is a problem for athletes when they are travelling away from home. In the 24 hours prior to major competition, team physicians generally prescribe norfloxacin (800 mg) or ciprofloxacin (1 g) with loperamide (4 mg) to provide rapid symptom relief. Athletes with chronic diarrhoea should be fully investigated to exclude any other abnormality (e.g. inflammatory bowel disease, malabsorptive disorders).

Treatment

The treatment of athletes with exercise-related diarrhoea is often difficult. Dietary changes should

include reduction of the fibre content of the diet in the 24 hours prior to intense competitive exercise. If the problem persists, prophylactic anti-diarrhoeal medication (such as loperamide) may be used; however, this should not be used on a regular basis. Antispasmodics (e.g. mebeverine) may be useful.

Training the gut

Studies as summarised by Jeukendrup (2017)[12] have demonstrated that the gastrointestinal system, and especially the stomach, has a remarkable trainability, much like many other bodily tissues. This has implications for athletes involved in endurance sports where carbohydrate replenishment is required (i.e. exercise lasting over 1 hour), with 60–90 grams of carbohydrate per hour recommended. The stomach has been shown to adapt to regular intake of large volumes of fluid and increased carbohydrates. Increased expression of the sodium-dependent glucose transport-1 (SGLT-1) proteins occurs when training with a high-carbohydrate diet, which supports the athlete's ability to process increased intakes during competition. It is therefore recommended that athletes include some training with high carbohydrate intake, to facilitate performance on race days. Further strategies designed to reduce GI distress during competition are summarised in Figure 12.1. Those who eat a regular ketogenic or low-carbohydrate diet, and may not be well adapted to processing increased glucose, are potentially at the greatest risk of GI discomfort in these circumstances.

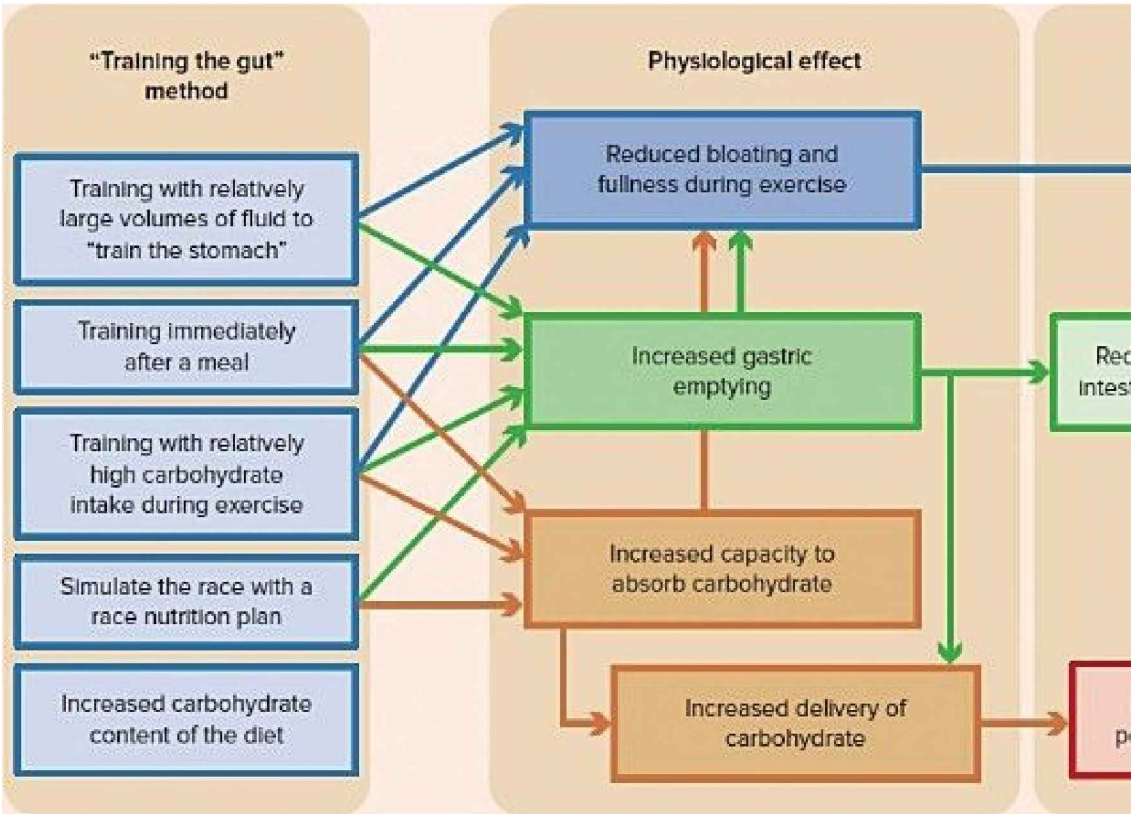


Figure 12.1 Strategies to reduce GI distress during physical activity.
JEUKENDRUP AE. TRAINING THE GUT FOR ATHLETES. SPORTS MEDICINE 2017;47:S101–10. HTTPS://LINK.SPRINGER.COM/ARTICLE/10.1007/S40279-017-0690-6[12]

GASTROINTESTINAL PATHOLOGIES

The following section will review some common pathologies of the GI system that may disrupt or reduce the exercise capacity of athletes or active individuals.

Lactose intolerance

A limited number of people lack the enzyme lactase, which is necessary for the digestion of lactose or milk sugar. Asian and African populations typically display an absence of lactase. Also, adult lactase has only about 5% of the activity of childhood lactase. Lactose intolerance leads to gastrointestinal disorders resulting in cramps, flatulence and diarrhoea.

Athletes suffering from lactose intolerance need to avoid dairy products, with the possible exception of yoghurt. The lactose in yoghurt is largely broken down by the bacterial cultures present. It is important that athletes who avoid lactose ensure an adequate dietary intake of calcium and protein via alternative sources, such as soy-based products (including milks, yoghurts,

cheeses and ice creams). An often unrecognised source of lactose is high-protein drinks and sports supplements.

Also, temporary lactose intolerance may follow acute infective diarrhoea (particularly if caused by rotavirus). Therefore, milk-based products should be among the last to be reintroduced to the athlete's diet after such an episode.

Coeliac disease

Coeliac disease is characterised by abnormal mucosa in the small intestine induced by a component of the gluten protein of wheat. Barley, rye and oats also contain gluten. Anaemia is often seen in athletes with coeliac disease, due to malabsorption of iron and folate. Howell–Jolly bodies may be seen on the blood film due to folate deficiency.

Prevalence data suggest that symptomatic or latent coeliac disease affects up to 1 in 200 people in most Western countries. It may not always present with the classic symptoms of diarrhoea and bloating; tiredness is a common presentation.[16] Laboratory testing may show high levels of IgA antiendomysial and IgA tissue transglutaminase antibodies. However, any of the IgA tests may be falsely negative in up to 3–5% of coeliac patients,[17] mainly in those with associated IgA deficiency.[1 8] Definitive diagnosis is via multiple small bowel biopsy, showing typical mucosal changes of subtotal villous atrophy.

Athletes diagnosed with coeliac disease are given comprehensive lists of alternative high-carbohydrate food sources and should consult a dietitian for assistance in planning a nutritionally adequate diet. Unfortunately, many people self-diagnose their symptoms as being due to gluten intolerance. They may reduce their gluten intake and note an improvement. It then becomes very difficult to convince these people that they need to go back onto a diet containing gluten for one month prior to having a small bowel biopsy to definitively prove the diagnosis (see Case study 'Nov ak Djokovic, tennis coeliac disease').

CASE STUDY

Alyx Treasure, high jump—Crohn's disease

Alyx Treasure is a Canadian high jumper. She began suffering from abdominal discomfort aged 17 and was subsequently diagnosed with Crohn's disease.

Diagnosis

Crohn's disease can present anywhere along the digestive tract. There is no specific diagnostic test. A combination of clinical history, physical examination, laboratory tests and imaging/endoscopy will support a clinical diagnosis. Colonoscopy remains the present gold standard.

Management

Having struggled to find a medication to control her symptoms, and following a period of hospitalisation, Alyx was prescribed a biologic. The biologic allowed her to return to school and continue in track and field.

The biologic allowed me to live a mostly normal life, but did have consequences to my training and life

in general. I had to go into the hospital to get my medication infused through IV therapy every 5 weeks which would take up to 5 hours at a time. The recovery from these infusions was the hardest hit to my training and would disable me from continuing to train at my normal level for anywhere from 2 to 7 days.

The biologic via IV therapy was continued throughout her college career and adjusted in 2016, in time for the Rio Olympic Games. The 2016 adjustment allowed Alyx to self-administer her biologic shot every 2 weeks. The impact of the new medication on her ability to train effectively was significant and it removed her concerns of regular hospitalisation. Ultimately these improvements contributed to a 5 cm improvement in her personal best and an Olympic final qualification.

Figure 12.2 Alyx Treasure, Canadian Olympic high jumper
CHRISTOPHER MORRIS/CORBIS VIA GETTY IMAGES

Conclusion

Biologic drugs are not a panacea therapy for Crohn's disease due to their immuno-suppressant side effects. Management involves a mixture of medication (pain relief, anti-inflammatories, antibiotics), supplements (if digestive absorption is affected), nutritional strategies and, in some cases, surgical intervention.

Alyx demonstrates that inflammatory bowel disease can be managed successfully with an individually tailored treatment plan to allow high-level athletic performance. She is now a spokesperson for Crohn's and Colitis Canada.

Crohn's disease and ulcerative colitis (inflammatory bowel disease—IBD)

Crohn's disease, as defined by the US National Institute of Diabetes and Digestive and Kidney

Diseases,[19] is a chronic inflammatory condition primarily affecting the small intestine and the early part of the large intestine. However, it can affect any part of the digestive tract and is placed in a category with other inflammatory bowel diseases such as ulcerative colitis. Complications of Crohn's may include intestinal obstruction, fistulas, abscesses, anal fissures and ulcers.

Ulcerative colitis presents as chronic, diffuse, superficial inflammation that starts in the rectum and extends continuously to potentially involve the entire colon (pancolitis). Small bowel involvement is absent. Patients with ulcerative colitis always present with rectal bleeding.

In addition to abnormalities of the digestive tract there are extra-intestinal manifestations involving the skin, liver, joints and eyes. Possibly the worst of the complicating factors for an athlete is the potential for malnutrition. The bowel is not able to fully absorb the vitamins and minerals as it would under normal conditions and therefore athletic performance may be impaired. Bone mineral density loss is a possibility due to impaired ability to absorb nutrients (vitamin D and calcium, in particular) and chronic use of steroids.[20] However, exercise has an overall beneficial effect on the management of IBDs and should therefore be encouraged.[21, 22]

FODMAPs

An additional complicating problem arises when fermentable dietary components cause gas production and distension in the gut, which then causes pain. FODMAP stands for:

- fermentable
- oligosaccharides (e.g. wheat or vegetables high in fructan, such as onions)
- disaccharides (e.g. lactose)
- monosaccharides (e.g. fructose)
- polyols (sugar alcohols, e.g. mannitol, sorbitol, zylol)—these are present in sports drinks.

The astute reader will notice that a lot of the above foods contain gluten. This explains why people who do not have true coeliac disease feel better when they eliminate gluten from their diet. However, this can come at a cost, as these foods often contain a lot of fibre (especially in the form of legumes), and lower dietary fibre intake results in constipation and has been linked to certain cancers.[23] FODMAP sensitivity is common, with an estimated 35% of people in some Western countries suffering from the problem.[24]

What solutions are there for the athlete who is sensitive to FODMAP foods?

1. Limit foods containing fructose. Typically, these include wheat, rye, barley, onions, legumes (e.g. peas) and garlic.
2. Space out foods containing a lot of fructose throughout the day (at least two hours between serves).
3. Sports nutrition bars, drinks and gels often contain added fructose. The clinician and nutritionist need to consider individual sensitivity to fructose and the effects of exercise on that individual.

4. Lactose is a disaccharide. Some athletes need to limit intake of milk, yoghurt, ice cream and soft cheese.
5. Polyols are only slowly absorbed in the small intestine. They are present in some chewing gums. Also, watch for sorbitol in stone fruit and mannitol in cauliflower or mushrooms.

It is now suggested that those wishing to undertake a low-FODMAP approach first try FODMAP elimination, then a short reintroduction, before finally coming to a personalisation.[25] This approach allows the athlete to gain the nutritional benefits of some high-FODMAP foods while avoiding GI discomfort.

Irritable bowel syndrome

Athletes who do not respond to manipulation of FODMAPs in their diet may be labelled as having irritable bowel syndrome (IBS). This is a very common gastrointestinal disorder that causes lower abdominal pain and constipation alternating with diarrhoea. The cause is not known, but there seems to be a strong association between the condition and the intestinal response to stress (e.g. sporting competition). Treatment includes a balanced fibre diet together with antispasmodic agents (e.g. dicyclomine).

PRACTICE PEARL

The elimination of certain foods in the diet should be done in conjunction with a nutritionist or dietician to support adherence, performance goals and good health.

Small intestinal bacterial overgrowth

Upper gut symptoms may be due to small intestinal bacterial overgrowth (SIBO), which is thought to be due to disruption of the migratory motor complex. It may result in malabsorption of carbohydrates, fat and vitamin B^{12}. It can also arise as a complication of the following disorders: infectious diarrhoea, malnutrition, malabsorption, hypothyroidism, inflammatory bowel disease and immunodeficiency. Treatment is typically with antibiotics (e.g. rifaximin or metronidazole), with evidence for the use of probiotics limited. Support to eliminate lactose from the diet and address nutritional deficiencies should be sought.

Page 182

Constipation

Constipation is a common problem in touring athletes, particularly in those who take long airline flights. The causes and solutions are outlined in Table 12.4.

Table 12.4 Constipation in the touring athlete

Potential causes	Recommended strategies
Disruption of usual daily routine	Remain well hydrated—drink fluids freely on the flight
Dry air in aircraft	Request special high-fibre airline meals (if available)

Jet lag	Obey the call to stool when it occurs
Anxiety over using shared bathroom facilities	Walk up and down the aircraft aisle
Difficulty in accessing these facilities during certain times in the flight	Judicious use of laxatives
Reduced dietary fibre in airline food	
Reduced fluid availability	
Long periods of sitting	

DIAGNOSTIC PATHWAY FOR ATHLETES WITH POTENTIAL GASTROINTESTINAL DISEASE

The conventional pathway for diagnosing GI disease includes blood tests—a full blood count, markers of inflammation such as C-reactive protein (CRP), plus serological testing for coeliac disease. CRP, while specific for inflammation, cannot localise it to the gut. Microbiological testing of faecal samples can be used to exclude an infective cause. Testing for faecal calprotectin can be helpful in determining whether or not an endoscopy is likely to be useful.[26] Disturbance to the mucosal architecture of the gut due to an inflammatory process results in leakage of calprotectin into the lumen and its subsequent excretion in faeces. The concentration of calprotectin in faeces correlates well with finding an inflammatory process at endoscopy. Conversely, if the faecal calprotectin test is negative, the athlete can usually be managed along standard lines for irritable bowel syndrome.

If symptomatic exercise-induced GI ischaemia is suspected, duplex ultrasound should be performed to rule out a haemodynamically significant stenosis of the splanchnic artery. If a significant stenosis is present, surgical treatment may be advised, especially if the athlete has ischaemic complaints in daily life. If there are no complaints in daily life, surgical treatment is unlikely to be indicated.[27]

NON-STEROIDAL ANTI-INFLAMMATORY DRUGS AND THE GASTROINTESTINAL TRACT

Non-steroidal anti-inflammatory drugs (NSAIDs) are used by up to 35% of athletes in competition.[28] During exercise, the reduction of gastrointestinal blood flow increases the potential for gut toxicity. Gastrointestinal adverse effects are the most common reason for cessation of use of these medicines, both in the general and the athletic populations. They can affect any portion of the gastrointestinal tract, as indicated in Table 12.5.

Table 12.5 Gastrointestinal-related adverse effects of NSAIDs

Site	Adverse effects
Oesophagus (common)	Reflux Upper gastrointestinal bleeding
Stomach and duodenum (common)	Gastritis Upper gastrointestinal bleeding Perforation
Small intestine (rare)	Increased permeability

Large intestine (uncommon)	Increased permeability Lower gastrointestinal bleeding

There are two groups of athletes who present for clinical evaluation. By far the most common are healthy individuals who experience dyspepsia with NSAID use. This affects about 10% of the population. Strategies which can be implemented include:

- using a traditional (non-specific) NSAID under cover of a proton pump inhibitor (PPI)[29]
- using a cyclooxygenase-2 (COX-2) agent
- using a COX-2 agent plus PPI—for patients at high risk
- avoiding NSAIDs altogether, and using paracetamol (acetaminophen) where analgesia alone is required (i.e. pain but no significant inflammation).

Page 183

Less common, but more serious, are the adverse effects of NSAIDs in those patients with known risk factors (age over 60 years, previous gastrointestinal bleeding, taking corticosteroids, or having diabetes or vascular disease). These people have over twice the risk of gastrointestinal adverse effects when taking NSAIDs. Over 80% of adverse events (gastrointestinal bleeding, perforation) are asymptomatic in this patient group, at least in the early phase. Because they are occurring in older, sicker people, they can be life-threatening. With the growing numbers of masters athletes, clinicians need to be alert to these conditions.

It was the high frequency of dyspepsia with the use of NSAIDs that prompted the development of COX-2 agents. Clinicians need to advise patients that, despite all the marketing hype, these agents are no more potent than traditional NSAIDs. Their main therapeutic advantage is in the patient who cannot tolerate traditional NSAIDs due to gastrointestinal upset.

Cyclooxygenase-2 agents do not reduce the risk of gastrointestinal upset to zero. Various tables of COX-2 selectivity have been published.[30] However, COX-2 selectivity is only relative, and other factors (e.g. drug dosage) also interact to contribute to the overall toxicity risk.

There is increasing recognition that inflammation plays much less of a role in sports injuries (e.g. tendinopathies) than previously thought.[31] Only use NSAIDs for conditions with inflammation.

PRACTICE PEARL

Reserve NSAID use for those injury problems where a significant inflammation is present (e.g. joint effusion).

PREVENTION OF GASTROINTESTINAL SYMPTOMS THAT OCCUR WITH EXERCISE

Many of the gut complaints experienced by runners are a direct result of the physical activity of

running, which causes jolting of the gastrointestinal tract and reduced blood supply to the cells. However, some relief can be gained by several dietary modifications. See box for advice on minimising gastrointestinal symptoms.

Dietary fibre intake prior to competition

To ensure that the gut has minimal food content prior to racing, it is necessary to reduce the fibre content of the diet in the days preceding the race. This means, in the two days prior to the competition, change from wholemeal and wholegrain varieties of rice, breads and cereals to the more refined alternatives. Avoid fresh fruit and vegetables with skin, legumes and heavy seasonings such as garlic, pepper and curry.

Runners who regularly suffer from diarrhoea or the urge to use their bowels regularly during a race may benefit from a liquid nutrition supplement during the last days preceding the competition. This will ensure that the gastrointestinal contents are minimised prior to the race. An alternative approach is to consume only fluids prior to competition on the day of the event.

Solid foods prior to the race

To ensure that the stomach is empty, it is important that the pre-event meal is consumed at least three hours before the race begins. However, in some athletes with a low gastric emptying rate, the pre-event meal may need to be accompanied by a prokinetic agent (e.g. domperidone) and eaten four to six hours prior to competition. Fluids, however, should still be consumed in the period leading up to the race.

Select the pre-event meal carefully

The pre-event meal should contain negligible amounts of fat and protein so that it will be easily digested by the time the event begins. Select from low-fibre high-carbohydrate foods, such as white rice, white bread, plain pastas, plain breakfast cereals (e.g. cornflakes, rice bubbles) and avoid adding any fats such as margarine, butter or creamy sauces. Simple carbohydrates such as honey, jam and syrup may be used to increase the energy value of the meal. Note that high-fructose foods (e.g. dried fruit, fruit juices, jam, soft drinks/sodas) are absorbed slowly, so large volumes may not be well tolerated if the athlete has a tendency for gastrointestinal upset.

Dehydration

It is important to drink small amounts frequently during the event, aiming to prevent thirst. During long events (more than 90 minutes) the athlete should choose a drink that contains some carbohydrate (up to 10% solution) and low concentrations of sodium and potassium. Concentrated drinks are more likely to cause symptoms. Practice drinking during training so that it becomes a habit in competitions.

Fat and protein intake during exercise

During ultra-endurance events where food may be consumed during the event, select items that contain minimum quantities of protein and fat. Fibre intake needs to be kept low and some runners may find liquid meal replacements a useful option. Boiled white rice, pasta,

pancakes with syrup, canned fruit, peeled potatoes, plain dry biscuits, and plain rolls or bread all make good choices. Practice food intake during training.

Minimising gastrointestinal tract symptoms when exercising—advice for athletes

1. Train and compete with your upper gut as empty as possible (at least 3 hours after a meal).
2. Limit the fat and protein content of your last meal before exercising.
3. Prevent dehydration—get used to drinking during training and long events.
4. Eat small amounts immediately before and during physical exertion to help with 'training the gut'.
5. Avoid high-fibre foods prior to competition.
6. Only take anti-inflammatory tablets (NSAIDs) or cyclooxygenase-2 inhibitors on the advice of a doctor, if you have an injury where inflammation plays a large role. Otherwise, use paracetamol (acetaminophen).
7. Always take NSAIDs on a full stomach.
8. If you have a family history of bowel or stomach cancer, consider regular screening examinations.
9. If you develop 'red flag' symptoms (e.g. upper or lower gastrointestinal bleeding, unintended weight loss), see your doctor and get these properly evaluated.
10. If pre-race nerves are a likely cause of gut symptoms, consult a sports psychologist.

Sports psychology

If pre-race nerves are a likely cause of gastrointestinal problems, it may be helpful to discuss race build-up with a sports psychologist. Proper management of anxiety can not only improve stomach and bowel problems but may also help maximise race performance.

Ongoing symptom management

Where an athlete continues to struggle with management of symptoms, it may be necessary to train at a steady-state heart rate of 5–10 bpm below the heart rate at which symptoms usually develop. This reduced exercise intensity may need to be continued for several months with a slow incremental resumption of previous levels of physical activity.[27]

CASE STUDY

Novak Djokovic, tennis—coeliac disease

Novak Djokovic is now consistently ranked among the pantheon of all-time tennis greats. Prior to 2010, despite reaching an extremely high standard of play, he began to suffer from symptoms similar to asthma and was prone to severe bouts of fatigue. This lead to inconsistency in his performance, which was observed by a physician watching him play who then encouraged Djokovic to undergo gluten

sensitivity testing.

Diagnosis

Blood tests: To be accurate, all coeliac disease blood tests require adherence to a gluten-containing diet. The tissue transglutaminase antibodies (tTG-IgA) test will be positive in about 98% of patients with coeliac disease who are on a gluten-containing diet.

Other tests to consider: IgA endomysial antibody (EMA); total serum IgA (used to check for IgA deficiency); deaminated gliadin peptide (DGP IgA and IgG).

Gluten challenge: If the athlete is on a gluten-free diet, a gluten challenge, to allow antibodies to build up in the bloodstream prior to testing, may be initiated. The current recommended gluten intake for the gluten challenge is two slices of wheat-based bread each day for 6–8 weeks. A gluten challenge should be supervised, and a biopsy ordered if symptoms are severe. This should not be done while pregnant.

Genetic testing: People with coeliac disease carry one or both of the HLA DQ2 and DQ8 genes, but these are also present in 25–30% of the general population. Carriers of the HLA DQ2 and/or DQ8 genes have an increased risk of developing coeliac disease, up from 1% (general population) to 3%.[14] Those with first-degree family members with coeliac disease have up to a 40% risk of developing the disease. A negative gene test excludes the possibility of developing coeliac disease, which may be valuable information for first-degree family members.

Biopsy: Small bowel biopsy remains the gold standard for diagnosing coeliac disease. However, many clinicians accept positive serology as diagnostic in the absence of IgA deficiency, particularly if a positive family history exists.

Management

The only current therapy for coeliac disease is a complete removal of gluten from the diet. Djokovic altered his diet from pizza and other gluten-heavy foods to one containing gluten-free pasta, brown rice and oatmeal plus other gluten-free carbohydrate-rich foods which ensured his body had its essential nutrient intake of fruit and leafy green vegetables. His 2013 book, *Serve to Win*, focuses on the benefits he associated with his new eating regime.[32]

In 2011, after changing his diet, Djokovic won 43 straight matches and has since extended his record to 14 Grand Slam titles.

Conclusion

Effective management of the athlete's diet can improve both disease management and performance. It is essential that athletes suffering from symptoms of lethargy, breathing difficulties and chest pain are screened for gastrointestinal concerns, once cardiac and other more life-threatening causes have been excluded.[33, 34, 35, 36]

REFERENCES

1. Casey E, Mistry DJ, MacKnight JM. Training room management of medical conditions: sports gastroenterology. *Clin Sports Med* 2005; 24(3): 525–40, viii.
2. de Vries E, Soerjomataram I, Lemmens VE et al. Lifestyle changes and reduction of colon cancer incidence in Europe: a scenario study of physical activity promotion and weight reduction. *Eur J Cancer* 2010; 46(14): 2605–16.
3. Waterman JJ, Kapur R. Upper gastrointestinal issues in athletes. *Curr Sports Med Rep* 2012; 11(2): 99–104.
4. de Oliveira EP, Burini RC, Jeukendrup A. Gastrointestinal complaints during exercise: prevalence, etiology, and nutritional recommendations. *Sports Med* 2014; 44 Suppl 1: S79–85.
5. Shawdon A. Gastro-oesophageal reflux and exercise. Important pathology to consider in the athletic population. *Sports Med* 1995; 20(2): 109–16.
6. Brouns F, Senden J, Beckers EJ et al. Osmolarity does not affect the gastric emptying rate of oral rehydration solutions. *J Parenter Enteral Nutr* 1995; 19(5): 403–6.
7. Rogers J, Summers RW, Lambert GP. Gastric emptying and intestinal absorption of a low-carbohydrate sport drink during exercise. *Int J Sport Nutr Exerc Metab* 2005; 15(3): 220–35.
8. Lanas A, Chan FKL. Peptic ulcer disease. Lancet 2017; 390: 613–24
9. Huang JQ, Sridhar S, Hunt RH. Role of Helicobacter pylori infection and non-steroidal anti-inflammatory drugs in peptic-ulcer disease: a meta-analysis. Lancet 2002; 359: 14–22.
10. Tscholl PM, Vaso M, Weber A, et al. High prevalence of medication use in professional football tournaments including the World Cups between 2002 and 2014: a narrative review with a focus on NSAIDs. Br J Sports Med. 2015 May;49(9):580-2. doi: 10.1136/bjsports-2015-094784.
11. Simons SM, Kennedy RG. Gastrointestinal problems in runners. *Curr Sports Med Rep* 2004; 3(2): 112–16.
12. Smetanka RD, Lambert GP, Murray R et al. Intestinal permeability in runners in the 1996 Chicago marathon. *Int J Sport Nutr Exerc Metab* 1999; 9(4): 426–33.
13. van Nieuwenhoven MA, Brouns F, Brummer RJ. Gastrointestinal profile of symptomatic athletes at rest and during physical exercise. *Eur J Appl Physiol* 2004; 91(4): 429–34.
14. Rao SS, Beaty J, Chamberlain M et al. Effects of acute graded exercise on human colonic motility. *Am J Physiol* 1999; 276 (5 Pt 1): G1221–6.

15. Jeukendrup AE. Training the gut for athletes. *Sports Med* 2017; 47(Suppl 1): 101–10.
16. Green HR, Cellier C. Celiac disease. *N Engl J Med* 2007; 357: 1731–43.
17. Celiac Disease Foundation. Screening. 2018. https://celiac.org/celiac-disease/understanding-celiac-disease-2/diagnosing-celiac-disease/screening/#QUxtUDXhHvFtXmQT.99.
18. Gastroenterological Society of Australia (2007) *Coeliac Disease* 4th ed. Available at http://www.gesa.org.au/resources/clinical-guidelines-and-updates/coeliac-disease/
19. National Institute of Diabetes and Digestive and Kidney Diseases. Definition & facts for Crohn's disease. 2017. https://www.niddk.nih.gov/health-information/digestive-diseases/crohns-disease/definition-facts.
20. Ali T, Lam D, Bronze MS et al. Osteoporosis in inflammatory bowel disease. *Am J Med* 2009; 122(7): 599–604.
21. Koon G, Atay O, Lapsia S. Gastrointestinal considerations related to youth sports and the young athlete. *Transl Pediatr* 2017; 6(3): 129–36.
22. Ng VK, Millard WM. Competing with Crohn's disease: management issues in active patients. *Phys Sportsmed* 2005; 33(11): 47–53.
23. Veronese N, Solmi M, Caruso MG et al. Dietary fiber and health outcomes: an umbrella review of systematic reviews and meta-analyses. *Am J Clin Nutr* 2018; 107(3): 436–44.
24. Barrett JS, Irving PM, Shepherd SJ et al. Comparison of the prevalence of fructose and lactose malabsorption across chronic intestinal disorders. *Aliment Pharmacol Ther* 2009; 30(2): 165–74.
25. Whelan K, Martin LD, Staudacher HM et al. The low FODMAP diet in the management of irritable bowel syndrome: an evidence based review of FODMAP restriction, reintroduction and personalisation in clinical practice. *J Hum Nutr Diet* 2018; 31(2): 239–55.
26. Walsham NE, Sherwood RA. Fecal calprotectin in inflammatory bowel disease. *Clin Exp Gastroenterol* 2016; 9: 21–9.
27. ter Steege RW, Geelkerken RH, Huisman AB et al. Abdominal symptoms during physical exercise and the role of gastrointestinal ischaemia: a study in 12 symptomatic athletes. *Br J Sports Med* 2012; 46(13): 931–5.
28. Tscholl P, Junge A, Dvorak J. The use of medication and nutritional supplements during FIFA World Cups 2002 and 2006. *Br J Sports Med* 2008; 42: 725–30.
29. Gupta M, Eisen GM. NSAIDs and the gastrointestinal tract. *Curr Gastroenterol Rep* 2009; 11: 345–53.
30. Riendeau D, Percival MD, Brideau C et al. Etoricoxib (MK-0663): preclinical profile and comparison with other agents that selectively inhibit cyclooxygenase-2. *J Pharmacol Exp Ther* 2001; 296: 558–66.
31. Paoloni JA, Milne C, Orchard J et al. Non-steroidal anti-inflammatory drugs in sports

medicine: guidelines for practical but sensible use. *Br J Sports Med* 2009; 43: 863–5.

32. Djokovic N. *Serve to Win: The 14-day gluten-free plan for physical and mental excellence*. New York: Zinc Ink, 2013.
33. https://www.amazon.ca/Serve-Win-Gluten-Free-Physical-Excellence/dp/0345548981
34. https://www.independent.co.uk/sport/tennis/revealed-the-diet-that-saved-novak-djokovic-8775333.html
35. https://www.telegraph.co.uk/men/active/10449779/Novak-Djokovic-diet-going-gluten-free-is-not-a-magic-cure.html
36. https://www.express.co.uk/life-style/health/428272/Novak-Djokovic-Going-gluten-free-was-a-real-game-changer

Chapter 13

Haematuria and other urinary symptoms

with CHRIS MILNE and PAUL BLAZEY

The doctors told me I would never run again, [but] I'm back running. They told me I would be on dialysis for the rest of my life, but I'm not. I had a kidney transplant, it was successful and I'm back doing what I love. So, if you just stay positive and stay focused on something you really want to achieve, you will do amazing things.

Aries Merritt, 110-metre hurdles world record holder

The kidneys are important but often neglected organs. Exercise can have significant effects on renal function. The most serious renal problem associated with exercise is rhabdomyolysis. Other common renal problems include post-exercise protein/haemoglobinuria and non-steroidal anti-inflammatory drug (NSAID)–induced renal dysfunction. Renal trauma may also be the result of a sports-related abdominal injury or trauma. There have been some well-documented cases of renal disease in athletes at the very top of their professions, including Jonah Lomu, the New Zealand rugby union star, and Aries Merritt, the US 2012 Olympic gold medallist in the 110-metre hurdles. Their stories are considered in case studies later in this chapter.

CLINICAL ANATOMY AND PHYSIOLOGY

Ordinarily, the kidneys are paired organs that lie under well-developed flank muscles.[1, 2] Kidneys receive high blood flow (approximately 20% of the total cardiac output at rest) and are composed of metabolically active cells. These cells are susceptible to hypoxia and tolerate this poorly. The tubular arrangement within the kidney uses a countercurrent mechanism to produce hypertonic urine.

The four major functions of kidneys are:

- to maintain salt and water balance

- to excrete nitrogen, mainly as urea
- to produce erythropoeitin and the vitamin D metabolite 1,25-dihydroxycholecalciferol
- to regulate blood pressure via the renin-angiotensin-aldosterone system.

Normal values for renal function at rest and with exercise are listed in Table 13.1.

Table 13.1 Renal function—normal values

	At rest	During exercise
Renal blood flow mL/min	1200	300
Glomerular filtration rate (GFR) mL/min	120	60
Concentrating ability:		
Urine osmolality 100–1200 mOsmol/kg water		
Serum osmolality 280–295 mOsmol/kg water		
Daily urine volume 400–4000 mL		
Obligatory water loss 840 mL*		

**Assumptions:*

- For each 3 g of protein ingested, about 1 g of urea will be produced.
- 1 g of urea equals approximately 17 mmol.
- Urine osmolality can be up to three times that of plasma.

It follows that 120 g of protein ingested per day provides 40 g of urea for excretion. This is about 680 mmol. At a urine osmolality three times that of plasma, 840 mL of obligatory water loss per day is required to excrete that nitrogen.

During exercise, physiological changes that have been observed are:

Page 188

- increased glomerular permeability
- increased excretion of red blood cells and protein into the urine
- renal vasoconstriction, especially of efferent arterioles
- increased filtration pressure
- relative stasis of blood in glomerular capillaries.

Collectively, these changes result in a degree of hypoxic damage to the nephron. In addition to the above, there is also decreased urine flow, mainly due to antidiuretic hormone (ADH) secretion.

EXERCISE-RELATED RENAL IMPAIRMENT

Exercise-related renal impairment usually occurs as a result of dehydration. Exercise results in fluid losses of 1–2 L/h, particularly in hot conditions. Replacement rarely matches this fluid loss, so a cascade of events may occur as depicted in Figure 13.1.

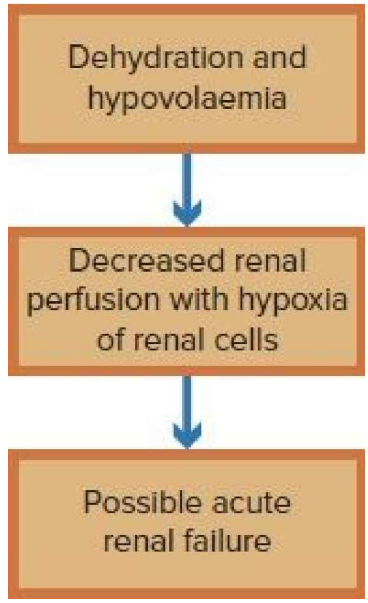


Figure 13.1 The cascade of events that can lead to renal impairment

In some cases, overly aggressive fluid replacement during exercise, especially in events lasting over four hours, can result in hyponatraemia. Prolonged exercise is known to cause non-osmotic release of ADH. The non-osmotic release of ADH in combination with salt loss from sweat and excessive fluid intake causes hyponatraemia.

Hyponatraemia occurs in slow athletes in long events. Up to 30% of long-distance runners may develop mild hyponatraemia (serum sodium in range 125–135 mmol/L). This is usually asymptomatic, but more severe drops (below 120 mmol/L) can result in cerebral oedema, seizures and even death. Until quite recently, athletes were encouraged to drink according to a predetermined schedule in endurance events. The obsessional athletes that rigorously stuck to these schedules were consequently at the greatest risk of developing hyponatraemia.

Current expert opinion on hydration is based on the proceedings of the second world conference on hyponatraemia in 2007.[3] Recommendations suggest starting any event well hydrated and drinking according to thirst rather than to a predetermined schedule.

RHABDOMYOLYSIS AND MYOGLOBINURIA

Rhabdomyolysis is the most serious renal condition associated with exercise. It is characterised as 'muscle cell meltdown'.[4] As a consequence of the breakdown of muscle cells, plus increased glomerular permeability, myoglobin (an oxygen transport protein) leaks into the urine. Serious sequelae may occur; in some cases, the condition is fatal. More commonly, acute renal failure with associated hyperkalaemia may ensue. Acute compartment syndrome is another recognised complication.

Rhabdomyolysis is predictable to some degree. Recognised risk factors include unaccustomed extreme exertion, especially in the heat, where dehydration and hypovolaemia are more common. Eccentric exercise is associated with greater damage to muscle fibres and Z bands, and in military reports the condition is referred to as the 'squat jump syndrome'. Rhabdomyolysis has been described in those undertaking *extreme* CrossFit training.[5] This form of exercise exemplifies the importance of unaccustomed high-level exertion in the genesis of the problem. Viral illnesses, metabolic disorders (e.g. diabetes) and certain drugs (e.g. statins, diuretics) are associated with the condition. It is more common in athletes with the sickle cell trait.[6]

Awareness of the above risk factors can be used to guide training to ensure an orderly progressive introduction of any eccentric exercise. Repeated bouts of the same type of exercise provoke less damage than the first bout.

PRACTICE PEARL

Rhabdomyolysis is a potentially fatal condition and requires hospital admission for close observation and active management.

Diagnosis relies on the history, including the risk factors listed above, plus examination findings, which include marked tenderness of the affected muscle groups and possibly hypovolaemia. Signs of serious causes of exercise-related collapse include altered mental status, systolic blood pressure less than 100 mmHg and heart rate greater than 100 bpm. The characteristic laboratory findings are of a grossly elevated serum creatine kinase (CK) level (over 10 000 IU/L) and myoglobin in the urine with a positive dipstick test.

Management consists of hospital admission, aggressive fluid replacement (4–11 L in the first 24 hours), cation exchange resins, forced diuresis and careful alkalinisation of the urine. Phosphate binders are also of benefit. In some cases, dialysis may be needed. Fasciotomy is indicated if associated compartment syndrome is present.

Page 189

OTHER EXERCISE-RELATED RENAL IMPAIRMENT CONCERNS

A number of other conditions exist that may cause renal symptoms or impairment. These are outlined below.

Footstrike haemolysis

Haemoglobinuria may occur as a result of footstrike haemolysis when running, and also with karate. Solutions for runners include well-cushioned shoes, use of viscoelastic inserts and running on soft surfaces. Karate exponents may need to modify their training.

Athletic pseudonephritis

The condition termed 'athletic pseudonephritis'[7] affects up to 20% of marathon runners who present with transient microscopic haematuria and proteinuria. In football players, red blood cells

have been identified in post-match urine samples. Repeat urine testing a few days later usually shows resolution of any abnormality.

Abrasions of the bladder wall in long-distance runners

A seminal investigation by Blacklock in 1977 reported haematuria in long-distance runners.[8] Cystoscopy showed abrasions of the bladder wall around the trigone. The postulated mechanism of damage was repeated impact of the flaccid posterior bladder wall against the trigone. The observed time course was recovery over several days. Preventive strategies include exercising with a partially full bladder and attention to pre-exercise fluid intake.

Renal trauma

Renal trauma can occur from a direct blow in boxing or a collision sport such as rugby union. Running can also cause transmitted shock to the kidneys. Most renal trauma can be managed non-surgically, but damage to the pedicle requires urgent surgical treatment to restore an adequate blood supply to the kidney.[1, 9]

CLINICAL APPROACH TO THE ATHLETE PRESENTING WITH HAEMATURIA

The presence of blood in the urine is an alarming symptom for any athlete. When assessing a patient, ask about any recent trauma in the flank or urethral area and check for a history of renal stones. The athlete should be questioned about any recent sore throat that could be a precursor of post-streptococcal glomerulonephritis. On examination, look for evidence of oedema or hypotension. Check for flank tenderness or evidence of urethral trauma. Investigations can usually be confined to urinalysis, to check for cell casts and urine culture. No other investigations are required unless the clinical picture suggests it.

At follow-up two to three days from the first sighting of blood in the urine, in most cases the haematuria will have settled. This tends to suggest that the haematuria is related to a benign exercise-related cause (see above).

Further evaluation should be reserved for those with persistent urinary abnormalities or a suspicious history. Testing should aim to identify the site of bleeding and the nature of the pathology causing bleeding. Relevant investigations include renal ultrasound (or intravenous urography [IVU] in some circumstances), urine cytology and cystoscopy.

The athlete with microscopic haematuria can resume normal activity. If macroscopic haematuria is present, the individual should rest until it clears. Management of renal disorders depends on the particular condition present. A discussion of management strategies is beyond the scope of this chapter.

CLINICAL APPROACH TO THE ATHLETE PRESENTING WITH PROTEINURIA

Proteinuria in athletes is typically picked up at a periodic medical screening examination. A small

amount of proteinuria is normal (up to 200 mg/day). Dipstick testing usually registers trace proteinuria at urinary protein levels of 100 mg/L. Orthostatic proteinuria is common in patients below the age of 30 (i.e. the majority of those athletes having their first medical screening). If the protein/creatinine ratio is less than 0.2 and urinalysis is otherwise normal, the diagnosis of orthostatic proteinuria is confirmed.[10]

With exercise, there is increased filtration of macro-molecules, especially albumin, and decreased tubular reabsorption of small molecular weight proteins. However, in most cases the proteinuria is transient and resolves within four hours of stopping exercise. Standard protocols recommend a repeat urinalysis 24–48 hours later. If the urine still contains protein then a 24-hour urine sample should be collected for protein, creatinine and protein electrophoresis. Serum creatinine, urea, electrolytes and glucose should be checked. If proteinuria exceeds 3 g/day, nephrology referral is indicated, as the likelihood of serious renal disease is high.

Lesser grades of exercise-related proteinuria are thought to be due to a variety of factors. These may include metabolic acidosis, some renal hypoxia, renal arteriole vasoconstriction and loss of the negative charge on the glomerular membrane.[11] Proteinuria appears to be proportional to exercise intensity. It is more common with running than cycling or swimming, at a given exercise intensity.[12]

Page 190

Non-steroidal anti-inflammatory drugs and the kidney

Figure 13.2 NSAID use when exercising is associated with a risk of renal impairment
SHUTTERSTOCK/WANNANC

The renal effects of NSAIDs are often overlooked, but exercise can amplify them and cause clinical problems. Non-steroidal anti-inflammatory drugs inhibit prostaglandin synthesis. This in turn causes renal vasoconstriction, with reduced urine output, leading to salt and water retention. The athlete who becomes dehydrated and is taking NSAIDs is at special risk. The prostaglandin inhibition may abolish the normal protective vasodilatation of afferent arterioles and contribute to acute oliguric renal failure. In addition, there is potassium retention due to decreased plasma renin activity and decreased aldosterone.[14]

Although rare, NSAIDs can cause interstitial nephritis and the nephrotic syndrome. They can occur from 2 weeks–18 months after commencing the NSAID and resolve up to one year after stopping it. There is no evidence that NSAIDs cause papillary necrosis, which is typically associated with phenacetin. Low-dose aspirin decreases platelet aggregation, conceivably contributing to haematuria.

The counsel of perfection is to never use NSAIDs when exercising. The fact that NSAIDs are in widespread use by people who exercise, with relatively few serious adverse consequences, attests to their relative safety. However, the clinician should be mindful that the longer and more intense the exercise bout, especially in high heat or humidity (see Chapter 23), the greater the risk it is to use NSAIDs when exercising.

Any decision to use NSAIDs should be made by a well-informed athlete after discussion with his or her doctor, with careful consideration of the benefits and risks in the individual case. If NSAID use is justified, then a preparation with a short half-life (e.g. ibuprofen) is likely to be safer than one with a long half-life.

Note: A systematic review demonstrated post-race increases in serum creatinine following endurance events (marathon and ultramarathon running) returned to normal within 48 hours.[13] This suggests no serious long-term effects can be attributed to participation in endurance events.

PRACTICE PEARL

The risk of renal impairment following exercise is exacerbated by NSAID use. Risks are greater with prolonged or high-intensity exercise, both of which significantly compromise renal blood flow.

CASE STUDY

Jonah Lomu, New Zealand rugby international—kidney disease

Jonah Lomu (Fig. 13.3) was an international rugby player for New Zealand and of Tongan descent. He developed nephrotic syndrome at the height of his career. Despite being diagnosed in 1994 Lomu was able to dominate the 1995 Rugby World Cup, carrying New Zealand to the final (where they lost to an inspired South African home team) capturing the wider public awareness in much the same way Tiger Woods did through golf and, more recently, Usain Bolt via athletics.

Figure 13.3 Rugby is a physically demanding sport. Despite being diagnosed with kidney disease, Jonah Lomu was able to play international-level rugby for many years
(C) INGRAM PUBLISHING / SUPERSTOCK

Lomu is a high-profile example of the increasing incidence of kidney disease among athletes from the Pacific Islands. Many athletes are not being diagnosed until severe kidney malfunction has developed.[15]

Despite treatment with immunosuppressive drugs, Lomu developed progressive renal impairment with anaemia. He received dialysis treatment but developed severe peripheral neuropathies and had to stop playing rugby. Subsequently he received a live-donor kidney transplant in 2004 and the peripheral neuropathy resolved. He was able to return to playing professional rugby around a year later but eventually retired due to ongoing complications of the disease.

Sadly, Jonah Lomu died suddenly on 18 November 2015, following a long flight during which he had experienced leg swelling. The cause of death was noted as pulmonary embolus. He was 40 years old. In addition to his sporting achievements, Lomu is remembered for his work as an active campaigner in attempting to reduce the effect of kidney disease, particularly in children.

EXERCISE AND THE PATIENT WITH RENAL IMPAIRMENT

Systematic reviews have recommended exercise as well as other lifestyle factors (Fig. 13.4) for those with renal impairment for improving physical fitness, walking capacity, cardiovascular dimensions (heart rate and blood pressure), health-related quality of life and nutritional parameters.[16, 17]

Page 192

https://www.sciencedirect.com. Due to rights and permissions restrictions, this content cannot be reproduced in a digital format. The content is available in the print edition at page 192.

Figure 13.4 Lifestyle factors contributing to the development of chronic kidney disease
FROM JOURNAL OF SCIENCE AND MEDICINE IN SPORT, 16(5), SMART NA, WILLIAMS AD, LEVINGER I, SELIG S, HOWDEN E, COOMBES JS, ET AL. EXERCISE & SPORTS SCIENCE AUSTRALIA (ESSA) POSITION STATEMENT ON EXERCISE AND CHRONIC KIDNEY DISEASE, 406-11, 2013, WITH PERMISSION FROM ELSEVIER

People with varying degrees of renal impairment can benefit from exercise provided they follow some simple rules:

1. Depending on the degree of renal impairment, there will be a reduction in the homeostatic function of the kidneys. The ability to excrete nitrogen due to this reduced kidney function will be compromised. We therefore advise against protein supplementation in any exercising individual with renal impairment.
2. As renal function decreases there may be associated hypertension. This needs to be well controlled, otherwise there will be an accelerated loss of the remaining functioning nephrons.
3. With significant renal impairment there is a drop in erythropoeitin production, which will result in anaemia. This, in turn, will restrict exercise capacity.

The Exercise and Sports Science Australia 2013 position statement recommended that individuals needed to perform aerobic exercise at greater than 60% capacity to realise the greatest benefits.[18] A 2016 *British Journal of Sports Medicine* review suggested that bouts of 30 minutes, up to three times a week, were required to observe clinically beneficial effects.[19] Many kidney patients report that low energy levels and fatigue are one of the main barriers to taking part in exercise, and therefore it is key for the medical and wider multidisciplinary team to reduce the reversible causes of this, such as the adverse effects of medication, sleep deprivation and shift work.[20]

PRACTICE PEARL

Renal impairment reduces protein excretion and therefore we advise against protein supplementation in exercising individuals with this condition.

PRACTICE PEARL

Utilising a multidisciplinary approach to addressing the reversible causes of fatigue can significantly improve the renal patient's ability to participate in physical activity.

The most common cause of renal function decline is increase in age. Most organ systems, including the renal system, function at an optimal level in young adulthood (age 20–30 years). With each passing decade over 30 years there is approximately a 10% loss of function. Additional

pathology such as hypertension or diabetes (type 1 or type 2) can accelerate this age-related decline. Collectively, these changes mean that the average 80-year-old has an estimated one-quarter of the renal function of a young adult.

Advanced renal disease is associated with fluid overload, electrolyte disturbances, muscle weakness, cardiac dysfunction, peripheral neuropathy and renal osteodystrophy. Dialysis may ameliorate some of these, but the definitive treatment is renal transplantation.

Exercise for patients with renal transplantation

Most nephrologists encourage regular exercise after kidney transplantation. Activities should include warm-up stretches followed by aerobic activity that progressively increases in duration and intensity as physical capabilities improve. All vigorous activities should be followed by a proper cool down.[21] Where climatic conditions are extreme (e.g. during high heat or humidity) or the patient is suffering from concurrent illness (e.g. influenza), exercise should be postponed. Chest pain, weakness and lightheadedness are indications to stop exercising and rest.

Most transplant units encourage participation in a wide variety of sports but counsel against boxing, martial arts and collision sports (e.g. rugby or American football).[22] There are reported cases of professional athletes in collision sports making a successful return to play. This would require management on a case-by-case basis in consultation with a nephrologist and transplant surgeon to guide decisions.

PRACTICE PEARL

Moderate training reduces exercise proteinuria in healthy individuals and in chronic renal disease.

For athletes wishing to return to collision sports, the transplanted kidney should be placed in a less vulnerable position (e.g. up under the ribcage). Immunosuppressive drugs will need to Page 193 be continued on a lifelong basis.

Similar to recommendations for exercise after kidney transplantation, traditional expert advice for individuals with one kidney has been to avoid contact (collision) sports.[23] However, investigations indicate that individuals with one kidney have a low risk of further renal injury from contact sports and their restriction from participating in physical activity is unsupported by available evidence.[1] Patient participation in contact sports remains a controversial issue and is best determined by a thorough, individualised assessment.[2]

PREVENTION OF RENAL COMPLICATIONS OF EXERCISE

Most causes of exercise-related renal impairment are preventable. Simple measures that athletes can adopt to minimise their risk are listed in the box. Clinicians involved in the assessment of a patient with a possible kidney problem should be mindful of the recommendations outlined to

support self-management where applicable.

Prevention of renal complications of exercise

- Remain well hydrated from day to day. Know your 'wet weight', particularly in hot weather, and regard any sudden weight loss as an indication of dehydration.
- Start any exercise bout well hydrated.
- During exercise, drink according to thirst.
- After exercise, drink freely in the first hour or two to replace fluids lost.
- Avoid anti-inflammatory drugs in the 48 hours prior to prolonged strenuous exercise.
- Weigh yourself daily.
- If you do not pass any urine in the 12 hours after an exercise bout, seek urgent medical advice.
- Do not ignore blood in the urine—it may have a serious cause.
- If travelling from a cool to a hot environment, acclimatise gradually to the conditions. Exercise initially in the coolest part of the day.
- If you exercise vigorously, do not restrict your salt intake.

CASE STUDY

Aries Merritt, 110-metre hurdles—kidney disease

I'm not even supposed to be running. Just me being here in the final is definitely a blessing.

Aries Merritt (Fig. 13.5) won Olympic gold in the 110-metre hurdles in London in 2012. He also set the and world record of 12.80 seconds over the distance in September 2012. However, less than a year later he began to suffer from tiredness and struggled in training, fading to sixth in the 2013 World Athletics Championships, despite his previous dominance over the distance.

Figure 13.5 Aries Merritt at the IAAF World Championships in Beijing, 2015
VCG/VCG VIA GETTY IMAGES

The New York Times in 2016 quoted the track star as saying he felt 'like a marshmallow' due to the presence of oedema in his legs, with food passing through him and swollen ankles.[24] He was hospitalised suffering from a renal condition known as focal segmental glomerulosclerosis (FSGS). This was complicated further by having contracted B19 parvovirus, which affected his ability to produce red blood cells and led to anaemia. In 2014, Merritt suffered extreme weight loss as his body lost the ability to filter protein, his kidney function having dropped to 15%. Merritt reported he could only train after spending several hours in the hospital which would allow him 'just to feel normal'. Despite these setbacks, and with the parvovirus controlled by intravenous immunoglobulin treatment, Merritt won a bronze medal at the 2015 World Athletics Championships in Beijing. Four days later he underwent a transplant, with his older sister providing the donor kidney.

Page 194

Merritt returned to the track and, despite missing out on the Rio Olympics by just 0.01 second, he competed in the 2017 London IAAF World Championships, placing fifth in the final.

If any athlete needed an inspiration to continue training despite renal pathology, Merritt provides a clear role model.

Sources: references 24, 25, 26, 27, 28

SUMMARY

- Renal impairment has the potential to be a life-limiting disease.
- Exercise can help to manage symptoms and enhance the effects of treatment.
- Aries Merritt exemplifies that with effective management it is possible to return to the highest level of competitive sport.
- Individuals undergoing therapy should be assessed and provided with a tailored physical activity program appropriate to their needs.

REFERENCES

1. Grinsell MM, Showalter S, Gordon KA et al. Single kidney and sports participation: perception versus reality. *Pediatrics* 2006; 118(3): 1019–27.
2. Holmes FC, Hunt JJ, Sevier TL. Renal injury in sport. *Curr Sports Med Rep* 2003; 2(2): 103–9.
3. Hew-Butler T, Ayus JC, Kipps C et al. Statement of the Second International Exercise-Associated Hyponatremia Consensus Development Conference, New Zealand, 2007. *Clin J Sport Med* 2008; 18(2): 111–21.
4. J Knochel, J. Risks and benefits and myoglobinuria. *Semin Nephrol* 1981; 18: 75–86.
5. Meyer M, Sundaram S, Schafhalter-Zoppoth I. Exertional and CrossFit-induced rhabdomyolysis. *Clin J Sport Med*. 2017 Jul 14. doi: 10.1097/JSM.0000000000000480. [Epub ahead of print]
6. Eichner ER. Sickle cell trait in sports. *Curr Sports Med Rep* 2010; 9(6):347–51.
7. Gardner KD, Jr. Athletic pseudonephritis; alteration of urine sediment by athletic competition. *J Am Med Assoc* 1956; 161(17): 1613–17.
8. Blacklock NJ. Bladder trauma in the long-distance runner: '10,000 metres haematuria'. *Br J Urol* 1977; 49(2): 129–32.
9. Bernard JJ. Renal trauma: evaluation, management, and return to play. *Curr Sports Med Rep* 2009; 8(2): 98–103.
10. M B. *Nephrology in sportspeople*. Malden: Blackwell Science, 1997.
11. B R. *Exercise and the kidney*. London: Blackwell, 2008.
12. Poortmans JR. Exercise and renal function. *Sports Med* 1984; 1(2): 125–53.
13. Hodgson L, Walter E, Venn R et al. Acute kidney injury associated with endurance events—is it a cause for concern? A systematic review. *BMJ Open Sport Exerc Med* 2017; 3(1): e000093.
14. Walker RJ, Fawcett JP, Flannery EM et al. Indomethacin potentiates exercise-induced reduction in renal hemodynamics in athletes. *Med Sci Sports Exerc* 1994; 26(11): 1302–6.
15. Cleaver D. Kidney concerns: 'huge problem' for Pasifika rugby players. 2018 [updated 25 March 2018]. http://www.nzherald.co.nz/sport/news/article.cfm?c_id=4&objectid=12019605.
16. Heiwe S, Jacobson SH. Exercise training for adults with chronic kidney disease. *Cochrane Database Syst Rev* 2011 (10): CD003236.
17. Heiwe S, Jacobson SH. Exercise training in adults with CKD: a systematic review and meta-analysis. *Am J Kidney Dis* 2014; 64(3): 383–93.

18. Smart NA, Williams AD, Levinger I et al. Exercise & Sports Science Australia (ESSA) position statement on exercise and chronic kidney disease. *J Sci Med Sport* 2013; 16(5): 406–11.
19. Phan K, Jia F, Kamper SJ. Effects of regular physical exercise training in adults with chronic kidney disease (PEDro synthesis). *Br J Sports Med* 2016; 50(5): 317–18.
20. Hannan M, Bronas UG. Barriers to exercise for patients with renal disease: an integrative review. *J Nephrol* 2017; 30(6): 729–41.
21. Cleveland Clinic Foundation. Exercise guidelines after kidney transplant. 2009.
22. Heffernan A, Gill D. Sporting activity following kidney transplantation. *Pediatr Nephrol* 1998; 12(6): 447–8.
23. Dyment PG, Goldberg B, Haefele SB et al. American Academy of Pediatrics Committee on Sports Medicine. Recommendations for participation in competitive sports. *Pediatrics* 1988; 81: 737–9.
24. Longman, J. Olympic hurdler isn't letting disease stand in his way. 2016. *New York Times*, https://www.nytimes.com/2016/07/08/sports/olympics/aries-merritt-hurdler-kidney-transplant.html.
25. https://www.flotrack.org/articles/6077588-after-surgery-transplant-aries-merritt-feels-the-best-he-has-in-5-years
26. http://www.espn.com/espn/feature/story/_/id/16942497/how-aries-merritt-recovered-kidney-transplant-reach-olympic-trials
27. https://en.wikipedia.org/wiki/Aries_Merritt
28. https://www.iaaf.org/news/feature/aries-merritt-kidney-transplant-2017

Chapter 14

Neurological conditions

with JAMES O'DONOVAN, SILKE APPEL-CRESSWELL and PAUL BLAZEY

Even when I have an off period, I can't go too crazy because the threat of having a seizure doesn't go away. As long as you're focused and dedicated—especially in a sport—there's no reason it should dictate your life.
Dai Greene, former 400-metre hurdles world champion

Neurological disorders are now the leading cause of disability in the world.[1] This chapter addresses the benefits of physical activity for some specific neurological conditions observed in regular clinical practice. The evidence base for treatments of these conditions has grown, with some research suggesting potential preventive as well as rehabilitative and management roles for physical activity in neurological conditions. Physical activity and effective functional mobility training (including sports participation) remain under-prescribed in the management of neurological conditions. The following sections provide a brief overview of cerebrovascular disease (stroke), Parkinson's disease (PD), multiple sclerosis and epilepsy, before discussing the effects of physical activity prescription in the prevention or management of these conditions.

CEREBROVASCULAR DISEASE (STROKE)

Stroke is a disease of the vascular supply to the brain. The effects of physical activity and its protective mechanisms for vascular disease are well established Physical activity can also provide a secondary preventative effect, alongside working as a rehabilitation tool post stroke.[2] A stroke is characterised by rapidly developing neurological symptoms of vascular origin resulting from brain ischaemia. This is the result of either an occlusion of the blood supply to the brain (thromboembolic) or a haemorrhage. Stroke remains the second highest cause of death in high-income countries and is top among middle-income areas, accounting for 14.6% of all deaths.[3]

Key concerns post stroke can be divided into three categories:

Physical

- muscle weakness or spasticity
- loss of sensation
- stiffness
- incontinence

Emotional

- mood disorder
- personality changes

Cognitive

- loss of memory
- poor concentration
- unable to problem solve or process information effectively
- visual neglect
- aphasia.

PRACTICE PEARL

Stroke-like signs such as hemiplegia and aphasia can occur during physical activity but may relate to the more common concern of transient hypoglycaemia. A finger prick test will support effective diagnosis.

Effects of physical activity on stroke mortality

Physically active men and women have a 25–30% reduced risk of stroke when compared with inactive men and women. Various physical activities, ranging from walking to occupational movement, provide benefits to men and women, uninfluenced by age or gender.

Page 196

Key data comes from observational studies as well as two meta-analyses of physical activity and stroke.[4, 5] The magnitude of the effect in those studies is shown in Table 14.1. The beneficial effects of higher levels of occupational physical activity are similar in extent to those seen in general physical activities, such as walking.

Table 14.1 Dose–response for the benefit of exercise in stroke: relative risks below 1.0 reflect relative protection against stroke

Median relative risk—all strokes	Men	Women
Moderate activity vs no/light activity	0.65	0.82
High activity vs no/light activity	0.72	0.72

Because the incidence of stroke is low for those younger than age 55 years, very few reports are available on the relation between physical activity and stroke morbidity or mortality in younger and middle-aged populations. There are, however, examples of elite athletes suffering from stroke; two of these are considered in greater detail in case studies in this chapter.

PRACTICE PEARL

Those suffering from unexplained dizziness, vision disturbance and/or drop attacks should be immediately referred for further investigation.

Effect of physical activity in the treatment of stroke

The ability of the body to recover and the neural plasticity of the brain are improved with motor relearning. Physical activity prescription should be incorporated into the management of those who have experienced a stroke. Charalambous et.al.[9] demonstrated that a high intensity Page 197 bout of physical activity was successful in enhancing the effects of motor relearning during rehabilitation. In most non-elite populations there should be an emphasis on aerobic exercise, muscle-strengthening activity, reduction of sedentary behaviour and risk management for secondary prevention of stroke.

CASE STUDY

Kris Letang, National Hockey League—stroke

Kris Letang is a National Hockey League (NHL) defenseman for the Pittsburgh Penguins, having played with them since 2006 (Fig. 14.1). He is a four-time NHL all-star and three-time Stanley Cup winner. In January 2014, Letang began feeling dizzy and nauseous, falling to the floor of his home before being assessed and given the all clear.

Figure 14.1 The Pittsburgh Penguins in action
SHUTTERSTOCK/JAI AGNISH

Diagnosis

Letang was initially cleared to travel with his teammates but was sent for further tests, including a magnetic resonance imaging (MRI) scan. The MRI revealed that Letang had suffered a stroke. Upon further evaluation Letang was discovered to have a congenital heart defect known as a patent foramen ovale (PFO), or hole between the atria.

Stroke in younger patients often presents from diverse causes, unlike in older generations, where it is predominantly of an ischaemic nature. Therefore a comprehensive examination of all potential causes is required.

Treatment

Letang was only 26 when the stroke occurred and due to his high level of fitness was able to undergo initial treatment with anticoagulation therapy and rehabilitation. PFO closure has been recommended as reducing the risk of secondary stroke by three of the most recent meta-analyses, offering advantages over normal medical management (anticoagulation therapy).[6–8] Although it is uncertain whether Letang underwent surgery, most contact sport participants are advised to undergo the percutaneous procedure, due to the risks of ongoing anticoagulant medication use. The use of anticoagulant therapy is of particular concern in contact sports such as ice hockey, rugby and American football. Letang returned to full competitive play in April 2014—only 6 weeks after the initial incident—and continued at the top level of the game. In 2016 he was part of the NHL all-star team.

Conclusion

Letang's experience demonstrates the need to be aware of the potential for ischaemic attacks, even in those whose age would traditionally suggest they would not be at risk.

Sources: references 76, 77, 78, 79

Once stroke patients have gone through the initial period of acute hospitalisation and subsequent inpatient/outpatient rehabilitation, their transition to home or community care can be improved through physical activity to improve fitness and motor functions. Hospitalisation generally causes deconditioning, and rehabilitation, while improving function, is usually lacking in aerobic intensity. In part, this may relate to the fear of causing further cerebrovascular problems and, to date, only a small number of studies have adequately addressed this issue.[10–12]

Greater aerobic fitness, muscle strength and endurance improve functional abilities such as walking. Treadmill and cycle training have also proven effective in this regard. An additional and important benefit of fitness training is improved self-confidence and general wellbeing. Increased endurance also seems to give individuals more confidence and energy to improve other activities. Duncan et.al. (2005),[13] in their consensus guidelines on post-stroke management, recommended physical activity and exercise programming to reduce the risk of further complications and promote a return to activities of daily living.

There are large benefits associated with resistance training across the physical, emotional and cognitive concerns associated with stroke.[14] A summary is listed below:

- reduced anxiety
- improved overall quality of life
- increased muscle strength, power and gait control (including walking velocity)
- greater focus and speed of information processing during tasks
- enhanced self-efficacy during functional activities, e.g. walking and stair climbing.

Evaluations of other forms of physical activity, including circuit classes, cardiorespiratory training, strength, flexibility and neuromuscular training, have all demonstrated benefits for the physical and mental health of stroke patients.[15–17] The impact of these benefits on maintaining functional autonomy should not be underestimated.

Despite the clear benefits, a limited number of stroke patients receive the appropriate assessment and support to improve their engagement in physical activity and take part in adjusted activities of daily living.[13]

Considerations in prescribing physical activity for stroke patients

Stroke patients have a mixture of risk factors that may preclude their ability to exercise, including an increased risk of falls, muscle weakness, exacerbated fatigue, autonomic dysfunction and haemodynamic instability. The haemodynamic instability of stroke patients has often been the greatest concern among clinicians. A thorough cardiovascular assessment and assessment of relevant risk factors needs to be performed prior to exercise prescription.

CASE STUDY

Bruce Tasker, British bobsleigh—stroke

Bruce Tasker is a 30-year-old British bobsleigh competitor who won a retrospective bronze medal in the 4-man team event at the Sochi 2014 Winter Olympic Games. He was due to compete in the event at the PyeongChang 2018 Winter Olympics but suffered a stroke only 2 months before the games.

Symptoms

Classic signs of a stroke presented while Tasker was relaxing at home; he experienced headache, dizziness and nausea prior to a brief syncope. He also had tingling in his left arm. This was followed by a second bout shortly after, which resulted in Tasker being admitted to the emergency department. He continued to feel unwell, complaining of visual and balance disturbances, before vomiting. It was reported that MRI confirmed the diagnosis of stroke. *Note:* it is more common for stroke diagnosis in the emergency department to come via computer tomography (CT) scan.

Treatment

Tasker was immediately placed on anticoagulent therapy, with his symptoms resolving soon after. He was discharged from hospital 3 days later. His return to intense physical activity had to be delayed until 6 months after the event, during which time anticoagulant medication continued. Following his recovery Tasker decided to retire from elite competition in October 2018.

Conclusion

Stroke is not always limited to older or unfit patient populations. Fortunately, this case study demonstrates that a high level of prior fitness may confer some benefits to those who suffer a stroke. Although two-thirds of stroke patients demonstrate at least one disability post-stroke, Tasker did not show any sign of long-term disability.

Sources: references 80, 81, 82, 83

A detailed analysis of the potential medications provided to stroke patients for the management of symptoms is beyond the scope of this chapter. The reader is encouraged to review pharmacological interventions and their potential to affect exercise ability prior to providing a physical activity prescription in all groups with neurological pathology.

PRACTICE PEARL

FAST, or Face–Arm–Speech–Time, the acronym used to promptly recognise stroke symptoms, is as applicable to elite athletes as to the elderly population. Prompt recognition allows the patient to begin antithrombolytic medication within the 4 hour 'golden window'.

PARKINSON'S DISEASE

Parkinson's disease (PD) has the fastest growing incidence of any neurological disorder, recently surpassing that of Alzeihmer's disease.[18] The incidence of PD increases sharply with age and, as the world population is ageing, the number of individuals affected is expected to increase exponentially. Figure 14.2 demonstrates the projected increase in those with a PD diagnosis by

2040.

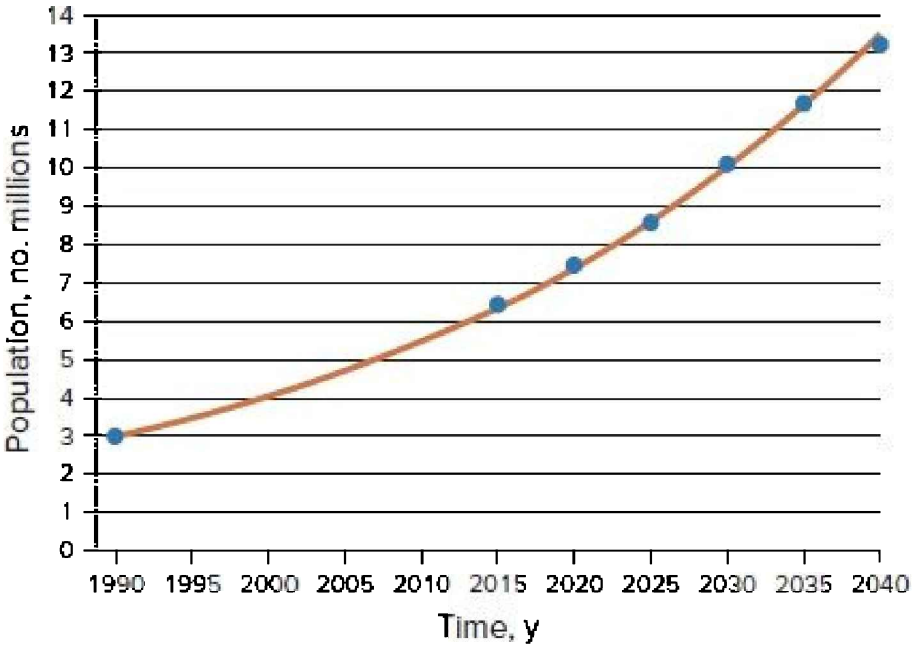


Figure 14.2 Estimated and projected number of individuals with Parkinson's disease, 1990–2040
BASED ON DATA FROM GLOBAL, REGIONAL, AND NATIONAL BURDEN OF NEUROLOGICAL DISORDERS DURING 1990–2015: A SYSTEMATIC ANALYSIS FOR THE GLOBAL BURDEN OF DISEASE STUDY 2015 GBD 2015 NEUROLOGICAL DISORDERS COLLABORATOR GROUP. PUBLISHED BY ELSEVIER LTD. DOI:HTTPS://DOI.ORG/10.1016/S1474-4422(17)30299-5

The increasing incidence and prevalence of PD raises much concern, especially when some believe that these estimates may be understated. Some researchers are describing this trend as 'the Parkinson pandemic' and suggest that this public health issue should be tackled with similar vigour to the case of any pandemic communicable disease.[18]

Parkinson's disease is a progressive neurodegenerative disorder. In addition to widespread neurodegeneration, the most prominent pathological feature of PD is a neuronal cell loss pattern at the substantia nigra of the basal ganglia, resulting in dopamine depletion, which leads to movement disorder. In addition, alpha-synuclein pathology (aggregation of abnormally folded proteins) and neuroinflammation mediated by astrocytes and microglia are typical pathological changes.[19] The clinical presentation is characterised by bradykinesia (slowed movement), resting tremor, postural instability and stiffness. Parkinson's disease is also associated with numerous non-motor symptoms (including mood disorder, apathy, sleep disturbance, cognitive impairment and a range of autonomic symptoms), some of which precede the motor dysfunction by more than a decade. A combination of all these factors can result in an individual having a sedentary lifestyle.[20] However, it is difficult to exclude reverse causality in studies of activity level in Parkinson's

patients. Preclinical PD may manifest years before as a reduction in activities or aversion to participating in physical activity. In addition, in more advanced PD, a fear of falling is common and can result in a reduction of outdoor activities.[21] Figure 14.3 demonstrates an average time Page 199 course for the development of the differing clinical symptoms associated with PD.

https://www.sciencedirect.com. Due to rights and permissions restrictions, this content cannot be reproduced in a digital format. The content is available in the print edition at page 199.

Figure 14.3 Clinical symptoms and time course of Parkinson's disease progression
REPRINTED FROM THE LANCET, 386(9996), KALIA LV, LANG AE. PARKINSON'S DISEASE, 896-912, 2015, WITH PERMISSION FROM ELSEVIER

PRACTICE PEARL

Practitioners should be alert to back pain and stiffness as potential early symptoms of Parkinson's disease. Clinicians should assess for the presence of other early symptoms such as loss of smell or constipation to guide diagnosis.

Parkinson's disease is a clinical diagnosis based on the presence of Parkinsonian motor features, namely bradykinesia, rigidity and resting tremor (which is absent in 30% of PD patients). Symptoms are classically unilateral initially, and over time become bilateral. Postural instability is typically a feature of more advanced disease. Patients normally respond well to pharmacological treatment with levodopa, showing a clear and dramatic reduction in PD symptoms. However, over time the drug becomes less effective and they will often slowly develop dyskinesias (involuntary choreiform movements). Frequently, there is olfactory loss and cardiac sympathetic denervation.[22]

Effect of physical activity in Parkinson's disease: prevention, disease modification and symptomatic benefit

Prospective evidence suggests that midlife, regular physical activity reduces the subsequent risk of PD in later years. Moderate to vigorous activity habits in midlife significantly reduced the risk of developing PD in three large prospective cohort observational studies.[23–25] In these studies, PD was significantly reduced with moderate to vigorous activities in patients aged 30–40, with a meta-analysis showing that males with the highest energy expenditure had 37% lower risk than those in the most sedentary group.[25] However, it is difficult to distinguish whether the association between physical activity and a lowered risk of PD can truly be explained by the preventive effects of activity alone, or by a decrease in baseline recreational activity as a result of preclinical PD.

The promising effects of physical activity in midlife may have implications for attenuating PD progression,[26] especially as we are starting to identify people who are at increased risk of PD, including:

- individuals with rapid eye movement sleep behaviour disorder
- family members of individuals with PD
- people who have reduced sense of smell
- people with chronic constipation
- people who carry a mutation in a PD susceptibility gene.

Combining different physical activity modalities is effective in improving motor symptoms and activities of daily living. In PD, activities that promote both a learning aspect to drive networks and an aerobic aspect to express molecules required to strengthen synaptic connections are likely to yield particular benefits.[27, 28] Accordingly, mind–body activities such as tai chi, yoga and dance have significant benefits for motor function, yet the aerobic (and most likely neuroprotective) aspect is relatively less than in, for example, treadmill or cycling training.[29] Table 14.2 summarises some of the benefits of physical activity for those with PD.

Table 14.2 Evidence from research to demonstrate benefits of physical activity in motor and non-motor symptoms of PD

Motor benefits	Non-motor benefits
• Cardiopulmonary fitness	• Reduced risk of mood disorder
• Walking speed and economy improved	• Improved cognitive function
• Muscle strength	• Improved health-related quality of life measures
• Improved functional mobility	• Reduced risk of osteoporosis
• Balance	• Improved sleep
• Posture	• Decreased fatigue
	• Decreased constipation

FROM STUDIES: MAK ET AL., 2017;[30] WU ET AL., 2017;[31] MURRAY ET AL., 2014;[32] BARHA ET AL., 2017;[33] REUTER ET AL., 2011;[34] CUGUSI ET AL., 2015;[35] SHULMAN ET AL., 2013;[36] CHUNG ET AL., 2016;[37] NI ET AL., 2016[38]

Treatment approaches specific to Parkinson's disease

Pharmacological and occasionally surgical management (i.e. deep brain stimulation) have long been the mainstays of PD treatment. Medications address the low levels of dopamine in the brain, either by replenishing the levels or mimicking its action. Medications address symptoms such as slowness, rigidity and tremor; however, with progression of the underlying neurodegenerative disease process, over time increased dosages are required, with subsequent raised risk of adverse effects. The most common drug prescribed is levodopa (L-dopa), which is metabolised to dopamine. Dopamine agonists, monoamine oxidase type B inhibitors and catechol-O-methyltransferase (COMT) inhibitors are also commonly utilised with this patient population. An understanding of these medications and common adverse effects is useful when treating PD patients.

All medications used in PD aim to enhance intracerebral dopamine concentrations or stimulate

dopamine receptors, and modify symptoms. Unfortunately, none of these drugs have proven to be neuroprotective or disease modifying. Dopaminergic medications are initiated when symptoms cause the patient disability or discomfort, with the goal of improving function and quality of life. Successful PD therapy should facilitate the maximum level of physical performance, and failure to achieve this should prompt the initiation or adjustment of medication. Drug-induced adverse reactions need to be considered, as listed in Table 14.3. Impulse control disorders, including pathological gambling, hyper-sexuality and compulsive spending, or doing any hobby or activity compulsively and with detrimental effects, occur more commonly with dopamine agonists. There have been cases where PD patients on this type of medication can become obsessed by physical activity, including excessive aimless walking.[40]

Table 14.3 Common drugs used to treat Parkinson's disease, including adverse effects

Drug category (name)	Actions	Adverse effects (relevant)
Levodopa (e.g. levodopa-carbidopa)	Increases dopamine levels in the brain	Low blood pressure, nausea, confusion, dyskinesias, dry mouth, dizziness, *on/off* effect resulting in motor fluctuations
Dopamine agonists (e.g. pramipexole, ropinirole, rotigotine, apomorphine)	Bind to and stimulate dopamine receptors in the brain	Nausea/vomiting, low blood pressure, sleep disturbances, sedation, dyskinesias, hallucinations, oedema, confusion, dry mouth, depression, headaches
Monoamine oxidase B inhibitors (e.g. selegiline, rasagiline)	Block the action of an enzyme (monoamine oxidase B) in the brain that breaks down dopamine	Agitation, insomnia, hallucinations, dizziness, nausea, pain, headache, sleep disturbances, runny nose, back pain, increased dyskinesias, postural hypotension, joint pain
Catechol-O-methyltransferase inhibitors (e.g. entacapone, tolcapone)	Block the action of an enzyme (catechol-O-methyltransferase) that breaks down dopamine (taken along with L-dopa)	Abdominal pain, back pain, constipation, nausea, diarrhoea, dyskinesias, orange discoloration of body fluids (harmless: entacapone)
Amantadine	Originally an antiviral drug, putative effect on dopamine, noradrenaline, NMDA-receptors, used to treat dyskinesias in PD	Dizziness, weakness, dry mouth, constipation, livedo reticularis, confusion, hallucinations

ADAPTED WITH PERMISSION FROM GALLO PM, EWING GARBER C. PARKINSON'S DISEASE: A COMPREHENSIVE APPROACH TO EXERCISE PRESCRIPTION FOR THE HEALTH FITNESS PROFESSIONAL. ACSM'S HEALTH & FITNESS JOURNAL 2011;15(4):8–17 COPYRIGHT © 2019 AMERICAN COLLEGE OF SPORTS MEDICNE HTTPS://JOURNALS.LWW.COM/ACSM-HEALTHFITNESS/PAGES/ARTICLEVIEWER.ASPX?YEAR=2011&ISSUE=07000&ARTICLE=00006&TYPE=FULLTEXT[39]

PRACTICE PEARL

Dopamine agonists should be avoided in patients with a history of addiction, obsessive-compulsive disorder or impulsive personality, due to an increased risk of developing impulse control disorders.

Considerations in planning a physical activity program for Parkinson's disease patients

It is important to have an understanding of stage of disease and disease severity, as this will help

categorise risks involved when initiating a physical activity program. This is important for calculating appropriate and realistic progressions for the patient, as well as for considering any necessary precautions. Interestingly, the risk of a patient falling is an inverted U-shaped curve (Fig. 14.4). Falls affect 35–90% of people with established PD and can lead to fractures, especially as osteoporosis is common in this population. PD patients who fall may suffer a spiral of negative psychosocial effects, such as an increased fear of falling and reduced physical activity. This can lead to an increase in the likelihood of nursing home admission.[41]

Page 201

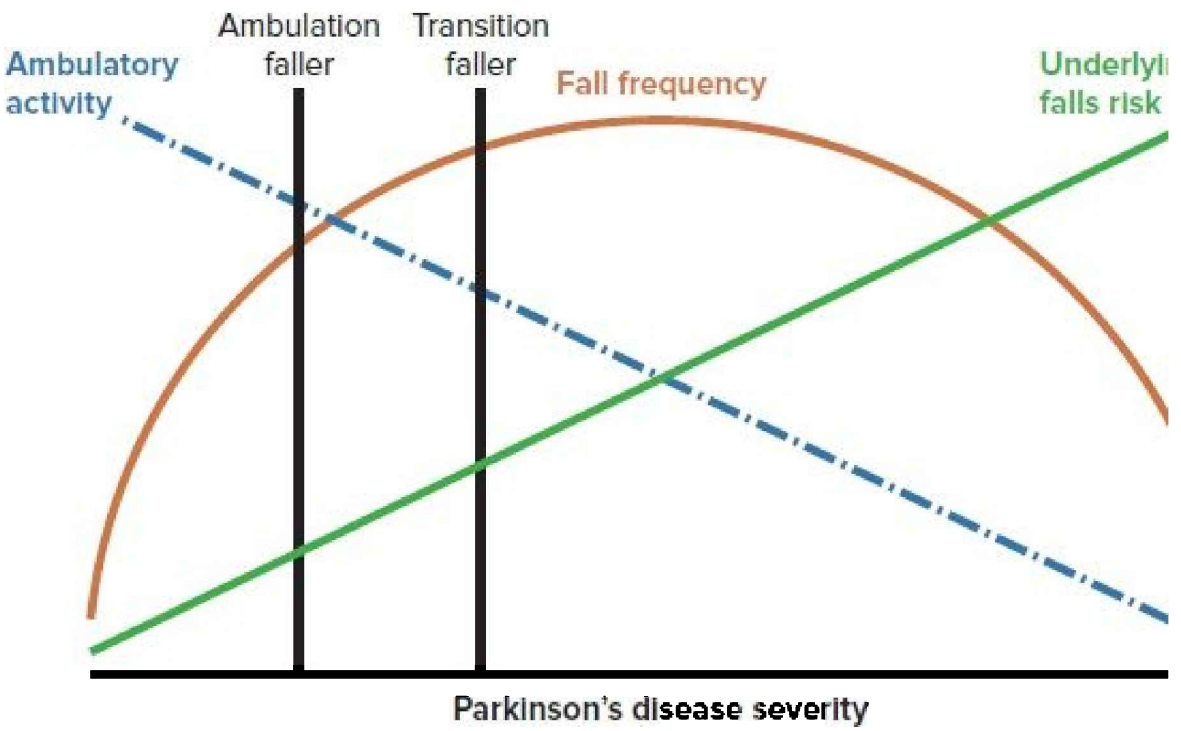


Figure 14.4 Schematic diagram of the relationship between activity and falls over time in PD. Fall frequency is thought to have an inverted U-shaped curve mediated by ambulatory activity which decreases as disease severity increases[42]

REPRINTED FROM PARKINSONISM & RELATED DISORDERS, 21(3), MACTIER K, LORD S, GODFREY A ET AL. THE RELATIONSHIP BETWEEN REAL WORLD AMBULATORY ACTIVITY AND FALLS IN INCIDENT PARKINSON'S DISEASE: INFLUENCE OF CLASSIFICATION SCHEME, 236-42, FIGURE 2, 2015, WITH PERMISSION FROM ELSEVIER

Motor fluctuations are important complications of levodopa therapy that evolve over time with progression of the disease. Motor fluctuations are alterations between periods of being *on,* during which the patient experiences a positive response to medication, and being *off,* during which the patient experiences a re-emergence of the Parkinson's symptoms suppressed during the *on* state.[43] It is important to ascertain the pattern, frequency and timing of *on*/*off* periods. *Off* periods are more common as the disease progresses, leading to reduced effectiveness of the medications over

time.[44]

Physical activity should be prescribed during an *on* period, and thus early morning activities may have to be delayed while medication takes effect. Most studies looking at the relationship of activity with the pharmacokinetics of levodopa have found no effect of increased activity on the efficacy of levodopa.[45] One study showed a trend towards absorption of the drug during physical activity, possibly due to accelerated mesenteric blood flow and thus resultant absorption.[46] In some patients, *off* periods are unpredictable, and the transitions from *on* to *off* can be sudden and unexpected, without an obvious relationship with the timing of levodopa dosing. In clinical practice, some patients require additional levodopa, for example 50–100 mg, before or during physical activity. Table 14.4 demonstrates some examples of effective physical activity interventions that can be prescribed for differing PD clinical symptoms.

Table 14.4 Physical activity recommendations based upon PD symptoms and severity

Symptom	Movement principles	Suggested activities
Rigidity Stooped posture and decreased range of motion in the neck, trunk, and hips	• Rotation • Reciprocal movement • Rhythmic movement • Extension exercises • Tall, 'charge up' posture	• Torso rotation exercises: – Kayaking – Golfing – Elbow to opposite knee – Side bends – Bow and arrow • Upper back strengthening exercises: – Rowing – Lat pull down • Pilates and yoga • Chest stretches
Bradykinesia Slow movements	• High effort, whole body movement • Wide base of support	• Walking and agility exercises • Lunging in all directions
Hypokinesia Small movements and narrow base	• Extensor muscle strengthening • BIG, fast steps • BIG, large arm swings	• Boxing • Kettlebell swings
Akinesia Impaired sequential coordination (includes freezing)	• Preplanning tasks • Quick change movements • Practice moving in small spaces • Understand and use external cues • Dual tasks • Sequential movements	• Walking and agility exercises • Obstacle courses • Quick turns in corners • Lunging in all directions • Boxing • Kettlebell swings
Impaired sensory integration Problems processing sensory information	• Practice balance on different surfaces • Reduce reliance on vision and external cues	• Stability ball exercises • BOSU ball exercises • Exercises with eyes closed • Exercises with head turns • Stand on a foam pad
Impaired balance	• Balance-specific exercises adding visual and surface changes • Weight shifting • Strengthening hips and legs	• Stability ball exercises • BOSU ball exercises • Kettlebell exercises • Lunging

- Tai Chi
- Boxing

ADAPTED WITH PERMISSION FROM GRANT (2018)[50] BRIAN GRANT FOUNDATION. EXERCISE FOR PARKINSON'S. 2018. HTTPS://BRIANGRANT.ORG/EXERCISE/

Dyskinesia consists of levodopa-related abnormal, involuntary movements, and encompasses a variety of involuntary movements, including chorea, dystonia and ballism. Dyskinesias tend to appear when the patient is *on* and are usually choreiform. Dyskinesia in the *off* state is more commonly dystonic and patients might struggle with walking or running due to foot inversion or toe flexion dystonia.

PRACTICE PEARL

Dystonia starting in adults with foot-related symptoms associated with walking or running may be an early symptom of PD.

Freezing of gait (FOG) can occur as a transient *off* phenomenon. During an episode of FOG, patients suddenly become immobilised for seconds to minutes at a time, usually when initiating walking in a confined space such as a doorway.[47] An episode of FOG can lead to falling, which is usually forward as the individual tries to move while their feet remain behind. This could happen in a busy gym class or between exercise machines. Movement strategies or cues that may help the patient 'get into gear' include shifting weight, making wider turns, concentrating on taking larger steps forward, and using visual imagery as if to step over an obstacle. A cane or laser cane (Fig. 14.5) may also be helpful for FOG. Similarly, turning can often be a challenge and is a fall risk scenario. Strategies and reinforcement to turn with a wide arc and increased steps are useful.

Page 202

Figure 14.5 Example of a laser cane, depicting a visual reference point to support those with FOG

Fatigue is an extremely common symptom in PD, affecting up to 50% of patients. When initiating activities, gradual progression of intensity and duration should be adopted, and adequate recovery periods should be allowed. PD patients often report that their fatigue improves with physical activity.[48] Excessive daytime sleepiness and unintended sleep episodes can occur in patients with Parkinson's disease. Some PD patients are prone to sleep attacks, where they are overcome by overwhelming sleepiness or fall asleep without warning.[49]

PRACTICE PEARL

Adherence to a regular medication dosing schedule is critical, and activity times should be coordinated with the schedule to optimise the ability to exercise. Occasionally, it is advisable to take an extra half to one tablet of levodopa before and/or during physical activity for maximum benefit.

CASE STUDY

Brian Grant, NBA—Parkinson's disease

Brian Grant played for five National Basketball Association (NBA) teams, including the Miami Heat and Los Angeles Lakers between 2000 and 2005. Over his career he amassed 7933 points and was renowned as one of the league's best defenders. He announced his diagnosis of early onset PD in 2009.

Diagnosis

Grant presented with weakness, primarily of his left jumping leg, and a resting tremor of his left hand, which was initially put down to stress.

Grant's diagnosis was likely based upon his medical history and physical examination. Investigations such as blood and urine assessment and brain imaging do not diagnose PD. Investigations may be utilised to rule out the presence of other medical conditions responsible for the patient's symptoms. PD will traditionally present with resting tremor, rigidity and bradykinesia.

Treatment

Grant initially self-medicated with supplements, which he suggested helped him to maintain his level of activity. However, when his resting tremor worsened, he began dopaminergic medication to control his symptoms. Grant has advocated the maintenance of an active lifestyle, and encourages others through his foundation. The Brian Grant Foundation has produced resources on Pilates, walking and high intensity interval training for PD patients. The resources include guides on matching physical activity to PD symptoms (see table 14.4).

Grant maintained his fitness and in 2012 was able to hike with members of his foundation and fellow individuals with PD to the top of Mount St Helens (8363 ft elevation).

Sources: references 84, 85, 86, 87

Risks of adverse events in prescribing physical activity to those with Parkinson's disease

Possible risks associated with increased physical activity in patients with PD, such as falls, have to be considered, and this should be done through pre-participation screening and evaluation. Paradoxically, physical activity can help prevent falls. As with the general older population, there is cardiovascular risk with an increase in moderate to vigorous physical activity. There is no difference for risk between PD and the normal population. The majority of studies that report risks or adverse effects conclude that the overall risk is low. The benefits of physical activity appear to far outweigh the potential adverse effects in PD.

MULTIPLE SCLEROSIS

Multiple sclerosis (MS) is a lifelong chronic demyelinating disease of the central nervous system. MS is thought to be largely an autoimmune response of the body triggered by an unknown factor

that results in an immune-mediated attack on the myelin sheath around nerve fibres. These attacks occur intermittently and can lead to progressive deterioration in physical and cognitive abilities. MS is more common in females aged 20–40 and its prevalence increases with increased distance from the equator. The incidence of MS is approximately 5 per 100 000 people worldwide, with substantial regional variation. Medical treatment reduces the frequency and severity of attacks.

Developing and maintaining muscle activity, strength and aerobic fitness are just as important for people with MS as for people without the condition. As the disease progresses over time, the need for improved functional capacity increases. After 15 years, 50% of patients with MS will require a walking aid to walk 100 metres; after 25 years, 50% will be confined to a wheelchair. There is strong evidence that physical activity improves muscle function, aerobic fitness, mobility and quality of life. The difficulty is that many patients with MS have reduced aerobic capacity for a variety of reasons.

Does physical activity prevent the onset of multiple sclerosis or cause exacerbations?

It cannot be confirmed that low physical activity is a contributory factor in the development of MS. However, research has demonstrated the beneficial effect of exercise on the release of neuroprotective molecules such as insulin-like growth factor 1 (IGF-1). Physical activity has demonstrated positive signs for slowing, reversing and in some cases preventing autoimmune diseases such as MS.[51, 52]

Physical activity for the management of multiple sclerosis

Physical activity in MS confers improvements in muscle function, aerobic fitness, quality of life and mobility.[53] Aerobic exercise in particular can improve both walking speed and distance in MS patients.[54] It is clear that physical activity, regardless of whether it is similar to the activities prescribed for healthy individuals or is modified to maintain function, is of great benefit to those with MS and therefore should be widely recommended. However, we currently have limited evidence upon which to base exercise prescription (e.g. type and amount) for MS patients.

Compared to people without MS, individuals with MS have lower levels of physical activity leading to reduced muscle mass, weakness and endurance. Reduced physical activity may in turn lead to less social interaction, restricted leisure activities and depression, affecting quality of life in individuals with MS.

Considerations in planning a physical activity program for those with multiple sclerosis

In individuals with MS, neurological function deteriorates sharply if core body temperature rises (Uhthoff's effect), due to the negative effect of temperature on the conduction velocity of demyelinated nerves.[55] Thus, environmental evaluation is important, and practical advice can include having a cool shower before and after activities. Wearing a cooling vest may be worthwhile.

More recent studies have looked at the effects of aquatic-based therapies, which allow for a mixture of strength, aerobic and proprioceptive exercises to be undertaken in a cool environment, with promising results.[56]

Fatigue can strongly influence activity adherence and approximately 90% of patients with MS experience fatigue; even in mild disease fatigue may be severe. The increased level of muscular fatigue is not correlated with muscular weakness, although muscular strength is also affected following a short period of exertion. This tiredness or fatigue affects all daily activities and quality of life. Management is complex and may include a longer period of recovery following exertion, planned rest, use of aids, short breaks to gain new strength during the physical activity regimen, assessment of sleep patterns and the use of medications.

Physical activity reduces overall fatigue and therefore should not be a contraindication to activity in individuals with MS.[57]

EPILEPSY

Epilepsy is a disorder of the central nervous system, characterised by mild, episodic losses of attention or sleepiness (petit mal), or by severe convulsions accompanied by the loss of consciousness (grand mal). It is defined by having recurrent unprovoked seizures.

Epilepsy is defined by the following International League Against Epilepsy (ILAE) guidelines, 2014:

1. At least two unprovoked (or reflex) seizures occurring >24 h apart
2. One unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years
3. Diagnosis of an epilepsy syndrome

Epilepsy is considered to be resolved for individuals who had an age-dependent epilepsy syndrome but are now past the applicable age or those who have remained seizure-free for the last 10 years, with no seizure medicines for the last 5 years.[58]

Non-epileptic related seizures are reported to occur in up to 15% of the general population across their lifetime. Despite its relatively high prevalence, with a worldwide prevalence of 50 million according the World Health Organization (2018),[59] the study of physical activity and its role in the management of epilepsy remains relatively low. The terms ‘seizure’, ‘epilepsy’, ‘convulsion’ and ‘fit’ are often used interchangeably. We use the term ‘seizure’ to refer to an epileptic seizure and the term ‘convulsion’ to describe the movements during an episode, without implying a specific aetiology.

PRACTICE PEARL

Neither single episodes of seizures during adolescence or adult life, nor febrile convulsions in infancy, constitute a diagnosis of epilepsy.

Once a suspected episode of epilepsy has been observed, it is routine to refer the patient for an electroencephalogram (EEG) to detect whether epileptiform activity is present.[60] Page 205 Sensitivity of EEG is relatively poor at 25–56% but specificity is higher, ranging from 78–98%.[61] The absence of epileptiform activity on EEG does not rule out the diagnosis, and it is important for the clinician to take a careful history to assess symptoms.

Effects of physical activity on the management of epilepsy

Regular physical activity is recommended for individuals with epilepsy.[62] In general, people with epilepsy report better seizure control when exercising regularly.[63] Occasionally, some individuals will have more seizures with physical activity and so every case must be treated individually.[64] Individuals with epilepsy do not have higher rates of injury in sport than those without epilepsy, and sport participation does not affect serum drug levels.

In a sample of more than 200 patients with epilepsy in Norway, activity patterns were similar to those of the average population.[62] In the majority of patients, physical activity had no adverse effects, while more than a third of patients claimed that regular activity contributed to better seizure control. Physical activity also reduces the risks of anxiety/depression and improves quality of life measures in individuals with epilepsy.[65] In 10% of patients, physical activity appeared to be a seizure precipitant, applying particularly to those with symptomatic partial epilepsy (i.e. underlying structural brain lesion). The risk of sustaining serious seizure-related injuries while exercising in this population was modest.[62]

Absolute and relative contraindications to sporting activities for individuals with epilepsy are shown in Table 14.5.

Table 14.5 Absolute and relative contraindications to sporting activities in individuals with epilepsy

Absolute	Relative (with supervision)
• Rock climbing • Flying • Hang-gliding • Pistol shooting • Scuba diving • Archery • Skydiving, parachuting • Motor racing	• Swimming • Cross-country skiing • Backpacking • Cycling • Downhill skiing

Management of a seizure in the sport setting

Seizures *nearly* always terminate spontaneously; they are rarely life threatening (see note). The patient usually does not feel pain or remember the seizure. The clinician observing or supervising a

seizure should have two aims. Firstly, protect the individual from injury. Secondly, observe the seizure closely to give an accurate description to the individual's physician. Do not put a knotted sheet or spoon in the individual's mouth and do not physically restrain them. After the seizure, the individual should be managed under the same protocols as an unconscious person. If a seizure lasts longer than 5 minutes one can consider medication to control the seizure, usually in the form of buccal midazolam or, more historically, rectal diazepam. Seizures are more likely at times of stress or infection/illness, and it is important to be aware of this with athletes. This is of particular relevance at times of high training intensity, or for example when entering a new training environment or competition.

Note: Certain forms of epilepsy may involve severe seizures that last longer than 30 minutes, sometimes termed 'convulsive status epilepticus'. It is beyond the scope of this chapter to consider management of these severe forms of seizure, but the reader is referred to guidance such as that provided by the National Institute for Health and Care Excellence (2016).[66]

Overall, people with epilepsy are able to participate in sport with few limitations. Family, friends, teammates and coaches should be made aware of the epilepsy diagnosis and understand what to do in the event of a seizure. This will contribute to removing unnecessary barriers to a normal active lifestyle for those with epilepsy.

PLANNING A PHYSICAL ACTIVITY PROGRAM FOR PATIENTS WITH A NEUROLOGICAL CONDITION

As well as the recommendations for specific types of training outlined in this section, the clinician planning a physical activity program for a patient with a neurological condition needs to consider the following:

1. All conditions must first be assessed for their severity, to determine the level at which any program can be initiated. Consider using a validated outcome measure for the condition (e.g. for Parkinson's, the MDS-UPDRS©).[67]
2. Attitudes towards physical activity must be assessed and current fitness established (e.g. is the patient deconditioned or do they have low self-efficacy in normal movement?)—the use of a universal tool questionnaire designed to assess physical activity readiness can aid the clinician to detect negative beliefs around physical activity and consider appropriate interventions (e.g. further counselling or education).
3. Consider screening measures for cardiovascular or respiratory concerns, and other medical issues prior to physical testing.

CASE STUDY

Dai Greene, 400-metre hurdles—epilepsy

I don't have any memory of what happened after that— I woke up later in hospital feeling really tired and all my muscles ached. The doctor told me I'd had an epileptic seizure

Dai Greene (Fig. 14.6) is a British athlete who won European, Commonwealth and world titles in the 400-metre hurdles between 2010 and 2011.

Figure 14.6 Dai Green former world 400m hurdle champion
COURTESY OF OLLY STABLER/DAI GREENE

Diagnosis

Greene was diagnosed with epilepsy at the age of 16, suffering a seizure following a night out with friends. He was able to identify triggers which included alcohol, tiredness and poor nutritional habits. He was assessed using EEG and diagnosed with idiopathic epilepsy—an inherited form of the condition.

Management

Greene began running hurdles in university and was prescribed lamotrigine. Despite the medication there was little change in his seizure control. He ceased medication in favour of controlling his epilepsy with a combination of lifestyle changes. Greene advised the biggest variable was his sleep. Ensuring his sleep pattern was regular and sufficient (i.e. >8 hours), alongside avoiding alcohol consumption and stress allowed him to reach the pinnacle of his sport.

Conclusion

Greene provides a good example of the benefits of physical activity and appropriate lifestyle measures in chronic disease management. He is now an ambassador for Youth Epilepsy UK.

4. Each individual needs to be assessed for optimal timing of activities. With PD, timing around *on* periods, with supportive medications or with deep brain stimulation, may be beneficial. For MS, periods of relapse and remission need to be considered, and activities should be reduced as necessary to allow successful completion and prevent potential demoralisation if failure occurs.

All neurological conditions need to be assessed for the presence of autonomic symptoms, awareness, non-motor symptoms (i.e. mood and cognitive status).

5. Symptoms or mood disorders such as depression or anxiety, fatigue and cognitive impairment may lead to attention difficulties. This should be taken into account in the design of physical activity programs, with a view to compliance and supervision.
6. Consider exercise testing to gain a baseline for current ability and to monitor change. Examples of relevant tests to consider are provided in Table 14.6.

Table 14.6 Examples of exercise tests for assessing aspects of physical performance in those with neurological disease

Page 207

Ability	Exercise test
• Balance	• Functional reach test, single-leg stance, pull tests, Berg balance scale (BBS)
• Gait observation	• 10-minute walk test
• Functional mobility	• Timed up-and-go test (TUAG), chair sit-to-stand, functional independence measure (FIM)
• Strength	• Arm cull, selective weight machines, chair rise test, dynamometer
• Aerobic	• 6-minute walk test, treadmill protocols (for those with mild disease take falls risk measures • Use of RPE (rating of perceived exertion, e.g. Borg scale), symptomology recordings, fatig
• Range of motion (ROM)/flexibility	• Goniometry, sit-and-reach test

7. Malnutrition related to dysphagia, or risk of seizure brought on by poor habits, can significantly impact the ability of an individual to engage in physical activity. All participants should be screened to ensure they are adequately hydrated and have eaten appropriately.
8. Physical activity prescription for specific neurological conditions is considered in the sections on each condition, above.
9. An important aspect of any physical activity prescription is the evaluation of outcomes at various intervals during the training. Evaluation of fitness and physical function provides feedback about the effectiveness of the training program and allows for further individualisation, as well as continued progression and motivation.

Physical activity prescription for neurological conditions

The main goals of physical activity for individuals with neurological conditions are to delay disability, prevent secondary complications, improve quality of life and slow disease progression. The benefits for patients with a neurological condition can be viewed from a general health perspective, given the positive health influences of physical activity discussed throughout this text. The positive effects on the brain and central nervous system, including some of the mediating effects of physical activity, are summarised in Figure 14.7. Many neurological conditions tend to develop in elderly people, who also have risks of various age-related morbidities that are known to benefit from being active, such as cardiovascular disease, diabetes mellitus, hypertension, hyperlipidaemia and osteoporosis.

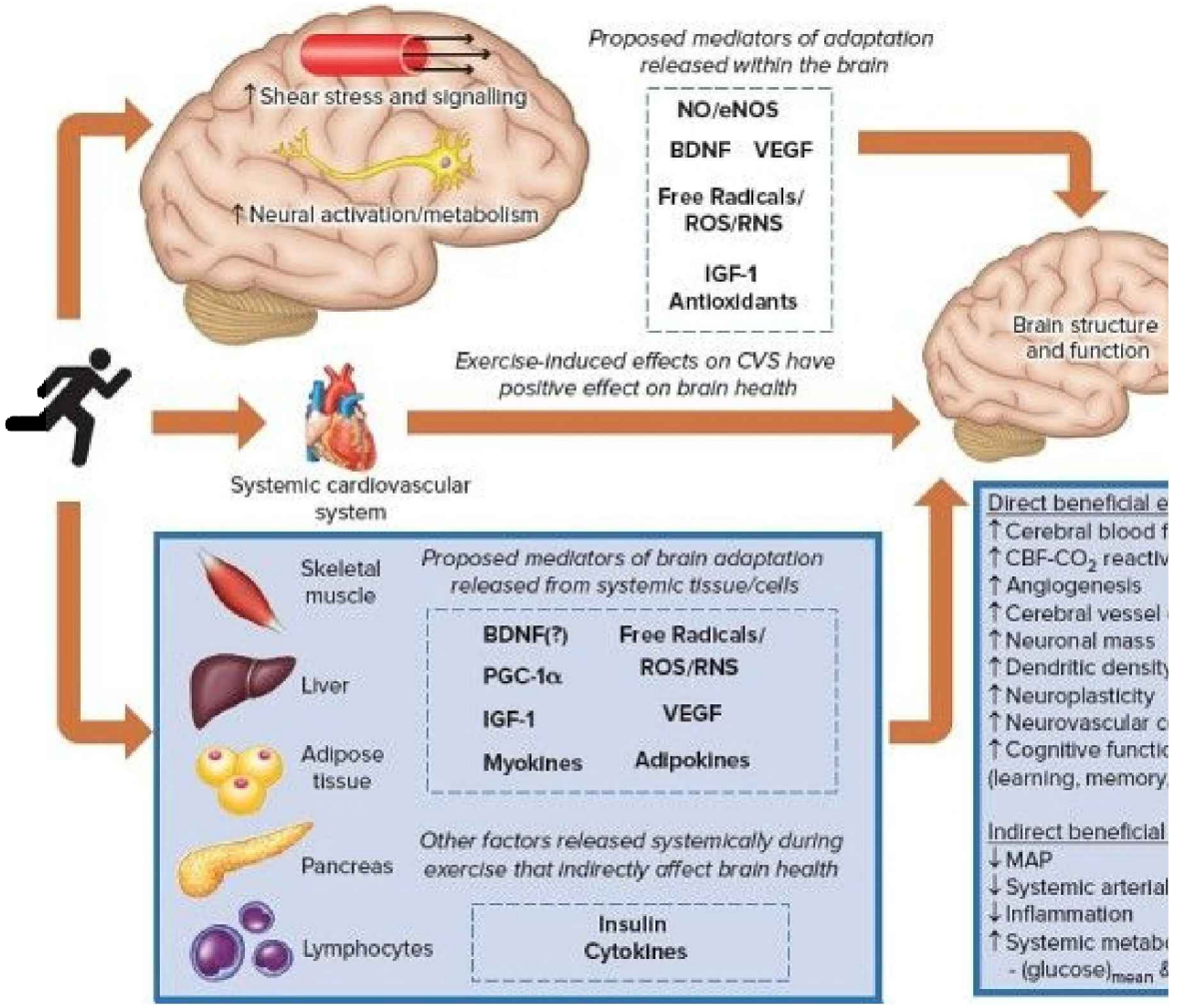


Figure 14.7 Proposed mechanisms by which physical activity may alter brain structure and function as well as lower the risk of brain-related dysfunction and disease via alterations in systemic function

BDNF, brain-derived neurotrophic factor; CBF, cerebral blood flow; CO_2, carbon dioxide; eNOS, endothelial nitric oxide synthase; IGF-1, insulin-like growth factor-1; MAP, mean arterial blood pressure; NO, nitric oxide; PGC-1α, peroxisome proliferator-activated receptor-γ coactivator; ROS, reactive oxygen species; RNS, reactive nitrogen species; VEGF, vascular endothelial growth factor

ADAPTED FROM LUCAS ET AL., JOURNAL OF CEREBRAL BLOOD FLOW & METABOLISM (35(6)) HIGH INTENSITY INTERVAL EXERVISE AND CEREBROVASCULAR HEALTH: CURIOSITY, CAUSE, AND CONSEQUENCE. PP.902-11 COPYRIGHT © 2015 REPRINTED BY PERMISSION OF SAGE PUBLICATIONS, INC.[68]

PRACTICE PEARL

The risk of mood disorders among those with neurological conditions is high and therefore it is important to address barriers to engagement in physical activity. These include, the patient's perception of the benefits, the belief that there is a lack of time, the fear of falls, low self-efficacy and apathy.

The majority of neurological conditions remain chronic and often progressive disorders. The ability of physical activity to support the management of these conditions should therefore necessitate an early diagnosis and prescription of an appropriate physical activity program. This prescription should be supplied when the individual is first diagnosed and continually reviewed on a regular, long-term basis.

Research into the ideal frequency and intensity of the different types of physical activity is ongoing, and the following recommendations should be seen as a guide rather than a definitive list. Most neurological rehabilitation programs need to consider the following types of activity. An example physical activity program for a PD patient is given in Table 14.7.

Table 14.7 Example physical activity program for a PD patient

	Aerobic	Resistance	Flexibility	Neuromuscular (proprioception/balance)
Type	Rhythmical activities using large muscle groups (e.g. cycling, walking, dancing, swimming)	Use of resistance machine weights, bands or bodyweight for strength training. For safety avoid free weights.	For all major muscle groups, particularly upper trunk/spine	Exercises involving motor skills, proprioceptive exercise training, tai chi, waltz, tango
Time	30–60 min (continuous or accumulated)	6–20 reps. 1 set may be effective, but 2–4 sets are required to increase strength	10–30 secs (30–60 secs may be better in older patients). 2–4 reps of each exercise	10–15 min/day, or for those at risk of falls 30–60 min accumulated over a week.
Intensity	Moderate or the equivalent of 40–60% of HRR or RPE-12 on the Borg Scale	Beginners–40–50% of 1RM. Novice/Intermediate–60–80% of 1RM	Hold to point of slight discomfort (scored 2–3/10 on an analogue scale)	Duration or frequency of participation can be increased
Frequency	3–5 days/week	2–3 days/week	2–3 days/week, but daily is optimal	2–3 days/week

Note: HRR – Heart rate reserve, RPE—Rate of perceived exertion, 1RM – 1 Repetition max.

Aerobic training

Lower-body exercises, using treadmills and cycle ergometers, have consistently resulted in improvements in cardiorespiratory fitness and maximal oxygen uptake. Weight-bearing cardiorespiratory exercise, such as walking, improves physical function, balance, coordination, dexterity and gait, particularly when performed at exercise intensities greater than usual self-selected walking pace.[69, 70] In an individual who has impaired balance, use of a cycle ergometer may prove a useful, safe and effective alternative aerobic exercise modality. If walking is used, assistive devices such as suspension harness equipment can be used to reduce the chances of falling

during treadmill walking.

Resistance training

Although not as widely studied as cardiorespiratory exercise, resistance training also demonstrates a variety of benefits, such as muscular fitness, decreased falls and gait speed.[71, 72] Currently, low intensity and high repetition is advised for sedentary older individuals. Emphasis on extensor muscles of the trunk and hip is important to prevent abnormal posture. A particular focus on the major muscles of the lower extremity may be beneficial to those at risk of falls.

Flexibility training

Flexibility training, including static stretching, may support the management of joint contractures, especially in those with spasticity.[16] Reduced spinal flexibility is a significant issue in PD, but early intervention may significantly reduce the progression of truncal stiffness and neck rigidity, which results in the characteristic stooped posture. Stretching guidelines recommend holding at the point of discomfort for an average of 30 seconds; however, this may need to be significantly increased in individuals with increased spasticity.

Neuromuscular training

Neuromuscular training comprises motor skills such as balance, coordination, gait and agility. Gait training is an important part of therapy for many patients with neurological conditions and may involve forced treadmill speeds and/or use of visual or auditory cues. Falls prevention education and activities are critical. It may also be necessary to prescribe assistive devices to support this form of training. Functional exercises such as sit-to-stand, step-ups, turning over and getting out of bed are important to improve neuromuscular control of balance and the maintenance of activities of daily living. Tai chi and more advanced dynamic activities such as kickboxing improve balance and coordination in those with MS.[73]

PRACTICE PEARL

Many neurological patients will suffer cognitive decline during the course of their illness. It is important to explain how to use all equipment, repeat instructions and provide a written physical activity prescription for all patients.

Goal-based motor training

Neurorehabilitation and physical activity research in PD has recently been focused on the application of physical activity that incorporates goal-based motor training, for the improvement or recovery of impaired or lost motor function.

Goal-based activity is the practice of certain activities that lead to improved performance. Treadmill walking has been useful in gait retraining.[74] Verbal feedback, or cues that draw attention to the motor task practice, may ease cognitive engagement to help consolidation of the learned behaviour that leads

to strengthening or modification of existing motor circuits. Similarly, with balance, tai chi focuses on dynamic postural control via activities that involve weight shifting. Individuals also become cognitively engaged while practising the control of their centre of gravity during maximal movements.[75] The addition of aerobic exercise and the benefits this confers in cerebral blood flow and trophic factor signalling are also postulated to lead to the potential for greater improvements in both rehabilitation and physical activity performance.[37]

The benefits of this approach may also be extrapolated and applied to stroke rehabilitation, where task repetition or motor relearning has long been applied to enhance the neuroplastic effects of rehabilitation.

SUMMARY

Physical activity has the potential to prevent and modify long-term symptoms and improve physical functioning and quality of life in a range of neurological conditions. For many of these conditions, appropriate activity management may convey a neuroprotective benefit. All of the neurological conditions discussed above should be managed with an appropriate physical activity prescription. This may be in the form of structured sports participation or may involve other forms of physical activity such as social prescriptions (e.g. 'The Green Prescription', discussed in Chapter 4).

The prevalence of neurological disease is increasing, and it is therefore essential that clinicians are able to support physical activity in neurological patients under their care.[1] Clinicians require a sound understanding of the principles of physical activity prescription and their application to physical activity interventions for those with a variety of neurological diseases.

REFERENCES

1. Global, regional, and national burden of neurological disorders during 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet Neurol* 2017; 16(11): 877–97.
2. D'Isabella NT, Shkredova DA, Richardson JA et al. Effects of exercise on cardiovascular risk factors following stroke or transient ischemic attack: a systematic review and meta-analysis. *Clin Rehabil* 2017; 31(12): 1561–72.
3. World Health Organization (WHO). WHO factsheets: The top ten causes of death. Geneva, 2007. http://www.who.int/mediacentre/factsheets/fs310.pdf.
4. Lee CD, Folsom AR, Blair SN. Physical activity and stroke risk: a meta-analysis. *Stroke* 2003; 34(10): 2475–81.
5. Wendel-Vos GCW, Schuit AJ, Feskens EJM et al. Physical activity and stroke: a meta-analysis of observational data. *Int J Epidemiol* 2004; 33(4): 787–98.
6. Mojadidi MK, Zaman MO, Elgendy IY et al. Cryptogenic stroke and patent foramen ovale. *J Am Coll Cardiol* 2018; 71(9): 1035–43.
7. Ntaios G, Papavasileiou V, Sagris D et al. Closure of patent foramen ovale versus medical therapy in patients with cryptogenic stroke or transient ischemic attack:

updated systematic review and meta-analysis. *Stroke* 2018; 49(2): 412–18.

8. Ahmad Y, Howard JP, Arnold A et al. Patent foramen ovale closure vs medical therapy for cryptogenic stroke: a meta-analysis of randomized controlled trials. *Eur Heart J* 2018: ehy121-ehy.
9. Charalambous CC, Helm EE, Lau KA et al. The feasibility of an acute high-intensity exercise bout to promote locomotor learning after stroke. *Top Stroke Rehabil* 2018; 25(2): 83–9.
10. Saunders DH, Greig CA, Young A et al. Physical fitness training for stroke patients. *Cochrane Database Syst Rev* 2004 (1): CD003316.
11. Pang MYC, Eng JJ, Dawson AS et al. The use of aerobic exercise training in improving aerobic capacity in individuals with stroke: a meta-analysis. *Clin Rehabil* 2006; 20(2): 97–111.
12. Gordon NF, Gulanick M, Costa F et al. Physical activity and exercise recommendations for stroke survivors: an American Heart Association scientific statement from the Council on Clinical Cardiology, Subcommittee on Exercise, Cardiac Rehabilitation, and Prevention; the Council on Cardiovascular Nursing; the Council on Nutrition, Physical Activity, and Metabolism; and the Stroke Council. *Stroke* 2004; 35(5): 1230–40.
13. Duncan PW, Zorowitz R, Bates B et al. Management of adult stroke rehabilitation care: a clinical practice guideline. *Stroke* 2005; 36(9): e100–43.
14. Gambassi BB, Coelho-Junior HJ, Schwingel PA et al. Resistance training and stroke: a critical analysis of different training programs. *Stroke Res and Treat* 2017; 2017: 11.
15. Belfiore P, Miele A, Galle F et al. Adapted physical activity and stroke: a systematic review. *J Sports Med Phys Fitness* 2017 Oct 24. doi: 10.23736/S0022-4707.17.07749-0.
16. Han P, Zhang W, Kang L et al. Clinical evidence of exercise benefits for stroke. *Adv Exp Med Biol* 2017; 1000: 131–51.
17. English C, Hillier SL, Lynch EA. Circuit class therapy for improving mobility after stroke. *Cochrane Database Syst Rev* 2017 (6): CD007513.
18. Dorsey ER, Bloem BR. The Parkinson pandemic—a call to action. *JAMA Neurol* 2018; 75(1): 9–10.
19. Kalia LV, Lang AE. Parkinson's disease. *Lancet* 2015; 386(9996): 896–912.
20. van Nimwegen M, Speelman AD, Hofman-van Rossum EJ et al. Physical inactivity in Parkinson's disease. *J Neurol* 2011; 258(12): 2214–21.
21. Pickering RM, Grimbergen YA, Rigney U et al. A meta-analysis of six prospective studies of falling in Parkinson's disease. *Mov Disord* 2007; 22(13): 1892–900.
22. Postuma RB, Berg D, Stern M et al. MDS clinical diagnostic criteria for Parkinson's disease. *Mov Disord* 2015; 30(12): 1591–601.
23. Chen H, Zhang SM, Schwarzschild MA et al. Physical activity and the risk of Parkinson disease. *Neurology* 2005; 64(4): 664–9.

24. Thacker EL, Chen H, Patel AV et al. Recreational physical activity and risk of Parkinson's disease. *Mov Disord* 2008; 23(1): 69–74.
25. Xu Q, Park Y, Huang X et al. Physical activities and future risk of Parkinson disease. *Neurology* 2010; 75(4): 341–8.
26. Stephenson R, Siderowf A, Stern MB. Premotor Parkinson's disease: clinical features and detection strategies. *Mov Disord* 2009; 24 Suppl 2: S665–70.
27. Jakowec MW, Wang Z, Holschneider D et al. Engaging cognitive circuits to promote motor recovery in degenerative disorders. Exercise as a learning modality. *J Hum Kinet* 2016; 52: 35–51.
28. Petzinger GM, Fisher BE, McEwen S et al. Exercise-enhanced neuroplasticity targeting motor and cognitive circuitry in Parkinson's disease. *Lancet Neurol* 2013; 12(7): 716–26.
29. Kwok JY, Choi KC, Chan HY. Effects of mind–body exercises on the physiological and psychosocial well-being of individuals with Parkinson's disease: a systematic review and meta-analysis. *Complement Ther Med* 2016; 29: 121–31.
30. Mak MK, Wong-Yu IS, Shen X et al. Long-term effects of exercise and physical therapy in people with Parkinson disease. *Nat Rev Neurol* 2017; 13(11): 689–703.
31. Wu PL, Lee M, Huang TT. Effectiveness of physical activity on patients with depression and Parkinson's disease: a systematic review. *PLoS ONE* 2017; 12(7): e0181515.
32. Murray DK, Sacheli MA, Eng JJ et al. The effects of exercise on cognition in Parkinson's disease: a systematic review. *Transl Neurodegener* 2014; 3(1): 5.
33. Barha CK, Galea LA, Nagamatsu LS et al. Personalising exercise recommendations for brain health: considerations and future directions. *Br J Sports Med* 2017; 51(8): 636–9.
34. Reuter I, Mehnert S, Leone P et al. Effects of a flexibility and relaxation programme, walking, and Nordic walking on Parkinson's disease. *J Aging Res* 2011; 2011: 232473.
35. Cugusi L, Solla P, Serpe R et al. Effects of a Nordic walking program on motor and non-motor symptoms, functional performance and body composition in patients with Parkinson's disease. *NeuroRehabilitation* 2015; 37(2): 245–54.
36. Shulman LM, Katzel LI, Ivey FM et al. Randomized clinical trial of 3 types of physical exercise for patients with Parkinson disease. *JAMA Neurol* 2013; 70(2): 183–90.
37. Chung CL, Thilarajah S, Tan D. Effectiveness of resistance training on muscle strength and physical function in people with Parkinson's disease: a systematic review and meta-analysis. *Clin Rehabil* 2016; 30(1): 11–23.
38. Ni M, Signorile JF, Mooney K et al. Comparative effect of power training and high-speed yoga on motor function in older patients with Parkinson disease. *Arch Phys Med Rehabil* 2016; 97(3): 345–54.e15.
39. Gallo PM, Ewing Garber C. Parkinson's disease: a comprehensive approach to

exercise prescription for the health fitness professional. *ACSM's Health Fit J* 2011; 15(4): 8–17.

40. Weiss HD, Marsh L. Impulse control disorders and compulsive behaviors associated with dopaminergic therapies in Parkinson disease. *Neurol Clin Pract* 2012; 2(4): 267–74.
41. Allen NE, Schwarzel AK, Canning CG. Recurrent falls in Parkinson's disease: a systematic review. *Parkinsons Dis* 2013; 2013: 906274.
42. Mactier K, Lord S, Godfrey A et al. The relationship between real world ambulatory activity and falls in incident Parkinson's disease: influence of classification scheme. *Parkinsonism Relat Disord* 2015; 21(3): 236–42.
43. Poewe W. Treatments for Parkinson disease—past achievements and current clinical needs. *Neurology* 2009; 72(7 Suppl): S65–73.
44. Bayulkem K, Lopez G. Nonmotor fluctuations in Parkinson's disease: clinical spectrum and classification. *J Neurol Sci* 2010; 289(1–2): 89–92.
45. Lopane G, Contin M, Scaglione C et al. The effect of a clinically practical exercise on levodopa bioavailability and motor response in patients with Parkinson disease. *Clin Neuropharmacol* 2010; 33(5): 254–6.
46. Reuter I, Harder S, Engelhardt M et al. The effect of exercise on pharmacokinetics and pharmacodynamics of levodopa. *Mov Disord* 2000; 15(5): 862–8.
47. Nutt JG. Motor fluctuations and dyskinesia in Parkinson's disease. *Parkinsonism Relat Disord* 2001; 8(2): 101–8.
48. Friedman JH. Fatigue in Parkinson's disease patients. *Curr Treat Options Neurol* 2009; 11(3): 186–90.
49. Swick TJ. Parkinson's disease and sleep/wake disturbances. *Parkinsons Dis* 2012; 2012: 205471.
50. Brian Grant Foundation. Exercise for Parkinson's. 2018. https://briangrant.org/exercise/.
51. Sharif K, Watad A, Bragazzi NL et al. Physical activity and autoimmune diseases: get moving and manage the disease. *Autoimmun Rev* 2018; 17(1): 53–72.
52. Motl RW, Sandroff BM. Exercise as a countermeasure to declining central nervous system function in multiple sclerosis. *Clin Ther* 2018; 40(1): 16–25.
53. White LJ, Dressendorfer RH. Exercise and multiple sclerosis. *Sports Med* 2004; 34(15): 1077–100.
54. Rampello A, Franceschini M, Piepoli M et al. Effect of aerobic training on walking capacity and maximal exercise tolerance in patients with multiple sclerosis: a randomized crossover controlled study. *Phys Ther* 2007; 87(5): 545–55.
55. Davis SL, Frohman TC, Crandall CG et al. Modeling Uhthoff's phenomenon in MS patients with internuclear ophthalmoparesis. *Neurology* 2008; 70(13 Pt 2): 1098–106.
56. Reynolds ER, Ashbaugh AD, Hockenberry BJ et al. Multiple sclerosis and exercise: a

literature review. *Curr Sports Med Rep* 2018; 17(1): 31–5.

57. Edwards T, Pilutti LA. The effect of exercise training in adults with multiple sclerosis with severe mobility disability: a systematic review and future research directions. *Mult Scler Relat Disord* 2017; 16: 31–9.
58. Fisher RS, Acevedo C, Arzimanoglou A. A practical clinical definition of epilepsy. *Epilepsia*, 2014. 55(4):475–482.
59. WHO. Epilepsy—factsheet. 2018. http://www.who.int/mediacentre/factsheets/fs999/en/.
60. Cervenka MC, Kaplan PW. Epilepsy. *Semin Neurol* 2016; 36(4): 342–9.
61. Smith SJ. EEG in the diagnosis, classification, and management of patients with epilepsy. *J Neurol Neurosurg Psychiatry* 2005; 76 Suppl 2: ii2–7.
62. Nakken KO. Physical exercise in outpatients with epilepsy. *Epilepsia* 1999; 40: 643–51.
63. Arida RM, Cavalheiro EA, da Silva AC et al. Physical activity and epilepsy: proven and predicted benefits. *Sports Med* 2008; 38(7): 607–15.
64. Howard GM, Radloff M, Sevier TL. Epilepsy and sports participation. *Curr Sports Med Rep* 2004; 3(1): 15–19.
65. Hafele CA, Freitas MP, da Silva MC et al. Are physical activity levels associated with better health outcomes in people with epilepsy? *Epilepsy Behav* 2017; 72: 28–34.
66. National Institute for Health and Care Excellence (NICE). Epilepsies: diagnosis and management. Clinical guideline [CG137]. January 2012, updated April 2018. https://www.nice.org.uk/guidance/cg137.
67. International Parkinson and Movement Disorder Society. Unified Parkinson's Disease Rating Scale (2008) Located at: https://www.movementdisorders.org/MDS-Files1/PDFs/Rating-Scales/MDS-UPDRS_English_FINAL.pdf.
68. Lucas SJE, Cotter JD, Brassard P et al. High-intensity interval exercise and cerebrovascular health: curiosity, cause, and consequence. *J Cereb Blood Flow Metab* 2015; 35(6): 902–11.
69. Fisher BE, Wu AD, Salem GJ et al. The effect of exercise training in improving motor performance and corticomotor excitability in people with early Parkinson's disease. *Arch Phys Med Rehabil* 2008; 89(7): 1221–9.
70. Herman T, Giladi N, Hausdorff JM. Treadmill training for the treatment of gait disturbances in people with Parkinson's disease: a mini-review. *J Neural Transm (Vienna)* 2009; 116(3): 307–18.
71. Falvo MJ, Schilling BK, Earhart GM. Parkinson's disease and resistive exercise: rationale, review, and recommendations. *Mov Disord* 2008; 23(1): 1–11.
72. Erickson KI, Raji CA, Lopez OL et al. Physical activity predicts gray matter volume in late adulthood: the Cardiovascular Health Study. *Neurology* 2010; 75(16): 1415–22.
73. Charron S, McKay KA, Tremlett H. Physical activity and disability outcomes in multiple sclerosis: a systematic review (2011–2016). *Mult Scler Relat Disord* 2018; 20:

169–77.

74. Herman T, Giladi N, Gruendlinger L et al. Six weeks of intensive treadmill training improves gait and quality of life in patients with Parkinson's disease: a pilot study. *Arch Phys Med Rehabil* 2007; 88(9): 1154–8.
75. Li F, Harmer P, Fitzgerald K et al. Tai chi and postural stability in patients with Parkinson's disease. *N Engl J Med* 2012; 366(6): 511–19.
76. https://en.wikipedia.org/wiki/Kris_Letang https://www.thestar.com/life/2014/02/07/why_did_26yearold_pittsburgh_penguin_kris_letang_have_a_stroke.html
77. https://www.theglobeandmail.com/sports/hockey/penguins-announce-letang-suffered-stroke/article16748171/
78. https://thehockeynews.com/news/article/pittsburghs-kris-letang-discusses-details-about-his-stroke
79. https://www.cbc.ca/sports/hockey/nhl/kris-letang-speaks-for-1st-time-after-stroke-1.2554317
80. https://en.wikipedia.org/wiki/Bruce_Tasker
81. https://www.bbc.com/sport/winter-olympics/42958489
82. https://www.theguardian.com/sport/2018/jan/11/british-bobsledder-bruce-tasker-winter-olympics-stroke
83. https://www.independent.co.uk/sport/olympics/winter-olympics/bruce-tasker-winter-olympics-2018-2014-medal-bobsleigh-a8155556.html
84. https://briangrant.org/https://www.si.com/nba/2018/05/02/brian-grant-parkinsons-disease-trail-blazers-heat-michael-j-fox-pat-riley
85. https://en.wikipedia.org/wiki/Brian_Grant 86. https://parkinsonslife.eu/ex-nba-player-brian-grant-opens-up-about-his-parkinsons-disease/
86. https://parkinsonslife.eu/ex-nba-player-brian-grant-opens-up-about-his-parkinsons-disease/
87. https://www.theplayerstribune.com/en-us/articles/brian-grant-lakers-parkinsons

Chapter 15

Rheumatological conditions

with CHRISTA JANSE VAN RENSBURG

I would go to the doctor and start crying. I couldn't help it. I just want a chance to play on the same field as other people, I want to feel normal, but as frightening as the diagnosis was, it was also a relief.

Venus Williams, seven-time Grand Slam winner, on being diagnosed with Sjögren's syndrome

Musculoskeletal complaints are common in individuals engaging in physical activity. However, not every clinical condition that presents to the sports clinic is due to a mechanical sports-related diagnosis. Athletes may have other systemic pathologies of a prolonged inflammatory nature that present as a mechanical injury. These chronic progressive inflammatory diseases may lead to joint pathology and even joint destruction in the most severe cases.

The clinician must be able to differentiate between a sports injury and possible rheumatological disease.[1–3] Prompt and effective treatment can modify disease progression, allowing the athlete to continue with their regular exercise program. Despite being diagnosed with Sjögren's syndrome in 2011, Venus Williams was able to maintain her elite level of competition with effective therapy, returning to a world top-five ranking and reaching further tennis Grand Slam finals in 2017.

Early intervention is even more important in the general population, where reduced medical support could result in greater risk of joint damage and disability. As always, a thorough history and clinical examination are essential.

The clinical key to diagnosing a rheumatological condition is to recognise the patient's clinical features that do not fit the typical pattern of a common sports-related condition and come to a differential diagnosis. Special investigations including relevant blood tests and imaging will help confirm the diagnosis.

In this chapter we discuss the clinical approach to diagnosing a patient with a musculoskeletal complaint that is not an acute sports injury. The focus is on rheumatological conditions.[1, 4]

AGE

Arthritis is often considered a condition of old age. This, however, does not hold true, as children are also affected. In fact, juvenile arthritis is well recognised and is an umbrella term used to describe all the inflammatory and autoimmune diseases that can develop in children younger than 16 years old.[2, 5]

Juvenile arthritis can manifest in many ways. One or many joints can be involved, and a complete history and physical examination should cover symptoms and signs like fever, skin rash and eye problems. Uveitis is an important complication affecting approximately one in every three individuals with autoimmune disease.[6]

There are five types of juvenile arthritis:[7, 8]

- systemic arthritis (Fig. 15.1a)
- oligoarthritis (pauci-articular disease) (Fig. 15.1b)
- polyarthritis (Fig. 15.1c, d)
- psoriatic arthritis
- enthesitis-related arthritis.

(a)

(b)

(c)

(d)

Figure 15.1 Various manifestations of juvenile idiopathic arthritis (JIA) (a) Systemic arthritis—Example of growth retardation in twins. (b) Oligoarthritis—a smaller number of joints are affected (c) Polyarthritis involves five or more joints (d) Polyarthritis may be experienced at any age and is not sex-specific
IMAGES COURTESY OF PROF. CHRISTA JANSE VAN RENSBURG

Adult onset arthritis can develop at almost any age. Ankylosing spondylitis (AS) is most common in young people in their twenties, while the average onset of rheumatoid arthritis (RA) is between 30 and 60 years of age. Although osteoarthritis (OA) usually presents in middle age, previous injury to a joint can make that joint more susceptible to early-onset OA.[5, 9]

SEX: MARS VERSUS VENUS

As in life, the different types of rheumatological diseases do not equally affect men and women.[5, 9, 10] Ankylosing spondylitis has a male to female ratio of 3:1, and gout can present in males at any

age, while a red flag raises if a premenopausal female presents with 'gout'. Rheumatoid arthritis has a definite predisposition in female patients. In general, females are more predisposed to arthritic disease (Table 15.1).[2, 11]

Table 15.1 Sex ratio in some of the most common rheumatological diseases[11–13]

Disease	Female/male ratio
Ankylosing spondylitis	1:3
Osteoarthritis—knee	1.5–4:1
Psoriatic arthritis	1:1
Rheumatoid arthritis	3:1
Sjögren's syndrome	9:1
Systemic lupus erythematosus	7:1
Systemic sclerosis	3:1

ANATOMICAL SITE

All anatomical structures around a joint are involved in arthritic disease; however, this is different to the involvement of a joint secondary to injury. The history and clinical picture help to distinguish between swelling and pain due to injury or to arthritis.[1]

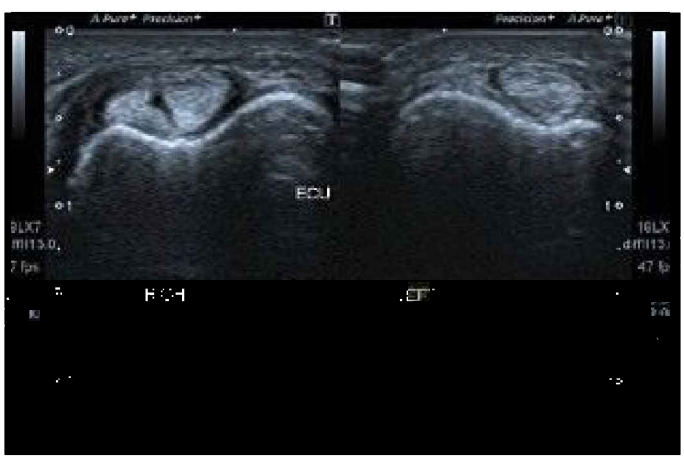
Although the joint (synovium and cartilage) is the focus, enthesopathies are quite common in rheumatic disease, especially in the spondyloarthropathy group.[12] Anatomical structures that need to form part of the differential diagnosis are discussed in Table 15.2.[14] Tissue pathology is also addressed in Chapter 4 of *Clinical Sports Medicine Volume 1: Injuries.*

Table 15.2 Anatomical structures involved in diagnoses

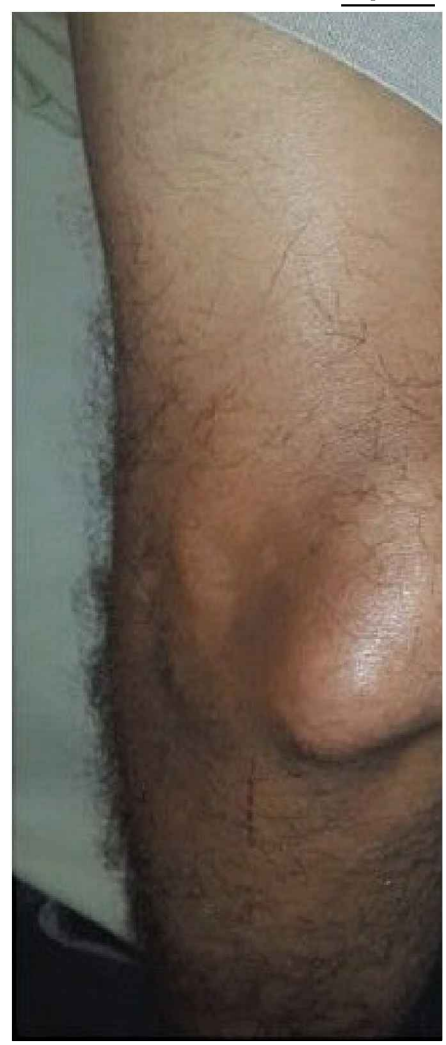
Anatomical structure	Diagnosis
Joint	Arthritis (inflammatory, infective, degenerative) Synovial cysts (Fig. 15.2a) Dislocation Subluxation Articular cartilage—osteochondritis, chondromalacia
Bone	Osteitis Apophysitis Periostitis Stress reactions Fracture
Muscle	Strain Tear Compartment syndrome
Ligament	Sprain Tear
Tendon	Tendinosis Tenosynovitis (Fig. 15.2b) Paratenonitis

	Tear
Bursa	Bursitis (Fig. 15.2c)
Other soft tissue	
– Skin	Nodules Rash Nail changes
– Nerve	Entrapment Neuropathy
Referred pain	Neural Vascular

(a)



(b)



(c)

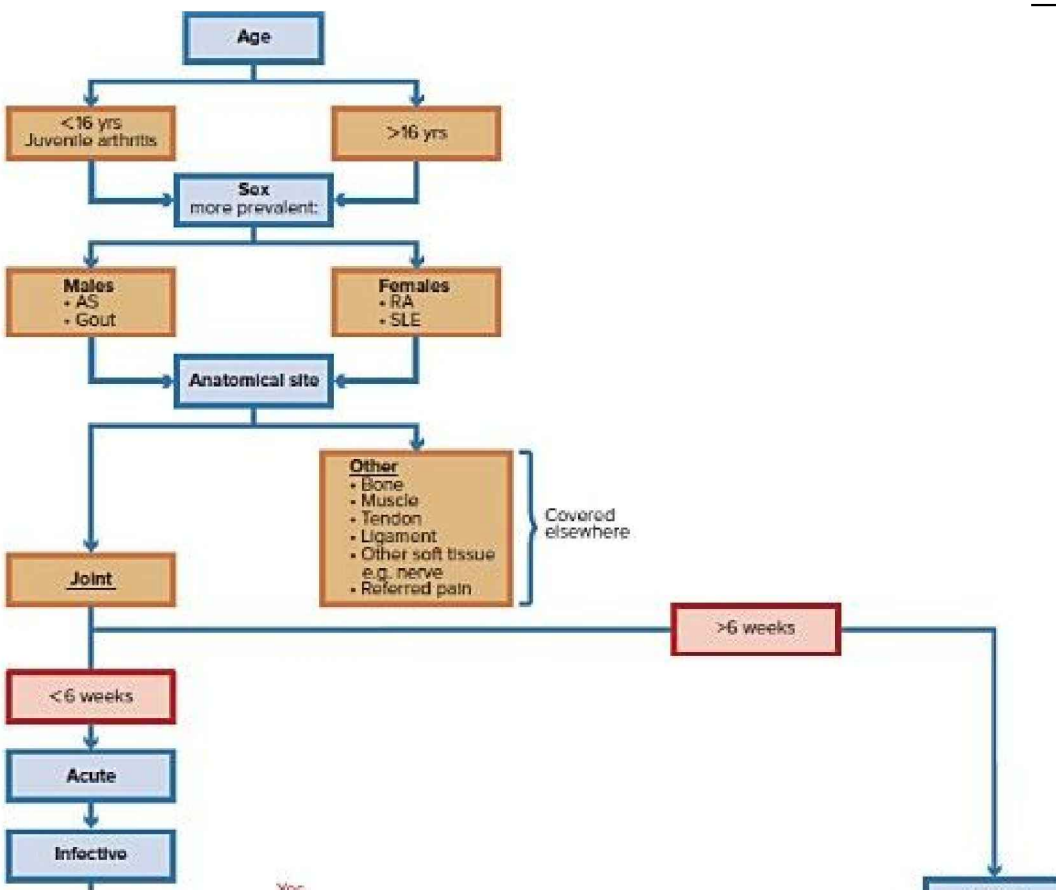
Figure 15.2 (a) Two very prominent synovial cysts above and below the knee joint line—smaller cysts are also likely to complement these large ones (b) Ultrasound showing tenosynovitis of the extensor carpi ulnaris tendon (right side) (c) The olecranon bursa is one of the more commonly affected bursae
IMAGES COURTESY OF PROF. CHRISTA JANSE VAN RENSBURG

PRACTICE PEARL

Consider the possibility of rheumatic disease where enthesopathy is part of the presenting complaint.

CLINICAL HISTORY

A complete subjective history and thorough physical examination are the cornerstones to diagnosis. Following a systematic approach, as presented in Figure 15.3, helps to cover all bases. The clinician should also have a high index of suspicion for inflammatory disorders if there is no history of trauma reported.



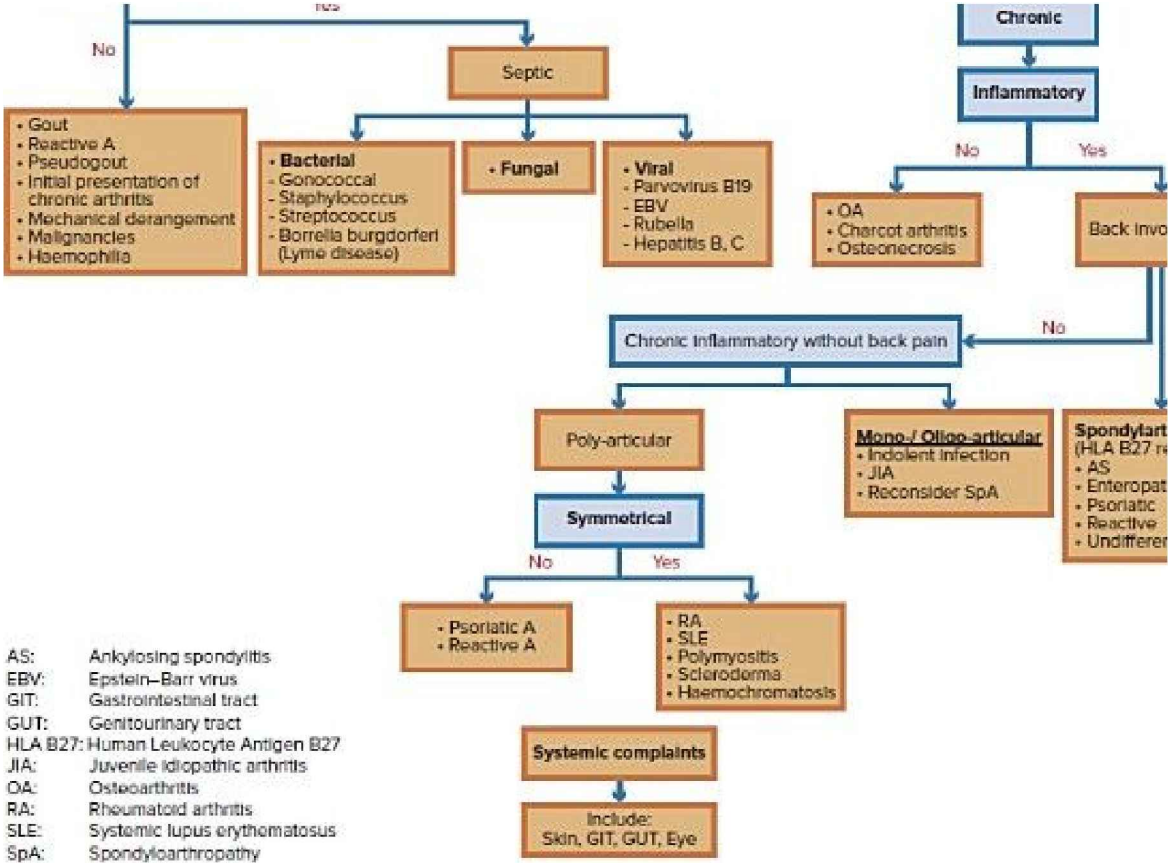


Figure 15.3 Algorithm for diagnosing a patient with a musculoskeletal complaint other than a sports injury
ADAPTED FROM FAUCI AS ET AL, HARRISON'S PRINCIPLES OF INTERNAL MEDICINE, 17TH EDITION, THE MCGRAW-HILL COMPANIES, INC.

PHYSICAL EXAMINATION

The physical examination does not only focus on the affected joint(s) but needs to include all systems, as extra-articular manifestations are quite a common phenomenon in arthritic disease (Table 15.3).

Features that suggest an inflammatory disorder[15]

- Insidious onset
- Prolonged stiffness after rest
- Pain worse at night
- Improvement with moderate activity
- Constitutional features (e.g. fever, malaise, weight loss)

- Elevated inflammatory blood markers (ESR, CRP)
- Good response to NSAIDs

CRP: C-reactive protein
ESR: Erythrocyte sedimentation rate
NSAIDs: Non-steroidal anti-inflammatory drugs

Important questions to cover in the rheumatological history

The history should guide the clinician to follow a systematic approach during the physical examination.

- Any history of trauma or overuse?
- Which joint or joints are affected?
- What is the timeline (acute vs chronic)?
- Is this the first incident or is it a recurring problem?
- Is there any inflammatory component?
- Was there any exposure to infective agents?
- Any treatment (non-pharmacological and/or pharmacological) used for the current problem?
- Is there any back involvement?
- Are there any systemic features? (refer Table 15.3)
  - fever
  - weight changes
  - skin involvement
  - eye involvement
- Are there any other extra-articular manifestations?

Table 15.3 Joint and extra-articular manifestations of rheumatological disease[16–20]

System	Sign	Disease
Musculoskeletal system	Small hand (MCP, PIP) and foot (MTP) joints	RA, psoriatic arthritis, pseudogout
	Hand (DIP, CMC joints)	OA
	Large (lower limb) joint synovitis	ReA, AS, psoriatic arthritis, EnA
	Restricted lumbar range of motion/sacroiliac tenderness	AS, ReA, psoriatic arthritis, EnA
	Enthesitis (Fig. 15.4a)	AS, ReA, psoriatic arthritis, EnA
	Tenosynovitis	RA, psoriatic arthritis, gout
General	Fever	Septic arthritis, acute gout, SLE
	Lymphadenopathy	Septic arthritis, malignant bone/soft tissue tumour, SLE

	Weight change	All inflammatory disorders
	Fatigue	All inflammatory disorders
Skin/mucous membranes	Psoriatic plaques (Fig. 15.4b, c), nail dystrophy (Fig. 15.4d)	Psoriatic arthritis
	Erythema nodosum (Fig. 15.4e)	Acute sarcoidosis
	Subcutaneous–Tophi –Nodules	Gout RA
	Nail fold infarcts, splinter haemorrhages	RA (vasculitis), SLE
	Circinate balanitis, keratoderma blennorrhagica (Fig. 15.4f)	ReA
	Pyoderma gangrenosum	EnA
	Erythema chronicum migrans	Lyme disease
	Malar (butterfly) rash	SLE
Eyes	Conjunctivitis	ReA
	Uveitis	AS, psoriatic arthritis, EnA, juvenile arthritis, SLE
	Dry eyes (and mouth)	Sjögren's syndrome (often associated with RA, SLE)
CV	Atherosclerosis (ischaemic heart disease)	All inflammatory diseases
	Pericarditis	RA, SLE, overlap syndrome
	Myocarditis	RA, SLE, overlap syndrome
	Endocarditis	RA, SLE, overlap syndrome
	Conduction disorders	SpA, SLE, overlap syndrome
Pulmonary	Pleural effusion	RA, SLE, overlap syndrome
	Nodules	RA
	Interstitial fibrosis	RA, overlap syndrome
GIT	Gastritis/PU	Mostly iatrogenic
	IBD (Crohn's/UC)	SpA
Renal	Glomerulonephritis	Mostly iatrogenic, SLE, overlap syndrome
	Interstitial renal disease	Mostly iatrogenic, SLE, overlap syndrome
Neurological	Carpal tunnel syndrome	RA, OA
	Peripheral neuropathy	RA (vasculitis), overlap syndrome
	Autonomic nervous system impairment	RA, SLE, Sjögren's syndrome, FM, SpA
	Myelopathy	RA, overlap syndrome
Haematological	Anaemia Microcytic Normocytic Macrocytic	 Iron deficiency, chronic disease Chronic disease Thyroid disorders, liver pathology, vitamin B_{12}/folate deficiency
	Neutropenia	RA, SLE, overlap syndrome
	Thrombocytopenia	RA, SLE, overlap syndrome, APS
	Thrombocytosis	RA, overlap syndrome

APS: Antiphospholipid syndrome
AS: Ankylosing spondylitis
CMC: Carpometacarpal
CV: Cardiovascular
DIP: Distal interphalangeal
EnA: Enteropathic arthritis

FM:	Fibromyalgia
GIT:	Gastrointestinal tract
IBD:	Inflammatory bowel disease
MCP:	Metacarpophalangeal
MTP:	Metatarsophalangeal
OA	Osteoarthritis
PIP:	Proximal interphalangeal
PU:	Peptic ulcer
RA:	Rheumatoid arthritis
ReA:	Reactive arthritis
SLE:	Systemic lupus erythematosus
SpA:	Spondyloarthropathy
UC:	Ulcerative colitis

The clinical presentation of patients is most likely to be reported or include one of the following key manifestations: Page 217

- single swollen joint (monoarthritis)
- multiple joint involvement (polyarthritis or polyarthralgia)
- low back pain and stiffness
- joint pain and 'pain all over'.

The single swollen joint (monoarthritis)

Consider monoarthritis in any patient presenting to the clinic with a single swollen joint and no history of trauma. The differential diagnoses in an active person presenting with a single swollen joint are presented in Table 15.4. Some of these conditions may also have an oligoarticular presentation, such as the crystal arthropathies, Lyme disease and the spondyloarthropathy group.[1]
6

Table 15.4 Differential diagnoses in the athlete presenting with a single swollen joint without a clear history of trauma Page 219

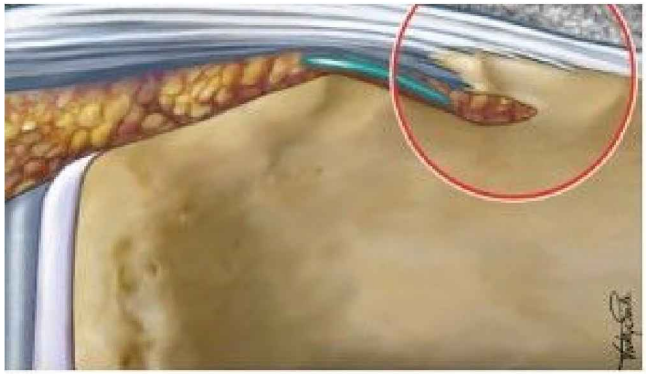
Common conditions	Less common conditions
• Septic arthritis • Crystal arthropathies: – Gout – Pseudogout • Lyme disease • Spondyloarthropathies: – Reactive arthritis – Psoriatic arthritis – Peripheral ankylosing spondylitis • Osteoarthritis	• Pigmented villonodular synovitis (Fig. 15.5) • Malignancies (e.g. synovial sarcoma) • Monoarticular rheumatoid arthritis • Sarcoidosis • Peripheral enteropathic arthritis • Haemophilia

Figure 15.5 MRI of pigmented villonodular synovitis of the knee

Non-infective causes of monoarthritis in the acute setting include gout, pseudogout and reactive arthritis. It may also be the initial presentation of chronic arthritis, and mechanical derangement is always a possibility. Life-threatening conditions like malignancies (e.g. synovial sarcoma) and haemophilia also need to be excluded.[21]

Septic arthritis

Septic arthritis is the most important diagnosis not to miss. It is the direct invasion of the joint by various microorganisms (bacteria, viruses, fungi and mycobacteria). The knee and hip joint are the most vulnerable, and the clinician should always have a high index of suspicion, especially in patients with prosthetic joints or who are immunocompromised.



(a)

(b)

(c)

(e)

(f)

(d)

Figure 15.4 Joint and extra-articular manifestations of rheumatological disease (a) Psoriatic enthesitis can manifest as a bone spur (circled)—unusual tendinopathies (e.g. distal patellar tendon rather than proximal insertion) should raise the clinician's suspicion of a possible spondyloarthropathy (b) Characteristic scales and red patches of psoriatic plaques on the forearm (c) Subtle psoriatic plaques behind the ear—examine here if spondyloarthropathy is in the differential diagnosis (d) Typical appearance of the nails in a patient with psoriatic arthropathy (e) Erythema nodosum in acute sarcoidosis (f) Keratoderma blennorrhagica in reactive arthritis—lesions which resemble those of psoriasis are commonly found on the palms or the soles of the foot
(E) IMAGE COURTESY OF RAHEEM B KHERANI

One of the most common organisms that causes septic arthritis is *Neisseria gonorrhoea.* Gonococcal arthritis is a rare complication of sexually transmitted infection and needs to be excluded among teens and young adults. Gonococcal arthritis may present with a skin rash and is treated with a dual antibiotic regimen, preferably ceftriaxone and azithromycin.[22]

Lyme disease

Lyme disease [vector: deer tick (*Ixodes scapulares*); bacteria: *Borrelia burgdorferi* (USA), *Borrelia afzelii* and *Borrelia garinii* (Europe)] is an infective disorder that has been reported in North America, China, Europe, Japan and Australia. It occurs most frequently in children 5–14 years of age and adults 40–50 years of age.

Patients involved in outdoor activities in high-risk areas are particularly subject to the potential hazard of contracting the disease. The disease is described in three phases, with arthritis occurring in the late stages. Usually only one or a few joins are affected, most commonly the knees. It can become chronic and simulates many other types of inflammatory arthritis. Treatment for Lyme disease is doxycycline, amoxicillin or cefuroxime.[23–25]

Gout

Gout (monosodium urate crystal deposition) affects mainly males and postmenopausal females. In the acute phase, it is characterised by recurrent attacks of monoarthritis—commonly at the great toe and also at the wrist (Fig. 15.6). If not managed well, it causes a chronic debilitating form of polyarthritis complicated by tophi, kidney stones and eventually urate nephropathy.

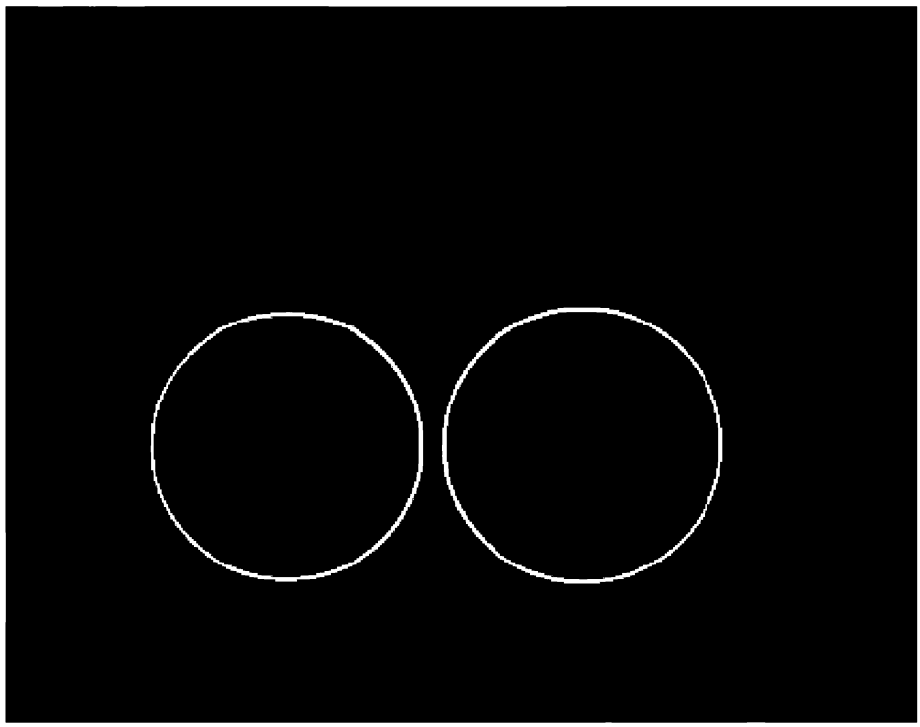
Figure 15.6 T1-weighted magnetic resonance (MR) image of the wrist showing the punched-out hypointense lesions characteristic of gout
IMAGE COURTESY OF DR MARK VELLEMAN

Lifestyle changes (diet, weight loss, exercise) combined with non-steroidal anti-inflammatory drugs (NSAIDs) and colchicine as needed may be enough to counter the disease in the early phase, but in the long term uric-acid- lowering drugs (probenecid, allopurinol, febuxostat) may be required.[21, 26]

Pseudogout

Pseudogout (calcium pyrophosphate deposition disease [CPPD]), also known as chondrocalcinosis, derived its name from its similarity to gout. It is more common in the elderly, is associated with degenerative arthritis, and acute attacks can be caused by dehydration and hyperparathyroidism.

The knee is most commonly affected (Fig. 15.7), but wrists, shoulders, hips and/or ankles may be involved. Attacks last for days to weeks and resolve spontaneously. Treatment is symptomatic relief of inflammation and prevention of dehydration.[26, 27]



(a)

(b)

Figure 15.7 Radiographs of pseudogout—chondrocalcinosis (a) Characteristic appearance of pseudogout in the knee—calcium pyrophosphate deposition occurs in the menisci of the knee (b) At the wrist the calcium pyrophosphate dihydrate deposition is in the triangular fibrocartilage (arrowed)
(A) IMAGE COURTESY OF DR MARK VELLEMAN

Reactive arthritis

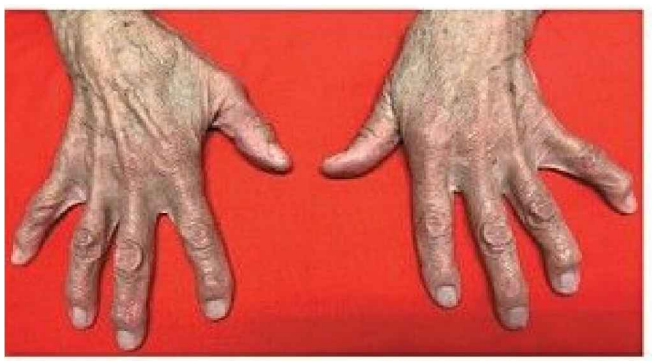
Reactive arthritis (previously called Reiter's syndrome) belongs to the spondyloarthropathy group and refers to arthritis that is not directly attributable to the infection itself but is caused by an immune reaction to a genital infection *(Chlamydia)* or bowel infection *(Salmonella, Yersinia, Campylobacter, Shigella)*. It is a painful, inflammatory arthritis, most commonly involving knees and ankles, although the toes, heels, fingers and lower back may also be affected. It occurs mostly in men aged 20–50, and some patients carry the HLA B27 gene. Gene carriers tend to have a more sudden and severe onset and are more likely to have prolonged symptoms. However, the diagnosis is based on clinical features and not on special investigations. Acute inflammation is treated with anti-inflammatory drugs, but disease-modifying anti-rheumatic drugs (DMARDs) may be required in the chronic phase.[28]

Osteoarthritis

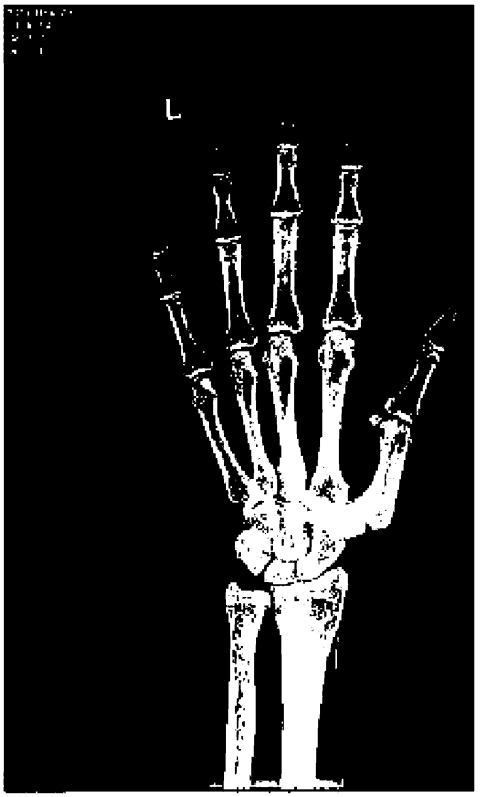
When a patient presents with musculoskeletal complaints of longer than 6 months duration, chronic arthritic disease comes into play. It helps to differentiate between inflammatory and non-inflammatory causes, as this narrows down the differential diagnosis.

Osteoarthritis (OA) is the most common rheumatological disease and can affect one or many joints. If only a few joints are involved, they are usually weight-bearing joints like the knee (Fig. 15. 8a) or hip. General OA (usually hereditary) also involves small hand joints, but unlike RA, the distal interphalangeal (DIP) joints (Heberden's nodes, Fig. 15.8b) are affected. Mucoid cysts, trigger fingers, carpal tunnel syndrome and carpometacarpal (CMC) (Fig. 15.8c) joint involvement often accompany hand OA. Trauma to a joint can lead to earlier onset of OA; for example, knee cruciate ligament injuries (Fig. 15.8d shows patellofemoral OA post-ACL injury), scaphoid fractures, etc.[29] Management of knee osteoarthritis is detailed in *Clinical Sports Medicine Volume 1: Injuries,* Chapters 35 and 37.

(a)



(b)



(c)

(d)

Figure 15.8 Images of osteoarthritis (a) Medial compartment osteoarthritis of the knee (b) Heberden's nodes at the distal interphalangeal joint (c) Carpometacarpal joint osteoarthritis (d) Patellofemoral joint osteoarthritis, which is prevalent de novo and also in younger people after ACL reconstruction
IMAGES (A), (C) AND (D) COURTESY OF EUGENE MARAIS RADIOLOGY, IMAGE (B) BY PROF. CHRISTA JANSE VAN RENSBURG

Unfortunately, there are still no disease modifying drugs for osteoarthritis. Page 222 Management includes:[30, 31]

a. education
b. non-pharmacological treatment—muscle strengthening, weight management, orthotics, braces, physical therapy modalities and assistive devices
c. pharmacological drugs—topical ointments (anti-inflammatories and capsaicin), oral analgesics, NSAIDs and SYSADOAs (symptomatic slow acting drugs in OA) (e.g. glucosamine, chondroitin)
d. intra-articular injections—cortisone and hyaluronic acid
e. surgery—arthroplasties, trigger finger release.

Other causes of chronic non-inflammatory joint disease include Charcot arthropathy and osteonecrosis. Both conditions progress to joint destruction and underline the old saying that 'prevention is better than cure'.[32, 33]

Multiple swollen joints (polyarthritis or polyarthralgia)

A patient with multiple joint pain (polyarthralgia) or multiple joint pain with synovitis (polyarthritis) occasionally presents to the sports and exercise medicine clinic. To make an accurate diagnosis, a systematic approach becomes vital. The differential diagnoses of a patient presenting with polyarthritis are listed in Table 15.5.[16]

Table 15.5 Conditions to consider when a patient presents with polyarthritis[16]

Common conditions	Less common conditions
• Rheumatoid arthritis • Viral arthritis: – Parvovirus B19 – Epstein–Barr virus • Polyarticular spondyloarthropathy: – Psoriatic arthritis – Reactive arthritis • Inflammatory osteoarthritis • Systemic lupus erythematosus	• Viral arthritis: – Hepatitis B, C – Rubella • Rheumatic fever • Enteropathic polyarthritis • Overlap syndrome* (Fig. 15.9) • Polyarticular gout/pseudogout • Haemochromatosis • Sjögren's syndrome

- Osteoarthritis

*Overlap syndrome is an autoimmune disease of connective tissue in which a person presents with symptoms of two or more diseases. Features of the following diseases are most commonly found: SLE, mixed connective tissue disease, systemic sclerosis, polymyositis, dermatomyositis, RA, Sjögren's syndrome, Raynaud's syndrome (Fig. 15.9), autoimmune thyroiditis, antiphospholipid antibody syndrome.[34]

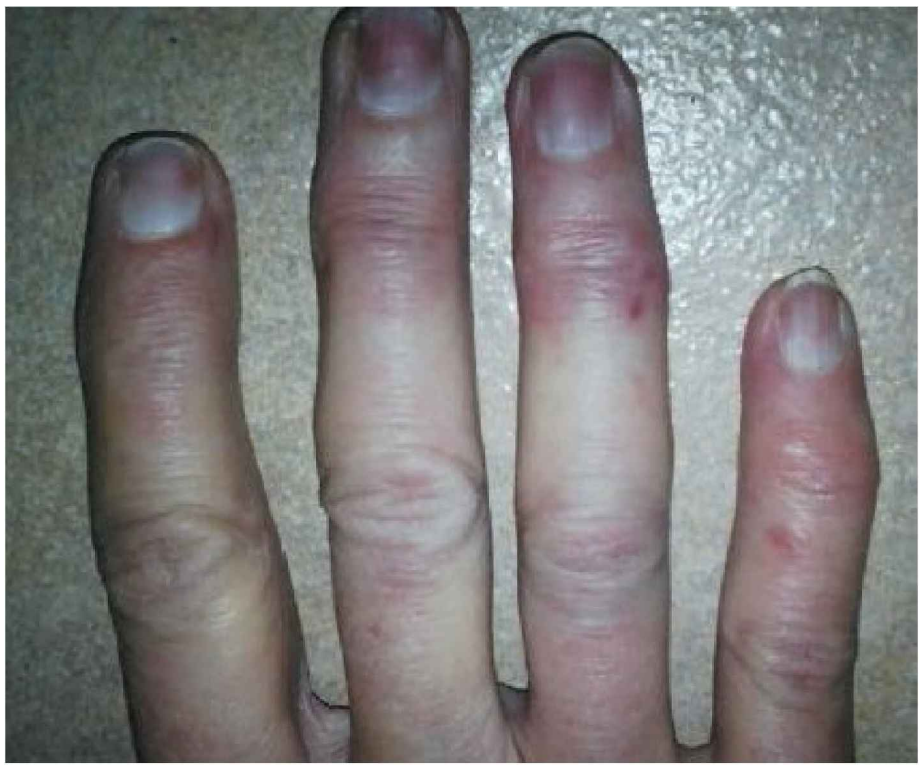
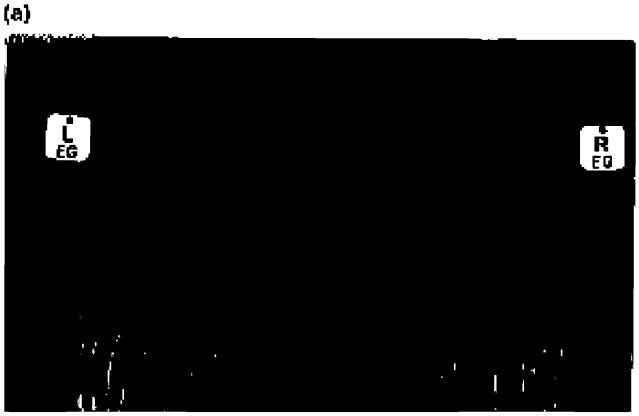


Figure 15.9 The characteristic white appearance of the fingers reflects the inadequate blood flow seen in Raynaud's syndrome
IMAGE COURTESY OF PROF. CHRISTA JANSE VAN RENSBURG

Rheumatoid arthritis

Rheumatoid arthritis (RA) is an autoimmune disease that attacks the joints in a symmetrical fashion. The primary joints are the small joints of the hands (proximal interphalangeal joints, metacarpophalangeal joints, Fig. 15.10a), wrists (Fig. 15.10b) and the feet (interphalangeal joints, metatarsophalangeal joints), as well as the cervical vertebrae, especially C1 and C2 (Fig. 15.10c). Cervical involvement often goes unnoticed but it is associated with the life-threatening risk of C1–2 subluxation. Therefore, cervical involvement of RA requires notification when referring patients for physical therapy or anaesthesia.

(a)



(c)

(d)

(b)

Figure 15.10 Clinical images highlighting the manifestations of rheumatoid arthritis (a) Radiograph showing rheumatoid erosions in the small joints of the hand (b) Rheumatoid erosions at the left wrist in particular (c) Sagittal MR image showing the complication of basilar invagination—a complication of C1–2 rheumatoid arthritis (d) Coronal T1 MR image of the knee showing bone oedema, effusion, geodes and meniscal displacement
(B) AND (C) IMAGES COURTESY OF EUGENE MARAIS RADIOLOGY (D) IMAGE COURTESY OF DR MARK VELLEMAN

As the disease progresses symptoms spread to other joints, such as the knees (Fig. 15.10d), elbows, shoulders and hips. All the inflammatory disorders, including RA, have a systemic burden. These extra-articular manifestations can involve the cardiovascular system, lungs, kidneys, eyes, skin, salivary glands, neural tissue and bone marrow (Table 15.3).

Periods of disease flares may alternate with periods of relative remission. The biological drugs (TNF α inhibitors, IL-6 blockers, T-cell co-stimulation modulators, B-cell inhibitors B-cell inhibition) have made a huge difference in the disease outcome. However, early diagnosis and onset of treatment with DMARDs, NSAIDs and corticosteroids also contribute to better response to treatment.[2, 35, 36]

Parvovirus B19

Young women (mothers or school teachers) caring for small children suffering from parvovirus B19 (fifth disease or 'slapped cheek' syndrome) can be affected with subsequent polyarthritis. This condition often resembles early RA, although symptoms and signs of parvovirus B19 polyarthritis usually improve within six weeks, whereas RA mostly follows a chronic and progressive course. There is no antiviral therapy available to treat the infection. Acetaminophen or NSAIDs usually provide symptomatic relief for post-infectious arthritis.[37]

Systemic lupus erythematosus

Page 224

Joint pain is one of the most common presenting complaints of females with systemic lupus erythematosus (SLE). There is, however, a wide array of other clinical manifestations, including skin (malar rash [Fig. 15.11], discoid lesions), oral ulcers, serositis (pleuritis, pericarditis), alopecia, photophobia, renal problems and neuropsychiatric involvement, that make it difficult to reach a diagnosis. The clinician should have a high index of suspicion in females with fatigue, non-specific joint pain disproportionate to swelling and some of the aforementioned symptoms.

Figure 15.11 The characteristic malar (across the cheeks) or 'butterfly' rash of systemic lupus erythematosus—this can be itchy
IMAGE COURTESY OF PROF. CHRISTA JANSE VAN RENSBURG

The arthritis component in SLE is non-erosive, and the differential diagnoses include drug-induced lupus, leukaemia, viral infections, fibromyalgia and many more. The disease course is also highly variable, ranging from indolent to fulminant.[38–40] Management depends on disease manifestations and severity. Hydroxychloroquine plays a central role in pharmacological management, as do NSAIDs, corticosteroids and immunosuppression medications (azathioprine, methotrexate, mycophenolate mofetil). Biological drugs such as belimumab and rituximab have shown mixed results for treatment of SLE.[41]

Low back pain and stiffness

A common presenting complaint is low back pain. It is crucial to distinguish between inflammatory and mechanical back pain as early as possible.

Chapter 29 in *Clinical Sports Medicine Volume 1: Injuries* covers mechanical back pain. The inflammatory disorders that can involve the back and the rest of the axial skeleton are grouped together as spondyloarthropathy. This group comprises chronic inflammatory diseases that share clinical immunological and radiological features. Diagnostic delays of 5–8 years have been reported. These diseases include:[12]

- ankylosing spondylitis

- enteropathic arthritis (ulcerative colitis, Crohn's disease)
- psoriatic arthritis
- reactive arthritis
- undifferentiated arthritis.

Extra-articular manifestations can be divided into a group related to the spondyloarthropathy concept (including skin, eye, gut or urogenital system involvement), or those reproducing chronic, long-term inflammation (involving the heart, lung, kidney and nerves). During the consultation, the clinician needs to ask about and observe for possible gastrointestinal complaints, skin and or nail involvement, recent urinary tract or bowel infection, enthesopathies and eye pathology. Uveitis is a well-described extra-articular manifestation of spondyloarthropathy. In fact, up to 77% of patients presenting with uveitis have undiagnosed spondyloarthropathy.[12, 42] Spondyloarthropathy-related manifestations (often at times the first manifestation) occur relatively frequently (20–60%) during disease evolution and may be related to axial or peripheral joint inflammation.[18]

Involvement of the sacroiliac joints is usually the first manifestation of axial disease (Fig. 15.12), and this has been included in the new diagnostic criteria developed by the Assessment of SpondyloArthritis International Society (ASAS).[42] A summary of the ASAS criteria is shown in Table 15.6.

(a)

(b)

Figure 15.12 Ankylosing spondylitis (a) T2-weighted coronal MR image of acute ankylosing spondylitis with hyperintense signal of bone oedema (arrows) in the sacroiliac joint (b) T2-weighted coronal MR image of chronic ankylosing spondylitis, also with bone oedema in the sacroiliac joint—in the chronic condition the signal is not as intense

IMAGES COURTESY OF DR MARK VELLEMAN

Table 15.6 ASAS classification criteria for axial spondyloarthritis

Classification criteria
Patients with back pain ≥3 months and age of onset <45 years and: • Sacroiliitis on imaging* plus ≥1 spondyloarthropathy feature** OR • Positive HLA B27 plus ≥2 spondyloarthropathy features**
* Sacroiliitis on imaging – Active (acute) inflammation on MRI highly suggestive of sacroiliitis associated with spondyloarthropathy OR – Definite radiographic sacroiliitis according to modified New York criteria
** Spondyloarthropathy features – Inflammatory back pain – Arthritis – Enthesitis (heel) – Uveitis – Dactylitis – Psoriasis (Fig. 15.4b) – Crohn's disease/ulcerative colitis – Good response to NSAIDs – Family history of spondyloarthropathy – HLA B27 – Elevated CRP

RUDWALEIT M, VAN DER HEIJDE D, LANDEWÉ R ET AL. THE ASSESSMENT OF SPONDYLOARTHRITIS INTERNATIONAL SOCIETY CLASSIFICATION CRITERIA FOR PERIPHERAL SPONDYLOARTHRITIS AND FOR SPONDYLOARTHRITIS IN GENERAL. ANN RHEUM DIS 2010.[42]

In a minority of patients, the major complaint is peripheral joint involvement. Patients can also present with sausage digits (Fig. 15.13). Approximately 90% of patients with ankylosing spondylitis are HLA B27 positive. This association is weaker for psoriatic arthritis, reactive arthritis and inflammatory bowel disease. In addition, 7% of the general population is positive for HLA B27 and shows no manifestation of disease.[12]

Figure 15.13 Sausage digits (dactylitis) are due to inflammation inside the toes and are a feature of peripheral joint involvement in ankylosing spondylitis
IMAGE COURTESY OF PROF. CHRISTA JANSE VAN RENSBURG

Ankylosing spondylitis

Ankylosing spondylitis is most common in young males, and the presenting symptom can be either back pain involving the gluteal areas (sacroiliac joints) or asymmetrical, mostly lower limb, joint swelling. Often these patients can recall episodes of tennis elbow, Achilles tendon and other enthesis-related problems. It is crucial to remember that double pathology is possible; for example, a cricket fast bowler can present with back pain that is attributable to both overload (spondylolysis/spondylolisthesis) and an inflammatory disorder (AS).[12]

PRACTICE PEARL

Multisport events allow for greater variation in movements and may provide a more holistic management strategy for patients suffering from multiple joint pain.

Psoriatic arthritis

Psoriatic arthritis has skin (Fig. 15.4b, c) and/or nail (Fig. 15.4d) involvement. Skin lesions can be present long before any articular manifestations. It has also been reported that nail involvement implies more serious arthritic disease. The joint involvement can mimic that of RA, as it is often symmetrical and affects upper and lower limbs. However, distal interphalangeal joints are also affected, which is not the case in RA.[43]

The management of the arthritic component of spondyloarthropathy includes NSAIDs, DMARDs in case of peripheral joint involvement, and biological drugs (TNFa inhibitors) for recalcitrant disease.[12]

Joint pain and 'pain all over'

The athlete with widespread joint or muscle pain who 'hurts all over' is a challenging presentation for any clinician. These patients often have frequent visits to the clinic, and it can be particularly satisfying to provide a diagnosis and offer the support they need. In many cases, the clinical examination does not reveal much. The differential diagnosis of this presentation is broad and includes the conditions listed in Table 15.5. Other possible diagnoses are highlighted in Table 15.7.

Table 15.7 Conditions in patients presenting with polyarthralgia

System	Cause
Drug-induced	Quinolones, acyclovir, vitamin A, clofibrate, beta blockers, statins
Infectious	Viral syndromes, vaccines
Endocrine	Hyper/hypothyroidism, hyperparathyroidism, corticosteroid withdrawal
Autoimmune	Polymyalgia rheumatica, inflammatory myositis
Neoplastic	Leukaemia
Psychiatric	Depression, somatisation disorder
Other	Fibromyalgia (chronic fatigue syndrome), silicone implant syndrome

CASE STUDY

Helgi Olafson, triathlete—ankylosing spondylitis

Several athletes, including golfer Phil Mickelson (psoriatic arthritis) and cricketer Michael Atherton (ankylosing spondylitis), managed their inflammatory arthritis while competing at the elite level. Many have been diagnosed early in their professional career but . . . have used physical activity to support the management of their disease. Helgi Olafson is one such athlete.

Olafson was diagnosed with ankylosing spondylitis at 19 years of age. Olafson adopted a program of up to 25 hours per week of exercise, as he trained for triathlons supplemented by pain medication to manage acute exacerbation of his symptoms. The combination of swimming, cycling and running allowed for a full-body approach to his training and prevented the potential complications of taking part in single-sport events. The multi-sport approach helped him to avoid the complications associated with prolonged flexed postures in ankylosing spondylitis.

Fibromyalgia

Fibromyalgia is a diagnosis of exclusion. It causes widespread pain, fatigue, memory problems, mood changes and an array of other symptoms. Although not life threatening and seemingly devoid of demonstrable muscle or joint damage, the condition can be devastating. The treatment is difficult and consists of biofeedback, sleep hygiene and medication. The role of exercise is controversial, and it is not recommended where the patient feels there is no benefit. FDA-approved drugs include pregabalin, duloxetine and milnacipran. Other antidepressants that are used off-label are tricyclics (e.g. amitriptyline), which relieve pain and improve sleep, and selective serotonin reuptake inhibitors (SSRIs), such as fluoxetine, paroxetine and sertraline, that relieve pain and improve mood.[44–46]

Page 227

Figure 15.14 Clinical images associated with ankylosing spondylitis (a) Sagittal plane radiograph of the 'bamboo spine' syndesmophytes (bony growth originating inside a ligament) characteristic of ankylosing spondylitis at C4–5. This image shows features of both ankylosing spondylitis and age-related joint changes (b) Lateral radiograph showing characteristic squaring of the vertebral bodies in ankylosing spondylitis

(A) IMAGE COURTESY OF DR J VAN DER MERWE

DIAGNOSIS

Special investigations (laboratory tests and imaging) can help to confirm diagnoses. These tests

should be requested in an appropriate fashion and clinicians should avoid falling into the trap of ordering an 'arthritis profile'. A summary of appropriate diagnostic tools is presented in Table 15.8.

Table 15.8 Diagnostic tools[21, 26, 39, 40, 47]

Disease	Lab tests	Imaging
Septic arthritis	**Blood** ↑ White cells • Neutrophils (bacterial) • Lymphocytes (viral) ↑ APR **Synovial fluid** • White cell count >100 000 per mm^3 • Culture of organism	Non-specific
Lyme disease	**Blood** Two-step testing process: 1. Enzyme immunoassay *or immunofluorescence assay* 2. Western blot	
Gout	**Blood** • Uric acid may be increased or normal • ↑ APR in acute attack **Synovial fluid** • MSU crystals (polarised light microscopy: birefringence, needle-shaped morphology)	**XR** ***Acute*** • Non-specific ***Chronic*** • Punched-out erosions with overhanging edges • Soft tissue nodules (tophi) **US** • Generic signs* • Double contour sign • Tophi **DECT** • Identify subclinical urate burden **MRI** • Generic signs** • Useful if gout presents in unusual location • Monitor management (tophi size)
Pseudogout	**Blood** • ↑ APR **Synovial fluid** • CPPD crystals (polarised light microscopy: variation in size and morphology of crystals; not all particles exhibit birefringence)	**XR** • Dense line within the cartilage that parallels the articular surface • Degenerative arthritis in unusual location **US** • Generic signs* • Calcific deposits
Osteoarthritis	**Blood** • No specific markers • APR mostly normal, but can be slightly elevated **Synovial fluid** • White cell count <2000 per mm^3	**XR** • Joint space narrowing • Subchondral cysts • Subchondral sclerosis • Osteophytes
Spondyloarthropathies	**Blood** • HLA B27 + (AS 90%; IBD, psoriatic arthritis and reactive arthritis 70%) • ↑ APR, *but* can be normal	**XR** (changes take long to develop, resulting in delayed diagnosis) • Sacroiliac joint: – Erosion – Sclerosis

	Reactive arthritis: **Synovial fluid** • White cell count 2000–100 000 mm^3 • No organisms cultured **Stool culture**—*Shigella, Salmonella, Yersinia, Campylobacter* **Urine culture**—*Chlamydia* **Vaginal swab**—*Chlamydia*	– Ankylosis • Spine: – Early changes are Romanus lesions ('shiny corners') and squaring of the vertebrae (Fig. 1 5.14b) – Later changes are formation of syndesmophytes (Fig. 15.14a) and calcification of the ligamentum flavum causing ankylosis (bamboo spine) • Hands and feet (psoriatic arthritis): – 'Pencil in cup' appearance – Contrary to RA, changes are asymmetrical and involve DIP joints **MRI** (sacroiliac joint) • Earlier changes than XR (high sensitivity, low specificity) • Bone marrow oedema • Contrast enhancement • Sclerosis • Erosions of the joint **NM** • As with MRI, earlier changes can be detected
Rheumatoid arthritis	**Blood** • ↑ APR • RF + (80%), low specificity • Anti-CCP + (60–70%), high specificity	**XR** • Soft tissue swelling • Peri-articular osteopenia • Joint space narrowing • Intra-articular erosions **US** • Generic signs* • Doppler activity **MRI** • Generic signs** • Earlier changes than XR
SLE	**Blood** • Leukopenia (<4 × 10^3 cells/μL on > 1 occasion) • Lymphopenia (<1500 cells/μL on > 1 occasion) • Thrombocytopenia (<100 × 10^3 cells/μL in the absence of offending medications) • Haemolytic anaemia • ANA >1:160—in the absence of medications associated with drug-induced lupus • Immunologic phenomena—dsDNA; anti-Smith antibodies; antiphospholipid antibodies; biologic false-positive serologic test results for syphilis, lupus erythematosus (LE) cells **Renal involvement** • Proteinuria (>0.5 g/day or 3 + positive on dipstick testing) or cellular casts (including red blood cells)	Radiologic studies focusing on joint pathology are non-specific
ANA:	Antinuclear antibodies	* Ultrasound generic signs are:

Anti-CCP:	Anti-cyclic citrullinated peptide antibodies
APR:	Acute phase reactants (ESR, CRP, ferritin, platelets)
CPPD:	Calcium pyrophosphate deposition disease
CRP:	C-reactive protein
CT:	Computed tomography
DECT:	Dual energy computed tomography
DIP:	Distal interphalangeal joint
dsDNA:	Double-stranded deoxyribonucleic acid
ESR:	Erythrocyte sedimentation rate
IBD:	Inflammatory bowel disease
MRI:	Magnetic resonance imaging
MSU:	Monosodium urate
NM:	Nuclear medicine scan
RF:	Rheumatoid factor
SLE:	Systemic lupus erythematosus
US:	Ultrasound
XR:	X-rays

- synovitis
- erosions
- effusions.

** MRI generic signs are:

- synovial thickening
- effusion
- bone erosion
- bone marrow oedema.

MANAGEMENT

The treatment of any rheumatological disease includes non-pharmacological and pharmacological management.[48–51] A considerable part of treatment involves patient education about the condition, as well as the correct use of medications and possible adverse effects. Other non-pharmacological management includes physical and occupational therapy, exercise programs, weight loss where indicated, orthoses and braces.

Non-pharmacological management

Physical activity forms an essential part of the management of rheumatoid arthritis, among other inflammatory conditions.[52, 53] The US Centers for Disease Control and Prevention[54] found that there has been an increase in physical activity counselling from physicians on all forms of arthritis from 52% to 61% (2002–2014). However, this suggests 40% of the 50 million sufferers in the USA alone are still not receiving appropriate physical activity guidance.

The UK National Institute for Health and Care Excellence guidelines[55–56] for the management of adults with rheumatoid arthritis and spondyloarthropathy state that all patients should be supported by a multidisciplinary team approach to work on exercises for enhancing joint flexibility and muscle strength and managing other functional impairments.

Other non-pharmacological recommendations include the use of orthotics and specialist podiatric assessment to support mobility for rheumatoid arthritis, and psychological therapies such as cognitive behavioural therapy and mindfulness when indicated (Chapters 21 and 22).

PRACTICE PEARL

Patients with rheumatoid arthritis and spondyloarthropathy require counselling on physical activity and may benefit from activity trackers to support adherence to their physical activity prescription.[54]

Pharmacological management

Pharmacological management for those suffering from rheumatological conditions has improved significantly, allowing athletes and those in the general population to maintain quality of life. The most common drugs prescribed are listed in Table 15.9.

Table 15.9 Medication for rheumatological conditions

Page 231

Symptomatic	Administration
Analgesics NSAIDs Corticosteroids	Oral Topical Intramuscular Intra-articular
Synthetic DMARDs	
Methotrexate	Oral/subcutaneous
Sulfasalazine	Oral
Leflunomide	Oral
Hydroxychloroquine (Chloroquine in some countries)	Oral
Azathioprine	Oral
Cyclosporine	Oral/intra-articular
Cyclophosphamide (cytophosphane)	Oral/intravenous/intra-articular
Biologic DMARDs (currently available; with ongoing development)	
TNFa inhibitors:	
Infliximab	Intravenous every 3 months
Etanercept	Subcutaneous weekly
Adalimumab	Subcutaneous every 2nd week
Golimumab	Subcutaneous monthly
Certolizumab	Subcutaneous twice weekly
Interleukin-6 inhibitors: Tocilizumab	Intravenous/subcutaneous monthly
Interleukin-12/23 inhibitors: Ustekinumab	Subcutaneous every 3 months
T-cell co-stimulation modulator: Abatacept	Intravenous/subcutaneous monthly
B-cell inhibitor: Rituximab	Intravenous (one course is 2 infusions separated by

CASE STUDY

Venus Williams, tennis—Sjögren's syndrome

I had swelling, and numbness and fatigue, which was really debilitating. I just didn't have any energy. It's not that you don't have energy; you just feel beat up.

Alongside her sister Serena, Venus Williams forms part of the most dominant family in female tennis history. She is a 7-time Grand Slam ladies' singles, 14-time Grand Slam ladies' doubles and 2-time

Grand Slam mixed doubles winner. In 2011, before her match at the US Open, Williams was forced to pull out due to the effects of Sjögren's syndrome. This signalled a peak in four years of increasing symptomatology.

Diagnosis

There are currently no readily accessible biomarkers for Sjögren's. This will often lead to delays in diagnosis. Instead, the clinician has to rely on a combination of tests, including blood (anti-nuclear antibodies, rheumatoid factor and erythrocyte sedimentation rate), eyes (Schirmer's test) and salivary production tests.

Management

Sjögren's is a lifelong autoimmune disease, but its effects on athletic performance can be managed with appropriate pharmacological intervention to reduce pain, humidifiers to help with acute dryness of the eyes and eye protection (e.g. goggles) when outdoors, and appropriate hydration strategies to combat salivary concerns.

Page 232

Ms Williams made considerable dietary changes including a move to a vegan diet and adopted a new exercise program to help manage her symptoms.

Autoimmune diseases such as Sjögren's can cause significant difficulties in daily training and competition for athletes. Having returned to the world top 5 in 2017 and making Grand Slam finals at both the Australian Open and Wimbledon, Williams provides an example of effective management of the disease.

Sources: references 59, 60, 61, 62, 63

SUMMARY

Many rheumatological conditions have not been covered in this chapter, such as dermatomyositis, polymyositis, systemic sclerosis and polymyalgia rheumatica. Clinicians should adopt a systematic approach and have a high index of suspicion in any patient presenting with joint pain. A simple heuristic is to treat every patient the same and not jump to conclusions. The clinician should always take a thorough history, do a comprehensive physical examination—addressing all medical issues relating to sport and exercise—and request the relevant investigations. All physiological systems should be considered (skin and axillaries, cardiovascular system, pulmonary, gastrointestinal tract, genitourinary tract, neurological) during the consultation, as this will help prevent misdiagnoses.

Once a diagnosis of a rheumatological condition is established, not all future symptoms and signs can be attributed to that diagnosis. The patient with arthritis may still contract common sports-related injuries and or illnesses. Prompt diagnosis and appropriate management will support the patient in maintaining their level of performance, or at least offer them the opportunity to continue at an appropriate level. The effects of continued sporting participation are disease dependent. Maintenance of the patient's physical and mental wellbeing through continued sporting participation should not be underestimated.

REFERENCES

1. Janse Van Rensburg DC. A clinical approach to rheumatological conditions mimicking sports injuries. *International SportMed Journal* 2001; 2(6): 1–4.
2. Barczyńska TA, Węgierska M, Z'uchowski P et al. Coexistence of rheumatoid

arthritis and ankylosing spondylitis. *Reumatologia* 2015; 53(5): 279.

3. Jennings F, Lambert E, Fredericson M. Rheumatic diseases presenting as sports-related injuries. *Sports Med* 2008; 38(11): 917–30.
4. Papadakis MA, McPhee SJ, Rabow MW. *Current medical diagnosis & treatment 2016*. 55th ed. New York, NY: McGraw-Hill Medical, 2016.
5. Helmick CG, Felson DT, Lawrence RC et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States: part I. *Arthritis Rheum* 2008; 58(1): 15–25.
6. Guly CM, Forrester JV. Investigation and management of uveitis. *BMJ* 2010; 341(7777): 821–6.
7. Mertelsmann-Voss C, Lyman S, Pan TJ et al. US trends in rates of arthroplasty for inflammatory arthritis including rheumatoid arthritis, juvenile idiopathic arthritis, and spondyloarthritis. *Arthritis Rheum* 2014; 66(6): 1432–9.
8. Cassidy JT, Levinson J, Bass J et al. A study of classification criteria for a diagnosis of juvenile rheumatoid arthritis. *Arthritis Rheum* 1986; 29(2): 274–81.
9. Urwin M, Symmons D, Allison T et al. Estimating the burden of musculoskeletal disorders in the community: the comparative prevalence of symptoms at different anatomical sites, and the relation to social deprivation. *Ann Rheum Dis* 1998; 57(11): 649–55.
10. Cross M, Smith E, Hoy D et al. The global burden of rheumatoid arthritis: estimates from the Global Burden of Disease 2010 study. *Ann Rheum Dis* 2014; 73(7): 1316–22.
11. van Vollenhoven RF. Sex differences in rheumatoid arthritis: more than meets the eye. *BMC Med* 2009; 7(1): 12.
12. Harper BE, Reveille JD. Spondyloarthritis: clinical suspicion, diagnosis, and sports. *Curr Sports Med Rep* 2009; 8(1): 29–34.
13. Litwic A, Edwards MH, Dennison EM et al. Epidemiology and burden of osteoarthritis. *Br Med Bull* 2013; 105(1): 185–99.
14. Kourilovitch M, Galarza-Maldonado C, Ortiz-Prado E. Diagnosis and classification of rheumatoid arthritis. *J Autoimmun* 2014; 48: 26–30.
15. Walker BF, Williamson OD. Mechanical or inflammatory low back pain. What are the potential signs and symptoms? *Man Ther* 2009; 14(3): 314–20.
16. Brukner P, Khan K. *Brukner & Khan's clinical sports medicine*. 4th ed. Sydney: McGraw-Hill, 2012.
17. Cojocaru M, Cojocaru IM, Silosi I et al. Extra-articular manifestations in rheumatoid arthritis. *Maedica (Buchar)* 2010; 5(4): 286–91.
18. Quintero SG, Romero-Sánchez C. Extra-articular manifestations of spondyloarthritis. 2016. https://pdfs.semanticscholar.org/dd8c/a3a0496cd37ed5e817c705c16a57357106c0.pdf
19. Martey C. Spotting the signs: extra-articular manifestations in rheumatology. 2017.

https://www.physiospot.com/opinion/spotting-the-signs-extra-articular-manifestations-in-rheumatology/.

20. Janse van Rensburg DC, Ker JA, Grant CC et al. Autonomic impairment in rheumatoid arthritis. *Int J Rheum Dis* 2012; 15(4): 419–26.
21. Chowalloor PV, Siew TK, Keen HI. Imaging in gout: a review of the recent developments. *Ther Adv Musculoskelet Dis* 2014; 6(4): 131–43.
22. Robbins R, Keith MP. Gonococcal arthritis. Last update 13 November 2017. https://emedicine.medscape.com/article/333612-overview#showall.
23. Steere AC. Diagnosis and treatment of Lyme arthritis. *Med Clin North Am* 1997; 81(1): 179–94.
24. Shiel W. Lyme disease. 2017. https://www.medicinenet.com/lyme_disease/article.htm.
25. Mead PS. Epidemiology of Lyme disease. *Infect Dis Clin North Am* 2015; 29(2): 187–210.
26. Dieppe P, Swan A. Identification of crystals in synovial fluid. *Ann Rheum Dis* 1999; 58(5): 261–3.
27. Higgins PA. Gout and pseudogout. *JAAPA* 2016; 29(3): 50–2.
28. Selmi C, Gershwin ME. Diagnosis and classification of reactive arthritis. *Autoimmun Rev* 2014; 13(4): 546–9.
29. Braun HJ, Gold GE. Diagnosis of osteoarthritis: imaging. *Bone* 2012; 51(2): 278–88.
30. Deveza LA, Bennell K. Management of knee osteoarthritis. 28 June 2017. https://www.uptodate.com/contents/management-of-knee-osteoarthritis.
31. Zhang W, Nuki G, Moskowitz R et al. OARSI recommendations for the management of hip and knee osteoarthritis: part III: changes in evidence following systematic cumulative update of research published through January 2009. *Osteoarthritis Cartilage* 2010; 18(4): 476–99.
32. Womack J. Charcot arthropathy versus osteomyelitis: evaluation and management. *Orthop Clin North Am* 2017; 48(2): 241–7.
33. Osmani F, Thakkar S, Vigdorchik J. The utility of conservative treatment modalities in the management of osteonecrosis: a systematic review. *Bull Hosp Jt Dis (2013)* 2017; 75(3): 186–93.
34. Iaccarino L, Gatto M, Bettio S et al. Overlap connective tissue disease syndromes. *Autoimmun Rev* 2013; 12(3): 363–73.
35. Gaffo A, Saag KG, Curtis JR. Treatment of rheumatoid arthritis. *Am J Health Syst Pharm* 2006; 63(24): 2451–65.
36. Singh JA, Saag KG, Bridges SL, Jr. et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis Rheumatol* 2016; 68(1): 1–26.
37. Moore TL. Parvovirus-associated arthritis. *Curr Opin Rheumatol* 2000; 12(4): 289–94.

38. Yu C, Gershwin ME, Chang C. Diagnostic criteria for systemic lupus erythematosus: a critical review. *J Autoimmun* 2014; 48: 10–13.
39. Wallace D. Overview of the management and prognosis of systemic lupus erythematosus in adults. Last update 13 December 2016. https://www.uptodate.com/contents/overview-of-the-management-and-prognosis-of-systemic-lupus-erythematosus-in-adults.
40. Bartels C. Systemic lupus erythematosus (SLE) treatment & management. Last update 14 November 2017. https://emedicine.medscape.com/article/332244-treatment.
41. Yildirim-Toruner C, Diamond B. Current and novel therapeutics in the treatment of systemic lupus erythematosus. *J Allergy Clin Immunol* 2011; 127(2): 303–12.
42. Rudwaleit M, Van Der Heijde D, Landewé R et al. The Assessment of SpondyloArthritis International Society classification criteria for peripheral spondyloarthritis and for spondyloarthritis in general. *Ann Rheum Dis* 2010: annrheumdis133645.
43. Gladman D, Antoni C, Mease P et al. Psoriatic arthritis: epidemiology, clinical features, course, and outcome. *Ann Rheum Dis* 2005; 64(Suppl 2): ii14–17.
44. Endresen GK. Fibromyalgia: a rheumatologic diagnosis? *Rheumatol Int* 2007; 27(11): 999–1004.
45. Häuser W, Eich W, Herrmann M et al. Fibromyalgia syndrome: classification, diagnosis, and treatment. *Dtsch Arztebl Int* 2009; 106(23): 383–91.
46. Pongratz DE, Sievers M. Fibromyalgia—symptom or diagnosis: a definition of the position. *Scand J Rheumatol* 2000; 29(113): 3–7.
47. Baraliakos X, Landewé R, Hermann K et al. Inflammation in ankylosing spondylitis: a systematic description of the extent and frequency of acute spinal changes using magnetic resonance imaging. *Ann Rheum Dis* 2005; 64(5): 730–4.
48. Janse van Rensburg DC, Ker JA, Grant CC et al. Effect of exercise on cardiac autonomic function in females with rheumatoid arthritis. *Clin Rheumatol* 2012; 31(8): 1155–62.
49. Nolte K, Janse van Rensburg DC. The role of exercise in the rehabilitation of ankylosing spondylitis. *International SportMed Journal* 2001; 2(4): 1–12.
50. Lorig KR, Ritter PL, Laurent DD et al. The internet-based arthritis self-management program: a one-year randomized trial for patients with arthritis or fibromyalgia. *Arthritis Care Res (Hoboken)* 2008; 59(7): 1009–17.
51. Barlow J, Wright C, Sheasby J et al. Self-management approaches for people with chronic conditions: a review. *Patient Educ Couns* 2002; 48(2): 177–87.
52. Janse van Rensburg DC, Viljoen M, Coertzen C, et al. Efficacy of an exercise programme on the functional capacity and disease activity in females with rheumatoid arthritis. *Sth Afr Orth J* 2010; 9(2): 34–43.

53. Nolte K, Janse van Rensburg DC, Sheasby J et al. Exercise prescription in the management of rheumatoid arthritis. *Sth Afr Fam Prac* 2013; 48(2): 345–9.
54. Hootman JM, Murphy LB, Omura JD et al. Health care provider counseling for physical activity or exercise among adults with arthritis — United States, 2002 and 2014. *Morb Mort Week Rep* 2018; 66(5152): 1398–1401.
55. National Guideline Centre (UK). Rheumatoid arthritis in adults: diagnosis and management. London: National Institute for Health and Care Excellence (UK); 2018 Jul. (NICE Guideline, No. 100.) Available from: https://www.ncbi.nlm.nih.gov/books/NBK519103/.
56. National Guideline Centre (UK). Spondyloarthritis in over 16s: diagnosis and management. London: National Institute for Health and Care Excellence (UK); 2017 Jun. (NICE Guideline, No. 65.) Available from: https://www.nice.org.uk/guidance/ng65
57. https://www.spondylitis.org/Spondylitis-Plus/helgi-olafson-1
58. https://www.arthritis-health.com/blog/interview-helgi-olafson-triathlete-ankylosing-spondylitis-part-1
59. https://en.wikipedia.org/wiki/Venus_Williams
60. http://edition.cnn.com/2014/03/20/sport/tennis/venus-williams-sjogrens-syndrome/index.html
61. https://youtu.be/eC4YFzlsk2Q
62. http://info.sjogrens.org/conquering-sjogrens/bid/303930/Venus-Williams-Opens-Up-about-Living-with-Sjogren-s
63. https://www.theguardian.com/sport/blog/2017/jul/17/venus-williams-longevity-diet-wimbledon-tennis

Chapter 16

Osteoarthritis

with DAVID HUNTER and PRIA KRISHNASAMY

The joint lubrication was not what it was when I was competing, and I decided that not having arthritis or rheumatism for the rest of my life was a lot more important to me than returning to the track.
Edwin Moses, former world and Olympic 400-metre hurdles champion, on his decision to retire

Osteoarthritis (OA) is increasingly recognised to be a heterogeneous disorder that can present with pain and functional limitations and affects the entire joint, including cartilage, synovial membrane, subchondral bone, ligaments and periarticular musculature.[1] It has traditionally been seen as a condition of the elderly but is increasingly presenting at a younger age.[2] Osteoarthritis has affected some of the most famous athletes of all time, from golfers Tiger Woods and Jack Nicklaus to NBA stars Shaquille O'Neal and Kobe Bryant. The previous edition of *Clinical Sports Medicine* quoted comedian Jack Benny as saying 'I don't deserve this award, but then I have arthritis and I don't deserve that either'. The question is: to what extent is OA preventable? Many sports carry a higher risk of joint injury and therefore supporting the older athlete to remain actively involved in sports and their activities of daily living is key to their long-term health.

The most recent definition of OA proposed by the Osteoarthritis Research Society International (OARSI) is:

> . . . a disorder involving movable joints characterised by cell stress and extracellular matrix degradation initiated by micro- and macro-injury that activates maladaptive repair responses including pro-inflammatory pathways of innate immunity. The disease manifests first as a molecular derangement (abnormal joint tissue metabolism) followed by anatomic, and/or physiologic derangements (characterised by cartilage degradation, bone remodelling, osteophyte formation, joint inflammation and loss of normal joint function), that can culminate in illness.[3]

It is anticipated that this definition will continue to be subject to regular refinement with advances in scientific evidence.[3,4]

Recent studies have attempted to classify OA into different phenotypes[5, 6] and subpopulations,[7] as a means of categorising clinical presentations, including aetiological factors, risk factors, mechanisms of disease and treatment effects. The most recent systematic review of knee OA phenotypes discusses the clinical relevance in each subgroup, with the subgroups being clinical phenotypes, imaging phenotypes and laboratory phenotypes.[6] The extension of these definitions to other joints affected by OA is yet to be determined.

EPIDEMIOLOGY

The total burden of disease for OA increased substantially between 1990 and 2015, with disability-adjusted life years (DALYs) increasing by 35%.[8] Osteoarthritis also has the highest prevalence among all joint diseases, and with increasing trends in obesity and joint injury—which are the two most important risk factors for OA—these figures will increase further. A systematic review concluded that individuals with obesity and previous knee trauma had a 2.6-fold and 3.9-fold risk of developing knee OA, respectively.[9] Other risk factors included hand OA, female gender and older age.[9]

Joint sites with the highest prevalence of OA are the hands (43.3%), followed by the knees (23.9%) and the hips (10.9%).[10] In the sporting context, a review by Gouttebarge and colleagues reported that the prevalence of OA in former elite athletes was higher than the general population.[11] In young and athletic individuals, there may be a higher predisposition to joint injuries due to time spent in the activities, which may result in higher likelihood of developing OA.[2] However, the relationship between physical activity, joint injury and the likelihood of developing OA is not linear. A recent systematic review reported that the overall prevalence of hip and knee OA was 13.3% in competitive runners, 3.5% in recreational runners and 10.2% in sedentary, non-running controls,[12] suggesting that recreational running has some protective mechanism against the development of OA. Another systematic review reported that there was an overall low quality of evidence from studies that have looked at the relationship between elite sports participation and OA, but an increased prevalence of OA in athletes with previous anterior cruciate ligament (ACL) injuries or meniscectomies.[13] A recent retrospective cross-sectional study of leisure-time runners showed that there was no increased risk of symptomatic or radiographic knee OA compared to non-runners.[14]

While there is an increased risk of hip and knee OA after suffering from joint injury, recreational sport has not shown an increased risk of OA.[13, 15] This is relevant as the benefits of regular physical activity are recognised as an important element in the holistic management of many of the comorbidities faced globally, including but not limited to obesity, cardiovascular disease and diabetes. Moreover, there is growing evidence that physical activity is associated with reduced systematic inflammation[16] and with reduced intra-articular inflammation.[17]

PRACTICE PEARL

All individuals without significant comorbidities should engage in regular physical activity. There is no evidence to suggest regular physical activity undertaken recreationally increases the risk of osteoarthritis (the use of the term DJD is pervasive but inaccurate).

PATHOPHYSIOLOGY

It is now accepted that OA has biomechanical, genetic, inflammatory and metabolic aetiologies.[1, 18–20] It is known that at least 50% of susceptibility to hand and hip OA can be attributed to genetic factors.[21] Whereas for knee OA, biomechanical effects have been associated with OA disease onset and progression.[22–24] Higher knee joint forces are thought to contribute to OA disease progression, where one unit of weight loss has been equated to about four units of reduction in knee joint forces.[22]

Pathophysiological mechanisms in OA are known to involve pro-inflammatory cytokines, such as interleukins (IL-6, IL-1ß, IL-8), tumour necrosis factor-alpha (TNFa) and pro-catabolic mediators,[25] cartilage ageing and senescence.[20] Metabolic syndromes, namely obesity, diabetes, hypertension and hyperlipidaemia, have also been implicated in OA pathogenesis.[19] For example, adipokines released by fat tissue have been thought to induce the expression of pro-inflammatory factors, and hyperglycaemia is thought to have deleterious effects on cartilage, mediated by oxidative stress and advanced-age glycation products (AGEs).[19]

CLINICAL HISTORY AND DIAGNOSIS

Pain is the defining clinical symptom at presentation of osteoarthritis, and relief from pain is a driver for seeking clinical care.[26] Pain aetiology in osteoarthritis is recognised to have a complex biopsychosocial model with the recognised contributors being extra-articular factors, joint-related factors and sensitisation of nociceptive pathways.[27, 28] More recently, sleep disturbance and depression have also been associated with pain progression in OA.[29]

Figure 16.1 is a diagrammatic representation of a biopsychosocial model of pain in relation to structural pathology in OA. This model highlights the multifactorial nature of OA and the need to approach its management as part of a multidisciplinary team, looking at physical, psychological and environmental barriers to managing OA. The older athlete in particular may struggle to come to terms with the psychological effects of reduced performance and, if they are still actively participating to a high level, may refrain from speaking out for fear of being removed from the field of play.

https://www.sciencedirect.com. Due to rights and permissions restrictions, this content cannot be reproduced in a digital format. The content is available in the print edition at page 235.

Figure 16.1 Biopsychosocial model depicting the relation of structural pathology to the experience of pain
REPRINTED FROM OSTEOARTHRITIS CARTILAGE, 21, HUNTER DJ, ET AL., 'STRUCTURAL CORRELATES OF PAIN IN JOINTS WITH OSTEOARTHRITIS', 91170-8, FIGURE 1, SEP 2013, WITH PERMISSION FROM ELSEVIER

Diagnosis of OA is based on clinical history and examination. General features in history consistent with a diagnosis of OA may include persistent pain, joint stiffness and reduced function. Clinical examination findings of OA include reduced range of movement, crepitus and bony enlargement.[31] Radiography can be used for confirmation of diagnosis, when uncertain or to exclude differential diagnoses. The sections below provide further details for diagnosis of hip, knee, ankle, foot, spine, shoulder, wrist and hand OA.

Hip osteoarthritis

Risk factors in hip OA include obesity, mechanical factors, physical activity and dysplasia.[32, 33] Although femoroacetabular impingement (FAI) has been proposed to be a precursor of hip OA, this relationship is conflicting, as FAI features have shown to be common in asymptomatic individuals.[3] [4] A clinical diagnosis of hip OA can be made if patients are over the age of 45 years, have activity-related joint pain and minimal duration of morning joint stiffness less than 30 minutes, Page 235 according to the UK National Institute of Health and Care Excellence (NICE).[35]

Common physical examination findings include a loss of hip range of motion into rotation and pain in the groin on movement. Plain radiography may be performed to aid diagnosis if the cause of symptoms is uncertain. However, it has been reported that hip pain was not necessarily present in many hips with radiographic osteoarthritis, and many hips with pain did not show radiographic hip osteoarthritis.[36] Hence, hip OA may be missed if diagnosis is based solely on radiographs.[36]

Knee osteoarthritis

Risk factors for knee OA include age over 50 years, female gender, higher body mass index (BMI), previous knee injury or malalignment, joint laxity, occupational or recreational usage, family history and presence of Heberden's nodes.[31] For patellofemoral OA, recognised risk factors include activities that increase the load in the patellofemoral joint (PFJ), such as descending stairs and squatting, quadriceps weakness and patella malalignment.[37]

Clinical history in knee OA may include usage-related pain, with symptoms worse towards the end of the day, relieved by rest, feelings of 'giving way', mild morning or inactivity stiffness, pain at night and impaired function.[31]

Typical clinical findings on examination include crepitus, painful and/or restricted range of movement, bony enlargement and absent or modest effusion.[31] Persons with higher structural severity of knee OA by the Kellgren-Lawrence (K-L) grade have been shown to have worse clinical scores,[38] and classical features on plain radiography of knee OA include focal joint space narrowing, osteophytes, subchondral bone sclerosis and subchondral cysts.

Magnetic resonance imaging (MRI), ultrasound, blood, urine and synovial tests are seldom

required for diagnosis of OA.[31] However, laboratory tests may be used to exclude inflammatory arthritis. These investigations (both radiography and lab tests), although possible adjuncts for confirmation of diagnosis, are typically not necessary.

Ankle osteoarthritis

Approximately 1% of the world's adult population is affected by ankle OA, with 79.5% of patients with ankle OA having a history of one or more ankle joint injuries.[39] There is a latency time between joint injury and ankle OA, reported to be an average of 20.9 years, depending on the type and severity of injury, age at time of injury, occurrence of complications and varus malalignment.[40] In a longitudinal study over 18 years, risk factors that were identified to predispose to development of ankle OA included fracture, fracture-dislocation, increased BMI, age 30 or older, and length of time since surgery.[41]

Clinical presentation may include pain with daily or sporting activities, which may persist after cessation of activities, and clinical signs may include stiffness and decreased range of movement of the tibiotalar joint.[42] Weight-bearing radiographs are recommended, including anteroposterior, lateral and mortise views.[42]

Foot osteoarthritis

Symptomatic radiographic foot OA affects one in six older adults,[43] and the prevalence of first metatarsophalangeal (MTP) OA has been estimated in middle-aged to older adults to be 6.3–39%.[44] Symptomatic midfoot OA has been estimated to be present in 12% of the population aged over 50 years,[45] whereas hindfoot OA is thought to be less common.[46] In a recent large cross-sectional study, population prevalence for individual foot joints was estimated as: 7.8% for the first MTP joint, 3.9% for the first cuneometatarsal joint, 6.8% for the second cuneometatarsal joint, 5.3% for the naviculocuneiform joint and 5.8% for the talonavicular joint.[43]

Clinical features may include pain and stiffness of the affected foot, swelling near the affected joint, limited range of movement, difficulty in walking and bony protrusions.[46] Physical function and quality of life may be significantly affected in persons with foot OA. The feet can also be affected by erosive OA, which can lead to progressive structural joint damage.[46] Traditionally, the Kellgren and Lawrence (K-L) grade has been used to grade OA stages, and more recently a foot-specific OA grading system has been described using weight-bearing dorso-plantar and lateral projections.[47, 48]

Spine osteoarthritis

Lumbar spine OA is common, with an estimated prevalence of 40–85%.[49, 50] The role of osteophyte formation and disc degeneration as components of spine OA has been debated in the literature.[49] However, a recent cross-sectional study alluded to differences between synovial facet joint OA and spine OA (disc space narrowing and vertebral osteophytes), reflected in differences in types of elevated biological markers, suggesting variation in phenotypes.[51]

Prevalence of intervertebral disc degeneration (DD) from large cross-sectional studies was estimated to be highest in the lumbosacral vertebrae,[52, 53] followed by the 5th and 6th cervical spines and the 6th and 7th thoracic spines.[52] Comparing incidence and progression rates for lumbar spine DD between men and women, a 4-year longitudinal study reported incidence rates to be 31.6% in men and 44.7% in women; and progression rates to be 52% in men and 60.4% in women.[54] In the athletic population, lumbar disc herniation and disc prolapse has a reported prevalence of up to 58%.[55] However, to date, it is unclear whether lumbar disc injury correlates with a higher rate of lower back pain or even pathology.[55]

Risk factors for lumbar spine disc degeneration include age, back pain and radiographic OA in the hip and knee.[56] Osteophyte formation has also been associated with manual labour and patterns of joint loading.[57] Studies in different sport settings have reported higher radiographic changes in the lumbar spine in shot-putters, discus throwers and high jumpers, than in runners.[58]

Besides pain, symptoms in spine OA can vary depending on the anatomical structures involved. For example, neurological symptoms such as radicular symptoms, paraesthesia, numbness and weakness can occur if spine OA compromises nearby neural structures. Plain radiographs should not be routinely used for non-specific low back pain, but may be used to provide further information on the origin of pain and to exclude pathology such as malignancy, fracture or infection, in the absence of radicular symptoms.[49, 59] MRI imaging findings have been reported to correlate poorly with levels of low back pain and disability.[60] Moreover, guidelines recommend the use of MRI in evaluation of patients with persistent low back pain and signs or symptoms of radiculopathy or spinal stenosis only if they are potential surgical candidates.[59]

Shoulder osteoarthritis

In a radiographic study, idiopathic OA of the glenohumeral joint was reported in 20% of symptomatic patients aged 60 and over.[61] A similar prevalence was reported in another study, with increasing age being recognised as a risk factor.[62] The prevalence of shoulder OA in former elite tennis players has been reported to be 33%.[63]

Clinical presentations of glenohumeral OA may include pain, globally reduced function and stiffness. Careful history taking in conjunction with clinical examination will help the clinician understand the cause of symptoms and detect presence of associated pathology that can occur with shoulder OA, such as rotator cuff pathology and frozen shoulder. Plain radiography has been recommended as a useful first-line investigation for shoulder pain, to identify bony and calcific changes and exclude tumours.[64]

Hand osteoarthritis

Risk factors for hand OA include age over 40 years, female gender, positive family history, occupational usage, obesity and finger joint injury.[65] Typical joint pattern involvement

for hand OA includes the distal and proximal interphalangeal and thumb base joints,

shorter duration of morning or inactivity stiffness, and symmetric distribution.[65] Heberden's and Bouchard's nodes are important clinical markers for hand OA, and some individuals are at increased risk of multiple joint involvement of OA.[65] Erosive hand OA is a subgroup of hand OA, targeting mainly the interphalangeal joints, with worse clinical and structural outcomes, such as subchondral erosion, ankylosis and inflammation.[65]

Diagnosis is clinical but, if unclear, can be confirmed with posteroanterior radiograph of both hands. Blood tests are not required for diagnosis of hand OA, but may be done to exclude differential diagnoses.[65]

PREVENTION

With a growing body of evidence and increased knowledge, we now know that OA is a complex disease with multiple aetiologies, and our understanding of its development and risk factors has improved, especially for hip and knee OA. Osteoarthritis may not be inevitable and prevention is a priority, with current clinical guidelines placing emphasis on early treatment with education, exercise and weight loss among the general population.[35, 66–69] This section describes preventive measures for OA, focusing on hip and knee OA, given the growing but currently limited body of literature of OA of the other joints.

Primary prevention strategies to reduce the risk of exposure, such as injury prevention and prevention of obesity during adolescence, are recommended.[70] Secondary prevention strategies include weight management and exercise interventions to improve proprioception, dynamic joint stability and muscle function after sustaining joint injury.[70]

Education

The first step in prevention of OA is understanding the disease, which includes information on how it occurs, its risk factors and how to prevent it—and then incorporating the elements into a patient-focused plan. Education and self-management is effective in improving adherence to non-pharmacological treatment.[71] Involving the patient in goal setting and establishing short- and long-term goals with regular follow-up improves compliance and efficacy of the prevention intervention.

When working with athletes, this education is likely to be in the form of specific preventive programs, with the education focused on prolonging the ability to participate in the selected sport as well as the longer term joint management.

Prevention of disease through diet and exercise

A large prospective study reported that a BMI over 30 was associated with a 2.81-fold increased risk of developing knee OA over 10 years.[72] Another prospective study over 22 years reported a 7-fold increased risk of developing knee OA with a BMI over 30.[73] A weight loss of 5.1 kg over 10 years has been shown to decrease the odds of developing OA by over 50%.[74] A comprehensive review of all modalities for weight management is beyond the scope of this chapter, but recognition that weight

loss is an important and modifiable factor in the prevention of OA is essential.

Joint injury prevention

Joint injury increases the risk of OA development, and strategies to prevent joint injury should be addressed. Joint injury prevention strategies include interventions that address modifiable intrinsic and extrinsic injury risk factors. Examples of modifiable intrinsic risk factors include body weight and physical fitness, including muscle function, strength, proprioception and stability. Modifiable extrinsic risk factors may include protective equipment such as knee braces, footwear and the environment (e.g. weather).

Prehabilitation

The term 'prehabilitation' (or 'prehab') has become widely used in sport-specific circles as a way of combating the potential joint injury risks associated with competitive sports participation. Participation at a competitive level in many sports, including soccer, rugby, cricket, distance running and football, increases the risk of developing osteoarthritis. Therefore, all sports medicine teams should develop an appropriate program of exercises that will complement sustained sporting participation of their athletes.

A 40% reduction was observed in lower limb injury rates among rugby players undertaking an injury prevention program that included balance, strength, power and agility exercises.[75] Neuromuscular and proprioceptive training exercises have been shown to prevent 50% of ACL injuries,[76] with a further study of over 11 000 athletes demonstrating a significant reduction in overall knee injury risk among soccer players.[77] Neuromuscular training aims to improve sensorimotor control and functional stabilisation of joints.[70] As further studies emerge that focus on the specific criteria for each sport to include in injury prevention programs, it is important that the methods with the greatest efficacy are shared and widely available to both clinicians and athletes. Programs should be included at all levels, including school, recreational and elite sport.

Current suggested methods for the development of greater resistance to injury have been to include cross-training to help prevent injury and practising alternative forms of movement (e.g. yoga for runners or swimming for soccer players). This may be especially important in the ageing athlete, who may need to be encouraged to move away from single-sport pursuits.[78] Sports governing bodies are now starting to make changes to the rules of their sports, to improve the long-term health of their participants, but these changes take time and will not happen fast.

One emerging field is the use of smartphone applications for monitoring loading in specific sports. These tools could potentially provide all athletes with the means necessary to analyse their participation levels and manage the risks of joint injury accordingly, by titrating their training when risks are identified.

PRACTICE PEARL

The use of load-monitoring systems, including smartphone applications, may help identify the risk of overtraining in single sports, and reduce risk of joint injury and osteoarthritis.

MANAGEMENT

Following an accurate clinical history and physical examination for individual joints affected by OA, as described above, a personalised management plan should be established. In the absence of a cure for OA, management should comprise education and active lifestyle management, including dietary and exercise interventions. Compliance with exercise and dietary interventions is often poor and, hence, providing education and instilling self-management skills in patients are important. Success often depends on patients taking part in the decision-making process of an agreed management plan and establishing short- and long-term goals that focus on improving patients' quality of life, with regular follow-up.

Weight management in osteoarthritis

Weight management forms an essential treatment arm in the management of persons with OA. Up to 50% symptomatic improvement in pain has been shown with 10% reduction in body weight.[79–81] Besides symptomatic improvement, preservation of structural OA disease has also been implicated with weight loss.[82] Higher BMI has been shown to have significant effect on the severity of knee OA [83] and has been associated with hip and knee replacement surgeries.[84] For every 1 kg of weight loss, peak knee load has been shown to be reduced by 2.2 kg, in obese individuals with knee OA.[85] Weight management, comprising strategies to improve nutritional awareness, reduction of portion size and modification of behaviours or triggers of unhealthy eating, should be included.[86]

Sports that require greater power and mass for success may pose a greater risk of developing joint pathology. Where a confirmed OA diagnosis is made, the risks of maintaining a high BMI may need to be discussed with the patient.

Table 16.1 describes management options that should be advocated and those that should be discouraged in OA, using a traffic-light system.

Table 16.1 Traffic-light system for osteoarthritis management

Assessments and diagnosis
Holistic assessment including consideration of: • *Modifiable risk factors*—overweight/obesity, joint alignment and injury/buckling • *Pain assessment and other musculoskeletal pain*—self-help strategies; analgesics use, frequency and adverse effects • *Social factors*—impact on activities of daily living and quality of life, recreational and occupational aspirations, participation restric • *Health beliefs and concerns*—previous knowledge of OA, expectations of treatment • *Psychological factors*—screen for depression, stresses in life, mood and quality of sleep • *Presence of support*—concerns of the main carer, isolation issues • *Influence of comorbidities*—e.g. falls risk
Unde
• *Imaging and blood tests* are not necessary to diagnose or monitor disease unless diagnosis is unclear, or staging for surgery. • *Imaging* should only be considered for atypical presentations if alternative (e.g. rheumatoid arthritis or gout) or additional diagnos
• Reactive, siloed care

- Glucosamine and chondroitin supplements
- Opioids

Principles for the diagnosis and management of osteoarthritis.
REPRODUCED AND MODIFIED WITH PERMISSION FROM HUNTER, DJ & BOWDEN, JL (2017) ARE YOU MANAGING OSTEOARTHRITIS APPROPRIATELY? *NAT REV RHEUMATOL* DOI:10.1038/NRRHEUM.2017.[87]

Exercise in the management of osteoarthritis

There have been concerns raised that physical activity may worsen OA. Muscle weakness that ensues with physical inactivity and with the disease itself may aggravate OA. Moreover, proprioception is reduced in persons with OA, compared to healthy individuals,[88, 89] which is associated with self-reported knee instability,[90] predisposing to an increased risk of falls. Patients with OA should be encouraged to engage and maintain regular low-impact exercise according to their preference and physical ability. The majority of the literature on the benefits of exercise in OA has focused on hip and knee OA. The most recent evidence of the benefits of exercise in hip and knee OA has been summarised below.

Exercise in hip osteoarthritis

There is high-quality evidence of a small to moderate effect that land-based exercises reduce pain and improve function in hip OA.[91] Currently, there is insufficient evidence for benefit in Page 239 pain and function from isolated strengthening exercises in hip OA, and the majority of trials have incorporated them as part of an exercise program with flexibility and functional exercise components.[92–94]

Neuromuscular exercise has been reported to moderately improve activities of daily living (ADL) and pain in patients with end-stage hip OA.[95] Tai chi has not been specifically studied in persons with hip OA; however, the general finding was that it is effective in the short term for reducing pain and disability in chronic musculoskeletal pain conditions.[96] A recent review reported moderate-quality evidence that aquatic exercise may have small, short-term and clinically relevant effects on pain, disability and quality of life (QoL) in persons with hip OA.[97] Nordic walking has been suggested to confer significant benefits that were greater than supervised strength training or home-based exercise alone, the use of walking poles allowing for a combination of strength and aerobic training benefits.[98] In persons with end-stage hip OA, preoperative exercise interventions have been reported to reduce pain in hip OA prior to hip replacement surgery.[95, 99]

According to World Health Organization (WHO) recommendations for physical activity, adults aged 18–64 should do at least 150 minutes of moderate-intensity aerobic physical activity throughout the week, or 75 minutes of vigorous-intensity aerobic physical activity throughout the week, or an equivalent combination of moderate- and vigorous-intensity activity.[100] The Page 240 application of this recommendation in persons with OA needs to be studied further.

A systematic review examined studies that have compared high-intensity versus low-intensity exercise in both hip and knee OA.[101] At present, there is insufficient evidence to conclude on the

effectiveness of high-intensity over low-intensity exercise programs in improving pain and physical function in OA, the minimal intensity for clinical effectiveness, or the maximum intensity patients with OA can tolerate.[101]

Exercise in knee osteoarthritis

For knee OA, land-based exercise has been shown to reduce pain, improve function and improve quality of life for 2–6 months after cessation of exercise.[102] The effect on pain and physical function did not differ between delivered treatment modalities of strengthening-only programs and combined programs.[102] A recent review reported that there is moderate-quality evidence that high-intensity resistance exercise demonstrated large and sustained improvement in knee muscle strength in knee OA patients.[103]

Cycling may be an alternative exercise option for persons with mild to moderate knee OA and has been shown to improve pain.[104] Other modalities of exercise such as tai chi have also been shown to improve pain, physical function, self-efficacy, depression and QoL scores in persons with knee OA.[105] In comparison to physical therapy, tai chi is reported to have similar clinical improvements in pain and physical function, but greater improvements in depression and the physical component of QoL, from a 12-week intervention program.[106] As with hip OA, aquatic exercise has been reported to have small, short-term and clinically relevant effects on pain, disability and QoL in persons with knee OA.[97] It is also suggested that hatha yoga can improve pain and perceived function in persons with knee OA.[107]

In patients with end-stage knee OA, neuromuscular exercises have been shown to improve ADL and pain, albeit with small effect sizes.[95] Preoperative exercise interventions have been reported to reduce pain in knee OA prior to knee replacement surgery.[95, 99] However, postoperative outcomes after total knee replacement (TKR) with preoperative exercise have been less promising.[108, 109] Huber et al. reported preoperative neuromuscular exercise had an additional small but non-significant improvement in functional assessments, compared to education alone in post-TKR patients.[108] These findings are supported by a recent review that concluded there is little evidence that preoperative physiotherapy had significant improvements in patient outcome scores, lower limb strength, pain, range of movement and hospital length of stay post-TKR.[110] However, the quality of evidence in the studies included in the review was reported to be moderate to poor and the studies had multimodal interventions with little information on exercise intensities.[110]

Although literature on rehabilitation programs post-ACL reconstruction is extensive,[111–117] few studies have addressed the important topic of exercise and knee OA, post-ACL reconstruction. Identification of exercise strategies that may delay or prevent knee OA development after ACL reconstruction is of interest, as an outcome we can potentially control. Shelbourne et al. recommended that exercise programs post-ACL reconstruction should aim to achieve and maintain full symmetric range of movement in the knee in the long term, to reduce the development of OA.[1, 18, 119] However, a recent systematic review reported that the relationship between rehabilitative

exercise for ACL injuries and long-term knee OA prevalence is inconclusive.[120]

Exercise prescription for osteoarthritis

Therapeutic effects of exercise for knee OA can be derived from various types of exercise.[102, 121, 122] Combining exercises that improve muscle strength, flexibility and aerobic capacity[121] or focusing on a single type of exercise that aims to improve strength, aerobic capacity or functional performance[122] have been among the recommended conclusions in recent reviews.

Exercise is an effective treatment for individuals with knee OA; however, reported effect sizes are modest.[102] One method to improve outcomes is by tailoring exercise programs to participant characteristics, as recommended by clinical guidelines.[66] Another may be by focusing future research on minimal thresholds for efficacy and maximal thresholds for safety in dose and intensity of the types of exercises prescribed.

Resistance training has significant benefits for older adults with knee OA. It is suggested that exercise prescription need only attain progressive overload of the structures, with no benefits recognised with high-load versus low-load resistance training. All forms of resistance training led to moderate improvements in both strength and functional measurements.[117]

Contraindications and precautions for exercise in patients with osteoarthritis

Exercise recommendations in patients with OA should consider precautions which are joint specific and systemic.

General contraindications for exercise specific to the joint would be presence of infection or an acute arthritic flare. Type and intensity of exercise chosen may depend on range of movement of the joints, strength of the muscles surrounding the joint and joint stability.

De Rooij et al. developed comorbidity-adapted exercise protocols for patients with knee OA, as comorbidities are highly prevalent in OA patients.[123] Three protocols were developed:

1. physiological adaptations—coronary disease, heart failure, hypertension, type 2 diabetes mellitus, chronic obstructive pulmonary diseases, obesity
2. behavioural adaptations—chronic non-specific pain, non-specific low back pain, depression
3. environmental adaptations—visual or hearing impairments.

Biomechanical interventions

The use of knee braces, knee sleeves and foot orthoses is recommended under the guidance of an appropriate specialist, such as an orthotist, physiotherapist or podiatrist, in the management of knee OA.[66] A tibiofemoral or patellofemoral brace and patellofemoral taping can be useful adjuncts in the management of knee OA. The evidence for the use of orthotics with a lateral wedge for medial tibiofemoral OA remains mixed; recommendations have included use of this type of device alongside bracing and foot orthotics, but further studies are needed before recommending this adjunct to therapy.[124] A walking stick (cane) is recommended for knee OA and is thought to help reduce pain and improve function,[66, 125] but extension of its use for OA of other joints needs

further research.

Psychological factors

It is important to offer reassurance to those affected by OA that they are experiencing a condition that is manageable. An alteration of ADL to support the management of a process the patient feels they can control may help prevent withdrawal from all exercise and its subsequent deleterious effects on both OA management and mental health. A systematic review of patient beliefs in managing their OA demonstrated those with a 'keep going' and activity modification attitude showed a greater propensity to take part in physical activity than those with existing beliefs that added to their feelings of a worsening disease process.[126]

The effects of psychological interventions in supporting OA management require further investigation, but the way in which OA is communicated to patients can have a substantial effect on their engagement in rehabilitation and prevention.

PRACTICE PEARL

Consider the effect of positive communication strategies when discussing OA with patients, to enhance their self-efficacy in performing and maintaining agreed management strategies.

Pharmacological management in osteoarthritis

Drug treatment in OA is important to support effective management and may prove complementary to achieving some of the exercise benefits outlined. Forms of pharmacological management are discussed below.

Non-steroidal anti-inflammatory drugs

Non-steroidal anti-inflammatory drugs (NSAIDs) have been shown to improve pain in hip and knee OA more than paracetamol.[127] However, there are also known adverse effects of NSAIDs, which include gastrointestinal (GI) and cardiovascular effects.[128] Hence, stratification of prescription should follow risk profiles for cardiovascular and GI; for example, naproxen may be prescribed for persons with high cardiovascular risk profiles.[128] In persons with high GI risk and low cardiovascular risk, a COX-2 selective inhibitor or non-selective NSAID with a proton pump inhibitor may be suitable.[128] In the older population, GI-adverse events may be increased and, hence, prescription of proton pump inhibitors is recommended.[66] Patients with renal impairment may need dose reduction, and treatment should be guided by indication, minimum dose and duration required for specific clinical requirements. Topical NSAIDs are a good alternative to oral NSAIDs for pain relief, with similar efficacies but without higher systemic adverse events.[129] For example, systemic exposure of diclofenac sodium gel 1% was reported to be 5- to 17-fold lower than oral diclofenac.[129]

Duloxetine

Duloxetine is a centrally acting serotonin and noradrenaline reuptake inhibitor (SNRI), and has been reported as efficacious and tolerable for the treatment of chronic pain in OA.[130] As discussed previously, pain in OA has a complex aetiology, and the role of central sensitisation in the chronic pain experience of OA patients is increasingly recognised.[131] Moreover, the reduction of pain with SNRIs was thought to be due to a direct analgesic effect, and independent of improvement in mood and anxiety.[132] A recent meta-analysis of randomised controlled trials (RCTs) reported that duloxetine had a greater reduction of pain, improved function and patient-rated improvement in function, and acceptable adverse effects after approximately 10–13 weeks of treatment.[132] Adverse events such as nausea, fatigue and constipation can occur and should be monitored.

Acetaminophen (paracetamol)

Paracetamol is no longer advocated as the first-line analgesia in the management of OA. A systematic review with meta-analysis showed that paracetamol had only minimal short-term benefits for patients with hip and knee OA.[133] Moreover, adverse effects from ingestion of paracetamol, such as abnormal liver function tests, gastrointestinal, renal and cardiovascular effects, are of concern,[134] and prescription should be limited to <4 g/day.

Opioids

Although opioids have a small to modest effect on pain, they have a higher and more frequent risk of adverse events.[66, 135] Examples of adverse events include nausea, constipation, dizziness, somnolence and vomiting.[136] Current guidelines recommend against any use of opioids for pharmacological management of osteoarthritis.

Disease-modifying osteoarthritis drugs

At present, although there are no disease-modifying osteoarthritis drugs (DMOADs) approved for use in OA, there are several promising candidates in the pipeline.[137] A recent review identified DMOADs that have been and are currently in clinical development and highlighted initiatives to develop biomarkers as drug development tools in OA trials.[137] Treatment of OA should be targeted and personalised,[138] taking account of the complexity of OA and with the understanding that one single therapy is unlikely to be effective.[139]

Intra-articular injections

Corticosteroids

Although intra-articular (IA) corticosteroids have been shown to provide pain relief in the short term (2–4 weeks),[140, 141] repeated injections are often administered. Long-term use of IA corticosteroids every 3 months for 2 years showed that there was no benefit for pain relief after 2 years.[140] Moreover, animal studies have alluded to potential cartilage damage occurring with regular IA corticosteroid injection.[142–144] A recent RCT reported that IA injection of triamcinolone

over 2 years resulted in significant cartilage volume loss and no significant difference in pain when compared to placebo.[145] Hence, the use of IA corticosteroids should be carefully considered, with short-term pain-relief benefits balanced against potential cartilage damage with repeated use in the long term. *Overall repeat corticosteroid injections are discouraged.*

Hyaluronic acid (viscosupplementation)

The evidence in the literature for IA hyaluronic acid (HA) injection has been conflicting, but the overall evidence shows that there is a small but clinically irrelevant benefit and an increased risk for serious adverse events.[146] A more recent systematic review of only double-blind, sham-controlled trials concluded that patients treated with HA injection for knee OA did not show clinically important differences over placebo.[147] Hence, treatment of IA hyaluronic acid for OA is generally not recommended.

Platelet-rich plasma

Current evidence in the use of platelet-rich plasma (PRP) in OA is suggestive of benefit; however, this derives from trials that are not of optimal quality. Platelet-rich plasma has been reported in systematic reviews to reduce pain and function when compared to control; however, moderate to high risk of bias was reported in the studies examined.[148, 149] To date, the effect of PRP on structural OA disease has not been studied, and PRP preparations in existing trials are heterogeneous. Hence, no firm conclusions on recommendations for PRP use in OA can be made at present.

Mesenchymal stem cell

Mesenchymal stem cells (MSCs) are progenitor cells that can be derived from various tissues such as blood, bone marrow, adipose tissue and skeletal muscle.[150] There is increasing interest in MSC due to its immunomodulatory and anti-inflammatory properties,[151] and MSC-based treatments have been examined in OA.[152, 153] However, current literature that has examined MSC-based treatments lacks consensus statements on optimum growth factor and culture conditions; methods of identification, isolation and characterisation; therapeutic strategy protocols; and established guidelines in clinical applications.[154] Further basic science research into understanding the biology of MSCs is needed, to better inform stem cell-based clinical trial research.[154] The use of MSCs in the treatment of osteoarthritis has not yet been proven to be safe or effective to support clinical use and lacks long-term data.[155] The Australasian College of Sports Physicians, in its current position statement, recommends that the use of MSCs fit within one of the following pathways: as part of a rigorous clinical research trial; or as an individualised innovative therapy that progresses to a clinical trial setting.[155]

CASE STUDY

Kristin Armstrong, road cycling—hip osteoarthritis

Even skipping a couple of days here and there will cause the deep dull pain to come back around, that pain is always a friendly reminder to get back on track.

Kristin Armstrong (Fig. 16.2) is a three-time US Olympic gold medallist, having won the women's road cycling time trial at the 2008 Beijing, 2012 London and 2016 Rio games. Armstrong was the first US athlete and first female rider to achieve three gold medals in the same discipline. Armstrong began her athletic career as a road runner and swimmer, competing in the 1999 Ironman Triathlon championships in Hawaii.

Figure 16.2 US Olympic gold medallist Kristin Armstrong competing in the Cycling Road Women's Individual Time Trial on Day 5 of the Rio 2016 Olympic Games. Armstrong has bilateral hip osteoarthritis, reported to be aggravated by running but relieved by cycling
PHIL WALTER/GETTY IMAGES

However, in 2001, aged just 27, Armstrong was diagnosed with osteoarthritis in both hips and advised to transition to cycling. That diagnosis was seven years prior to her first Olympic medal success. To manage her osteoarthritis, Armstrong combined cycling with a stretching and yoga routine, walked regularly and maintained a lower weight.

Exercise alongside appropriate medication to manage exacerbations and, where appropriate, activity modification (possibly even changing exercise discipline) can all be utilised to manage osteoarthritis, in both the recreational and elite athlete. Clinicians should work with patients to identify appropriate exercise management strategies based upon patients' own interests and goals.

Sources: references 167, 168, 169

Supplements

Eicosapentaenoic acid (EPA; 20:5 n-3) and docosahexaenoic acid (DHA; 22:6 n-3) are compounds found in fish oil that are thought to have analgesic properties, through regulation of inflammation.[156] However, a recent systematic review reported that fish oil does not reduce pain in osteoarthritis.[157] In animal models of osteoarthritis, curcumin has been shown to suppress gene expression of inflammatory mediators and reduce OA disease progression.[158] In humans, RCTs have shown short-term improvement in pain and function with curcumin,[159–162] and although promising, studies with larger subjects and longer follow-up are needed.

Evidence for the efficacy of glucosamine and chondroitin in OA literature has been conflicting. Glucosamine has been reported to have a similar effect to placebo for pain in independent investigator-initiated trials.[135] Similarly, the treatment of knee OA with glucosamine, chondroitin and their combinations did not achieve a clinically important difference in pain or function, compared to placebo.[163] Meta-analysis of the research suggests that clinically there are no medium- to long-term benefits for pain or joint function.[162]

Topical agents

As discussed, topical NSAIDs may be of benefit. A further topical agent that has been recommended by OARSI is capsaicin cream.[66] The cream utilises the active ingredient found in chilli to reduce substance P markers and therefore reduce inflammation, and has been backed with good quality RCT data. However, it is only recommended for use with knee OA.

When to refer for surgical intervention

Surgical referral in OA should be reserved for when conservative measures fail. Structural radiographic changes and patient symptoms do not necessarily follow similar trajectories. The indication for surgery should be based on persistent moderate to severe symptoms that include worsening pain, physical function and quality of life, despite adequate conservative management.

The type of surgery in knee and hip OA should be limited to joint replacement, and in younger patients, where appropriate, an osteotomy may be considered. Arthroscopic debridement involving

partial meniscectomy, debridement or both was shown to have no benefit at 1 to 2 years after surgery for knee OA.[164] Arthroscopy should be reserved for patients presenting clear clinical mechanical symptoms of locking, supported by imaging evidence.[165] In patients with asymptomatic meniscal tear, a course of physical therapy is recommended before considering arthroscopy.[165]

Improvement in pain and function with surgery in knee OA has been demonstrated in a randomised trial of surgery over non-surgical treatment.[166] However, the trial also reported a higher number of serious adverse events with surgery, compared to non-surgical management.[166] Hence, consideration for surgical intervention referrals should be based not only on weighing relative benefits and risks, but also taking account of possible unfavourable post-surgical pain outcomes, such as preoperative pain levels, and the presence of comorbidities.[167]

SUMMARY

- Physical activity is essential in the maintenance of joint health and for the prevention of osteoarthritis.
- Too much physical activity (e.g. elite sports participation) or injury to a joint can result in osteoarthritis.
- Injury resulting in joint damage is second only to obesity as a leading risk factor for osteoarthritis.
- Increased awareness of risk, with appropriate injury prevention programs, is critical for all sports, at all levels, and should be the primary focus of clinicians advising patients participating in physical activity, particularly where the focus is on a single-discipline sport.

REFERENCES

1. Rahmati M, Mobasheri A, Mozafari M. Inflammatory mediators in osteoarthritis: a critical review of the state-of-the-art, current prospects, and future challenges. *Bone* 2016; 85: 81–90. doi: 10.1016/j.bone.2016.01.019.
2. Amoako AO, Pujalte GG. Osteoarthritis in young, active, and athletic individuals. *Clin Med Insights Arthritis Musculoskelet Disord* 2014; 7: 27–32. doi: 10.4137/CMAMD.S14386.
3. Kraus VB, Blanco FJ, Englund M et al. Call for standardized definitions of osteoarthritis and risk stratification for clinical trials and clinical use. *Osteoarthritis Cartilage* 2015; 23(8): 1233–41. doi: 10.1016/j.joca.2015.03.036.
4. Mobasheri A, Bay-Jensen AC, van Spil WE et al. Osteoarthritis year in review 2016: biomarkers (biochemical markers). *Osteoarthritis Cartilage* 2017; 25(2): 199–208. doi: 1 0.1016/j.joca.2016.12.016.
5. Dell'Isola A, Allan R, Smith SL et al. Identification of clinical phenotypes in knee osteoarthritis: a systematic review of the literature. *BMC Musculoskelet Disord* 2016; 17(1): 425. doi: 10.1186/s12891-016-1286-2.
6. Deveza LA, Melo L, Yamato TP et al. Knee osteoarthritis phenotypes and their

relevance for outcomes: a systematic review. *Osteoarthritis Cartilage* 2017; 25(12): 1926–41. doi: 10.1016/j.joca.2017.08.009.

7. Bierma-Zeinstra SM, Verhagen AP. Osteoarthritis subpopulations and implications for clinical trial design. *Arthritis Res Ther* 2011; 13(2): 213. doi: 10.1186/ar3299.
8. GBD 2015 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet* 2016; 388(10053): 1545–602. doi: 10.1016/s0140-6736(16)31678-6.
9. Blagojevic M, Jinks C, Jeffery A et al. Risk factors for onset of osteoarthritis of the knee in older adults: a systematic review and meta-analysis. *Osteoarthritis Cartilage* 2010; 18(1): 24–33. doi: 10.1016/j.joca.2009.08.010.
10. Pereira D, Peleteiro B, Araujo J et al. The effect of osteoarthritis definition on prevalence and incidence estimates: a systematic review. *Osteoarthritis Cartilage* 2011; 19(11): 1270–85. doi: 10.1016/j.joca.2011.08.009.
11. Gouttebarge V, Inklaar H, Backx F et al. Prevalence of osteoarthritis in former elite athletes: a systematic overview of the recent literature. *Rheumatol Int* 2015; 35(3): 405–18. doi: 10.1007/s00296-014-3093-0.
12. Alentorn-Geli E, Samuelsson K, Musahl V et al. The association of recreational and competitive running with hip and knee osteoarthritis: a systematic review and meta-analysis. *J Orthop Sports Phys Ther* 2017; 47(6): 373–90. doi: 10.2519/jospt.2017.7137.
13. Tran G, Smith TO, Grice A et al. Does sports participation (including level of performance and previous injury) increase risk of osteoarthritis? A systematic review and meta-analysis. *Br J Sports Med* 2016; 50: 1459–66. doi: 10.1136/bjsports-2016-096142.
14. Lo GH, Driban JB, Kriska AM et al. Is there an association between a history of running and symptomatic knee osteoarthritis? A cross-sectional study from the Osteoarthritis Initiative. *Arthritis Care Res (Hoboken)* 2017; 69(2): 183–91. doi: 10.1002/acr.22939.
15. Vignon E, Valat JP, Rossignol M et al. Osteoarthritis of the knee and hip and activity: a systematic international review and synthesis (OASIS). *Joint Bone Spine* 2006; 73(4): 442–55. doi: 10.1016/j.jbspin.2006.03.001.
16. Warnberg J, Cunningham K, Romeo J et al. Physical activity, exercise and low-grade systemic inflammation. *Proc Nutr Soc* 2010; 69(3): 400–6. doi: 10.1017/S0029665110001928.
17. Hyldahl RD, Evans A, Kwon S et al. Running decreases knee intra-articular cytokine and cartilage oligomeric matrix concentrations: a pilot study. *Eur J Appl Physiol* 2016; 116(11–12): 2305–14. doi: 10.1007/s00421-016-3474-z.

18. Felson DT. Osteoarthritis as a disease of mechanics. *Osteoarthritis Cartilage* 2013; 21(1): 10–15. doi: 10.1016/j.joca.2012.09.012.
19. Zhuo Q, Yang W, Chen J et al. Metabolic syndrome meets osteoarthritis. *Nat Rev Rheumatol* 2012; 8(12): 729–37. doi: 10.1038/nrrheum.2012.135.
20. Mobasheri A, Batt M. An update on the pathophysiology of osteoarthritis. *Ann Phys Rehabil Med* 2016; 59(5–6): 333–9. doi: 10.1016/j.rehab.2016.07.004.
21. Spector TD, MacGregor AJ. Risk factors for osteoarthritis: genetics. *Osteoarthritis Cartilage* 2004; 12(Suppl): S39–44. doi: 10.1016/j.joca.2003.09.005.
22. Messier SP, Gutekunst DJ, Davis C et al. Weight loss reduces knee-joint loads in overweight and obese older adults with knee osteoarthritis. *Arthritis Rheum* 2005; 52(7): 2026–32. doi: 10.1002/art.21139.
23. Bennell KL, Bowles KA, Wang Y et al. Higher dynamic medial knee load predicts greater cartilage loss over 12 months in medial knee osteoarthritis. *Ann Rheum Dis* 2011; 70(10): 1770–4. doi: 10.1136/ard.2010.147082.
24. Vincent KR, Conrad BP, Fregly BJ et al. The pathophysiology of osteoarthritis: a mechanical perspective on the knee joint. *PM R* 2012; 4(5 Suppl): S3–9. doi: 10.1016/j.pmrj.2012.01.020.
25. Liu-Bryan R, Terkeltaub R. Emerging regulators of the inflammatory process in osteoarthritis. *Nat Rev Rheumatol* 2014; 11(1): 35–44. doi: 10.1038/nrrheum.2014.162.
26. Malfait AM, Schnitzer TJ. Towards a mechanism-based approach to pain management in osteoarthritis. *Nat Rev Rheumatol* 2013; 9(11): 654–64. doi: 10.1038/nrrheum.2013.138.
27. Neogi T. The epidemiology and impact of pain in osteoarthritis. *Osteoarthritis Cartilage* 2013; 21(9): 1145–53. doi: 10.1016/j.joca.2013.03.018.
28. Kidd B. Mechanisms of pain in osteoarthritis. *HSS J* 2012; 8(1): 26–8. doi: 10.1007/s11420-011-9263-7.
29. Parmelee PA, Tighe CA, Dautovich ND. Sleep disturbance in osteoarthritis: linkages with pain, disability, and depressive symptoms. *Arthritis Care Res (Hoboken)* 2015; 67(3): 358–65. doi: 10.1002/acr.22459.
30. Hunter DJ, Guermazi A, Roemer F et al. Structural correlates of pain in joints with osteoarthritis. *Osteoarthritis Cartilage* 2013; 21(9): 1170–8. doi: 10.1016/j.joca.2013.05.017.
31. Zhang W, Doherty M, Peat G et al. EULAR evidence-based recommendations for the diagnosis of knee osteoarthritis. *Ann Rheum Dis* 2010; 69(3): 483–9. doi: 10.1136/ard.2009.113100.
32. Zhang W, Doherty M, Arden N et al. EULAR evidence based recommendations for the management of hip osteoarthritis: report of a task force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). *Ann Rheum Dis* 2005; 64(5): 669–81. doi: 10.1136/ard.2004.028886.

33. Aresti N, Kassam J, Nicholas N et al. Hip osteoarthritis. *BMJ* 2016; 354: i3405. doi: 10.1136/bmj.i3405.
34. Frank JM, Harris JD, Erickson BJ et al. Prevalence of femoroacetabular impingement imaging findings in asymptomatic volunteers: a systematic review. *Arthroscopy* 2015; 31(6): 1199–204. doi: 10.1016/j.arthro.2014.11.042.
35. National Institute for Health and Care Excellence (NICE). *Osteoarthritis: care and management*. London, 2014.
36. Kim C, Nevitt MC, Niu J et al. Association of hip pain with radiographic evidence of hip osteoarthritis: diagnostic test study. *BMJ* 2015; 351: h5983. doi: 10.1136/bmj.h5983.
37. Mills K, Hunter DJ. Patellofemoral joint osteoarthritis: an individualised pathomechanical approach to management. *Best Pract Res Clin Rheumatol* 2014; 28(1): 73–91. doi: 10.1016/j.berh.2014.01.006.
38. Herman A, Chechik O, Segal G et al. The correlation between radiographic knee OA and clinical symptoms—do we know everything? *Clin Rheumatol* 2015; 34(11): 1955–60. doi: 10.1007/s10067-015-2871-8.
39. Brown TD, Johnston RC, Saltzman CL et al. Posttraumatic osteoarthritis: a first estimate of incidence, prevalence, and burden of disease. *J Orthop Trauma* 2006; 20(10): 739–44. doi: 10.1097/01.bot.0000246468.80635.ef.
40. Horisberger M, Valderrabano V, Hintermann B. Posttraumatic ankle osteoarthritis after ankle-related fractures. *J Orthop Trauma* 2009; 23(1): 60–7. doi: 10.1097/BOT.0b013e31818915d9.
41. Lübbeke A, Salvo D, Stern R et al. Risk factors for post-traumatic osteoarthritis of the ankle: an eighteen year follow-up study. *Int Orthop* 2012; 36(7): 1403–10. doi: 10.1007/s00264-011-1472-7.
42. Barg A, Pagenstert GI, Hugle T et al. Ankle osteoarthritis: etiology, diagnostics, and classification. *Foot Ankle Clin* 2013; 18(3): 411–26. doi: 10.1016/j.fcl.2013.06.001.
43. Roddy E, Thomas MJ, Marshall M et al. The population prevalence of symptomatic radiographic foot osteoarthritis in community-dwelling older adults: cross-sectional findings from the clinical assessment study of the foot. *Ann Rheum Dis* 2015; 74(1): 156–63. doi: 10.1136/annrheumdis-2013-203804.
44. Trivedi B, Marshall M, Belcher J et al. A systematic review of radiographic definitions of foot osteoarthritis in population-based studies. *Osteoarthritis Cartilage* 2010; 18(8): 1027–35. doi: 10.1016/j.joca.2010.05.005.
45. Thomas MJ, Peat G, Rathod T et al. The epidemiology of symptomatic midfoot osteoarthritis in community-dwelling older adults: cross-sectional findings from the Clinical Assessment Study of the Foot. *Arthritis Res Ther* 2015; 17: 178. doi: 10.1186/s13075-015-0693-3.
46. Iagnoco A, Rizzo C, Gattamelata A et al. Osteoarthritis of the foot: a review of the

current state of knowledge. *Med Ultrason* 2013; 15(1): 35–40. doi: 10.11152/mu.2013.2066.151.ai1ofr2.

47. Kalichman L, Hernandez-Molina G. Midfoot and forefoot osteoarthritis. *Foot (Edinb)* 2014; 24(3): 128–34. doi: 10.1016/j.foot.2014.05.002.
48. Menz HB, Munteanu SE, Landorf KB et al. Radiographic classification of osteoarthritis in commonly affected joints of the foot. *Osteoarthritis Cartilage* 2007; 15(11): 1333–8. doi: 10.1016/j.joca.2007.05.007.
49. Goode AP, Carey TS, Jordan JM. Low back pain and lumbar spine osteoarthritis: how are they related? *Curr Rheumatol Rep* 2013; 15(2): 305. doi: 10.1007/s11926-012-0305-z.
50. Battié MC, Videman T, Parent E. Lumbar disc degeneration: epidemiology and genetic influences. *Spine* 2004; 29(23): 2679–90. doi: 10.1097/01.brs.0000146457.83240.eb.
51. Goode AP, Nelson AE, Kraus VB et al. Biomarkers reflect differences in osteoarthritis phenotypes of the lumbar spine: the Johnston County Osteoarthritis Project. *Osteoarthritis Cartilage* 2017; 25(10): 1672–9. doi: 10.1016/j.joca.2017.07.007.
52. Teraguchi M, Yoshimura N, Hashizume H et al. Prevalence and distribution of intervertebral disc degeneration over the entire spine in a population-based cohort: the Wakayama Spine Study. *Osteoarthritis Cartilage* 2014; 22(1): 104–10. doi: 10.1016/j.joca.2013.10.019.
53. Cheung KM, Karppinen J, Chan D et al. Prevalence and pattern of lumbar magnetic resonance imaging changes in a population study of one thousand forty-three individuals. *Spine* 2009; 34(9): 934–40. doi: 10.1097/BRS.0b013e3181a01b3f.
54. Teraguchi M, Yoshimura N, Hashizume H et al. Progression, incidence, and risk factors for intervertebral disc degeneration in a longitudinal population-based cohort: the Wakayama Spine Study. *Osteoarthritis Cartilage* 2017; 25(7): 1122–31. doi: 10.1016/j.joca.2017.01.001.
55. Reiman MP, Sylvain J, Loudon JK et al. Return to sport after open and microdiscectomy surgery versus conservative treatment for lumbar disc herniation: a systematic review with meta-analysis. *Br J Sports Med* 2016; 50(4): 221–30. doi: 10.1136/bjsports-2015-094691.
56. Hassett G, Hart DJ, Manek NJ et al. Risk factors for progression of lumbar spine disc degeneration: the Chingford Study. *Arthritis Rheum* 2003; 48(11): 3112–17. doi: 10.1002/art.11321.
57. Ozturk A, Ozkan Y, Ozdemir RM et al. Radiographic changes in the lumbar spine in former professional football players: a comparative and matched controlled study. *Eur Spine J* 2008; 17(1): 136–41. doi: 10.1007/s00586-007-0535-3.
58. Schmitt H, Dubljanin E, Schneider S et al. Radiographic changes in the lumbar spine in former elite athletes. *Spine* 2004; 29(22): 2554–9.

59. Chou R, Qaseem A, Snow V et al. Diagnosis and Treatment of Low Back Pain: a Joint Clinical Practice Guideline from the American College of Physicians and the American Pain Society. *Ann Intern Med* 2007; 147(7): 478–91. doi: 10.7326/0003-4819-147-7-200710020-00006.
60. Jarvik JG, Hollingworth W, Heagerty PJ et al. Three-year incidence of low back pain in an initially asymptomatic cohort. *Spine* 2005; 30(13): 1541–8. doi: 10.1097/01.brs.0000167536.60002.87.
61. Kerr R, Resnick D, Pineda C et al. Osteoarthritis of the glenohumeral joint: a radiologic-pathologic study. *AJR Am J Roentgenol* 1985; 144(5): 967–72. doi: 10.2214/ajr.144.5.967.
62. Kobayashi T, Takagishi K, Shitara H et al. Prevalence of and risk factors for shoulder osteoarthritis in Japanese middle-aged and elderly populations. *J Shoulder Elbow Surg* 2014; 23(5): 613–19. doi: 10.1016/j.jse.2013.11.031.
63. Maquirriain J, Ghisi JP, Amato S. Is tennis a predisposing factor for degenerative shoulder disease? A controlled study in former elite players. *Br J Sports Med* 2006; 40(5): 447–50. doi: 10.1136/bjsm.2005.023382.
64. Chaudhury S, Gwilym SE, Moser J et al. Surgical options for patients with shoulder pain. *Nat Rev Rheumatol* 2010; 6(4): 217–26. doi: 10.1038/nrrheum.2010.25.
65. Zhang W, Doherty M, Leeb BF et al. EULAR evidence-based recommendations for the diagnosis of hand osteoarthritis: report of a task force of ESCISIT. *Ann Rheum Dis* 2009; 68(1): 8–17. doi: 10.1136/ard.2007.084772.
66. McAlindon TE, Bannuru RR, Sullivan MC et al. OARSI guidelines for the non-surgical management of knee osteoarthritis. *Osteoarthritis Cartilage* 2014; 22(3): 363–88. doi: 10.1016/j.joca.2014.01.003.
67. Hochberg MC, Altman RD, April KT et al. American College of Rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. *Arthritis Care Res (Hoboken)* 2012; 64(4): 465–74.
68. Zhang W, Moskowitz RW, Nuki G et al. OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. *Osteoarthritis Cartilage* 2008; 16(2): 137–62. doi: 10.1016/j.joca.2007.12.013.
69. Jordan KM, Arden NK, Doherty M et al. EULAR Recommendations 2003: an evidence based approach to the management of knee osteoarthritis: Report of a Task Force of the Standing Committee for International Clinical Studies Including Therapeutic Trials (ESCISIT). *Ann Rheum Dis* 2003; 62(12): 1145–55. doi: 10.1136/ard.2003.011742.
70. Roos EM, Arden NK. Strategies for the prevention of knee osteoarthritis. *Nat Rev Rheumatol* 2016; 12(2): 92–101. doi: 10.1038/nrrheum.2015.135.
71. Du S, Yuan C, Xiao X et al. Self-management programs for chronic musculoskeletal

pain conditions: a systematic review and meta-analysis. *Patient Educ Couns* 2011; 85(3): e299–310. doi: 10.1016/j.pec.2011.02.021.

72. Grotle M, Hagen KB, Natvig B et al. Obesity and osteoarthritis in knee, hip and/or hand: an epidemiological study in the general population with 10 years follow-up. *BMC Musculoskelet Disord* 2008; 9: 132. doi: 10.1186/1471-2474-9-132.
73. Toivanen AT, Heliovaara M, Impivaara O et al. Obesity, physically demanding work and traumatic knee injury are major risk factors for knee osteoarthritis—a population-based study with a follow-up of 22 years. *Rheumatology (Oxford)* 2010; 49(2): 308–14. doi: 10.1093/rheumatology/kep388.
74. Felson DT, Zhang Y, Anthony JM et al. Weight loss reduces the risk for symptomatic knee osteoarthritis in women: the Framingham study. *Ann Intern Med* 1992; 116(7): 535–9.
75. Attwood MJ, Roberts SP, Trewartha G et al. Efficacy of a movement control injury prevention programme in adult men's community rugby union: a cluster randomised controlled trial. *Br J Sports Med* 2018; 52: 368–74. doi: 10.1136/bjsports-2017-098005.
76. Gagnier JJ, Morgenstern H, Chess L. Interventions designed to prevent anterior cruciate ligament injuries in adolescents and adults: a systematic review and meta-analysis. *Am J Sports Med* 2013; 41(8): 1952–62. doi: 10.1177/0363546512458227.
77. Grimm NL, Jacobs JC, Jr., Kim J et al. Anterior cruciate ligament and knee injury prevention programs for soccer players: a systematic review and meta-analysis. *Am J Sports Med* 2015; 43(8): 2049–56. doi: 10.1177/0363546514556737.
78. Batt ME. Physical activity for the ageing athlete: the importance of maintaining musculoskeletal health. *Br J Sports Med* published online 2018; 52: 145–6. doi: 10.1136/bjsports-2017-098427.
79. Christensen R, Bartels EM, Astrup A et al. Effect of weight reduction in obese patients diagnosed with knee osteoarthritis: a systematic review and meta-analysis. *Ann Rheum Dis* 2007; 66(4): 433–9. doi: 10.1136/ard.2006.065904.
80. Christensen R, Henriksen M, Leeds AR et al. Effect of weight maintenance on symptoms of knee osteoarthritis in obese patients: a twelve-month randomized controlled trial. *Arthritis Care Res (Hoboken)* 2015; 67(5): 640–50. doi: 10.1002/acr.22504.
81. Messier SP, Mihalko SL, Legault C et al. Effects of intensive diet and exercise on knee joint loads, inflammation, and clinical outcomes among overweight and obese adults with knee osteoarthritis: the IDEA randomized clinical trial. *JAMA* 2013; 310(12): 1263–73. doi: 10.1001/jama.2013.277669.
82. Bliddal H, Leeds AR, Christensen R. Osteoarthritis, obesity and weight loss: evidence, hypotheses and horizons—a scoping review. *Obes Rev* 2014; 15(7): 578–86. doi: 10.1111/obr.12173.

83. Muehleman C, Margulis A, Bae WC et al. Relationship between knee and ankle degeneration in a population of organ donors. *BMC Med* 2010; 8: 48. doi: 10.1186/1741-7015-8-48.
84. Wendelboe AM, Hegmann KT, Biggs JJ et al. Relationships between body mass indices and surgical replacements of knee and hip joints. *Am J Prev Med* 2003; 25(4): 290–5.
85. Aaboe J, Bliddal H, Messier SP et al. Effects of an intensive weight loss program on knee joint loading in obese adults with knee osteoarthritis. *Osteoarthritis Cartilage* 2011; 19(7): 822–8. doi: 10.1016/j.joca.2011.03.006.
86. Fernandes L, Hagen KB, Bijlsma JW et al. EULAR recommendations for the non-pharmacological core management of hip and knee osteoarthritis. *Ann Rheum Dis* 2013; 72(7): 1125–35. doi: 10.1136/annrheumdis-2012-202745.
87. Hunter DJ, Bowden JL. Therapy: are you managing osteoarthritis appropriately? *Nat Rev Rheumatol* 2017; 13: 703–4. doi: 10.1038/nrrheum.2017.160.
88. Koralewicz LM, Engh GA. Comparison of proprioception in arthritic and age-matched normal knees. *J Bone Joint Surg Am* 2000; 82-A(11): 1582–8.
89. Hassan BS. Effect of pain reduction on postural sway, proprioception, and quadriceps strength in subjects with knee osteoarthritis. *Ann Rheum Dis* 2002; 61(5): 422–8. doi: 10.1136/ard.61.5.422.
90. van der Esch M, van der Leeden M, Roorda LD et al. Predictors of self-reported knee instability among patients with knee osteoarthritis: results of the Amsterdam osteoarthritis cohort. *Clin Rheumatol* 2016; 35(12): 3007–13. doi: 10.1007/s10067-016-3411-x.
91. Fransen M, McConnell S, Hernandez-Molina G et al. Exercise for osteoarthritis of the hip. *Cochrane Database Syst Rev* 2014 (4): CD007912. doi: 10.1002/14651858.CD007912.pub2.
92. Fernandes L, Storheim K, Sandvik L et al. Efficacy of patient education and supervised exercise vs patient education alone in patients with hip osteoarthritis: a single blind randomized clinical trial. *Osteoarthritis Cartilage* 2010; 18(10): 1237–43. doi: 10.1016/j.joca.2010.05.015.
93. Krauss I, Steinhilber B, Haupt G et al. Exercise therapy in hip osteoarthritis—a randomized controlled trial. *Dtsch Arztebl Int* 2014; 111(35–36): 592–9. doi: 10.3238/arztebl.2014.0592.
94. Juhakoski R, Tenhonen S, Malmivaara A et al. A pragmatic randomized controlled study of the effectiveness and cost consequences of exercise therapy in hip osteoarthritis. *Clin Rehabil* 2011; 25(4): 370–83. doi: 10.1177/0269215510388313.
95. Villadsen A, Overgaard S, Holsgaard-Larsen A et al. Immediate efficacy of neuromuscular exercise in patients with severe osteoarthritis of the hip or knee: a secondary analysis from a randomized controlled trial. *J Rheumatol* 2014; 41(7):

1385–94. doi: 10.3899/jrheum.130642.

96. Hall A, Copsey B, Richmond H et al. Effectiveness of tai chi for chronic musculoskeletal pain conditions: updated systematic review and meta-analysis. *Phys Ther* 2017; 97(2): 227–38. doi: 10.2522/ptj.20160246.

97. Bartels EM, Juhl CB, Christensen R et al. Aquatic exercise for the treatment of knee and hip osteoarthritis. *Cochrane Database Syst Rev* 2016; 3: CD005523. doi: 10.1002/14651858.CD005523.pub3.

98. Bieler T, Siersma V, Magnusson SP et al. In hip osteoarthritis, Nordic walking is superior to strength training and home-based exercise for improving function. *Scand J Med Sci Sports* 2017; 27(8): 873–86. doi:10.1111/sms.12694.

99. Wallis JA, Taylor NF. Pre-operative interventions (non-surgical and non-pharmacological) for patients with hip or knee osteoarthritis awaiting joint replacement surgery—a systematic review and meta-analysis. *Osteoarthritis Cartilage* 2011; 19(12): 1381–95. doi: 10.1016/j.joca.2011.09.001.

100. World Health Organization (WHO): Global Strategy on Diet, Physical Activity and Health. Geneva, 2011.

101. Regnaux JP, Lefevre-Colau MM, Trinquart L et al. High-intensity versus low-intensity physical activity or exercise in people with hip or knee osteoarthritis. *Cochrane Database Syst Rev* 2015 (10): CD010203. doi: 10.1002/14651858.CD010203.pub2.

102. Fransen M, McConnell S, Harmer AR et al. Exercise for osteoarthritis of the knee. *Cochrane Database Syst Rev* 2015; 1: CD004376. doi: 10.1002/14651858.CD004376.pub3.

103. Zacharias A, Green RA, Semciw AI et al. Efficacy of rehabilitation programs for improving muscle strength in people with hip or knee osteoarthritis: a systematic review with meta-analysis. *Osteoarthritis Cartilage* 2014; 22(11): 1752–73. doi: 10.1016/j.joca.2014.07.005.

104. Salacinski AJ, Krohn K, Lewis SF et al. The effects of group cycling on gait and pain-related disability in individuals with mild-to-moderate knee osteoarthritis: a randomized controlled trial. *J Orthop Sports Phys Ther* 2012; 42(12): 985–95. doi: 10.2519/jospt.2012.3813.

105. Wang C, Schmid CH, Hibberd PL et al. Tai chi is effective in treating knee osteoarthritis: a randomized controlled trial. *Arthritis Rheum* 2009; 61(11): 1545–53. doi: 10.1002/art.24832.

106. Wang C, Schmid CH, Iversen MD et al. Comparative effectiveness of tai chi versus physical therapy for knee osteoarthritis: a randomized trial. *Ann Intern Med* 2016; 165(2): 77–86. doi: 10.7326/M15-2143.

107. Cheung C, Wyman JF, Bronas U et al. Managing knee osteoarthritis with yoga or aerobic/strengthening exercise programs in older adults: a pilot randomized controlled trial. *Rheumatol Int* 2017; 37(3): 389–98. doi: 10.1007/s00296-016-3620-2.

108. Huber EO, Roos EM, Meichtry A et al. Effect of preoperative neuromuscular training (NEMEX-TJR) on functional outcome after total knee replacement: an assessor-blinded randomized controlled trial. *BMC Musculoskelet Disord* 2015; 16: 101. doi: 10.1186/s12891-015-0556-8.
109. McKay C, Prapavessis H, Doherty T. The effect of a prehabilitation exercise program on quadriceps strength for patients undergoing total knee arthroplasty: a randomized controlled pilot study. *PM R* 2012; 4(9): 647–56. doi: 10.1016/j.pmrj.2012.04.012.
110. Kwok IH, Paton B, Haddad FS. Does pre-operative physiotherapy improve outcomes in primary total knee arthroplasty? A systematic review. *J Arthroplasty* 2015; 30(9): 1657–63. doi: 10.1016/j.arth.2015.04.013.
111. Kruse LM, Gray B, Wright RW. Rehabilitation after anterior cruciate ligament reconstruction: a systematic review. *J Bone Joint Surg Am* 2012; 94(19): 1737–48. doi: 10.2106/JBJS.K.01246.
112. Wright RW, Preston E, Fleming BC et al. A systematic review of anterior cruciate ligament reconstruction rehabilitation: part II: open versus closed kinetic chain exercises, neuromuscular electrical stimulation, accelerated rehabilitation, and miscellaneous topics. *J Knee Surg* 2008; 21(3): 225–34.
113. Coppola SM, Collins SM. Is physical therapy more beneficial than unsupervised home exercise in treatment of post surgical knee disorders? A systematic review. *Knee* 2009; 16(3): 171–5. doi: 10.1016/j.knee.2008.09.001.
114. Wright RW, Preston E, Fleming BC et al. A systematic review of anterior cruciate ligament reconstruction rehabilitation: part I: continuous passive motion, early weight bearing, postoperative bracing, and home-based rehabilitation. *J Knee Surg* 2008; 21(3): 217–24.
115. Glass R, Waddell J, Hoogenboom B. The effects of open versus closed kinetic chain exercises on patients with ACL deficient or reconstructed knees: a systematic review. *N Am J Sports Phys Ther* 2010; 5(2): 74–84.
116. Cooper RL, Taylor NF, Feller JA. A systematic review of the effect of proprioceptive and balance exercises on people with an injured or reconstructed anterior cruciate ligament. *Res Sports Med* 2005; 13(2): 163–78. doi: 10.1080/15438620590956197.
117. Kristensen J, Franklyn-Miller A. Resistance training in musculoskeletal rehabilitation: a systematic review. *Br J Sports Med* 2012; 46(10): 719–26. doi: 10.1136/bjsm.2010.079376.
118. Shelbourne KD, Freeman H, Gray T. Osteoarthritis after anterior cruciate ligament reconstruction: the importance of regaining and maintaining full range of motion. *Sports Health* 2012; 4(1): 79–85. doi: 10.1177/1941738111430201.
119. Shelbourne KD, Urch SE, Gray T et al. Loss of normal knee motion after anterior cruciate ligament reconstruction is associated with radiographic arthritic changes

after surgery. *Am J Sports Med* 2012; 40(1): 108–13. doi: 10.1177/0363546511423639.

120. Duncan KJ, Chopp-Hurley JN, Maly MR. A systematic review to evaluate exercise for anterior cruciate ligament injuries: does this approach reduce the incidence of knee osteoarthritis? *Open Access Rheumatol* 2016; 8: 1–16. doi: 10.2147/OARRR.S81673.
121. Uthman OA, van der Windt DA, Jordan JL et al. Exercise for lower limb osteoarthritis: systematic review incorporating trial sequential analysis and network meta-analysis. *BMJ* 2013; 347: f5555. doi: 10.1136/bmj.f5555.
122. Juhl C, Christensen R, Roos EM et al. Impact of exercise type and dose on pain and disability in knee osteoarthritis: a systematic review and meta-regression analysis of randomized controlled trials. *Arthritis Rheumatol* 2014; 66(3): 622–36. doi: 10.1002/art.38290.
123. de Rooij M, van der Leeden M, Avezaat E et al. Development of comorbidity-adapted exercise protocols for patients with knee osteoarthritis. *Clin Interv Aging* 2014; 9: 829–42. doi: 10.2147/CIA.S55705.
124. Parkes MJ, Maricar N, Lunt M et al. Lateral wedge insoles as a conservative treatment for pain in patients with medial knee osteoarthritis: a meta-analysis. *JAMA* 2013; 310(7): 722–30. doi: 10.1001/jama.2013.243229.
125. Jones A, Silva PG, Silva AC et al. Impact of cane use on pain, function, general health and energy expenditure during gait in patients with knee osteoarthritis: a randomised controlled trial. *Ann Rheum Dis* 2012; 71(2): 172–9. doi: 10.1136/ard.2010.140178.
126. Kanavaki AM, Rushton A, Efstathiou N et al. Barriers and facilitators of physical activity in knee and hip osteoarthritis: a systematic review of qualitative evidence. *BMJ Open* 2017; 7(12): e017042. doi: 10.1136/bmjopen-2017-017042.
127. Pincus T, Koch GG, Sokka T et al. A randomized, double-blind, crossover clinical trial of diclofenac plus misoprostol versus acetaminophen in patients with osteoarthritis of the hip or knee. *Arthritis Rheum* 2001; 44(7): 1587–98. doi: 10.1002/1529-0131(200107)44:7<1587::aid-art282>3.0.co;2-x.
128. Scarpignato C, Lanas A, Blandizzi C et al. Safe prescribing of non-steroidal anti-inflammatory drugs in patients with osteoarthritis—an expert consensus addressing benefits as well as gastrointestinal and cardiovascular risks. *BMC Med* 2015; 13: 55. doi: 10.1186/s12916-015-0285-8.
129. Kienzler JL, Gold M, Nollevaux F. Systemic bioavailability of topical diclofenac sodium gel 1% versus oral diclofenac sodium in healthy volunteers. *J Clin Pharmacol* 2010; 50(1): 50–61. doi: 10.1177/0091270009336234.
130. Citrome L, Weiss-Citrome A. A systematic review of duloxetine for osteoarthritic pain: what is the number needed to treat, number needed to harm, and likelihood to be helped or harmed? *Postgrad Med* 2012; 124(1): 83–93. doi: 10.3810/pgm.2012.01.2521.

131. Lluch E, Torres R, Nijs J et al. Evidence for central sensitization in patients with osteoarthritis pain: a systematic literature review. *Eur J Pain* 2014; 18(10): 1367–75. doi: 10.1002/j.1532-2149.2014.499.x.
132. Wang ZY, Shi SY, Li SJ et al. Efficacy and safety of duloxetine on osteoarthritis knee pain: a meta-analysis of randomized controlled trials. *Pain Med* 2015; 16(7): 1373–85. doi: 10.1111/pme.12800.
133. Machado GC, Maher CG, Ferreira PH et al. Efficacy and safety of paracetamol for spinal pain and osteoarthritis: systematic review and meta-analysis of randomised placebo controlled trials. *BMJ* 2015; 350: h1225. doi: 10.1136/bmj.h1225.
134. Roberts E, Delgado Nunes V, Buckner S et al. Paracetamol: not as safe as we thought? A systematic literature review of observational studies. *Ann Rheum Dis* 2016; 75(3): 552–9. doi: 10.1136/annrheumdis-2014-206914.
135. Zhang W, Nuki G, Moskowitz RW et al. OARSI recommendations for the management of hip and knee osteoarthritis: Part III: changes in evidence following systematic cumulative update of research published through January 2009. *Osteoarthritis Cartilage* 2010; 18(4): 476–99. doi: 10.1016/j.joca.2010.01.013.
136. Avouac J, Gossec L, Dougados M. Efficacy and safety of opioids for osteoarthritis: a meta-analysis of randomized controlled trials. *Osteoarthritis Cartilage* 2007; 15(8): 957–65. doi: 10.1016/j.joca.2007.02.006.
137. Karsdal MA, Michaelis M, Ladel C et al. Disease-modifying treatments for osteoarthritis (DMOADs) of the knee and hip: lessons learned from failures and opportunities for the future. *Osteoarthritis Cartilage* 2016; 24(12): 2013–21. doi: 10.1016/j.joca.2016.07.017.
138. Mobasheri A. The future of osteoarthritis therapeutics: targeted pharmacological therapy. *Curr Rheumatol Rep* 2013; 15(10): 364. doi: 10.1007/s11926-013-0364-9.
139. Hunter DJ. Pharmacologic therapy for osteoarthritis—the era of disease modification. *Nat Rev Rheumatol* 2011; 7(1): 13–22. doi: 10.1038/nrrheum.2010.178.
140. Bellamy N, Campbell J, Robinson V et al. Intraarticular corticosteroid for treatment of osteoarthritis of the knee. *Cochrane Database Syst Rev* 2006 (2): CD005328. doi: 10.1002/14651858.CD005328.pub2.
141. Bannuru RR, Natov NS, Obadan IE et al. Therapeutic trajectory of hyaluronic acid versus corticosteroids in the treatment of knee osteoarthritis: a systematic review and meta-analysis. *Arthritis Rheum* 2009; 61(12): 1704–11. doi: 10.1002/art.24925.
142. Behrens F, Shepard N, Mitchell N. Alterations of rabbit articular cartilage by intra-articular injections of glucocorticoids. *J Bone Joint Surg Am* 1975; 57(1): 70–6.
143. Behrens F, Shepard N, Mitchell N. Metabolic recovery of articular cartilage after intra-articular injections of glucocorticoid. *J Bone Joint Surg Am* 1976; 58(8): 1157–60.
144. Hochberg MC, Altman RD, Brandt KD et al. Guidelines for the medical management of osteoarthritis. Part II. Osteoarthritis of the knee. American College of

Rheumatology. *Arthritis Rheum* 1995; 38(11): 1541–6.

145. McAlindon TE, LaValley MP, Harvey WF et al. Effect of intra-articular triamcinolone vs saline on knee cartilage volume and pain in patients with knee osteoarthritis: a randomized clinical trial. *JAMA* 2017; 317(19): 1967–75. doi: 10.1001/jama.2017.5283.
146. Rutjes AW, Juni P, da Costa BR et al. Viscosupplementation for osteoarthritis of the knee: a systematic review and meta-analysis. *Ann Intern Med* 2012; 157(3): 180–91. do i: 10.7326/0003-4819-157-3-201208070-00473.
147. Jevsevar D, Donnelly P, Brown GA et al. Viscosupplementation for osteoarthritis of the knee: a systematic review of the evidence. *J Bone Joint Surg Am* 2015; 97(24): 2047–60. doi: 10.2106/JBJS.N.00743.
148. Laudy AB, Bakker EW, Rekers M et al. Efficacy of platelet-rich plasma injections in osteoarthritis of the knee: a systematic review and meta-analysis. *Br J Sports Med* 2015; 49(10): 657–72. doi: 10.1136/bjsports-2014-094036.
149. Shen L, Yuan T, Chen S et al. The temporal effect of platelet-rich plasma on pain and physical function in the treatment of knee osteoarthritis: systematic review and meta-analysis of randomized controlled trials. *J Orthop Surg Res* 2017; 12(1): 16. doi: 1 0.1186/s13018-017-0521-3.
150. Phinney DG, Prockop DJ. Concise review: mesenchymal stem/multipotent stromal cells: the state of transdifferentiation and modes of tissue repair—current views. *Stem Cells* 2007; 25(11): 2896–902. doi: 10.1634/stemcells.2007-0637.
151. Uccelli A, Moretta L, Pistoia V. Mesenchymal stem cells in health and disease. *Nat Rev Immunol* 2008; 8(9): 726–36. doi: 10.1038/nri2395.
152. Cui GH, Wang YY, Li CJ et al. Efficacy of mesenchymal stem cells in treating patients with osteoarthritis of the knee: a meta-analysis. *Exp Ther Med* 2016; 12(5): 3390–400. doi: 10.3892/etm.2016.3791.
153. Borakati A, Mafi R, Mafi P et al. A systematic review and meta-analysis of clinical trials of mesenchymal stem cell therapy for cartilage repair. *Curr Stem Cell Res Ther* 2018; 13(3): 215–25. doi: 10.2174/1574888x12666170915120620.
154. Mobasheri A, Kalamegam G, Musumeci G et al. Chondrocyte and mesenchymal stem cell-based therapies for cartilage repair in osteoarthritis and related orthopaedic conditions. *Maturitas* 2014; 78(3): 188–98. doi: 10.1016/j.maturitas.2014.04.017.
155. Osborne H, Anderson L, Burt P et al. Australasian College of Sports Physicians—position statement: the place of mesenchymal stem/stromal cell therapies in sport and exercise medicine. *Br J Sports Med* 2016; 50(20): 1237–44. doi: 10.1136/bjsports-20 15-095711.
156. Calder PC. Marine omega-3 fatty acids and inflammatory processes: effects, mechanisms and clinical relevance. *Biochim Biophys Acta* 2015; 1851(4): 469–84. doi: 1 0.1016/j.bbalip.2014.08.010.
157. Senftleber NK, Nielsen SM, Andersen JR et al. Marine oil supplements for arthritis

pain: a systematic review and meta-analysis of randomized trials. *Nutrients* 2017; 9(1): 42. doi: 10.3390/nu9010042.

158. Zhang Z, Leong DJ, Xu L et al. Curcumin slows osteoarthritis progression and relieves osteoarthritis-associated pain symptoms in a post-traumatic osteoarthritis mouse model. *Arthritis Res Ther* 2016; 18(1): 128. doi: 10.1186/s13075-016-1025-y.
159. Nakagawa Y, Mukai S, Yamada S et al. Short-term effects of highly-bioavailable curcumin for treating knee osteoarthritis: a randomized, double-blind, placebo-controlled prospective study. *J Orthop Sci* 2014; 19(6): 933–9. doi: 10.1007/s00776-014-0633-0.
160. Madhu K, Chanda K, Saji MJ. Safety and efficacy of *Curcuma longa* extract in the treatment of painful knee osteoarthritis: a randomized placebo-controlled trial. *Inflammopharmacology* 2013; 21(2): 129–36. doi: 10.1007/s10787-012-0163-3.
161. Panahi Y, Rahimnia AR, Sharafi M et al. Curcuminoid treatment for knee osteoarthritis: a randomized double-blind placebo-controlled trial. *Phytother Res* 2014; 28(11): 1625–31. doi: 10.1002/ptr.5174.
162. Liu X, Machado GC, Eyles JP et al. Dietary supplements for treating osteoarthritis: a systematic review and meta-analysis. *Br J Sports Med* 2018; 52: 167–75. doi: 10.1136/bjsports-2016-097333.
163. Sawitzke AD, Shi H, Finco MF et al. Clinical efficacy and safety of glucosamine, chondroitin sulphate, their combination, celecoxib or placebo taken to treat osteoarthritis of the knee: 2-year results from GAIT. *Ann Rheum Dis* 2010; 69(8): 1459–64. doi: 10.1136/ard.2009.120469.
164. Thorlund JB, Juhl CB, Roos EM et al. Arthroscopic surgery for degenerative knee: systematic review and meta-analysis of benefits and harms. *BMJ* 2015; 350: h2747. doi: 10.1136/bmj.h2747.
165. Katz JN, Brownlee SA, Jones MH. The role of arthroscopy in the management of knee osteoarthritis. *Best Pract Res Clin Rheumatol* 2014; 28(1): 143–56. doi: 10.1016/j.berh.2014.01.008.
166. Skou ST, Roos EM, Laursen MB et al. A randomized, controlled trial of total knee replacement. *N Engl J Med* 2015; 373(17): 1597–606. doi: 10.1056/NEJMoa1505467.
167. Hawker GA, Badley EM, Borkhoff CM et al. Which patients are most likely to benefit from total joint arthroplasty? *Arthritis Rheum* 2013; 65(5): 1243–52. doi: 10.1002/art.37901.
168. https://en.wikipedia.org/wiki/Kristin_Armstrong
169. https://jointhealth.org/programs-jhmonthly-view.cfm?id=137
170. https://www.nytimes.com/2009/11/01/sports/cycling/01cycling.html?mtrref=www.google.com&gwh=B8EEC0508EA6EFB6E19687D5EF3B5517&gwt=pay

Chapter 17

Osteoporosis—physical activity for bone health

with HEATHER M MACDONALD, LEIGH GABEL and HEATHER A McKAY

A recurrent theme in this volume of *Clinical Sports Medicine* is the irrefutable data that regular physical activity prevents a host of chronic diseases.[1, 2] With respect to bone, various international position statements spell out that weight-bearing physical activity is essential to build a strong and healthy skeleton during childhood, maintain bone mass and strength during adult years, and mitigate skeletal decline as we age.[1, 3, 4]

In this chapter we:

- summarise the key evidence demonstrating that physical activity promotes bone health
- discuss how to maximise bone health during maturation
- discuss the prevention of bone mineral loss and osteoporosis in adults
- highlight contemporary non-pharmacological and pharmacological approaches for treating bone loss across the age spectrum.

KEY EVIDENCE—HOW BONE ADAPTS TO PHYSICAL ACTIVITY AND EXERCISE

Bone has a remarkable ability to adapt its mass, structure and strength to match functional demands including those associated with weight-bearing activity. Functional adaptation of bone is determined by strain (deformation of bone tissue), with muscle forces imposing the largest strain on the skeletal system during voluntary activities.[5, 6]

A 'mechanostat' feedback system keeps bone strains within a 'physiological window', by adjusting bone mass and structure. The key load-sensing cells in bone are osteocytes, and they react strongly to changes in their environment to initiate key cell signalling pathways involved in

mechanotransduction (the process by which bone converts a biophysical force into a cellular response). Osteocytes accommodate (switch off) when receiving steady-state signals.[7] Thus, in the absence of varied stimuli, bone cells desensitise to loading.

PRACTICE PEARL

When prescribing an exercise program, vary the type and nature of the exercise to ensure the continued response of bone mass.

These principles of bone adaptation to loading are summarised in the late Professor Charles Turner's three rules for bone adaptation to mechanical stimuli:

- bone adaptation is driven by dynamic rather than static loads (i.e. cyclic not continuous)
- only a short duration of loading is needed to initiate bone adaptation
- bone cells accommodate and become less responsive to routine loading.

These three rules should guide exercise prescription that targets bone health across the lifespan.[8] If we use these three rules within the FITT principles (Chapters 3 and 4), an effective exercise program for bone health will have the following features:

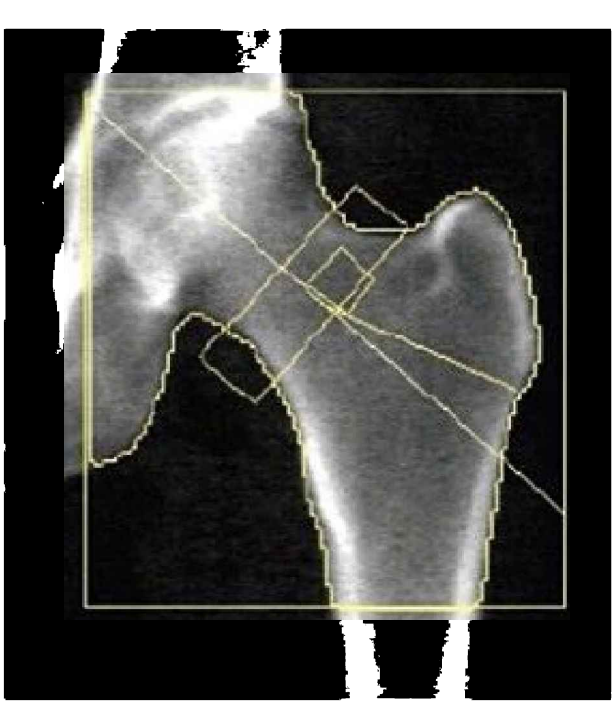
- *Frequency*—Short, frequent bouts of weight-bearing activity are effective. This refers to daily, or multiple times daily, load (physical activity or exercise).
- *Intensity*—High-impact exercises (or high strain from muscle on bone) promote bone adaptation better than low-intensity activities.
- *Time*—Short bouts (5–10 min or less) separated by rest periods are more effective than a continuous bout with the same amount of total load.
- *Type*—Activities that include multidirectional and irregular loading patterns ('surprises') are more effective than exercises involving repetitive strain distributions.

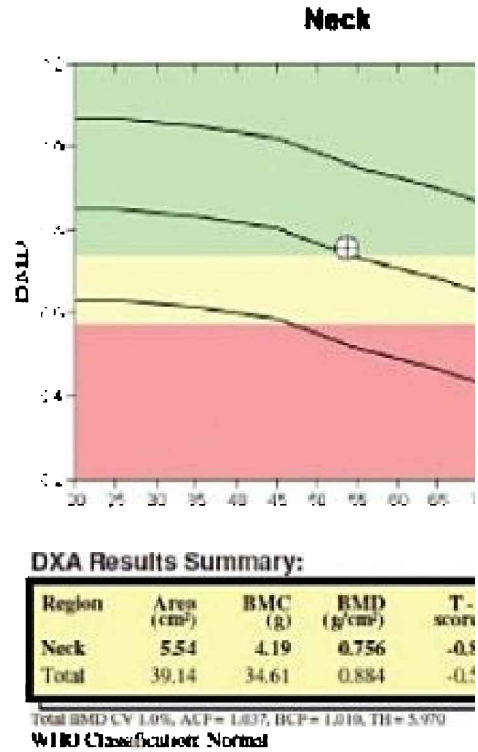
The clinical implications of these principles are very well proven in clinical studies. Regular walking and other low-intensity activities are insufficient to prevent bone loss at clinically relevant sites, such as the lumbar spine in healthy postmenopausal women.[9, 10] Athletes in sports Page 246 such as gymnastics,[11] soccer,[12, 13] tennis, squash[14] and weightlifting[15] that are associated with high- or odd-impact loading have greater bone mass and superior bone structure compared with less active individuals. Benefits of sports participation on bone health (mechanical competence) often remain evident in retired middle-aged and older athletes, particularly those who started training during childhood.[16]

Understanding how bone adaptation to physical activity is measured —'inside the black box'

Dual-energy X-ray absorptiometry (DXA) (Fig. 17.1) is the clinical gold standard for assessing bone mineral density (areal BMD or aBMD, g/cm^2) and bone mineral content (BMC, g), and for diagnosing osteoporosis. DXA may also be used to assess bone adaptation to exercise in all age groups. BMD and BMC are surrogate measures for bone strength and predict fragility fractures at the population level.[17]

Figure 17.1 (a) DXA scanner





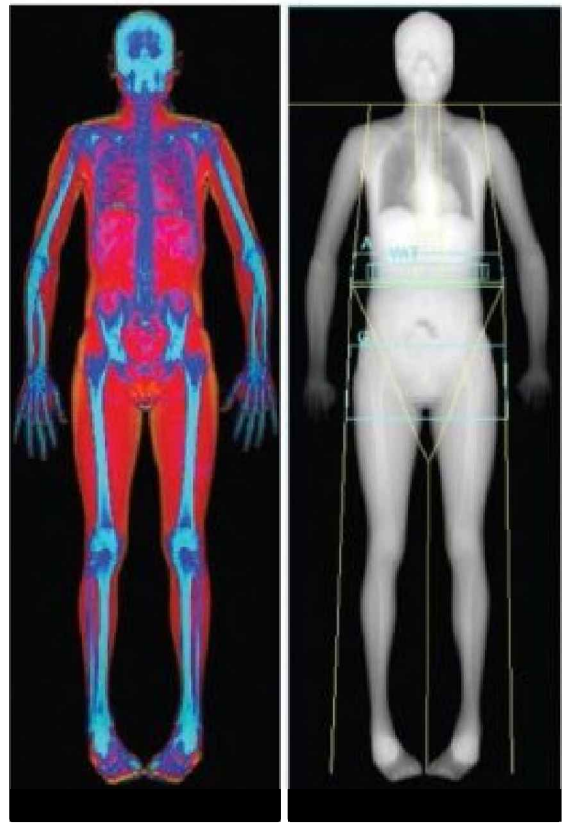
DXA Results Summary:

Region	Area (cm²)	BMC (g)	BMD (g/cm²)	T-score
Neck	5.54	4.19	0.756	-0.8
Total	39.14	34.61	0.884	-0.5

Total BMD CV 1.0%, ACF= 1.037, BCF= 1.019, TH= 5.970

WHO Classification: Normal

Figure 17.1 (b) Output from DXA scan showing hip sub-regions for a healthy 53-year-old white female (H: 162.4cm, W:66.8kg)



Body Composition Results

Region	Fat Mass (g)	Lean + BMC (g)	Total Mass (g)	% Fat	%Fat Percentile YN	AM
Total	9028	54704	63732	14.2	14	9

(c)

Figure 17.1 (c) Output from DXA scan showing total body composition analysis of a 33-year-old white male distance runner

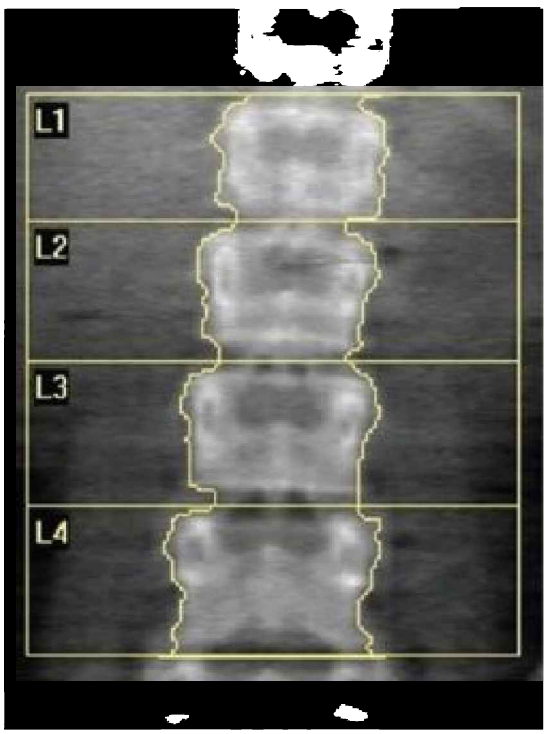
In clinical practice, DXA scanning for bone is limited to the proximal femur and its subregions (femoral neck and greater trochanter), the lumbar spine and the radius. Whole body DXA scans may be performed when evaluation of body composition (i.e. bone-mineral free lean mass and fat mass) is of interest. Benefits of DXA include:

- a low effective dose of radiation (approximately 1 μSv for the hip or spine scan)
- accuracy and precision (coefficient of variation less than 2%)
- efficient scanning duration

- ability to measure bone mass at various sites
- identification of individuals at risk of fracture
- availability of reference data for children and adults.[18]

DXA scan reports provide unadjusted (raw) values of BMD and BMD Z- and T-scores (Fig. 17.2). Age is a major determinant of BMD, thus unadjusted values are useful when comparing values between individuals of the same age and sex. To help clinicians interpret BMD results, they are reported as Z-scores—standard deviations (SD) compared with the normal data for those of the same age as the patient—and T-scores—standard deviations related to a young adult.

Page 247



DXA Results Summary:

Region	Area (cm^2)	BMC (g)	BMD (g/cm^2)	T sco
L1	10.43	7.95	0.762	-2
L2	11.59	8.71	0.752	-2
L3	13.19	9.19	0.696	-3
L4	15.71	8.51	0.542	-4
Total	50.92	34.35	0.675	-3

Total BMD CV 1.0%, ACF = 1.022, BCF = 0.994, TH = 5.772
WHO Classification: Osteoporosis
Fracture Risk: High

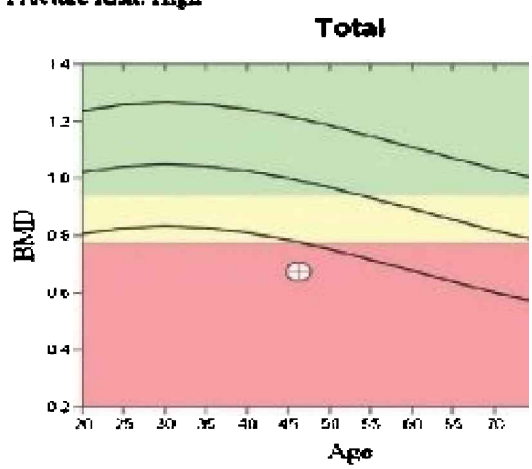


Figure 17.2 DXA scan of the lumbar spine from a 46-year-old Caucasian woman with osteoporosis (H:149.6cm, W:39.1kg). Figures demonstrate raw values for BMD, T-score, Z-score and reference curve for age-graded BMD (normal = green, low bone density = yellow, osteoporosis = red)

T-scores are the most commonly used clinical outcome measure. Osteoporosis is defined by the World Health Organization (WHO) as a T-score < -2.5. This refers to an individual with BMD 2.5 standard deviations below that of the average 30 year old. T-scores for femoral neck BMD can be combined with other clinical risk factors such as age, body size and fracture history to determine an individual's 10-year probability of hip fracture using the FRAX® algorithm (www.sheffield.ac.uk/FRAX/in

dex.aspx).[19] Importantly, T-scores should not be used to evaluate children who have not reached peak bone mass. This occurs in females at approximately age 15–17 years and males at age 16.5–18.5 years, on average.[20, 21]

When using DXA to monitor the bone response to exercise intervention (i.e. before and after DXA scans), clinicians should be aware of the magnitude of change required to be statistically significant (least significant change, LSC). A change of <2% in BMD should be considered 'no change' from a clinical perspective.

The reader whose clinical work involves DXA on a regular basis will be aware of the limitations of the method. We refer the interested reader to the open access paper by Professors Blake and Fogelman for a balanced discussion.[18]

Beyond DXA—contemporary tools that measure bone's response to physical activity

Contemporary imaging tools such as peripheral quantitative computed tomography (pQCT) and high-resolution peripheral quantitative computed tomography (HR-pQCT, Fig. 17.3) characterise bone in more detail than DXA. Peripheral QCT systems are small purpose-built scanners used to measure cortical and trabecular BMD of the appendicular skeleton at a resolution of 0.2–1.0 mm.[22] Common measurement sites include distal and shaft sites of the tibia and radius, where single 2.3 mm thick bone cross-sections are imaged to derive outcomes such as total bone cross-sectional area (mm^2), cortical thickness (mm) and cortical and trabecular BMD (g/cm^3).

https://www.sciencedirect.com. Due to rights and permissions restrictions, this content cannot be reproduced in a digital format. The content is available in the print edition at page 248.

Figure 17.3 Peripheral quantitative computed tomography (QCT) scans. (a) raw image of a cross-section of the tibia (cortical bone) (b) image prepared to allow calculations of bone strength
MACDONALD ET AL. (2009).39

Estimates of bone strength can be obtained by combining bone geometry and BMD measures into a bone strength index (BSI) at distal sites or a strength-strain index (SSI) at shaft sites.[23] These measures allow investigators to see where bone has been laid down in response to exercise. Bone will adapt anatomically (i.e. on a particular surface, at a particular location in bone—not equally along the whole bone). Furthermore, cortical bone and trabecular bone respond differently to load, which can be observed using pQCT and HR-pQCT.

Research is needed to establish the clinical utility of pQCT and HR-pQCT and establish standard image acquisition and analysis protocols.

MAXIMISING BONE HEALTH DURING ADOLESCENCE AND EARLY ADULTHOOD

There are current guidelines to recommend exercise for the prevention and management of osteoporosis across the lifespan.[1, 3, 24] These are based on of randomised controlled trials conducted in both children and adults. Childhood and adolescence are crucial times when the adoption of lifelong behaviours including physical activity can help prevent osteoporosis in later life.[25] During the two years of peak linear growth (11–13 years of age in girls and 12–14 years in boys, on average), more than one quarter of adult bone mass is gained.[26] Further, bones tend to reach peak density (strength) by the end of adolescence. This means bone mass, size and strength all reach their plateau during the late teens and early twenties (Fig. 17.4).[21, 27]

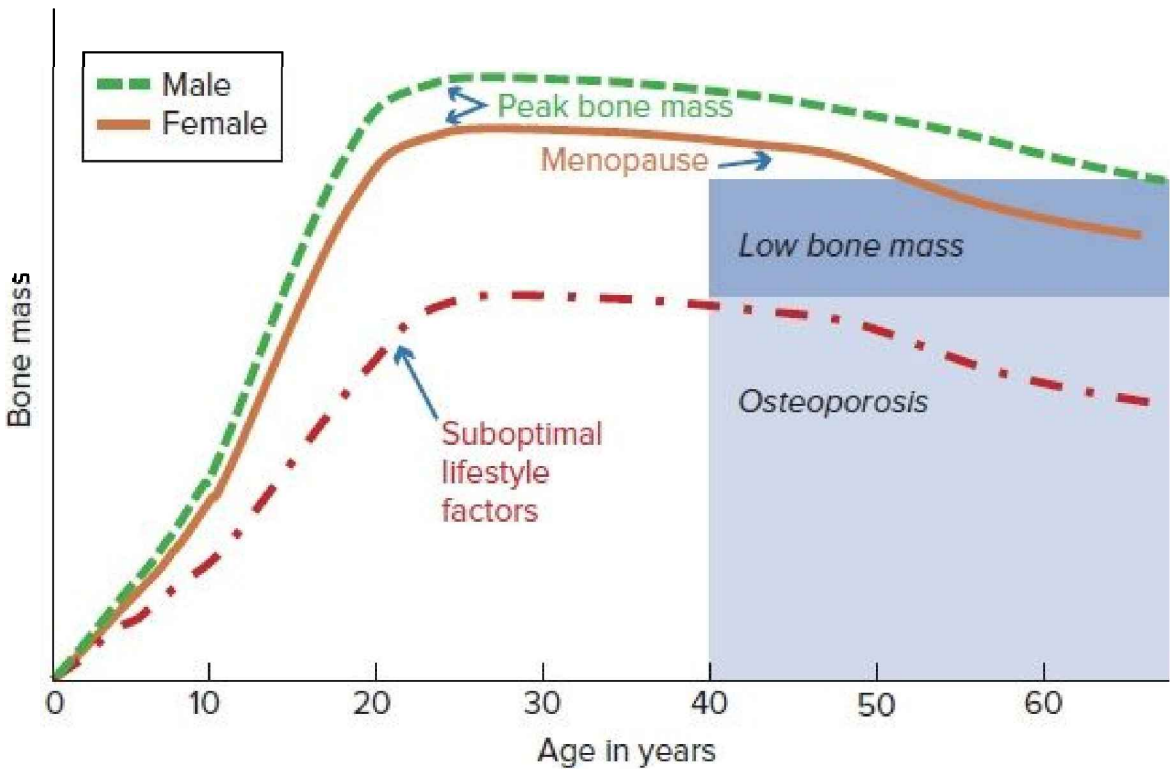


Figure 17.4 Bone mass across the lifespan with optimal and suboptimal lifestyle choices.
REPRINTED BY PERMISSION FROM SPRINGER NATURE: OSTEOPOROSIS INTERNATIONAL 27(4):1281-386, THE NATIONAL OSTEOPOROSIS FOUNDATION'S POSITION STATEMENT ON PEAK BONE MASS DEVELOPMENT AND LIFESTYLE FACTORS: A SYSTEMATIC REVIEW AND IMPLEMENTATION RECOMMENDATIONS, WEAVER CM, GORDON CM, JANZ KF, ET AL. COPYRIGHT 2016[28]

intervention

Action Schools! BC (AS! BC) was a school-based physical activity intervention implemented in British Columbia, Canada that included a bone-loading component. As an active school model, AS! BC provided tools for schools and teachers to increase physical activity opportunities for children throughout the day.[37] The main bone-loading program within AS! BC, 'Bounce at the Bell', required students to perform three daily episodes of 3-minute jumping activities; this was repeated four times per week during a 16-month intervention period.[38, 39] The classroom component of AS! BC encouraged teachers to deliver an additional 15 min/day of classroom-based physical activity, which could involve weight-bearing activities such as skipping. The results, shown in Table 17.1, demonstrate signs of enhanced bone strength accrual at the femoral neck (5%, as estimated with hip structure analysis) among girls in the most compliant schools, when compared with a control group of peers and against expected bone mineral increases for their age group.[40] Boys demonstrated an increased bone mass accrual at the lumbar spine and bone strength accrual at the tibial midshaft. At the tibia, exercising boys gained more strength in regions of the bone cross-section, where bending loads would theoretically be greatest during jumping.[41]

Page 249

Table 17.1 Study results demonstrating baseline data and changes between control and intervention groups for a school-based physical activity model

Page 250

	BOYS				GIRLS			
	Control (n = 62)		Intervention (n = 151)		Control (n = 55)		Intervention (n = 142)	
	Baseline	Change (95% CI)	Baseline	Change (95% CI)	Baseline	Change (95% CI)	Baseline	Change (95% CI)
Age at baseline (years)	10.3 (0.7)	–	10.2 (0.5)	–	10.2 (0.5)	–	10.2 (0.6)	–
Age at follow-up (years)	11.4 (0.6)	–	11.4 (0.6)	–	11.4 (0.5)	–	11.4 (0.6)	–
No. Asian/Caucasian/other	32/19/11	–	85/52/14	–	30/19/6	–	78/45/19	–
Maturity offset at follow-up	-1.9 (1.2)	–	-2.2 (1.5)	–	-0.54 (0.64)	–	-0.50 (0.68)	–
Height (cm)	141.7 (6.9)	6.7 (6.3, 7.1)	141.5 (7.4)	6.9 (6.5, 7.2)	139.7 (6.7)	8.2 (7.7, 8.7)	141.0 (7.5)	7.5 (7.2, 7.8)
Sitting height (cm)	75.0 (3.5)	2.9 (2.5, 3.3)	74.2 (3.6)	2.9 (2.6, 3.2)	73.5 (3.4)	4.2 (3.8, 4.5)	74.4 (3.8)	3.5 (3.3, 3.8)
Weight (kg)	40.7 (10.2)	6.3 (5.5, 7.1)	37.4 (9.7)	5.6 (5.2, 6.0)	33.8 (6.5)	6.4 (5.6, 7.1)	36.1 (8.4)	6.0 (5.6, 6.5)
TB lean mass (kg)	26.8 (4.6)	4.3 (3.9, 4.8)	25.8 (3.8)	4.1 (3.8, 4.4)	23.2 (3.9)	4.8 (4.3, 5.2)	24.2 (4.1)	4.3 (4.0, 4.6)
TB fat mass (kg)	11.8 (6.2)	1.6 (1.1, 2.2)	9.6 (6.0)	1.1 (0.7, 1.4)	8.8 (3.8)	1.1 (0.7, 1.6)	10.0 (4.9)	1.1 (0.8, 1.4)
Long jump (cm)	132.6 (19.4)	6.4 (2.6, 10.2)	133.5 (17.2)	10.2 (7.8, 12.6)	121.1 (15.1)	3.7 (0.4, 7.0)	121.0 (14.0)	9.9 (7.3, 12.4)
Vertical jump (cm)	28.2 (5.2)	2.4 (1.2, 3.7)	27.8 (5.7)	4.2 (3.3, 5.2)	25.3 (5.3)	3.3 (2.0,	25.2	3.4 (2.5,

						4.6)	(4.6)	4.2)
Average PA score (/5)*	2.7 (0.4)	–	2.8 (0.4)	–	2.6 (0.3)	–	2.5 (0.5)	–
Average load time (hours/week)*	6.6 (3.9)	–	6.9 (4.2)	–	4.1 (3.2)	–	4.2 (3.2)	–
Average dietary calcium (mg/day)*	930[460]	–	937[432]	–	797[363]	–	894[467]	–

SD = standard deviation
CI = confidence interval
PA = physical activity
Means, SD, CI were determined without accounting for clustering.
Values are mean (SD) for baseline and mean (95% CI) for change (unless otherwise indicated).
* Physical activity and dietary calcium variables are the average of 5 reports.
REPRINTED BY PERMISSION FROM SPRINGER NATURE: OSTEOPOROSIS INTERNATIONAL 19: 1445, 'DOES A NOVEL SCHOOL-BASED PHYSICAL ACTIVITY MODEL BENEFIT FEMORAL NECK BONE STRENGTH IN PRE- AND EARLY PUBERTAL CHILDREN?', H. M. MACDONALD, S. A. KONTULAINEN, M. A. PETIT ET AL, COPYRIGHT 2008

This period of peak adolescent growth and bone accrual provides a critical window of opportunity when weight-bearing exercise or physical activity has its greatest influence on bone mass and strength.[29– 32] School-based studies, with data obtained from large, diverse groups of children, indicate that short bouts of high-impact physical activity during adolescence enhance bone mass and strength accrual (see box 'Action Schools! BC' and Table 17.1 for an example of an effective intervention).[32] Participation in recreational physical activity and competitive sport during childhood also benefits bone accrual. Children and youth who participate in more leisure-time physical activity, particularly at a vigorous intensity, have greater bone mass and stronger bones than their less active peers.[26, 33–36]

Interventions such as those used in AS! BC increase the feasibility of wide-scale physical activity programs. Programs that target bone health in children and youth may be incorporated into the regular physical education curriculum. Further studies, including Larsen et al. (2017),[42] demonstrated children who participated in small-sided ball games (e.g. 3-on-3) and circuit strength training over 10 months gained more total body aBMD and leg BMC, as compared with children in control schools (Table 17.2).

Table 17.2 RCT examples of school-based exercise programs for children and youth that demonstrated improved bone mineral accrual

Study	Intervention	
Larsen et al. (2017)[42]	Small-sided ball games Circuit strength training	3 times per week for 40 min; 3-on-3 soccer, basketball or floorball 3 times per week for 40 min; 30 s all-out exercise followed by 45 s rest. 6–10 stations of plyometric and strength exercises: jumps, sit-ups, push-ups, as well as static strength training using upper and lower body and core. Other half of period playing games.
Macdonald et al.	AS! BC program,	5 times per week for 15 min; variety of activities: skipping, dancing, circuits, simple resistance exercise 3 times per day, 4 times per week, ~3 min: 5–12 countermovement or side-to-side jumps per session

(2007)[39–41]	classroom action Bounce at the Bell	performed in the classroom
Morris et al. (1997)[43]	Strength-building circuit	3 times per week for 30 min. 10 exercise stations, 1 min per station; progressive increases from one set of 10 reps to three sets: arms (biceps, triceps), chest (pectoralis major), back (latissimus dorsi, trapezius), trunk, shoulder (deltoids), abdominals and legs (quadriceps, hamstrings, gastrocnemius, soleus)

Young athletes such as gymnasts, who experience ground reaction forces greater than 10 times their body weight, consistently demonstrate greater bone strength (by pQCT) in the upper and lower limbs as compared with their non-gymnast peers.[44, 45] Similar sport-related benefits in bone mass and strength are also evident in young athletes in other weight-bearing sports including tennis,[46] running[47] and soccer.[48] Importantly, these sport-related benefits in bone mass and strength are optimised when training begins during this critical window of opportunity in pre- and early puberty.[14, 49] Further, athletes who begin training during childhood may maintain their bone mass and strength advantage well into adulthood, even after a significant period of detraining (see Case study).[16]

A case for caution

While the osteogenic potential of weight-bearing exercise is not disputed, high levels of exercise combined with inadequate energy intake can compromise bone health,[51, 52] particularly in girls who experience menstrual dysfunction (see Case study 'Bobby Clay'; see also Chapter 29 for a discussion on relative energy deficiency in sport, RED-S). Clinicians need to be alert to symptoms of disordered eating,[53] particularly anorexia nervosa, which negatively influences all aspects of bone health including bone turnover, BMD and bone strength.[54]

PRACTICE PEARL

RED-S, although observed more commonly in females, can affect both sexes. Males presenting with hypogonadism should be monitored and advised on the risks to their future bone health accordingly.

At the other end of the activity spectrum, many youths may not be reaching their bone health potential due to a lack of physical activity and increasing sedentary behaviours. Today's youth spend most (60%) of their day sedentary (defined as <1.5 metabolic equivalents, or METs).[55] Thus, clinicians should encourage their young patients to participate in recommended levels of moderate to vigorous physical activity (MVPA) (i.e. 60 minutes per day of MVPA with muscle and bone strengthening activities at least 3 days per week) while limiting sedentary time to no more than 2 hours each day.[56]

CASE STUDY

94-year-old former Major League Baseball pitcher

Professor Stuart Warden of Indiana University studied a 94-year-old former Major League Baseball (MLB) pitcher who began throwing at age 6 and threw for 33 years.[50] The former player had detrained (retired) 55 years prior to undergoing bone assessment. During his career, he pitched with his non-dominant arm (due to a reported need for left-handed pitchers); thus, contralateral differences between throwing and non-throwing arms were attributed to the mechanical demands of throwing, not to arm dominance. Peripheral QCT was used to assess bone structure, density and strength at the midshaft of his humerus (Fig. 17.5). Despite no differences in cortical bone mineral content between arms, his throwing arm was 14% larger (CSA) and 15% stronger (polar moment of inertia), compared to his non-throwing arm. Thus, even after five decades of detraining, the influence of physical activity performed in his youth and early adulthood appears to have conferred lifelong benefits for his bone size and strength.

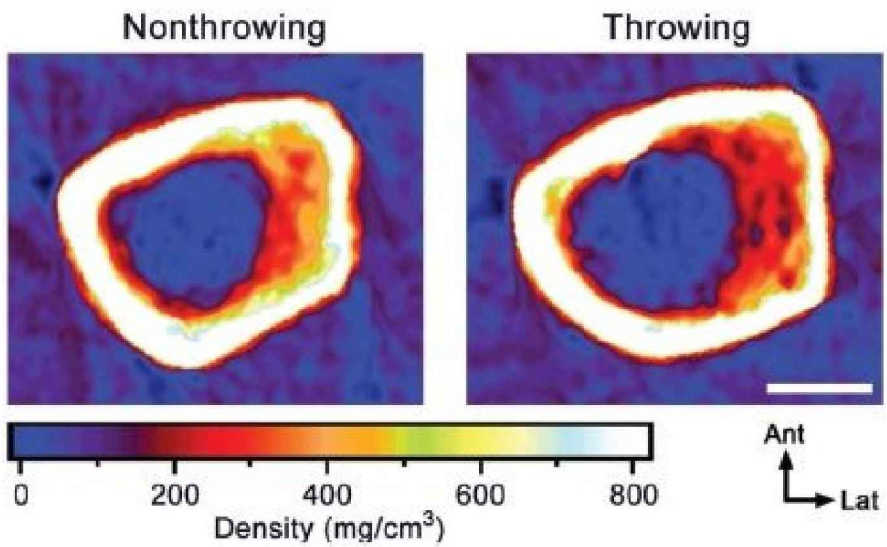


Figure 17.5 Peripheral QCT image of the mid-humerus in the non-throwing/dominant arm and throwing/non-dominant arm of a 94-year-old former baseball pitcher. The subject's throwing arm is significantly larger in cross-sectional area and medullary canal area compared to the non-throwing arm, despite similar cortical thickness. Since mechanical strength of the humerus midshaft scales exponentially with the distribution of bone material from the neutral axis, the throwing arm is substantially stronger, even with the same amount of bone material as the non-throwing arm
'S. J. WARDEN AND S.M. MANTILA ROOSA, 'PHYSICAL ACTIVITY COMPLETED WHEN YOUNG HAS RESIDUAL BONE BENEFITS AT 94 YEARS OF AGE: A WITHIN-SUBJECT CONTROLLED CASE STUDY', J MUSCULOSKELET NEURONAL INTERACT 2014; 14(2):239-243, FIGURE 1

PRACTICE PEARL

Physical activity levels decline precipitously during the teenage years. This is a key period for promoting healthy lifestyle behaviours and improved bone health.

CASE STUDY

Bobby Clay, British athletics—osteoporosis

'Each time something breaks, I feel another part of who I am disappear.'

Bobby Clay (Fig. 17.6) is a middle-distance runner for Great Britain who won gold in the 1500 metres at the European Juniors in 2015. However, years of high training volume and insufficient nutrition led to symptoms such as an absence of menstruation (amenorrhoea). Bobby had completed a successful injury-free summer season when she fractured her foot while swimming, which led to her seeking medical attention.

Figure 17.6 Bobby Clay, after winning gold in the 1500 metres at the 2015 European junior championships in Eskilstuna, Sweden
GETTY/JOOSEP MARTINSON

Diagnosis

Osteoporosis was diagnosed by DXA, following her initial fracture. She was 20 years old.

Treatment plan

Improved nutrition and hormone replacement therapy (HRT) were recommended to regulate menstruation.

Conclusion

The absence of menstruation resulted in reduced oestrogen and increased bone resorption. This is a symptom of an energy deficit and relates to overtraining in elite athletes (RED-S, see Chapter 29). Clinicians should discuss menstruation and training with young female athletes, their parents and coaches.

EXERCISE PRESCRIPTION FOR BONE HEALTH IN MIDDLE-AGED AND OLDER ADULTS—STRATIFIED BY FRACTURE RISK

After age 40, bone mass declines by approximately 0.5% each year, irrespective of sex or ethnicity, and significant age-related declines in bone structure and strength are also evident in women and men.[57–59] Thus, the primary role of exercise is to maintain adult bone mass and strength, attenuating bone loss.

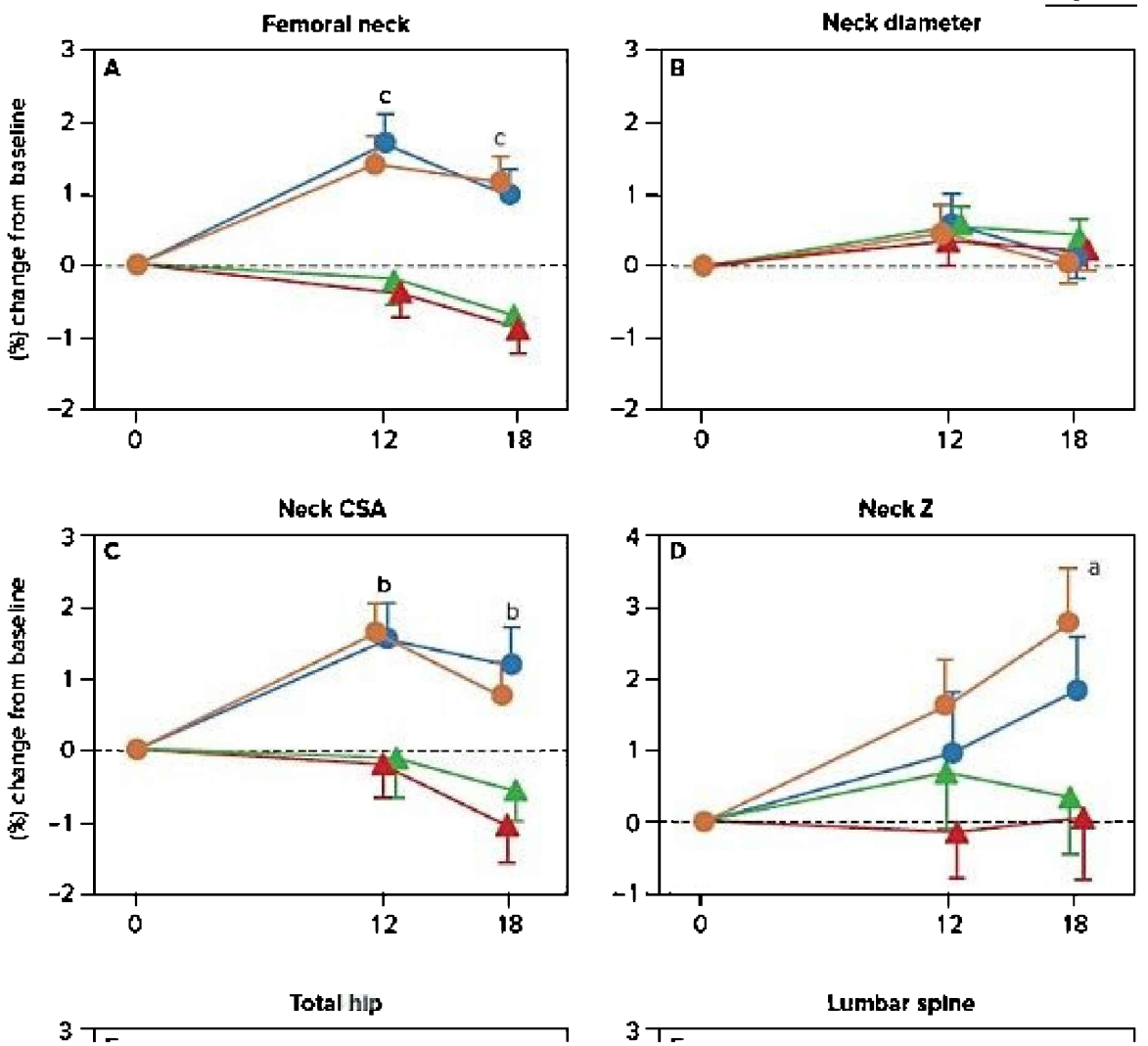
Current recommendations[3, 4, 60, 61] are based on data that show moderate- to high-impact weight-bearing activities and high-intensity resistance training will maintain (or slightly increase) bone mass in middle-aged women and men. Such activity may prevent bone loss in older adults. While exercise-related gains in bone mass in adults are small (1–3%), even these small gains or attenuation of age-related bone loss may reduce fracture risk. For a thorough review of this evidence, most of which focuses on DXA-derived bone mass, the reader is directed to systematic reviews that focus on pre- and postmenopausal women[62–68] and men.[69, 70]

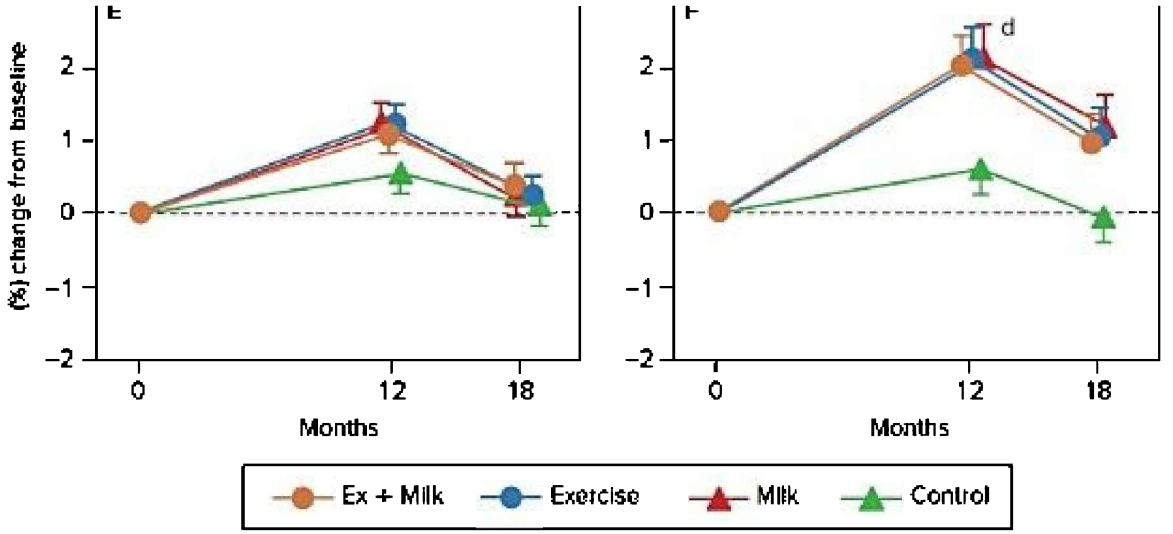
When prescribing exercise to a middle-aged or older adult to target bone health, clinicians should first consider the individual's current bone health (e.g. BMD by DXA), together with risk factors for falls and fracture.[4] Common risk factors may include age, frailty, sarcopenia, family history of osteoporosis, history of fracture or falls.

In their recent position statement for Exercise and Sport Science Australia, Beck et al. (2016) outlined exercise prescription guidelines based upon best available evidence for individuals according to their level of risk for a low-trauma fracture (see Table 17.3).[4] Balance training is recommended in addition to impact loading and resistance training, particularly in individuals who are at moderate or high risk for fracture. Chapter 31 discusses physical activity strategies that will help prevent falls in older people. Recommended weight-bearing activity involves loads 2–4 times body weight, depending on the risk group. Thus, current exercise prescription guidelines acknowledge there is limited evidence to support a protective effect of walking or other low-impact activities on aBMD, particularly at the lumbar spine.[9, 65] Across all groups, exercise programs should be accompanied by sufficient calcium and vitamin D, while also considering comorbidities and the safety of participants.[4]

Exercise prescription for low-risk individuals

Low-risk individuals have normal BMD (T-score above -1.0 SD), function well in daily life and have no clinical risk factors for falls or fracture. Exercise prescription for this group aims to maximise bone mass and strength and improve muscle strength through a combination of high-impact activities (e.g. multidirectional jumps and hops) and progressive resistance training targeting major muscle groups and back extension. For example, this type of combined exercise program increased hip BMD (measured on DXA) by almost 3% and spine BMD by 1% in women aged 20–35 who participated in a 2-year program.[73] A similar multimodal program for older men aged 50–79 years (described below) increased femoral neck bone strength and lumbar spine trabecular BMD by 2%.[74] (Fig. 17.7) The physical activity training provided a 25% improvement in leg muscle strength, a 0.6 kg increase in total body lean mass and a 1.1 kg reduction in fat mass.[75]





Mean unadjusted percentage changes (±SE) from baseline in femoral neck aBMD (A), diameter (B), cross-sectional area (CSA) (C), and section modulus (D), and total hip (E) and lumbar spine (L¹–L4) aBMD (F) according to treatment group. No exercise-by-calcium-vitamin D_3 interactions were detected [a], $P < 0.05$, [b], $P < 0.01$, [c], $P < 0.001$ for main effect of exercise vs. no exercise. [d], $P < 0.01$ ex + milk, exercise, milk > controls.

Figure 17.7 Results of study into the effects of physical activity and calcium intake on bone health
SONJA KUKULJAN ET AL. INDEPENDENT AND COMBINED EFFECTS OF CALCIUM-VITAMIN D3 AND EXERCISE ON BONE STRUCTURE AND STRENGTH IN OLDER MEN: AN 18-MONTH FACTORIAL DESIGN RANDOMIZED CONTROLLED TRIAL. *THE JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM* (2011) 96 (4): 955-963, DOI: 10.1210/JC.2010-2284. REPRODUCED BY PERMISSION OF OXFORD UNIVERSITY PRESS ON BEHALF OF THE ENDOCRINE SOCIETY

Adherence to exercise programs may prove challenging in working adults, due to competing life demands.[76] Thus, clinicians may consider bone-loading programs that can be conducted with simple exercises spread throughout the day. One researched example consisted of five bouts of 10 vertical jumps (approximately 3 times body weight; landing with flexion of the ankles, knees and hips followed by heel strike; walking on the spot between bouts), 6 days/week for 5 months. This regime increased hip BMD by almost 3% in premenopausal women (aged 38 years, on average).[77]

Effective multimodal exercise programs for low-risk individuals

Program 1

American women aged 20–35 years from two universities trained three times each week for 1 hour with the first and last 10 minutes of each class for warm-up and cool-down activities.[73] The remaining time was spent in one of three different types of exercise.

- *Type 1:* Circuit of exercise stations and high-impact aerobic activities (1–2 minutes at each): push-ups, sit-ups, arm curls with dumbbells, military presses with dumbbells. Special emphasis was

placed on augmenting the gluteus maximus, quadriceps, erector spinae and shoulder girdle muscles. Lifts were from ground level and moderate weights were used (3–12 lb (1.3–5.4 kg) dumbbells, 16–36 lb (2.7 –16.3 kg) barbells and 0.5–2.5 lb (0.2 – 1.1 kg) ankle/wrist weights). Participants progressively increased their weight load over the 2 years.

- *Type 2:* Similar strengthening exercises as type 1 but the class participated in unison rather than at separate stations and with little aerobic activity after the initial warm-up.
- *Type 3:* Vigorous, high-impact aerobic workout to get heart rate up to 70–85% of maximum. Step benches were added in year 2.

This program incorporated both resistance training and impact exercise, and demonstrated increases in BMD in premenopausal women.

Program 2

Healthy Australian men aged 50–79 years performed three supervised training sessions per week for 18 months in local community centres.[75] Each session lasted 60–75 minutes with the following activities:

- 5–10 minutes of warm-up
- 6–8 moderate- to high-intensity progressive resistance training exercises
- 3 moderate-impact weight-bearing exercises interspersed with moderate- to high-impact weight-bearing exercises.

Resistance training

This combined upper and lower body machine and free weights with core strength exercises.

Frequency and intensity: For the first 12 weeks, 3 sets of 15–20 repetitions at 50–60% of 1 RM; thereafter, volume was prescribed at two sets of 8–12 reps: first, a warm-up set at 60–65% of 1 RM; and second, a single training set at 60–70% of 1 RM for the first 4 weeks of each 12-week training cycle and 80–85% of 1 RM for the remaining 8 weeks. During the last 6 months exercises switched from maximal strength to high-velocity power-based training (e.g. squats or leg presses, lunges, hip abduction/adduction, seated row/latissimus pull-downs, back extension).

Weight-bearing exercises

Frequency: Three sets of 10 exercises, which progressed to 20 repetitions, interspersed between resistance training exercises.

Intensity: Peak ground reaction forces varied from 1.5–9.7 times body weight.

Type: Single- and double-foot landings, bench stepping and jumping off 15 cm and 30 cm benches. Activities were varied or progressed in magnitude, rate and direction by increasing the height of the jumps and/or including more complex movement patterns.

This RCT was designed to assess the benefits of fortified milk, exercise or the two combined against a control group. It demonstrated that older, community-dwelling men can safely participate in a multicomponent exercise program and achieve significant bone health benefits using physical activity interventions *without* the need for supplementation.

Individuals who lack access to equipment or do not wish to join structured programs can be encouraged to participate in regular leisure-time physical activity to target bone

health. Men who are more physically active in their leisure time have greater BMD[78] and bone strength,[79] as compared with less active men. Similarly, women aged 36–57 years who take part in MVPA were positively associated with a higher femoral neck BMD compared to less active peers.[80]

Exercise prescription in moderate-risk individuals

Moderate-risk individuals are those women and men with low bone mass (T-score -1.0 to -2.5 SD) and/or risk factors for fracture (described above). Exercise prescription in this group aims to preserve or improve bone mass and strength and improve muscle strength, power and balance.[4] Specifically, combination exercise programs that involve high-impact weight-bearing activity and progressive resistance training are recommended. The intensity of the impact activities may be moderate in nature compared with those undertaken by low-risk individuals (Table 17.3). The 16-year Erlangen Fitness Osteoporosis Prevention Study (EFOPS) program in Germany (see box) was an example of one combined exercise program designed for early postmenopausal (1–8 years) women at moderate risk for osteoporosis.[81–84] In addition to maintaining BMD at the spine and hip in exercising women, EFOPS reduced risk of major osteoporotic fractures by 60%,[85] similar to the reduction observed in pharmacological trials.[86, 87] Benefits for the exercising women included increased muscle strength and physical fitness, with a reduction in back pain. The study also suggested a reduction in risk factors for heart disease, including lipid levels.[84]

Table 17.3 Exercise prescription for the prevention and management of osteoporosis according to level of risk for fragility fracture.

Page 256

Exercise mode	Exercise components	Low-risk* individuals (prevention of OP)	Moderate-risk** individuals (prevention of OP)	High-risk*** individuals (management of OP and prevention of falls)
Impact loading	Vertical and multidirectional jumping, bounding, hopping, skipping rope, drop jumps and bench stepping. Progress bodyweight (BW) intensity by increasing heights for activities such as bounding and drop jumping, adding weighted vests and changing directions. Impact loading can be interspersed between balance and resistance training exercises.	Intensity: High-impact activities † (>4 × BW), as tolerable Frequency: 4–7 d/wk Sets/repetitions: 50 jumps per session (3–5 sets of 10–20 repetitions with 1–2 min rest between sets)	Intensity: Moderate- to high-impact activities†† (>2 × BW), as tolerable Frequency: 4–7 d/wk Sets/repetitions: 50 jumps per session (3–5 sets of 10–20 repetitions with 1–2 min rest between sets)	Intensity: Moderate-impact activities ††† (2–3 × BW), within the limits of pain, increasing as tolerated. Frail individuals will require a period of progressive resistance training (PRT) to develop adequate strength to perform some impact activities. Frequency: 4–7 d/wk Sets/repetitions:

				Aim to work up to 50 repetitions over time (5 sets of 10 repetitions with 1–2 min rest between sets).
Resistance training (RT)	8 exercises per session targeting major muscle groups attached to the hip and spine, including (on a rotating system): weighted lunges, hip abduction/adduction, knee extension/flexion, plantarflexion/dorsiflexion, back extension, reverse chest flys and abdominal exercises, or a smaller number of compound movements such as squats and deadlifts.	Intensity: High to very high (80–85% of 1 RM; ≥ 16 on Borg 6–20 point RPE scale or 'very hard')¥ Frequency: 2 d/wk Sets/repetitions: 2–3 sets of 8 repetitions Consider including high velocity (rapid) RT exercises to enhance muscle power and function. Avoid deep forward spine flexion. Training in technique and supervision is essential.	Intensity: High to very high (80–85% of 1 RM; ≥ 16 on Borg 6–20 point RPE scale or 'very hard')¥ Frequency: 2 d/wk Sets/repetitions: 2–3 sets of 8 repetitions Consider including high velocity (rapid) RT exercises to enhance muscle power and function. Avoid deep forward spine flexion. Training in technique and supervision is essential.	Intensity: High to very high (80–85% of 1 RM; ≥ 16 on Borg 6–20 point RPE scale or 'very hard')¥ Frequency: 2 d/wk Sets/repetitions: 2–3 sets of 8 repetitions Consider including high velocity (rapid) RT exercises to enhance muscle power and function. Avoid deep forward spine flexion. Training in technique and supervision is essential.
Balance training	Standing and moving exercises with gradual reduction in base of support to standing on one foot, perturbing the centre of mass with leaning and reaching then regaining balance with minimal use of support from the upper extremities. E.g. tai chi, single-leg stance, tandem stance, tandem walk, backwards, sideways and crossover walks, circle and pivot turning, figure-of-eight walks, stepping over and avoiding obstacles, walking on uneven surface. Progress by altering surface (foam mats) and reducing base of support, longer or faster steps, heel-and-toe walks, raised arms walk, withdrawing vision during balance tasks and dual tasking (e.g. cognitive tasks such as counting backwards or naming animals, combined with balance activities).	Intensity: Challenging Frequency: Incorporate balance activities where possible into strength and impact elements of the exercise program. Tasks performed with eyes closed should be done in proximity to a railing or other secure support.	Intensity: Challenging Frequency: 4 sessions/wk Sets/repetitions: 30 min of a variety of balance exercises per session; at least 10 s per balance exercise and at least 10 steps forward and back for mobility exercises, increasing as tolerated to longer durations. Could be accomplished within other exercise bouts during the course of a	Intensity: Challenging Frequency: 4 sessions/wk Sets/repetitions: 30 min of a variety of balance exercises per session; at least 10 s per balance exercise and at least 10 steps forward and back for mobility exercises, increasing as tolerated to longer durations. Could be accomplished within other exercise bouts during the course of a

	week. Tasks performed with eyes closed should be done in proximity to a railing or other secure support.	week. Frail individuals should be supervised to prevent falls while performing balance training. Activity should be within reach of secure support (e.g. rails).

* Low-risk = asymptomatic individual with normal BMD (T-score above -1.0 SD) and functional status, and no clinical risk factors for falls or fracture

** Moderate-risk = low bone mass (T-score -1.0 to -2.5 SD) and/or certain clinical or functional risk factors for fracture

*** High-risk = very low bone mass (T-score less than -2.5 SD/osteoporosis) and/or a number of clinical or functional risk factors for fracture

† High-impact activities (>4 × BW) include landings from exertional jumps such as high vertical jumps, star jumps, tuck jumps, and drop landings; including within sports such as volleyball, basketball, gymnastics, ballet, Australian rules football, etc.

† Moderate- to high-impact activities (>2 × BW) include all of the activities listed for the moderate- and high-impact categories (adapted from Weeks and Beck71).

††† Moderate-impact activities (2–3 × BW) include running, stride jumps, jump rope, side steps, highland-type dancing, jump take offs and hops; including within sports such as racquet sports, track events, most field sports and martial arts that include frequent jumps.

¥ Rate of progression of RT for novice exercisers should be 50%, 60%, 70% and 80% of 1 RM for the first 4 sessions to ensure correct technique and appropriate muscle conditioning. Intensity and rate of progression will vary based on level of individual risk within each category.

Challenging = attempting a level not yet mastered (i.e. the entire time, distance or activity cannot be completed without losing balance)

Abbreviations: BW body weight; OP osteoporosis; RM repetition maximum, the maximum weight that can be lifted once; RPE rating of perceived exertion (Borg 6–20 point scale categories of RPE intensity72).

REPRINTED FROM *JOURNAL OF SCIENCE AND MEDICINE IN SPORT*, 20(5), BECK BR, DALY RM, SINGH MAF, ET AL. EXERCISE AND SPORTS SCIENCE AUSTRALIA (ESSA) POSITION STATEMENT ON EXERCISE PRESCRIPTION FOR THE PREVENTION AND MANAGEMENT OF OSTEOPOROSIS, 438-45, 2017, WITH PERMISSION FROM ELSEVIER

Exercise prescription for high-risk individuals

High-risk individuals are those with osteoporosis (T-score less than -2.5 SD), previous fracture(s) and/or multiple risk factors for fracture.[4] Clinicians may confront challenges when prescribing exercise to this group, including modification for mobility or postural concerns and to mitigate the risk of falls and fractures.[94] An expert panel recently recommended that individuals with osteoporosis or osteoporotic vertebral fracture:

1. participate in multicomponent exercise programs that include both resistance and balance training and
2. combine recommended levels of aerobic exercise (e.g. 150–300 minutes per week of moderate-intensity aerobic physical activity or 75–150 minutes per week of vigorous aerobic physical activity) with balance and resistance training.

Based on these recommendations, exercise training workshops for healthcare professionals and exercise practitioners are now offered in Canada (www.bonefit.ca). Importantly, exercise prescription in older adults should consider functional and clinical risk factors for falls and fracture such as age, frailty, sarcopenia, presence of back pain, mobility and vision, among others.[4] A conservative approach to exercise that focuses on muscle function and balance may be required for individuals with these key risk factors.[4]

Most resistance-training protocols designed for high-risk individuals typically involve slow-velocity contractions (2–4 seconds) at a moderate to high percentage of maximal force (80–85% of 1 RM). However, high-velocity resistance training (rapid concentric (lifting phase) movements that maximise movement speed and muscle force), which is safe and effective for improving functional outcomes in older adults,[95] also benefits femoral neck and lumbar spine BMD in postmenopausal women with low bone mass.[96] Exercises may need to be supervised and assessed on a case-by-case basis with those individuals most at risk.

Given the current 'crisis in the treatment of osteoporosis' with respect to pharmacological treatment,[98] clinicians should see elderly women and men as ideal candidates to participate in regular physical activity to promote bone health, among the large number of benefits as outlined in Chapters 1 and 2. Clinicians who have influence in their communities can help advocate for the scaling up of effective interventions. Clinicians can work with local communities to try to overcome barriers to participation, such as feeling isolated and lack of readily accessible transport.[99]

Can physical activity reduce fractures?

It costs drug companies hundreds of millions of dollars to perform a randomised trial designed to demonstrate fracture reduction as an outcome. No government has prioritised such a level of funding for an exercise RCT to demonstrate fracture reduction.[100] There are, however, trials that can make us confident to prescribe exercise with the goal of preventing facture. In Germany, there were fewer fractures among women in an exercise group after 16 years.[85] Mayo Clinic physiatrist Dr Mersheed Sinaki reported lower incidence of vertebral fractures among postmenopausal women who 10 years prior had taken part in a 2-year intervention involving progressive, resistive back-strengthening exercises.[101]

Effective multimodal exercise programs for moderate-risk individuals—Erlangen Fitness Osteoporosis Prevention Study[81, 83, 84]

The EFOPS protocol:

- 2 supervised group classes of 60–65 min per week

- 2 home training sessions of 20–25 min per week
- 49–50 weeks/year throughout 16 years
- Focus on high exercise intensity (i.e. high strain magnitude)

Group classes

- 20–25 minutes of low- and high-impact aerobic dance exercises with heart rates (HR) of 70–85% HR_{max} and peak ground reaction forces (GRF) of ≈ 2–3 × body mass were applied using interval training (i.e. 2–4 min high intensity intermitted by 1–2 min of lower intensity).
- 4 × 15 reps of different multilateral jumping exercises (GRF of ≈ 3–4.5 × body mass) with varying movement velocity and 30 seconds of rest between the jumping sequences were introduced at 6 months.
- One resistance exercise session per week on machines and one session per week using isometric exercises with resistance bands and free weights.
- All main muscle groups were addressed by 12–15 different exercises. Specific emphasis was placed upon lower and upper back strengthening (5 exercises) and hip/lower limb exercises (4–5 exercises).
- After an initial 7-month conditioning phase, an exercise program with 12 weeks of either linearly or non-linearly periodised high-intensity resistance exercise (1–4 sets, 4–12 reps, 70–90% of 1 RM, 2–3 min rest) intermitted by 4–6 weeks of lower intensity but higher volume (2–3 sets, 20–25 reps, 50–55% of 1 RM, 1–2 min rest) was introduced.
- After 3 years, movement velocity was consistently varied during the high-intensity periods, with periods of explosive (concentric phase only), moderate or very slow (up to. (up to 4 seconds concentric-2 second static-4 seconds eccentric) velocity.

Home training

The 20–25 min home training session was introduced after 5 months and included:

- a 5–10 min warm-up sequence with different rope-skipping exercises (80–120 reps)
- intense isometric and dynamic resistance exercises (10 min)
- stretching and flexibility exercises (5 min).

Exercises were extensively practised in the group sessions before the intervention and replaced every 3–6 months with progressions or a varied exercise *dependent on ability.* The complexity, intensity and impact of the exercises were gradually increased up to year 4. During the first 5 years, the individual load prescription was based on 1 RM tests, thereafter on the number of repetitions combined with the rate of perceived exertion (RPE; Borg CR-10 scale). After year 8, the number of high-impact elements during the aerobic dance sequence was reduced in favour of movements with a more challenging character, for static and dynamic balance and general coordination. The complexity and impact of the jumping exercises were reduced (peak GRF ≤ 3–3.5 × body weight) during the last 4 study years. The improvements observed in the exercise group are summarised in Figure 17.8.

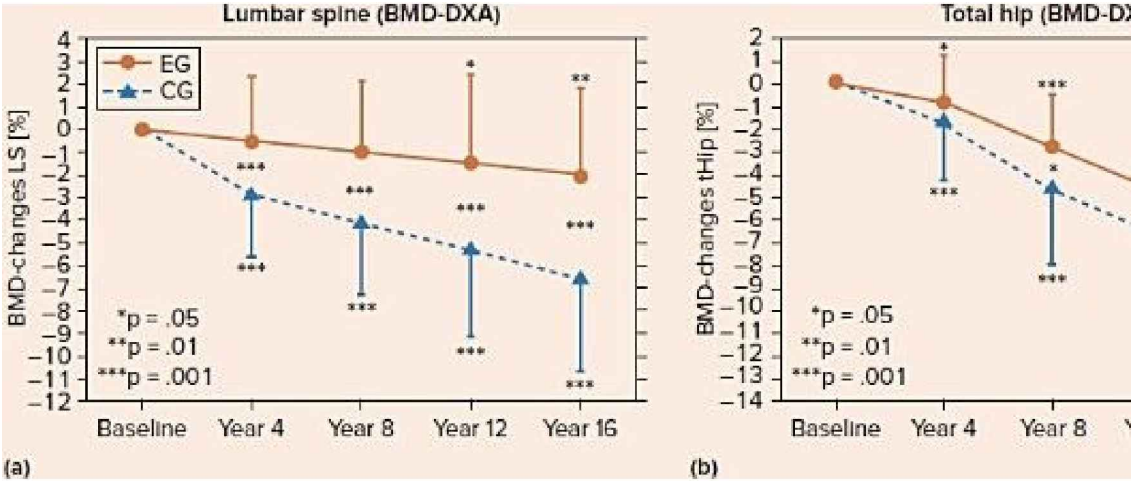


Figure 17.8 Changes in lumbar spine and total hip BMD across the 16-year EFOPS study
DATA FROM EFOPS STUDY: KEMMLER W, ENGELKE K, VON STENGEL S. LONG-TERM EXERCISE AND BONE MINERAL DENSITY CHANGES IN POSTMENOPAUSAL WOMEN--ARE THERE PERIODS OF REDUCED EFFECTIVENESS? JOURNAL OF BONE AND MINERAL RESEARCH. 2016;31(1):215-22 © AMERICAN SOCIETY FOR BONE AND MINERAL RESEARCH

Better Bones and Balance™—the challenge of maintaining active lives in the community

Importantly, there remains a gap between evaluation of effective exercise programs and implementation of these programs at large in the real-world context. This is particularly important since benefits of exercise on BMD are lost after cessation of training.[88, 89] We know of only one program that has proven effective for maintaining BMD and decreasing fall risk in postmenopausal women in a controlled environment[90, 91] that was subsequently translated into the community setting. Better Bones and Balance (BBB) (http://extension.oregonstate.edu/physicalactivity/bbb/) involves lower-body resistance training with weighted vests along with impact and balance exercises. The program began in 1995 and has expanded from Oregon, USA, where the program originated, to neighbouring counties and elsewhere within that state. Certified training for instructors is available. Although participation in BBB in the community setting has not yet proven effective for preventing bone loss in postmenopausal women,[92] the program successfully supports older women to meet physical activity guidelines.[93]

LIFTMOR trial—do not rule out heavy loading—a reminder for individualised exercise prescription

Within the resistance training component of the Too Fit to Fracture guidelines, moderate-intensity exercises (70–80% of 1 RM, 8–15 repetitions) are recommended for individual muscle groups.[94] However, in the recent Australian LIFTMOR (Lifting Intervention For Training Muscle and Osteoporosis Rehabilitation) trial, older women with low bone mass safely participated in challenging exercises like squats and deadlifts (Fig. 17.9).[97] Eight months of supervised high-intensity resistance and impact training (HiRIT) (twice weekly for 30 minutes; 5 sets of 5 repetitions, >85% of 1 RM; deadlift, overhead press and back squat for resistance training and jumping chin-ups with drop landings for impact loading) improved lumbar spine and femoral neck BMD and functional performance (i.e. muscle strength, timed up-and-go test, sit-to-stand test) and reduced kyphosis in exercising women (Fig. 17.10).[97]

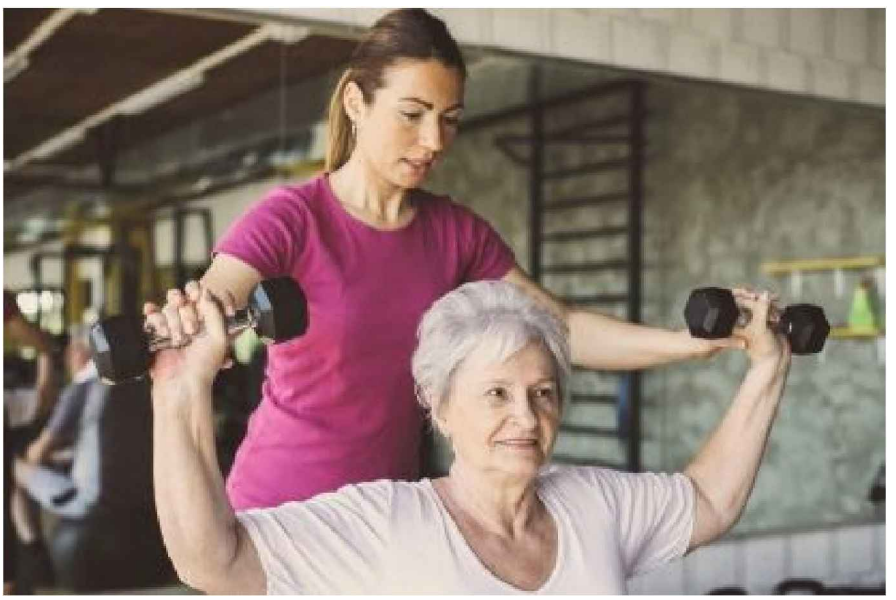


Figure 17.9 Postmenopausal women at moderate to high risk for osteoporotic fracture can safely and feasibly improve their bone mass
LIDERINA/SHUTTERSTOCK

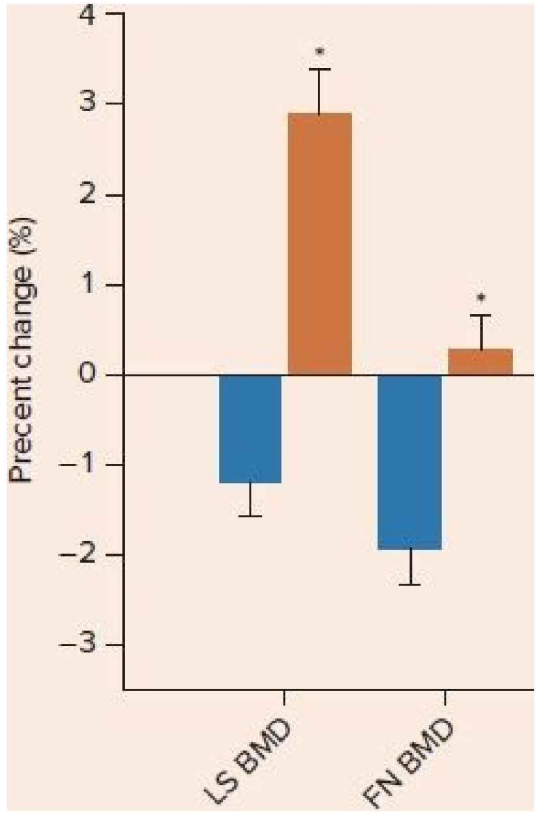


Figure 17.10 LIFTMOR trial showing effects on Lumbar Spine (LS) and Femoral Neck (FN) bone mineral density (BMD) of heavy resistance training

JOHN WILEY AND SONS, JOURNAL OF BONE AND MINERAL RESEARCH, 'HIGH-INTENSITY RESISTANCE AND IMPACT TRAINING IMPROVES BONE MINERAL DENSITY AND PHYSICAL FUNCTION IN POSTMENOPAUSAL WOMEN WITH OSTEOPENIA AND OSTEOPOROSIS: THE LIFTMOR RANDOMIZED CONTROLLED TRIAL', , STEVEN L WATSON, BENJAMIN K WEEKS, LISA J WEIS, ET AL, OCT 4, 2017, VOL 33, ISSUE 2, FIG 2.A P10 © AMERICAN SOCIETY FOR BONE AND MINERAL RESEARCH[17]

This program highlights that, contrary to common assumptions, postmenopausal women at moderate to high risk for osteoporotic fracture can safely and feasibly participate in HiRIT and, in doing so, improve their bone mass. Clinicians who deem that an appropriate level of supervision and patient comprehension is present may consider prescribing this type of exercise program for community-dwelling patients.

Cohort studies indicate that physically active adults have a 20–60% lower risk of hip fracture compared with sedentary adults.[100, 102, 103] Even moderate levels of physical activity (e.g. walking less than 30 min/day) can protect against fragility fractures.[104, 105] Regular physical activity does not, however, appear to protect against vertebral fractures.[102, 103]

Page 260

MASTERS ATHLETES: SPECIAL BONE HEALTH CONSIDERATIONS

I wasn't running very fast, and I was nearing the end of the run. I came off the asphalt onto the grass, and that's when I felt my right leg crack. I'd been feeling a little soreness for a while, so I think I was running on a stress fracture.

Bill Rogers, former men's marathon world record holder, shortly before being diagnosed with osteoporosis aged 56

Older athletes may underestimate their risk of fracture and osteoporosis because they have heard that exercise protects against weakening bones. However, an individual's bones are not protected simply because they are an athlete. There is little evidence that activities with regular loading patterns such as walking, cycling or long-distance running will augment BMD. Older endurance athletes, particularly runners who do not exercise apart from running, may be at increased risk of fracture due to existing low bone strength and density.

Despite a mature skeleton, masters athletes can improve their bone structure and strength with targeted weight-bearing and resistance-training exercises. Coaches and clinicians should specifically encourage older endurance athletes to complement their endurance training with high-impact or resistance-training exercises.

Masters runners

Masters and middle-aged runners with high-impact loading histories (e.g. sprinters) consistently demonstrate stronger bones than their non-active peers. Middle- and long-distance runners also display more favourable bone structure and strength compared with non-active peers; however, the magnitude of bone health advantage scales with training speeds and bone strains (e.g. sprinters > middle-distance > long-distance > sedentary).[106] A recent study of masters sprint athletes in Finland showed that intensive strength, sprint and plyometric training led to 2–3% increases in bone strength.[107]

Masters cyclists

Non weight-bearing sports such as cycling typically do not provide benefits for bone health. Yet, sports injuries and fractures are relatively common in the sport, with hip fractures a serious concern in older cyclists. As athletes of any age can break their hip when falling off a bicycle, older athletes who train in slippery conditions may consider wearing hip protectors over their cycling shorts.

Cyclists should be encouraged to complement their training with short bouts of high-impact, weight-bearing exercise and/or resistance training 2–3 times per week, mimicking principles described by Turner et al.[8]

The effect of cycling on bone health tends to vary based on type of cycling (sprint vs distance) and whether cycling is complemented by weight-bearing exercise. Endurance cyclists have lower bone mass and BMD and are roughly 50% more likely to meet criteria for osteopenia/osteoporosis compared with non-athletes.[108] This phenomenon can be partially mitigated by weight training or impact exercises.[108] Sprint cyclists have greater bone strength at the tibia and radius compared

with non-athletes; sprint cyclists who also engaged in lower-body resistance training had greater tibial bone strength than their fellow sprint cyclists who did not do resistance training.[106]

SUMMARY

- Regular weight-bearing physical activity or exercise is essential to optimising bone mass and strength accrual during childhood and adolescence, maintaining bone mass and strength during adulthood and preventing bone loss in the later years.
- Short bouts of high-impact physical activity enhance bone mass and strength accrual in children and adolescents.
- Multicomponent exercise programs that incorporate both progressive resistance training and impact loading should be recommended to individuals who are at low, moderate or high risk of sustaining an osteoporotic fracture.
- High-intensity resistance training may also offer promise as an effective exercise program for individuals at high risk for fracture.
- Masters athletes, particularly those involved in non-weight bearing sports, should complement their training with impact exercise and resistance training to maintain bone health.

REFERENCES

1. World Health Organization (WHO). Global Recommendations on Physical Activity for Health. Geneva, Switzerland: 2010.
2. Warburton DER, Nicol CW, Bredin SSD. Health benefits of physical activity: the evidence. *CMAJ* 2006; 174(6): 801–9.
3. Kohrt WM, Bloomfield SA, Little KD et al. American College of Sports Medicine Position Stand: physical activity and bone health. *Med Sci Sports Exerc* 2004; 36(11): 1985–96.
4. Beck BR, Daly RM, Singh MAF et al. Exercise and Sports Science Australia (ESSA) position statement on exercise prescription for the prevention and management of osteoporosis. *J Sci Med Sport* 2017; 20(5): 438–45.
5. Burr DB. Muscle strength, bone mass, and age-related bone loss. *J Bone Miner Res* 1997; 12(10): 1547–51.
6. Lanyon LE. Functional strain in bone tissue as an objective, and controlling stimulus for adaptive bone remodelling. *J Biomech* 1987; 20(11–12): 1083–93.
7. Turner CH. Toward a mathematical description of bone biology: the principle of cellular accommodation. *Calcif Tissue Int* 1999; 65(6): 466–71.
8. Turner CH, Robling AG. Designing exercise regimens to increase bone strength. *Exerc Sport Sci Rev* 2003; 31(1): 45–50.

9. Ma D, Wu L, He Z. Effects of walking on the preservation of bone mineral density in perimenopausal and postmenopausal women: a systematic review and meta-analysis. *Menopause* 2013; 20(11): 1216–26.
10. Martyn-St James M, Carroll S. Meta-analysis of walking for preservation of bone mineral density in postmenopausal women. *Bone* 2008; 43(3): 521–31.
11. Erlandson MC, Kontulainen SA, Chilibeck PD et al. Former premenarcheal gymnasts exhibit site-specific skeletal benefits in adulthood after long-term retirement. *J Bone Miner Res* 2012; 27(11): 2298–305.
12. Nikander R, Kannus P, Rantalainen T et al. Cross-sectional geometry of weight-bearing tibia in female athletes subjected to different exercise loadings. *Osteoporos Int* 2010; 21(10): 1687–94.
13. Nilsson M, Ohlsson C, Mellström D et al. Sport-specific association between exercise loading and the density, geometry, and microstructure of weight-bearing bone in young adult men. *Osteoporos Int* 2013; 24(5): 1613–22.
14. Kontulainen S, Sievänen H, Kannus P et al. Effect of long-term impact-loading on mass, size, and estimated strength of humerus and radius of female racquet-sports players: a peripheral quantitative computed tomography study between young and old starters and controls. *J Bone Miner Res* 2003; 18(2): 352–9.
15. Heinonen A, Sievänen H, Kannus P et al. Site-specific skeletal response to long-term weight training seems to be attributable to principal loading modality: a pQCT study of female weightlifters. *Calcif Tissue Int* 2002; 70(6): 469–74.
16. Warden SJ, Mantila Roosa SM, Kersh ME et al. Physical activity when young provides lifelong benefits to cortical bone size and strength in men. *Proc Natl Acad Sci U S A* 2014; 111(14): 5337–42.
17. Marshall D, Johnell O, Wedel H. Meta-analysis of how well measures of bone mineral density predict occurrence of osteoporotic fractures. *BMJ* 1996; 312(7041): 1254–9.
18. Blake GM, Fogelman I. The role of DXA bone density scans in the diagnosis and treatment of osteoporosis. *Postgrad Med J* 2007; 83(982): 509–17.
19. Kanis JA, Borgstrom F, De Laet C et al. Assessment of fracture risk. *Osteoporos Int* 2005; 16(6): 581–9.
20. Crabtree NJ, Arabi A, Bachrach LK et al. Dual-energy X-ray absorptiometry interpretation and reporting in children and adolescents: the revised 2013 ISCD Pediatric Official Positions. *J Clin Densitom* 2014; 17(2): 225–42.
21. Baxter-Jones ADG, Faulkner RA, Forwood MR et al. Bone mineral accrual from 8 to 30 years of age: an estimation of peak bone mass. *J Bone Miner Res* 2011; 26(8): 1729–39.
22. Manske S, Macdonald H, Nishiyama K et al. Clinical tools to evaluate bone strength. *Clin Rev Bone Miner Metab* 2010; 8(3): 122–34.
23. Kontulainen SA, Johnston JD, Liu D et al. Strength indices from pQCT imaging

predict up to 85% of variance in bone failure properties at tibial epiphysis and diaphysis. *J Musculoskelet Neuronal Interact* 2008; 8(4): 401–9.

24. International Osteoporosis Foundation. Exercise recommendations. https://www.iofbonehealth.org/exercise-recommendations.
25. Bailey DA, McCulloch R. Osteoporosis: are there childhood antecedents for an adult health problem? *Can J Pediat* 1992; 4(5): 130–4.
26. Bailey DA, McKay HA, Mirwald RL et al. A six-year longitudinal study of the relationship of physical activity to bone mineral accrual in growing children: the University of Saskatchewan Bone Mineral Accrual Study. *J Bone Miner Res* 1999; 14(10): 1672–9.
27. Gabel L, Macdonald HM, McKay HA. Sex differences and growth-related adaptations in bone microarchitecture, geometry, density, and strength from childhood to early adulthood: a mixed longitudinal HR-pQCT study. *J Bone Miner Res* 2017; 32(2): 250–63.
28. Weaver CM, Gordon CM, Janz KF et al. The National Osteoporosis Foundation's position statement on peak bone mass development and lifestyle factors: a systematic review and implementation recommendations. *Osteoporos Int* 2016; 27(4): 1281–386.
29. Gunter KB, Almstedt HC, Janz KF. Physical activity in childhood may be the key to optimizing lifespan skeletal health. *Exerc Sport Sci Rev* 2012; 40(1): 13–21.
30. Hind K, Burrows M. Weight-bearing exercise and bone mineral accrual in children and adolescents: a review of controlled trials. *Bone* 2007; 40(1): 14–27.
31. MacKelvie KJ, Khan KM, McKay HA. Is there a critical period for bone response to weight-bearing exercise in children and adolescents? A systematic review. *Br J Sports Med* 2002; 36(4): 250–7; discussion 257.
32. Tan VPS, Macdonald HM, Kim S et al. Influence of physical activity on bone strength in children and adolescents: a systematic review and narrative synthesis. *J Bone Miner Res* 2014; 29(10): 2161–81.
33. Forwood MR, Baxter-Jones AD, Beck TJ et al. Physical activity and strength of the femoral neck during the adolescent growth spurt: a longitudinal analysis. *Bone* 2006; 38(4): 576–83.
34. Gabel L, Macdonald HM, Nettlefold L et al. Physical activity, sedentary time, and bone strength from childhood to early adulthood: a mixed longitudinal HR-pQCT study. *J Bone Miner Res* 2017; 32(7): 1525–36.
35. Gabel L, Macdonald HM, Nettlefold L et al. Bouts of vigorous physical activity and bone strength accrual during adolescence. *Pediatr Exerc Sci* 2017; 29(4): 465–75.
36. Janz KF, Gilmore JME, Levy SM et al. Physical activity and femoral neck bone strength during childhood: the Iowa Bone Development Study. *Bone* 2007; 41(2): 216–22.
37. McKay HA, Macdonald HM, Nettlefold L et al. Action Schools! BC implementation:

from efficacy to effectiveness to scale-up. *Br J Sports Med* 2015; 49(4): 210–18.

38. McKay HA, MacLean L, Petit M et al. 'Bounce at the Bell': a novel program of short bouts of exercise improves proximal femur bone mass in early pubertal children. *Br J Sports Med* 2005; 39(8): 521–6.
39. Macdonald HM, Cooper DML, McKay HA. Anterior-posterior bending strength at the tibial shaft increases with physical activity in boys: evidence for non-uniform geometric adaptation. *Osteoporos Int* 2009; 20(1): 61–70.
40. Macdonald HM, Kontulainen SA, Petit MA et al. Does a novel school-based physical activity model benefit femoral neck bone strength in pre- and early pubertal children? *Osteoporos Int* 2008; 19(10): 1445–56.
41. Macdonald HM, Kontulainen SA, Khan KM et al. Is a school-based physical activity intervention effective for increasing tibial bone strength in boys and girls? *J Bone Miner Res* 2007; 22(3): 434–46.
42. Larsen MN, Nielsen CM, Helge EW et al. Positive effects on bone mineralisation and muscular fitness after 10 months of intense school-based physical training for children aged 8–10 years: the FIT FIRST randomised controlled trial. *Br J Sports Med* 2018; 52(4): 254–60.
43. Morris FL, Naughton GA, Gibbs JL et al. Prospective ten-month exercise intervention in premenarcheal girls: positive effects on bone and lean mass. *J Bone Miner Res* 1997; 12(9): 1453–62.
44. Burt LA, Greene DA, Ducher G et al. Skeletal adaptations associated with pre-pubertal gymnastics participation as determined by DXA and pQCT: a systematic review and meta-analysis. *J Sci Med Sport* 2013; 16(3): 231–9.
45. Ward KA, Roberts SA, Adams JE et al. Bone geometry and density in the skeleton of pre-pubertal gymnasts and school children. *Bone* 2005; 36(6): 1012–18.
46. Ducher G, Bass SL, Saxon L et al. Effects of repetitive loading on the growth-induced changes in bone mass and cortical bone geometry: a 12-month study in pre/peri- and postmenarcheal tennis players. *J Bone Miner Res* 2011; 26(6): 1321–9.
47. Greene DA, Naughton GA, Briody JN et al. Bone strength index in adolescent girls: does physical activity make a difference? *Br J Sports Med* 2005; 39(9): 622–7; discussion 627.
48. Lozano-Berges G, Matute-Llorente Á, González-Agüero A et al. Soccer helps build strong bones during growth: a systematic review and meta-analysis. *Eur J Pediatr* 2018; 177(3): 295–310.
49. Kannus P, Haapasalo H, Sankelo M et al. Effect of starting age of physical activity on bone mass in the dominant arm of tennis and squash players. *Ann Intern Med* 1995; 123(1): 27–31.
50. Warden SJ, Mantila Roosa SM. Physical activity completed when young has residual bone benefits at 94 years of age: a within-subject controlled case study. *J*

Musculoskelet Neuronal Interact 2014; 14(2): 239–43.

51. Mountjoy M, Sundgot-Borgen J, Burke L et al. The IOC Consensus Statement: Beyond the Female Athlete Triad—Relative Energy Deficiency in Sport (RED-S). *Br J Sports Med* 2014; 48(7): 491–7.
52. Ackerman KE, Holtzman B, Cooper KM et al. Low energy availability surrogates correlate with health and performance consequences of Relative Energy Deficiency in Sport. *Br J Sports Med* 2018: bjsports-2017-098958.
53. Golden NH, Schneider M, Wood C et al. Preventing obesity and eating disorders in adolescents. *Pediatrics* 2016; 138(3): e20161649.
54. Thornton D, Gordon CM. Restrictive eating disorders and skeletal health in adolescent girls and young women. *Calcif Tissue Int* 2017; 100(5): 449–60.
55. Colley RC, Garriguet D, Janssen I et al. Physical activity of Canadian children and youth: accelerometer results from the 2007 to 2009 Canadian Health Measures Survey. *Health Rep* 2011; 22(1): 15–23.
56. Tremblay MS, Carson V, Chaput J-P et al. Canadian 24-Hour Movement Guidelines for Children and Youth: An Integration of Physical Activity, Sedentary Behaviour, and Sleep. *Appl Physiol Nutr Metab* 2016; 41(6 Suppl 3): S311–27.
57. Burt LA, Hanley DA, Boyd SK. Cross-sectional versus longitudinal change in a prospective HR-pQCT study. *J Bone Miner Res* 2017; 32(7): 1505–13.
58. Burt LA, Liang Z, Sajobi TT et al. Sex- and site-specific normative data curves for HR-pQCT. *J Bone Miner Res* 2016; 31(11): 2041–7.
59. Macdonald HM, Nishiyama KK, Kang J et al. Age-related patterns of trabecular and cortical bone loss differ between sexes and skeletal sites: a population-based HR-pQCT study. *J Bone Miner Res* 2011; 26(1): 50–62.
60. American College of Sports Medicine, Chodzko-Zajko WJ, Proctor DN et al. American College of Sports Medicine position stand. Exercise and physical activity for older adults. *Med Sci Sports Exerc* 2009; 41(7): 1510–30.
61. NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy. Osteoporosis prevention, diagnosis, and therapy. *JAMA* 2001; 285(6): 785–95.
62. Howe TE, Shea B, Dawson LJ et al. Exercise for preventing and treating osteoporosis in postmenopausal women. *Cochrane Database Syst Rev* 2011(7): CD000333.
63. Kelley GA, Kelley KS, Kohrt WM. Exercise and bone mineral density in premenopausal women: a meta-analysis of randomized controlled trials. *Int J Endocrinol* 2013; 2013: 741639.
64. Marques EA, Mota J, Carvalho J. Exercise effects on bone mineral density in older adults: a meta-analysis of randomized controlled trials. *Age (Dordr)* 2012; 34(6): 1493–515.
65. Martyn-St James M, Carroll S. A meta-analysis of impact exercise on

postmenopausal bone loss: the case for mixed loading exercise programmes. *Br J Sports Med* 2009; 43(12): 898–908.

66. Sañudo B, de Hoyo M, Del Pozo-Cruz J et al. A systematic review of the exercise effect on bone health: the importance of assessing mechanical loading in perimenopausal and postmenopausal women. *Menopause* 2017; 24(10): 1208–16.
67. Xu J, Lombardi G, Jiao W et al. Effects of exercise on bone status in female subjects, from young girls to postmenopausal women: an overview of systematic reviews and meta-analyses. *Sports Med* 2016; 46(8): 1165–82.
68. Zhao R, Zhang M, Zhang Q. The effectiveness of combined exercise interventions for preventing postmenopausal bone loss: a systematic review and meta-analysis. *J Orthop Sports Phys Ther* 2017; 47(4): 241–51.
69. Kelley GA, Kelley KS, Tran ZV. Exercise and bone mineral density in men: a meta-analysis. *J Appl Physiol (1985)* 2000; 88(5): 1730–6.
70. Kemmler W, Shojaa M, Kohl M et al. Exercise effects on bone mineral density in older men: a systematic review with special emphasis on study interventions. *Osteoporos Int* 2018; 29(7): 1493–504.
71. Weeks BK, Beck BR. The BPAQ: a bone-specific physical activity assessment instrument. *Osteoporos Int* 2008; 19(11): 1567–77.
72. American College of Sports Medicine Position Stand. The recommended quantity and quality of exercise for developing and maintaining cardiorespiratory and muscular fitness, and flexibility in healthy adults. *Med Sci Sports Exerc* 1998; 30(6): 975–91.
73. Friedlander AL, Genant HK, Sadowsky S et al. A two-year program of aerobics and weight training enhances bone mineral density of young women. *J Bone Miner Res* 1995; 10(4): 574–85.
74. Kukuljan S, Nowson CA, Sanders KM et al. Independent and combined effects of calcium-vitamin D3 and exercise on bone structure and strength in older men: an 18-month factorial design randomized controlled trial. *J Clin Endocrinol Metab* 2011; 96(4): 955–63.
75. Kukuljan S, Nowson CA, Sanders K et al. Effects of resistance exercise and fortified milk on skeletal muscle mass, muscle size, and functional performance in middle-aged and older men: an 18-mo randomized controlled trial. *J Appl Physiol (1985)* 2009; 107(6): 1864–73.
76. McArthur D, Dumas A, Woodend K et al. Factors influencing adherence to regular exercise in middle-aged women: a qualitative study to inform clinical practice. *BMC Womens Health* 2014; 14: 49.
77. Bassey EJ, Rothwell MC, Littlewood JJ et al. Pre- and postmenopausal women have different bone mineral density responses to the same high-impact exercise. *J Bone Miner Res* 1998; 13(12): 1805–13.

78. Strope MA, Nigh P, Carter MI et al. Physical activity-associated bone loading during adolescence and young adulthood is positively associated with adult bone mineral density in men. *Am J Mens Health* 2015; 9(6): 442–50.
79. Cousins JM, Petit MA, Paudel ML et al. Muscle power and physical activity are associated with bone strength in older men: the osteoporotic fractures in men study. *Bone* 2010; 47(2): 205–11.
80. Wu F, Wills K, Laslett LL et al. Moderate-to-vigorous physical activity but not sedentary time is associated with musculoskeletal health outcomes in a cohort of Australian middle-aged women. *J Bone Miner Res* 2017; 32(4): 708–15.
81. Kemmler W, Engelke K, von Stengel S. Long-term exercise and bone mineral density changes in postmenopausal women—are there periods of reduced effectiveness? *J Bone Miner Res* 2016; 31(1): 215–22.
82. Kemmler W, von Stengel S, Bebenek M et al. Exercise and fractures in postmenopausal women: 12-year results of the Erlangen Fitness and Osteoporosis Prevention Study (EFOPS). *Osteoporos Int* 2012; 23(4): 1267–76.
83. Engelke K, Kemmler W, Lauber D et al. Exercise maintains bone density at spine and hip—EFOPS: a 3-year longitudinal study in early postmenopausal women. *Osteoporos Int* 2006; 17(1): 133–42.
84. Kemmler W, Lauber D, Weineck J et al. Benefits of 2 years of intense exercise on bone density, physical fitness, and blood lipids in early postmenopausal osteopenic women: results of the Erlangen Fitness Osteoporosis Prevention Study (EFOPS). *Arch Intern Med* 2004; 164(10): 1084–91.
85. Kemmler W, Bebenek M, Kohl M et al. Exercise and fractures in postmenopausal women. Final results of the controlled Erlangen Fitness and Osteoporosis Prevention Study (EFOPS). *Osteoporos Int* 2015; 26(10): 2491–9.
86. Neer RM, Arnaud CD, Zanchetta JR et al. Effect of parathyroid hormone (1-34) on fractures and bone mineral density in postmenopausal women with osteoporosis. *N Engl J Med* 2001; 344(19): 1434–41.
87. McCloskey EV, Johansson H, Oden A et al. Denosumab reduces the risk of osteoporotic fractures in postmenopausal women, particularly in those with moderate to high fracture risk as assessed with FRAX. *J Bone Miner Res* 2012; 27(7): 1480–6.
88. Englund U, Littbrand H, Sondell A et al. The beneficial effects of exercise on BMD are lost after cessation: a 5-year follow-up in older post-menopausal women. *Scand J Med Sci Sports* 2009; 19(3): 381–8.
89. Winters KM, Snow CM. Detraining reverses positive effects of exercise on the musculoskeletal system in premenopausal women. *J Bone Miner Res* 2000; 15(12): 2495–503.
90. Shaw JM, Snow CM. Weighted vest exercise improves indices of fall risk in older

women. *J Gerontol A Biol Sci Med Sci* 1998; 53(1): M53–8.

91. Snow CM, Shaw JM, Winters KM et al. Long-term exercise using weighted vests prevents hip bone loss in postmenopausal women. *J Gerontol A Biol Sci Med Sci* 2000; 55(9): M489–91.
92. McNamara A, Gunter K. The influence of participation in Better Bones and Balance^{TM} on skeletal health: evaluation of a community-based exercise program to reduce fall and fracture risk. *Osteoporos Int* 2012; 23(6): 1813–22.
93. McNamara AJ, Pavol MJ, Gunter KB. Meeting physical activity guidelines through community-based group exercise: 'Better Bones and Balance'. *J Aging Phys Act* 2013; 21(2): 155–66.
94. Giangregorio LM, Papaioannou A, Macintyre NJ et al. Too Fit To Fracture: exercise recommendations for individuals with osteoporosis or osteoporotic vertebral fracture. *Osteoporos Int* 2014; 25(3): 821–35.
95. Tschopp M, Sattelmayer MK, Hilfiker R. Is power training or conventional resistance training better for function in elderly persons? A meta-analysis. *Age Ageing* 2011; 40(5): 549–56.
96. Gianoudis J, Bailey CA, Ebeling PR et al. Effects of a targeted multimodal exercise program incorporating high-speed power training on falls and fracture risk factors in older adults: a community-based randomized controlled trial. *J Bone Miner Res* 2014; 29(1): 182–91.
97. Watson SL, Weeks BK, Weis LJ et al. High-intensity resistance and impact training improves bone mineral density and physical function in postmenopausal women with osteopenia and osteoporosis: the LIFTMOR randomized controlled trial. *J Bone Miner Res* 2018; 33(2): 211–20.
98. Khosla S, Shane E. A crisis in the treatment of osteoporosis. *J Bone Miner Res* 2016; 31(8): 1485–7.
99. Rodrigues IB, Armstrong JJ, Adachi JD et al. Facilitators and barriers to exercise adherence in patients with osteopenia and osteoporosis: a systematic review. *Osteoporos Int* 2017; 28(3): 735–45.
100. Moayyeri A. The association between physical activity and osteoporotic fractures: a review of the evidence and implications for future research. *Ann Epidemiol* 2008; 18(11): 827–35.
101. Sinaki M, Itoi E, Wahner HW et al. Stronger back muscles reduce the incidence of vertebral fractures: a prospective 10 year follow-up of postmenopausal women. *Bone* 2002; 30(6): 836–41.
102. Gregg EW, Pereira MA, Caspersen CJ. Physical activity, falls, and fractures among older adults: a review of the epidemiologic evidence. *J Am Geriatr Soc* 2000; 48(8): 883–93.
103. Qu X, Zhang X, Zhai Z et al. Association between physical activity and risk of

fracture. *J Bone Miner Res* 2014; 29(1): 202–11.

104. Feskanich D, Willett W, Colditz G. Walking and leisure-time activity and risk of hip fracture in postmenopausal women. *JAMA* 2002; 288(18): 2300–6.
105. Stattin K, Michaëlsson K, Larsson SC et al. Leisure-time physical activity and risk of fracture: a cohort study of 66,940 men and women. *J Bone Miner Res* 2017; 32(8): 1599–606.
106. Wilks DC, Winwood K, Gilliver SF et al. Bone mass and geometry of the tibia and the radius of master sprinters, middle and long distance runners, race-walkers and sedentary control participants: a pQCT study. *Bone* 2009; 45(1): 91–7.
107. Suominen TH, Korhonen MT, Alen M et al. Effects of a 20-week high-intensity strength and sprint training program on tibial bone structure and strength in middle-aged and older male sprint athletes: a randomized controlled trial. *Osteoporos Int* 2017; 28(9): 2663–73.
108. Nichols JF, Rauh MJ. Longitudinal changes in bone mineral density in male master cyclists and nonathletes. *J Strength Cond Res* 2011; 25(3): 727–34.

Chapter 18

Infections

with ZAFAR IQBAL and HASAN TAHIR

Guillermo Varela to miss German Cup final with infected tattoo and furious Frankfurt end his loan. The Manchester United loanee's infected arm artwork has spelled the premature end of his time at the Bundesliga club. Varela was instructed not to get the tattoo by Eintracht Frankfurt's club doctor ahead of the club's DFB-Pokal showdown against Borussia Dortmund on Saturday, but the 24-year-old decided to get it anyway.

www.fourfourtwo.com, 24 May 2017

Athletes are subject to the same infections as the rest of the community; however, certain circumstances in sport may increase their susceptibility to infections. Athletes involved in team sports have close contact with teammates, which increases the likelihood of spread of infection. In addition, team members often share food and drink, particularly with the increased use of squeeze bottles during exercise.

In this chapter we:

- review the relationships between exercise/activity and infections
- discuss whether athletes should exercise or train when suffering an infection
- discuss management of a range of specific infections in athletes according to the region of presentation—skin, respiratory, gastrointestinal and liver etc.
- outline national infection prevention strategy guidelines.

EXERCISE AND INFECTION

There is considerable debate regarding the relationship between exercise and infection. It is important, first, to consider the relationship between exercise and the immune system and then examine whether there is an increased incidence of infection associated with intense exercise. Finally, we discuss when an athlete can train and play with an infection.

Exercise and the immune system

The immune system can be considered as two complementary parts.[1] First is the innate immune system, which is non-specific regarding host defence. Its components include the skin, mucous membranes, phagocytes, natural killer (NK) cells, cytokines and complement factors. The latter two elements control and mediate immune function and help activate T- and B-lymphocytes, key parts of the acquired immune system. In contrast to the innate system, the acquired system protects the body against specific infectious agents during both initial and subsequent attacks.[1]

The body's first line of defence consists of skin and mucous membranes, which can be impaired by temperature, wind, sun, humidity and trauma. Many upper respiratory pathogens are airborne and affected by airflow patterns, mechanical barriers and ciliary action in the respiratory tract.[1]

During exercise, the athlete switches from nasal to mouth breathing, and this can increase deposition of harmful particles in the lower respiratory tract. It also causes an increase in cooling and drying of the respiratory mucosa, which slows ciliary movement and increases mucous viscosity.[2]

Natural killer cells express spontaneous cytolytic activity against cells infected with viruses.[1] NK cell counts increase 150–300% immediately after high-intensity exercise lasting less than 1 hour. Within 30 minutes of the end of such high-intensity exercise, however, NK cell counts fall below pre-exercise levels.[3] NK cell activity increases by 40–100% in response to acute exercise of less than 1 hour in duration and falls to 25–40% below pre-exercise levels 1–2 hours into recovery time. Intense exercise lasting longer than 1 hour causes no rise in NK cell activity. There is, however, a more profound and sustained drop in NK cell activity in recovery, which is likely to be a cortisol-induced effect.[4]

Macrophages phagocytose foreign particles, present antigens to lymphocytes, and also produce lymphocyte-stimulating cytokines.[2] Acute strenuous exercise increases the macrophage count and several aspects of macrophage function. Long-term training seems to attenuate the macrophage response to acute exercise, but the resulting macrophage function is still found to be greater than in untrained subjects.[3]

Cytokines are produced by and mediate communication between immune and non-immune cells and are divided into pro-inflammatory and anti-inflammatory types. Pro-inflammatory cytokines such as tumour necrosis factor-alpha (TNFa), interleukin-1 (IL-1) and interleukin-6 (IL-6) are increased with acute exercise. IL-6 levels can increase up to 100-fold after a marathon. Anti-inflammatory cytokines such as interleukin-10 (IL-10) and IL-1 receptor antagonist (IL-1ra) also increase with exercise.

Neutrophils are capable of phagocytosis, both alone and in response to antigen-dependent defences.[1] Neutrophil counts increase with acute exercise, most likely due to demargination, several hours after exercise, a cortisol-induced phenomenon. Acute moderate exercise increases neutrophil activity, but acute intense exercise suppresses it.[3] Endurance training reduces several aspects of neutrophil function compared with being sedentary. It seems that long-term moderate training increases neutrophil counts whereas intense training decreases them.[3]

The acquired portion of the immune system has the ability to form a memory and attack specific foreign particles that have invaded the body previously. The main components of this system are T- and B-lymphocytes and plasma cell–secreted antibodies. Overall, lymphocyte counts increase with acute exercise. Lymphocyte counts and B-cell function are decreased after intense exercise, but not after moderate exercise.

Antibody production, most notably of IgA, is impaired by intense prolonged exercise.[1] Cross-country skiers have low baseline salivary IgA levels, which further decline after racing. Studies of longitudinal changes in salivary IgA levels in swimmers have yielded conflicting results.[1] IgG does not seem to be affected as much by intense training, although some elite athletes show a small decrease during peak training.[2]

Among the T-lymphocytes are the $CD4^+$ (T-helper) and $CD8^+$ (T-suppressor) cells. A ratio of $CD4^+$ to $CD8^+$ cells of 1.5:1 is considered necessary for proper cellular immune function. Heavy exercise decreases this ratio by decreasing $CD4^+$ cells and increasing $CD8^+$ cells. A decreased $CD4^+$ count also diminishes cytokine output, which decreases NK cell and macrophage activation and B-cell proliferation.[2]

The brief period of immunosuppression after acute intense physical activity, when ciliary action, mucosal IgA levels, NK cell count and activity, T-lymphocyte count and $CD4^+$ to $CD8^+$ ratio are decreased, is an immunological 'open window', during which an athlete may be more susceptible to infection.

Exercise and clinical infections

Given the measurable changes in the immune system with exercise, are athletes more susceptible to infections? It has been suggested that compared with a sedentary lifestyle, the risk of infection is reduced with regular moderate exercise.[5] There is a temporary depression of several aspects of the immune system lasting up to 24 hours after acute bouts of prolonged exercise.[6] A number of studies have been performed examining the incidence of upper respiratory tract infection and exercise. The results are conflicting, although there is some evidence that there is an increased incidence of upper respiratory tract infections in the days after intense training.[7]

Nieman[8] has proposed the J curve (Fig. 18.1). According to this theory, regular moderate exercise decreases the risk of upper respiratory tract infection to below that of sedentary individuals, whereas strenuous intense exercise increases the risk above that of sedentary individuals. The exact frequency, duration, type and intensity of exercise required to optimally lower one's risk of infection or to adversely increase the risk of infection, remain to be determined.

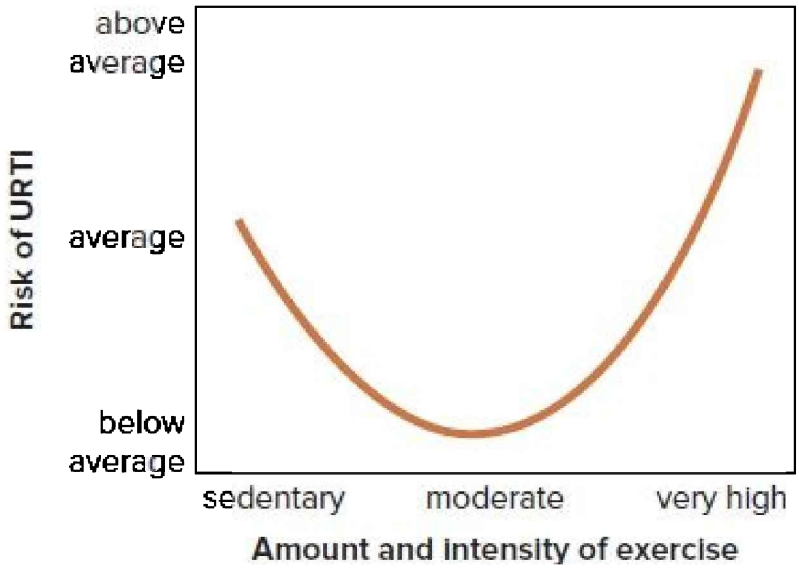


Figure 18.1 The association between exercise and susceptibility to upper respiratory tract infection
FROM NIEMAN (2000) <REF 8:NIEMAN D. IS INFECTION RISK LINKED TO EXERCISE WORKLOAD? MEDICINE & SCIENCE IN SPORTS & EXERCISE 2000; 32(7): S406–11 © 2019 AMERICAN COLLEGE OF SPORTS MEDICINE HTTPS://JOURNALS.LWW.COM/ACSM-MSSE/FULLTEXT/2000/07001/IS_INFECTION_RISK_LINKED_TO_EXERCISE_WORKLOAD_.5.ASPX.>[8]

Foster[9] proposed identifiable parameters of training that related to illness. He related Page 263 the incidence of common illness to indices of training load and noted a correspondence between spikes in the indices of training and subsequent (within 10 days) illness, and computed individual thresholds that allowed for optimal explanation of illnesses. On these calculations, 84% of illnesses could be explained by a preceding spike in training load above the individual training threshold. However, 55% of the excursions above the threshold were accomplished without a related illness. A subsequent study failed to support Foster's theory.[10]

Infection and athletic performance

Infection or subclinical infection is commonly used to explain poor athletic performance. Infection may compromise muscle enzyme activity and muscle strength. Impaired muscle metabolism has also been demonstrated using magnetic resonance imaging (MRI). Exercise performed during illness also requires greater cardiopulmonary effort. These findings may theoretically lead to a detrimental effect of infection on performance. See the box for a discussion of the issue of whether an athlete should train during illness.

A number of studies have been performed at the Australian Institute of Sport, in Canberra, examining the relationship between mild illness and sporting performance. An initial study in elite swimmers did not show any statistically significant decrease in performance in competition in those who had suffered a minor illness in the month leading up to competition.[11]

In a group of elite middle-distance and distance runners, illness-affected runners reported a higher perceived training intensity. However, laboratory-based measures of performance showed little change in physical work capacity.[10] A third study in another group of elite swimmers suggested that mild illness had a trivial effect on the competitive performances of female swimmers and a substantial though small harmful effect in male swimmers. In this study it was noted that, although the mean harmful effects were trivial to small, the chances of harm for individuals were substantial.[11]

PRACTICE PEARL

If symptoms are above the neck (runny nose, nasal congestion, sore throat) and not associated with symptoms below the neck (fever, malaise, muscle aches, severe cough, gastrointestinal), then the athlete may commence training at half intensity for 10 minutes. If symptoms do not worsen, then the training session can continue as tolerated. This differentiation between the two forms of viral illness is known as the 'neck check'.[12, 17]

COMMON INFECTIONS IN ATHLETES

Athletes are subject to the same infections as those suffered by the rest of the community; however, as mentioned above, in certain circumstances in sport there may be an increase in the susceptibility to infections.

Pathogens may be transmitted by contact, the airborne route, or by the food and water route (Table 18.1).

Table 18.1 Summary of epidemiology and outbreak management considerations for organisms responsible for infections in children participating in organised sports[18] Page 264

Pathogens primarily transmitted by contact sports

Pathogen or disease	Transmission	Risk factors	Rn, Dx, Rx	Prevention	Outbreaks and other considerations
S. aureus including MRSA	Contact	Contact sports, wounds (turf injuries in football or soccer), wrestling, rugby, judo and gymnastic mats, sharing equipment	Rn: folliculitis, skin abscess, cellulitis, impetigo	Good personal hygiene, wound care, avoid sharing equipment, refrain from use of common tubs, cosmetic shaving, cleaning of high-touch surfaces	Involve public health authorities for outbreaks
			Dx: Gram stain, culture of lesions		Topical mupirocin depending on susceptibilities
			Rx: cephalexin, TMP–SMX or doxycycline based on susceptibility for 10 d		–

GABHS	Contact, droplet	Skin contact in impetigo/erysipelas, droplet in pharyngitis	Rn: impetigo, erysipelas, pharyngitis, cellulitis	Good hygiene, not sharing water bottles, equipment	Topical mupirocin if limited skin lesions
			Dx: rapid antigen detection test for GABHS if sore throat and no viral symptoms, Gram stain, culture of lesions Rx: treat if positive; culture skin lesions with amoxicillin or penicillin; if penicillin allergic, macrolide; all for 10 d except azithromycin for 5 d		Azithromycin for serious penicillin allergy
B. cereus	Contact, contaminated food	Sharing sunscreen, penetrating trauma, contaminated environment	Rn: honey-crusted skin lesions; rarely, necrotising fasciitis: if contaminated food, nausea, vomiting, diarrhoea and cramps Dx: Gram stain, culture of lesions, identification of enterotoxin from food if contaminated food Rx: usually IV vancomycin or linezolid for severe skin infections, supportive for foodborne	Good personal hygiene, avoid sharing equipment, sunscreen	Involve public health authorities for outbreaks
HSV	Contact with infected individual; reactivation 1° infection	Skin contact, wrestling, abraded skin, sun induced (e.g. skiing)	Rn: cropped vesicles	Valacyclovir prophylaxis, proper cleaning equipment	Page 265 Identification and isolation of infected people
			Dx: viral PCR of skin lesion Rx: adolescents, valacyclovir for 7 d		Valacyclovir –
Molluscum contagiosum	Contact	Sharing towels, underlying eczema	Rn: pearly papule with central umbilication	Avoid skin contact with infected people; no specific treatment is uniformly efficacious	Outbreaks have been reported
			Dx: clinical Rx: 10% KOH, cryotherapy		
T. capitis (T. tonsurans), T. corporis	Contact	Skin contact, wrestlers, judo practitioners	Rn: scaly plaque, alopecia	In settings of high infection rates, in consultation with infectious diseases expert, consider fluconazole prophylaxis, 100 mg, once daily for 3 d, at season onset and repeat in 6 wk	Griseofulvin contraindicated in pregnancy
			Dx: KOH prep, culture Rx: oral itraconazole, terbinafine, griseofulvin ± 1% terbinafine gel or 2% ketoconazole cream		Topical for limited area *T. corporis* –
T. pedis	Contact	Common shower, skin contact, swimmers, skaters,	Rn: scaly, itchy eruption on feet	Good personal hygiene	–

		marathon runners			
			Dx: KOH prep, culture Rx: children 12 y or older, topical 0.77% ciclopirox cream or gel BID for 4 wk, 1% terbinafine gel OD for 1 wk, naftifine ointment BID for 4 wk. Oral terbinafine for 1 wk	Foot powder after bathing Careful drying between toes after showers	
				Daily change of socks Periodic cleaning of footwear	Page 266
T. cruris	Contact	Heat, humidity, hyperhidrosis, contaminated towels, hotel bedroom sheets	Rn: scaly, itchy eruption in groin area	Put on socks before underwear if *T. pedis* present	–
			Dx: KOH prep, culture Rx: children 12 y or older, 1% terbinafine gel OD for 1 wk	Dry crural folds after bathing Use separate towel to dry groin and other parts of body	
Verruca vulgaris (caused by subtypes of HPV)	Contact	Wrestlers, sharing of equipment, bare feet in common shower areas	Rn: painless warts on hands and feet and under nails, firm hyperkeratotic papules	Avoid contact with known infected people, no sharing of equipment and towels; wear rubber-soled thongs or sandals in communal showers	–
			Dx: clinical Rx: none or curettage, liquid nitrogen, laser removal or application of salicylic acid		
S. *scabiei* (scabies)	Contact	Wrestlers	Rn: + + pruritic rash, interdigital webs	–	Evaluate sparring partners; treat suspected cases Itching is attributable to hypersensitivity reaction and may not subside for weeks; not indication of treatment failure
			Rx: topical permethrin 5% cream to whole body below neck (not pregnant women), remove by bathing after 8–14 h; oral ivermectin, 2 doses 1 wk apart for children > 15 kg (not widely approved and not for pregnant girls), 10% crotamiton cream or lotion or precipitated sulfur 4–8%		
Pediculus capitis (head lice)	Contact	Sharing clothing, equipment	Rn: visible lice on hair shaft, pruritus	Although risk of spread is low, sharing of combs, hair brushes, hats and hair ornaments	Clearance by health care professional before resuming sport Page 267

				is not recommended	
			Dx: clinical: seeing nits, nymphs or adult lice with naked eye or hand lens	No need to treat contacts prophylactically	Rinse hair after topical pediculicide application over a sink rather than shower or bath to limit skin exposure and use warm water instead of hot to limit absorption resulting from vasodilatation
			Rx: manual removal of nits by fine-toothed combing. Start with over-the-counter topical 1% permethrin lotion or pyrethrin combined with piperonyl butoxide; repeat in 7 d; resistance reported, see text for options	–	–
Infectious mononucleosis caused by Epstein–Barr virus	Close contact	Adolescent group settings	Rn: exudative pharyngitis, splenomegaly; serum antibody panel	Counsel regarding close contact and avoiding sharing drinks, utensils	Avoid contact sports until recovered and spleen no longer palpable (typically ~3–4 wk)
			Dx: heterophile antibody test (>4 y of age), IgM antibodies versus viral capsid antigen, Epstein–Barr nuclear antigen Rx: supportive		
Pathogens primarily transmitted by airborne route					
Varicella	Skin, airborne	Close community contact	Rn: crops of papules, vesicles, crusts; can be confused with HSV Dx: PCR of vesicular fluid Rx: usually none, oral acyclovir or valacyclovir for 7 d	Ensure varicella vaccine is given	Ensure fully vaccinated or history of disease for all exposed people Avoid salicylates during infection –
Measles (rubeola)	Droplet, airborne	International venues, underimmunised populations	Rn: febrile prodrome, morbilliform rash	Ensure ACIP/AAP-recommended MMR vaccine is given	Involve public health authorities for single case
			Dx: PCR of urine and nasopharyngeal specimens, rubeola serology Rx: supportive		
Pathogens primarily transmitted by droplet route					
Mumps	Droplet	Crowded settings, underimmunised populations	Rn: parotitis	Ensure ACIP/AAP-recommended MMR vaccine is given	Involve public health authorities for single case
			Dx: PCR of saliva, serology Rx: supportive		
Influenza	Droplet	Close community contact	Rn: febrile upper respiratory tract during influenza season	Ensure ACIP/AAP-recommended influenza vaccine is given seasonally	Prioritise treatment of those who have increased risk for influenza complications (e.g.

					asthma, heart and/or lung disorders, metabolic disorders, immune compromised)
			Dx: culture, rapid molecular tests Rx: oseltamivir if identified in first 2 d, for 5 d		
Pertussis	Droplet	Close community contact	Rn: paroxysmal cough for ≥2 wk	Ensure ACIP/AAP-recommended Tdap is given; identify and intervene with chemoprophylaxis in outbreaks	Involve public health authorities for outbreaks (>2 cases in closed population)
			Dx: PCR of nasopharyngeal swab specimen Rx: azithromycin for 5 d		
N. meningitidis	Droplet	Close community contact	Rn: bacteremic presentation, shock, purpura	Ensure meningococcal vaccine is given	Involve public health authorities for single case; if serogroup B involved, meningococcal B vaccine
			Dx: Gram stain, culture Rx: begin with intravenous cefotaxime or ceftriaxone; penicillin once diagnosis confirmed		
Shigella	Contaminated food or water; person to person	Commonly attendedRn: diarrhoea, blood event, restaurant related	Hand hygiene		Involve public health authorities for outbreaks
			Dx: culture stool Rx: TMP–SMX, ciprofloxacin depending on susceptibilities		
Giardia	Contaminated food or water	Public pools, swimmers	Rn: watery diarrhoea Dx: stool antigen test Rx: metronidazole or nitazoxanide	Hand hygiene	–
Cryptosporidia	Contaminated food or water	Public pools, swimmers	Rn: watery diarrhoea Dx: stool examination Rx: nitazoxanide	Hand hygiene	Hand hygiene
Norovirus	Contaminated food or water; person to person	Common environment	Rn: abrupt onset of vomiting, watery diarrhoea Dx: clinical RT-PCR Rx: supportive	Hand hygiene	Involve public health authorities for outbreaks
Leptospirosis	Contaminated water	Triathletes, fresh water swimming, skin wounds	Rn: fever and headache, myalgia (can mimic influenza) Dx: enzyme-linked immunosorbent assay IgM Rx: intravenous penicillin G first choice, risk of Jarish–Herxheimer reaction; also cefotaxime, ceftriaxone and doxycycline; supportive care	Swimmers avoid immersion or swallowing potentially contaminated water Protective clothing, boots in contaminated water	–

REPRODUCED WITH PERMISSION FROM JOURNAL PEDIATRICS, DAVIES HD, JACKSON MA, RICE SG, ET AL. INFECTIOUS DISEASES ASSOCIATED WITH ORGANISED SPORTS AND OUTBREAK CONTROL. VOL. 140(4), PAGES 2017-2477, COPYRIGHT © 2017 BY THE AAP

Should an athlete train during illness?

One of the most difficult dilemmas facing the clinician and the athlete is to decide whether or not to train or compete in the presence of a viral illness.

It is important to differentiate those athletes suffering from viral illness into two groups—those with symptoms restricted to one system, usually the upper respiratory tract, and those with generalised symptoms. An athlete with an upper respiratory tract infection manifesting itself as a sore throat, runny nose or headache who is afebrile should be allowed to continue with mild to moderate training, below 80% of VO_2max.

Exercise in moderately fit and active people with an upper respiratory tract infection does not prolong or intensify the illness.[5]

Modification of the training program may involve increased skill training with less anaerobic or endurance training for the period of the illness.

Those athletes with systemic symptoms of general malaise, excessive fatigue, muscle pains and tenderness, temperature in excess of 38°C (100°F), or a resting heart rate greater than 10 beats per minute above normal should avoid any athletic activity until the systemic symptoms and signs return to normal or near normal. Activity should then be gradually resumed.

Engaging in intensive exercise during an infection has been associated with an increased risk of heat exhaustion,[12] post-viral fatigue syndrome[13, 14] and viral myocarditis.[15]

There is no evidence that exercise will affect the severity or duration of an illness.[16] If symptoms of viral illness are generalised, athletes should not train intensively nor compete. If symptoms are confined to one area (e.g. sore throat), then they can train moderately.

Strenuous exercise can result in a transient depression of leukocyte function, thereby increasing the risk of developing an infection.[19] Other factors leading to an increased risk of infection include lack of sleep, mental stress and poor nutrition.[19] During exercise the higher rate and depth of breathing increases the exposure of bacteria and virus to the lungs. Prolonged exercise in the heat may allow entry of gut bacterial endotoxins into the circulation due to an increase in gut permeability. There is also a post-exercise immune function depression when the exercise is prolonged (more than 90 minutes), of moderate to high intensity (55–75% aerobic capacity) and accompanied by reduced food intake.[7]

It has been shown that in major international games, including Summer and Winter Olympic Games lasting 9–18 days, 6–17% of athletes suffered an illness episode. The incidence of illness appeared to be higher in winter compared with Summer Olympic Games and more common in female athletes than males.[20] The most common illnesses in the majority of the studies, with 40–60% of all acute illness episodes, affected the respiratory tract. Other systems commonly affected by illness were the gastrointestinal system (10–20%), skin (10–15%) and genitourinary system (5–10%).[20]

The accurate diagnosis, management and prevention of infections is important, to limit disruption of training and subsequent impact on performance. An acute illness can affect several organ systems resulting in a reduction in exercise performance. The systemic effects include decreasing muscle strength, decreased aerobic capacity, impaired motor function and altered metabolic function. Sports-related infections can cause serious complications and even epidemics that sideline entire teams.

We review infections according to their clinical presentation—those affecting skin, the respiratory system and the gastrointestinal tract.

Skin infections

Skin infections occur more commonly in athletes than sedentary individuals.[21] Athletes are at risk for skin infections because of several factors. These include skin-to-skin contact with other athletes, athletic equipment including gloves or pads, which can be difficult to sanitise, and sharing of personal toiletries. In many sports there is an increased likelihood of skin trauma such as abrasions and lacerations. Further, increased sweating and occlusive clothing form the perfect environment for skin infections. Skin infections may be due to viruses (e.g. herpes simplex, molluscum contagiosum, warts), bacteria (e.g. impetigo, folliculitis, otitis externa) or fungi (e.g. tinea, scabies, lice).

Viral skin infections

Contact sports such as wrestling or rugby have a higher rate of viral skin infections than non-contact sports.[21] Training environments may promote the transmission of some viral infections via fomites, such as weights, mats, weight benches, pool decks and communal showers.[22] The three main viral infections that affect athletes are herpes simplex, molluscum contagiosum and warts (verrucae).

Herpes simplex virus infections

Herpes simplex virus (HSV-1) skin infections occur in athletes, particularly among wrestlers (herpes gladiatorum) and rugby forwards (herpes rugbeiorum or 'scrum pox'). The virus is transmitted through skin-to-skin contact. Outbreaks have been reported particularly among wrestlers, and a major epidemic threatened the 2007 Minnesota high school wrestling season but was contained due to suspension of the competition and enforcement of an 8-day isolation period.[2] [3] A review of a recent outbreak suggested that there is a 33% probability of transmission if herpes develops on a sparring partner.[24]

In contact sports, lesions are common on the head and may involve the eyes, leading to conjunctivitis or blepharitis (infection of the eyelids). HSV infections can be extremely painful and may be accompanied by systemic symptoms such as fever and malaise. These symptoms represent the prodrome, but not every episode of HSV has a prodrome.

After an incubation period of 5–10 days, asymptomatic shedding of viral particles and the development of clinical lesions may occur. The vesicles rupture quickly and crust over within a few

days. Crusted lesions last 5–7 days and may take 2–3 weeks to heal completely.[21] The diagnosis is made on the typical appearance of the herpes lesions and can be confirmed with viral cultures.

Herpes labialis (cold sores) typically appear at mucocutaneous junctions, especially on the lip. They may affect snow skiers and others who are exposed to cold stress or to increased ultraviolet solar radiation at high altitudes. In healthy patients, the infection is self-limited and does not usually require treatment. However, one may consider systemic treatment if lesions are noticed within 72 hours, to reduce outbreaks and suppress herpes recurrences.

Treatment of HSV is with oral acyclovir or valacyclovir immediately with the onset of prodromal symptoms, for 7–10 days. Topical acyclovir is not helpful. The earlier the antiviral is taken, the more effective it is.

Herpes simplex virus is highly contagious and no one should compete in a contact sport until the scabs have dried and there are no further vesicles, ulcers or drainage. In the USA, where high school and college wrestling is a popular sport, organisations have imposed strict rules. The National Collegiate Athletic Association's (NCAA) rules state that an athlete must:[25]

Page 271

- be free of systemic symptoms (fever, malaise etc.)
- have developed no new blisters for 72 hours before the examination
- have no moist lesions; all lesions must be dried and have progressed to a firm adherent crust
- have been on appropriate systemic antiviral therapy for at least 120 hours before and at the time of the meet or tournament
- not cover active herpetic infections to participate.

As HSV is not eliminated, recurrences may occur, particularly at times of undue physical or psychological stress. Recurrent attacks are usually milder, lasting only five days. Treatment is the same but a shorter course.

None of these recommendations, however, are evidence based. On the basis of virus shedding studies in herpes genitalis, the athlete can probably return to competition 4–7 days after a recurrent outbreak,[24] whereas others recommend removing the athlete from practice and competition for 8 days.[26]

Molluscum contagiosum

Molluscum contagiosum, which mainly affects children, is characterised by discrete white to skin-coloured, umbilicated papules that are 3–5 mm (~0.2 in.) in diameter. It is caused by a virus from the Poxviridae family.[21] The papules are more common in swimmers, gymnasts and wrestlers and are commonly seen on the hands, forearms and face. They are generally asymptomatic and spread by skin-to-skin contact. One report noted that 8% of 1500 cross-country runners developed molluscum contagiosum.[27] The origin of this epidemic was unclear, but is likely related to sharing of towels and close contact.

Treatment is generally recommended, particularly if an athlete participates in a contact sport.

The infection is self-limited but may take months or even years to resolve without treatment.[21] The most common method of treatment is application of liquid nitrogen or curettage. NCAA wrestling guidelines require curettage or removal of molluscum before the athlete participates in meets or tournaments. Single or localised lesions can be covered with Opsite or Bioclusive™, and subsequently Pro-Wrap and stretch tape, thus allowing the wrestler to compete in the tournament.[25] Patients should be educated about prevention of spread of the disease—by use of separate towels and other measures of basic hygiene.

Warts (verrucae)

Warts, or verrucae, are caused by infection with various forms of the human papillomavirus (HPV). They are commonly seen on the hands and feet and tend to be hard and have a verrucous surface. Infectivity is low, but warts are transmitted either by direct skin-to-skin contact or through fomites such as swimming pool decks and showers. Warts are frequently spread by autoinoculation from shaving, scratching or other skin trauma. Plantar warts can be painful and should be treated.

Visual inspection is usually sufficient for diagnosis. The main challenge is distinguishing a wart from a callus. Warts do not retain the normal fingerprint lines on the hands and feet that corns and calluses do. A wart on the surface of the foot can also be distinguished from a callus by paring the lesion down with a no. 15 blade. Warts will have 10–15 pinpoint black spots that are thrombosed capillaries. Once the wart has been pared down it can be treated with liquid nitrogen.

Athletes can return to competition as soon as warts have been treated, but the warts should remain covered until completely resolved.[21] The NCAA guidelines for wrestlers state that athletes with single or a few scattered lesions should be treated before the meet or tournament. Wrestlers who have multiple warts on the face that cannot be adequately covered by a mask or who have multiple warts on the body that cannot be adequately covered will be disqualified.[25]

Bacterial skin infections

Staphylococci (80%) and streptococci (10%) are the most common bacterial organisms causing skin infections. They may present as various conditions such as impetigo, folliculitis, furunculosis and boils.[28]

Impetigo

Impetigo is a skin infection that is easily spread from person to person; it is particularly common in sports with close skin-to-skin contact, such as wrestling and the various football codes. Impetigo has two different presentations—bullous and non-bullous—with multiple lesions affecting the face or extremities.

The bullous form typically begins as multiple fluid-filled vesicles that either coalesce or individually enlarge, forming blister-like lesions that eventually collapse centrally. The centre has a classic honey-crusted lesion that, when removed, reveals erythematous plaques draining serous fluid.

Non-bullous impetigo originates as small vesicles or pustules with erythematous bases and honey-coloured crusts which also drain fluid. Breaks in the skin provide an avenue for bacterial

invasion. Patients are typically afebrile, but enlarged lymph glands may be present.[28]

In most cases the diagnosis is made clinically; it can be confirmed with bacterial cultures when necessary. Impetigo may resolve spontaneously but when the disorder is widespread treatment should be implemented, either with topical (fucidic acid [fusidate sodium] or mupirocin) or oral (flucloxacillin or clarithromycin if penicillin allergic) antibiotics for 7 days.[29] It has been advocated that topical disinfectants are not nearly as efficient as antibiotics and therefore should be avoided.[30]

CASE STUDY

Blake Griffin, NBA—*Staphylococcus aureus*

Blake Griffin is an American professional basketball player for the Detroit Pistons. He is a five-time NBA All-Star, former Rookie of the Year and slam dunk contest champion.

Diagnosis

In early 2015, Griffin was struggling to play due to a troublesome right elbow.

He has had to deal with bursitis in his right elbow throughout his career and routinely has it drained during the season. After having his elbow drained, and struggling to perform in the following two games, the team trainer sent Griffin to the hospital to get his elbow examined.

Griffin was found to have a staph infection in his elbow and was ruled out for 4 to 6 weeks.

Management

Griffin was sent for surgery to remove the infection, due to concern about possible septic complications, and was treated with a short course of antibiotics. Fortunately, he was able to return to play roughly 6 weeks post surgery.

Conclusion

There has been a growing concern in recent years about the incidence of infections among athletes. Staph is the most commonly transmitted bacterial skin infection in athletes. The infection can take a number of forms, as outlined within this chapter. All clinicians and members of the medical team should be suspicious of potential skin infections, and should consider bacterial cultures in order to rule out methicillin-resistant staph aureus (MRSA)—a serious staph infection that is resistant to many common antibiotics. For further information about MRSA, see the box below.

Figure 18.2 Scanning electron micrograph view of clumps of staphylococcus aureus bacteria
18PERCENTGREY/123RF;JANICE HANEY CARR/CENTER FOR DISEASE CONTROL (CDC)

Sources: references 85, 86, 87, 88

PRACTICE PEARL

Those who have suffered turf burns, cuts, are undergoing regular treatment that involves skin infiltration (e.g. injections) or who have had recent surgery should be monitored closely and treated immediately with an appropriate antibiotic if signs of infection present.

Scratching should be resisted because of the highly contagious nature of the infection; an antihistamine is sometimes prescribed. All lesions should be covered during contact sport. The NCAA wrestling guidelines state that the athlete must take antibiotics for 72 hours before competition and be free from any new skin lesion for 48 hours.[31]

Folliculitis, furunculosis (boils) and carbuncles

Folliculitis is a superficial infection of the upper portion of the hair follicle and surrounding areas, characterised by mildly tender papules or pustules surrounded by erythema.

Furunculosis (boil) is an infection of the deeper hair follicle cavity; the lesions usually contain pus and present as large, well-defined erythematous and fluctuant nodules that commonly occur in areas of increased sweating and friction, such as the buttock, belt line, anterior thigh and axilla.[32]

Page 273

A carbuncle describes confluent infection of multiple, contiguous hair follicles, like multiple boils, in which the infection is limited to the subcutaneous tissue.

Local treatment of these infections includes using chlorhexidine and applying saline or aluminium subacetate soaks/compresses for 15 minutes, twice daily. Widespread infection should be treated with anti-staphylococcal antibiotics (e.g. flucloxacillin 500 mg four times a day for 7–14 days). Boils and abscesses may require incision and drainage.

Pseudomonas or 'hot-tub' folliculitis is usually contracted in spas or hot tubs. Symptoms appear from 6 hours to 5 days after bathing in contaminated water and include generalised malaise, low-grade fever and headache, accompanied by a pustular rash commonly appearing in the axilla, perineum or buttocks. The rash is usually self-limiting and disappears after 7–14 days. These infections are prevented by adequate filtration and chlorination of the baths.

Folliculitis may also occur after a vigorous massage (especially when insufficient lubricant is used) or after leg waxing or shaving.

Fungal and mite skin infections

Fungal skin infections are common among athletes because of the presence of sweat and use of occlusive clothing or footwear.

Tinea

The most common fungal skin infections are tinea pedis (athlete's foot) and tinea cruris (jock itch). Topical antifungal cream (e.g. clotrimazole, miconazole, ketoconazole) is effective in most cases of tinea pedis and cruris. This should be applied 2–3 times per day over the affected areas for 2–4 weeks. Moist infections between the toes resolve more quickly with the addition of drying powders.

PRACTICE PEARL

Preventive measures include regular changes of socks, shorts and underwear, the use of foot powders and regular cleaning of shower facilities.

Resistant cases should be referred to a dermatologist for alternative medications. Oral therapy (e.g. terbinafine, griseofulvin or itraconazole) is generally required, after confirmation of diagnosis, for tinea infections of the scalp, hair and nails.

MRSA—methicillin-resistant *Staphylococcus aureus*

The rise in community-acquired MRSA within the general population has also been found to be a cause of outbreaks of skin infections among athletes, particularly among those involved in contact sports. MRSA initially shows up as small, red bumps that may resemble a spider bite, a pimple or boil and can be accompanied by fever and rash. In athletes the majority of MRSA infections primarily affect soft tissues; but if allowed to enter the bloodstream an infection could result in sepsis, with a need for immediate medical attention.

Athletes with existing skin diseases may have chronic colonisation with *Staphylococcus A* and may be predisposed to recurrent infections. Skin breaks caused in play and poor hygiene practices have been identified as the primary risk factors in transmission. Up to 23% of athletes have been found to have colonisation with MRSA, but high colonisation alone does not appear sufficient to trigger an outbreak.[33]

Management of MRSA outbreaks requires the screening of players for carriage along with use of a topical nasal mupirocin therapy twice daily for 5 days for those found to have colonisation.[34] It may also be necessary to utilise chlorhexidine washes alongside maintaining extra vigilance in personal hygiene practices among all team members. The screening process for MRSA in the athlete requires assessment of primary culture sites of infection including nasal passages and any open skin lesions.

All known infections should have cultures taken for the known causative agent and tested for antimicrobial susceptibility. The application of empirical antibiotics should be considered pending results.[18] Antibiotic choices should be guided by knowledge of the local patterns of MRSA susceptibility.

PRACTICE PEARL

Key hygiene behaviours are needed to minimise the risk of obtaining or spreading infection in organised sports. Primary care physicians and trainers can help reinforce such educational messages.

Tinea gladiatorum is a fungal infection that is transmitted through skin-to-skin contact in wrestlers. It is the second most common skin infection in wrestlers after herpes, with a prevalence of between 20% and 75%. Although it is fairly benign, it can have major effects on the ability of the wrestler to compete. Screening of all wrestlers and disinfection of mats can help reduce spread.[35]

Onychomycosis

Onychomycosis is a fungal nail infection, typically caused by *Tricophyton rubrum* or *T. mentagrophytes.* It is common among athletes, particularly those who swim in pools, use communal showers, or have chronic tinea pedis and wear occlusive footwear.[36] The infection results from migration of the fungus under the distal nail plate leading to a nail bed infection that results in discoloration of the nail plate. Subungual debris then forms and the nail plate becomes distorted, thickened and separated from the nail bed. Over time the nail plate becomes brittle and crumbles.[3] [7] Treatment requires a long-term commitment with either an oral antifungal agent or topical nail lacquer.[38]

Scabies

Scabies mites are easily transmitted through skin-to-skin contact. Once on the skin surface the mite burrows into the epidermis. In a first-ever infection a person will usually develop symptoms in between two and six weeks.

Infestation manifests as small linear burrows and/or vesicles characteristically in axillary skin folds, finger and toe web spaces, the flexor surface of the wrists, the extensor surfaces of the elbows and knees, periumbilicus, genitalia, buttocks and lateral foot. The most prominent symptom is severe itching.

Confirmation of the diagnosis can be made by direct microscopic visualisation of mites from an infected papule. Topical therapy with acaricides, such as permethrin 5% cream or malathion 0.5% liquid, is very effective if applied twice, at one week apart. It is also important to treat close contacts. Bedding, clothing and towels used during the previous three days should be washed in hot water and dried in a hot dryer.

Pediculosis (lice)

Lice can occur on the body (pediculosis corporis), head (pediculosis capitis) and genitalia (pediculosis pubis); they are spread by close physical contact.[37] Once a person is infested, it can take 7–10 days for the nit (louse egg) to hatch. Patients may describe night-time itching and may develop an inflammatory reaction to scratching. As bites emerge, they appear as 2–4 mm (<0.25 in.) red papules on an erythematous base. Diagnosis can be confirmed by direct visualisation. Various over-the-counter medications are available for head lice. Most involve application to the scalp once and, if required, again 7 days later. In addition, a fine comb should be used to remove nits, and all clothing, bed linen and sporting equipment should be washed and dried in a hot dryer or discarded.

Respiratory and ear, nose and throat infections

The major ear, nose and throat infections include various forms of influenza and infectious mononucleosis (IM). IM brings with it the risk of splenic enlargement and, thus, splenic rupture in athletes (see below). Ear infections are a common problem in water sports.

Viral

Infections of the upper and lower respiratory tracts are common, especially during winter months. A survey of British athletes in 30 different Olympic sports found that infection was the cause of

missed training in 33% of cases.[39] Adults experience between two and four episodes of respiratory illnesses per year. It is thought that similar symptoms can be due to allergy or inflammation caused by dry, cold or polluted air.[40] In the vast majority of cases, respiratory tract infections are due to viruses. Over 200 different viruses can cause upper respiratory tract infections; those commonly involved are the adenovirus, influenza virus, echovirus, cytomegalovirus and rhinovirus. They may cause rhinitis, pharyngitis, bronchitis or pneumonia.

Treatment is usually aimed at controlling the accompanying fever and reducing the symptoms. Some symptomatic treatments are on the list of substances banned by the World Anti-Doping Agency (WADA, see Chapter 34). Antibiotics should not be used unless bacterial infection is suspected.

Influenza

Influenza (flu) is a common viral infection occurring in winter months. The flu season typically begins in November and continues until April in the temperate northern hemisphere, and lasts from April to October in the southern hemisphere. There are a number of strains of influenza virus; the predominant strain tends to vary from year to year.

Influenza can be a debilitating illness with systemic symptoms such as fever, malaise and myalgia. It is recommended that susceptible individuals, such as the elderly and those with a chronic illness, have annual influenza immunisation.

Athletes may wish to have annual influenza immunisation as the illness may result in their missing a considerable period of competition and training. Athletes involved in team sports may wish to be immunised because of the possibility of spread among team members. However, there is conflicting evidence for the effectiveness of influenza immunisation in healthy adults.

A 2010 Cochrane review noted that 'influenza vaccines have a modest effect in reducing influenza symptoms and working days lost' in healthy adults, but found no evidence of prevention of complications, such as pneumonia or transmission.[41] Some recently developed anti-influenza drugs are showing promise as a possible treatment for those who are in the early stages of the illness.

Infectious mononucleosis

The Epstein–Barr virus (EBV) causes infectious mononucleosis (IM), also known as 'glandular fever' or 'mono'. The incidence of IM is highest in adolescence and early adulthood, with 1–3% of American college students reported to become infected each year.[42] Many clinicians believe that the incidence of IM is higher in athletes who are training intensely, but there are no studies to support (or refute) this claim.

Clinical perspective

The severity of the infection appears to increase with age. Children infected by the Epstein–Barr virus develop a flu-like illness. Adolescents and young adults typically develop symptoms of fatigue, sore throat, malaise, headache and, less commonly, myalgia, nausea and vomiting.

Examination of the typical 15- to 19-year-old patient reveals an exudative pharyngitis and swollen cervical lymph nodes. A fever of 39–40°C (102–104°F) is common. Splenomegaly due to lymphocyte infiltration occurs in about 50% of cases and peaks in the second or third week of the illness. A similar clinical picture may be seen with cytomegalovirus infection, toxoplasmosis and primary infection with HIV.

PRACTICE PEARL

Patients with infectious mononucleosis who are treated with ampicillin or amoxicillin often develop a diffuse macular rash. Older patients have an increased tendency to develop complications of infectious mononucleosis, such as hepatitis or thrombocytopenia (reduced platelet count).

The virus is spread through close contact, especially saliva (e.g. via kissing). The incubation period is usually between 30 and 50 days after exposure to the virus, and the illness lasts between 5 and 15 days. However, tiredness may be more prolonged and, in some patients, may continue for a number of months.

Investigations

Investigations usually reveal a moderately raised white cell count (10–20 × 10^9/L) with an increase in the number of lymphocytes (50% or more of total white blood cell count). Between 10% and 20% of these lymphocytes are usually described as 'atypical'. Mild thrombocytopenia (platelet count <140 × 10^9/L) occurs in approximately 50% of patients. Liver function test abnormalities occur in approximately 75% of patients. The development of jaundice, however, is uncommon. Enlargement of the spleen may be confirmed on ultrasound.

Confirmation of IM is usually made serologically. The presence of heterophile antibodies can be seen in 85–90% of acute EBV infections. Most clinical laboratories use some form of latex agglutination method, such as the monospot or Paul–Bunnell tests. These tests are usually positive in the second week of illness. False negative results occur but other diagnoses (e.g. cytomegalovirus, HIV, toxoplasmosis) should be considered in the presence of a negative monospot result.

In the 10–15% who never develop a positive monospot test result, EBV-specific antibodies are measured. Most laboratories provide IgM and IgG antibody results. The IgM assay is positive in an acute infection and remains so for 1–2 months. The IgG antibodies tend to persist for life so are not indicative of current infection, only that a previous infection has occurred.

Treatment

Treatment of IM involves symptomatic treatment to reduce fever and sore throat. IM is not particularly contagious despite the relatively high incidence in adolescents and young adults. There is no need for isolation of the athlete with IM. Many people have adequate antibody levels

because of childhood exposure.

The athlete with IM should rest from sporting activity until all acute symptoms have resolved.

Risk of splenic rupture in infectious mononucleosis

The incidence of splenic rupture in cases of IM is thought to be between only 0.1% and 0.2%.[43, 44] Contact and collision sports should be avoided while the spleen is enlarged, as splenic rupture can be fatal. Most reports of splenic ruptures have occurred during the first three weeks of illness and so it is thought that spleen vulnerability peaks in this period.[44] The dilemma for the treating clinician is how to determine that the spleen size has returned to normal. If the spleen is palpable, then it is clearly enlarged. However, many enlarged spleens are not palpable.

Ultrasound is used to measure spleen size. Simple linear ultrasonographic measurements are often used, but there is uncertainty as to the normal size. An upper limit for normal of 12 cm length, 7 cm width and 4 cm thickness has been proposed, but spleen size varies considerably between individuals, although it correlates reasonably well with body size. Unfortunately, very few individuals have previous ultrasonic measurement of the spleen with which to compare the post- infective size.

Page 276

As the majority of spleen ruptures have occurred within 21 days of the onset of symptoms, most expert clinicians advise allowing return to play after that period, remembering that there is still a slight possibility of rupture at a later date; these risks should be clearly outlined to the patient. See Putukian et al.[44] for a detailed discussion of this issue. There have been some attempts made to protect the spleen from contact for collision sports, such as protective braces in basketball, but it is unclear whether these are effective.[45]

PRACTICE PEARL

Peak splenic enlargement by ultrasound occurred within 2–3.5 weeks and splenomegaly resolved within 4–6 weeks of the onset of symptoms of infectious mononucleosis.[44]

Bacterial

Otitis externa

Otitis externa is a diffuse inflammation of the skin lining the external auditory meatus that can be caused by either *Pseudomonas* or *Staphylococcal aureus* infection. This is sometimes known as 'swimmer's ear', as it is exacerbated by moisture, but also by trauma of the ear canal with cotton buds or finger nails.

Otitis externa presents as a painful itch or discharge from the external ear. Pain is aggravated by traction on the tragus of the ear. The external auditory canal is usually swollen and tender and may be filled with debris.

Page 277

CASE STUDY

Mark Cavendish, British track and road cycling—Epstein–Barr virus

British cyclist Mark Cavendish has won 30 separate stages of the Tour de France, has an Olympic silver medal in the omnium track cycling and has won the points race in all three of the major European tours (La Vuelta, the Giro d'Italia and the Tour de France).

Diagnosis

In early 2017 he was suffering from unexplained fatigue, which was initially attributed to an ankle injury. Due to ongoing fatigue he was sent for further blood tests, which revealed he had contracted the Epstein–Barr virus or mononucleosis (mono).

Management

Cavendish was managed with a regular monitoring program of daily questionnaires on his sleep, general health and tiredness level, alongside regular blood tests. His return to competition and heavy training was carefully titrated, based on both his subjective reports and the objective data from his blood markers.

Anti-VCA (viral capsid antigen) IgG appears around 2–4 weeks after infection with mono and then slowly falls to lower levels, but is likely to remain present for the rest of the patient's lifetime. Anti-EA (early antigen) is another common marker that is elevated, indicating an active mono infection. This antigen also falls to occasionally undetectable levels, but may remain present in a large percentage of individuals.

Conclusion

Cavendish was able to return to full training 6 weeks after the initial diagnosis. His story echoes that of many other athletes who have suffered from the disease, and have experienced an unexplained drop in performance. In this case there were no complications from the infection, but it should be noted the infection can also lead to chronic fatigue syndrome as a result of the viral effects on the immune system. This complication was ultimately responsible for the retirement of former world top-10 Swedish tennis professional Robin Söderling at the age of only 26.

Figure 18.3 Tour de France, 2007
MIKE COLEMAN./ALAMY
Sources: references 89, 90, 91, 92, 93

Treatment is by irrigation to remove purulent debris, protection from exposure to water and mechanical trauma (e.g. avoiding ear plugs), and application of antibiotic and steroid combination drops (e.g. Gentisone® HC, Sofradex®, Kenacomb®). There is a high incidence of recurrent infection.

Recurrences may be limited by the use of drying agents such as 5% acetic acid (Aquaear®) before and after swimming and the insertion of water-resistant earplugs. Another simple preventive measure is shaking water out of the ear after swimming and drying the area with a hair dryer.

Otitis media

Otitis media is inflammation of the middle ear and is sometimes associated with upper respiratory tract infections, which may be viral or bacterial. Clinical features include ear pain and an inflamed or bulging ear drum. Most (80%) recover without antibiotics; nasal decongestants may help.[46] Diving should be avoided until there is normal tympanic membrane movement, as indicated by Valsalva or tympanometry, due to risk of membrane rupture at depths greater than 1.5 m. Swimming should only be resumed if there is an intact tympanic membrane.

Gastrointestinal and liver infections

Acute gastroenteritis

Acute gastroenteritis remains a major public health concern worldwide. The norovirus (an RNA virus) causes approximately 90% of epidemic non-bacterial outbreaks of gastroenteritis around the world.[47] The viruses are transmitted by contaminated food or water surfaces and person-to-person contact. Because outbreaks of norovirus infection often occur in closed or semi-closed communities (such as hospitals and hotels), it can quickly spread among sports teams where athletes are in close contact. Many norovirus outbreaks have been traced to food that was handled by one infected person.[48]

The symptoms of a norovirus gastroenteritis usually start between 12 and 48 hours after the initial infection; the first symptom is usually nausea, followed by projectile vomiting and watery diarrhoea. The symptoms normally last 12–60 hours. Norovirus is rapidly inactivated by either sufficient heating or by chlorine-based disinfectants. For the affected individual it is important to ensure good hydration and paracetamol for any fever. It is important to limit the spread of the virus and therefore the affected player should be isolated as soon as symptoms appear; he or she should not be in contact with other players until having been symptom-free for at least 48 hours.

Traveller's diarrhoea

Traveller's diarrhoea has been defined as 'an increase in frequency of bowel movements to three or more loose stools per day during a trip abroad, usually to a less economically developed region'.[49]

Limited attacks of diarrhoea occur frequently among athletes in international competition. Agents that may cause traveller's diarrhoea include *Escherichia coli, Campylobacter,* rotavirus, *Salmonella, Shigella* and *Giardia lamblia.*

The high incidence of diarrhoea among travellers is thought to be due to changes in the normal bacterial flora of the food and water in foreign countries. The traveller is exposed to different bacteria to which he or she is not already immune.

The attack of diarrhoea usually occurs in the first week after arrival, and commonly lasts between 24 and 48 hours. It is often associated with mild fever, abdominal pain and malaise. Although the majority of these illnesses settle quickly, athletic performance may be affected during the attack and for some time afterwards.

Because of the potential effect on performance, attention has been paid to possible methods of preventing traveller's diarrhoea. Avoidance of local water and raw foods that may have been washed in water (e.g. salads) is recommended. However, in spite of these precautions infection may still occur.

Prophylaxis

There is some evidence that probiotics such as freeze-dried cultures or yoghurts may help prevent traveller's diarrhoea.[50] As it is not yet known what preparation and dose is best, this is not a current recommendation.

Antibiotic prophylaxis remains controversial.[51] When deciding whether or not to use this approach, the athlete and physician must take into account any underlying medical illnesses, the importance of the competition, compliance of the traveller with food precautions and individual preference. Antibiotics may cause mild or in some cases serious, allergic reactions.

PRACTICE PEARL

For prophylaxis, recommended antibiotics include norfloxacin (400 mg/day) and ciprofloxacin (500 mg/day). These should be commenced on arrival in the foreign country and continued until the athlete has been back home for 48 hours.

Trimethoprim–sulfamethoxazole and doxycycline were popular for prophylaxis in the 1990s, but resistance is common now. Bismuth subsalicylate is less effective than antibiotic prophylaxis.

Treatment

The vast majority of cases will be managed at home with oral rehydration. Most are self-limiting illnesses that do not require medical intervention. Antidiarrhoeal medications (e.g. loperamide) can be used for logistical reasons, particularly while travelling. Antibiotics can shorten symptoms, but they are only indicated if diarrhoea is severe, bloody or persists for more than 48 hours. Ideally, where it is needed, antibiotic therapy should be guided by microbiology advice, with the benefit of the results of the stool sample and sensitivities determined thereby. Where empirical

treatment is needed, ciprofloxacin 500 mg twice daily for three days is the usual choice. However, in travellers from South Asia and South-east Asia, quinolone resistance is common and azithromycin (off-licence) is the preferred choice. Studies show these antibiotics reduce the course from an average of 3 days to an average of 1.5 days.[49] If diarrhoea persists for more than 5–7 days, infections such as giardiasis should be considered; this can be treated with a single dose of tinidazole (2 g). More persistent diarrhoea should be investigated.

Hepatitis

Viral hepatitis is neither a single disease condition nor is it caused by a single viral agent. There are a multitude of viral causes, including hepatitis A, B, C, D, E, cytomegalovirus, Epstein–Barr, herpes simplex and adenovirus to name but a few.

The commonest group is the hepatitis group of viruses, of which at least five distinct types have been identified: hepatitis A (HAV), hepatitis B (HBV), hepatitis C (HCV), hepatitis delta or D (HDV) and hepatitis E (HEV).

The sport-specific risks of hepatitis are discussed in the box 'Athletes and risk of hepatitis'.

Hepatitis A

Hepatitis A virus (HAV) infection occurs worldwide. HAV is spread via the faecal–oral route, and is more prevalent in low socioeconomic areas in which a lack of adequate sanitation and poor hygienic practices facilitate spread of the infection. HAV infection, the symptoms of which can develop 2–6 weeks from infection, usually results in an acute, self-limiting illness, typically lasting up to 8 weeks, and may include vomiting, abdominal pain and diarrhoea.[52] It rarely leads to fulminant hepatic failure.[53]

The diagnosis of acute HAV infection is made by the detection of anti-HAV antibodies in a patient with the typical clinical presentation. Treatment is supportive. Approximately 85% of individuals who are infected with HAV have full clinical and biochemical recovery within three months, and nearly all have complete recovery by six months.[54] Safe and effective vaccines against HAV are available, and athletes working or travelling in countries that have a high or intermediate rate of HAV infection should be immunised; immunisation can last for 20 years.

Hepatitis B (HBV)

About a third of the world's population has been infected with HBV at one point in their lives, including 343 million who have chronic infections.[55] Another 129 million new infections occurred in 2013.[56] Over 750 000 people die of hepatitis B each year. About 300 000 of these are due to liver cancer.[57]

The predominant mode of transmission of HBV varies in different geographical areas. Perinatal infection is the predominant mode of transmission in high prevalence areas.[58]

In comparison, horizontal transmission, particularly in early childhood, accounts for most cases of chronic HBV infection in intermediate prevalence areas, while unprotected sexual intercourse and intravenous drug use in adults are the major routes of spread in low prevalence areas.[59]

The spectrum of clinical manifestations of HBV infection varies in both acute and chronic disease. During the acute phase, manifestations range from subclinical or anicteric hepatitis to icteric hepatitis and, in some cases, fulminant hepatitis. During the chronic phase, manifestations range from an asymptomatic carrier state to chronic hepatitis, cirrhosis and hepatocellular carcinoma. Extrahepatic manifestations can also occur with both acute and chronic infection.

The percentage of patients who progress from acute to chronic hepatitis B is determined primarily by the age at infection. The rate is approximately 90% for a perinatally acquired infection, 20–50% for infections acquired between the age of one and five years and less than 5% for an adult-acquired infection.[60] Chronic carriers of hepatitis B pose a problem regarding their current infectivity risk to others. They should be assessed regularly by a hepatitis specialist for further tests, including hepatitis B DNA load, to determine how active their condition is and thus their infectivity is.

Treatment for acute hepatitis B is mainly supportive. In addition, appropriate measures should be taken to prevent infection in exposed contacts. The main aim of treatment for chronic hepatitis B is to suppress replication before there is irreversible liver damage. Treatment strategies for chronic hepatitis B include interferon, lamivudine, adefovir, dipivoxil, telbivudine, entecavir and tenofovir. Many new treatments are undergoing testing. Thus, an approach to the care of patients with HBV is evolving rapidly.

The infection has been preventable by vaccination since 1982, and this is recommended by the World Health Organization in the first day of life if possible. Two or three more doses are required at a later time for full effect. This vaccine works about 95% of the time.

PRACTICE PEARL

Any athlete involved in a contact or collision sport should be immunised against HBV.

Any athlete involved in a contact or collision sport should be immunised against HBV. The hepatitis B vaccine (Engerix®-B) has a zero-, one- and six-month schedule. Immunity should be assessed 1–4 months after the last course of the vaccine, by means of a blood test. If the athlete does not produce an adequate response then he or she may need a booster or testing to exclude past or current hepatitis B infection.

Athletes and risk of hepatitis

Athletes are at risk of developing hepatitis mainly as a result of activity unrelated to sport (e.g. sexual contact, sharing needles); however, a small theoretical risk of virus contamination during certain types of athletic activity does exist. The mode of transmission of viral hepatitis from an infected individual

varies depending upon the specific viral agent, although some overlap does exist (Table 18.2).

Table 18.2 Transmission of viral hepatitis

Virus	Transmission	Chronic carrier	Vaccine	Disease severity
HAV	Food	No	Yes	Not severe, disappears on its own
HBV	Blood, sexual intercourse, mother-to-child	Yes	Yes	No severe symptoms
HCV	Blood, sexual intercourse, mother-to-child	Yes	No	No severe symptoms
HDV	Blood, sexual intercourse, mother-to-child	Yes	No	Severe, high mortality rate
HEV	Food	No	No	Moderate

Infection with HAV or HEV is likely to occur as a result of exposure to contaminated food or beverages. The risk of infection is particularly high during international travel to areas with poor hygienic conditions where HAV and HEV are endemic.[61] Direct transmission of HAV or HEV during sports participation has not been described;[62] however, outbreaks of hepatitis among groups of athletes have been reported, the most famous of which involved 90 members of an American college football team after an infected group of children contaminated the drinking water used during practice.[63]

For athletes, exposure to blood-borne pathogens such as HBV and HCV is also much more likely to occur during activities not related to sport, such as unprotected sexual activity, using injectable drugs such as anabolic steroids, sharing personal items such as razors, and tattooing and body piercing. However, there is the potential for horizontal transmission of HBV and HCV while playing sports, especially contact or collision sports. In a study in wrestlers who were found to be chronic carriers of hepatitis B, it was discovered that sweat may be another means of hepatitis B transmission, as the hepatitis B DNA load was similar in the sweat to that of the serum.[64]

The concentration of HBV in blood is higher than that of HIV, and HBV is also more stable in the environment; therefore, the risk of transmission of HBV is much (actually 50–100 times) greater than the risk of transmission of HIV.[65] HBV is also more environmentally stable, is resistant to alcohol and some detergents and capable of surviving on environmental surfaces for more than 7 days.

The blood of an infected athlete may contaminate the skin or mucous membranes of other athletes or staff. Two reports of transmission of HBV among Japanese athletes have been described, one in sumo wrestling[66] and the other in American football at the University of Okayama.[67]

There has been only one report of HBV transmission in a non-contact sport.[68] Between 1957 and 1963, there were 568 cases of hepatitis B reported among Swedish athletes participating in the sport of orienteering. It was thought that the most likely route of contamination was the use of water contaminated with infected blood to clean the wounds on multiple individuals who were cut by thorns and bushes during the competition.

There have been no documented cases of HCV transmission during sporting activity,[62] but there has been a documented case during bloody fisticuffs, which was thought to have occurred when the two participants shared a common handkerchief to wipe their bleeding wounds.[69] There has also been a report of three soccer players from one amateur club contracting HCV as a result of sharing a syringe to inject intravenous vitamin complexes.[70]

It is clear that the risk of transmission of both HBV and HCV during sport is very low and there is no reason why infected individuals should not be allowed to compete. All carriers should have regular follow-up by specialists to monitor viral activity and any systemic effects. It has been shown in a group of Taiwanese runners that chronic HBV carriers, compared with non-HBV carriers, had greater increases in ALT, AST and total bilirubin during a 7-day ultramarathon, indicating that the liver function

of carriers is more highly impacted in these races.[71] There is the dilemma of allowing infected athletes to compete without disclosing their status to team members and opposition.

In those who have not been immunised and who experience a known or high-risk exposure to HBV, post-exposure prophylaxis with immune globulin should be administered. Post-exposure immunisation with HBV vaccine can attenuate or prevent acute HBV.

Hepatitis C

Infection with the hepatitis C virus (HCV) can result in both acute and chronic hepatitis. The acute process is most often asymptomatic; if symptoms are present, they usually abate within a few weeks. Acute infection rarely causes hepatic failure. Acute hepatitis C typically leads to chronic infection; 60–80% develop chronic hepatitis (abnormal liver enzymes). Chronic hepatitis C is usually slowly progressive; it may not result in clinically apparent liver disease in many patients if the infection is acquired later in life. Approximately 20–30% of chronically infected individuals develop cirrhosis over a period of 20–30 years.

Chronic hepatitis C is the most common cause of chronic liver disease and the most frequent indication for liver transplantation in the USA. The decision to offer antiviral therapy to a treatment-naive patient is usually straightforward when there is a detectable viral load, significant chronic hepatitis and fibrosis on liver biopsy, and an absence of contraindications to treatment.

Treatment is with combination therapy with peginterferon plus ribavirin. The duration of therapy depends on the patient's HCV genotype. Genotypes 1 and 4 have lower response rates and require longer courses of treatment (48 weeks) compared with HCV genotypes 2 or 3 (24 weeks).

Hepatitis D

Hepatitis D virus (HDV) is often referred to as 'hepatitis delta virus' or 'delta agent'. Although HDV can replicate autonomously, the simultaneous presence of HBV is required for complete virion assembly and secretion. As a result, individuals with hepatitis D are always dually infected with HDV and HBV. Acute HBV and HDV co-infection tends to be more severe than acute HBV infection alone and is more likely to result in fulminant hepatitis.

Hepatitis E

Hepatitis E virus (HEV) is an enterically-transmitted acute viral hepatitis. The epidemiology of HEV is similar to that of HAV. Hepatitis E virus generally causes a self-limiting acute infection, although fulminant hepatitis can develop. The clinical signs and symptoms in patients with typical hepatitis E are similar to those seen with other forms of acute viral hepatitis, although the disease appears to be relatively more severe than hepatitis A.

The diagnosis of HEV is based on the detection of HEV in serum or stool by PCR (polymerase chain reaction) or by the detection of IgM antibodies to HEV. Treatment is supportive.

An effective vaccine against HEV has been developed, but is not yet commercially available. Travellers to endemic areas (i.e. Asia, Africa, the Middle East and Central America) should engage in practices that may prevent infection, such as avoiding drinking water of unknown purity, or

eating uncooked shellfish, fruits or vegetables.

Acute viral hepatitis and physical activity

In those patients with acute viral hepatitis, strict bed rest and avoidance of all physical activity are no longer thought to be necessary. Acute hepatitis infection should be viewed just as other viral infections, and the ability to play should be based on clinical signs and symptoms such as fever, fatigue or hepatomegaly.[72] Hepatomegaly (80%) and splenomegaly (10–20%) may persist after other symptoms have settled. Contact and collision sports should be avoided until the organomegaly has resolved.[61]

Other infections

Human immunodeficiency virus

The human immunodeficiency virus (HIV) pandemic has spread to every country in the world and has infected 59 million people worldwide, including 20 million who have already died.[73] HIV infection is usually acquired through sexual intercourse, exposure to contaminated blood or perinatal transmission. Risk factors for HIV transmission include viral load, lack of circumcision, sexual risk, presence of ulcerative sexually transmitted diseases, nitrate inhalant use, and host and genetic factors.[74–76]

Infection with HIV initially causes a flu-like illness. This is followed by an asymptomatic period characterised by replication of the HIV virus and antibody formation. The length of this period is variable but may last months or years. This is followed by the development of acquired immunodeficiency syndrome (AIDS), which may present as a variety of diseases associated with the suppression of immunity. These include *Pneumocystis carinii* pneumonia, Kaposi's sarcoma, cytomegalovirus infection, cryptosporidiosis and lymphoma.

The presence of HIV antibodies can be detected a short time after the initial exposure, usually within three months. Practising safe sex and avoiding direct contact with blood or blood products can reduce the risk of HIV infection. There is an extremely slight risk of acquiring HIV from contact on the sporting field, from an HIV carrier bleeding from an open wound or from bloodstained clothing. This risk has been described as being 'exceedingly low' and is estimated to be between one per million and one per 85 million game contacts.[77]

There are no confirmed reports of HIV transmission during sport, although there has been one possible transmission during a football match[78] and a number of reports of transmission Page 281 during bloody street fights.[79, 80]

Attention to the guidelines described in the box will reduce this risk. Medical personnel attending bleeding players must make every attempt to stop the bleeding and remove all exposed blood. If bleeding cannot be controlled, the player should be removed from the field of play. Medical staff should always wear gloves when treating a bleeding wound.

The optimal level of participation and competition in an HIV-affected athlete remains unknown. Healthy, asymptomatic athletes with HIV may continue in competition and exercise without restriction but should avoid overtraining. Athletes with AIDS may remain physically active and

continue training on a symptom-related basis but should avoid strenuous exercise and reduce activity during acute illness.

Sexually transmitted infections

More than 20 different sexually transmitted infections have been identified and should be considered with any patient with testicular pain, penile/urethral discharge, prostatitis, urethritis, dyspareunia, dysuria or genital warts.

It should be noted that a patient may have more than one sexually transmitted disease and should be screened and tested accordingly. This is particularly important in athletes, who need to be aware that sexually transmitted infections have been shown to also cause other symptoms that could affect their athletic performance. These include reactive arthritis, which is an autoimmune condition that develops in response to an infection in another part of the body. By the time the patient presents with symptoms of arthritis, the trigger infection has been cured or is in remission in chronic cases, thus making determination of the initial cause difficult. It was reported in a case study of 10 professional athletes with persistent knee injuries that eight had sexually acquired reactive arthritis.[81]

Tetanus

Tetanus is caused by *Clostridium tetani,* which is normally found in soil and faeces; it only flourishes in dead tissue and produces a toxin that targets anterior horn cells (in the spinal cord). A tetanus-prone injury is defined as 'an injury where there has been a puncture type of wound, significant devitalised tissue or contact with soil or manure', which is something that should be considered with all open-wound injuries in athletes, especially on the playing field. The incubation period is 2–24 days. Initially there is muscle spasm at the injury site; the spasms then progress to the muscles of the face, neck and spine. It can also cause autonomic dysfunction.

Diagnosis is by clinical assessment, with no definitive laboratory test. The single most important step in preventing tetanus infection is good wound cleaning with debridement of dead tissue. Human antitetanus immunoglobulin is given intramuscularly, together with parenteral penicillin. Wound toilet should also be carried out.

If the immune status of a patient is not known, the patient should be assumed to be non-immune. For tetanus, a total of five doses of vaccine at the appropriate intervals are considered to give lifelong immunity. If the risk of tetanus is especially high (e.g. the wound is contaminated with soil), human antitetanus immunoglobulin should be given to provide immediate additional protection.

PREVENTIVE MEASURES AND REDUCING RISK OF INFECTIONS

As with any medical condition, prevention is better than cure and so it is important that all athletes are advised to report any illness immediately to their doctor. By isolating the infected individual, or preventing him or her from mixing with others, the risk of spread is reduced. Where possible, the athlete's doctor should consider screening for sexually transmitted infections and conditions for which vaccines may be available.

Athletes should also be educated about good hygiene procedures, such as hand washing or using antibacterial hand gels, and not sharing drink bottles (or at least not making direct contact with the mouth and instead squirting the fluid into the mouth). See the national guidelines in the box.

As athletes may compete or reside almost anywhere around the globe, one should consider the appropriate travel immunisations and malaria chemoprophylaxis if required. The clinician should always enquire about the player's travel history, in case he or she has been in contact with an exotic illness.

National position statements on infectious diseases

Sports medicine authorities in Australia, the USA and Canada have all produced national position statements[82–84] on infectious diseases, with particular reference to HIV and hepatitis B. These are summarised below.

A number of blood-borne infectious diseases can be transmitted during body contact and collision sports. The more serious include HIV/AIDS and hepatitis infections. These diseases may be spread by contact with infected:

Page 282

- blood
- saliva (excluding HIV)
- perspiration (excluding HIV)
- semen and vaginal fluids.

The following recommendations will reduce the risk of disease transmission. All open cuts and abrasions must be reported and treated immediately.

Players

1. It is the players' responsibility to maintain strict personal hygiene, as this is the best method of controlling the spread of these diseases.
2. It is strongly recommended that all participants involved in contact sport be vaccinated with hepatitis B vaccine.
3. Players with prior evidence of these diseases must obtain advice and clearance from a physician prior to participation.

Team areas

1. It is the clubs' responsibility to ensure that dressing rooms are clean and tidy. Particular attention should be paid to hand basins, toilets and showers. Adequate soap, paper hand towels, brooms and disinfectants must be available at all times.
2. Communal bathing areas (e.g. spas) should be strongly discouraged.
3. Spitting or urinating in team areas must not be permitted.
4. All clothing, equipment and surfaces contaminated by blood must be considered potentially infectious and treated accordingly. Clothing soiled with blood and other body fluids should be washed in hot, soapy water.
5. Sharing of towels, face washers and drink containers should be avoided.
6. All personnel working in team areas should be vaccinated against hepatitis B.

7. In all training areas, open cuts and abrasions must be reported and treated immediately.
8. Athletes should not share personal items, such as razors, toothbrushes and nail clippers.
9. Athletes must cover areas of broken skin with an occlusive dressing before and during participation.
10. Disposable vinyl or latex gloves should be worn to avoid contact with blood or other bodily fluids visibly tinged with blood and any object such as equipment, bandages or uniforms contaminated with these fluids.
11. Athletes with active bleeding should be removed from competition as soon as possible and the bleeding stopped. Wounds should be cleaned with soap and water. Skin antiseptics may be used if soap and water are not available. Wounds must be covered with an occlusive dressing that remains intact during play, before athletes return to competition.
12. Equipment and playing areas contaminated with blood must be cleaned until all visible blood is gone and then disinfected with an appropriate germicide such as a freshly made bleach solution containing one part bleach in 10 parts of water. The decontaminated equipment or area should be in contact with the bleach solution for at least 30 seconds. The area may be wiped with a disposable cloth after the minimum contact time or be allowed to air dry.

Referees and game officials

1. These officials must report all open cuts and abrasions at the first available opportunity.
2. All contaminated clothing and equipment must be replaced prior to the player being allowed to resume play.
3. If bleeding should recur, the above procedure must be repeated.
4. If bleeding cannot be controlled and the wound securely covered, the player must not continue in the game.
5. Those who officiate in body contact and collision sports should be vaccinated against hepatitis B.

Education

1. There is an obligation upon all relevant sporting organisations to provide suitable information on associated risk factors and prevention strategies for these diseases.
2. The safe handling of contaminated clothing, equipment and surfaces must be brought to the attention of all players and ancillary staff.
3. In the event of a player, official or member of the ancillary staff being found to be suffering from such a blood-borne disease (e.g. hepatitis B, HIV), that person cannot resume training or play, nor be involved in any team or match, until cleared by his or her local medical officer or the team physician.

REFERENCES

1. Metz JP. Upper respiratory tract infections: who plays, who sits? *Curr Sports Med Rep* 2003; 2: 84–90.
2. Shepard RJ, Shek PN. Exercise, immunity, and susceptibility to infection: a J-shaped relationship? *Phys Sportsmed* 1999; 27(6): 47–71.

3. Woods J, Davis J, Smith J et al. Exercise and cellular innate immune function. *Med Sci Sports Exerc* 1999; 31: 57–66.
4. Nieman D. Nutrition, exercise and immune system function. *Clin Sports Med* 1999; 18: 537–48.
5. Nieman DC, Henson DA, Austin MD et al. Upper respiratory tract infection is reduced in physically fit and active adults. *Br J Sports Med* 2011; 45(12): 987–92.
6. Walsh NP, Gleeson M, Shephard RJ et al. Position statement. Part one: immune function and exercise. *Exerc Immunol Rev* 2011; 17: 6–63.
7. Gleeson M, Bishop NC. URI in athletes: are mucosal immunity and cytokine responses key risk factors? *Exerc Sport Sci Rev* 2013; 41(3): 148–53.
8. Nieman D. Is infection risk linked to exercise workload? *Med Sci Sports Exerc* 2000; 32(7): S406–11.
9. Foster C. Monitoring training in athletes with reference to overtraining syndrome. *Med Sci Sports Exerc* 1998; 30: 1164–8.
10. Fricker PA, Pyne DB, Saunders PU et al. Influence of training loads on patterns of illness in elite distance runners. *Clin J Sport Med* 2005; 15(4): 246–52.
11. Pyne DB, McDonald W, Gleeson M et al. Mucosal immunity, respiratory illness, and competitive performance in elite swimmers. *Med Sci Sports Exerc* 2001; 33: 348–53.
12. Primos WA, Jr. Sports and exercise during acute illness: recommending the right course for patients. *Phys Sportsmed* 1996; 24(1): 44–54.
13. Budgett R. Fatigue and underperformance in athletes: the overtraining syndrome. *Br J Sports Med* 1998; 32: 107–10.
14. Parker S, Brukner P, Rosier M. Chronic fatigue syndrome and the athlete. *Sports Med Train Rehab* 1996; 6: 269–78.
15. Friman G, Wesslen L. Infections and exercise in high-performance athletes. *Immunol Cell Biol* 2000; 78: 510–22.
16. Weidner T, Schurr T. Effect of exercise on upper respiratory tract infection in sedentary subjects. *Br J Sports Med* 2003; 37: 304–6.
17. Eichner E. Infection, immunity, and exercise: what to tell your patients. *Phys Sportsmed* 1993; 21: 125.
18. Davies HD, Jackson MA, Rice SG et al. Infectious diseases associated with organized sports and outbreak control. *Pediatrics* 2017; 140(4). Published online: 25 September 2017. doi: 10.1542/peds.2017-2477.
19. Walsh NP, Gleeson M, Pyne DB et al. Position statement. Part two: maintaining immune health. *Exerc Immunol Rev* 2011; 17: 64–103.
20. Schwellnus M, Soligard T, Alonso JM et al. How much is too much? (Part 2). International Olympic Committee consensus statement on load in sport and risk of illness. *Br J Sports Med* 2016; 50(17): 1043–52.

21. Cyr PR. Viral skin infections: preventing outbreaks in sports settings. *Phys Sportsmed* 2004; 32(7): 33–8.
22. Rush S. Sports dermatology. *ACSMs Health Fit J* 2002; 6(4): 24–6.
23. Anderson BJ. Managing herpes gladiatorum outbreaks in competitive wrestling: the 2007 Minnesota experience. *Curr Sports Med Rep* 2008; 7(6): 323–7.
24. Anderson BJ. The effectiveness of valacyclovir in preventing reactivation of herpes gladiatorum in wrestlers. *Clin J Sport Med* 1999; 9(2): 86–90.
25. National Collegiate Athletic Association (NCAA). *2014–15 NCAA Sports Medicine Handbook*. 25th ed. Indianapolis, IN: NCAA, 2014.
26. Johnson R. Herpes gladiatorum and other skin diseases. *Clin Sports Med* 2004; 23: 473–84.
27. Mobacken H, Nordin P. Molluscum contagiosum among cross-country runners. *J Am Acad Dermatol* 1987; 17: 519–60.
28. Ibrahim F, Khan T, Pujalte GG. Bacterial skin infections. *Prim Care* 2015; 42(4): 485–99.
29. Joint Formulary Committee. *British National Formulary* (74). London: BMJ Group and Pharmaceutical Press, 2017.
30. Hartman-Adams H, Banvard C, Juckett G. Impetigo: diagnosis and treatment. *Am Fam Physician* 2014; 90(4): 229–35.
31. Bubb RG. *Wrestling Rules and Interpretations*. Indianapolis, IN: NCAA, 2002.
32. Levy JA. Common bacterial dermatoses. *Phys Sportsmed* 2004; 32(6): 33–9.
33. Creech CB, Saye E, McKenna BD et al. One-year surveillance of methicillin-resistant *Staphylococcus aureus* nasal colonisation and skin and soft tissue infections in collegiate athletes. *Arch Pediatr Adolesc Med* 2010; 164(7): 615–20.
34. Kirkland EB, Adams BB. Methicillin-resistant *Staphylococcus aureus* and athletes. *J Am Acad Dermatol* 2008; 59(3): 494–502.
35. Hedayati MT, Afshar P, Shokohi T et al. A study on tinea gladiatorum in young wrestlers and dermatophyte contamination of wrestling mats from Sari, Iran. *Br J Sports Med* 2007; 41: 332–4.
36. Seraly MF, Fuerst ML. Diagnosing and treating onychomycosis. *Phys Sportsmed* 1998; 26(8): 58–67.
37. Winokur RC, Dexter WM. Fungal infections and parasitic infestations in sports. *Phys Sportsmed* 2004; 32(10): 23–33.
38. De Berker D. Fungal nail disease. *N Engl J Med* 2009; 360: 2108–16.
39. English Institute of Sport. *Injury and Illness in Great Britain Sport*. Olympiad review August 2009. English Institute of Sport, 2009.
40. Bermon S. Airway inflammation and upper respiratory tract infection in athletes: is there a link? *Exerc Immunol Rev* 2007; 13: 6–14.

41. Jefferson T, Di Pietrantonj C, Rivetti A et al. Vaccines for preventing influenza in healthy adults. *Cochrane Database Syst Rev* 2010 Jul 7; (7): CD001269.
42. Brodski AL, Heath CW. Infectious mononucleosis: epidemiological patterns at United States colleges and universities. *Am J Epidemiol* 1972; 96: 87–93.
43. Hosey RG, Kriss V, Uhl TL et al. Ultrasonographic evaluation of splenic enlargement in athletes with acute infectious mononucleosis. *Br J Sports Med* 2008; 42: 974–7.
44. Putukian M, O'Connor F, Stricker P et al. Mononucleosis and athletic participation: an evidence-based subject review. *Clin J Sport Med* 2008; 18(4): 309–15.
45. Shah N, Richards D. Facilitating sport participation with a customised spleen guard: a case of a basketball player with splenomegaly. *Clin J Sport Med* 2008; 18(1): 92–5.
46. Ramakrishnan K, Sparks RA, Berryhil WE. Diagnosis and treatment of otitis media. *Am Fam Physician* 2007; 76(11): 1650–8.
47. Lindesmith L, Moe C, Marionneau S et al. Human susceptibility and resistance to Norwalk virus infection. *Nat Med* 2003; 9(5): 548–53.
48. Koopmans M, Duizer E. Foodborne viruses: an emerging problem. *Int J Food Microbiol* 2004; 90(1): 23–41.
49. Barrett J, Brown M. Travellers' diarrhoea. *BMJ* 2016; 353: i1937.
50. Guandalini S. Probiotics for prevention and treatment of diarrhea. *J Clin Gastroenterol* 2011; 45 Suppl: S149–53.
51. Young MA, Fricker PA, Maughan RJ et al. The travelling athlete: issues relating to the Commonwealth Games, Malaysia, 1998. *Clin J Sport Med* 1998; 8: 130–5.
52. Matheny SC, Kingery JE. Hepatitis A. *Am Fam Physician* 2012; 86(11): 1027–34.
53. Taylor RM, Davern T, Munoz S et al. Fulminant hepatitis A virus infection in the United States: incidence, prognosis, and outcomes. *Hepatology* 2006; 44: 1589.
54. Koff RS. Review article: vaccination and viral hepatitis—current status and future prospects. *Aliment Pharmacol Ther* 2007; 26(10): 1285–92.
55. GBD 2015 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet* 2016; 388(10053): 1545–602.
56. Schilsky ML. Hepatitis B '360'. *Transplant Proc* 2013; 45(3): 982–5.
57. Global Burden of Disease Study 2013 Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2015; 386(9995): 743–800.
58. Wiseman E, Fraser MA, Holden S et al. Perinatal transmission of hepatitis B virus: an Australian experience. *Med J Aust* 2009; 190(9): 489–92.
59. Kim WR. Epidemiology of hepatitis B in the United States. *Curr Hep Rep* 2007; 6(1): 3–

8.
60. Lok AS, McMahon BJ. Chronic hepatitis B: update 2009. *Hepatology* 2009; 50: 661.
61. Harrington DW. Viral hepatitis and exercise. *Med Sci Sports Exerc* 2000; 32: S422–30.
62. Anish EJ. Viral hepatitis: sports-related risk. *Curr Sports Med Rep* 2004; 3: 100–6.
63. Morse LJ, Bryan JA, Hurley JP et al. The Holy Cross college football team hepatitis outbreak. *JAMA* 1972; 219: 706–8.
64. Bereket-Yücel S. Risk of hepatitis B infections in Olympic wrestling. *Br J Sports Med* 2007; 41(5): 306–10.
65. Kordi R, Wallace WA, Orchard J. Blood borne infections in sport: risks of transmission, methods of prevention, and recommendations for hepatitis B vaccination; commentary. *Br J Sports Med* 2004; 38(6): 678–84.
66. Kashiwagi S, Hayashi J, Ikematsu H et al. An outbreak of hepatitis B in members of a high school sumo wrestling club. *JAMA* 1982; 248: 213–14.
67. Tobe K, Matsuura K, Ogura T et al. Horizontal transmission of hepatitis B virus among players of an American football team. *Arch Intern Med* 2000; 160: 2541–5.
68. Ringertz O, Zetterberg B. Serum hepatitis among Swedish track finders. An epidemiological study. *N Engl J Med* 1967; 276: 540–6.
69. Bourlière M, Halfon P, Quentin Y et al. Covert transmission of hepatitis C virus during bloody fisticuffs. *Gastroenterology* 2000; 119(2): 507–11.
70. Parana R, Lyra L, Trepo C. Intravenous vitamin complexes used in sporting activities and transmission of HCV in Brazil. *Am J Gastroenterol* 1999; 94: 857–8.
71. Chou SL, Chou MY, Wang YH et al. The impact of chronic carrier of hepatitis B virus on liver function in a 7-day ultramarathon race. *J Chin Med Assoc* 2016; 79(4): 179–84.
72. American Medical Society for Sports Medicine (AMSSM), American Academy of Sports Medicine (AASM). Human immunodeficiency virus and other blood-borne pathogens in sports. *Clin J Sport Med* 1995; 5(3): 199–204.
73. UNAIDS. *Report on the global AIDS epidemic*, 2004. Bangkok, Thailand: 2004.
74. Dorak MT, Tang J, Penman-Aguilar A et al. Transmission of HIV-1 and HLA-B allele-sharing within serodiscordant heterosexual Zambian couples. *Lancet* 2004; 363(9427): 2137–9.
75. Grey RH, Wawer MJ, Brookmeyer R et al. Probability of HIV-1 transmission per coital act in monogamous, heterosexual, HIV-1-discordant couples in Rakai, Uganda. *Lancet* 2001; 357(9263): 1149–53.
76. Quinn TC, Wawer MJ, Sewankambo N et al. Viral load and heterosexual transmission of human immunodeficiency virus type 1. Rakai Project Study Group. *N Engl J Med* 2000; 342(13): 921–9.
77. Brown L, Drotman P, Chu A et al. Bleeding injuries in professional football: estimating the risk for HIV transmission. *Ann Intern Med* 1995; 122: 271–4.

78. Torre D. Transmission of HIV-1 infection via a sports injury. *Lancet* 1990; 335: 1105.
79. Ippolito G, Del Paggio P, Arici C et al. Transmission of zidovudine-resistant HIV during a bloody fight. *JAMA* 1994; 272: 433–4.
80. O'Farrell N, Tovey SJ. Transmission of HIV-1 infection after a fight. *Lancet* 1992; 339: 246.
81. Coghlan A. Shagged out. *New Scientist* 1999 Aug 7; (2198): 5–7.
82. Sports Medicine Australia. Policy. Infectious diseases. https://sma.org.au/sma-site-content/uploads/2017/08/infdisease.pdf
83. The American Medical Society for Sports Medicine and the American Orthopaedic Society for Sports Medicine (1995). Human immunodeficiency virus (HIV) and other blood-borne pathogens in sports, Joint Position Statement (online). www.amssm.org /hiv.html
84. Robinson J. The Canadian Academy of Sport Medicine (1999). Position statement, HIV as it relates to sport (online). www.casm-acms.org/
85. https://www.usatoday.com/story/sports/nba/clippers/2015/02/08/blake-griffin-out-injury-staph-infection-elbow-los-angeles-all-star-game/23078561/
86. https://www.nba.com/clippers/blake-griffin-getting-surgery-elbow-infection
87. https://en.wikipedia.org/wiki/Blake_Griffin
88. https://www.latimes.com/sports/clippers/clippersnow/la-sp-cn-blake-griffin-staph-infection-nazarian-20150208-story.html
89. https://en.wikipedia.org/wiki/Mark_Cavendish
90. https://www.theguardian.com/sport/2017/apr/12/mark-cavendish-diagnosed-epstein-barr-virus-cycling
91. https://www.cyclist.co.uk/news/2834/mark-cavendish-back-on-his-bike-after-epstein-barr-virus
92. www.telegraph.co.uk/cycling/2017/04/12/mark-cavendish-cancels-upcoming-races-diagnosed-glandular-fever/
93. https://www.bbc.com/sport/cycling/39578254

Chapter 19

The tired athlete

SANDRA MEJAK

Fatigue makes cowards of us all.
Vince Lombardi, NFL coach

Tiredness is a common complaint among both athletes and the general population. Training to improve sporting performance involves stressing the body for adaptation to occur. This leads to acute fatigue, which settles with appropriate recovery. Excessive physical and mental stress can be thought of as anchoring one end of a continuum, where complete inactivity represents the other end. When stress and recovery are in balance the outcome is optimal sporting performance in a healthy body.

More broadly, any negative stressor can lead to fatigue, just as any positive influence assists recovery, rather than just the sum of exercise and rest. If the balance is not right, tiredness can occur, as can other problems. It is therefore easy to conceptualise that the causes of tiredness are endless. This chapter focuses on common non-medical and medical causes. It also covers myalgic encephalomyelitis/chronic fatigue syndrome, which is a debilitating but less common condition. Ta ble 19.1 shows a list of causes of tiredness in the athlete.

When assessing a fatigued athlete, the practitioner must have a systematic approach, led with the common causes in mind, while looking for red flags. The common causes are often very obvious and, if reversible with behaviour modification alone, do not need investigation.

Table 19.1 Causes of tiredness in the athlete

Common non-medical	Common medical	Less common	Not to be missed
Sub-optimal sleep	Viral illness	Hypothyroidism	Malignancy
Social factors	Respiratory tract infections	Diabetes mellitus	Cardiac failure
Lifestyle factors	Infectious mononucleosis	Chronic fatigue	Adrenal disease
Overtraining	Other common infections	syndrome	Renal disease
Inadequate carbohydrate	Respiratory	Other nutritional	Liver disease
intake	Asthma	Malabsorption	Infectious

Timing of carbohydrate intake	Chronic sinusitis / Allergic rhinitis	e.g. coeliac disease	Bacterial endocarditis
Inadequate protein intake	Psychological	Eating disorders	Hepatitis
Inadequate hydration	Depression		HIV
Iron deficiency	Anxiety		Malaria
	Medication		Meningitis
	Prescription		Encephalitis
	Alcohol		Neuromuscular disorders
	Caffeine		Other malabsorption
	Endocrine		Inflammatory bowel disease
	Polycystic ovarian syndrome (PCOS)		Pregnancy
	Insulin resistance		Post-concussive syndrome
			SLE and other autoimmune conditions

When taking a history, it should be noted that particular symptoms are often not specific to one cause. It is also important to understand that many of the causes are interrelated, either being on a spectrum of disease, or by cause and effect. Some of these commonly observed clinical clusters are listed in Table 19.2.

Page 284

Table 19.2 Clusters of pathology associated with tiredness in the athlete

1	2	3
Relative energy deficiency in sport	Polycystic ovarian syndrome (PCOS)	Respiratory infections
Overtraining syndrome	Insulin resistance	Asthma
Eating disorders	Impaired glucose tolerance	Allergic rhinitis
Endocrine disorders	Diabetes	

ASSESSMENT OF THE TIRED ATHLETE

Because of the very many medical conditions that can lead to an athlete complaining of tiredness, the clinician should be sure to schedule an appropriate length appointment. The history has elements that relate to both sport and medicine, and the physical examination must be done very thoroughly because conditions such as numerous cancers, serious infectious diseases and endocrine disturbances may be present. Despite such a detailed work-up, there may be nothing to show the patient—further underscoring the importance of making sure there is time to communicate. Investigation can vary from nothing at all to a very detailed work-up—depending on the history and physical examination.

History

The nature of the athlete's tiredness itself needs to be taken in detail. This should include:

- How long has the athlete been tired?
- Are or were there any particular triggers?
- What is the pattern of tiredness:
  - constant or only post-exercise

  - certain venues (suggesting allergy)
  - certain seasons
  - certain conditions (e.g. hot weather—dehydration)?
- Has there been a past history of tiredness?
- How tired is the athlete?

History of medications, caffeine, alcohol, supplements, tobacco and other drugs should be taken.

Training diary

A comprehensive training history is crucial:

- sessions and type
- volume (hours or kilometres per week)
- intensity
- time of day
- spikes and increases
- number, timing and duration of competitions
- any deterioration in performance noted
- recovery time and practices
- any baseline performance values to compare with, particularly at anaerobic threshold
- periodisation.

Sleep history

The athlete's sleep patterns should be noted:

- Sleep/wake time
- Duration of sleep
- Quality of sleep. The athlete may wear an activity tracker which logs this.
- Is there any suggestion of sleep apnoea or snoring?
- What is the athlete's routine prior to bed?

Nutrition diary

A food diary of 3–7 days is very useful when assessing for deficiencies of macronutrients and micronutrients. The clinician should also check whether there is any known current (or past) nutrient deficiency.

Symptoms of medical conditions

This list focuses on features of common medical causes, but a brief general medical history should also be taken. Family history may also be revealing.

- Respiratory symptoms such as cough, wheeze, atypical shortness of breath to suggest asthma. Is there regular animal contact?
- Infective respiratory symptoms—sore throat, nasal congestion
- Gastrointestinal symptoms—diarrhoea and abdominal pain (which would suggest causes such as malabsorption, inflammatory bowel disease, irritable bowel)
- Cardiac symptoms—chest pain, palpitations, shortness of breath
- Rheumatological patterns of pain, iritis, rashes
- Generalised neurological or muscle diseases may be suggested by weakness or muscle twitches.
- A more detailed endocrine history to include:
  - possibility of pregnancy
  - menstrual abnormalities—amenorrhoea, oligomenorrhoea or menorrhagia
  - polyuria and polydipsia, suggestive of diabetes
  - body weight that does not match the individual's energy balance—this could suggest a thyroid condition, polycystic ovarian syndrome (PCOS) or insulin resistance
  - thyroid symptoms, including myalgia and arthralgia
- Myalgias or arthralgias

Page 285

Other biopsychosocial stressors

Other relevant biopsychosocial factors should be noted, including:

- Demands such as relationships, school, work and travel
- Psychological:
  - mood
  - depression, anxiety, performance anxiety
  - eating disorder. At a simple level this can include a history of weight fluctuations, disturbed body image, fear of weight gain, bingeing and purging. Questionnaires such as the LEAF-Q (Low Energy Availability in Females Questionnaire)[1] or the Eating Disorder Examination interview[2] (the gold standard) could be performed, either as screening or if there is a higher suspicion.
- Performance concerns such as upcoming selection or competition, coach or team issues.

There are other tools that can be utilised for assessing fatigue, stress and exertion. These include: Profile of Mood States (POMS), Iceberg Profile, recovery–stress questionnaire specific to sport (RESTQ-Sport), and Borg's rating of perceived exertion (RPE) scale.

Examination

Perform a focused physical examination to determine whether there are any signs of the medical causes of fatigue; in most cases this will be normal. Examine for jaundice and pallor, as signs of liver disease and anaemia, respectively. The respiratory tract should be examined for signs of

infection or asthma, including the ear, nose, throat and lymph nodes. Include a full cardiac examination. The abdomen should be palpated for signs of organomegaly. Assess anthropometry by body mass index, body fat percentage estimate, waist girth, or a simple visual estimate. Pubertal stage assessment is relevant if amenorrhoea or oligomenorrhoea is present. Signs of purging, such as dental erosions and parotid gland enlargement, may be seen in athletes with eating disorders. Look for signs of thyroid disease, such as goitre, dry or oily skin and loss of the outer third of eyebrows. Hirsutism and acne may be signs of PCOS. Visual field defects are a sign of a pituitary tumour.

Investigations

The clinician may feel pressure to perform a series of tests to look for a medical cause or deficiency to explain and treat the tiredness. It is, however, very reasonable to initially do no investigations at all if a simple explanation for the tiredness is discovered. In this case a short trial of treatment is indicated. If the patient recovers, your diagnosis is likely confirmed.

If investigations are performed, the choice of primary investigations is based on three factors. The first is to investigate for common causes, such as iron studies and haemoglobin for iron deficiency. The second consideration is ease of testing, such as a urine dipstick, which can be done instantly and costs very little.

The third factor determining choice of initial tests is findings from the history and examination. Under this banner certain tests (looking for causes and consequences of causes) could be considered; however there is never an indication to do all of these at the same time.

Other selective blood tests to consider are: a full blood count, blood film, erythrocyte sedimentation rate, C-reactive protein, urea, electrolytes, vitamin B^{12}, folate, vitamin D, calcium, zinc, magnesium, coeliac serology, thyroid function test, parathyroid hormone, glucose, creatine kinase and liver function test. A screen for infectious diseases could include serology for hepatitis A, B and C, toxoplasmosis, cytomegalovirus, Epstein–Barr virus (EBV), Ross River fever and Barmah Forest fever in endemic areas. Humoral immune status could be assessed with serum immunoglobulins, including IgG subclasses, IgM deficiency and IgA deficiency. A rheumatological screen could start with an antinuclear antibody test and, if positive, be followed up with other specific autoimmune serology if indicated, including extractable nuclear antigen, double-stranded DNA and complement levels. Allergy can be assessed by measuring total IgE, allergen-specific IgE, and radioallergosorbent test (RAST). Other hormones to test can include follicle stimulating hormone, luteinising hormone, prolactin, oestradiol, a pregnancy test and androgen profile (testosterone and dehydroepiandosterone [DHEA]).

Salivary tests could include EBV DNA, looking for reactivation, and salivary immunoglobulins.

Other tests based on history and examination findings may include respiratory tests, such as spirometry, bronchial challenge tests or chest X-ray. Allergy tests, such as skin prick testing, should be considered in asthmatics and those where allergies are suspected. Electrocardiogram and echocardiogram tests may be considered for heart abnormalities. A pelvic ultrasound can show PCOS or a structural reason for amenorrhoea. Bone mineral density may be considered when there has been inadequate nutritional intake.

COMMON NON-MEDICAL CAUSES

Poor sleep

It is surprising how often simple factors such as poor sleep are overlooked as causes of tiredness. Insufficient sleep is prevalent in our society. Evidence-based consensus is that adults need at least 7 hours of sleep for optimal health.[3] Even more sleep is required by adolescents and children.[4] Sleep can be deficient in its duration, quality, timing of sleep onset and waking. Sleep can be disturbed by many factors, including conditions such as insomnia, obstructive sleep apnoea, restless legs syndrome, circadian rhythm disorders, jet lag and factors in an athlete's schedule.

Inadequate sleep hinders recovery from exercise.[5, 6] It is needed to assist with memory consolidation and learning, and sleep disruption may be associated with decreased ability to learn and improve skills necessary for team performance.[7] Improving sleep improves on-field performance.[8]

Strong data exist linking poor sleep to fatigue-related accident and injury in other populations, such as transportation workers and in the military. There is less strong evidence in the athletic population. Sleeping fewer than 6 hours or having inadequate rest was associated with injury in young athletes,[9] and adolescents sleeping more than 8 hours were less likely to be injured.[10]

Dysfunctional sleep decreases immune function. Graded associations between sleep duration and efficiency (percentage of time actually asleep) have been linked to increased susceptibility to the common cold, with efficiency being the primary and independent predictor.[11] Those with less than an average 7 hours per night were 3 times more likely to develop a common cold after exposure to a common cold virus than those who slept 8 or more hours. Those with a sleep efficiency less than 92% were 5.5 times more likely to get a cold than those with greater than 97% efficiency. Measurable reduced natural killer cell activity, increased pro-inflammatory cytokines, attenuation of antibody response to hepatitis A and influenza[12–16] have been attributed to poor sleep.

Dysfunctional sleep may be the cause or effect of other conditions such as overtraining syndrome or depressed mood.[17] Inadequate sleep can affect hunger hormones, and may make one crave fatty foods.[18–20] It harms memory, vision, decision making, cognitive performance and motor skills.[21–24] It causes autonomic nervous system imbalance.[25] Sleep symptoms are commonly seen after concussion and should be managed appropriately, as poor sleep can exacerbate or prolong any concussion symptoms.[26]

Chronic sleep deprivation has been linked to higher risks of diabetes,[27] cardiovascular disease,[28] obesity[29] and depression.

Non-functional overreaching and overtraining syndrome

It should first be noted that successful training must involve overload training, which leads to acute fatigue, but with appropriate recovery leads to positive adaptation. This is termed functional

overreaching (FOR). If the balance between appropriate training stress and adequate recovery is disrupted, an abnormal training response may occur; performance can stagnate or decrease with increased training. Another way of putting this is that an athlete reaches their 'tipping point', and that each athlete has a different tipping point. This is called non-functional overreaching (NFOR). These definitions suggest that the difference between NFOR and overtraining is the amount of time needed for performance restoration, not the type or duration of training. The diagnosis of overtraining syndrome (OTS) versus NFOR can often only be made retrospectively when the time course of recovery can be appreciated.[17] NFOR is far more prevalent than the severe condition of overtraining syndrome.

Definitions and diagnosis involving OTS are not standardised, making conclusions difficult. Synonyms used in the literature around overreaching include staleness, burnout, failure adaptation, under-recovery and unexplained underperformance syndrome. It is also important to note that there is inter-individual variability found in both response to training load and recovery required and in clinical features of overtraining. Table 19.3 best summarises the definitions.

Table 19.3 Overtraining syndrome definitions

Condition	Previously used synonyms	Definition	Performance decrement	Outcome
Functional overreaching	Short-term overreaching	Increased training leading to a temporary performance decrement and with improved performance after rest	Days to weeks	Acute fatigue, then positive adaptation
Non-functional overreaching	Long-term overreaching, staleness, burnout, failure adaptation, underrecovery	Intense training leading to a longer performance decrement but with full recovery after rest Accompanied by increased psychologic and/or neuroendocrinologic symptoms	Weeks to months	Negative due to symptoms and possible loss of training time
Overtraining syndrome	Unexplained underperformance syndrome	Consistent with extreme nonfunctional overreaching but with: 1.Longer performance decrement (>2 months) 2.More severe symptomatology and maladapted physiology (psychologic, neurologic, endocrinologic, immunologic systems) 3.Accompanied by an additional stressor beyond excessive training load 4.Not explained by other diseases	Months +	Negative due to symptoms and possible end to athletic career

ADAPTED FROM KREHER JB, SCHWARTZ JB. SPORTS HEALTH (4(2)) OVERTRAINING SYNDROME: A PRACTICAL GUIDE. PP.128–38 COPYRIGHT (C) 2012 REPRINTED BY PERMISSION OF SAGE PUBLICATIONS, INC.65

Many detrimental effects of overtraining have been noted in various studies of NFOR/OTS, although the exact effects are highly variable between studies and none can be used to diagnose the condition. One individual may have any combination of effects, and one may also have those same effects without overreaching or overtraining.

By definition, OTS is a syndrome. Although the basis of the syndrome as described is excessive training, it is acknowledged that there is a multifactorial aetiology and that training is not necessarily the sole causative factor. Several confounding factors can contribute to OTS, as is the case with tiredness itself. A short list of these would include: nutritional factors such as inadequate calories, carbohydrate or protein; recovery time and practices; environmental factors such as heat, cold and altitude; illness; sleep dysfunction; and other stressors. Selye's general adaptation syndrome framework helps to explain how these other factors contribute.[30]

Potential negative effects are summarised in Table 19.4.

Table 19.4 Summary of detrimental effects of overtraining syndrome

Psychological	Physiological	Biochemical	Hormonal/neurological	Immune
Central changes in neurotransmitter function	Performance decline	Glycogen depletion	Hypothalamic-pituitary-adrenal hormonal axis maladaption	Decreased systemic immunity – innate and adaptive
Increased fatigue	Fatigue	Glycogenolysis and glucose transport down-regulated Insulin-like growth factor increases	Hypothalamic-pituitary-gonadal hormonal axis maladaption	Decreased mucosal immunity
Mood disturbance –tension, depression, anger, fatigue, confusion, irritability, agitation	Bradycardia	Catabolism increases	Sympathetic-adrenal-medullary axis maladaption	Increased URTIs
Loss of motivation	Tachycardia	Mild insulin resistance	Fatigue – thought to be due to central neurotransmitter	Decreased salivary IgA
Decreased reaction time	Hypertension	Diminished maximal lactate concentration (with exercise), but differences are sometimes subtle and within measurement error No lactate changes in strength athletes	Delayed menarche	Reduced bacterially stimulated neutrophil degranulation response
Lack of concentration	Restlessness	Elevated CK	Oligomenorrhoea	Reduced natural killer cell activity
Insomnia	Heavy, sore, stiff muscles	Decreased plasma glutamine	Amenorrhoea	T-cell increased activation
Awakening unrefreshed	Anorexia		Decreased libido (men)	
Anhedonia	Weight loss		Decreased plasma testosterone / cortisol ratio	

ADAPTED WITH PERMISSION FROM MEEUSEN R, DUCLOS M, FOSTER C ET AL. PREVENTION, DIAGNOSIS, AND TREATMENT OF THE OVERTRAINING SYNDROME: JOINT CONSENSUS STATEMENT OF THE EUROPEAN COLLEGE

Prevalence

It is difficult to provide exact prevalence data because of the changes in definition over time, and because not all studies clearly indicated the timeframe of data collection. It is noted that Page 287 NFOR/OTS predominantly occurs in endurance sports. Among collegiate swimmers and other endurance athletes the rate has been reported as 10%.[31] Survey studies of elite runners report 60% of females and 64% of males indicate experiencing at least one previous episode of OTS, with a career rate of 33% in non-elite adult runners.[32, 33] The rate is higher in faster performers.[34, 35] If there is NFOR/OTS early in an athlete's career, there is a much higher chance of a subsequent episode.[36]

Diagnosis

Given that a hallmark of OTS is the inability to sustain intense exercise, performance testing to determine whether there has been a decrease in performance is considered to be essential for the diagnosis.[37–39] Time-o-figue tests at anaerobic threshold, and tests of fixed duration at anaerobic threshold are the most useful tests. Tests of increasing intensity are not as sensitive.[40–42] Weaknesses in these methods of performance testing include the necessity of baseline tests, poor reproducibility and standardisation, and the inability to make them specific to many sports. In the absence of quality standardised performance tests, index training sessions performed within the athlete's sport may be useful.

Unfortunately, there is no diagnostic tool that can detect NFOR/OTS. As a result, it is clinical, retrospective, and only diagnosed after excluding other conditions. Many tests have been investigated. Often, they are not useable beyond a research context, as spot observations of biochemical markers vary widely, even though general patterns have been observed in various studies. Specifically, for this reason, this section will not focus on the biochemical changes.

For a biomarker to be a reliable indicator for the onset of OTS, it should be sensitive to the training load and ideally be unaffected by other factors. Changes in the marker should occur before the establishment of OTS, and changes in response to acute exercise should be distinguishable from chronic changes. Ideally, it should be easy to measure, with a quickly available result, and not too expensive or invasive. Unfortunately, no such biomarker has been found, despite many being studied.

Biomarkers that have been recognised in some studies as being able to estimate training load and the body's response are: salivary immunoglobulin A,[43] plasma testosterone/ cortisol ratio;[38, 44, 45] and overnight urinary cortisol/cortisone ratio.[46] Markers that have been recognised in some studies as being able to estimate oxidative stress of exercise are reduced/oxidised glutathione ratio and urinary isoprostanes.[47]

Physiologic markers that have been recognised in some studies to show evidence of training load

and the body's response but have not been able to differentiate overreaching conditions Page 288 are: resting heart rate (HR) (increase); maximal HR (a decrease of 5–10 beats per minute);[1] [7] and HR variability (decrease).[48, 49] Heart rate variability seems to be a good tool in theory, but studies show either no change or inconsistent results in NFOR and OTS subjects. Another weakness of HR variability is that there is no standardised method of measuring it.

Physiologic markers that have been recognised in some studies to show evidence of being able to differentiate NFOR and overtraining conditions (but not overtraining from NFOR) are: decreased maximal lactate on performance testing,[50] and decreased maximal HR at lactate threshold with incrementally increasing exercise.[51]

The greatest promise for differentiating FOR from NFOR, and NFOR from OTS, is combined performance and biomarker testing. A two-bout exercise protocol performance test combined with hormonal testing of adrenocorticotropic hormone (ACTH) and prolactin has shown promise.[37] Hormone response (ACTH and prolactin) to a first and second exercise bout is measured. In FOR, the circulating concentrations of both hormones increase after both tests, but less so after the second. In NFOR, both hormones are markedly higher after the second exercise bout. In OTS, there is an extremely large increase in circulating concentrations of both hormones after the first test, followed by a complete suppression in the second exercise bout.

Athletes with NFOR/OTS consistently report elevations in negative moods (tension, Page 289 depression, anger, fatigue and confusion). Mood state exhibits a predictable dose–response relationship with training, whereby mood disturbances increase as training loads rise, with peak training and peak mood disturbance coinciding. Conversely, training tapers usually result in a reduction in negative moods and an increase in vigour, such that at the end of a taper mood is positive. It is therefore useful to assess mood as part of regular monitoring of an athlete, although no assessment can be used to diagnose NFOR/OTS. Reducing training according to mood state monitoring may be useful in reducing OTS.

The Profile of Mood States (POMS) questionnaire is a common tool for assessing mood.[52] Research reveals that as few as two days of intensified training can result in significant increases in POMS measures, which precede changes in biomarkers. In OTS, depression increases the most of all POMS variables, so may be specific to OTS but not FOR. The Iceberg Profile is a graphical representation of the POMS and has an iceberg shape when mood is positive.[33, 53, 54] In healthy athletes during peak overload training, POMS fatigue and vigour show the largest shift, but depression increases the least, whereas in athletes showing signs of OTS, depression increases the most of all POMS variables, with some reports indicating that up to 80% of affected athletes show signs of clinical depression.[33] This has led to tests of mood state monitoring as a means to modulate training load (both up and down), with the goal of reducing the incidence of OTS. There are many variants of POMS questionnaires, varying from sport-specific to non sport-specific, and training-specific (e.g. Training Distress Scale) versus general.

The Training Distress Scale (TDS) was developed as a seven-item tool (five depression and two anger items), based on analyses of POMS data from 186 healthy and overtrained college swimmers.[5]

[5] The TDS was more accurate in identifying OTS athletes, compared with POMS total mood disturbance scores or depression scores.

Kenttä et.al. created a POMS energy index measure by subtracting fatigue from vigour scores.[56] They found energy index scores were responsive to both training stress and recovery, whereas depression scores were unchanged, suggesting the index could be used to reduce NFOR during intense but brief training cycles.

Several sport-specific OTS scales have been developed using theoretical assumptions about what psychological and behavioural factors should be associated with OTS. Among them, the most extensively studied has been the Recovery–Stress Questionnaire for Athletes (RESTQ-Sport),[57] a 77-item questionnaire encompassing 19 separate factors that assess both overtraining and recovery responses in injury and athletes. RESTQ is responsive to changes in training load, particularly in athletes with signs of OTS.[58]

Relatively new but promising tools in the early detection of NFOR and OTS are psychomotor speed tests (using tests of reaction time and attention). The studies on them strongly suggest that central fatigue is an early (and maybe the earliest) manifestation of overreaching, and that complexity is an important mediating variable in the relationship between overreaching and brain functioning. Reaction time tests[59–62] have been studied in cyclists, with reaction time decreasing significantly with a significant increase in training.

Weaknesses in using mood states and other factors are: they can be influenced by stressors unrelated to training and recovery; it can be unclear which baseline mood scores to compare training scores to; there can be a degree of faking answers; care must be taken determining at exactly what point in time they are measured; and coaches and athletes can be sceptical.

Prevention

The overwhelming impression is that emphasis needs to be on prevention of NFOR and OTS (mostly by appropriate periodisation of the training program, with careful focus on including and executing appropriate recovery in the training program), and early diagnosis. To achieve these, one must maintain accurate records of performance. Training load (RPE × minutes) should be recorded, monitored and periodised. GPS data can be incorporated. Monotony should be avoided, and training individualised.[63, 64] Training can and needs to include intensity for adaptation to occur, but recovery strategies, including at least one day off per week, should be implemented.[65]

A regular performance test is essential. A time-to-fatigue test at anaerobic threshold is best. Alternatively, a standard distance test, designed to test the athlete near their anaerobic threshold is the next best.

A close relationship between athlete, coach, doctor and the whole sports science and medicine team can help monitor for warning signs and alter training according to stressors such as illness. The athlete and team support should be alert to a stasis in performance with the same or higher perceived effort. Another sign can be starting a session well but losing the ‘finishing kick’.[64, 66]

It can be useful to measure some simple physiological markers as markers of training load and

the body's response, including weight, morning HR, maximal HR and HR variability. Maximal lactate is useful although a little harder.

Attention to non-training or recovery contributing factors, such as mood state monitoring, daily wellbeing measures, stressors, nutrition and sleep, is important; and it is important to recognise that it is more than just training load and recovery that affect the overall state of the athlete. Other stressors should be periodised the same as training is periodised.

Treatment

Treatment often requires a period of complete or partial rest from training. The period of rest required depends on the severity of the NFOR/OTS. Recognising Selye's general adaptation syndrome framework,[30] address all modifiable contributing factors including nutritional intake. Medical conditions need to be ruled out as an alternative cause of the fatigue, and treated. Athletes need to be educated for both prevention and treatment of NFOR/OTS and, in particular, a decline in performance should not be managed with the knee-jerk reaction of increasing training.

Relative energy deficiency in sport

Relative energy deficiency in sport (RED-S) was previously known as the female athlete triad, with the last iteration of the triad being described in 2007 by the American College of Sports Medicine, recognising it as a continuous spectrum, with energy availability, menstrual function and bone health being the three interrelated components on the spectrum.[67] In 2014 the female athlete triad was renamed by the International Olympic Committee (IOC), in its updated consensus statement, as 'RED-S', to recognise changes in the understanding of the condition: that it can also affect males; and that it involves more than just inadequate intake, menstrual abnormalities and decreased bone mineral density.[68] For more detail on this topic refer to Chapter 29 or the 2014 IOC consensus statement. Fatigue, as a result of the negative energy balance, is a feature of RED-S.

Definition

The core understanding of RED-S is that it is caused by energy deficiency leading to inadequate support of the range of body functions involved in optimal health and performance, although it is recognised that it can be caused by too high a training load. With the revised understanding of RED-S, it is now very similar to overtraining syndrome, in both the causes and effects.

Effects

Note that, as with OTS, the combination of systems involved and the threshold for their dysfunction varies among individuals. Figure 19.1 summarises the health consequences of RED-S.

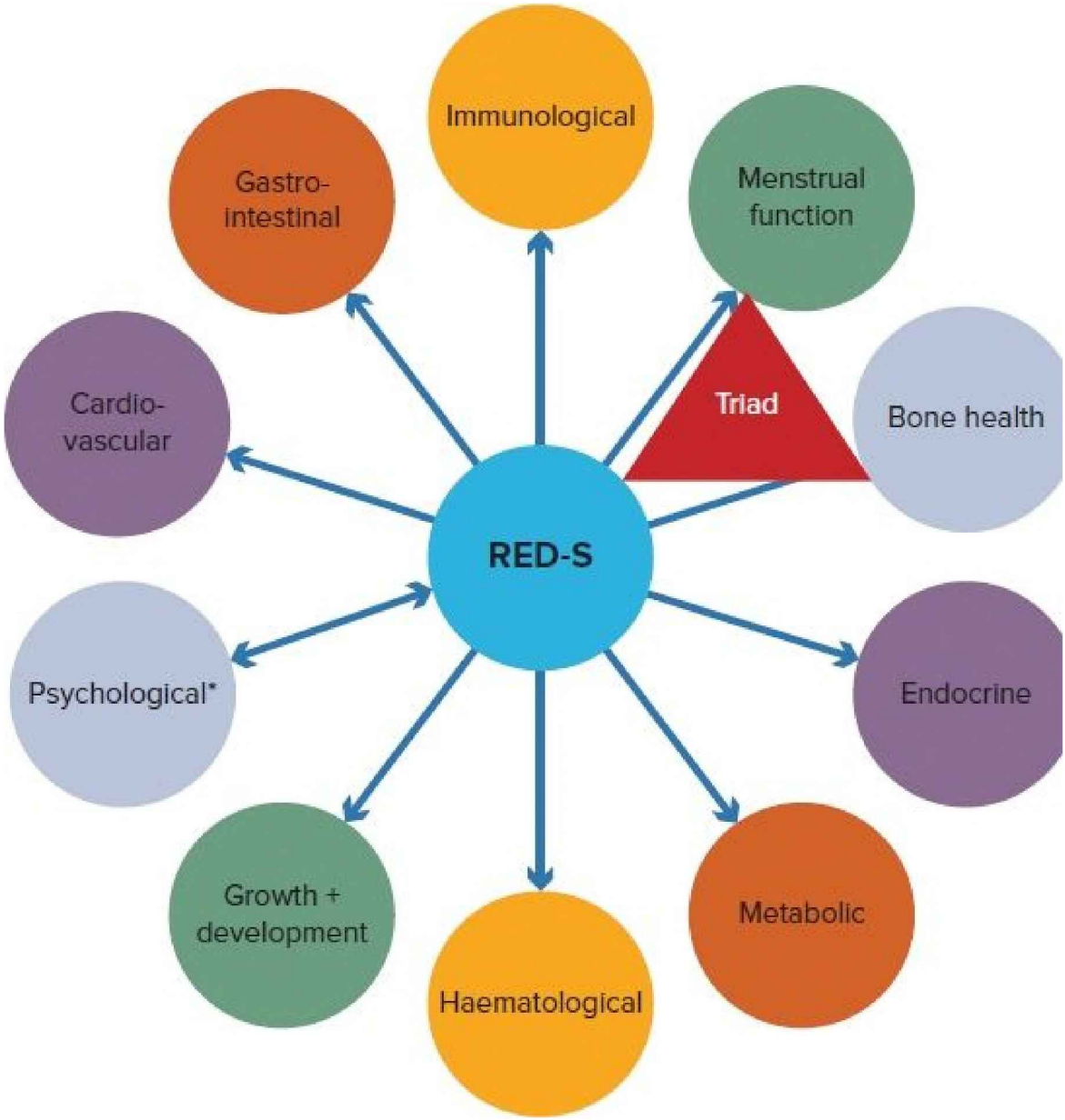


Figure 19.1 There are many body systems affected by RED-S.
REPRODUCED WITH PERMISSION MOUNTJOY M, SUNDGOT-BORGEN J, BURKE L, ET AL. THE IOC CONSENSUS STATEMENT: BEYOND THE FEMALE ATHLETE TRIAD—RELATIVE ENERGY DEFICIENCY IN SPORT (RED-S). BR J SPORTS MED 2014;48(7):491–769; ORIGINAL CONCEPT: CONSTANTINI NW. MEDICAL CONCERNS OF THE DANCER. BOOK OF ABSTRACTS. FIMS WORLD CONGRESS OF SPORTS MEDICINE BUDAPEST, 2002:151.

Diagnosis

There is no objective diagnostic laboratory test for RED-S. There is also no consensus on which

screening tool has best efficacy; and the screening tools do not include men. Symptoms of RED-S can be subtle, so one must look for suspect signs, such as disordered eating, weight loss, lack of normal growth and development, menstrual dysfunction, recurrent injuries and illnesses, decreased performance and mood changes. The measurement of energy availability requires expertise and is generally imprecise.

Treatment

Treatment of RED-S is much like that for OTS, in that the energy intake needs to be increased and/or the energy output needs to be decreased.

COMMON UNDIAGNOSED, UNTREATED OR UNDERTREATED MEDICAL CAUSES

In an often-quoted article studying 41 athletes who presented with persistent fatigue and/or recurrent infections, a cause was found on screening blood work in 68% of cases. The most common were partial humoral immune deficiency (28%), non-fasting hypoglycaemia (28%), unresolved viral infections (27%), allergic disease (15%), sleep disorders (15%), asthma (13%), upper airway dysfunction (5%), iron depletion (3%), and one case of a thyroid disorder. A positive antinuclear antibody was detected in 21% of the athletes, without any evidence of autoimmune disorders. Evidence of Epstein–Barr virus reactivation was detected in 22% of the athletes tested. Eighty-six per cent of the athletes assessed scored positive on a fatigue scale, and 55% presented with what were defined as recurrent infections (range 4–28). Most infections were described as upper respiratory tract infections.[70]

Infective causes of fatigue

We discuss two common categories of infective causes of tiredness in the athletic setting.

Respiratory tract infections

Viral respiratory tract infections are common, and athletes average 2.7 respiratory tract infections per athlete per year.[71] Not only do they cause tiredness, but they also add a stressor to the body and may contribute to other conditions such as NFOR, OTS and RED-S. There is also evidence of a higher incidence of injuries during illness.[72]

Infectious mononucleosis

Sore throat, fever and lymphadenopathy are often referred to as the classic triad of infectious mononucleosis (glandular fever/Epstein–Barr virus),[73] but the most common symptoms are sore throat and fatigue. Prodromal symptoms of headache, fatigue (often severe), anorexia and myalgia often precede the classic symptoms by 3–5 days.[74]

Prevalence of infectious mononucleosis is not higher in athletes, but athletes seem to experience a milder disease. Ninety per cent of individuals are seropositive by age 30, and most infections occur between 15 and 25 years of age.

Return to sport should not occur before three weeks after onset of symptoms, as this is the

period in which splenic rupture can occur and may occur with or without trauma.[75] The athlete should be afebrile, with resolution of symptoms, and should feel well enough to play.

Most athletes recover in 4–6 weeks, but recovery can take as long as 3 months. Reactivation is a common cause of oropharyngitis in young adults,[76] and is associated with upper respiratory tract infection symptoms in competitive athletes[77] and further salivary shedding. Fatigue can be prolonged post-infection, but probably represents relapses of the condition, so it is important to follow the return-to-sport guidelines to prevent that.

Cytomegalovirus is less common, but presents similarly to infectious mononucleosis.

See Chapter 18 and Case study: Mark Cavendish, British track and road cycling—Epstein-Barr virus for further discussion on infectious mononucleosis.

Non-infective causes of fatigue

Often overlooked, there are at least five common categories of non-infectious causes of tiredness among athletes.

Nutritional

Inadequate nutritional intake may cause prolonged fatigue, especially in those undertaking intense bouts of exercise. Common theories of there being an optimal window for post-exercise refuelling are still to be proven. The International Society of Sports Nutrition highlights the need for specific amounts of carbohydrate replenishment only in sports where less than a 4-hour window is present between competition.[78]

Note: For further discussion on nutrition and sport please review Chapter 6.

It is estimated that 10% of energy needs are via protein, and protein in the diet is essential to replace protein catabolism from muscle contraction. The mechanism by which inadequate protein intake causes fatigue is unclear. Acute or chronic dehydration can also cause fatigue.

Iron deficiency

Iron is essential to oxidative metabolism. It is needed for oxygen utilisation in haemoglobin and myoglobin. The electron transport chain, which is the final step in oxidative ATP synthesis, depends on haemes-containing cytochromes, therefore it is required for aerobic metabolism.[79] Decreased iron stores (even without anaemia) decrease VO_2max[80] and submaximal aerobic capacity.

Iron deficiency prevalence is higher in females and endurance athletes. Exercise increases iron loss; therefore, athletes need 30–70% more iron than non-athletes. The prevalence of iron deficiency in females is 20–50% (more common in females due to menstrual blood loss and lower intake) and in males 4–50%.[81, 82]

There is 0.9–1.2 mg of daily basal iron loss; 0.6 mg per day is lost via the gastrointestinal tract; 0.08 mg per day is lost via urine; and 0.2–0.3 mg per day is lost via sweat. Physical activity increases loss from all of these. When menstruating, 0.6–0.9 mg per day is lost in menstrual blood.

The general consensus is that an athlete should receive iron supplementation if ferritin is below 30 ng/mL, but some athletes may perform better at a higher ferritin level.[83]

Respiratory

According to the Australian Bureau of Statistics (ABS)[84], in 2014–15 the prevalence of asthma in the general adult population was 11%. The prevalence in cold weather athletes is 11–50%.[85] It is often undiagnosed, as symptoms do not correlate with lung function tests.

Rhinitis is an inflammation of nasal mucous membranes that manifests as sneezing, pruritus, rhinorrhoea and especially congestion with nasal obstruction. Rhinitis is caused by allergy in 50% of cases. Other causes include infection, hormonal changes, medications and irritants.[86] According to the ABS[84], 20% of Australians had allergic rhinitis in 2014–15, with the most common age group being 15–59 years.

A high proportion (almost all) of individuals with allergic rhinitis have asthma or develop it later,[86, 87] but only 50% of individuals with asthma have allergic rhinitis.[88] Allergic rhinitis with nasal obstruction can hinder performance through effects on ventilation, impaired sleep from nasal obstruction and other symptoms, and by worsening asthma. Allergic rhinitis can worsen asthma in the following ways:[89]

- Upper airway obstruction lowers the trigger for mouth breathing, which increases breathing of colder, drier air and decreases filtration of particles, both of which can exacerbate asthma.
- Inflammation in the upper airway induces an immune response in the upper and lower airway (unified airway model of asthma) and vice versa, by early and late phase immune responses.
- It is noted that when there are more severe symptoms of rhinitis, there are more night-time awakenings caused by asthma.

Treatment of the upper airway with intranasal corticosteroid reduces bronchial hyperresponsiveness, asthmatic symptoms and emergency room visits. Well-trained athletes had a marked reduction in exercise-induced bronchospasm only one week after commencing this treatment.

Psychological

Estimates based on ABS data for 2007[90] suggest that affective disorder prevalence is 6.2%. Specific sport cohorts suggest anecdotally similar or higher rates of incidence of anxiety and depression in athletes.

Alcohol, caffeine and medications

Alcohol, acting as a central nervous system depressant, can cause fatigue after ingestion. Although it causes drowsiness and induces sleep, hours later it causes an increase in adrenaline, which disrupts sleep. It also inhibits release of antidiuretic hormone (ADH), making an individual more likely to wake up needing to urinate overnight. Alcohol withdrawal also causes fatigue.

Caffeine, although a stimulant, can cause fatigue. Studies suggest effects vary between individuals. Caffeine prolongs sleep latency, shortens total sleep duration and preserves the dream phases.[91] There is some evidence for a dose–response relationship between caffeine and sleep structure. Generally, more than 200 mg of caffeine is required to affect sleep significantly.[92, 93]

Tolerance to caffeine's effects on sleep may occur but results vary.[94, 95] Some studies suggest that these differences might reflect varying individual sensitivity to caffeine, possibly related to differing rates of caffeine metabolism. Indeed, poor sleepers are reported to metabolise caffeine at a lower rate. There is some evidence that tolerance to caffeine-related sleep disturbances may develop, in that heavy coffee drinkers appear to be less sensitive to such disturbances than light coffee drinkers. Tolerance to sleep latency and quality has been shown to develop over a period of days.

Some individuals develop a tolerance to caffeine. More caffeine is needed to have the same effect, and without repeat dosing daytime tiredness ensues. Withdrawal from caffeine in this way commonly causes fatigue.

Medications including beta blockers, anxiolytics, antidepressants and antihistamines have long been recognised as affecting sleep.

Endocrine causes of fatigue

Diabetes and impaired glucose tolerance are both associated with excessive daytime sleepiness, when controlling for sleep apnoea, obesity, depression and age.[96] Daytime sleepiness is reported very frequently by women with PCOS, in whom insulin resistance is a common metabolic abnormality.[97–99] Excessive daytime sleepiness is associated with PCOS even when obesity is not present,[98] and it seems likely that excessive daytime sleepiness is associated with glucose dysregulation and insulin resistance, independent of sleep apnoea or obesity.[99–101]

Polycystic ovarian syndrome

The prevalence of PCOS is 5–10% of women, as a conservative estimate, but higher if the European Society for Human Reproduction and Embryology (ESHRE) and the American Society for Reproductive Medicine (ASRM) criteria are used. Athletes exhibit reduced symptoms of the syndrome (obesity, skin changes), although the same incidence of the ovarian findings, which suggests that exercise is treating the clinical manifestations.

Patients with PCOS have symptoms of fatigue, menstrual abnormalities, hyperandrogenism, infertility, hirsutism, obesity, sleep apnoea, acanthosis nigricans, metabolic syndrome, and often sit somewhere on the spectrum of insulin resistance to diabetes mellitus.

Medical management is aimed at the treatment of metabolic derangements, anovulation, hirsutism and menstrual irregularity. Diet and exercise are the first line treatments for the metabolic derangements, and can even reduce the cysts. As with insulin resistance (see below) reduction of carbohydrate intake is the key to management.

Metformin improves insulin resistance and decreases hyperinsulinaemia in patients with PCOS. Evidence suggests that metformin frequently improves ovulation rates in women with PCOS. Management of infertility should be via referral to a reproductive endocrinologist. Hirsutism can be treated by hair removal, weight reduction, oral contraception, spironolactone (note that this is banned in sport) or eflornithine. Menstrual irregularity can be treated with an oral contraceptive, which not only inhibits ovarian androgen production but also increases sex hormone binding globulin (SHBG) production.

PRACTICE PEARL

The key to management of PCOS and insulin resistance is reduction of dietary carbohydrate intake.

Insulin resistance

Patients with insulin resistance can present with difficulty losing weight or maintaining a healthy weight; irregular, heavy, absent or late periods; and fatigue. They can be slim.

Insulin resistance is a precursor to impaired glucose tolerance and diabetes. A patient can go from insulin resistance to type 2 diabetes mellitus in as little as 10 years. Other consequences of insulin resistance are high triglycerides, low high-density lipoprotein, increased uric acid, premature atherosclerosis, fatty liver, low testosterone in men, high testosterone in women, hypertension, acanthosis nigricans and skin tags.

Treatment involves lifestyle changes including diet (reduced carbohydrate intake) and exercise, and metformin therapy. Treating insulin resistance will reduce mental stress, reduce fatigue and prevent diabetes.

LESS COMMON MEDICAL CAUSES

Hypothyroidism

The symptoms and signs of hypothyroidism include fatigue, myalgias, arthralgias and decreased exercise tolerance. The symptoms may take years to develop. In Australia and other iodine-rich countries, the most common cause is autoimmune thyroiditis (Hashimoto's disease). Worldwide, the most common cause is iodine deficiency. Prevalence of hypothyroidism is 3.7% in the USA. Worldwide, the iodine deficiency rate is 31%. It is more common in females and older individuals.

Treatment usually involves thyroxine tablets. Once thyroxine is commenced, clinical improvement occurs in 3–5 days, but thyroid stimulating hormone levels take months to return to normal.

Diabetes mellitus

Rates of diagnosed diabetes mellitus are higher than insulin resistance; however, it is rarely diagnosed by a sport and exercise physician. Prevalence in Australia is 7% if the estimated numbers of undiagnosed cases are included. Symptoms of uncontrolled diabetes include polyuria, polydipsia,

loss of weight (type 1), tiredness and fatigue, and a propensity for infections.

Myalgic encephalomyelitis/chronic fatigue syndrome

Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) affects over one million people in the USA and at least a quarter of a million in the UK. It is characterised by overwhelming fatigue with a substantial loss of physical and mental stamina. Such symptoms following physical or mental exertion can persist for hours, days or weeks and are not relieved by rest or sleep. The degree of tiredness can range from being unable to attend school or work, to being Page 294 wheelchair dependent and bed bound. Diagnosis is clinical, after other medical causes are ruled out. By definition, fatigue must have lasted longer than 6 months (can be intermittent), but ME/CFS can be provisionally diagnosed and treated before then.

Cardinal features are malaise and a worsening of symptoms following minimal physical or mental exertion or orthostatic stress. Other core symptoms are impaired physical and/or cognitive function, fatigue, sleep disturbance, cognitive symptoms and pain. Onset can be sudden, gradual, or a sudden worsening of mild fatigue. Some or all symptoms are present every day. An acute onset of fever and viral-like symptoms is common, and CFS can follow a known illness such as infectious mononucleosis.[102]

Prevalence and aetiology

The prevalence of ME/CFS is 0.1–0.5% in the paediatric population, and 0.42% of the adult population in the USA, but 84–91% of adult patients who fit the diagnostic criteria have not been diagnosed.[103, 104] Females are four times more likely to have the condition.[105] The exact cause is unknown. It is unlikely that chronic fatigue has a single aetiology in an individual patient.

The main theory is that there is an occult infection causing active persistent infection or latent symptoms after the pathogen has been cleared from the body; the condition is a multisystem physical illness. Psychological factors are secondary, not primary. It is not a psychiatric condition. The most important factor associated with developing chronic fatigue syndrome is the severity of the initial infective illness, as reflected by the number of days spent in bed with acute symptoms.[106]

Diagnosis

The diagnosis of ME/CFS is difficult to confirm in the absence of any definitive sign or test. It is often a diagnosis of exclusion. A number of conditions have symptoms that overlap with those of ME/CFS. The two most significant are fibromyalgia and depression. The major presenting symptom in fibromyalgia is usually widespread muscle and joint pain, but fatigue is nearly always present. Fibromyalgia is characterised by the presence of multiple tender points in the muscles. Trigger points are also frequently seen in patients with CFS and form an important part of the treatment. Fatigue is often the primary presenting symptom in patients with depression, and many of the symptoms described in CFS are found in depressive patients.

Clinical diagnostic worksheets, both adult and paediatric, can be found in the International Association for Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (IACFS/ME) 'Primer for

Clinical Practitioners' publications, which can be found on its website (http://iacfsme.org/ME-CFS-Primer-Education.aspx).[107]

Comorbidities

Comorbidities are seen frequently in patients with ME/CFS. These include cognitive problems, unrefreshing or disturbed sleep, generalised or localised pain, light-headedness, symptoms in multiple organ systems and orthostatic intolerance.[108] Orthostatic intolerance refers to a group of conditions in which symptoms worsen with upright posture and are improved but not always abolished by lying down. They include light-headedness, white-outs or blackouts of the visual field, visual dimming, mental fog, headaches, nausea, pain and shortness of breath. Orthostatic intolerance can be diagnosed on history and with a 10-minute standing test (record blood pressure and heart rate each minute, after a 5-minute period of lying supine). It can be missed with the standard 1-minute post-standing blood pressure test.

Treatment

The natural history of ME/CFS includes a group of patients who make very gradual improvement over a period of months and sometimes years. Treatment includes acknowledging that the patient has a real problem, providing symptom relief and supporting the patient. The most common fatigue triggers should be identified and addressed. Whether graded exercise therapy or cognitive behavioural therapy are useful is controversial. A major UK study (the PACE trial[109]) was published in 2011 and reported that those elements (exercise, behavioural therapy) were superior to the usual specialist care. However, the clinical measures of success were rather small—a 60 m greater distance in the 6-minute walk test and a level still below normal. Patient groups contested the findings, and there has been a lot of discussion about methodological flaws in the study. Our clinical advice is to use a shared decision-making approach on a case-by-case basis. Overexertion can cause exacerbation of symptoms in some patients. Medications may be required for comorbidities such as pain, insomnia, depression and orthostatic intolerance.

Coeliac disease

Coeliac disease is a common immune-mediated systemic condition, manifested by small intestinal enteropathy triggered by exposure to gluten. In Australia, coeliac disease is estimated to have a prevalence of 1.2% in men and 1.9% in women.[110] It is a cause of fatigue and is not always accompanied by the symptoms of malabsorption, such as diarrhoea and abdominal pain.
Other common sequelae include weight loss and growth failure. Fifty-six per cent of the population carry one or both of the genes (HLA DQ2 and HLA DQ8). In Australia, it is estimated 80% of people with coeliac disease are undiagnosed.[111]

CASE STUDY

Michelle Akers, Team USA soccer—chronic fatigue syndrome

Michelle Akers (Fig. 19.2) is an American former soccer player who won two World Cups and one Olympic gold medal with Team USA. Akers is regarded as one of the greatest female soccer players of all time. In 2004, she was one of only two female soccer players named on FIFA's list of the 125 greatest living soccer players. However, following the initial World Cup triumph of 1991, she was diagnosed with CFS, having suffered from exhaustion after the tournament.

Figure 19.2 Michelle Akers playing for Team USA
GETTY IMAGES/RICK STEWART/ALLSPORT

Sources: references 113, 114, 115, 116, 117

Diagnosis

Akerman first noticed increasing fatigue when performing basic activities of daily living, and was advised to rest. Her symptoms included fatigue, dizziness, migraines, night sweats, upset stomach and metabolic concerns. Ultimately, following no forthcoming diagnosis, she collapsed post-match in 1993. In 1994, following an echocardiogram, heart stress tests and blood tests, Akers was diagnosed with the Epstein–Barr virus (mononucleosis), which had subsequently affected her immune system, leading to CFS and neurally mediated hypotension (NMH).

Management

Akers was placed on a strict dietary regimen that included multivitamins, antioxidants, B complex vitamins, magnesium and CoQ10. In addition to dietary control, Akers was given salt tablets and advised to remain hydrated to prevent the effects of hypotension. She was also advised to maintain her regular physical activity and avoid becoming sleep deprived.

Conclusion

Although no cure exists for CFS, Akers was able to play on at the elite level of soccer long after the onset of her symptoms and up to her retirement some six years post-diagnosis. Lifestyle adaptations were necessary to allow her to manage her CFS, but this should be framed in the context of maintaining one's activities of daily living over the longer term.

Eating disorders

Eating disorders cause fatigue via inadequate calorie intake and hormonal imbalance. The prevalence of anorexia is estimated to be 1% in the general population, with bulimia estimated at 1–3%.[112] Prevalence is higher in female athletes, aesthetic sports and low body weight–advantage sports.

SUMMARY

Fatigue is a common presentation in athletes, either self-referred or referred via their coaches and support staff. Remember that the various causes of tiredness do not usually occur in isolation and that those causes can contribute to the other negative outcomes. While there are many common and obvious causes, care must be taken to be vigilant for less common medical causes.

REFERENCES

1. Melin A, Tornberg AB, Skouby S et al. The LEAF questionnaire: a screening tool for the identification of female athletes at risk for the female athlete triad. *Br J Sports Med* 2014; 48(7): 540–5.
2. Fairburn C, Cooper Z, O'Connor M. Eating disorder examination (edition 16.0D). In: Fairburn C. *Cognitive behavior therapy and eating disorders*. New York: Guilford Press,

2008: 265–308.

3. Watson NF, Badr MS, Belenky G et al. Recommended Amount of Sleep for a Healthy Adult: a Joint Consensus Statement of the American Academy of Sleep Medicine and Sleep Research Society. *Sleep* 2015; 38(6): 843–4.
4. Paruthi S, Brooks LJ, D'Ambrosio C et al. Recommended Amount of Sleep for Pediatric Populations: a Consensus Statement of the American Academy of Sleep Medicine. *J Clin Sleep Med* 2016; 12(6): 785–6.
5. Malhotra RK. Sleep, recovery, and performance in sports. *Neurol Clin* 2017; 35(3): 547–57.
6. Vyazovskiy VV, Delogu A. NREM and REM sleep: complementary roles in recovery after wakefulness. *Neuroscientist* 2014; 20(3): 203–19.
7. Walker M, Stickgold R. It's practice, with sleep, that makes perfect: implications of sleep-dependent learning and plasticity for skill performance. *Clin Sports Med* 2005; 24(2): 301–17.
8. Mah CD, Mah KE, Kezirian EJ et al. The effects of sleep extension on the athletic performance of collegiate basketball players. *Sleep* 2011; 34(7): 943–50.
9. Luke A, Lazaro RM, Bergeron MF et al. Sports-related injuries in youth athletes: is overscheduling a risk factor? *Clin J Sport Med* 2011; 21(4): 307–14.
10. Von Rosen P, Frohm A, Kottorp A et al. Too little sleep and an unhealthy diet could increase the risk of sustaining a new injury in adolescent elite athletes. *Scand J Med Sci Sports* 2017; 27(11): 1364–71.
11. Cohen S, Doyle WJ, Alper CM et al. Sleep habits and susceptibility to the common cold. *Arch Intern Med* 2009; 169(1): 62–7.
12. Irwin MR, Wang M, Campomayor CO et al. Sleep deprivation and activation of morning levels of cellular and genomic markers of inflammation. *Arch Intern Med* 2006; 166(16): 1756–62.
13. Opp MR, Born J, Irwin MR. Sleep and the immune system. In: Ader R, ed. *Psychoneuroimmunology*. 4th ed. Burlington, MA: Elsevier Academic Press, 2007; 1: 579–618.
14. Vgontzas AN, Zoumakis E, Bixler EO et al. Adverse effects of modest sleep restriction on sleepiness, performance, and inflammatory cytokines. *J Clin Endocrinol Metab* 2004; 89(5): 2119–26.
15. Lange T, Perras B, Fehm HL et al. Sleep enhances the human antibody response to hepatitis A vaccination. *Psychosom Med* 2003; 65(5): 831–5.
16. Spiegel K, Sheridan JF, Van Cauter E. Effect of sleep deprivation on response to immunization. *JAMA* 2002; 288(12): 1471–2.
17. Meeusen R, Duclos M, Foster C et al. Prevention, Diagnosis, and Treatment of the Overtraining Syndrome: Joint Consensus Statement of the European College of Sport Science and the American College of Sports Medicine. *Med Sci Sports Exerc*

2013; 45(1): 186–205.

18. Nishiura C, Noguchi J, Hashimoto H. Dietary patterns only partially explain the effect of short sleep duration on the incidence of obesity. *Sleep* 2010; 33(6): 753–7.
19. Weiss A, Xu F, Storfer-Isser A et al. The association of sleep duration with adolescents' fat and carbohydrate consumption. *Sleep* 2010; 33(9): 1201–9.
20. Chaput JP, Despres JP, Bouchard C et al. Longer sleep duration associates with lower adiposity gain in adult short sleepers. *Int J Obes* 2012; 36(5): 752–6.
21. Frank MG, Benington JH. The role of sleep in memory consolidation and brain plasticity: dream or reality? *Neuroscientist* 2006; 12(6): 477–88.
22. Edwards BJ, Waterhouse J. Effects of one night of partial sleep deprivation upon diurnal rhythms of accuracy and consistency in throwing darts. *Chronobiol Int* 2009; 26(4): 756–68.
23. Reyner LA, Horne JA. Sleep restriction and serving accuracy in performance tennis players, and effects of caffeine. *Physiol Behav* 2013; 120: 93–6.
24. Jarraya S, Jarraya M, Chtourou H et al. Effect of time of day and partial sleep deprivation on the reaction time and the attentional capacities of the handball goalkeeper. *Biol Rhythm Res* 2014; 45(2): 183–91.
25. Zhong X, Hilton HJ, Gates GJ et al. Increased sympathetic and decreased parasympathetic cardiovascular modulation in normal humans with acute sleep deprivation. *J Appl Physiol (1985)* 2005; 98(6): 2024–32.
26. McCrory P, Meeuwisse W, Dvorak J et al. Consensus Statement on Concussion in Sport–the 5th International Conference on Concussion in Sport held in Berlin, October 2016. *Br J Sports Med* 2017; 51(11): 838–47.
27. Tasali E, Leproult R, Ehrmann DA et al. Slow-wave sleep and the risk of type 2 diabetes in humans. *Proc Natl Acad Sci U S A* 2008; 105(3): 1044–9.
28. Morris CJ, Purvis TE, Hu K et al. Circadian misalignment increases cardiovascular disease risk factors in humans. *Proc Natl Acad Sci U S A* 2016; 113(10): E1402–11.
29. Chaput JP, Sjodin AM, Astrup A et al. Risk factors for adult overweight and obesity: the importance of looking beyond the 'big two'. *Obes Facts* 2010; 3(5): 320–7.
30. Cunanan AJ, DeWeese BH, Wagle JP et al. The general adaptation syndrome: a foundation for the concept of periodization. *Sports Med* 2018; 48(4): 787–97.
31. Raglin J, Wilson G. Overtraining and staleness in athletes. In: Hanin YL, ed. Emotions in sport. Champaign, IL: Human Kinetics, 2000: 191–207.
32. Morgan W, O'Connor P, Ellickson K et al. Personality structure, mood states, and performance in elite male distance runners. *Int J Sport Psych* 1988; 19: 247–63.
33. Morgan W, O'Connor P, Sparling P et al. Psychological characterization of the elite female distance runner. *Int J Sports Med* 1987; 8(Suppl 2): 124–31.
34. Kenttä G, Hassmén P, Raglin J. Training practices and overtraining syndrome in Swedish age-group athletes. *Int J Sports Med* 2001; 22: 460–5.

35. Matos N, Winsley R, Williams C. Prevalence of nonfunctional overreaching/overtraining in young English athletes. *Med Sci Sports Exerc* 2011; 43: 1287–94.
36. Raglin J. Overtraining and staleness: psychometric monitoring of endurance athletes. In: Murphey M, Tennant LK, Singer RN, eds. *Handbook of research on sport psychology*. New York: Macmillan, 1993: 840–50.
37. Meeusen R, Piacentini MF, Busschaert B et al. Hormonal responses in athletes: the use of a two bout exercise protocol to detect subtle differences in (over)training status. *Eur J Appl Physiol* 2004; 91: 140–6.
38. Urhausen A, Gabriel H, Kindermann W. Blood hormones as markers of training stress and overtraining. *Sports Med* 1995; 20: 251–76.
39. Budgett R, Newsholme E, Lehmann M et al. Redefining the overtraining syndrome as the unexplained underperformance syndrome. *Br J Sports Med* 2000; 34: 67–8.
40. Halson SL, Jeukendrup AE. Does overtraining exist? An analysis of overreaching and overtraining research. *Sports Med* 2004; 34: 967–81.
41. Halson S, Lancaster G, Jeukendrup A et al. Immunological responses to overreaching in cyclists. *Med Sci Sports Exerc* 2003; 35(5): 854–61.
42. Urhausen A, Gabriel H, Weiler B et al. Ergometric and psychological findings during overtraining: a long-term follow-up study in endurance athletes. *Int J Sports Med* 1998; 19: 114–20.
43. Mackinnon LT. Chronic exercise training effects on immune function. *Med Sci Sports Exerc* 2000; 32(7 Suppl): S369–76.
44. Duclos M. A critical assessment of hormonal methods used in monitoring training status in athletes. *Int Sportmed J* 2008; 9(2): 55–66.
45. Lehmann M, Foster C, Dickhuth HH et al. Autonomic imbalance hypothesis and overtraining syndrome. *Med Sci Sports Exerc* 1998; 30(7): 1140–5.
46. Gouarne C, Groussard C, Gratas-Delamarche A et al. Overnight urinary cortisol and cortisone add new insights into adaptation to training. *Med Sci Sports Exerc* 2005; 37(7): 1157–67.
47. Margonis K, Fatouros IG, Jamurtas AZ et al. Oxidative stress biomarkers responses to physical overtraining: implications for diagnosis. *Free Radic Biol Med* 2007; 43(6): 901–10.
48. Urhausen A, Kindermann W. Diagnosis of overtraining—what tools do we have? *Sports Med* 2002; 32: 95–102.
49. Costill DL, Flynn MG, Kirwan JP et al. Effects of repeated days of intensified training on muscle glycogen and swimming performance. *Med Sci Sports Exerc* 1988; 20: 249–54.
50. Meeusen R, Duclos M, Gleeson M et al. Prevention, Diagnosis, and Treatment of the Overtraining Syndrome: ECSS Position Statement 'Task Force'. *Eur J Sport Sci* 2006;

6(1): 1–14.

51. Le Meur Y, Hausswirth C, Natta F et al. A multidisciplinary approach to overreaching detection in endurance trained athletes. *J Appl Physiol (1985)* 2013; 114(3): 411–20.

53. McNair BM, Lorr M, Doppleman LE. *Profile of mood states manual*. San Diego, CA: Educational & Industrial Testing Service, 1971.

54. Morgan W, Brown D, Raglin J et al. Psychological monitoring of overtraining and staleness. *Br J Sports Med* 1987; 21: 107–14.

55. Raglin J, Morgan W, O'Connor P. Changes in mood state during training in female and male college swimmers. *Int J Sports Med* 1991; 12: 585–9.

56. Raglin J, Morgan W. Development of a scale for use in monitoring training-induced distress in athletes. *Int J Sports Med* 1994; 15: 84–8.

57. Kenttä G, Hassmén P, Raglin J. Mood state monitoring of training and recovery in elite kayakers. *Eur J Sport Sci* 2006; 6(4): 245–53.

58. Kellmann M, Kallus K. *Recovery-stress questionnaire for athletes*. Champaign, IL: Human Kinetics, 2001.

59. Kellmann M, Gunther K. Changes in stress and recovery in elite rowers during preparation for the Olympic Games. *Med Sci Sports Exerc* 2000; 32(3): 676–83.

60. Rietgens G, Kuipers H, Adam J et al. Physiological, biochemical and psychological markers of strenuous training-induced fatigue. *Int J Sports Med* 2005; 26: 16–26.

61. Nederhof E, Lemmink K, Visscher C et al. Psychomotor speed: possibly a new marker for overtraining syndrome. *Sports Med* 2006; 36(10): 817–28.

62. Nederhof E, Lemmink K, Zwerver J et al. The effect of high load training on psychomotor speed. *Int J Sports Med* 2007; 28(7): 595–601.

63. Nederhof E, Zwerver J, Brink M et al. Different diagnostic tools in nonfunctional overreaching. *Int J Sports Med* 2008; 29(7): 590–7.

64. Kenttä G, Hassmén P. Overtraining and recovery: a conceptual model. *Sports Med* 1998; 26(1): 1–16.

65. Kreher JB, Schwartz JB. Overtraining syndrome: a practical guide. *Sports Health* 2012; 4(2): 128–38.

66. Bruin G, Kuipers H, Keizer HA et al. Adaptation and overtraining in horses subject to increasing training loads. *J Appl Physiol (1985)* 1994; 76: 1908–13.

67. Budgett R. Fatigue and underperformance in athletes: the overtraining syndrome. *Br J Sports Med* 1998; 32(2): 107–10.

68. Nattiv A, Loucks AB, Manore MM et al. American College of Sports Medicine Position Stand: the Female Athlete Triad. *Med Sci Sports Exerc* 2007; 39: 1867–82.

69. Mountjoy M, Sundgot-Borgen J, Burke L et al. The IOC Consensus Statement: Beyond the Female Athlete Triad—Relative Energy Deficiency in Sport (RED-S). *Br J Sports*

Med 2014; 48: 491–7.

70. Reid VL, Gleeson M, Williams N et al. Clinical investigation of athletes with persistent fatigue and/or recurrent infections. *Br J Sports Med* 2004; 38(1): 42–5.
71. Fricker PA, Gleeson M, Flanagan A et al. A clinical snapshot: do elite swimmers experience more upper respiratory illness than non-athletes? *Clin Exerc Physiol* 2000; 2: 155–8.
72. Alonso J-M, Tshcoll PM, Engebretson L et al. Occurrence of injuries and illness during the 2009 IAAF World Athletics Championships. *Br J Sports Med* 2010; 44: 1100–5.
73. Luzuriaga K, Sullivan JL. Infectious mononucleosis. *N Engl J Med* 2010; 362: 1993–2000.
74. Harris MD. Infectious diseases in athletes. *Curr Sports Med Rep* 2011; 10(2): 84–9.
75. Putukian M, O'Connor FG, Stricker PR et al. Mononucleosis and athletic participation: an evidence-based subject review. *Clin J Sport Med* 2008; 18(4): 309–15.
76. Yoda K, Sata T, Kurata T et al. Oropharyngotonsillitis associated with nonprimary Epstein–Barr virus infection. *Arch Otolaryngol Head Neck Surg* 2000; 126(2): 185–93.
77. Gleeson M, Pyne D, Austin J et al. Epstein–Barr virus reactivation and upper-respiratory illness in elite swimmers. *Med Sci Sports Exerc* 2002; 34(3): 411–7.
78. Kerksick CM, Arent S, Schoenfeld BJ et al. International Society of Sports Nutrition Position Stand: Nutrient Timing. *J Int Soc Sports Nutr* 2017; 14: 33.
79. Beard JL, Tobin B. Iron status and exercise. *Am J Clin Nutr* 2000; 72(2 Suppl): 594S–7S.
80. Davies KJ, Maguire JJ, Brooks GA et al. Muscle mitochondrial bioenergetics, oxygen supply, and work capacity during dietary iron deficiency and repletion. *Am J Physiol* 1982; 242(6): E418–27.
81. Clement DB, Lloyd-Smith DR, Macintyre JG et al. Iron status in Winter Olympic sports. *J Sports Sci* 1987; 5(3): 261–71.
82. Rowland TW, Black SA, Kelleher JF. Iron deficiency in adolescent endurance athletes. *J Adolesc Health Care* 1987; 8(4): 322–6.
83. Eichner ER. Pearls and pitfalls: everyone needs iron. *Curr Sports Med Rep* 2012; 11(2): 50–1.
84. Australian Bureau of Statistics (ABS) 2016. National Health Survey: First Results, 2014–15. ABS Cat no. 4364.0.55.001. Canberra: ABS.
85. Wilber RL, Rundell KW, Szmedra L et al. Incidence of exercise-induced bronchospasm in Olympic winter sport athletes. *Med Sci Sports Exerc* 2000; 32: 723–37.
86. Dykewicz, MS. 7. Rhinitis and sinusitis. *J Allergy Clin Immunol* 2003; 111(2 Suppl): S520–9.
87. Passalacqua G, Ciprandi G, Canonica GW. The nose–lung interaction in allergic

rhinitis and asthma: united airways disease. *Curr Opin Allergy Clin Immunol* 2001; 1: 7–13.

88. Settipane RJ, Hagy GW, Settipane GA. Long-term risk factors for developing asthma and allergic rhinitis: a 23-year follow-up study of college students. *Allergy Proc* 1994; 15: 21–5.
89. Fisher LH, Davies MJ, Craig TJ. Nasal obstruction, the airway, and the athlete. *Clin Rev Allergy Immunol* 2005; 29: 151–8.
90. Australian Bureau of Statistics. Mental Health of Young People, 2007. Prevalence of mental disorders. http://www.abs.gov.au/ausstats/abs@.nsf/Latestproducts/4840.0.55.001Main%20Features42007?opendocument&
91. Clark I, Landolt HP. Coffee, caffeine, and sleep: a systematic review of epidemiological studies and randomized controlled trials. *Sleep Med Rev* 2017; 31: 70–8.
92. Brezinova V. Effect of caffeine on sleep: EEG study in late middle age people. *Br J Clin Pharmacol* 1974; 1(3): 203–8.
93. Drapeau C, Hamel-Herbert I, Robillard R et al. Challenging sleep in aging: the effects of 200 mg of caffeine during the evening in young and middle-aged moderate caffeine consumers. *J Sleep Res* 2006; 15(2): 133–41.
94. Hollingworth HL. The influence of caffein alkaloid on the quality and amount of sleep. *Am J Psychol* 1912; 23(1): 89–100.
95. Yang A, Palmer AA, de Wit H. Genetics of caffeine consumption and responses to caffeine. *Psychopharmacology (Berl)* 2010; 211(3): 245–57.
96. Bixler EO, Vgontzas AN, Lin HM et al. Excessive daytime sleepiness in a general population sample: the role of sleep apnea, age, obesity, diabetes, and depression. *J Clin Endocrinol Metab* 2005; 90(8): 4510–5.
97. Dunaif A. Insulin resistance and the polycystic ovary syndrome; mechanism and implications for pathogenesis. *Endocr Rev* 1997; 18: 774–800.
98. Vgontzas AN, Legro RS, Bixler EO et al. Polycystic ovary syndrome is associated with obstructive sleep apnea and daytime sleepiness: role of insulin resistance *J Clin Endocrinol Metab* 2001; 86(2): 517–20.
99. Tasali E, Van Cauter E, Ehrmann DA. Relationships between sleep disordered breathing and glucose metabolism in polycystic ovary syndrome. *J Clin Endocrinol Metab* 2006; 91: 36–42.
100. Fogel RB, Malhotra A, Pillar G et al. Increased prevalence of obstructive sleep apnea syndrome in obese women with polycystic ovary syndrome. *J Clin Endocrinol Metab* 2001; 86(3): 1175–80.
101. Gopal M, Duntley S, Uhles M et al. The role of obesity in the increased prevalence of obstructive sleep apnea syndrome in patients with polycystic ovarian syndrome. *Sleep Med* 2002; 3(5): 401–4.

102. Katz BZ, Shiraishi Y, Mears CJ et al. Chronic fatigue syndrome after infectious mononucleosis in adolescents. *Pediatrics* 2009; 124(1): 189–93.
103. Reyes M, Nisenbaum R, Hoaglin DC et al. Prevalence and incidence of chronic fatigue syndrome in Wichita, Kansas. *Arch Intern Med* 2003; 163: 1530–6.
104. Jason LA, Richman JA, Rademaker AW et al. A community-based study of chronic fatigue syndrome. *Arch Intern Med* 1999; 159(18): 2129–37.
105. Nijhof SL, Maijer K, Bleijenberg G et al. Adolescent chronic fatigue syndrome: prevalence, incidence, and morbidity. *Pediatrics* 2011; 127(5): e1169–75.
106. Jason LA, Katz BZ, Shiraishi Y et al. Predictors of post-infectious chronic fatigue syndrome in adolescents. *Health Psychol Behav Med* 2014; 2(1): 41–51.
107. Rowe PC, Underhill RA, Friedman KJ et al. Myalgic encephalomyelitis/chronic fatigue syndrome diagnosis and management in young people: a primer. *Front Pediatr* 2017; 5: 121.
108. Stewart JM, Gewitz MH, Weldon A et al. Orthostatic intolerance in adolescent chronic fatigue syndrome. *Pediatrics* 1999; 103(1): 116–21.
109. White PD, Goldsmith KA, Johnson AL et al; PACE trial management group. Comparison of adaptive pacing therapy, cognitive behaviour therapy, graded exercise therapy, and specialist medical care for chronic fatigue syndrome (PACE): a randomised trial. *Lancet* 2011; 377(9768): 823–36 doi: 10.1016/S0140-6736(11)60096-2.
110. Anderson RP, Henry MJ, Taylor R et al. A novel seronegative approach determines the community prevalence of celiac disease and informs improved diagnostic pathways. *BMC Med* 2013; 11: 188.
111. Anderson RP. Coeliac disease is on the rise. *Med J Aust* 2011; 194: 278–9.
112. Bratland-Sanda S, Sundgot-Borgen J. Eating disorders in athletes: overview of prevalence, risk factors and recommendations for prevention and treatment, *Eur J Sport Sci*. 2013; 13: 499-508, doi: 10.1080/17461391.2012.740504.
113. https://en.wikipedia.org/wiki/Michelle_Akers
114. https://www.biography.com/people/michelle-akers-21321911
115. https://www.washingtonpost.com/archive/sports/1999/06/04/akerss-exhausting-opponent/00e07c5d-38e7-4163-9a0f-9c12ac03bf7f/?noredirect=on&utm_term=.657fd57a4b09
116. https://www.webmd.com/fitness-exercise/features/michelle-akers-cfids#1
117. https://www.ussoccer.com/stories/2014/03/17/13/59/michelle-akers-bows-out-of-olympics-due-to-injury-womens-soccer-legend-retires-from-international-pl

Chapter 20

Cancer

with DANIEL FRIEDMAN, MARCOS AGOSTINHO, KRISTIN CAMPBELL and KATHRYN H SCHMITZ

Even though I'm not running anymore, we still have to try to find a cure for cancer. Other people should go ahead and try to do their own thing now.

Terry Fox (1958–1981) Canadian athlete, humanitarian and cancer research activist

Cancer is the second leading cause of death globally and is responsible for nearly 9 million deaths annually—equivalent to 1 in 6 deaths worldwide.[1] In the USA, 38% of women and 42% of men will be diagnosed with cancer in their lifetimes.[2] With an ageing and rapidly expanding population, cancer is more prevalent than ever and incident cases are projected to rise by about 70% over the next two decades.[1]

The first recorded case of cancer was in Egypt in 1500 BCE.[3] Compared to the days of pharaohs and hieroglyphics, we may be living longer but many of us are also *living sicker.* Modern physical and social environments are not conducive to healthy lifestyles, and overwhelming levels of physical inactivity (among other non-communicable disease risk factors) are exposing our cells and biological processes to greater stress than in the past.

For many years we have understood that regular moderate to vigorous physical activity reduces the risk of breast and colon cancer. By 2018, that list had expanded to include a reduced risk for cancers of the bladder, blood, endometrium, head and neck, kidney, liver, lung, oesophagus and stomach.[4, 5] The underlying biological mechanisms responsible for physical activity's protective effects for cancer are being unravelled; epidemiologists and basic scientists now realise that physical activity has a much larger role to play in clinical oncology than initially thought.

In this chapter we explore:

- the clinical work-up of the patient with cancer, in brief
- physical activity's role:

  - in the primary prevention of different types of cancer
  - as an adjunct treatment for cancer
  - in maximising the quality of life in patients recovering from cancer
- considerations in prescribing physical activity to the patient with, or recovering from, cancer.

A BRIEF OVERVIEW OF CANCER

Cancer comes from the Greek word *karkinos,* meaning 'crab,' first used by Hippocrates to describe carcinomas.[3] Cancer cells develop in a multistep process[6] in which several mutations are required to gradually transform normal cells into malignant ones. This progressive series of alterations comprises inherited or acquired genetic mutations in tumour suppressor genes, oncogenes and/or mismatch repair genes.

Without the regulation of normal cell signalling, cancer cells continue to divide, replicate and accumulate, instead of undergoing apoptosis (programmed cell death) when damaged. In a nutshell, cancer can be thought of as cell programming gone wrong. This can occur in different cells throughout the body (Table 20.1).

Table 20.1 Most common causes of cancer death worldwide by type

Cancer type	Deaths
Lung	1 690 000
Liver	777 000
Colorectal	774 000
Stomach	754 000
Breast	571 000

ADAPTED FROM WORLD HEALTH ORGANIZATION CANCER FACT SHEET(2018)[1]

Although over 200 different types of cancer exist, they share common traits or hallmarks, first described by Hanahan and Weinberg nearly 20 years ago as 'organizing principle[s] for rationalizing the complexities of neoplastic disease'.[7, 8] These hallmarks include:

- sustaining proliferative signalling
- evading growth suppressors

Cancer—not just one disease

Cancer can be grouped into more specific categories based on organ or tissue involvement, or location. Most cancers include subtypes, defined by anatomy, histology or genomics. Examples of common cancer types include:

- carcinoma—originating from skin or tissue that lines or covers internal organs made up of epithelial cells

- sarcoma—originating from bone, muscle, fat and blood vessels being made up of supportive or connective tissue
- leukaemia—abnormal blood cells, originating from blood-forming tissues, giving rise to the circulation of these cells in the blood throughout the body
- lymphoma and myeloma—originating from cells of the immune system
- glioma and astrocytoma—originating from cells of the central nervous system.

- resisting cell death
- enabling replicative immortality
- inducing angiogenesis
- activating invasion and metastasis.

More recently, Hanahan and Weinberg proposed four new hallmarks,[8] namely:

- abnormal metabolic pathways
- evading the immune system
- genome instability
- inflammation.

For more information about the molecular and cellular basis of cancer, we recommend *The Biology of Cancer* by Robert Weinberg.[9]

How does cancer present?

Cancer presentation varies and depends on location, size, and extent of invasion and metastasis. Classic symptoms associated with cancer include:

- unintentional, unexplained weight loss
- fatigue
- night sweats
- unexplained cough
- blood present in urine or faeces
- change in bowel habits or bladder function
- skin changes
- unexplained pain or unusual swelling.

Often no specific symptoms manifest, so it is important to reduce risk factors and undergo recommended screening specific to certain age groups. Individuals with known risk factors for cancer (see box) and considered at risk should be informed of potential cancer symptoms and be

evaluated by a clinician.

How is cancer diagnosed?

In conjunction with a thorough history and examination, imaging, molecular diagnostics and biopsy techniques can be utilised separately or in combination to help diagnose cancer. Biopsy remains the gold standard in cancer diagnosis—this enables cancers to be graded and staged. Grading refers to how abnormal tumour cells (and tissue) look under the microscope. Stages of cancer are determined by spread of the original tumour. Characterising cancer in this way helps guide treatment and allows clinicians to provide a more accurate prognosis.

How is cancer treated?

Cancer therapy must be individualised and may include chemotherapy, radiotherapy, hormonal therapy, targeted immunotherapy and/or surgery.

Most cancer patients will undergo surgery, and about half of cancer patients undergo radiotherapy,[11] which can be delivered before or after surgery, alone or with concomitant chemotherapy. Approximately half of cancer patients also receive chemotherapy, which is taken orally or delivered intravenously, on defined schedules that are cyclical in nature. Immunotherapies are often delivered cyclically via infusion as well. Hormonal therapies are often used in breast and prostate cancers, while tumour-specific monoclonal antibody therapies have been established in recent decades as one of the most successful therapeutic strategies for both haematological malignancies and solid tumours.[12]

The mode of delivery, schedule and frequency are unique to cancer type, but often include frequent appointments for a defined duration. Anti-cancer therapy usually extends over many months and, in some cases, years.

Exercise can decrease the adverse effects of anti-cancer therapy and can aid in recovery following therapy, as discussed later in this chapter.

PRACTICE PEARL

Anti-cancer therapies are constantly changing. To best understand a patient's exercise tolerance and provide a safe exercise prescription, it is essential to understand the patient's treatments and anticipate body systems that will be adversely affected.

Modifiable risk factors that can reduce the burden of cancer

While tobacco use is the most important risk factor for cancer and is responsible for over 20% of all cancer-related deaths,[10] clinicians must consider all other modifiable risk factors to help patients reduce their chances of developing cancer. Clinicians should educate the public about these risk

factors and support interventions that modify exposure to risk factors, to decrease the overall burden of disease. Public health agencies and cancer charities often provide free promotional material (Fig. 20.1).

General modifiable risk factors for cancer include:[1]

- tobacco use, including cigarettes and smokeless tobacco
- being overweight or obese (Chapter 7)
- unhealthy diet, low fruit and vegetable intake (Chapter 6)
- **physical inactivity**
- alcohol consumption
- sexually transmitted human papillomavirus (HPV) infection
- ionising and ultraviolet radiation
- indoor smoke from household use of solid fuels.

Figure 20.1 The Canadian Cancer Society provides a range of educational material to support prevention and management of cancer
WITH PERMISSION OF THE CANADIAN CANCER SOCIETY

CASE STUDY

Terry Fox, Marathon of Hope—osteogenic sarcoma

Terry Fox, quoted at the beginning of the chapter, was only 18 years old when he was diagnosed with osteogenic sarcoma—a cancer that mainly affects adolescents and young adults.[13] After crashing his car in 1976, Fox emerged with a sore knee and again felt knee pain a month later, which continued to intensify over the coming months. He presented to hospital, where he was diagnosed with the bone cancer and had his leg amputated soon after. Fox then underwent 16 months of chemotherapy.

While in hospital, Fox was so overcome by the suffering of other cancer patients that he decided to run across Canada to raise money for cancer research, in a journey he called 'The Marathon of Hope'.

In 1980, Fox ran halfway across Canada, wearing a prosthetic leg (Fig. 20.2). He completed nearly a marathon per day for 143 days. On day 143, already having raised C$23 million for cancer research, he was forced to stop due to cough and chest pain caused by metastases. Fox was the youngest person to be awarded the Order of Canada, in 1980, and won the Lou Marsh Award, given to Canada's top athlete, in the same year.

Figure 20.2 Terry Fox running in his 'Marathon of Hope'
GETTY IMAGES/BETTMANN

In the following months, Fox received multiple chemotherapy treatments and experimental interferon therapy; however the cancer continued to metastasise. In 1981, at 22 years of age, Fox was readmitted to hospital due to pneumonia, fell into a coma and died.

Fox left behind a legacy and has since been described as one of the greatest Canadian athletes ever. To date, over C$750 million has been raised for cancer research in Fox's name, through the annual *Terry Fox Run,* which is held across Canada and in other countries.[14]

PHYSICAL ACTIVITY FOR THE PRIMARY PREVENTION OF CANCER

Decades of epidemiological research have repeatedly identified physical activity as a protective factor against a number of cancers. In 2008, the US Physical Activity Guidelines Advisory Committee concluded that 'a moderate, inverse relationship existed between increased levels of physical activity and reduced risks of breast and colon cancers'.[15]

For example, epidemiological data from 73 studies reviewed in 2010 demonstrated a 25% reduction in the risk of developing breast cancer among the most physically active women, compared with those who are least active.[16] A 2012 meta-analysis suggested that the risk of breast cancer decreases by 5% for every 2 hours/week increment in moderate plus vigorous recreational physical activity.[17] Increased physical activity is associated with reduced risk of all breast cancer subtypes, regardless of hormone receptor status.[18] With regards to colon cancer, meta-analyses also suggest a 25% lower risk for the most active groups.[19, 20]

In 2017, a new Physical Activity Guidelines Advisory Committee was convened by the US Department of Health and Human Services. The review completed by this new committee added to

the list, concluding that 'strong evidence demonstrates that greater amounts of physical activity are associated with reduced risk of developing cancers of the bladder, endometrium, oesophagus, kidney, and stomach' (Table 20.2).[4] However, they concluded that there is limited evidence suggesting an association between increased physical activity and decreased risks of haematological, head and neck, ovary, pancreas and prostate cancers. Further, a landmark 2016 study by Moore et al., which pooled data from over 1.4 million adults, found that high levels of leisure-time physical activity were associated with lower risks of myeloid leukaemia, myeloma and cancer of the liver.[5]

Table 20.2 Summary of associations of physical activity and sedentary behaviour with specific cancers by evidence grade

Cancer	Evidence grade
Physical activity protects against:	
Bladder, breast, colon, endometrium, oesophagus, renal, gastric	Strong
Lung	Moderate
Haematological, head and neck, ovary, pancreas, prostate	Limited
Brain	None available
No effect of physical activity:	
Thyroid	Limited
Rectal	Limited
Sedentary behaviour increases risk of:	
Endometrium, colon, lung	Moderate

ADAPTED FROM PHYSICAL ACTIVITY GUIDELINES ADVISORY COMMITTEE SCIENTIFIC REPORT (2018)[4]

Conversely, greater levels of sedentary behaviour are reported to increase the risk of developing cancer, particularly endometrial, colon and lung cancer.[4]

Most evidence about the association between physical activity and cancer risk is based on observational studies that use self-reported measures of leisure-time or recreational physical activity (Fig. 20.3). A 2015 meta-analysis that revealed the inverse linear relationship between household physical activity and cancer risk found a 16% lower overall cancer risk in the most active compared with the least active. Increasing an individual's household physical activity by 10 MET (metabolic equivalent) hours per week or 1 hour/week was associated with a 1% reduction of cancer risk.[21]

Page 301

https://www.sciencedirect.com. Due to rights and permissions restrictions, this content cannot be reproduced in a digital format. The content is available in the print edition at page 301.

Figure 20.3 Physical activity reduces the risk for a number of diseases—5 hours of physical activity per

week reduces breast and colon cancer risk by about 25%.
THE LANCET, 380(9836), KAHN ET AL, SPORT AND EXERCISE AS CONTRIBUTORS TO THE HEALTH OF NATIONS, 59-64, 2012, WITH PERMISSION FROM ELSEVIER

How does physical activity prevent cancer?

Physical activity, or more specifically exercise, involves 'bouts of strenuous exertion that challenge whole-body homeostasis and provoke widespread adaptations in cells, tissues and organ systems'[22] (see Chapter 2). Being active causes diverse biological, epigenetic, metabolic and inflammatory changes in the body that occur both acutely and over time.[23] However, while biomechanical and metabolic adaptations from physical activity have been extensively studied in skeletal muscle, much less is known about physical activity's effects on cancerous or pre-cancerous cells.[24]

In a seminal paper written by McTiernan in 2008, it was proposed that physical activity is linked to cancer protection through exercise-dependent reductions in cancer risk factors, such as sex hormones, insulin and insulin-like growth factor-1, and inflammatory markers (Fig. 20.4).[25] Subsequent research has focused on exploring McTiernan's hypothesis, and has outlined additional mechanisms that may link physical activity and exercise to cancer prevention.[26]

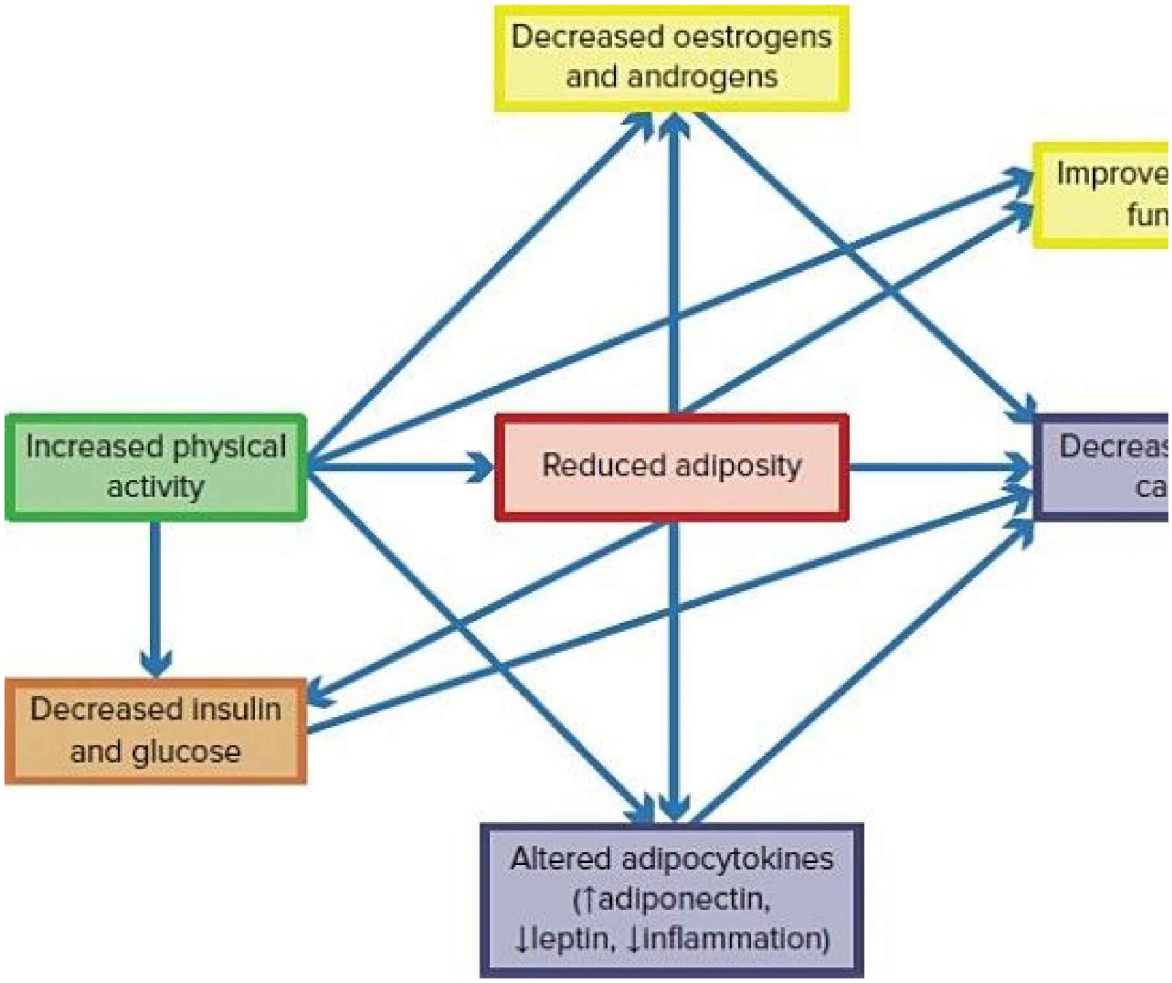


Figure 20.4 In her classic 2008 review, Professor Anne McTiernan proposed that physical activity could reduce cancer risk via several mechanisms
REPRINTED BY PERMISSION FROM SPRINGER NATURE: NATURE REVIEWS CANCER VOLUME 8, PAGES 205–211, MECHANISMS LINKING PHYSICAL ACTIVITY WITH CANCER, MCTIERNAN A., COPYRIGHT 2008[25]

The following sections review some of the biological changes that occur during and after physical activity that have the potential to influence cancer-promoting or progression pathways.

Insulin-like growth factor-1 promotes cell growth

Insulin-like growth factor-1 (IGF-1) is a peptide hormone, similar in molecular structure to insulin, that plays a key role in the regulation of cell growth. When bound to its receptor, IGF-1 activates a number of signalling pathways that inhibit apoptosis, promote cell growth, mitosis and angiogenesis.[27] A landmark case-control study from 1993 found higher plasma concentrations of

IGF-1 in women with breast cancer than in women without,[28] and more recent analysis of data from 17 prospective studies revealed a significant positive association between IGF-1 and breast cancer risk, with a 28% increase in risk for women with the highest levels of IGF-1, compared to those with the lowest.[29]

Similarly, a 2008 analysis of 12 prospective studies showed a significant positive association between IGF-1 levels and prostate cancer risk in men, with a 38% increase in risk for men with the highest levels of IGF-1, compared to those with the lowest.[30]

Insulin-like growth factor-1 concentration can change in response to nutritional changes, such as decreasing caloric intake and protein restriction,[31] and it has been found that individuals with high intakes of protein from dairy products have higher levels of IGF-1.[32] Although there is evidence that dairy products and perhaps other animal proteins may be important determinants of IGF-1, the impact of our dietary choices on IGF-1 is still up for debate.

Exercise, on the other hand, has been shown to lower IGF-1, and this reduction is associated with a near 50% reduction in cancer-specific deaths.[33]

Energy imbalance and insulin resistance promote cancer development

Physical activity reduces plasma insulin concentrations, leading to increased insulin sensitivity and glucose metabolism in breast cancer survivors[34] and in men with prostate cancer receiving androgen suppression therapy.[35] As Thomas et al. summarise in their 2017 scientific review,[23] 'hyperglycaemia and hyperinsulinaemia secondary to insulin resistance are associated with an increased risk of cancer, poorer prognostic features at presentation, higher risk of relapse after initial treatment and more rapid progression in men with hormone-refractory prostate cancer'. Further, elevated levels of C-peptide, an endogenous marker of insulin secretion, are associated with a significantly increased risk of prostate cancer-specific mortality.[36]

Energy intake that exceeds energy expenditure (e.g. eating too much or exercising too little) is one of the main drivers of weight gain and obesity (Chapter 7), which is estimated to be responsible for 20% of cancer cases.[37] Leptin (a neuropeptide cytokine) and oestrogen, both generated in adipose cells, promote breast cancer directly, as well as through insulin signalling pathways via enhanced angiogenesis and cell proliferation.[38]

Adiponectin, an adipokine cytokine that is secreted from white adipose tissue and is inversely correlated with adiposity, breast and prostate cancer risk,[39] is notably reduced in obesity and type 2 diabetes.[40] Adiponectin suppresses the inactivation of nitric oxide, which reduces tumour cell-induced platelet aggregation[41]—a process by which tumour cells cloak themselves with platelets to protect from natural killer cell-mediated killing.[42]

Physical activity increases antioxidant pathways and enhances immunity

Physical activity produces reactive oxidative species that increase oxidative stress on DNA, which is met with an upregulation of antioxidant genes and a subsequent increased production of

antioxidant enzymes.[43] Physically active individuals have greater levels of antioxidant enzymes, which may increase their defence against environmental and ingested carcinogens.[44, 45]

During physical activity, increased levels of catecholamines (dopamine, adrenaline and noradrenaline) stimulate the recruitment of leukocytes, resulting in elevated levels of neutrophils, natural killer cells, $CD4^+$ T cells and B cells, which lead to heightened immune surveillance against malignant processes (Fig. 20.5).[46, 47]

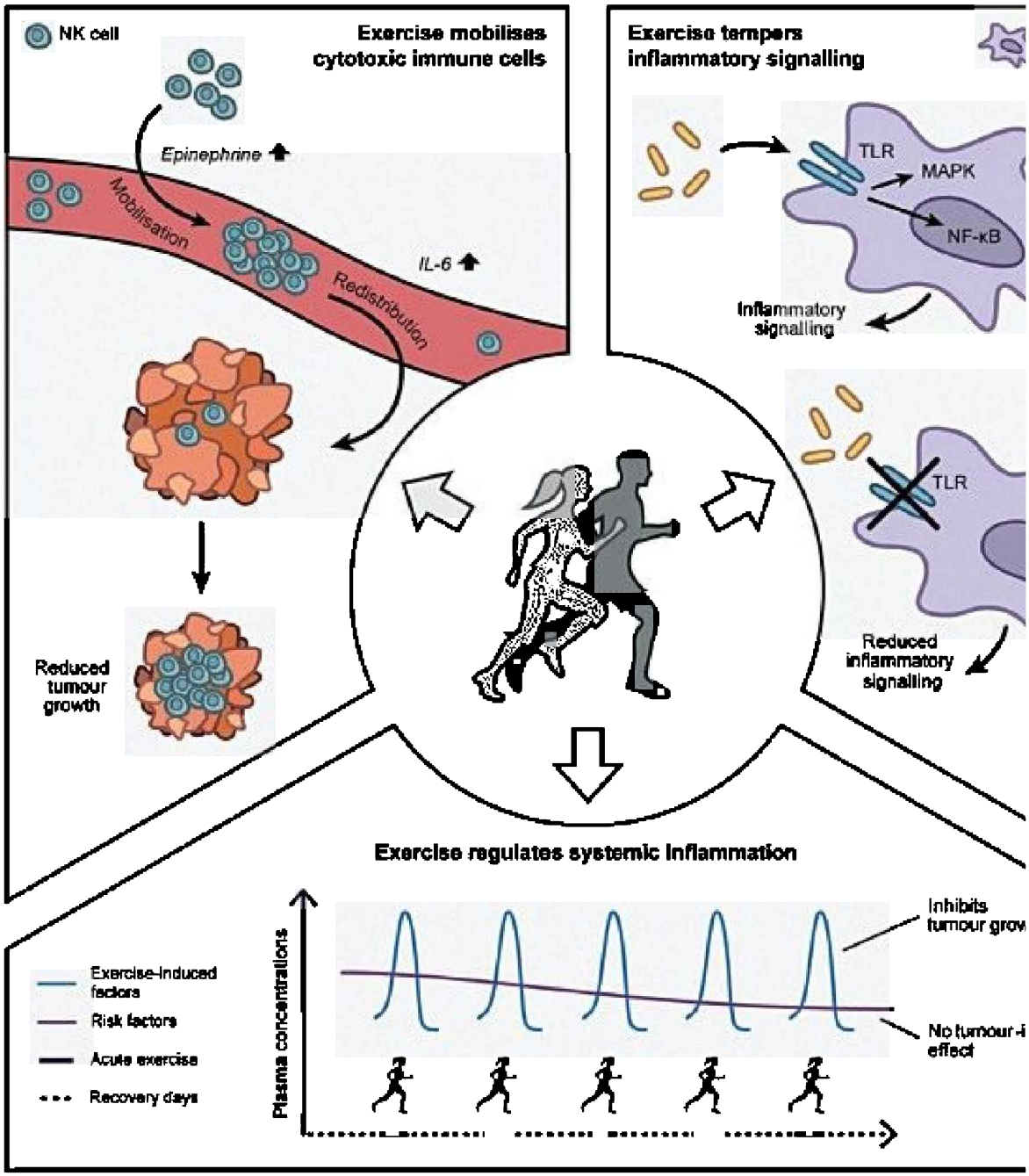


Figure 20.5 The effect of exercise on regulation of immune cell function, tempering inflammatory signalling and regulation of systemic inflammation[50] NK = natural killer; IL-6 = interleukin 6; TLR = toll-like receptor; MAPK = mitogen-activated protein kinase; NF-kB = nuclear factor kappa-light-chain-enhancer of

activated B cells.

ADAPTED FROM PORTLAND PRESS, LTD, EXERCISE PROTECTS FROM CANCER THROUGH REGULATION OF IMMUNE FUNCTION AND INFLAMMATION. BIOCHEMICAL SOCIETY TRANSACTIONS. HOJMAN P VOL45(4), PAGES 905-11. 2017 HTTP://WWW.BIOCHEMSOCTRANS.ORG/CONTENT/45/4/905; PERMISSION CONVEYED THROUGH COPYRIGHT CLEARANCE CENTER, INC.

Elevated levels of inflammatory markers, seen in individuals with chronic inflammation due to obesity, sedentary behaviour and poor diet,[48] are weakly associated with increased cancer incidence and strongly associated with increased risk of cancer-specific mortality.[49]

Physical activity's epigenetic effects on gene expression, DNA repair and telomere length

Physical activity influences the expression of genes via epigenetic biochemical alterations to chromosomes, such as histone modifications, DNA methylation, expression of microRNAs and changes in chromatin structure.[51]

Physical activity also has epigenetic effects on telomeres, the sequences of nucleotides at the end of the chromosomes that protect the integrity of information-carrying DNA and are shortened with each cell division, helping to prevent their deregulation by protecting them from transcription errors.[51] Telomere length decreases with age, and higher levels of physical activity are related to longer telomere lengths.[52] In patients with early prostate cancer, those who Page 304 are regularly active and eat in a healthy manner have longer telomeres and reduced prostate-specific antigen progression (a tumour marker for prostate cancer, as well as a biomarker for other conditions) compared with controls.[53]

Other notable biological processes of physical activity that may protect against cancer include:[23]

- increased production of heat shock proteins, which have been found to have cytoprotective functions
- increased production of irisin, a trans-membrane messenger protein that reduces cancer cell proliferation, migration and viability
- increased sunlight exposure (when being active outdoors) and subsequently vitamin D levels, which have been linked to lower incidence of cancers and cancer-specific mortality.

PHYSICAL ACTIVITY AS AN ADJUNCT TREATMENT FOR CANCER

Despite the indisputable evidence that physical activity is safe, feasible and beneficial for people with cancer, even for the most frail and advanced-stage patients,[11] physical activity currently plays a limited role in clinical oncology. Perhaps this is due to a lack of recognition of the positive effects of physical activity on cancer and treatment outcomes, or perhaps it is a fault of the healthcare system in which we find ourselves. Regardless, physical activity has therapeutic value at all points along the cancer continuum and should be an integrated component of every management plan, in conjunction with conventional anti-cancer therapy.

In this section, we will discuss the benefits of physical activity as an adjunct treatment for cancer and review the current physical activity guidelines for patients with cancer.

Physical activity decreases the adverse effects of anti-cancer therapy

Anti-cancer therapy does not come without adverse effects. In the process of killing cancer cells, many anti-cancer therapies also destroy healthy non-cancerous cells, leaving many patients with substantially diminished physical function and performance limitations.[54, 55] The adverse effects of anti-cancer therapy may be immediate, resolving over a period of weeks, or may be persistent, lasting years after therapy is completed.[11]

The sequelae of anti-cancer therapy are not unique to one specific type of treatment and include adverse effects such as fatigue, pain, cardiovascular and pulmonary complications, endocrine changes, musculoskeletal fatigue and weakness, immune alterations, gastrointestinal upset, skin changes and changes in body composition.[11]

Physical activity during and after treatment can prevent physical decline and improve cardiorespiratory fitness, functional status, strength and flexibility, body composition, immune function, self-esteem and mood, depression, anxiety and stress levels. Whether physical activity can mitigate the cognitive decline associated with treatment is still being debated. Physical activity during treatment can reduce the number and severity of adverse effects, including nausea, fatigue, pain and lymphoedema (more specific to breast cancer survivors).[11, 56]

A 2016 Cochrane review asked whether exercise during chemotherapy, radiotherapy or both helped to reduce treatment side effects. The review concluded that exercise during adjuvant treatment for breast cancer results in less fatigue, improved physical fitness and cancer site–specific quality of life, as well as cognitive function. The authors concluded that 'both aerobic and resistance exercise can be regarded as beneficial for individuals with adjuvant therapy-related side effects'.[57]

Physical activity enhances anti-cancer therapy drug tolerance

Another important clinical benefit of physical activity during anti-cancer therapy is the potential to improve treatment tolerance. If physical activity can help manage debilitating adverse effects of anti-cancer therapy, patients may be more likely to comply with treatment.

In a 2007 randomised controlled trial of over 250 breast cancer patients undergoing chemotherapy, treatment completion rates were significantly better among patients who engaged in resistance training, compared to usual care.[58]

A more recent randomised controlled trial of 230 patients undergoing adjuvant chemotherapy for breast cancer found that moderate- to high-intensity exercise during chemotherapy has a beneficial effect on cardiorespiratory fitness, muscle strength, fatigue and chemotherapy completion rates, compared to low-intensity home-based exercise or usual care. Benefits were also found for symptom burden (e.g. nausea and vomiting, pain, constipation) and return to work.[59]

Physical activity promotes overall survival

Higher physical activity levels are associated with prolonged overall survival and extending disease-free intervals in patients with breast, colon and prostate cancer.[60]

In a landmark self-report study based on responses from the Nurses' Health Study, women with breast cancer who engaged in regular physical activity after diagnosis had prolonged overall survival and disease-free intervals, with the greatest benefits noted in women who performed 9–15 MET hours/week (equivalent to walking 3–5 hours/week). Even patients who walked more than 1 hour/week obtained a protective effect.[61]

Likewise, physical activity decreases colon cancer mortality.[62] However, compared to Page 305 breast cancer, higher levels of physical activity—at least 18 MET hours/week—may be required to see beneficial effects. A 2012 systematic review of six cohort studies concluded that physical activity in patients with colorectal cancer reduces colon cancer-specific and all-cause mortality, with some evidence of a dose–response relationship.[63]

A more recent (2017) systematic review that included data from nearly 70 000 cancer patients concluded that 'superior levels of exercise following a cancer diagnosis were associated with a 28–44% reduced risk of cancer-specific mortality, a 21–35% lower risk of cancer recurrence and a 25–48% decreased risk of all-cause mortality'.[60]

However, this evidence is from observational studies and does not prove cause and effect. In addition, it is unclear whether exercise is associated with improved disease outcomes in patients diagnosed with other types of cancer. There is insufficient evidence to determine whether the degree of protection varies according to cancer type, stage or treatment regimen. Knowledge is also lacking regarding the exercise dosage (think FITT principle—Chapter 4) that shows the most promise for improving disease outcomes.

Physical activity benefits patients with advanced cancer

Physical activity also has a role in the setting of advanced cancer—cancer that is unlikely to be cured by current cancer treatments, but can be managed such that people can live with cancer for several years. Patients inevitably suffer impaired physical function due to disease progression and the effects of anti-cancer therapy. A 2012 systematic review that examined 16 studies involving more than 500 patients with advanced cancer reported that aerobic exercise, group exercise or physical activity rehabilitation programs improved physical fitness and function and increased feelings of 'vitality'.[64]

Physical activity may also be helpful during palliative care for cancer patients, to help alleviate symptoms and increase their wellbeing. An exercise intervention for patients receiving palliative care has the potential to improve physical activity performance outcomes, including walking distance, sit-to-stand time and improvements in reach, as well as fatigue and emotional function.[65] Physical activity interventions in palliative care settings help bring a structure to everyday life and may also help patients increase their daily routine capabilities.[66]

CASE STUDY

Jarryd Roughead AFL—melanoma

He's given me the all-clear to get back into living normal life and getting back to doing things I want, which is playing footy and living my life.

Jarryd Roughead, a four-time premiership player for the Hawthorn Hawks in the Australian Football League (Fig. 20.6), was diagnosed with melanoma in 2015. The melanoma was found and removed from his lip in 2015 and Roughead missed two games of the regular season. However, in May 2016, he was diagnosed with a recurrence of melanoma, confirmed by biopsy after imaging revealed four small spots on his lung, and his football career was placed on hold indefinitely.

Roughead commenced a 12-month targeted immunotherapy program, in which he was prescribed a novel monoclonal antibody. Monoclonal antibodies are antibodies that are made by identical immune cells that are all clones of a unique parent cell. In cancer treatment, they bind only to cancer cell-specific antigens and induce an immune response against the target cancer cells, essentially boosting the body's immune response against the cancer.

After 8 months of immunotherapy, Roughead revealed that he had a complete response from the treatment, was cancer-free and had been cleared to return to playing football at the national level. At the beginning of the 2017 season, Roughead was appointed the new captain of Hawthorn and had PET scans every 3 weeks for ongoing monitoring.

Figure 20.6 Melanoma
SHUTTERSTOCK /AUSTRALIS PHOTOGRAPHY
Sources: references 83, 84, 85

Physical activity counselling for patients with cancer—how to do it

To successfully counsel the patient with cancer requires pre-exercise testing followed by exercise advice.

Pre-exercise testing for patients with cancer

Cancer and subsequent anti-cancer therapies create a variety of challenges for organs and bodily systems involved in performing physical activity. Each patient with cancer experiences different symptoms, complications and adverse effects from treatment, so clinicians should implement pre-exercising testing before providing written physical activity prescriptions and tailored programs to patients.

Before commencing pre-exercise testing, clinicians must be aware of a patient's medical history, including comorbidities and exercise contraindications, as well as understand the most common adverse effects associated with the patient's specific treatment.

The American College of Sports Medicine (ACSM) has developed guidelines for the pre-exercise testing of patients with cancer,[67] focusing on general as well as cancer site-specific recommendations for the medical assessment (Table 20.3).

Table 20.3 Pre-exercise medical assessments for patients with cancer[11]

Cancer site	Breast	Prostate	Colon	Adult haematologic (no HSCT)	Adult HSCT	Gynaecologic
General medical assessments recommended prior to exercise	Evaluate for peripheral neuropathies and musculoskeletal morbidities secondary to treatment, regardless of time since treatment. If there has been hormonal therapy or known metastatic disease of the bone, evaluate fracture risk and discern what is safe prior to starting exercise. Patients with known cardiac conditions require medical assessment. There is always a risk that bone metastases or cardiotoxicity secondary to cancer treatments will go undetected and so exercise professionals should consult with a patient's medical team to discern likelihood if deemed appropriate.					
Cancer site-specific medical assessments recommended prior to exercise	Evaluate for arm/shoulder morbidity	Evaluate muscle strength and wasting	Patients should be evaluated as having established consistent and proactive infection prevention behaviours, prior to engaging in exercise training more vigorous than a walking program.	None	None	Evaluate for lower extremity lymphoedema prior to vigorous aerobic exercise or resistance training. Patients with morbid obesity may require additional medical assessment.

HSCT: haematopoietic stem cell transplantation

SCHMITZ KH, COURNEYA KS, MATTHEWS C ET AL. AMERICAN COLLEGE OF SPORTS MEDICINE ROUNDTABLE ON EXERCISE GUIDELINES FOR CANCER SURVIVORS. MEDICINE & SCIENCE IN SPORTS & EXERCISE 2010;42(7):1409-26 © 2019 AMERICAN COLLEGE OF SPORTS MEDICINE HTTPS://JOURNALS.LWW.COM/ACSM-MSS

Once a patient has been medically cleared for exercise, standard exercise testing methods may be appropriate. Similar to patients without cancer, the ACSM underlines that no assessments are required in most cancer survivors to commence a program of light-intensity walking, progressive strength training or flexibility.[67]

Exercise prescription for patients with cancer

According to the ACSM, exercise is safe both during and after treatment for all types of cancer.[11] However, a single, precise FITT-based prescription (Chapter 4) is inappropriate given the diversity of the population affected by cancer (see Table 20.4).

Table 20.4 Exercise prescription for patients with cancer[67]

	Aerobic	Resistance	Flexibility
Frequency	3–5 days/week	2–3 days/week	≥ 2 days/week
Intensity	Moderate to vigorous	Start with low resistance (<30% of 1 repetition max.) and progress with smallest increments possible	Move through range of motion as tolerated
Time	75 min/week of vigorous intensity or 150 min/week of moderate intensity or an equivalent combination of the two	At least 1 set of 8–12 repetitions	10–30 s hold for static stretching
Type	Prolonged, rhythmic activity using large muscle groups (e.g. walking, cycling, swimming)	Free weights, resistance machines, weight-bearing functional tasks (e.g. sit-to-stand) targeting all major muscle groups	Stretching or range of motion exercises for all major muscle groups Address specific areas of joint or muscle restriction that may have resulted from treatment with steroids, radiation or surgery

AMERICAN COLLEGE OF SPORTS MEDICINE, ACSM'S GUIDELINES FOR EXERCISE TESTING AND PRESCRIPTION. TENTH ED, WOLTERS KLUWER, 2017, P. 305

The ACSM's FITT-based exercise prescription is based on limited literature.[67] Clinicians should identify that exercise recommendations will vary across the cancer continuum and at all times require individualisation to accommodate each patient.

A 2012 Cochrane review of 56 studies that included nearly 5000 participants concluded that moderate- or vigorous-intensity exercise during cancer treatment provided greater improvements than light exercise in quality of life, physical function, anxiety, fatigue and sleep disturbances.[68]

High-intensity activity versus low-intensity activity—what is the evidence?

There is increasing evidence highlighting the benefits of shorter bursts of high-intensity exercise for the general population, as discussed in Chapter 4. In recent years, there has also been a growing body of evidence that supports the inclusion of high-intensity physical activity as a viable component of cancer

rehabilitation.

Pilot studies have shown that women with early-stage breast cancer can perform high-intensity interval training (HIIT) safely.[69, 70]

In a 2018 randomised controlled trial, 182 Swedish women with breast cancer who planned to receive adjuvant chemotherapy were randomly allocated to perform either resistance training with concurrent HIIT (RT-HIIT) or concurrent moderate-intensity aerobic training and HIIT (AT-HIIT) twice a week for 16 weeks or receive 'usual care'.[71] The intervention groups commenced exercise training three days after the second chemotherapy session. The trial found that 16 weeks of RT-HIIT counteracts cancer-related fatigue and self-reported cognitive problems and reduces symptom burden. AT-HIIT improved patients' emotional functioning and self-reported pain. Both AT-HIIT and RT-HIIT showed benefits for the patients' quality of life.

However, more research is needed to understand how HIIT can be used in individuals with other cancer types or more advanced disease.

PRACTICE PEARL

A supervised, moderate- to high-intensity, combined resistance and aerobic exercise prescription may be appropriate for some patients with breast cancer undergoing adjuvant chemotherapy. A home-based, low-intensity physical activity prescription is a viable alternative for women who are unable or unwilling to follow a higher intensity program.[59]

Special considerations when prescribing exercise for cancer patients

The following summarises important considerations when prescribing exercise for cancer patients, as outlined in the ACSM's Guidelines for Exercise Testing and Prescription.[67]

- Compared to patients without cancer, slower progression may be needed. If progression leads to an increase in adverse symptoms or complications, any element of FITT can be reduced until tolerated.
- Patients with compromised immune function should avoid public gyms and swimming pools until their white blood cell counts return to safe levels.
- Heart rate may be less reliable for monitoring exercise intensity for cancer patients undergoing treatment. Instead, patients may be advised to follow perceived exertion to monitor intensity.[72]
- Patients with lymphoedema should wear a compression sleeve during resistance training.
- Several short bouts per day rather than a single bout to meet recommendations may be advised and better tolerated, especially during active treatment.
- Patients receiving chemotherapy or radiotherapy may suffer from debilitating fatigue that can restrict their ability to exercise. All patients should be advised to avoid physical inactivity whenever possible.
- Patients with bone metastases are at increased risk of fractures, so modifications to the exercise prescription will likely be required.
- Identify when exercising at home or in a medical setting is advisable, such as after a bone marrow transplant or when immunosuppressed for another reason.
- Patients undergoing radiation should avoid chlorine exposure (e.g. swimming pools) to irradiated skin.
- Patients with severe anaemia, a worsening condition or an active infection should not perform exercise immediately following surgery.

- The exercise prescription should anticipate that patients receiving chemotherapy may experience fluctuating symptoms during treatment cycles, so recommendations should be modified accordingly.

Putting exercise into practice in clinical oncology

When our daughter got her relapse, doctors suggested to enrol her in the program. We were told that the first studies just got published, showing that physical activity improves chemotherapy-induced neurological deficits as well as concentration. She has been taking part in PASTEC for two years. In the first year, it took place every Saturday and they did alternatively fine motor skills and endurance/strength training. Now, it is fortnightly and the main emphasis is on discovering new activities.[73]

Promotion of Therapeutic Sports Activity for Children with Cancer (PASTEC) is an out-of-hospital exercise training program for children with cancer, developed by the paediatric haematology-oncology unit of the Lausanne University Hospital and the Sport and Health Centre of the University Sports Centre of Dorigny, in Lausanne, Switzerland.

PASTEC offers children with cancer a weekly opportunity to participate in a range of sports and activities, as well as take part in local events such as local fun runs (Fig. 20.7). The goals of the program are:

- to evaluate the benefits of physical activity on improving the physical abilities and quality of life in children undergoing anti-cancer therapy

Figure 20.7 PASTEC offers children with cancer a weekly opportunity to participate in a range of sports and activities

SHUTTERSTOCK / LORIMER IMAGES

- to develop in-school support for teachers so that children with cancer can be reintegrated into the most normal school physical activity program possible.

For more information, see www2.unil.ch/css/pastec [French].

PHYSICAL ACTIVITY'S ROLE IN SURVIVORSHIP

A 'cancer survivor' is defined as a person who has been diagnosed with cancer, from the time of diagnosis through the remainder of his or her life.[74]

There has been an increase in the number of cancer survivors over the past several decades due to improvements in early detection of first malignancies and more effective treatments.[75] In 2014, the 5-year relative survival rate after cancer diagnosis for all cancers was about 70%— almost a 20% improvement compared to the previous two decades.[76] As more people are surviving cancer, more people are forced to suffer the enduring complications of the disease and its treatment.

Page 309

Physical activity is an attractive intervention that can alleviate many of the sequelae related to cancer and help patients return to the health status they had prior to diagnosis (Table 20.5). Just as at other points of the cancer continuum, regular physical activity is safe and should be integrated into a patient's management alongside conventional anti-cancer therapies.[77]

Table 20.5 Benefits of regular physical activity for cancer survivors

Associated with improvements in:	Associated with a lower risk of:
• weight management	• death and all-cause mortality
• cardiorespiratory fitness	• cancer recurrence
• muscular strength and endurance	• type 2 diabetes
• quality of life	• cardiovascular disease
• fatigue	
• psychosocial factors	

GARCIA DO, THOMSON CA. PHYSICAL ACTIVITY AND CANCER SURVIVORSHIP. NUTRITION IN CLINICAL PRACTICE 2014;29(6):768-79 © AMERICAN SOCIETY FOR PARENTERAL AND ENTERAL NUTRITION.78

Exercise prescription for cancer survivors

According to the ACSM guidelines,[67] overall recommendations for survivors of cancer are consistent with the physical activity guidelines for the general population—that is, to work up to 150 minutes of moderate-intensity aerobic physical activity throughout the week (Chapter 4).

Survivors who have completed therapy can gradually and incrementally increase exercise duration when tolerated and without exacerbation of symptoms.

PRACTICE PEARL

Cancer survivors should be advised to avoid sedentary behaviour and to return to normal daily activities as quickly as possible, as tolerated.

Cancer survivors often have specific rehabilitation needs related to chemotherapy, radiotherapy, surgery or the cancer itself. For example, lymph node dissection and or axillary radiation and clearance can lead to lymphoedema in breast cancer survivors, which can limit exercise ability and enjoyment. Chemotherapy can leave survivors with peripheral neuropathies, and the resulting pain and paraesthesia can likewise affect a patient's ability and desire to be active.

Clinicians should consider referral to a rehabilitation specialist (see box) for cancer survivors with complex rehabilitation needs.

Safety precautions and contraindications to physical activity for cancer survivors

Given the destructive nature of cancer and its treatment, specific precautions may be warranted for exercising survivors, especially while receiving cancer treatment (as outlined above under 'Special considerations when prescribing exercise for cancer patients'). That said, we also want to take care not to erect barriers to activity for survivors. A balanced approach that maximises both access to activity and safety should be sought. The issues that may be of particular safety concern include peripheral neuropathies or ataxia. Some safety precautions and contraindications to physical activity for cancer survivors after cancer treatment include the following:[79–82]

- Survivors who have completed a bone marrow transplant are advised to avoid public pools and gyms for one year after transplantation because of the risk of infection.
- Clinicians should beware of the potential risk for cardiotoxicity in patients who have received particular types of of chemotherapy or other cancer treatments.
- Survivors with peripheral neuropathies or ataxia should be advised to perform activity that does not require balance (e.g. stationary reclining bicycle rather than walking on a treadmill).
- Clinicians should beware of fracture risk in patients with known bone metastases or who have been treated with hormone or androgen deprivation therapy.

The multidisciplinary cancer rehabilitation team

- Oncologist
- Rehabilitation specialist (physiatrist)
- Physiotherapist
- Rehabilitation nurse

- Occupational therapist
- Lymphoedema therapist
- Recreational therapist
- Dietitian
- Social worker
- Mental health professionals
- Exercise professionals

CASE STUDY

Gabriele Grunewald, running—adenoid cystic carcinoma and papillary thyroid cancer

The mental boost I get from my daily run has become so important to me and is something I wish I could share with every cancer survivor.

Gabriele 'Gabe' Grunewald was an American professional middle-distance runner who finished fourth in the 2012 US Olympic Trials and won the USA Championship indoor 3000 metres in 2014. Her personal best in the 1500 metres of 4:01.48 made her the 11th fastest performer in US history.

In 2009, at age 22, Gabe was diagnosed with adenoid cystic carcinoma that manifested as a small tumour on her parotid gland. After surgical removal of the tumour, Gabe completed a 3-month course of radiotherapy and slowly started training again soon after. The following year, Gabe went on to have one of her best seasons ever, setting a school record and placing second at the National Collegiate Athletic Association championships in the 1500 metres.

However, in October 2010, Gabe's clinicians discovered papillary thyroid cancer during routine follow-up imaging for the initial adenoid cystic carcinoma. She promptly had a thyroidectomy and neck dissection to remove affected lymph nodes. In December 2011, Gabe finished her thyroid cancer protocol with radioactive iodine treatment. Returning to running, she went on to win her first national title, in 2014 in the 3000 metres at the US Indoor National Championships.

In August 2016, Gabe's husband noticed a firmness in her abdomen when hugging her. A CT scan revealed a large mass on her liver, which was confirmed as a metastatic recurrence of adenoid cystic carcinoma. Later that month, Gabe had a right hepatectomy to remove the cancer.

In March 2017, a follow-up CT scan revealed multiple small tumours in Gabe's liver. In June, she commenced chemotherapy and competed at the USA Outdoor Track & Field Championships (Fig. 20.8), before beginning an immunotherapy clinical trial in July and then radiotherapy in October.

In 2017, the hashtag #BraveLikeGabe was started on Twitter in support of Gabe and, in 2018, she founded the Brave Like Gabe Foundation, to share her story, connect with other patients, support rare cancer research and empower cancer survivors through physical activity.

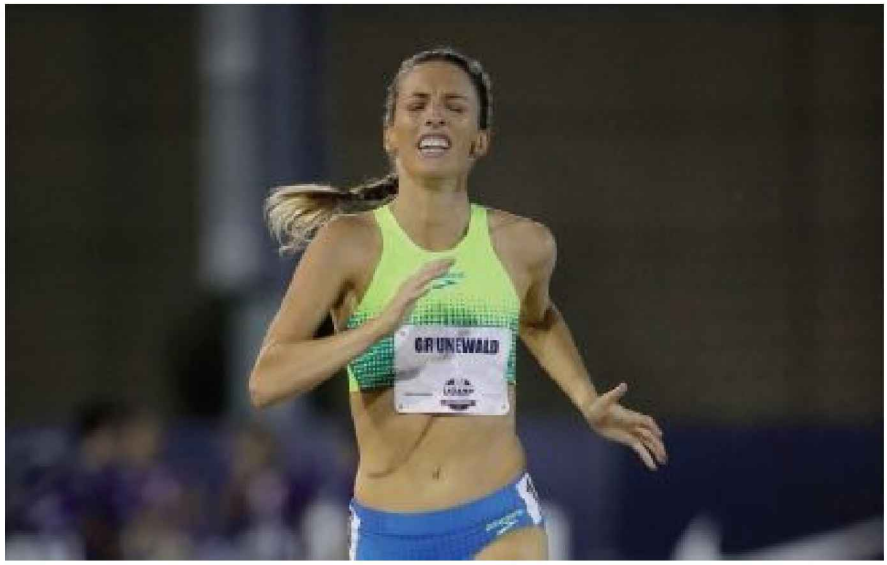


Figure 20.8 Gabe had over half her liver surgically removed in 2016. She returned to compete in the USATF 2017 Championships despite having ongoing therapy for her carcinoma
ANDY LYONS/GETTY IMAGES

Gabe's legacy

In 2018, while still undergoing immunotherapy Gabe set her sights on making the 2020 Olympics in Tokyo. Unfortunately, on June 11th, 2019 she passed away following a liver infection and further complications as a result of her condition.

Gabe leaves behind the legacy of someone who competed successfully at the highest level of her sport, despite seemingly insurmountable odds. Perhaps more importantly, she is the epitome of the word *brave* and should stand as an inspiration to those with cancer to continue to strive for their goals and fight on. For more information on her story and her Brave Like Gabe Foundation visit https://bravelikegabe.org.

REFERENCES

1. World Health Organization (WHO). Cancer—fact sheet 2018. Updated February 2018. Geneva, 2018. http://www.who.int/mediacentre/factsheets/fs297/en/.
2. American Cancer Society. Lifetime risk of developing or dying from cancer. Updated 23 March 2016. https://www.cancer.org/cancer/cancer-basics/lifetime-probability-of-developing-or-dying-from-cancer.html.
3. Sudhakar A. History of cancer, ancient and modern treatment methods. *J Cancer Sci*

Ther 2009; 1(2): 1–4.

4. 2018 Physical Activity Guidelines Advisory Committee Scientific Report. Washington, DC: US Department of Health and Human Services, 2018.
5. Moore SC, Lee IM, Weiderpass E et al. Association of leisure-time physical activity with risk of 26 types of cancer in 1.44 million adults. *JAMA Intern Med* 2016; 176(6): 816–25.
6. Vogelstein B, Kinzler KW. The multistep nature of cancer. *Trends Genet* 1993; 9(4): 138–41.
7. Hanahan D, Weinberg RA. The hallmarks of cancer. *Cell* 2000; 100(1): 57–70.
8. Hanahan D, Weinberg RA. Hallmarks of cancer: the next generation. *Cell* 2011; 144(5): 646–74.
9. Weinberg RA. *The biology of cancer*. 2nd ed. New York: Garland Science, 2013.
10. GBD 2015 Risk Factors Collaborators. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet* 2016; 388(10053): 1659–724.
11. Schmitz KH, Courneya KS, Matthews C et al. American College of Sports Medicine roundtable on exercise guidelines for cancer survivors. *Med Sci Sports Exerc* 2010; 42(7): 1409–26.
12. Scott AM, Allison JP, Wolchok JD. Monoclonal antibodies in cancer therapy. *Cancer Immun* 2012; 12: 14.
13. Geller DS, Gorlick R. Osteosarcoma: a review of diagnosis, management and treatment strategies. *Clin Adv Hematol Oncol* 2010; 8(10): 705–18.
14. Terry Fox Foundation. Terry's story. 2018. http://www.terryfox.org/terrys-story/.
15. Physical Activity Guidelines Advisory Committee. Physical Activity Guidelines Advisory Committee Report, 2008. Washington, DC: US Department of Health and Human Services, 2008.
16. Lynch BM, Neilson HK, Friedenreich CM. Physical activity and breast cancer prevention. *Recent Results Cancer Res* 2011; 186: 13–42.
17. Wu Y, Zhang D, Kang S. Physical activity and risk of breast cancer: a meta-analysis of prospective studies. *Breast Cancer Res Treat* 2013; 137(3): 869–82.
18. Neilson HK, Farris MS, Stone CR et al. Moderate-vigorous recreational physical activity and breast cancer risk, stratified by menopause status: a systematic review and meta-analysis. *Menopause* 2017; 24(3): 322–44.
19. Robsahm TE, Aagnes B, Hjartaker A et al. Body mass index, physical activity, and colorectal cancer by anatomical subsites: a systematic review and meta-analysis of cohort studies. *Eur J Cancer Prev* 2013; 22(6): 492–505.
20. Wolin KY, Yan Y, Colditz GA et al. Physical activity and colon cancer prevention: a meta-analysis. *Br J Cancer* 2009; 100(4): 611–16.

21. Shi Y, Li T, Wang Y et al. Household physical activity and cancer risk: a systematic review and dose–response meta-analysis of epidemiological studies. *Sci Rep* 2015; 5: 14901.
22. Gabriel BM, Zierath JR. The limits of exercise physiology: from performance to health. *Cell Metab* 2017; 25(5): 1000–11.
23. Thomas RJ, Kenfield SA, Jimenez A. Exercise-induced biochemical changes and their potential influence on cancer: a scientific review. *Br J Sports Med* 2017; 51(8): 640–4.
24. Neufer PD, Bamman MM, Muoio DM et al. Understanding the cellular and molecular mechanisms of physical activity-induced health benefits. *Cell Metab* 2015; 22(1): 4–11.
25. McTiernan A. Mechanisms linking physical activity with cancer. *Nat Rev Cancer* 2008; 8(3): 205–11.
26. Brown JC, Winters-Stone K, Lee A et al. Cancer, physical activity and exercise. *Compr Physiol* 2012; 2(4): 2775–809.
27. Yu H, Rohan T. Role of the insulin-like growth factor family in cancer development and progression. *J Natl Cancer Inst* 2000; 92(18): 1472–89.
28. Peyrat JP, Bonneterre J, Hecquet B et al. Plasma insulin-like growth factor-1 (IGF-1) concentrations in human breast cancer. *Eur J Cancer* 1993; 29A(4): 492–7.
29. Key TJ, Appleby PN, Reeves GK et al. Insulin-like growth factor 1 (IGF1), IGF binding protein 3 (IGFBP3) and breast cancer risk: pooled individual data analysis of 17 prospective studies. *Lancet Oncol* 2010; 11(6): 530–42.
30. Roddam AW, Allen NE, Appleby P et al. Insulin-like growth factors, their binding proteins and prostate cancer risk: analysis of individual patient data from 12 prospective studies. *Ann Intern Med* 2008; 149(7): 461–71, w83–8.
31. Thissen JP, Ketelslegers JM, Underwood LE. Nutritional regulation of the insulin-like growth factors. *Endocr Rev* 1994; 15(1): 80–101.
32. Qin LQ, He K, Xu JY. Milk consumption and circulating insulin-like growth factor-I level: a systematic literature review. *Int J Food Sci Nutr* 2009; 60 Suppl 7: 330–40.
33. Haydon AMM, MacInnis RJ, English DR et al. Effect of physical activity and body size on survival after diagnosis with colorectal cancer. *Gut* 2006; 55(1): 62–7.
34. Ligibel JA, Campbell N, Partridge A et al. Impact of a mixed strength and endurance exercise intervention on insulin levels in breast cancer survivors. *J Clin Oncol* 2008; 26(6): 907–12.
35. Hvid T, Winding K, Rinnov A et al. Endurance training improves insulin sensitivity and body composition in prostate cancer patients treated with androgen deprivation therapy. *Endocr Relat Cancer* 2013; 20(5): 621–32.
36. Ma J, Giovannucci E, Mucci L et al. Prediagnostic body-mass index, plasma C-peptide concentration, and prostate cancer-specific mortality in men with prostate cancer: a long-term survival analysis. *Lancet Oncol* 2008; 9(11): 1039–47.

37. De Pergola G, Silvestris F. Obesity as a major risk factor for cancer. *J Obes* 2013; 2013: 291546.
38. Schmidt S, Monk JM, Robinson LE et al. The integrative role of leptin, oestrogen and the insulin family in obesity-associated breast cancer: potential effects of exercise. *Obes Rev* 2015; 16(6): 473–87.
39. Booth A, Magnuson A, Fouts J et al. Adipose tissue, obesity and adipokines: role in cancer promotion. *Horm Mol Biol Clin Investig* 2015; 21(1): 57–74.
40. Simpson KA, Singh MA. Effects of exercise on adiponectin: a systematic review. *Obesity (Silver Spring)* 2008; 16(2): 241–56.
41. Restituto P, Colina I, Varo JJ et al. Adiponectin diminishes platelet aggregation and sCD40L release. Potential role in the metabolic syndrome. *Am J Physiol Endocrinol Metab* 2010; 298(5): E1072–7.
42. Gay LJ, Felding-Habermann B. Contribution of platelets to tumour metastasis. *Nat Rev Cancer* 2011; 11(2): 123–34.
43. Gupta-Elera G, Garrett AR, Robison RA et al. The role of oxidative stress in prostate cancer. *Eur J Cancer Prev* 2012; 21(2): 155–62.
44. Gomez-Cabrera MC, Domenech E, Vina J. Moderate exercise is an antioxidant: upregulation of antioxidant genes by training. *Free Radic Biol Med* 2008; 44(2): 126–31.
45. Kojda G, Hambrecht R. Molecular mechanisms of vascular adaptations to exercise. Physical activity as an effective antioxidant therapy? *Cardiovasc Res* 2005; 67(2): 187–97.
46. Radom-Aizik S, Zaldivar F, Haddad F et al. Impact of brief exercise on peripheral blood NK cell gene and microRNA expression in young adults. *J Appl Physiol (1985)* 2013; 114(5): 628–36.
47. Wang JS, Weng TP. Hypoxic exercise training promotes antitumour cytotoxicity of natural killer cells in young men. *Clin Sci (Lond)* 2011; 121(8): 343–53.
48. Monteiro R, Azevedo I. Chronic inflammation in obesity and the metabolic syndrome. *Mediators Inflamm* 2010; 2010: 289645.
49. Il'yasova D, Colbert LH, Harris TB et al. Circulating levels of inflammatory markers and cancer risk in the health aging and body composition cohort. *Cancer Epidemiol Biomarkers Prev* 2005; 14(10): 2413–18.
50. Hojman P. Exercise protects from cancer through regulation of immune function and inflammation. *Biochem Soc Trans* 2017; 45(4): 905–11.
51. Ntanasis-Stathopoulos J, Tzanninis JG, Philippou A et al. Epigenetic regulation on gene expression induced by physical exercise. *J Musculoskelet Neuronal Interact* 2013; 13(2): 133–46.
52. Arsenis NC, You T, Ogawa EF et al. Physical activity and telomere length: impact of aging and potential mechanisms of action. *Oncotarget* 2017; 8(27): 45008–19.

53. Ornish D, Lin J, Chan JM et al. Effect of comprehensive lifestyle changes on telomerase activity and telomere length in men with biopsy-proven low-risk prostate cancer: 5-year follow-up of a descriptive pilot study. *Lancet Oncol* 2013; 14(11): 1112–20.
54. Ness KK, Wall MM, Oakes JM et al. Physical performance limitations and participation restrictions among cancer survivors: a population-based study. *Ann Epidemiol* 2006; 16(3): 197–205.
55. Jones LW, Courneya KS, Mackey JR et al. Cardiopulmonary function and age-related decline across the breast cancer survivorship continuum. *J Clin Oncol* 2012; 30(20): 2530–7.
56. Ballard-Barbash R, George SM, Alfano CM et al. Physical activity across the cancer continuum. *Oncology (Williston Park)* 2013; 27(6): 589, 592.
57. Furmaniak AC, Menig M, Markes MH. Exercise for women receiving adjuvant therapy for breast cancer. *Cochrane Database Syst Rev* 2016; 9: CD005001.
58. Courneya KS, Segal RJ, Mackey JR et al. Effects of aerobic and resistance exercise in breast cancer patients receiving adjuvant chemotherapy: a multicenter randomized controlled trial. *J Clin Oncol* 2007; 25(28): 4396–404.
59. van Waart H, Stuiver MM, van Harten WH et al. Effect of low-intensity physical activity and moderate- to high-intensity physical exercise during adjuvant chemotherapy on physical fitness, fatigue and chemotherapy completion rates: results of the PACES randomized clinical trial. *J Clin Oncol* 2015; 33(17): 1918–27.
60. Cormie P, Zopf EM, Zhang X et al. The impact of exercise on cancer mortality, recurrence and treatment-related adverse effects. *Epidemiol Rev* 2017; 39(1): 71–92.
61. Holmes MD, Chen WY, Feskanich D et al. Physical activity and survival after breast cancer diagnosis. *JAMA* 2005; 293(20): 2479–86.
62. Denlinger CS, Engstrom PF. Colorectal cancer survivorship: movement matters. *Cancer Prev Res (Phila)* 2011; 4(4): 502–11.
63. Ballard-Barbash R, Friedenreich CM, Courneya KS et al. Physical activity, biomarkers and disease outcomes in cancer survivors: a systematic review. *J Natl Cancer Inst* 2012; 104(11): 815–40.
64. Albrecht TA, Taylor AG. Physical activity in patients with advanced-stage cancer: a systematic review of the literature. *Clin J Oncol Nurs* 2012; 16(3): 293–300.
65. Oldervoll LM, Loge JH, Paltiel H et al. The effect of a physical exercise program in palliative care: a phase II study. *J Pain Symptom Manage* 2006; 31(5): 421–30.
66. Gulde I, Oldervoll LM, Martin C. Palliative cancer patients' experience of physical activity. *J Palliat Care* 2011; 27(4): 296–302.
67. American College of Sports Medicine. ACSM's Guidelines for exercise testing and prescription. 10th ed. Philadelphia, PA: LWW, 2017.
68. Mishra SI, Scherer RW, Snyder C et al. Exercise interventions on health-related

quality of life for people with cancer during active treatment. *Cochrane Database Syst Rev* 2012 (8): CD008465.

69. Schulz SVW, Laszlo R, Otto S et al. Feasibility and effects of a combined adjuvant high-intensity interval/strength training in breast cancer patients: a single-center pilot study. *Disabil Rehabil* 2018; 40(13): 1501–8.
70. Schmitt J, Lindner N, Reuss-Borst M et al. A 3-week multimodal intervention involving high-intensity interval training in female cancer survivors: a randomized controlled trial. *Physiol Rep* 2016; 4(3): e12693.
71. Mijwel S, Backman M, Bolam KA et al. Highly favorable physiological responses to concurrent resistance and high-intensity interval training during chemotherapy: the OptiTrain breast cancer trial. *Breast Cancer Res Treat* 2018; 169(1): 93–103.
72. Scharhag-Rosenberger F, Kuehl R, Klassen O et al. Exercise training intensity prescription in breast cancer survivors: validity of current practice and specific recommendations. *J Cancer Surviv* 2015; 9(4): 612–19.
73. Cornevin A, Carrard J. Swiss Junior Doctors and Undergraduate Perspective on Sport and Exercise Medicine Blog Series. *BJSM* 2017. http://blogs.bmj.com/bjsm/2017/07/31/exercise-oncology-part-23-lets-put-practice/.
74. Centers for Disease Control and Prevention (CDC). Cancer survivors—United States, 2007. *MMWR Morb Mortal Wkly Rep* 2011; 60(9): 269–72.
75. McCabe MS, Bhatia S, Oeffinger KC et al. American Society of Clinical Oncology Statement: Achieving High-Quality Cancer Survivorship Care. *J Clin Oncol* 2013; 31(5): 631–40.
76. Siegel R, Ma J, Zou Z et al. Cancer statistics, 2014. *CA Cancer J Clin* 2014; 64(1): 9–29.
77. Fong DYT, Ho JWC, Hui BPH et al. Physical activity for cancer survivors: meta-analysis of randomised controlled trials. *BMJ* 2012; 344: e70.
78. Garcia DO, Thomson CA. Physical activity and cancer survivorship. *Nutr Clin Pract* 2014; 29(6): 768–79.
79. Doyle C, Kushi LH, Byers T et al. Nutrition and physical activity during and after cancer treatment: an American Cancer Society guide for informed choices. *CA Cancer J Clin* 2006; 56(6): 323–53.
80. Speck RM, Courneya KS, Masse LC et al. An update of controlled physical activity trials in cancer survivors: a systematic review and meta-analysis. *J Cancer Surviv* 2010; 4(2): 87–100.
81. Pinto BM, Ciccolo JT. Physical activity motivation and cancer survivorship. *Recent Results Cancer Res* 2011; 186: 367–87.
82. McTiernan A. Obesity and cancer: the risks, science and potential management strategies. *Oncology (Williston Park)* 2005; 19(7): 871–81; discussion 881–2, 885–6.
83. http://www.afl.com.au/news/2015-07-02/hawk-roughead-has-melanoma-removed-from-lip

84. “Roughead faces fight as cancer spreads”. heraldsun.com.au 17 May 2016.
85. “Roughead to start 12-month treatment”. hawthornfc.com.au

Chapter 21

Physical activity in the prevention and treatment of depression

with GUY FAULKNER, MARK DUNCAN and PAUL BLAZEY

It's like a weight is pressing down on you. There are days when you just can't get out of bed. You cannot face the world. You tell yourself simple things like: 'Just get to the kitchen and get a glass of water'. But not being able to do something so basic is frightening.

Ian Thorpe, Australian swimmer and five-time Olympic gold medallist

Depression is a prevalent and debilitating psychiatric disorder. Its early age of onset and persistence combine to create substantial premature morbidity and mortality.[1] Depression causes individual distress, functional, occupational and relationship impairment, reduced quality of life and societal economic cost.[2]

International prevalence of depression across lifetime and 1-year incidences for high-income countries are 14.6% and 5.5%, respectively. This compares to 11.1% and 5.9% in low- to middle-income countries.[3] Globally, more than 350 million people suffer from depression, and it is predicted that by 2030 it will be the leading cause of disease burden (Fig. 21.1).[4] The World Health Organization's (WHO) global burden of disease report highlighted mental disorders specifically as being the leading cause of lost healthy years of living for females aged 15–44 years.[4] Canadian studies have backed this finding, with the prevalence of major depressive disorder highest among females and younger age groups.[5]

Rank	2004 Disease or Injury	2030 Disease or I
1	Lower respiratory infections	Unipolar depressive di
2	Diarrhoeal diseases	Ischaemic heart dise
3	Unipolar depressive disorders	Road traffic accide
4	Ischaemic heart disease	Cerebrovascular dis
5	HIV/AIDS	COPD
6	Cerebrovascular disease	Lower respiratory infe
7	Prematurity and low birth weight	Hearing loss, adult o
8	Birth asphyxia and birth trauma	Refractive errors
9	Road traffic accidents	HIV/AIDS
10	Neonatal infections and other	Diabetes mellitus
13	COPD	11 Neonatal infections a
14	Refractive errors	12 Prematurity and low bi
15	Hearing loss, adult onset	15 Birth asphyxia and bir
19	Diabetes mellitus	18 Diarrhoeal disea

COPD = chronic obstructive pulmonary disease

Figure 21.1 Ten leading causes of burden of disease, world, 2004 and 2030
ADAPTED FROM WHO, (2008)[4]

FORMS OF DEPRESSION

Depression can be subdivided into several different forms, some of which are specific to certain populations, age groups and areas of the world (e.g. seasonal affective disorder, SAD). This chapter will focus on the two primary forms of depression outlined below.

Major or unipolar depression

Unipolar depression is characterised by symptoms which persist for most of the day, nearly every day for at least two weeks. These symptoms may interfere with the person's ability to work, sleep, study, eat or enjoy life. Episodes may be standalone and never reoccur, but more often, a person

will experience several episodes over their lifetime.[6]

Bipolar depression or dysthymia

Depressive symptoms that last for longer than two years are classified as bipolar. A person diagnosed with this form of depression may have episodes of major depression along with periods of less severe symptoms.

DIAGNOSIS

Depression is associated with a range of symptoms, including low energy, lack of interest, low self-worth, and sometimes overwhelming feelings of sadness and anxiety. The current classification of depression is based on the *Diagnostic and Statistical Manual of Mental Disorders,* 5th edition (DSM-5®, 2013; Table 21.1), or 'Recurrent depressive episodes' in the International Classification of Diseases, 10th revision (ICD-10), classification of mental and behavioural disorders.[7, 8]

Table 21.1 Criteria for major depressive episode taken from DSM-5[8]

An individual must be experiencing *five* (or more) of the following symptoms during the same 2-week period. Symptoms must represent a change from previous function. At least one of the symptoms should be either *depressed mood* or *loss of interest or pleasure.*

1. Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g. feels sad, empty, hopeless) or observation made by others (e.g. appears tearful). Note: In children and adolescents, can be irritable mood
2. Markedly diminished interest or pleasure in all or almost all activities most of the day, nearly every day (as indicated by either subjective account or observation)
3. Significant weight loss when not dieting or weight gain (e.g. a change of more than 5% of body weight in a month) or decrease or increase in appetite nearly every day. Note: In children, consider failure to make expected weight gains
4. Insomnia or hypersomnia nearly every day
5. Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down)
6. Fatigue or loss of energy nearly every day
7. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick)
8. Diminished ability to think or concentrate or indecisiveness, nearly every day (either by subjective account or as observed by others)
9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide

Note: Do not include symptoms that are clearly due to a general medical condition or mood-incongruent delusions or hallucinations.

A range of patient-rated and clinician-rated scales can be used for screening, diagnosis and monitoring depression outcomes. A common clinician-rated scale is the Hamilton Depression Rating Scale (HAM-D), while the Patient Health Questionnaire (PHQ-9) is a commonly used patient-rated scale.[9, 10] A quick two-question screen ('In the last month, have you been bothered by little interest or pleasure in doing things?' and 'In the last month, have you been feeling down, depressed or hopeless?') has been recommended as an effective and simple approach for screening in clinical practice.[2, 11]

MANAGEMENT

A common approach to treatment adopts a stepped care model.[12] In stepped care models, patients typically start with a low-intensity evidence-based treatment that might include education and what is termed 'self-management'—developing skills to manage depression and associated treatments, physical and psychosocial consequences and lifestyle modifications.

Progress is monitored systematically and those patients who do not respond adequately step up to a subsequent treatment of higher intensity. In many cases, this could include pharmacological treatments (selective serotonin reuptake inhibitors, SSRIs; tricyclic antidepressants, TCAs; monamine oxidase inhibitors, MAOIs) or psychological treatments (cognitive behavioural therapy, CBT; interpersonal therapy, IPT; and behavioural activation, BA)—both are recommended as first-line treatments of depression.[13, 14]

PRACTICE PEARL

Teammates, coaches, clubs and the media all need to have an understanding of the value of mental health and wellbeing, and its potential effects on performance.

PHYSICAL ACTIVITY AND DEPRESSION

Physical activity has an important role to play as a low-intensity evidence-based treatment that should be considered before initiating intensive therapeutic approaches or while awaiting further treatment.

The specific physiological mechanisms through which physical activity acts to both prevent and manage depression remain up for debate. It is thought the benefits of physical activity on mental health and depression are a combination of physiological, psychological, social, and neurological effects (Fig. 21.2).

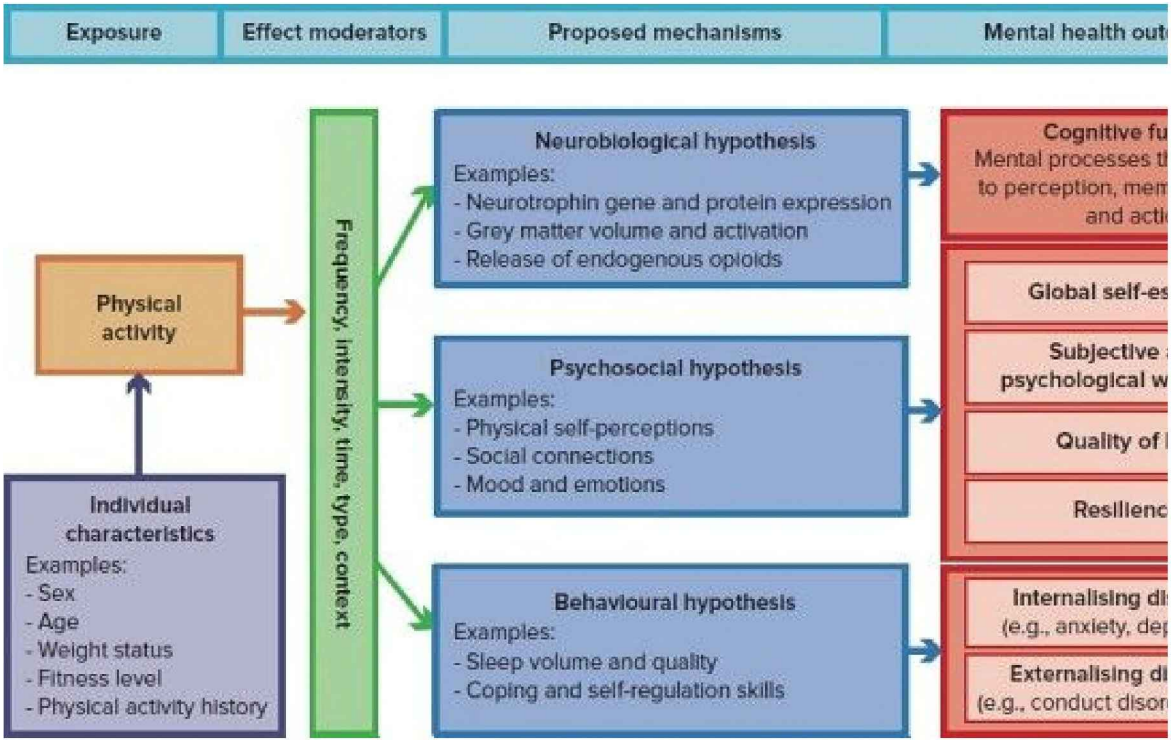


Figure 21.2 Proposed mechanisms by which physical activity benefits those with depression
REPRODUCED WITH PERMISSION FROM JOURNAL PEDIATRICS, 'PHYSICAL ACTIVITY FOR COGNITIVE AND MENTAL HEALTH IN YOUTH: A SYSTEMATIC REVIEW OF MECHANISMS', LUBANS D, RICHARDS J, HILLMAN C, ET AL., VOL. 138(3), COPYRIGHT © 2016 BY THE AAP

- *Physiological:* Physical activity boosts the production of endorphins and endocannabinoids, chemicals that support relaxation, the ability to feel pleasure, and reduce sensations of pain. The production of cortisol 'stress hormone' is reduced.
- *Psychological:* Regular physical activity increases feelings of self-esteem, self-efficacy and boosts self-worth.[15] Exercise may also disperse negative thoughts.
- *Social:* Regular face-to-face interaction (e.g. fitness classes and team sports) boosts mood and can help to prevent depression.
- *Neurological:* Physical activity helps your brain to use and produce more dopamine and serotonin – chemicals known to confer a positive frame of mind. Physical activity will boost blood flow to the brain, and has been shown to boost memory.[16]

Physical activity has demonstrated a therapeutic effect and should be offered to those suffering from mild to moderate depression or depressive symptoms.[17–19] Physical activity may also be offered in conjunction with psychological therapies to gain maximal therapeutic effect, although

the clinical effectiveness of this remains up for debate.[20]

We outline four clear reasons for clinicians to consider physical activity prescription for those suffering from depression:

1. *Physical activity can be a cost-effective alternative for those who prefer not to use medication or who cannot access therapy.* Antidepressants offer both short- and long-term benefit for some individuals. However, important problems remain, such as delayed therapeutic onset, limited efficacy in milder depression and the existence of treatment-resistant depression.[21] Additionally, adherence remains low, in part because of patient concerns about adverse effects or in a sports setting issues related to performance, doping and the risk of stigmatisation.[8, 22] Psychological counselling treatment, such as cognitive behavioural therapy, can be costly and difficult to access. In Canada for example, publicly funded CBT remains limited and in most care settings is only available to those with private health insurance, or who can afford to pay themselves.[23]

Page 314

Have mental health concerns achieved parity of esteem with - physical.injury?

There is a great appetite to address mental health issues within sport and things are improving, but the support for athletes is nowhere near adequate. I believe that football and sport in general can lead the way.—Clarke Carlisle, footballer and Mind ambassador[24]

In some sports it has been suggested that showing mental illness is a sign of lacking the competitive fortitude required. This has caused many athletes to conceal their mental health battles, but fortunately this has started to change, with long-term efforts by health agencies and governments to change the public and sporting perception of mental health.[8]

Unfortunately, media reports still exist of players engaging in on-field abuse, mocking those who have gone public about their battle with depressive illness.[25] This follows a 2017 case of an Australian rules footballer being mocked by a journalist on social media.[26]

The question remains whether clinicians and sporting organisations truly create the ideal environment for athletes to be open with teammates, coaches and healthcare staff.

Physical activity can be self-sustaining, in turn improving the potential of the individual to self-manage and enhance their internal locus of control over their condition. Pharmacological and psychotherapeutic treatments, usually have a specified endpoint with relapse risks associated to withdrawal.

2. *Physical activity is associated with negligible deleterious adverse effects.* In contrast, common adverse events associated with antidepressant medication include headache, nausea, agitation, sedation, sexual dysfunction, diminished mental acuity and memory, weight gain and metabolic abnormalities.[27]

3. *Physical activity is an effective method for improving important aspects of physical health.* Individuals with depression have elevated mortality compared to the general population.[28] Cardiovascular and metabolic disease are major contributing factors to premature mortality and morbidity. In turn, individuals with depression engage in significantly less physical activity and demonstrate higher sedentary behaviour than healthy controls.[29] The promotion of physical activity should be incorporated into mental health care for this reason alone. However, the promotion of physical activity and exercise for mental health should be seen as a 'win–win' situation with physical and potentially mental health benefits accruing.[30]
4. *Physical activity follows current evidence-based practice.* There is now evidence that exercise works in clinical trials. The antidepressant effects observed post physical activity are similar to those of psychological treatments and antidepressant medication.

Physical activity—a preventive role?

Thirty studies examined the relationship between physical activity and depression. Twenty-five found a significant, inverse relationship between baseline physical activity and follow-up depression. This suggests that physical activity prevents the onset of depression.[31]

A clear dose–response relationship between physical activity and reduced depression was not readily apparent. However, there was evidence that any level of physical activity, including low levels, can prevent future depression.[32] Further, everyday activities such as walking appear to confer a benefit. Meeting the recommended levels of physical activity, established for physical health benefits, appear equally appropriate for preventing depression. Study data suggests that individuals who are currently active should sustain their physical activity habits and those who are inactive should initiate a physically active lifestyle.

Page 315

Depression among athletes

Depression is prevalent among elite athletes, who were once perceived to be superheroes immune to mental weakness. High-profile athlete suicides related to major depressive episodes have included Robert Enke (soccer) and Rick Rypien (ice-hockey). Incidents such as these have raised the awareness of mental health concerns among athletes, prompting increased media coverage. Hypothesised causes for depression in athletes currently include:

- the pressures of modern-day professional sport, including external expectations
- shortened careers due to injury or lengthy periods on the sidelines
- loss of self-identity at retirement
- overtraining.[36–38]

There is also the question of whether playing collision sports and suffering chronic traumatic encephalopathy (CTE) may augment the risk of depression.[39] Hart et al. (2013)[40] observed that ageing or experienced US National Football League (NFL) players showed an increased risk of depressive symptoms compared to the general population and had evidence of changes to their cerebral grey

matter.

Many top athletes are now speaking about their experiences of managing mental health concerns but reports are likely to underestimate the prevalence because of the social stigma attached to all mental illness. This perhaps explains why many athletes report problems towards the end of their career or after retirement when risks may be perceived as lower.

The clinician involved in supporting an athlete at the elite level is ideally positioned to identify athletes who may not admit to their depression, and to address concerns raised by athletes under their care. Clinicians can help to address mental health concerns by asking questions (see Chapter 22 for advice on how to raise the issue with athletes) and supporting the promotion of lifelong mental wellbeing as well as physical health.

Three systematic reviews focused on the protective effect of cardiorespiratory fitness (CRF)—mostly running or walking interventions—on depression.[33–35] All reviews concluded that an inverse relationship existed between CRF and depressive symptoms. Individuals with low CRF and medium CRF demonstrate an increased risk of developing depression compared with their more active peers. Physical activity can also provide a stimulus to engage in outdoor activities. The affects of low sunlight exposure in people living further from the equator leading to Seasonal Affective Disorder (SAD) are well documented. Although a discussion on the effects of sunlight and the consequent vitamin D production in individuals is beyond the scope of this chapter, it should not be neglected as an important variable in the prevention of altered mental health.

PRACTICE PEARL

Patients should be advised that even small amounts of physical activity can confer a benefit to their mental health and wellbeing.

Efficacy of using physical activity to treat depression

Meta analyses have consistently demonstrated the beneficial effects of physical activity compared to no intervention.[41–44]

A Cochrane review identified 39 randomised controlled trials (RCTs), and a meta-analysis of these studies showed a moderate effect size for exercise versus no treatment control conditions.[18] Over the long-term, if physical activity is discontinued the beneficial effects diminish. Therefore, it is important to consider how patients can be supported to maintain their activity through support networks or social groups and found no significant difference. Four trials (n = 300) compared exercise with pharmacological treatment and found no significant difference. The conclusion from this would be that physical activity is at least equal to psychological therapy or pharmacological treatments for treatment effect but, as previously mentioned, has fewer adverse effects. Physical activity when compared to psychological therapy and pharmacological treatment is equally effective.[18]

Physical activity has less documented side-effects. Therefore primary strategies for managing

depression should focus on the facilitation of physical activity in patients.

In perhaps the strongest trial to date, the effects of aerobic exercise were compared to the administration of sertraline therapy among 156 older adults with depression.[45] Participants were randomised to either aerobic exercise (three times per week at 70–85% of their heart rate reserve), sertraline (an SSRI antidepressant), or combined sertraline and exercise for 16 weeks. After 16 weeks of treatment, patients in all three groups exhibited significant reductions in depressive symptoms. Ten months after the study commenced, remitted participants (those who no longer met diagnostic criteria for depression) in the exercise group had significantly lower relapse rates than participants in the medication group.[44] Notably, patients who continued to exercise over the 6-month follow-up period following the intervention were 50% less likely to relapse.

PRACTICE PEARL

For physical activity interventions to be successful they need to be maintained over the long term.

Overall, exercise appears to be as effective in the short term as psychological or pharmacological therapies and is *another* evidence-based option for patients and treatment providers to consider. In Canada, exercise is now recommended as a first-line monotherapy for mild to moderate depression and as a second-line adjunctive treatment for moderate to severe depression.[45]

Exercise prescription—what is the dose?

Thirty minutes of supervised aerobic exercise performed 3 days per week for at least 8 weeks is effective for reducing depressive symptoms.[46-50]

Very few studies have examined strength training or combinations of aerobic and strength training. At present no advantage has been observed when comparing aerobic to strength-based activity. Resistance-based training is known to produce a significant reduction in depressive symptoms amongst the elderly.[51, 52] In addition, resistance training improves sleep quality, which concurrently may reduce symptoms of both depression and anxiety.[53, 54]

Given no evidence of harm, a sound recommendation is to engage in muscle and bone strengthening activities using major muscle groups at least twice a week. Such a recommendation is in line with common international guidelines for physical activity.

Interventions that are structured and supervised demonstrate stronger antidepressant effects, while dropout is minimised in interventions delivered by team members with specific training in exercise prescription.[55, 56]

A pragmatic concern for clinicians is the question of whether structures exist for referring individuals with depression to supervised exercise programs that include physical activity counselling by qualified practitioners. Where these are in place the practical exercise prescriptions

presented in Table 21.2 may be appropriate. To help prevent relapse, patients should be encouraged to continue with their exercise routines beyond the 9-week prescription or once symptoms have subsided.

Table 21.2 Practical exercise prescription example

Type of training	Time	Intensity	Frequency
Supervised aerobic exercise 8–9 weeks (e.g. cycling, gym class etc.)	30 min to 1 hr	Moderate	3–5 times per week
Muscle and bone strengthening activities using major muscle groups (may include gym-based lifting or other resistance exercise)	Dependent on session but may include round of 6 weighted exercises or could be class-based for up to 1 hr	Moderate	2–3 times per week

Caution is needed in being overly prescriptive about the exercise dosage for depression. The best dose is likely to be the one that is enjoyable and sustainable. Encouraging and supporting individuals with depression to 'move more and sit less', irrespective of exercise prescription, is likely a sound approach to start with for many patients. Individually tailoring the exercise dose to suit the patient's preferences and circumstances is critical, as will be structuring the exercise experience to promote feelings of competence, control and companionship.[57] Reflecting the symptomatology of depression, 'low mood', 'lack of energy' and 'being too tired' are particularly salient barriers to engaging in all activities.[58] Employing a range of behaviour change techniques targeting these emotional barriers will probably be needed for some patients to reduce negative emotions, develop opportunities for self-assessment of the affective consequences of exercise and provide emotional support.[59]

Developing psychological skills for managing exercise behaviour may assist patients in long-term adherence to their exercise routine even after achieving symptom remission or once formal support is no longer available. For further reading on facilitating patient physical activity as a long-term self-management technique, refer to Chapter 5 and the discussion on behaviour change.

Interactions of exercise with drug therapy

Little research has been done to evaluate the interactions between medications and exercise therapy.[60] Both acute responses to exercise and chronic adaptations may alter the pharmacokinetics of medications. For example, blood flow to the liver is altered during acute bouts of exercise, and body composition is altered due to chronic exercise. In turn, these changes may influence drug pharmacokinetics (i.e. absorption, distribution, metabolism and excretion).[60] Monoamine oxidase inhibitors and atypical antidepressants that target the norepinephrine system (as opposed to serotonin as the primary target) combined with exercise increase the amount of brain-derived neurotrophic factor (BDNF) expression. BDNF is a

neurochemical that may play a role in the anti-depressive effects of both medications and exercise.[61, 62]

Figure 21.3 At present no advantage has been observed when comparing aerobic to strength-based activity in the treatment of depression. The prescribed exercise experience should promote feelings of competence, control and companionship

There appears to be little difference in adverse events between exercise conditions and usual care controls or medication, where reported.[18] For example, when Blumenthal et al. (1999) compared combined sertraline and exercise to sertraline alone, both groups had an equal number of dropouts due to adverse events suggesting that the combination did not confer any additional risk over medication alone.[45] In fact, adding exercise to antidepressant treatment may have an additive effect. When followed up at 10 months, the same trial observed higher rates of ongoing remission in the combined treatment arm than in those managed with medication alone. Continued exercise behaviour after the trial finished, positively predicted remission status.[46]

In sum, there is little evidence demonstrating that exercise interferes with antidepressant medication. It remains more likely that adverse effects from medication, such as insomnia, sleepiness, weight gain and headaches, may serve as additional barriers to motivating patients to become or remain active.

Contraindications to exercise

As with other clinical populations, pre-screening for comorbid conditions is necessary. Tools such as the Physical Activity Readiness Questionnaire for Everyone (PAR-Q+) are simple to administer

and can be used to confirm that a patient is physically able to exercise without additional precautions.

Figure 21.4 Adding exercise to antidepressant treatment may have an additive effect
DOLGACHOV/123RF

PSYCHOLOGICAL THERAPIES

Many studies have evaluated the benefits of concurrent psychological therapies alongside exercise. Although it remains beyond the scope of this chapter to consider the specific application of this intervention in detail. Psychological therapies such as cognitive behavioural therapy (CBT) should be considered as stand alone or complimentary treatments for those with depressive symptoms. CBT has proven an effective therapy for depression in controlled trials, with or without physical activity as an adjunct therapy.[64] Chapter 22 further discusses the use of CBT in the management of mental health disorders.

PHARMACOLOGICAL MANAGEMENT

A detailed discussion of the pharmacological management of depression is beyond the scope of this chapter. However, where both physical activity and psychological therapies have failed to address concerns, medication remains an option. Medication for the treatment of all psychiatric disorders has gone through revolutionary change in the last three decades, and discovery of new drugs with fewer adverse effects occurs every year. A recent study suggests medications prescribed to the athlete or physically active patient differ from those offered to the general population.[65]

Since there is inherent benefit and risk to using medication, one must proceed to pharmacotherapy in the sporting arena with an air of caution. It is important to understand that

the potential negative impact of medication on athletic performance may dissuade an athlete from using this treatment modality. The sports medicine clinician must remember that medication alone is not a universal cure and is often more successful in conjunction with another therapy, such as physical activity or CBT. Clinicians must also be aware of the prohibited substance list and possible performance-enhancing effects of drugs when prescribing to elite athletes.

PRACTICE PEARL

Patients suffering from depressive symptoms who have failed to respond to physical activity interventions or CBT, or who have severe symptoms such as psychosis, should be referred for specialist psychological assessment and support.

SUMMARY

Depression is about to become the leading cause of lost healthy years of life, Physical activity is an effective management strategy in the prevention and rehabilitation of depression but is not a panacea. All health professionals should be aware of the benefits of prescribing physical activity and develop strategies to support patients with depression to remain active.

- Depression is just as likely to affect competitive athletes as the general population, and at times of high stress (e.g. competition, injury, retirement) may do so in numbers that exceed those observed in the general population.
- Physical activity is an important component of any treatment plan for a person suffering from depression, but the titration and type of activity may need to be adjusted, especially in elite athletes who already exceed physical activity guidelines.
- More novel strategies that alter the external pressures by allowing time away from competition or support the athlete to maintain fitness without sticking to the same activities may be an option.
- Generally, a lack of physical activity appears to contribute to the development of depression or may be the result of a depressive episode.
- It is important that clinicians have an understanding of how physical activity can support the long-term management of depression, promoting heightened self-efficacy and self-management strategies.

REFERENCES

1. Kessler RC. The costs of depression. *Psychiatr Clin North Am* 2012; 35(1): 1–14.
2. Lam RW, McIntosh D, Wang J et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 Clinical Guidelines for the Management of Adults with Major Depressive Disorder: section 1. disease burden and principles of care. *Can J Psychiatry* 2016; 61(9): 510–23.

3. Kessler RC, Bromet EJ. The epidemiology of depression across cultures. *Annu Rev Public Health* 2013; 34: 119–38.
4. Mathers C, Fat D, Boerma J. The Global Burden of Disease: 2004 Update. World Health Organization (WHO), Geneva, 2008.
5. Patten SB, Williams JV, Lavorato DH et al. Descriptive epidemiology of major depressive disorder in Canada in 2012. *Can J Psychiatry* 2015; 60(1): 23–30.
6. National Institute of Mental Health (NIMH). Depression Basics. In: NIH Publication No. TR 16-3561. Revised. 2016. https://www.nimh.nih.gov/health/publications/depression/depressionbasics-508-01112017_150043.pdf.
7. World Health Organization (WHO). The ICD-10 classification of mental and behavioural disorders: diagnostic criteria for research. Geneva, Switzerland: WHO, 1992.
8. American Psychiatric Association (APA). *Diagnostic and statistical manual of mental disorders (DSM-5®)*. 5th ed. Arlington, VA: APA, 2013.
9. Hamilton M. A rating scale for depression. *J Neurol Neurosurg Psychiatry* 1960; 23: 56–62.
10. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med* 2001; 16: 606–13.
11. Bosanquet K, Bailey D, Gilbody S et al. Diagnostic accuracy of the Whooley questions for the identification of depression: a diagnostic meta-analysis. *BMJ Open* published online 9 December 2015. doi: 10.1136/bmjopen-2015-008913.
12. Firth N, Barkham M, Kellett S. The clinical effectiveness of stepped care systems for depression in working age adults: a systematic review. *J Affect Disord* 2015; 170: 119–30.
13. Kennedy SH, McIntyre RS, Blier P et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 Clinical Guidelines for the Management of Adults with Major Depressive Disorder: section 3. pharmacological treatments. *Can J Psychiatry* 2016; 61(9): 540–60.
14. Parikh SV, Quilty LC, Ravitz P et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 Clinical Guidelines for the Management of Adults with Major Depressive Disorder: section 2. psychological treatments. *Can J Psychiatry* 2016; 61(9): 524–39.
15. Lubans D, Richards J, Hillman C et al. Physical activity for cognitive and mental health in youth: a systematic review of mechanisms. *Pediatrics* 2016; 138(3): e20161642.
16. Loprinzi, P.D., Frith, E., Edwards, M.K. et al. The Effects of Exercise on Memory Function Among Young to Middle-Aged Adults: Systematic Review and Recommendations for Future Research. *American Journal of Health Promotion*. 2018. 32(3), 691–704. https://doi.org/10.1177/0890117117737409

17. Phillips C. Physical activity modulates common neuroplasticity substrates in major depressive and bipolar disorder. *Neural Plast* 2017; 2017: 7014146.
18. Cooney G, Dwan K, Greig C et al. Exercise for depression. *Cochrane Database Syst Rev* 2013 (9): CD004366.
19. Rimer J, Dwan K, Lawlor DA et al. Exercise for depression. *Cochrane Database Syst Rev* 2012(7):CD004366. doi: 10.1002/14651858.CD004366.pub5.
20. Sukhato K, Lotrakul M, Dellow A et al. Efficacy of home-based non-pharmacological interventions for treating depression: a systematic review and network meta-analysis of randomised controlled trials. *BMJ Open* 2017; 7(7): e014499.
21. Penn E, Tracy DK. The drugs don't work? Antidepressants and the current and future pharmacological management of depression. *Ther Adv Psychopharmacol* 2012; 2: 179–88.
22. Hunot VM, Horne R, Leese MN et al. A cohort study of adherence to antidepressants in primary care: the influence of antidepressant concerns and treatment preferences. *Prim Care Companion J Clin Psychiatry* 2007; 9: 91–9.
23. Payne KA, Myhr G. Increasing access to cognitive-behavioural therapy (CBT) for the treatment of mental illness in Canada: a research framework and call for action. *Healthc Policy* 2010; 5(3): e173–85.
24. Mind. Performance matters: mental health in elite sport, 2018. https://www.mind.org.uk/media/1085139/Mental-Health-and-Elite-Sport.pdf.
25. BBC News. Players taunted footballer over depression. 2 February 2018. https://www.bbc.com/news/uk-scotland-42901550.
26. Smith S. Australian sports reporter mocked player's mental health in tweet. Imediaethics. 6 June 2017. https://www.imediaethics.org/australian-soccer-reporter-mocked-players-mental-health-tweet-apologizes/, accessed 15 February 2018.
27. Anderson HD, Pace WD, Libby AM et al. Rates of 5 common antidepressant side effects among new adult and adolescent cases of depression: a retrospective US claims study. *Clin Ther* 2012; 34(1): 113–3.
28. Walker ER, McGee RE, Druss BG. Mortality in mental disorders and global disease burden implications: a systematic review and meta-analysis. *JAMA Psychiatry* 2015; 72(4): 334–41.
29. Schuch FB, Vancampfort D, Firth J et al. Physical activity and sedentary behavior in people with major depressive disorder: a systematic review and meta-analysis. *J Affect Disord* 2017; 210: 139–50.
30. Mutrie N, Faulkner G. Physical activity: positive psychology in motion. In: Linley PA, Joseph S, eds. *Positive Psychology in Practice*. John Wiley & Sons, 2012. doi: 10.1002/9780470939338.ch9.
31. Mammen G, Faulkner G. Physical activity and the prevention of depression: a systematic review of prospective studies. *Am J Prev Med* 2013; 45(5): 649–57.

32. Hamer M, Stamatakis E, Steptoe A. Dose–response relationship between physical activity and mental health: the Scottish Health Survey. *Br J Sports Med* 2009; 43(14): 1111–14.
33. Baumeister SE, Leitzmann MF, Bahls M et al. Associations of leisure-time and occupational physical activity and cardiorespiratory fitness with incident and recurrent major depressive disorder, depressive symptoms, and incident anxiety in a general population. *J Clin Psychiatry* 2017; 78(1): e41–7.
34. Schuch FB, Vancampfort D, Sui X et al. Are lower levels of cardiorespiratory fitness associated with incident depression? A systematic review of prospective cohort studies. *Prev Med* 2016; 93: 159–65.
35. Papasavvas T, Bonow RO, Alhashemi M et al. Depression symptom severity and cardiorespiratory fitness in healthy and depressed adults: a systematic review and meta-analysis. *Sports Med* 2016; 46(2): 219–30.
36. Rice SM, Purcell R, de Silva S et al. The mental health of elite athletes: a narrative systematic review. *Sports Med* 2016; 46(9): 1333–53.
37. Bauman NJ. The stigma of mental health in athletes: are mental toughness and mental health seen as contradictory in elite sport? *Br J Sports Med* 2016; 50(3): 135–6.
38. Wolanin A, Gross M, Hong E. Depression in athletes: prevalence and risk factors. *Curr Sports Med Rep* 2015; 14(1): 56–60.
39. Kontos AP, Deitrick JM, Reynolds E. Mental health implications and consequences following sport-related concussion. *Br J Sports Med* 2016; 50(3): 139–40.
40. Hart J, Jr., Kraut MA, Womack KB et al. Neuroimaging of cognitive dysfunction and depression in aging retired National Football League players: a cross-sectional study. *JAMA Neurol* 2013; 70(3): 326–35.
41. Kvam S, Kleppe CL, Nordus IH et al. Exercise as a treatment for depression: a meta-analysis. *J Affect Disord* 2016; 202: 67–86.
42. Danielsson L, Noras AM, Waern M et al. Exercise in the treatment of major depression: a systematic review grading the quality of evidence. *Physiother Theory Pract* 2013; 29(8): 573–85.
43. Josefsson T, Lindwall M, Archer T. Physical exercise intervention in depressive disorders: meta-analysis and systematic review. *Scand J Med Sci Sports* 2014; 24(2): 259–72.
44. Silveira H, Moraes H, Oliveira N et al. Physical exercise and clinically depressed patients: a systematic review and meta-analysis. *Neuropsychobiology* 2013; 67(2): 61–8.
45. Blumenthal JA, Babyak M, Moore KA et al. Effects of exercise training on older patients with major depression. *Arch Intern Med* 1999; 159(19): 2349–56.
46. Babyak M, Blumenthal JA, Herman S et al. Exercise treatment for major depression: maintenance of therapeutic benefit at 10 months. *Psychosom Med* 2000; 62(5): 633–8.

47. Ravindran AV, Balneaves LG, Faulkner G et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 Clinical Guidelines for the Management of Adults with Major Depressive Disorder: section 5. complementary and alternative medicine treatments. *Can J Psychiatry* 2016; 61(9): 576–87.
48. Perraton LG, Kumar S, Machotka Z. Exercise parameters in the treatment of clinical depression: a systematic review of randomized controlled trials. *J Eval Clin Pract* 2010; 16(3): 597–604.
49. Stanton R, Reaburn P. Exercise and the treatment of depression: a review of the exercise program variables. *J Sci Med Sport* 2014; 17(2): 177–82.
50. Nyström M, Neely G, Hassmén P et al. Treating major depression with physical activity: a systematic overview with recommendations. *Cogn Behav Ther* 2015; 44(4): 341–52.
51. Singh NA, Clements KM, Fiatarone MA. A randomized controlled trial of progressive resistance training in depressed elders. *J Gerontol A Biol Sci Med Sci* 1997; 52(1): M27–35.
52. Singh NA, Stavrinos TM, Scarbek Y et al. A randomized controlled trial of high versus low intensity weight training versus general practitioner care for clinical depression in older adults. *J Gerontol A Biol Sci Med Sci* 2005; 60(6): 768–76.
53. Kovacevic A, Mavros Y, Heisz JJ et al. The effect of resistance exercise on sleep: a systematic review of randomized controlled trials. *Sleep Med Rev* 2018; 39: 52–68. doi: 10.1016/j.smrv.2017.07.002.
54. Alley JR, Mazzochi JW, Smith CJ et al. Effects of resistance exercise timing on sleep architecture and nocturnal blood pressure. *J Strength Cond Res* 2015; 29(5): 1378–85. d oi: 10.1519/jsc.0000000000000750.
55. Stubbs B, Vancampfort D, Rosenbaum S et al. Dropout from exercise randomized controlled trials among people with depression: a meta-analysis and meta regression. *J Affect Disord* 2016; 190: 457–66.
56. Chalder M, Wiles NJ, Campbell J et al. Facilitated physical activity as a treatment for depressed adults: randomised controlled trial. *BMJ* 2012; 344: e2758.
57. Deci EL, Eghrari H, Patrick BC et al. Facilitating internalization: the self-determination theory perspective. *J Pers* 1994; 62(1): 119–42.
58. Glowacki K, Duncan M, Gainforth H et al. Barriers and facilitators to physical activity and exercise among adults with depression: a scoping review. *Ment Health Phys Act* 2017; 13: 108–19.
59. Cane J, Richardson M, Johnston M et al. From lists of behaviour change techniques (BCTs) to structured hierarchies: comparison of two methods of developing a hierarchy of BCTs. *Br J Health Psychol* 2015; 20: 130–50.
60. McLaughlin M, Jacobs I. Exercise is medicine, but does it interfere with medicine? *Exerc Sport Sci Rev* 2017; 45: 127–35.

61. Russo-Neustadt AA, Alejandre H, Garcia C et al. Hippocampal brain-derived neurotrophic factor expression following treatment with reboxetine, citalopram, and physical exercise. *Neuropsychopharmacology* 2004; 29: 2189–99.
62. Russo-Neustadt AA, Ha T, Ramirez R et al. Physical activity–antidepressant treatment combination: impact on brain-derived neurotrophic factor and behavior in an animal model. *Behav Brain Res* 2001; 120: 87–95.
63. McRae D. Ian Thorpe: 'I was surrounded by people but had this intense loneliness'. *The Guardian* 13 November 2012. https://www.theguardian.com/sport/2012/nov/12/ian-thorpe-swimming-depression.
64. Bernard P, Romain A-J, Caudroit J et al. Cognitive behavior therapy combined with exercise for adults with chronic diseases: systematic review and meta-analysis. *Health Psychol* 2018; 37(5): 433–50.
65. Reardon CL, Creado S. Psychiatric medication preferences of sports psychiatrists. *Phys Sportsmed* 2016; 44(4): 397–402.

Chapter 22

Anxiety disorders

with SAUL MARKS and PAUL BLAZEY

When I let my enormous chimp out, I start thinking like a pessimist. I have a tremendous sense of foreboding, wondering about the what ifs, about crashes and mistakes.

Chris Hoy, six-time Olympic track cycling gold medallist, in a 2009 BBC interview

High-level sporting competition comes with high levels of pressure for athletes and their support staff. Anxiety in athletes carries both performance enhancing benefits and the potential to see athletes 'choke' under the pressure of the big race or event. It has affected top athletes across the whole spectrum of sport, from David Beckham (soccer—obsessive compulsive disorder) to Missy Franklin (Olympic gold medal swimmer—panic attacks).

Direct financial incentives and sponsorship deals, the media obsession with winners and losers, peer and family pressure, and a host of other social pressures all come together in modern-day sport at the top level. Sporting organisations often portray the ability to deal with this pressure as part of displaying the mental toughness required to compete, and this can predispose athletes, especially those yet to establish themselves, to say they are coping.[1] This may internalise concerns and lead to mental health disorders such as anxiety and depression (Chapter 21). These can also manifest in physical forms such as conditions affecting the gastrointestinal, respiratory or cardiovascular systems (Chapters 10–12).

This chapter discusses the range of anxiety disorders most often seen in both recreational and elite athletes. We outline the principles of clinical management for athletes suffering from anxiety disorders.

EPIDEMIOLOGY

The Anxiety and Depression Association of America (ADAA) states that as of 2018 anxiety disorders are the most common mental health complaint affecting US citizens, with 18.1% of the population

affected each year.[2] Risk factors can include, but are not limited to, genetic predisposition, brain chemical imbalance, life events and personality. More specific to athletes, there is an inherent risk that participating in elite sport can predispose them to factors or situations that may negatively impact upon their mental health (Table 22.1).

Table 22.1 Elite sport participation risks contributing to possible mental health concerns

Elite sport participation risks		
Poor performance or perceived poor performance by the athlete	Family or relationship issues	Immunological suppression and infection
Mental burnout	Concussion	Gastrointestinal symptoms
Conflicts with coaches or teammates	Lack of playing time	Increased incidence of allergies
Overtraining	Gambling/alcohol abuse	Iron deficiency
Changes in importance of sport, expectations of self/parents, role of sport in life	Debilitating injury or illness, resulting in surgery or loss of playing time	Violence—being assaulted, a victim of domestic violence, automobile accident, or merely witnessing a personal injury or assault on a family member, friend or teammate
School or work issues due to increased time demands	Increased risk for sudden cardiac death	Eating disorders, or significant dieting or weight loss

ADAPTED FROM HUGHES AND LEAVEY (2012),[3] AND NCAA (2013)[4]

The risk of athletes suffering from anxiety has been identified in studies across all sports. One Australian study showed up to 46.4% of athletes having symptoms of a mental health disorder. This figure is consistent with findings from other countries.[5, 6] Furthermore, it has been demonstrated that if those involved in high-level competition have feelings of career dissatisfaction they are prone to showing signs of anxiety or mental distress. These were present in 26.8% of one sample of UK athletes.[6] Further risks were identified in systematic reviews for those approaching or in retirement and those suffering from an injury which had forced a reduction in participation.[7]

Anxiety disorders often arise from a maladaptive response to stress. Harnessing the stressors that come with striving for peak physical performance can result in Olympic gold medals and world championship-winning performances (Fig. 22.1).

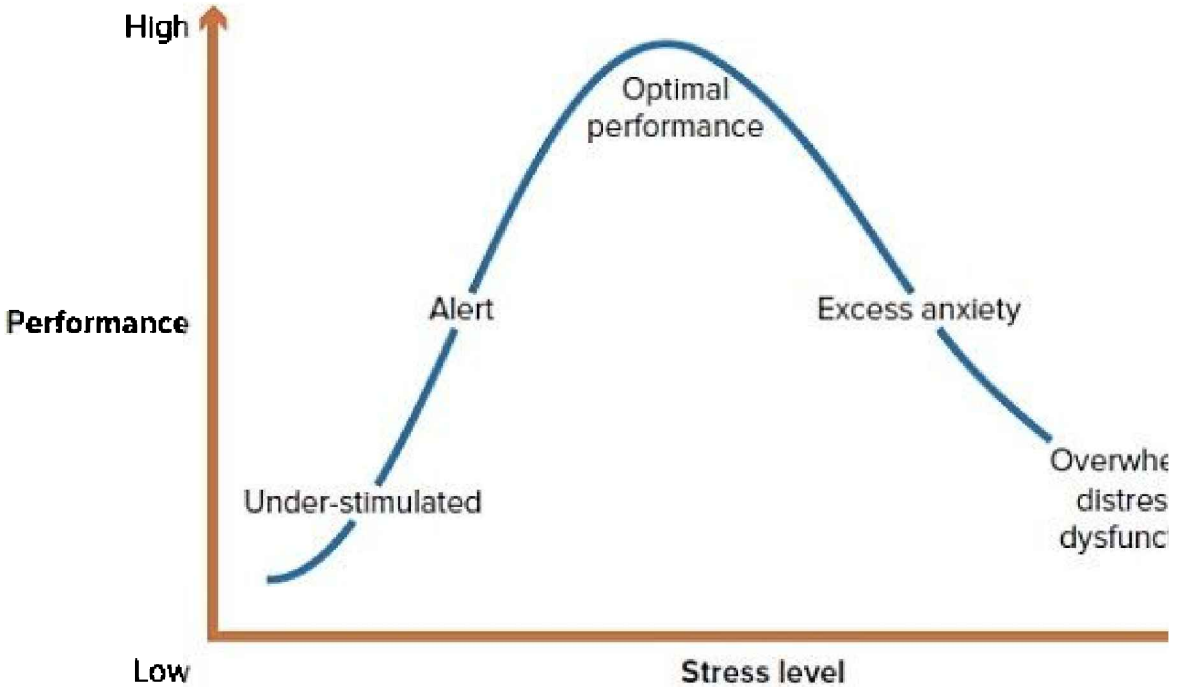


Figure 22.1 Adaptation of the Yerkes–Dodson curve for stress and performance. The shape of the blue curve is characteristic of each person. Some may perform well at a wide range of stress levels (with a flatter top to their response curve). The winning athlete is able to adapt to the constantly changing stress level that is an inherent part of sport; obtaining a blue line in the above graph that approaches almost flat and horizontal is the sign of a psychologically well-adapted athlete. Some, however, need support to prevent anxiety and self-doubt, even at moderate stress levels. Anxiety in moderation is likely to enhance performance by increasing alertness; the relationship between anxiety and performance follows a similar shape to the blue line[8]

The risk for anxiety disorders and other mental health concerns in athletes who fade away from the limelight either not having met their own (internal) or others (external e.g. family, fans, agents) expectations is high and provides the multidisciplinary medical team with a challenge to both identify and manage individuals appropriately (see box). This can prove especially complicated outside elite athletics, where often a sole physician may be expected to identify symptoms and support the athlete without an extended team. In this situation it is important that the clinician is aware of signs and symptoms of anxiety disorders, to support early diagnosis and prevention or treatment. When unsure of the diagnosis, referral to a psychiatrist for assistance, ideally a sports psychiatrist or a psychiatrist with experience of athletes may be necessary. Common signs and symptoms of an anxiety disorder are shown in Table 22.2.

Page 320

Table 22.2 Signs and symptoms of anxiety disorder

Page 321

Signs and symptoms		
Changes to sleeping patterns	Legal issues or fighting, problems with authority	Sweating
Feeling apprehensive or powerless	Negative self-talk	Feeling weak or tired
Having a sense of impending danger, panic or doom	Frequent complaints of injuries, illness or fatigue	Withdrawal from social contact
Breathing rapidly	Sudden weight loss	Problems concentrating, focusing or remembering
Trembling	Loss of interest in previously enjoyable activities	Gambling, alcohol or substance abuse
Irritability and mood swings	Increased heart rate at rest	Feeling out of control

ADAPTED FROM NATIONAL INSTITUTE OF MENTAL HEALTH, (2016)[9]

Note: The signs and symptoms above, such as sweating and apprehension, may be observed in normal pre-competition athletes, but it is specifically when these symptoms begin to impact performance or when multiple symptoms present that further investigation is warranted.

PRACTICE PEARL

Awareness of the signs and symptoms of anxiety and changes in the behaviour of those you support is crucial to supporting and managing anxiety disorders.

THE ANXIETY DISORDERS

As signs and symptoms alone cannot be relied upon to diagnose an individual, it is important to know the anxiety disorders commonly observed in all individuals to help guide further discussion. Athletes are not unique—anxiety disorders may present similarly in all populations. Table 22.2 has a list of the common signs and symptoms. The presence of any singular sign or symptom does not constitute diagnosis, and as illustrated in Figure 22.1, a degree of anxiety is useful to performance.

Generalised anxiety disorder

Generalised anxiety disorder (GAD) is defined as having suffered from chronic (>6 months), heighted sense of tension or worry above that which is considered normal. Most sufferers have a negative expectation on the outcome of events and may tend to worry excessively about money, health, family or work. They are often unable to relax and often suffer from insomnia. Sometimes the source of the worry is more specific to their sporting pursuits, and the rigours of training can be a triggering factor.

Generalised anxiety disorder can present with physical symptoms such as fatigue, insomnia or difficulty sleeping, muscle tension, headaches, irritability and poor concentration. There may also be associated autonomic changes leading to the athlete feeling lightheaded or breathless and symptoms such as urinary frequency.

Panic disorder or panic attack

Panic disorder, as defined by the Canadian Psychological Association (2014), is marked by repeated

attacks of panic that occur unexpectedly in the absence of any situational threat.[10] These attacks build to a peak rapidly (usually in 10 minutes or less) and are often accompanied by a sense of imminent danger or impending death and an urge to escape. They leave the individual emotionally drained, frightened, feeling vulnerable and anxious about their health. The person will often avoid situations or events that may predispose them to recurrent attacks.

Obsessive compulsive disorder or obsessional neurosis

For many athletes, the highly repetitive and regimented nature of training and eating can contribute to the development of obsessive compulsive disorder (OCD). Daily routines and repetition to achieve mastery are part of many sporting environments. Superstitions and rituals are extremely common in the world of sport, with small, short and infrequent rituals being a functional way of reducing anxiety. However, if ritualistic behaviours increase, they can incapacitate the athlete, both in and outside the sporting environment.

Obsessive compulsive disorder or obsessional neurosis is characterised by compulsive actions and/or obsessive thoughts. Common compulsions at home may include excessive cleaning and repeated checking of doors, with sufferers unable to ignore their intrusive thoughts. Sport-specific examples include the bouncing of the ball before a serve in tennis (observed in high-level players such as Rafael Nadal) and baulking (stopping) at the end of the board when attempting to land a perfect hurdle while diving (possibly due to negative feelings about one's ability to perform the dive). Both provide examples of a player being unable to begin their movement or performance due to psychological interference. Other common examples of thoughts that impede actions include fears such as:

- losing the competition
- not performing to the expected level
- sustaining injury or illness
- harming others in the process of participation
- not meeting external expectations.

Post-traumatic stress disorder

The athletes' history may help to guide a post-traumatic stress disorder (PTSD) diagnosis. Much like those involved in traumatic events outside of sporting competition, some athletes will be involved in accidents, such as suffering a major injury during a skiing event or requiring surgery following an injury suffered on the field of play. The traumatic memory may lead to the development of PTSD, The fear of participating in the same or similar future events may lead to significant reductions in the ability to perform at the previous level (e.g. speed or intensity). Symptoms of PTSD can include flashbacks and nightmares of the event, as well as avoidance and hypervigilance.

Agoraphobia, social anxiety and simple phobia

Agoraphobia (fear of public areas or open spaces) or social phobias have the potential to arise as secondary to other mental health concerns such as depression. Following a panic attack an athlete

may display signs of social phobia, especially around competitive environments. This is often the result of the fear of appearing inadequate in comparison to those around them. This corresponds with other social phobias characterised by a fear of making a fool of oneself.[11]

Debilitating performance anxiety

Often seen as a subset of social anxiety but of particular concern among athletes is performance anxiety. It is most often observed among people who are expected to demonstrate great skill or convey authority while under the public eye. It is defined by Powell (2004) as 'strong but delimited fears that severely compromise an individual's capacity to execute a task at a level that could be reasonably expected, which is crucial to that person's normal adjustment'.[12] This has been known to affect people across many differing backgrounds, from sports and theatre, to politicians and statesmen. In sports where the recovery from physical injury can significantly alter performance, the effects of performance anxiety have been documented to delay the rate of recovery.[13, 14] The differences between social phobia and debilitating performance anxiety can be seen in Table 22.3.

Table 22.3 Distinguishing debilitating performance anxiety from two other social phobia subtypes: a clinical model

	Social phobia	Non-generalised/specific social phobia	Debilitating performance anxiety
Overall impairment	More pervasive	Less pervasive	Limited
Focus of fears	Most interactions with others	One or few interactions with others	Limited to specific performance situations
Expectations of self	Low	Moderate	High
Fear of scrutiny by others	Primary	Primary	Secondary
Anticipatory anxiety	High	High	Variable
Commitment to feared task	Avoidant	Ambivalent	Committed

ADAPTED FROM POWELL, (2004)[12]

NEED TO KNOW

Resources and advice on managing conditions and supporting athletes with anxiety disorders are available from the Association of Applied Sports Psychology. A link is provided at the end of the chapter.

PRACTICE PEARL

In clinical consultations it may be useful to discuss potential performance anxiety, to support the identification of management strategies.

CLINICAL PRACTICE AND MANAGEMENT

There are no proven diagnostic tests for anxiety disorder, with attempts to elucidate a specific biomarker ongoing.[15] Where an athlete expresses thoughts of suicide they should *always* be referred for further assessment by a qualified mental health practitioner. An athlete or patient presenting in mental health crisis can be supported by following the core principles outlined in Table 22.4.

Table 22.4 Principles for responding to someone in a mental health crisis

Core elements in responding to mental health crises:
1. Provide timely access to supports and services.
2. Provide services in the *least restrictive* manner.
3. Ensure peer support is available.
4. Spend adequate time with the individual in crisis.
5. Consider the context of the individual's overall plan of services when providing emergency interventions.
6. Ensure that individuals with appropriate training and demonstrable competence to evaluate and effectively intervene with the prob
7. Ensure that individuals in a self-defined crisis are not turned away.
8. Ensure that interveners have a comprehensive understanding of the crisis.
9. Help the individual to regain a sense of control.
10. Attend to issues of culture, gender, race, age, sexual orientation, health literacy and communication needs of the individual being s
11. Respect individual rights.
12. Ensure services are trauma-informed.
13. Note recurring crises and consider whether they signal problems in assessment or care.
14. Take meaningful measures to reduce the likelihood of future emergencies.

ADAPTED FROM GUIDANCE OF THE US CENTER FOR MENTAL HEALTH SERVICES (2009)[16]

All those involved with supporting athletes have a role in identifying when anxiety may be affecting an individual beyond what is considered the individuals baseline level. The US National Collegiate Athletic Association (NCAA) has produced a guide for athletes, coaches and college staff to support the identification of mental health concerns in individuals and facilitate an understanding of what can be done to support athletes (see resources at end of the chapter).[17] Table 22.5 outlines some of the barriers to seeking help as well as facilitators. Those involved with supporting teams are encouraged to foster an environment that promotes open discussion of mental health with a goal of achieving improved wellbeing as well as sporting performance.

Table 22.5 Barriers and facilitators to seeking help. The list is ranked from most common (top) to least common (bottom)

Page 324

Barriers	Facilitators

• Stigma	• Education and awareness of mental health issues and/or services
• Lack of problem awareness	• Social support
• Difficulty in or not willing to express emotion	• Encouragement from others
• Lack of time	• Accessibility (e.g, money, transport, location)
• Denial of problem	• Positive relationship with service staff
• Not sure who to ask for help	• Confidentiality
• Fear of what might happen	• Time
• Worried about affecting ability to play / train	• Integration into everyday life
• Belief that it would not help	• Positive past experiences
• Not accessible	• Ease of expressing emotion and openness

ADAPTED FROM PUTUKIAN, (2016)[18]

CASE STUDY

Ricky Williams, NFL—social anxiety disorder

Following therapy I was able to start acting like the real Ricky Williams again.

Ricky Williams (Fig. 22.2) is a retired NFL running back, who primarily played for the Miami Dolphins in a career spanning 12 seasons. He was considered aloof by teammates and the media and was known for conducting post-game interviews still in his helmet and shaded visors. He was often unable to look those with whom he was talking in the eye and was initially described as being excessively shy. In a later interview, reproduced for the Anxiety and Depression Association of America, he described difficulties leaving the house outside of training or game days and concerns over meeting fans in the street. In his own words:

I felt extremely isolated from my friends and family because I couldn't explain to them what I was feeling. I had no idea what was wrong with me.

Following the advice of friends, Williams eventually sought help and was diagnosed with social anxiety disorder. He reported feeling like a weight was lifted from his shoulders. He was able to begin a program combining medication and cognitive behavioural therapy that addressed his social inhibition. He also utilised yoga, which provided both an exercise outlet and the benefits of practising mindfulness to control his anxiety.

Sources: references 41, 42, 43, 44

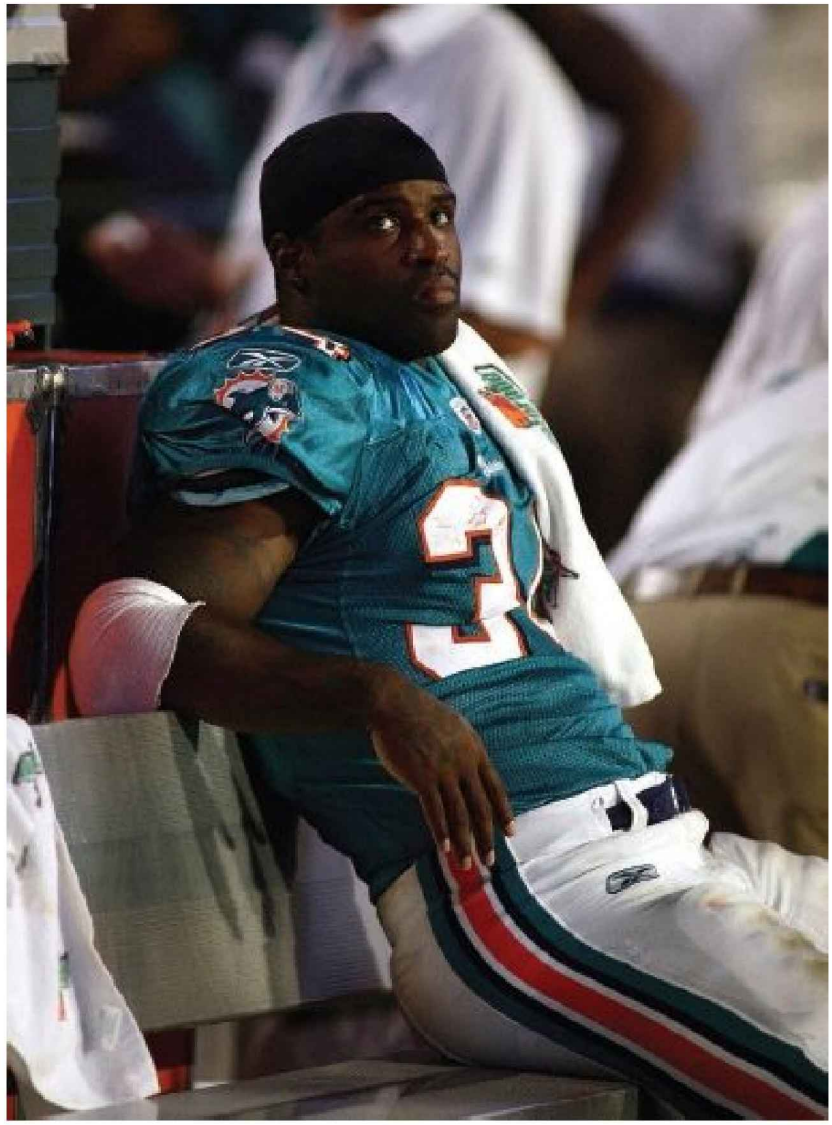


Figure 22.2 Ricky Williams, pictured while still playing for the Miami Dolphins, now speaks regularly about his anxiety and alternative coping strategies, including the use of marijuana
MARC SEROTA/GETTY IMAGES

For clinicians managing anxiety disorders it is important to identify maladaptive behaviours and to address any identified barriers. It may be necessary to facilitate access to the appropriate care (i.e. referral to psychiatric services).

Screening

Screening for anxiety disorders requires the use of questionnaires such as the state trait anxiety inventory (STAI) or the Beck anxiety inventory (BAI). Both require the athlete to self-report on their current thoughts and feelings. The athlete is scored on a Likert scale, to assess the level of anxiety they are experiencing. The BAI is the recommended tool of the NCAA, in its guide to managing the mental health of athletes; however, there has been some criticism that this index does not sufficiently differentiate anxiety from depression.[19]

The competitive environment is likely to exacerbate any underlying anxiety in an athlete. Internal and external pressures may culminate following years of training for a single event. One suggested potential tool for evaluating the level of pre-competition anxiety in athletes has been the measurement of heart rate variability (HRV). Those with a high HRV prior to competition have been shown to experience larger autonomic system changes due to increased levels of anxiety. Measurement of HRV may support the identification of those suffering abnormal levels of pre-competition anxiety. Management strategies can then be formulated to support athletes during competition.[20]

Approaching an athlete about a potential mental health and wellbeing concern

It is often difficult to approach an athlete suspected of suffering from an undiagnosed anxiety disorder. Athletes may fear stigmatisation from others following a formal diagnosis of a mental health disorder. To elicit a positive response from the individual and to ensure that the full spectrum of the disorder can be examined, it may be necessary to utilise open questions such as:[4]

- How are things going for you?
- Tell me, what is going on?
- Your behaviour (identify specific behaviour in question) has made me concerned for you. Can you tell me what is going on, or is there something I need to understand or know about why this incident happened?

It has been highlighted that one of the key pillars to successful management includes the cultivation of a supportive training environment that fosters mental wellbeing and resilience.[19] This includes the necessity for coaches and other team members to develop an open-minded and non-judgmental milieu, with cross-cultural understanding of the entire group embracing people from diverse backgrounds. In fact, support, empathy and passive listening, from family, friends, coaches, teammates, the multidisciplinary team or a therapist, is the first and least intrusive way to start treating any mental health challenge.

PRACTICE PEARL

In the event of a panic attack presenting with chest pain, a cardiac event or other medical problem should first be ruled out before attempting to calm the athlete. A panic attack is a diagnosis of exclusion.

Retirement and mental health disorders

You know, athletes die two times. It's true. Once your career is over, you've got to recreate yourself in a way that other people just don't have to.

This quote, from former Australian national-level basketballer Lauren Jackson, was delivered in a 2017 interview for the Australian ABC network, as part of a documentary focusing on athlete mental health. She poignantly describes a loss or 'death' of her sense of self, and her apprehension and fear of recreating or regenerating a new, productive and worthy direction in her life. It is now well established that retirement is one of the key risk points for athletes who develop a mental health condition. Regardless of whether athletes leave the sport due to injury, burnout, reduced performance due to age, or a combination, this period is a key milestone in an athletic career. This does not have to be confined to those in elite sport, who may suffer this landmark at an earlier age. It can also affect those who have to consider stopping their previous recreational activities or modifying them.

Many former athletes report not being ready for the change in routines or the lack of a routine that they were used to when training daily. Libby Trickett, Olympic swimmer, another interviewed in the documentary, said:

I had nothing outside of swimming. I tried to create something outside of swimming, so I was doing university, but it wasn't necessarily a passion.

Anxiety over coming to the end of one's career with declining performance and potentially the loss of lucrative contracts is a real concern.

Members of the medical team and those involved in general practice have a duty of care to their athletes to support them through this period with appropriate advice and referrals. Support for those in the professional ranks may be available through professional associations, but the availability of specialists is not consistent across all sports. Extra consideration may need to be given to those outside the professional environment who lack an extended support team. Physicians should develop a network and professional dialogue with local or regional mental health services, so that they are able to provide support and guidance in an appropriate manner.

PRACTICE PEARL

Retirement is a key transition phase for all athletes at risk of mental health disorders, including anxiety. Physicians should engage with athletes early to discuss potential post-career plans and identify potential anxiety concerns.

Physical activity as a management strategy for mental health

In recent years more emphasis has been given to regular physical activity in the maintenance of good mental health. The American Psychological Association (2018) highlights physical activity as an important tool for teaching individuals to manage anxiety, suggesting that exercise that stresses the bodily systems in manageable doses builds both physical and mental resilience.[21]

Overall exercise has been identified as a positive tool for the management of mental health

conditions, especially in the young, where excessive screen time has become a cause for concern in the development of mental illness.[22] As discussed in Chapter 21, it has been shown that exercise can act as a protective mechanism against mental illness, especially depression but also anxiety disorders.[11, 23] A systematic review found that exercise was an important part of therapy, alongside medication and cognitive behavioural therapy, and provided a significant reduction in anxiety compared with control subjects.[24] Jayakody et al. (2013) added that both forms of physical activity (aerobic and anaerobic) were beneficial adjuncts to the treatment of anxiety disorders.[25]

It is acknowledged that in practice those suffering from anxiety may struggle to engage with exercise therapy. Referral to a specialist team for regular follow-up may be necessary to prevent high dropout rates.[26]

The ADAA (2018) and the Association for Applied Sports Psychology (2006) recommend that for those suffering from anxiety disorders, exercise can help to manage their problems. In line with this they recommend adherence to general exercise guidelines for all populations utilising exercise for health, for example:[2, 27]

- 5 × 30: jog, walk, cycle or dance 3–5 times a week for 30 minutes.
- Set small daily goals and aim for daily consistency rather than perfect workouts. It is better to walk every day for 15–20 minutes than to wait until the weekend for a 3-hour fitness marathon. Frequency is most important.
- Find forms of exercise that are fun or enjoyable. Extroverted people often prefer class or group activities. Introverts may prefer solo pursuits.
- Distract yourself with audiobooks, podcasts or music played on a mobile device. Many people find it is more fun to exercise while listening to something they enjoy.
- Recruit an exercise buddy. It is often easier to stick to your exercise routine when you commit to exercise with a friend, partner or colleague.
- Be patient when you start a new exercise program. Most sedentary people require 4–8 weeks to feel coordinated and sufficiently in shape so that exercise feels easier.

Page 326

PRACTICE PEARL

When recommending that someone suffering from anxiety disorder takes up physical activity, it is important to warn them that their symptoms may initially increase in the new activity before improving.

The elite athlete's level of exercise often far exceeds these recommendations, and it often requires specialist support of a qualified mental health practitioner to identify the risks of continued participation versus some time away from training. If participation in an exercise regime is deemed safe, then it should be continued with the necessary support and advice outlined

above (e.g. in conjunction with cognitive behavioural therapy). Facilitating a supportive environment, is key to successful treatment.

Cognitive behavioural therapy

Cognitive behavioural therapy (CBT) is a well-established therapy for anxiety disorders. The UK National Institute for Health and Care Excellence guidelines (2005) for managing OCD and body dysmorphic disorder advise the use of combined CBT and selective serotonin reuptake inhibitors (SSRIs) for adults.[28] Due to the risk of adverse effects from SSRIs, children are recommended to be offered CBT alone, with pharmacological management (e.g. sertraline) initiated if no response is observed at 12 weeks. CBT is effective in managing episodes of depressive illness and generalised anxiety disorder.[29, 30] CBT that includes exposure to potentially negative stimuli in a controlled environment can achieve positive results.[31–33] It was found that group-delivered CBT combined with exercise was particularly helpful for managing social phobias.[25] Motivational interviewing techniques have been suggested as an adjunct to enhance the effectiveness of CBT.[34]

Multimodal positive mental imagery is an effective technique to support the reduction of pre-competition anxiety in athletes.[35]

Cognitive behavioural therapy alongside physical activity is considered a first-line therapy in motivated individuals who do not wish to proceed with pharmacological management. Adverse effects and performance detriments are a significant consideration before prescribing medication for anxiety. The team dealing with an athlete suffering from anxiety disorder, should understand CBT and know when to refer appropriately to a sports psychiatrist or other qualified CBT practitioner.

Although it is beyond the scope of this chapter to discuss CBT in its entirety, one of the central concepts utilised focuses on the concept ‘mind over mood’. Self-awareness of thoughts and feelings in a specific situation, can support a transition from rigid negative thinking to positive thoughts, changing behavioural and emotional outcomes. This concept is alluded to by Dr Steve Peters, who is credited with supporting the performances of Team GB’s gold-medal-winning cyclists. One idea concerns taming one’s own ‘monkey mind’, our own primal instinct in order to control performance anxiety.

Pharmacotherapy

Medication for the treatment of all psychiatric disorders has gone through revolutionary change in the last three decades, and discovery of new drugs with fewer adverse effects occurs every year. Since there is inherent benefit and risk to using medication, one must proceed to pharmacotherapy in the sporting arena with caution. It is important to understand that the potential negative impact of medication on athletic performance may dissuade an athlete from using this treatment modality. The sports medicine clinician must remember that medication alone is not a panacea and is more successful in conjunction with another therapy, such as CBT and a healthy lifestyle, including regular exercise, as described above.[37, 38] Clinicians and athletes must have an awareness of the prohibited substance list and possible performance-enhancing effects of drugs.

Selective serotonin reuptake inhibitors (or SSRI's) have become the mainstay of treatment for anxiety disorders. Though there is a role for benzodiazepines, they are considered only under acute exacerbations of anxiety. The athlete patient will develop tolerance and dependence if there is prolonged use. The sports medicine clinician needs to choose the SSRI that is best tolerated by the patient, using the adverse effect profile of each SSRI to guide them. For example, escitalopram is an SSRI with a low adverse effect profile and is well tolerated. Choosing the right SSRI for an athlete is an art as well as a science. Remember to work with the athlete patient, carefully listening to their feedback on their response to the medication and any difficulties they may be experiencing with adverse effects, both in their sports performance and during activities of daily living.

Page 327

CASE STUDY

Jonny Wilkinson, England rugby union—debilitating performance anxiety

The team was outside in a huddle waiting for me. I was supposed to be giving the 'come on we can do this' speech and I was a shivering wreck in the toilet.

Jonny Wilkinson is best known for scoring the winning drop goal in the 2003 Rugby World Cup final. He still holds the record for most points scored in rugby world cups and is known for his perfectionist goal-kicking tendencies.

Wilkinson suffered from injuries throughout his career, which threatened to prevent him from regaining his best form. This caused anxiety, as he expressed how closely his sense of self was intertwined with Wilkinson the rugby player, as opposed to Wilkinson the person. Following his retirement Wilkinson discussed his anxiety and the significant impact it had on him and his performance.

When I was playing rugby, I wore a rugby shirt and dissolved into what I was doing. The problem was my attachment to that idea of who I was meant I never took that shirt off. I became more and more attached to it.[36]

Treatment

Wilkinson is open about his utilisation of talking therapies and having a strong support network. He practised yoga to support his rehabilitation. He endorses interventions such as mindfulness and CBT, He now works with the mental health charity Mind to support people to address their mental health concerns using the same methods, alongside physical activity.

Sources: references 36, 45, 46, 47

Short-acting benzodiazepine drugs are useful for panic attacks, especially in their acute phase. Long acting benzodiazepines can be chosen in the early treatment phase of any anxiety disorder, before an SSRI has been titrated to an effective therapeutic dose.[39] While medication can play a big role in the treatment of an anxiety disorder in the athlete, it should be used alongside one or several of the treatment modalities mentioned. The patient presenting with refractory anxiety should be referred to a psychiatrist, preferably one with a knowledge of sports psychiatry.

This can support identification of the correct combination of psychopharmacology, CBT and other treatments.

SUMMARY

I'd been working closely with the Newcastle doctor, Graeme Wilkes, on my physical injuries and this one occasion I went and visited him again but this time I let it all go. I didn't talk to him about my groin, I told him about my head. Jonny Wilkinson, in his autobiography, *Jonny*[40]

The modern sporting environment often exposes individuals to pressures that can result in the development of anxiety disorders.

- There is evidence of an increased incidence of mental illness, especially anxiety disorders and depression, among elite athletes.
- Screening for career dissatisfaction may prove a valuable tool for early diagnosis; similarly, identifying at-risk groups, such as those nearing retirement or suffering from injury, may be worthwhile.
- The management of anxiety disorders and all mental health concerns requires a multidisciplinary approach. The physician is often the cornerstone of the management plan, acting as a signpost for the athlete. They can support the athlete to access the necessary therapy (e.g. CBT and pharmacological management) or resources to help support them through their concerns.
- It is essential that all members of the medical team support the identification of athletes at risk from anxiety disorders and are aware of the signs and symptoms. If anxiety is managed appropriately, performance levels can be maintained or enhanced.

RESOURCES

Page 328

- For more on the topic of managing mental health and harnessing the powers of mental strength to enhance performance, listen to the British Journal of Sports Medicine discussion with Dr Steve Peters, former Team GB Olympic sports psychiatrist (available at multiple podcast outlets)
- Association for Applied Sports Psychology resources— www.appliedsportpsych.org/resources.
- Useful guides for supporting students and others with their mental health and wellbeing can be found on the NCAA website:
  - 2018 interactive guide—http://www.ncaa.org/sport-science-institute/mental-health-educational-resources/
  - 2016 mental health best practices consensus document—www.ncaa.org/sites/default/files/HS_Mental-Health-Best-Practices_20160317.pdf.

REFERENCES

1. Bauman NJ. The stigma of mental health in athletes: are mental toughness and mental health seen as contradictory in elite sport? *Br J Sports Med* 2016; 50(3): 135–6.
2. Anxiety and Depression Association of America. Exercise for Stress and Anxiety. 2018. https://adaa.org/living-with-anxiety/managing-anxiety/exercise-stress-and-anxiety.
3. Hughes L, Leavey G. Setting the bar: athletes and vulnerability to mental illness. *Br J Psychiatry* 2012; 200(2): 95–6.
4. National Collegiate Athletic Association (NCAA). 2013–14 NCAA Sports Medicine Handbook. Indianapolis, IN: NCAA, 2013.
5. Gulliver A, Griffiths KM, Mackinnon A et al. The mental health of Australian elite athletes. *J Sci Med Sport* 2015; 18(3): 255–61.
6. Foskett RL, Longstaff F. The mental health of elite athletes in the United Kingdom. *J Sci Med Sport* 2018; 21(8): 765–70.
7. Rice SM, Purcell R, De Silva S et al. The mental health of elite athletes: a narrative systematic review. *Sports Med* 2016; 46(9): 1333–53.
8. Calvo F. Yerkes–Dodson principle. 2018. https://franzcalvo.wordpress.com/category/behavior-stress/page/2/.
9. National Institute of Mental Health (NIMH). Anxiety Disorders. 2016. https://www.nimh.nih.gov/health/topics/anxiety-disorders/index.shtml.
10. Gauthier J. 'Psychology Works' fact sheet: panic disorder. Canadian Psychological Association, 2014. https://www.cpa.ca/docs/File/Publications/FactSheets/PsychologyWorksFactSheet_PanicDisorder.pdf.
11. Professional Associations for Physical Activity (Sweden). *Physical activity in the prevention and treatment of disease*. 2nd ed. Stockholm: Swedish National Institute of Public Health, 2010.
12. Powell DH. Treating individuals with debilitating performance anxiety: an introduction. *J Clin Psychol* 2004; 60(8): 801–8.
13. Forsdyke D, Smith A, Jones M et al. Psychosocial factors associated with outcomes of sports injury rehabilitation in competitive athletes: a mixed studies systematic review. *Br J Sports Med* 2016; 50(9): 537–44.
14. Covassin T, Beidler E, Ostrowski J et al. Psychosocial aspects of rehabilitation in sports. *Clin Sports Med* 2015; 34(2): 199–212.
15. Bandelow B, Baldwin D, Abelli M et al. Biological markers for anxiety disorders, OCD and PTSD: a consensus statement. Part II: neurochemistry, neurophysiology and

neurocognition. *World J Biol Psychiatry* 2017; 18(3): 162–214.

16. Center for Mental Health Services. Practice Guidelines: Core Elements for Responding to Mental Health Crises. Rockville, MD: Substance Abuse and Mental Health Services Administration (SAMHSA), 2009.
17. National Collegiate Athletic Association. Supporting Student-Athlete Mental Wellness. 2018. http://www.ncaa.org/sport-science-institute/supporting-student-athlete-mental-wellness.
18. Putukian M. The psychological response to injury in student athletes: a narrative review with a focus on mental health. *Br J Sports Med* 2016; 50(3): 145–8.
19. National Collegiate Athletic Association. Mental Health Best Practices—Inter-Association Consensus Document: Best Practices for Understanding and Supporting Student-Athlete Mental Wellness. 2016. http://www.ncaa.org/sites/default/files/HS_Mental-Health-Best-Practices_20160317.pdf.
20. Fortes LS, da Costa BDV, Paes PP et al. Influence of competitive-anxiety on heart rate variability in swimmers. *J Sports Sci Med* 2017; 16(4): 498–504.
21. American Psychological Association. Exercise fuels the brain's stress buffers. 2018. http://www.apa.org/helpcenter/exercise-stress.aspx.
22. Biddle SJ, Asare M. Physical activity and mental health in children and adolescents: a review of reviews. *Br J Sports Med* 2011; 45(11): 886–95.
23. Bäckmand H, Kaprio J, Kujala UM et al. Physical and psychological functioning of daily living in relation to physical activity: a longitudinal study among former elite male athletes and controls. *Aging Clin Exp Res* 2006; 18(1): 40–9.
24. Stubbs B, Vancampfort D, Rosenbaum S et al. An examination of the anxiolytic effects of exercise for people with anxiety and stress-related disorders: a meta-analysis. *Psychiatry Res* 2017; 249: 102–8.
25. Jayakody K, Gunadasa S, Hosker C. Exercise for anxiety disorders: systematic review. *Br J Sports Med* 2014; 48(3): 187–96.
26. Daley A. (2016) Depression and anxiety. In Clow A, Edmunds S, eds. *Physical Activity and Mental Health*. Champaign, IL: Human Kinetics.
27. Monsma EV. Disordered eating and the controlling aspects of aesthetic sports. Association for Applied Sports Psychology, 2006. http://www.appliedsportpsych.org/resources/resources-for-coaches/disordered-eating-and-the-controlling-aspects-of-aesthetic-sports/.
28. National Institute for Health and Care Excellence (NICE). Obsessive-compulsive disorder and body dysmorphic disorder: treatment. NICE clinical guideline (CG31), 2005. https://www.nice.org.uk/guidance/cg31.
29. Health Quality Ontario. Psychotherapy for major depressive disorder and generalized anxiety disorder: a health technology assessment. *Ont Health Technol Assess Ser* 2017; 17(15): 1–167.

30. Driot D, Bismuth M, Maurel A et al. Management of first depression or generalized anxiety disorder episode in adults in primary care: a systematic metareview. *Presse Med* 2017; 46(12 Pt 1): 1124–38.
31. Swedish Council on Health Technology Assessment (SBU). Treatment of anxiety disorders: a systematic review. SBU yellow report no. 171/1+2. Stockholm: SBU, 2005.
32. Carpenter JK, Andrews LA, Witcraft SM et al. Cognitive behavioral therapy for anxiety and related disorders: a meta-analysis of randomized placebo-controlled trials. *Depress Anxiety* 2018; 35(6): 502–14.
33. Skapinakis P, Caldwell D, Hollingworth W et al. A systematic review of the clinical effectiveness and cost-effectiveness of pharmacological and psychological interventions for the management of obsessive-compulsive disorder in children/adolescents and adults. *Health Technol Assess* 2016; 20(43): 1–392.
34. Randall CL, McNeil DW. Motivational interviewing as an adjunct to cognitive behavior therapy for anxiety disorders: a critical review of the literature. *Cogn Behav Pract* 2017; 24(3): 296–311.
35. Coelho RW, Keller B, Kuczynski KM et al. Use of multimodal imagery with precompetitive anxiety and stress of elite tennis players. *Percept Mot Skills* 2012; 114(2): 419–28.
36. Squires N. Jonny Wilkinson exclusive: England rugby hero opens up on mental health problems. *Daily Express* 24 March 2018. https://www.express.co.uk/sport/rugby-union/935231/Jonny-Wilkinson-Toulon-Dave-Alfred-rugby-union-anxiety-coach-captain.
37. Reardon CL, Factor RM. Sport psychiatry: a systematic review of diagnosis and medical treatment of mental illness in athletes. *Sports Med* 2010; 40(11): 961–80.
38. Reardon CL. The sports psychiatrist and psychiatric medication. *Int Rev Psychiatry* 2016; 28(6): 606–13.
39. Reardon CL, Factor RM. The use of psychiatric medication by athletes. In: Baron DA, Reardon CL, Baron SH, eds. *Clinical sports psychiatry: an international perspective*. Chichester, UK: Wiley-Blackwell, 2013: 157–65.
40. Wilkinson J. *Jonny: my autobiography*. London, UK: Headline Publishing Group, 2012.
41. https://en.wikipedia.org/wiki/Ricky_Williams
42. http://articles.latimes.com/2002/jul/24/sports/sp-williams24
43. https://adaa.org/living-with-anxiety/personal-stories/ricky-williams-story-social-anxiety-disorder
44. https://genesight.com/5-famous-people-you-didnt-know-have-anxiety-disorder/
45. https://www.amazon.ca/Jonny-My-Autobiography-Wilkinson/dp/0755313402
46. https://www.express.co.uk/sport/rugby-union/935231/Jonny-Wilkinson-Toulon-Dave-Alfred-rugby-union-anxiety-coach-captain

47. https://www.time-to-change.org.uk/blog/jonny-wilkinson-%E2%80%93-physical-and-mental-battle-sporting-hero

PART C

Environment

Chapter 23

Heat

with SÉBASTIEN RACINAIS

As far as you will be having the race in Tokyo in mid summer, none of the measures, even a pile of all measures, can ensure safety.

Professor Yokohari discussing heat stress risks facing runners at the 2020 Tokyo Olympics where temperatures could reach 39°C

In April 2018, temperatures at the London Marathon reached 24.1°C, with more than 100 people taken to hospital suffering heat-related illness. This pales in comparison to the projected temperatures for athletes competing at the Tokyo 2020 Olympics where in August 2018 temperatures reached a sizzling 39°C. Temperature has been recognised as a critical indicator of health for centuries and is still routinely measured as one of the four primary vital signs. Despite our improvements in monitoring body temperature, incidences of heat stroke have increased over past decades, and it accounts for more deaths than all other natural disasters combined.[1] Heat stroke is the second highest cause of death in sport after cardiac conditions.[2] In addition to associated health issues, heat stress has a large effect on exercise performance. Yes, warming up enhances performance during high-intensity efforts, but an increase in whole-body core temperature during prolonged exercise in hot and/or humid environments limits performance by taxing the circulatory system and may lead to the development of heat-related illness.[3] In this chapter we explore the current scientific knowledge regarding acute and chronic responses to exercising in the heat, and provide practical recommendations and guidelines for clinicians, medical teams, event organisers and athletes.

BIOPHYSICS OF HEAT EXCHANGE

Core temperature fluctuates during the day between ∽36.5 and ∽37.5°C. When exposed to a cold or hot environment, humans maintain homeostasis through both behavioural thermoregulation

(e.g. clothing, sheltering) and autonomic thermoregulation (e.g. sweating, vasodilation/constriction). Skin temperature and environmental conditions can induce both positive and negative heat exchange (i.e. heat gain and loss, respectively) via radiation, convection and conduction (Fig. 23.1).

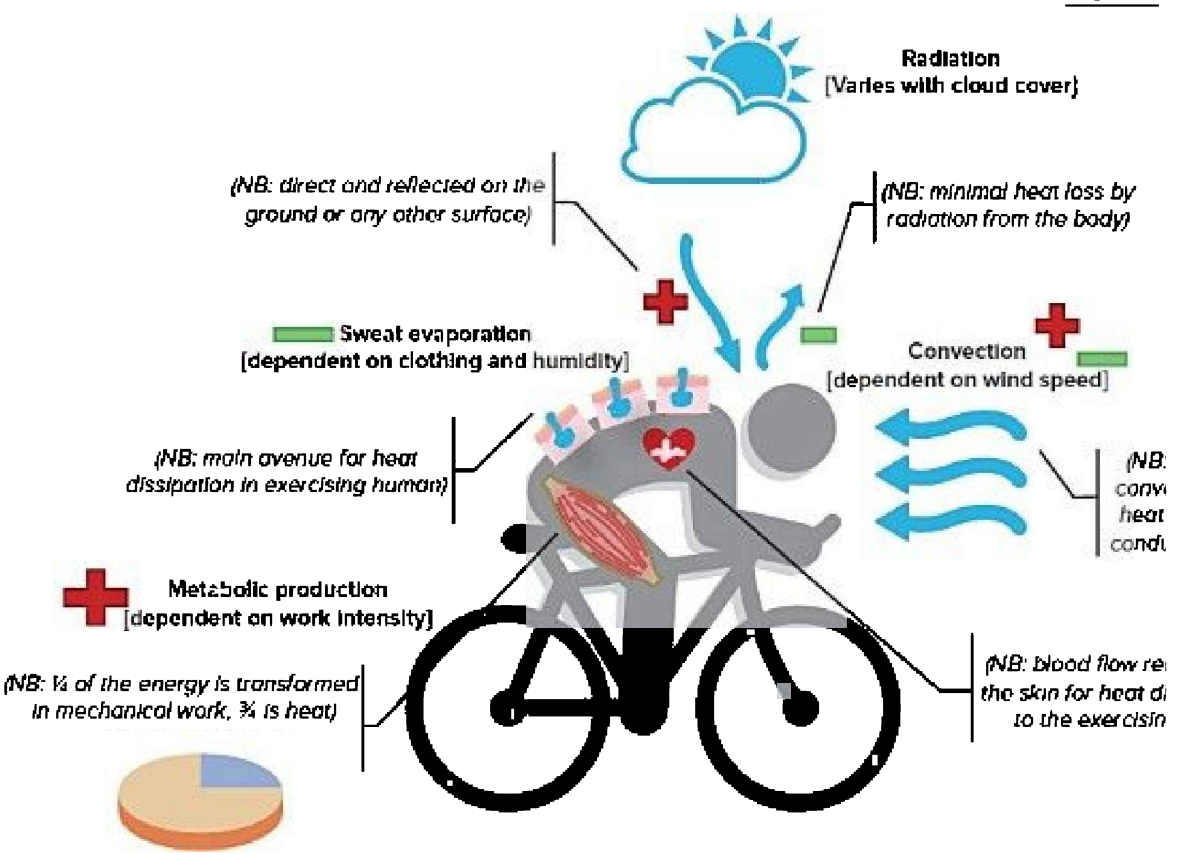


Figure 23.1 Factors that influence heat gain and heat loss during exercise

Humans possess the innate ability to sweat, allowing for heat loss through evaporative mechanisms. Evaporation is the primary avenue of heat loss when exercising in the heat, where the evaporation of sweat (i.e. transformation of a liquid into a gas) serves to dissipate thermal energy. As such, dripping of sweat does not allow for heat dissipation, and warm and humid environments (e.g. tropical) that limit evaporation are more challenging than hot and dry environments (e.g. desert). Maintaining homeostasis requires reaching an equilibrium between metabolic heat production and heat gain or loss (Fig. 23.1). The ability of humans to turn energy into mechanical output is estimated at 25% or less, the remaining 75% of energy consumed generates heat. This heat generated by muscle contractions induces a large initial increase in muscle temperature,[4]

thereafter driving an increase in core temperature.[5] Although exact absolute values of muscle temperature are dependent on the depth of measurement, muscle of interest, environmental conditions and intensity of contraction, it is ∾35°C at rest and will exceed core temperature after engaging in physical activity to remain between 0.65 and 0.95°C higher.[5]

If the increase in metabolic production is not matched by an increase in heat dissipation, this heat is stored. If environmental conditions allow for a match between heat loss and heat gain, then heat storage is transient and athletes will reach a plateau in core temperature. Otherwise, environments limiting heat loss (e.g. protective clothing) below heat gain generate an uncompensated heat elevation leading to a physiological stress on the body.

The pre-optic/anterior hypothalamus has been considered a 'thermostat', maintaining a core temperature 'set point'. Based on thermal sensory information, this thermostat activates effector responses to decrease body temperature (e.g. sweating, increasing skin blood flow) or increase temperature (e.g. shivering, decreasing skin blood flow).[6] This set point is considered relatively stable (i.e. allowing a circadian variation around 37°C), except in case of fever, where it is readjusted to promote a febrile response.

BENEFICIAL ACUTE RESPONSES TO HEAT PRODUCTION

An increase in body temperature is not necessarily detrimental to the health and performance of an athlete. For example, most athletes perform preconditioning exercises or warm-ups to increase their muscle temperature. This is particularly beneficial for high-intensity performance.[7] Some key benefits of generating heat within the body are outlined in the box.

DETRIMENTAL RESPONSES TO HEAT STRESS

If exercise is prolonged and atmospheric conditions overwhelm the body's mechanisms of homeostatic temperature regulation, hyperthermia can occur. This can cause several physiological responses within the body that limit the performance capability of the athlete and, if unchecked, may result in exertional heat illness.

Benefits of warming up prior to physical activity

- Increased contraction and nerve conduction velocity[8–10]
- Decreased viscous resistance of muscle and joints[11, 12]
- Increased local vasodilation, with improved substrate delivery and metabolite removal[13–15]
- Increased rate of force development and power due to a breakdown in cross-bridges maintaining muscle tone and posture at rest[16, 17]
- Improved mental focus and ability to practice mental imagery[18, 19]
- Cardiovascular preparation for high-intensity exercise with reduced risk of abnormal

electrocardiographic response (e.g. cardiac ischaemia)[20, 21]

Hyperthermia

While a moderate rise in muscle temperature enhances explosive skeletal muscle performance, the development of thermal strain (i.e. an elevation in core, skin and muscle temperature) impairs aerobic performance.[22–24] There is a notable increase in skin blood flow, largely related to the narrowing of the core-to-skin temperature gradient.[25–27] It had been suggested that this redistribution and peripheral pooling of blood reduced ventricular filling pressure, end-diastolic volume and stroke volume (Fig. 23.2).[28] However, it is now considered that the reduction in stroke volume is also due to an increase in intrinsic heart rate.[29–31]

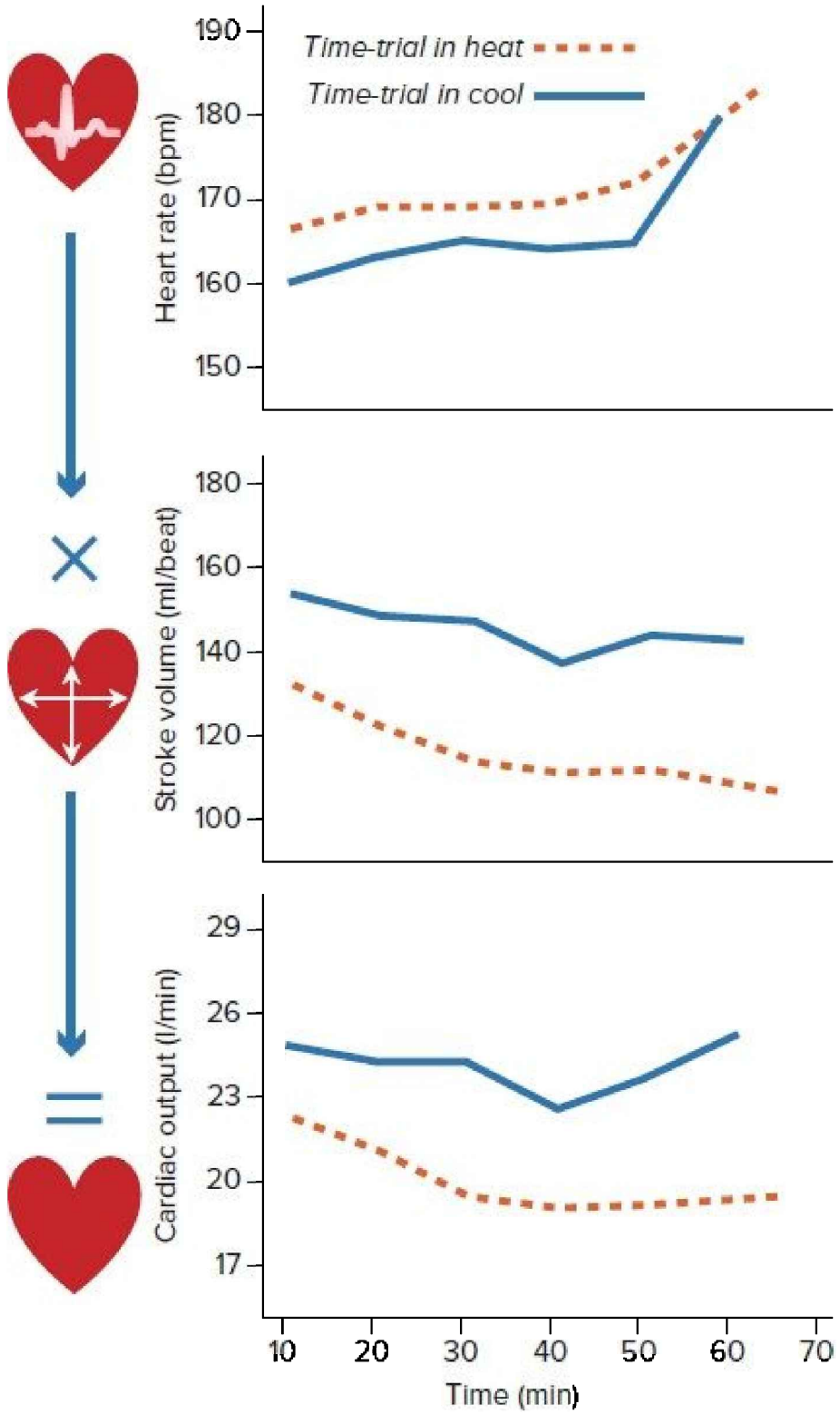

Time-trial in heat
Time-trial in cool
Heart rate (bpm)
190
180
170
160
150
Stroke volume (ml/beat)
180
160
140
120
100
Cardiac output (l/min)
29
26
23
20
17
10
20
30
40
50
60
70
Time (min)

Figure 23.2 Changes in heart rate and stroke volume that influence cardiac output in the heat and during cool conditions

REDRAWN WITH DATA FROM ROWELL LB, (1974)[28]

Attaining maximum or near maximum heart rate decreases maximum cardiac output[32, 33] and forces the cardiovascular system towards a functional limit at submaximal workloads and oxygen uptake.[34–36] This reduction in cardiovascular reserve increases the relative exercise intensity and perceived exertion for a given workload[32, 33, 37–39] making circulatory/cardiovascular strain the primary limiting factor for prolonged exercise in the heat.[23, 24, 40, 41] Athletes are therefore generally able to initiate a simulated or competitive event at the same intensity in hot or temperate environments, but then progressively reduce their absolute intensity (Fig. 23.3) to maintain a similar relative intensity in both environments.[24, 43]

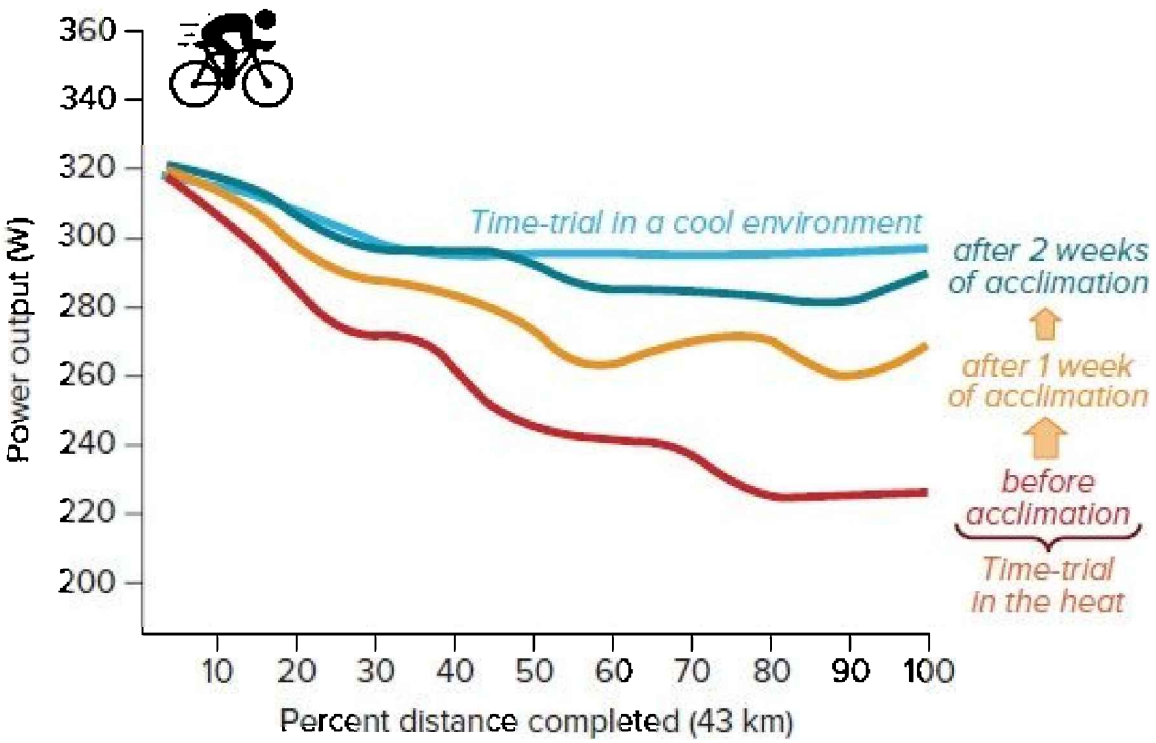


Figure 23.3 Athletes begin a simulated or competitive event at the same intensity in hot or temperate environments, but then progressively reduce their absolute intensity (power output) to maintain a similar relative intensity in both environments REDRAWN WITH DATA FROM PÉRIARD JD ET AL.[41]

Results of laboratory studies indicate that hyperthermia reduces voluntary activation[44, 45] by affecting both the peripheral transmission and the supraspinal generation of the neural drive (Fig.

23.4).[45] While a moderate increase in core temperature can initially improve cognitive function,[46] hyperthermia ultimately impairs cognitive processing.[47, 48] Complex tasks are affected more than simple tasks.[49–53] Impaired cognitive function has been linked to a reduction in the available cognitive resources due to the unpleasantness of hyperthermia and to an increase in impulsivity in hyperthermic humans.[53–55] For a good example of altered decision making, see the chapter case study on Jonathan Brownlee.

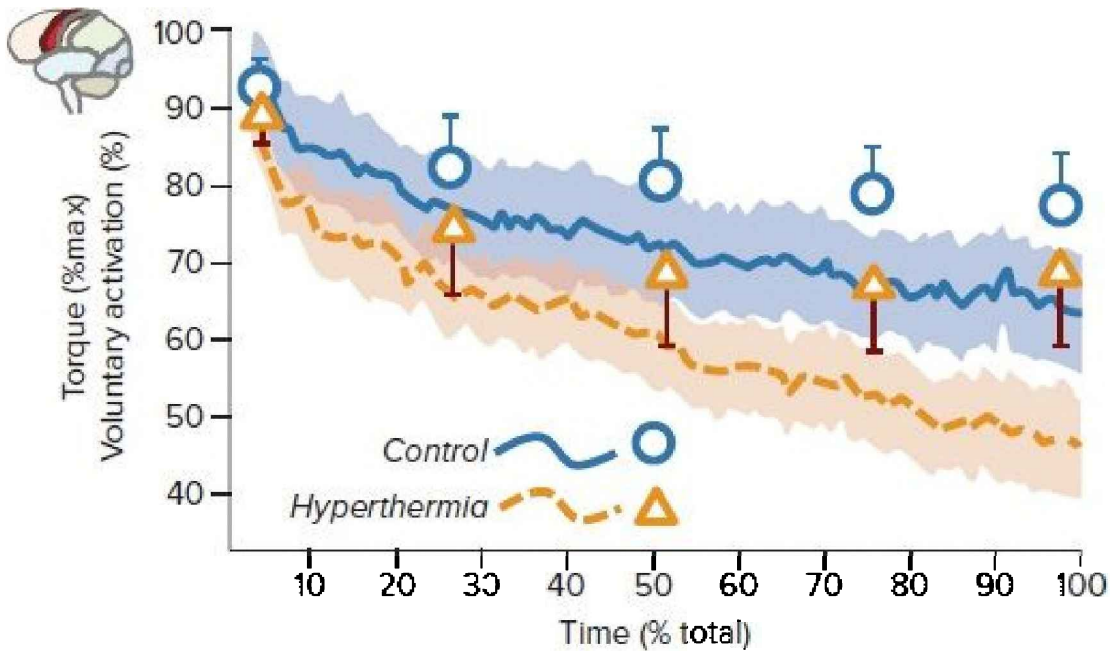


Figure 23.4 Torque and voluntary activation decrease over time more rapidly in hot than temperate conditions REDRAWN WITH DATA FROM RACINAIS S, ET AL[42]

Exertional heat illness

Beyond impairing performance, environmental heat stress and physical activity interact to increase the risk of exertional heat illness (EHI). As detailed in the flow chart of the possible outcomes of exercising in hot and humid conditions (Fig. 23.5), there is a continuum of medical conditions, ranging in severity.

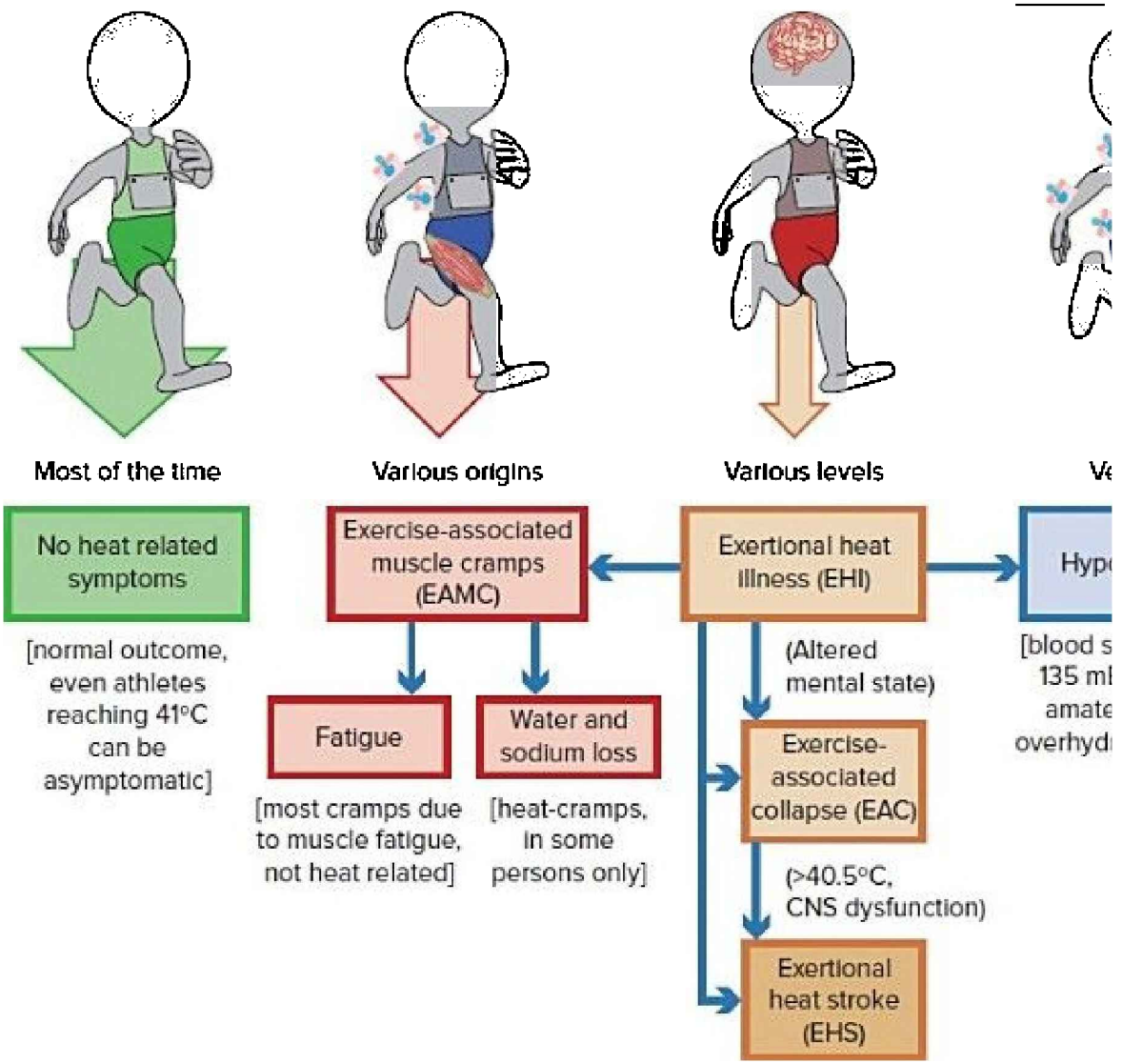


Figure 23.5 Potential complications of exercise in the heat

The most severe of these EHI-related conditions are potentially fatal and characterised by high body temperatures, profound central nervous system (CNS) dysfunction (e.g. combativeness, delirium, seizures and coma), as well as organ and tissue damage. Unlike classic heat stroke, which is primarily observed in vulnerable and immunocompromised populations during seasonal heat waves, exertional heat stroke occurs in healthy young individuals performing strenuous physical activity. Accordingly, it is difficult to identify individuals at risk of EHI. Heat stroke and other EHIs often occur in the presence of risk factors such as extreme environmental conditions, medication

and drug use, compromised health status and underlying genetic conditions.[1]

PRACTICE PEARL

Heat acclimatisation can decrease the risk of EHI in athletes or others expected to undertake physical activity in a hot or humid environment.

As a rectal temperature above 40°C is used in the diagnosis of exertional heat stroke, and most laboratory studies have defined a temperature between 39°C and 40°C as an ethical criterion for exercise cessation, some have considered the existence of a critical core temperature. However, peak core temperatures of 41.5-41.7°C have been observed during cycling and running competitions in hot ambient conditions.[43] The development of fatigue during exercise in the heat is a multifactorial phenomenon, largely under cardiovascular, cardiorespiratory and psychological influences.[32, 48]

ADAPTATIONS TO CHRONIC OR REPEATED EXPOSURES

Humans rely on behavioural responses to survive in cold environments, such as manufacturing clothes, building houses and mastering fire (i.e. the possibility to generate warmth). We conversely have a large autonomic capacity to adapt when repeatedly exposed to heat. Exercise capacity in the heat depends on thermoregulatory responses (e.g. sweating) and their cardiovascular consequences (e.g. increase in heart rate)–both of which adapt progressively when heat exposure is repeated (Fig. 23.7).

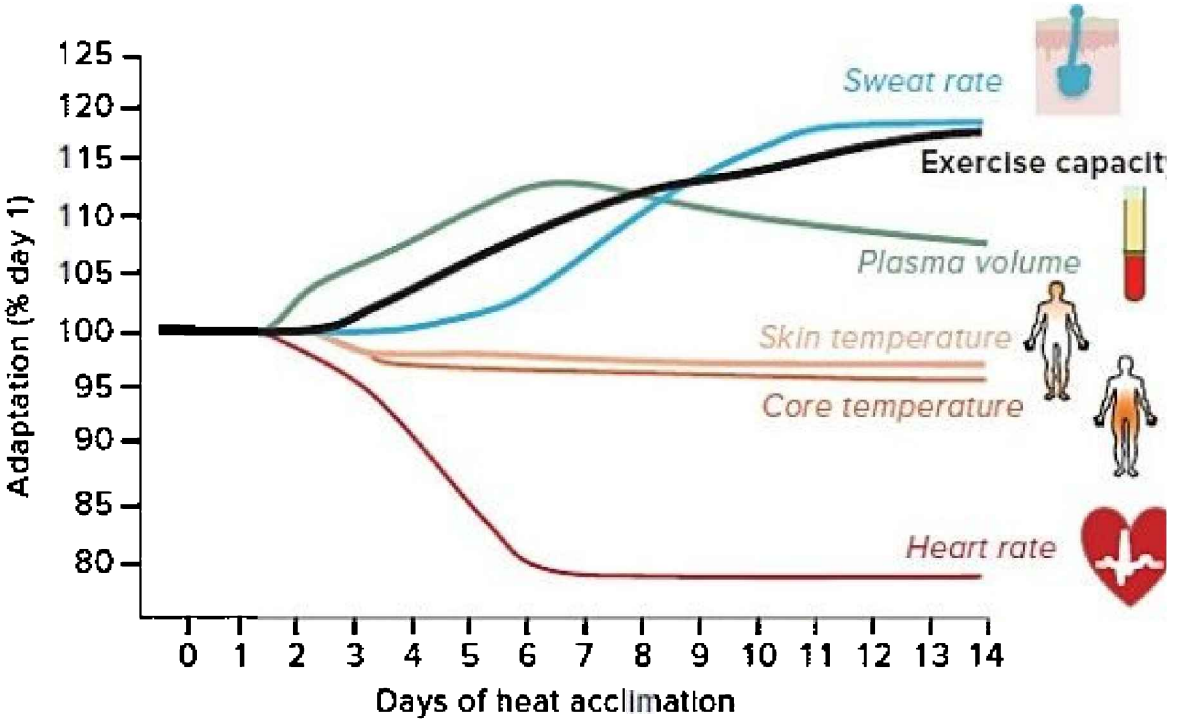


Figure 23.7 Adaptation with heat acclimatisation REDRAWN WITH DATA FROM PÉRIARD JD, ET AL.[42]

CASE STUDY

Jonathan Brownlee, triathlon—exertional heat illness

Jonathan Brownlee is one of the most successful triathletes of all time, having won the world triathlon title in 2012, and Olympic medals in London 2012 and Rio 2016 (his brother Alistair won gold on both occasions).

In 2016, while trying to regain the world championship title in the final race of the season, both brothers endured the extreme heat and humidity of Cozumel, Mexico. Following the swim and the bike legs of the race, Jonathan entered the final run section of the race but began to lose control of his lower limbs and cognitive functions just 400 metres from the finish. With a decrease in his voluntary muscle contraction, his central drive took over as a protective mechanism.

Alistair, who was in third place, recognised his brother's situation and proceeded to collect him and run with him, carrying him over the line (Fig. 23.6). Jonathan missed out on the world title by four points but, importantly, was able to receive immediate medical attention at the finish line. This example demonstrates that even with appropriate support and acclimatisation procedures, heat illness can affect anyone. Medical event directors are encouraged to be aware of the tell-tale signs of heat-related illness and ensure staff are appropriately trained to manage acute cases.

Figure 23.6 Alistair Brownlee supports brother Jonathan to the finish line of the ITU Cozumel Triathlon event. Jonathan was suffering clear signs of heat-related illness

ALEXANDER KOERNER/GETTY IMAGES

Source: references *130, 131, 132*

Sweat rate

The adaptations in sweat rate and sweat content were among the first described responses in heat acclimatisation. In the 1930s, Dill et al. conducted several experiments on the adaptations in sweat during heat acclimatisation, showing that the concentration of salt in sweat (sodium $[Na^+]_{sweat}$) decreased after a few days exposure to a hot environment.[56] By the end of the 1930s, it was accepted that heat acclimatisation increased sweat rate[57] and decreased sodium $[Na^+]_{sweat}$ concentration.[58] The increase in sweat rate has even been proposed to be the principal adaptive mechanism following heat acclimatisation, as it allows an increase in evaporative cooling.[59] These early observations are still regarded as some of the main responses in heat acclimatisation (Fig. 23. 7). The provocation of inducing profound sweating is considered a key determinant of successful acclimatisation, along with increased body (core and skin) temperature and skin blood flow.[60–62]

Changes in blood volume

Blood plasma volume expansion is a transient phenomenon only,[63, 64] likely due to a decrease in the level of physiological stress (i.e. the stimulus driving adaptation) when acclimatisation develops. Recent studies suggest that plasma volume would remain expanded if the adaptation stimulus is maintained constant by clamping core temperature during acclimatisation.[65, 66] This increase is, however, largely variable between individuals, as plasma volume expansion following

acclimatisation ranges from 3–27% (Fig. 23.7).[65–68] In addition, an artificial increase in plasma volume does not appear to improve thermoregulatory function[69, 70] and, therefore, the role of plasma volume expansion in response to heat acclimatisation is now debated. Nevertheless, even if plasma volume does not lead to improved exercise capacity, changes in haematocrit correlate to the changes in physical performance in the heat following short-term acclimatisation and thus represent a valuable indicator of individual responses.[71–73]

Cardiovascular adaptations

Heat acclimatisation improves evaporative cooling. This, in turn, lowers skin temperature relative to rectal temperature and thus increases the internal thermal gradient facilitating the heat flow to the surface.[67, 74] This ultimately improves heat transfer via blood flow, 'sparing' blood for the rest of the circulation[67] and thus relieving the circulatory strain.[74] A decrease in heart rate for a given exercise intensity is considered a clinical sign of heat acclimatisation and is still considered as one of the main indicators of heat acclimatisation (Fig. 23.7).[75_76]

PRACTICE PEARL

Using heart-rate based training programs can support athletes to acclimatise to hot or humid conditions by allowing them to work out at a similar physiological stress level to their usual environment while adapting to their new settings.

Kinetics of acclimatisation: short and long-term adaptations

Heat acclimatisation occurs in two phases; with the initial phase encompassing a decrease in heart rate and temperature threshold for sweating within 2–3 days, followed by a later increase in sweat rate for a given temperature and improved fatigue resistance.[75] Heat acclimatisation is now considered a relatively rapid process that begins from the first day of exposure, with 75–80% of the adaptations occurring in the first 4–7 days (Fig. 23.7).[76, 77] However, even if athletes benefit from a few days of acclimatisation[78–80] they may require 6–10 days to achieve near complete cardiovascular and sudomotor adaptations,[73, 67, 81] and 2 weeks to optimise aerobic performance in hot environments.[43]

HYDRATION, DEHYDRATION AND HYPONATRAEMIA

The elevated sweat rate when exercising in the heat can induce dehydration if fluid losses are not partly replaced via fluid consumption. A reduction in total body water induces a proportional decrease in plasma volume and increase in plasma osmolality.[61] This hypovolaemia and hyperosmolality is associated with an increase in the core temperature threshold for vasodilation and sweating at the onset of exercise,[82, 83] which in turn reduces the sweat rate for a given core temperature and hence attenuates evaporative heat loss during exercise.[84]

Dehydration decreases cardiac filling and challenges blood pressure regulation.[85–87] Dehydration exceeding 2% of body weight may increase the rate of heat storage and the cardiovascular strain, and hence reduce exercise capacity in the heat.[88–91] Despite this, it is common for endurance athletes to manage this loss of body weight and continue to perform at an extremely high level. At the 2014 Berlin Marathon Dennis Kimetto set the men's marathon world record of 2:02:57, despite losing 10% of his body weight.

Hydration

The necessity to provide hydration when exercising in the heat has been known for over a century.[92–94] Hyperhydration has been observed to lower core temperature and increase sweating during heat exposure.[94] While physical conditioning enables increased work performance regardless of hydration status,[95] research currently suggests that acclimatisation to a lack of water is impossible [92] and that heat acclimatisation does not protect against dehydration.[95]

However, it should be considered that progressively reaching dehydration by the end of an exercise bout will be less detrimental compared with reaching dehydration early or starting an exercise bout hypohydrated. Some researchers suggest that the negative effects of dehydration are overemphasised by sports beverage companies[97] and that athletes should simply drink to thirst.[98–100] Drinking to thirst may be appropriate in many settings, but not in circumstances where severe dehydration is expected due to both ambient conditions and exercise duration.[101]

PRACTICE PEARL

Endurance athletes should begin exercise well hydrated and attempt to contain their progressive dehydration to less than 2%.

Fluid quantity and composition

Given the difficulty in rehydrating while exercising, coupled with relatively slow fluid absorption rates (~1.2 L/h), it is critical to start the exercise well hydrated and have a proper hydration strategy throughout the planned activity. A standard value cannot be provided, as sweat rates commonly range from 1–3 L/h.[102–104] Personal hydration strategies have to be designed based on previous experience, event duration and environmental conditions.

Beyond fluid quantity, fluid composition is critical. The main electrolyte lost in sweat is sodium (20–70 mEq/L),[105–106] and supplementation during exercise is often required for heavy and 'salty' sweaters to maintain plasma sodium balance. Heavy sweaters may deliberately increase sodium (i.e. salt) intake prior to and following hot weather training and competition to maintain sodium balance (e.g. 3.0 g of salt added to 0.5 L of a carbohydrate-electrolyte drink). To this effect, the US Institute of Medicine[107] has highlighted that public health recommendations regarding sodium ingestion do not apply to individuals who lose large volumes of sodium in sweat, such as athletes

training or competing in the heat.

Hyponatraemia and sodium deficit

Although muscle cramps are primarily related to muscle fatigue, some cramps may be prompted by dehydration and electrolyte deficit.[108] If sweat sodium losses are not compensated by proper hydration and feeding, sodium deficits reaching 20–30% of the exchangeable sodium pool may prompt muscle cramping.[108] Fluid containing 0.5–0.7 g/L of sodium is therefore recommended for exercise in hot environments lasting longer than one hour.[108–111] Athletes experiencing regular muscle cramps may increase the sodium supplementation to 1.5 g/L of fluid.[112]

Severe sodium deficit may lead to hyponatraemia, a condition where blood sodium concentrations fall below the normal range of 135–145 mEq/L. Hyponatraemia is due to excess hypotonic fluid absorption, generally during slow and long races. Whereas most marathon runners become dehydrated during the race, some slower runners may conversely overhydrate,[113] with an associated risk of hyponatraemia (Fig. 23.5).[114] The predisposing factors related to developing hyponatraemia include substantial weight gain, a racing time above four hours, female sex and low body mass index.[115, 116] As such, while there is impetus to minimise dehydration and body mass losses to below approximately 2%, recreational athletes undertaking prolonged exercise in hot environments should be careful not to overhydrate.

GUIDELINES FOR MEDICAL COVERAGE OF COMPETITIVE EVENTS IN THE HEAT

To cope with medical conditions that are likely to occur during sports events held in hot or humid ambient conditions, practical steps should be taken. Algorithms for the diagnosis of EHI conditions complement the standard algorithms used by the medical team in temperate ambient conditions (Fig. 23.8).[2] For example, assessing responsiveness and cardiac functions remains the first step before assessing rectal temperature.[2] As presented below, successful outcomes depend on forward planning to allow for rapid treatment on the day of the event.

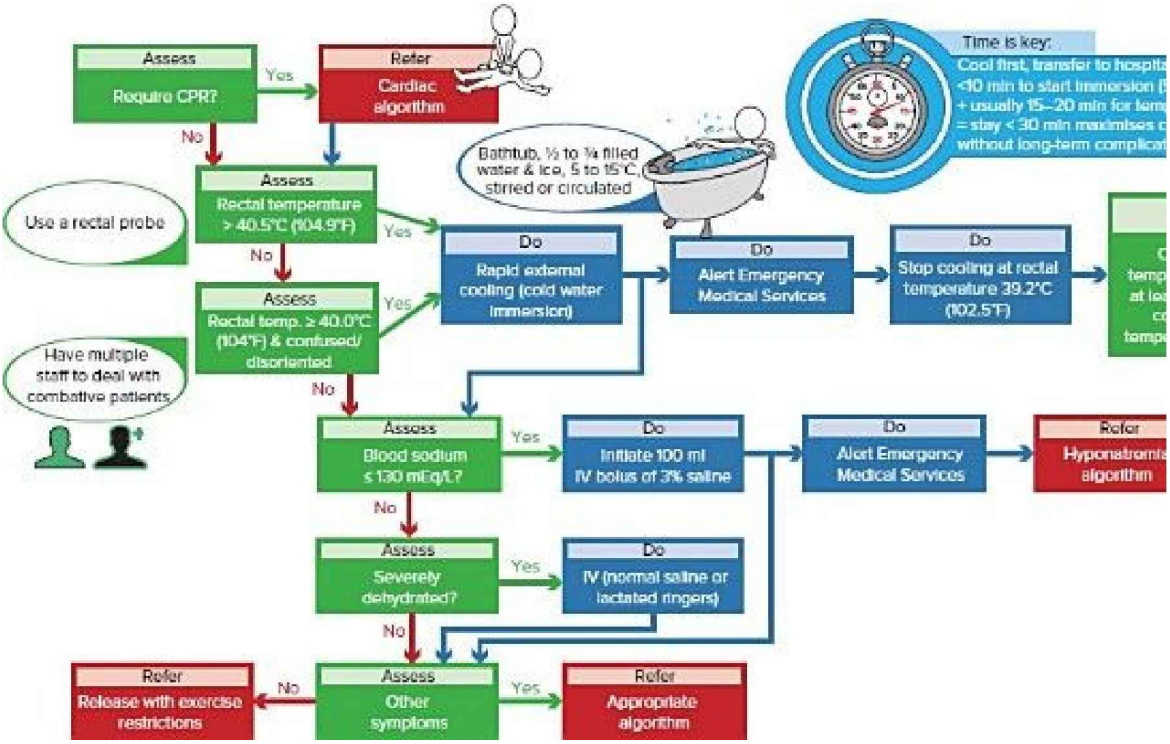


Figure 23.8 Algorithm for the management of patients with exertional heat illness COURTESY OF SEBASTIEN RACINAIS AND DOUGLAS CASA.

Facilities and equipment recommendations

A rectal thermometer is the main tool for the diagnosis of exertional heat stroke. The thermometer should include a flexible probe (to be inserted 10 cm beyond the anal sphincter) and a monitor reading up to 43°C. It is also recommended to have lubricating gel (to facilitate insertion), as well as cleansing wipes and a box for sterilisation, or disposable covers for the rectal probes. In addition, a portable blood sodium analyser (e.g. i-Stat®) is the main tool used for the diagnosis of hyponatraemia.

Ice-water immersion is the gold standard for treating heat stroke. A bathtub (or an inflatable paddling pool) half to three-quarters filled with water and ice should be readily available and considered the primary treatment in the event of heat stroke. Water temperature should be 5–15°C and it should be stirred or circulated continuously to maximise its cooling effect. Faster cooling occurs at lower temperatures. As such, the supply of ice should be planned in sufficient quantity.

Page 338

Vital signs should be continuously monitored during treatment. The medical tent should also provide drinking water, oral rehydration salts, salty food, bouillon cubes, Styrofoam cups, microwave oven, normal and hypertonic intravenous (IV) saline, glucagon, ondansetron, anti-seizure medication, IV cannulas, stopcock connections, needles, tourniquets, non-latex gloves,

sharps and biohazard disposal containers, alcohol wipes, gauze, tape, stretchers, wheelchairs, digital scales, emergency treatment tables, tables for supply access and organisation, and a phone for calling for transport or support. A laminated sheet listing emergency contact phone numbers should be prominently displayed.

Medical team training

Appropriate diagnosis and triage is the first step following an incident, and their effectiveness is largely based on staff training. The algorithms for the most common and most threatening conditions should be printed and clearly visibly displayed in the medical tent and the heat treatment unit (where available, e.g. close to the ice bath). The medical team should also be familiar with the specific equipment located in the heat treatment unit, including the rectal thermometer, the ice bath and the portable blood sodium analyser.

MEDICAL MANAGEMENT

In general, if an athlete is unresponsive upon arrival, the delivery of treatment should be according to the cardiac care algorithm of the medical team, and rectal temperature should be assessed to exclude exertional heat stroke (EHS). If an athlete is responsive, the assessment should include a brief history, vital signs, rectal temperature and blood sodium. In the absence of a specific medical condition, the appropriate management will largely be based on rectal temperature, a rectal temperature above 40°C with signs of confusion will be treated as heat stroke (Fig. 23.8).

Exertional heat stroke

The two EHS diagnostic criteria are a rectal temperature above 40°C and CNS dysfunction, such as dizziness, collapse, confusion, irrational behaviour, hysteria, aggressiveness, disorientation, seizures or coma. Other potential signs and symptoms include a hot, wet skin, dehydration, tachycardia, hyperventilation, hypotension, vomiting and diarrhoea.

Cold-water immersion up to the neck is considered the most effective strategy for the treatment of EHS. As soon as a diagnosis of EHS has been established, athletes should be immersed in ice water. It is critical to minimise the time an athlete's core temperature remains above 40°C. The goal is to lower body core temperature to less than 39°C within 30 minutes of collapse. Ice water should be circulated and maintained at 5–15°C, with faster cooling occurring at lower temperatures. Rapid cooling maximises the likelihood of preventing cell destruction during this period of extreme hyperthermia. Cooling should be at a rate of 0.1°C/min (0.18°F/min) or faster when cooling begins immediately, and not less than 0.15°C/min (0.27°F/min) if cooling is delayed longer than 20–30 min after collapse.[117] Cooling will be stopped once the athlete's rectal temperature reaches 39.2°C (approximately 9 minutes), to avoid subsequent hypothermia due to the 'after-drop effect'. Thereafter, athletes should be monitored for 15 minutes and then, if appropriate, transferred to hospital once safe temperatures have been attained, for follow-up (including blood analyses).

PRACTICE PEARL

Symptoms of exertional heat stroke can mimic those of head injury. In hot/humid environments a high-level of suspicion of heat-related illness should be maintained.

Exercise-associated muscle cramps

Muscle cramps are mainly due to excessive muscle fatigue. Initial responses should include gentle passive stretching along with oral rehydration (including salt capsules and salty food–but salt tablets should be avoided as they can cause gastrointestinal irritation). If there are no improvements within 20 minutes, secondary measures should include IV hydration with normal saline following a prior assessment of blood sodium concentration, to exclude hyponatraemia. Vital signs should be monitored continuously.

Heat syncope and exercise-associated collapse

Exercise-associated collapse (EAC) occurs in athletes unable to stand or walk unaided as a result of light-headedness, faintness and dizziness, or syncope, after completion of an exertional event or on ceasing exercise. On cessation of activity, the secondary muscle pump no longer assists in venous return, and large volumes of blood may pool in the lower extremities, contributing to EAC.

A collapsed athlete should be treated for EAC by moving the athlete into an appropriate position (i.e. supine with legs elevated). Intravenous infusions may be provided where there is loss of consciousness, in case of signs of severe dehydration; or, if the patient is able, oral rehydration can commence. Vital signs, rectal temperature and blood sodium concentration should be monitored. A low blood sodium concentration suggests hyponatraemia.

Page 339

Exercise-associated hyponatraemia

Hyponatraemia is defined by a decrease in serum or plasma sodium concentration below the normal range of 135–145 mEq/L. It is due to excess hypotonic fluid absorption (i.e. a larger fluid absorption than the fluid loss through sweat and urination). It is a rare but dangerous condition in sport. It is generally associated with slow and long races (e.g. marathon time above four hours) and substantial weight gain, although weight loss can also occur. Female sex and a low body mass index have been suggested as risk factors for hyponatraemia.

The diagnosis for establishing hyponatraemia is based on plasma or serum sodium concentration, with values of 130–135 mEq/L representing mild hyponatraemia, 125–129 mEq/L moderate hyponatraemia, and below 125 mEq/L severe hyponatraemia. Table 23.1 lists the clinical symptoms of hyponatraemia, which usually appear below 130 mEq/L, with the approximate threshold for coma being around ~120 mEq/L.

Table 23.1 Signs and symptoms of acute exertional hyponatraemia

- change of mental status
- coma
- combative behaviour
- nausea
- somnolence
- physical exhaustion
- vomiting
- tingling
- muscular weakness

- headache
- dizziness
- muscle twitching
- grand mal seizures
- encephalopathy
- disorientation
- confusion
- incoordination
- cardiac arrest
- respiratory arrest
- pulmonary oedema or cerebral oedema

Note: These signs and symptoms are closely aligned with those of EAC and EHS, therefore a sodium concentration check should always be performed.

Ensuing treatment depends on the severity of hyponatraemia and the associated symptoms. It ranges from ingesting salted crackers for a conscious athlete with mild hyponatraemia, to intravenous hypertonic saline (3%) as well as transport to hospital for more severe cases. Hypertonic saline should be discontinued when blood sodium concentration reaches 128–130 mEq/L.

CASE STUDY

Korey Stringer, NFL—exertional heat stroke

Korey Stringer was an American college and professional football player, who was an offensive tackle for the Minnesota Vikings in the NFL for six seasons.

In 2001, at a pre-season training camp, Stringer suffered EHS. He collapsed, had breathing difficulties and was vomiting. He was rushed to hospital, where he registered a core temperature of 43°C. Less than 24 hours later, Stringer died from multisystem organ failure related to the EHS.

Stringer was in full gear (helmet and shoulder pads) on a day with high humidity and temperatures above 30° C, leading many experts to suggest Stringer's death could have been avoided. Following his death, and thanks to campaigning by his wife, Kelci, the Korey Stringer Institute was established to promote the avoidance of sudden death in sports.[118]

Following investigations into Stringer's death, the NFL agreed to provide further guidance to help avoid sudden deaths. Following the adoption of these guidelines, deaths related to EHS have dramatically reduced in high school sports. Clinicians should follow guidelines and advise coaches to avoid scheduling training in the hottest part of the day and to take regular drink breaks (Fig. 23.9).

Source: references 133, 134, 135, 136

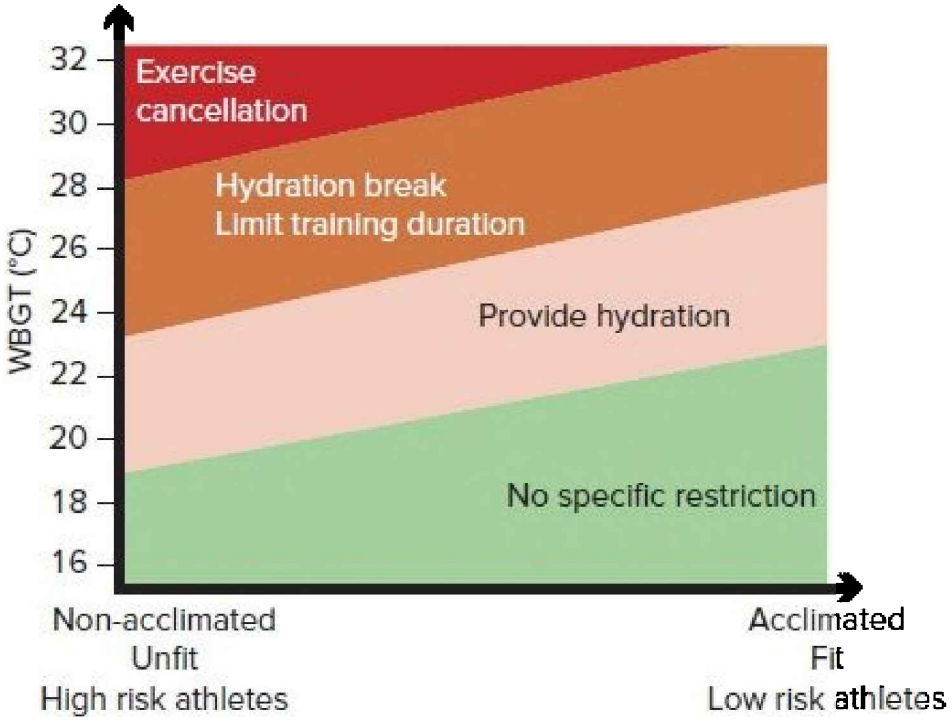


Figure 23.9 Graph demonstrating the fluctuating risk of EHI for varying WBGT temperatures with varying levels of fitness and acclimation

Note variation in risk can also depend upon the existence of co morbidities, whether exercise is low/high intensity or whether exercise is intermittent/ continuous. WBGT refers to wet-bulb globe temperature. WBGT is used to estimate the effect of temperature, humidity, wind speed (wind chill) and radiation (usually sunlight) on humans and is expressed as a measure of temperature (°C/F).

Guidelines for organising competitive events in the heat

The following guidelines should be utilised to support the organisation of events in the heat.

Scheduling

In cases of severe heat or humidity, adapting the event schedule may prevent excessive radiant heat from the sun or humidity adversely affecting the athletes. From a medical perspective, endurance events should be scheduled in the early morning or late afternoon (i.e. at times when temperature and solar radiation are lowest). Notably, an early start means that the environmental temperature will increase during the event, while simultaneously a participant's temperature will increase due to exertion. This may represent a risk for slower athletes. Humidity is as important as temperature and scheduling should avoid the most humid time of day.

Information

Once the event has been scheduled and the environmental conditions have been identified, the most important protective measure is to communicate this information to the medical team and the athletes. The following information, along with the questions and answers presented in the next box, represents

some of the standard questions raised by athletes and staff. These questions and answers were distributed as a leaflet to all athletes participating in the 2016 UCI Road Cycling World Championship in Qatar.[119]

Figure 23.10 Competitors were provided with information leaflets to support their preparation for extreme heat exposure at the 2016 World Road Cycling Championships, Doha, Qatar

ADAM HODGES/SHUTTERSTOCK

For major international events, organisers should also inform spectators. Organisers of the 1996 Summer Olympic Games in Atlanta, USA, sent leaflets on managing the heat to all ticket purchasers, and this is now commonplace in large mass participation events.

The impact of heat stress on various levels and types of sporting event

Organisers should be aware that the impact of heat stress varies based on the type of event and the level of the participants.

Events of shorter duration (e.g. under 15 minutes) are less affected by conditions of high heat or humidity, as they usually do not last long enough to increase whole-body temperature to levels that can affect health and performance. However, a long and intense warm-up will further increase temperature. The same will happen in the case of repeated bouts of exercise, such as during athletics meetings or rugby 7s tournaments. Measures should therefore be directed towards preventing large increases in temperature during warm-up and optimising cooling between exercise bouts (e.g. cooling fans, shaded areas, hydration).

Athletes participating in prolonged high-intensity events of greater than 20 minutes duration are likely to be most affected by heat stress. Maintaining a high exercise intensity for an extended period of time induces significant heat production, leading to a large increase in body temperature. Countermeasures should include heat acclimatisation, hydration and the availability of medical services well prepared to treat heat illness.

Ultra-endurance events (e.g. several hours) are generally performed at a lower intensity. However,

sustaining an elevated sweat rate for prolonged periods is likely to lead to hydration issues, if not managed appropriately. Elite athletes tend to dehydrate, whereas some amateur athletes tend to overhydrate. Countermeasures should be directed towards athlete education and providing sufficient opportunities to drink and rest.

Increasing participation in mass endurance events has led to larger numbers of amateur participants. This should lead medical teams to consider instigating measures to protect participants outside of competition time (e.g. limiting waiting time and providing shade before and after the event). Organisers of major events should also consider measures to educate and protect spectators. The public and participants in mass races are less likely to have undergone heat acclimatisation procedures and thus may be at greater risk for developing heat-related medical needs.

The specific effects of heat on females and junior athletes

Young athletes, especially those in their mid to late teens, experience large body weight and sodium losses, due to a pubertal increase in sweating, and do not always hydrate as well as adults. Young athletes and their coaches should pay particular attention to their hydration status and heat acclimatisation strategy. Females have lower sweat rates than males during high-intensity exercise in the heat and may reach higher core temperatures in a shorter period, potentially putting them at greater risk of developing heat illness. It is therefore important for female athletes to heat acclimatise in order to increase their sweat response and decrease the rise in body temperature associated with exercising in the heat.

On the day of the event

During the event, organisers should provide appropriate support to the athletes and their medical teams. Support to the athletes includes providing sufficient hydration opportunities, by having an appropriate number of feeding stations, providing bottles as well as food (e.g. fruit) and sodium (e.g. electrolytes, salty snacks). Athletes should have access to shaded and fanned rest areas before and after competition, as well as during the race for mass participation events (e.g. at designated medical points along the route).

Event modification

An important component of forward planning by event organisers is to develop clear guidelines and a plan for modifying the event in the case of (predetermined) extreme environmental conditions. Some major sporting federations have adapted their rules to allow modifications for hot or humid conditions:

- the Fédération Internationale de Football (FIFA) allows for an additional cooling and hydration break after 30 minutes of each half when the defined environmental criteria are met
- the Union Cyclistes Internationale (UCI) has adopted an extreme weather protocol allowing course modification if required by the weather conditions on race day
- the International Tennis Federation (ITF) and the Women's Tennis Association (WTA) allow for longer breaks between play during warmer competition days.

Organisers should nominate a panel (including medical personnel) to provide recommendations for last-minute modifications to the event. The decision to alter the event should be based on the temperature and humidity at the time of the event (both absolute values and relative to the seasonal values), the duration and type of event, as well as the level and preparedness of the participants.

Note that a given environmental condition that is bearable for athletes mid-season can be a risk at the beginning of the season, when they may not yet be heat acclimatised. As such, the first unseasonably hot days of the year (early spring, summer) are to be approached with caution.

Guidelines for training and competing in the heat

Here we address frequently asked questions raised by athletes and their staff.

What is the best way to prepare for exercise in the heat?

The best way to prepare for competing in the heat is to heat acclimatise. Some degree of heat acclimatisation is achieved by regular training, even in cool conditions, but the most efficient method for obtaining all benefits is to train in conditions similar to those expected during the competition. The most notable adaptations of the body to repeated training in the heat include an increased sweat rate, a decreased heart rate at a given intensity, a better retention of electrolytes and a decreased body core temperature. These adaptations will not only contribute to enhanced performance in the heat, but also to minimised risk of developing heat illness.

How much time is required to heat acclimatise?

Most adaptations develop within 7–10 days, but performance may keep increasing for two weeks. Importantly, there are large individual differences between athletes in the rate and magnitude of adaptations related to heat acclimatisation. As such, athletes preparing for an event to be held in hot and/or humid conditions should train in a similar environment for two weeks prior to competition. Conducting an initial heat acclimatisation camp several weeks before the event may increase the speed at which adaptation reoccurs in a pre-competition camp.

Are there alternative ways to heat acclimatise in a cold environment?

If it is not possible to train in the same environment as will be encountered during the competition, most adaptations can be acquired by artificially simulating heat during indoor training (e.g. via an environmental chamber, or an alternative heat source with no fan). It is also possible to use passive heat acclimatisation techniques such as hot-water immersion or sauna bathing for 30–40 minutes post-training. Water temperature should be 40–43°C, to induce adaptation while remaining tolerable (this can be easily measured with a floating pool thermometer). Although these techniques are not as specific as exercise heat acclimatisation, they can be used before travelling to events in a hot environment, to reduce the time required for acclimatisation on arrival.

What can an athlete do on the day of the event to prevent heat stress?

Minimise unnecessary heat exposure and heat gain prior to competing whenever possible. Athletes should warm up in the shade. Athletes may consider external pre-cooling methods (ice-vests, cold towels or fanning) and internal methods (cold fluid or ice slurry ingestion). A practical approach might be the use of fans and commercially available ice-cooling vests during warm-up, which can provide effective cooling without affecting optimal muscle temperature and function. Any cooling method should be tested and individualised during training to minimise disruption to the athlete on the day of the competition due to unexpected adverse effects or discomfort.

How much do I drink when exercising in the heat?

During exercise, it is recommended that hydration regimens be individualised to each athlete based on their sweat rate, to prevent excessive body mass loss. This individual prescription has to remain within the limits of how much fluid can be absorbed (~1.2 L/h). It is also important to recognise that hydration regimens should never result in overhydration, as this can result in serious health consequences (i.e. hyponatraemia).

Simple techniques such as measuring body weight before and after exercise can help athletes to

assess fluid loss through sweating and estimate their hydration needs and status. During training camps, athletes can monitor change in morning body weight (post-void), urine colour or urine specific gravity, to detect a change in hydration status, based on a series of daily measurements. For example, a decrease in morning body weight of 2% or more is suggestive of dehydration.

What should I drink when exercising in the heat?

During exercise lasting longer than one hour, it is advisable to add electrolyte tablets or the equivalent pinch of salt to water, especially for athletes prone to experiencing muscle cramping. It is also advisable to include 30–60 g of carbohydrates per hour for exercise lasting longer than one hour, and up to 90 g/h for events lasting over 2.5 hours. This can be achieved through a combination of fluids and solid foods. Following training or competing in the heat, recovery drinks should include sodium, carbohydrates and protein to optimise recovery. The preferred method of rehydration is through the consumption of fluids with foods, including salty food.

Are there any other precautions the athlete should take?

Athletes should protect their eyes by wearing UV-blocking sunglasses in a dark tint (i.e. grade 3) and their skin by using non-greasy sunscreen. Lightly coloured clothing can also minimise the effect of the sun's radiation, but clothing should not impair sweat evaporation. Other preventive measures include external pre-cooling (e.g. ice-vest), internal pre-cooling (e.g. ice slushy) and combining different cooling strategies. Athletes should also adapt their clothing (e.g. mesh clothing, well-ventilated helmets).

Future directions: from heat stress to heat therapy

Although exercising in the heat can challenge health and performance, it can also be a therapeutic opportunity for clinicians. For example, repeated passive heat exposure may induce mitochondrial adaptations,[120] promote muscle capillary growth[121] and improve cardiovascular health,[122] potentially benefiting patients with limited exercise capabilities. In addition, absolute intensity is lower for a given relative intensity when exercising in the heat.[32] This may therefore benefit injured athletes who need to maintain their fitness during a period of reduced loading.

Heat stress can facilitate hypertrophy in cultured cells[123, 124] or animals.[125] Heat stress also increases protein content and facilitates the recovery of atrophied muscle after an immobilisation period,[126] and has been shown to increase recovery following chemically induced muscle injury in rats.[127] Repeated passive heat exposures improve muscle cross-sectional area[128] and muscle function in humans (Fig. 2 3.11).[129] As such, heat exposures may be used with athletes and patients during a period of musculoskeletal unloading, such as post-surgical immobilisation.

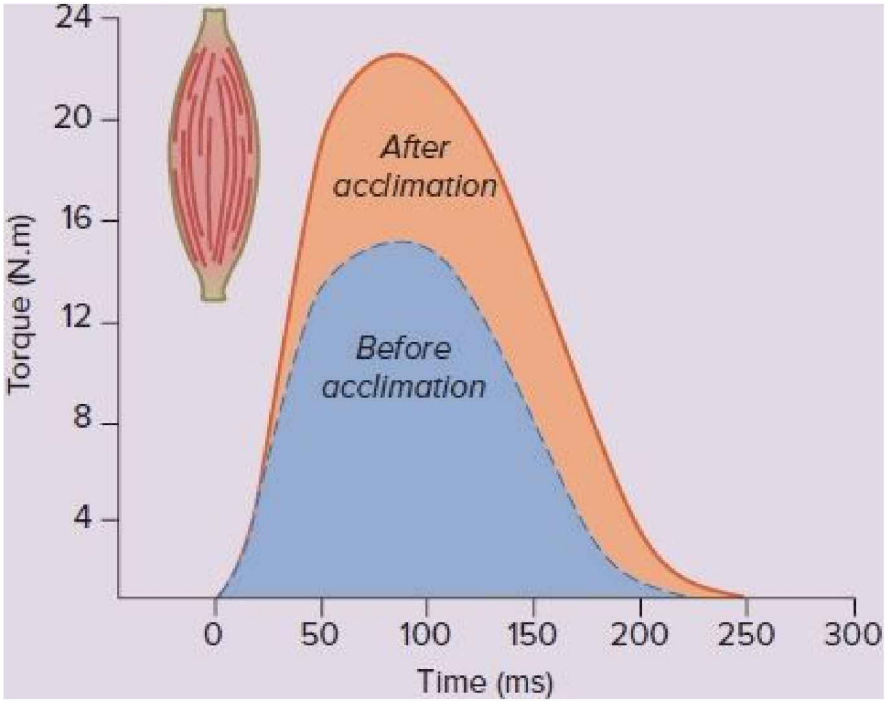


Figure 23.11 Repeated heat exposure increases muscle contractility

COURTESY OF SÉBASTIEN RACINAIS

SUMMARY

Humans have large autonomic adaptation capacities to heat. To acclimatise to heat, athletes should train in the heat for at least one week and ideally two weeks before an event. While exercising in the heat, one should also be careful to undertake exercise in a euhydrated state and minimise body water deficits through proper rehydration during exercise (without overhydrating). Although heat acclimatisation is the most important countermeasure, there are also a range of cooling methods that can reduce thermal and physiological strain, especially when the environmental conditions are non-compensable.

Medical teams should be aware of and trained on the continuum of heat-related conditions and be equipped to deal with them. This includes having clear algorithms for athlete management, rectal probes and a sodium analyser for diagnosis, and cold baths for treatment. Prevention includes minimising the thermal load (e.g. timing of the event, shade), allowing recovery periods (e.g. hydration and cooling) and providing relevant information in advance (e.g. booklets on acclimatisation).

REFERENCES

1. Leon LR, Bouchama A. Heat stroke. *Compr Physiol* 2015; 5(2): 611–47. doi: 10.1002/cphy.c140017.

2. Stearns RL, Casa DJ, O'Connor F et al. Exertional heat stroke. In: Casa DJ, Stearns RL, eds. *Preventing sudden death in sport and physical activity*. 2nd ed. Burlington: Jones & Bartlett Learning, 2017: 71–96.
3. Racinais S, Cocking S, Périard JD. Sports and environmental temperature: from warming-up to heating-up. *Temperature (Austin)* 2017; 4(3): 227–57.
4. González-Alonso J, Quistorff B, Krustrup P et al. Heat production in human skeletal muscle at the onset of intense dynamic exercise. *J Physiol* 2000; 524(Pt 2): 603–15.
5. Saltin B, Gagge AP, Stolwijk JA. Muscle temperature during submaximal exercise in man. *J Appl Physiol* 1968; 25(6): 679–88.
6. Havenith G, Fiala D. Thermal indices and thermophysiological modeling for heat stress. *Compr Physiol* 2016; 6(1): 255–302.
7. Asmussen E, Bøje O. Body temperature and capacity for work. *Acta Physiol Scand* 1945; 10: 1–22.
8. Close R, Hoh JF. Influence of temperature on isometric contractions of rat skeletal muscles. *Nature* 1968; 217(5134): 1179–80.
9. Racinais S, Oksa J. Temperature and neuromuscular function. *Scand J Med Sci Sports* 2010; 20 Suppl 3: 1–18.
10. Ward MR, Thesleff S. The temperature dependence of action potentials in rat skeletal muscle fibres. *Acta Physiol Scand* 1974; 91(4): 574–6.
11. Buchthal F, Kaiser E, Knappeis GG. Elasticity, viscosity and plasticity in the cross striated muscle fibre. *Acta Physiol Scand* 1944; 8: 16–37.
12. Wright V, Johns RJ. Quantitative and qualitative analysis of joint stiffness in normal subjects and in patients with connective tissue diseases. *Ann Rheum Dis* 1961; 20: 36–46.
13. Karvonen J. Warming up and its physiological effects. *Acta Universitatis Ouluensis* 1978; 31.
14. McCutcheon LJ, Geor RJ, Hinchcliff KW. Effects of prior exercise on muscle metabolism during sprint exercise in horses. *J Appl Physiol (1985)* 1999; 87(5): 1914–22.
15. Theorell H. The effect of temperature on myoglobin. *Biochem Z* 1934; 73: 268.
16. Davidoff RA. Skeletal muscle tone and the misunderstood stretch reflex. *Neurology* 1992; 42(5): 951–63.
17. Proske U, Morgan DL, Gregory JE. Thixotropy in skeletal muscle and in muscle spindles: a review. *Prog Neurobiol* 1993; 41(6): 705–21.
18. Bishop D. Warm up I: potential mechanisms and the effects of passive warm up on exercise performance. *Sports Med* 2003; 33(6): 439–54.
19. Malareki I. Investigation of physiological justification of so-called 'warming up'. *Acta Physiol Pol* 1954; 5: 543–6.

20. Barnard RJ, Gardner GW, Diaco NV et al. Cardiovascular responses to sudden strenuous exercise—heart rate, blood pressure, and ECG. *J Appl Physiol* 1973; 34(6): 833–7.
21. Barnard RJ, MacAlpin R, Kattus AA et al. Ischemic response to sudden strenuous exercise in healthy men. *Circulation* 1973; 48(5): 936–42.
22. González-Alonso J, Teller C, Andersen SL et al. Influence of body temperature on the development of fatigue during prolonged exercise in the heat. *J Appl Physiol (1985)* 1999; 86(3): 1032–9.
23. Cheuvront SN, Kenefick RW, Montain SJ et al. Mechanisms of aerobic performance impairment with heat stress and dehydration. *J Appl Physiol (1985)* 2010; 109(6): 1989–95.
24. Périard JD, Racinais S. Self-paced exercise in hot and cool conditions is associated with the maintenance of %$\dot{V}O_2$peak within a narrow range. *J Appl Physiol (1985)* 2015; 118(10): 1258–65.
25. Johnson JM. Regulation of skin circulation during prolonged exercise. *Ann N Y Acad Sci* 1977; 301: 195–212.
26. Johnson JM, Park MK. Reflex control of skin blood flow by skin temperature: role of core temperature. *J Appl Physiol Respir Environ Exerc Physiol* 1979; 47(6): 1188–93.
27. Johnson JM. Nonthermoregulatory control of human skin blood flow. *J Appl Physiol (1985)* 1986; 61(5): 1613–22.
28. Rowell LB. Human cardiovascular adjustments to exercise and thermal stress. *Physiol Rev* 1974; 54(1): 75–159.
29. Fritzsche RG, Switzer TW, Hodgkinson BJ et al. Stroke volume decline during prolonged exercise is influenced by the increase in heart rate. *J Appl Physiol (1985)* 1999; 86(3): 799–805.
30. Coyle EF, González-Alonso J. Cardiovascular drift during prolonged exercise: new perspectives. *Exerc Sport Sci Rev* 2001; 29(2): 88–92.
31. Trinity JD, Pahnke MD, Lee JF et al. Interaction of hyperthermia and heart rate on stroke volume during prolonged exercise. *J Appl Physiol (1985)* 2010; 109(3): 745–51.
32. Bassett DR, Howley ET. Limiting factors for maximum oxygen uptake and determinants of endurance performance. *Med Sci Sports Exerc* 2000; 32(1): 70–84.
33. di Prampero PE. Factors limiting maximal performance in humans. *Eur J Appl Physiol* 2003; 90(3–4): 420–9.
34. Sawka MN, Young AJ, Cadarette BS et al. Influence of heat stress and acclimation on maximal aerobic power. *Eur J Appl Physiol Occup Physiol* 1985; 53(4): 294–8.
35. Arngrïmsson SA, Stewart DJ, Borrani F et al. Relation of heart rate to percent VO_2 peak during submaximal exercise in the heat. *J Appl Physiol (1985)* 2003; 94(3): 1162–8.
36. Wingo JE, Lafrenz AJ, Ganio MS et al. Cardiovascular drift is related to reduced

maximal oxygen uptake during heat stress. *Med Sci Sports Exerc* 2005; 37(2): 248–55.

37. Robertson RJ. Central signals of perceived exertion during dynamic exercise. *Med Sci Sports Exerc* 1982; 14(5): 390–6.
38. Cabanac M. Sensory pleasure optimizes muscular work. *Clin Invest Med* 2006; 29(2): 110–16.
39. Racinais S, Girard O. Neuromuscular failure is unlikely to explain the early exercise cessation in hot ambient conditions. *Psychophysiology* 2012; 49(6): 853–65.
40. Ely BR, Ely MR, Cheuvront SN et al. Evidence against a 40 degrees C core temperature threshold for fatigue in humans. *J Appl Physiol (1985)* 2009; 107(5): 1519–25.
41. Périard JD, Cramer MN, Chapman PG et al. Cardiovascular strain impairs prolonged self-paced exercise in the heat. *Exp Physiol* 2011; 96(2): 134–44.
42 Racinais S, Périard JD, Karlsen A, et al. Effect of heat and heat acclimatization on cycling time trial performance and pacing. Med Sci Sports Exerc. 2015;47(3):601–606.
43. Byrne C, Lee JKW, Chew SAN, et al. Continuous thermoregulatory responses to mass-participation distance running in heat. Med Sci Sports Exerc 2006;38:803-10. Racinais S, Moussay S, Nichols D, Travers G, Belfekih T. Schumacher Y, Périard JD. Core temperature up to 41.5ºC during the UCI Road Cycling World Championships in the heat. *Br J Sports Med*. 2018 (in press)
44. Morrison S, Sleivert GG, Cheung SS. Passive hyperthermia reduces voluntary activation and isometric force production. *Eur J Appl Physiol* 2004; 91(5–6): 729–36.
45. Racinais S, Gaoua N, Grantham J. Hyperthermia impairs short-term memory and peripheral motor drive transmission. *J Physiol* 2008; 586(Pt 19): 4751–62.
46. Schmit C, Hausswirth C, Le Meur Y et al. Cognitive functioning and heat strain: performance responses and protective strategies. *Sports Med* 2017; 47(7): 1289–302.
47. Cian C, Barraud PA, Melin B et al. Effects of fluid ingestion on cognitive function after heat stress or exercise-induced dehydration. *Int J Psychophysiol* 2001; 42(3): 243–51.
48. Hocking C, Silberstein RB, Lau WM et al. Evaluation of cognitive performance in the heat by functional brain imaging and psychometric testing. *Comp Biochem Physiol A Mol Integr Physiol* 2001; 128(4): 719–34.
49. Pilcher JJ, Nadler E, Busch C. Effects of hot and cold temperature exposure on performance: a meta-analytic review. *Ergonomics* 2002; 45(10): 682–98.
50. Hancock PA, Vasmatzidis I. Effects of heat stress on cognitive performance: the current state of knowledge. *Int J Hyperthermia* 2003; 19(3): 355–72.
51. Gaoua N, Grantham J, El Massioui F et al. Cognitive decrements do not follow neuromuscular alterations during passive heat exposure. *Int J Hyperthermia* 2011; 27(1): 10–19.

52. Gaoua N, Grantham J, Racinais S et al. Sensory displeasure reduces complex cognitive performance in the heat. *J Environ Psychol* 2012; 32: 158–63.
53. Gaoua N, Racinais S, Grantham J et al. Alterations in cognitive performance during passive hyperthermia are task dependent. *Int J Hyperthermia* 2011; 27(1): 1–9.
54. Gosling CM, Gabbe BJ, McGivern J et al. The incidence of heat casualties in sprint triathlon: the tale of two Melbourne race events. *J Sci Med Sport* 2008; 11(1): 52–7.
55. Nybo L, González-Alonso J. Critical core temperature: a hypothesis too simplistic to explain hyperthermia-induced fatigue. *Scand J Med Sci Sports* 2015; 25: 4–5.
56. Dill DB, Jones BF, Edwards HT et al. Salt economy in extreme dry heat. *J Biol Chem* 1933; 100(3): 755–67.
57. Adolph EF, Dill DB. Observations on water metabolism in the desert. *Am J Physiol* 1938; 123(2): 369–78.
58. Dill DB, Hall FG, Edwards HT. Changes in composition of sweat during acclimatization to heat. *Am J Physiol* 1938; 123(2): 412–19.
59. Eichna LW, Park CR, Nelson N et al. Thermal regulation during acclimatization in a hot, dry (desert type) environment. *Am J Physiol* 1950; 163(3): 585–97.
60. Sawka MN, Wenger CB, Pandolf KB. Thermoregulatory responses to acute exercise-heat stress and heat acclimation. In: Fregly MJ, Blatteis CM, eds. *Handbook of physiology*. New York, NY: Comprehensive Physiology, 1996: 157–85.
61. Sawka MN, Leon LR, Montain SJ et al. Integrated physiological mechanisms of exercise performance, adaptation, and maladaptation to heat stress. *Compr Physiol* 2011; 1(4): 1883–928.
62. Racinais S, Alonso JM, Coutts AJ et al. Consensus recommendations on training and competing in the heat. *Scand J Med Sci Sports* 2015; 25: 6–19.
63. Wyndham CH, Williams CG, Morrison JF et al. Tolerance of very hot humid environments by highly acclimatized Bantu at rest. *Br J Ind Med* 1968; 25(1): 22–39.
64. Senay LC. Effects of exercise in the heat on body fluid distribution. *Med Sci Sports* 1979; 11(1): 42–8.
65. Patterson MJ, Stocks JM, Taylor NAS. Sustained and generalized extracellular fluid expansion following heat acclimation. *J Physiol* 2004; 559(Pt 1): 327–34.
66. Patterson MJ, Stocks JM, Taylor NAS. Whole-body fluid distribution in humans during dehydration and recovery, before and after humid-heat acclimation induced using controlled hyperthermia. *Acta Physiol (Oxf)* 2014; 210(4): 899–912.
67. Nielsen B, Hales JR, Strange S et al. Human circulatory and thermoregulatory adaptations with heat acclimation and exercise in a hot, dry environment. *J Physiol* 1993; 460: 467–85.
68. Périard JD, Travers GJS, Racinais S et al. Cardiovascular adaptations supporting human exercise-heat acclimation. *Auton Neurosci* 2016; 196: 52–62.
69. Sawka MN, Coyle EF. Influence of body water and blood volume on

thermoregulation and exercise performance in the heat. *Exerc Sport Sci Rev* 1999; 27: 167–218.

70. Watt MJ, Garnham AP, Febbraio MA et al. Effect of acute plasma volume expansion on thermoregulation and exercise performance in the heat. *Med Sci Sports Exerc* 2000; 32(5): 958–62.
71. Racinais S, Mohr M, Buchheit M et al. Individual responses to short-term heat acclimatisation as predictors of football performance in a hot, dry environment. *Br J Sports Med* 2012; 46(11): 810–15.
72. Racinais S, Buchheit M, Bilsborough J et al. Physiological and performance responses to a training camp in the heat in professional Australian football players. *Int J Sports Physiol Perform* 2014; 9(4): 598–603.
73. Karlsen A, Nybo L, Norgaard SJ et al. Time course of natural heat acclimatization in well-trained cyclists during a 2-week training camp in the heat. *Scand J Med Sci Sports* 2015; 25 Suppl 1: 240–9.
74. MacDonald DKC, Wyndham CH. Heat transfer in man. *J Appl Physiol* 1950; 3(6): 342–64.
75. Ladell WS. Assessment of group acclimatization to heat and humidity. *J Physiol* 1951; 115(3): 296–312.
76. Périard JD, Racinais S, Sawka MN. Adaptations and mechanisms of human heat acclimation: applications for competitive athletes and sports. *Scand J Med Sci Sports* 2015; 25: 20–38.
77. Shapiro Y, Moran D, Epstein Y. Acclimatization strategies— preparing for exercise in the heat. *Int J Sports Med* 1998; 19 Suppl 2: S161–3.
78. Sunderland C, Morris JG, Nevill ME. A heat acclimation protocol for team sports. *Br J Sports Med* 2008; 42(5): 327–33.
79. Garrett AT, Rehrer NJ, Patterson MJ. Induction and decay of short-term heat acclimation in moderately and highly trained athletes. *Sports Med* 2011; 41(9): 757–71.
80. Chalmers S, Esterman A, Eston R et al. Short-term heat acclimation training improves physical performance: a systematic review, and exploration of physiological adaptations and application for team sports. *Sports Med* 2014; 44(7): 971–88.
81. Lorenzo S, Halliwill JR, Sawka MN et al. Heat acclimation improves exercise performance. *J Appl Physiol (1985)* 2010; 109(4): 1140–7.
82. Nadel ER, Fortney SM, Wenger CB. Effect of hydration state of circulatory and thermal regulations. *J Appl Physiol Respir Environ Exerc Physiol* 1980; 49(4): 715–21.
83. Fortney SM, Wenger CB, Bove JR et al. Effect of hyperosmolality on control of blood flow and sweating. *J Appl Physiol Respir Environ Exerc Physiol* 1984; 57(6): 1688–95.
84. Montain SJ, Latzka WA, Sawka MN. Control of thermoregulatory sweating is altered

by hydration level and exercise intensity. *J Appl Physiol (1985)* 1995; 79(5): 1434–9.

85. González-Alonso J, Mora-Rodríguez R, Below PR et al. Dehydration reduces cardiac output and increases systemic and cutaneous vascular resistance during exercise. *J Appl Physiol (1985)* 1995; 79(5): 1487–96.
86. González-Alonso J, Calbet JA, Nielsen B. Muscle blood flow is reduced with dehydration during prolonged exercise in humans. *J Physiol* 1998; 513(Pt 3): 895–905.
87. Stöhr EJ, González-Alonso J, Pearson J et al. Dehydration reduces left ventricular filling at rest and during exercise independent of twist mechanics. *J Appl Physiol (1985)* 2011; 111(3): 891–7.
88. Adolph EF. *Physiology of Man in the Desert*. New York: Interscience, 1947.
89. Sawka MN, Toner MM, Francesconi RP et al. Hypohydration and exercise: effects of heat acclimation, gender, and environment. *J Appl Physiol Respir Environ Exerc Physiol* 1983; 55(4): 1147–53.
90. Sawka MN. Physiological consequences of hypohydration: exercise performance and thermoregulation. *Med Sci Sports Exerc* 1992; 24(6): 657–70.
91. González-Alonso J, Mora-Rodríguez R, Coyle EF. Stroke volume during exercise: interaction of environment and hydration. *Am J Physiol Heart Circ Physiol* 2000; 278(2): H321–30.
92. MacLaren A. *Training, in Theory and Practice*. London, England: Macmillan and Company, 1866.
93. Shelley WB. You're in the army now: World War II flame-thrower research at Fort Knox. *Int J Dermatol* 2007; 46(3): 323–9.
94. Pitts GC, Johnson RE. Work in the heat as affected by intake of water, salt and glucose. *Am J Physiol* 1944; 142: 253–9.
95. Moroff SV, Bass DE. Effects of overhydration on man's physiological responses to work in the heat. *J Appl Physiol* 1965; 20(2): 267–70.
96. Buskirk ER, Iampietro PF, Bass DE. Work performance after dehydration: effects of physical conditioning and heat acclimatization. *J Appl Physiol* 1958; 12(2): 189–94.
97. Cohen D. The truth about sports drinks. *BMJ* 2012; 345: e4737.
98. Goulet EDB. Effect of exercise-induced dehydration on time-trial exercise performance: a meta-analysis. *Br J Sports Med* 2011; 45(14): 1149–56.
99. Goulet EDB. Effect of exercise-induced dehydration on endurance performance: evaluating the impact of exercise protocols on outcomes using a meta-analytic procedure. *Br J Sports Med* 2013; 47(11): 679–86.
100. Wall BA, Watson G, Peiffer JJ et al. Current hydration guidelines are erroneous: dehydration does not impair exercise performance in the heat. *Br J Sports Med* published online 20 September 2013. doi: 10.1136/bjsports-2013-092417.
101. Cotter JD, Thornton SN, Lee JK et al. Are we being drowned in hydration advice? Thirsty for more? *Extrem Physiol Med* 2014; 3(1): 18.

102. Adams WC, Fox RH, Fry AJ et al. Thermoregulation during marathon running in cool, moderate, and hot environments. *J Appl Physiol* 1975; 38(6): 1030–7.
103. Bergeron MF, Maresh CM, Armstrong LE et al. Fluid-electrolyte balance associated with tennis match play in a hot environment. *Int J Sport Nutr* 1995; 5(3): 180–93.
104. Shirreffs SM, Sawka MN, Stone M. Water and electrolyte needs for football training and match-play. *J Sports Sci* 2006; 24(7): 699–707.
105. Costill DL. Sweating: its composition and effects on body fluids. *Ann N Y Acad Sci* 1977; 301: 160–74.
106. Verde T, Shephard RJ, Corey P et al. Sweat composition in exercise and in heat. *J Appl Physiol Respir Environ Exerc Physiol* 1982; 53(6): 1540–5.
107. Institute of Medicine (US). *DRI, Dietary Reference Intakes for Water, Potassium, Sodium, Chloride, and Sulfate*. Washington DC: National Academies Press, 2004.
108. Bergeron MF. Muscle cramps during exercise—is it fatigue or electrolyte deficit? *Curr Sports Med Rep* 2008; 7(4): S50–5.
109. Casa DJ. Exercise in the heat. II. Critical concepts in rehydration, exertional heat illnesses, and maximizing athletic performance. *J Athl Train* 1999; 34(3): 253–62.
110. von Duvillard SP, Braun WA, Markofski M et al. Fluids and hydration in prolonged endurance performance. *Nutrition* 2004; 20(7–8): 651–6.
111. American College of Sports Medicine, Sawka MN, Burke LM et al. American College of Sports Medicine position stand. Exercise and fluid replacement. *Med Sci Sports Exerc* 2007; 39(2): 377–90.
112. Bergeron MF. Heat cramps: fluid and electrolyte challenges during tennis in the heat. *J Sci Med Sport* 2003; 6(1): 19–27.
113. Zouhal H, Groussard C, Minter G et al. Inverse relationship between percentage body weight change and finishing time in 643 forty-two-kilometre marathon runners. *Br J Sports Med* 2011; 45(14): 1101–5.
114. Noakes TD, Goodwin N, Rayner BL et al. Water intoxication: a possible complication during endurance exercise. *Med Sci Sports Exerc* 1985; 17(3): 370–5.
115. Noakes TD. Overconsumption of fluids by athletes. *BMJ* 2003; 327(7407): 113–14.
116. Almond CSD, Shin AY, Fortescue EB et al. Hyponatremia among runners in the Boston Marathon. *N Engl J Med* 2005; 352(15): 1550–6.
117. Casa DJ, McDermott BP, Lee EC et al. Cold water immersion: the gold standard for exertional heatstroke treatment. *Exerc Sport Sci Rev* 2007; 35(3) 141-149.
118. Korey Stringer Institute. Wet bulb globe temperature monitoring. https://ksi.uconn.edu/prevention/wet-bulb-globe-temperature-monitoring/.
119. Racinais S, Palfreeman R, Schumacher YO et al. Beat the heat. http://www.ephysiol.com/international-sports-federations/UCIen
120. Tamura Y, Matsunaga Y, Masuda H et al. Postexercise whole body heat stress

additively enhances endurance training-induced mitochondrial adaptations in mouse skeletal muscle. *Am J Physiol Regul Integr Comp Physiol* 2014; 307(7): R931–43.

121. Kuhlenhoelter AM, Kim K, Neff D et al. Heat therapy promotes the expression of angiogenic regulators in human skeletal muscle. *Am J Physiol Regul Integr Comp Physiol* 2016; 311(2): R377–91.
122. Brunt VE, Howard MJ, Francisco MA et al. Passive heat therapy improves endothelial function, arterial stiffness and blood pressure in sedentary humans. *J Physiol* 2016; 594(18): 5329–42.
123. Yamashita-Goto K, Ohira Y, Okuyama R et al. Heat stress facilitates stretch-induced hypertrophy of cultured muscle cells. *J Gravit Physiol* 2002; 9(1): P145–6.
124. Goto K, Okuyama R, Sugiyama H et al. Effects of heat stress and mechanical stretch on protein expression in cultured skeletal muscle cells. *Pflugers Arch* 2003; 447(2): 247–53.
125. Uehara K, Goto K, Kobayashi T et al. Heat-stress enhances proliferative potential in rat soleus muscle. *Jpn J Physiol* 2004; 54(3): 263–71.
126. Goto K, Honda M, Kobayashi T et al. Heat stress facilitates the recovery of atrophied soleus muscle in rat. *Jpn J Physiol* 2004; 54(3): 285–93.
127. Kojima A, Goto K, Morioka S et al. Heat stress facilitates the regeneration of injured skeletal muscle in rats. *J Orthop Sci* 2007; 12(1): 74–82.
128. Goto K, Oda H, Kondo H et al. Responses of muscle mass, strength and gene transcripts to long-term heat stress in healthy human subjects. *Eur J Appl Physiol* 2011; 111(1): 17–27.
129. Racinais S, Wilson MG, Périard JD. Passive heat acclimation improves skeletal muscle contractility in humans. *Am J Physiol Regul Integr Comp Physiol* 2017; 312(1): R101–7.
130. https://youtu.be/_OLjy_rZbZ4
131. https://www.theguardian.com/sport/video/2016/sep/19/alistair-brownlee-gives-chance-win-helps-brother-jonny-video
132. https://www.theguardian.com/sport/2016/sep/19/alistair-brownlee-jonny-world-triathlon-series https://www.bbc.com/sport/triathlon/37402716
133. https://en.wikipedia.org/wiki/Korey_Stringer
134. www.nytimes.com/2001/08/02/sports/pro-football-heat-kills-a-pro-football-player-nfl-orders-a-training-review.html
135. https://ksi.uconn.edu/2017/08/01/korey-stringers-death-lingers-on-a-final-trip-to-mankato-espn/
136. https://ksi.uconn.edu/about/koreys-story/

Chapter 24

Cold

with MIKE TIPTON

Man in the cold is not necessarily a cold man.
David Bass, Yale University environmental physiologist, 1960

Sports and physical activity often take place in cold environments. Normal deep body homeostatic temperature in humans is around 37°C (99°F). When ambient air temperature drops below 28°C, the human body must either reduce heat loss (e.g. via insulation) or produce sufficient heat through activity to maintain homeostasis. Hypothermic injury results when these conditions are not met. At the 2018 Winter Olympics, in PyeongChang, temperatures reached - 14°C (-7°F), leading to significant challenges for the athletes. As discussed in the previous chapter thermally induced injuries, including drowning, are a common cause of death in people undertaking sport. The primary focus of this chapter is to:

- review thermoregulation of the human body in cold environments
- demonstrate how to measure environmental and body temperatures in the cold
- look at the impact of cold on performance
- discuss the effects of cold air and water: medical risks and mitigation
- briefly review treatment approaches to freezing and non-freezing cold injuries and health screening for sport in cold environments.

THERMOREGULATION IN THE COLD

For the body to be in heat balance, the physical routes of heat exchange (conduction, convection, evaporation and radiation) must match heat production or gain, such that heat storage or debt does not occur. This is important biophysical knowledge, but what is sometimes forgotten is that alongside these physical pathways lies a thermoregulatory system attempting to maintain thermal homeostasis. To achieve homeostasis there are thermal sensors distributed throughout the body,

especially the skin and central nervous system. These transient receptor potential cation channels can respond, or be inhibited by, heat and cold. They are also activated by different chemical stimuli (e.g. menthol: TRPM8 'cold'; capsaicin: TRPM1 'hot'), hence the use of such chemicals in cooling or warming products. It is worth noting these effects are primarily sensory.

The distribution of cold and warm receptors varies throughout the body. Again, this is interesting, but for the clinician it is the relative sensitivity of the different body sites for determining thermoregulatory effector responses that is perhaps more useful. In this regard, the hierarchy for the thermoregulatory effector responses (skin blood flow, sweating, shivering) is:

Deep body temperature → Mean skin temperature → Local skin temperature

The predominance of deep body temperature (T_{db}) in determining thermoregulatory effector responses explains, for example, why hand immersion in cold water can be used to cool hyperthermic individuals (skin blood flow 3 L/min), but hand immersion in warm water will not rewarm hypothermic individuals (skin blood flow 20 mL/min).[1, 2] It also explains why the best way to avoid cold injuries to the extremities is to maintain, or raise slightly, deep body temperature and thereby maintain blood flow (heat supply) to the hands (Fig. 24.1). As T_{db} falls, the body will withdraw blood from the extremities, physiologically amputating and thereby 'sacrificing' them in an attempt to maximise body insulation and protect essential deep body organs.

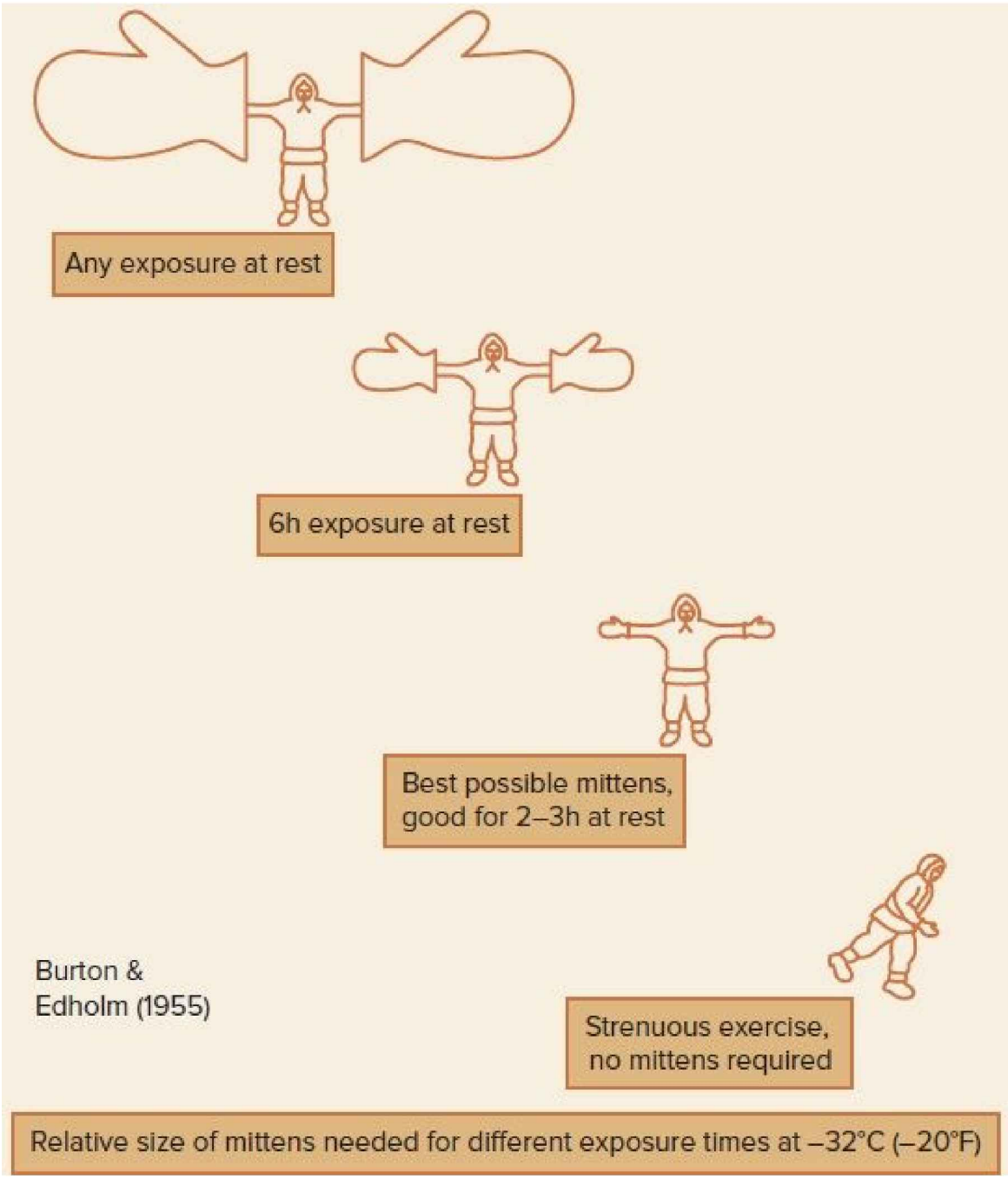


Figure 24.1 Impact of exercise (raised deep body temperature) on blood flow to the hands and the maintenance of hand skin temperature (avoidance of cold injury)

ADAPTED FROM BURTON & EDHOLM (1955)[3]

Deep body temperature increases with exercise; it will do this in all air environments. For the clinician, the critical information is whether or not an increase or fall in T_{db} is 'compensable', that is, whether the thermoregulatory system of an individual can move them into thermal balance, albeit at a higher or lower deep body temperature (in the thermoregulatory zone). One needs to worry less about an individual with a raised or lowered deep body temperature that is stable (in quasi steady-state/heat balance) than someone at the same deep body temperature whose temperature is increasing or falling; it is those individuals, whose thermoregulatory system is being overwhelmed, who will become hyperthermic or hypothermic.

Page 346

Effect of cold environments on the cardiovascular and respiratory systems

Vasoconstriction may lead to fluid shifts by increasing the central blood volume, thus causing a cold diuresis. This diuresis, in conjunction with the increased fluid loss from respiration and sweat during exercise, may reduce total circulating volume. On rewarming, peripheral vessels dilate and cause a fluid shift to the periphery, with a further reduction in central circulation. Decreased cardiac output occurs because of a combination of reduced circulatory volume, myocardial depression and impaired electrical conductance.

Impaired conductance results in a decreased heart rate and ECG changes, with prolongation of all intervals. The presence of a J wave in the ST segment is indicative of hypothermia.

Atrial fibrillation may occur and usually reverts with rewarming. Ventricular fibrillation may occur and may be refractory to treatment at very low temperatures.

Cold water exposure results in hyperventilation with a resultant respiratory heat and water loss, especially if the air over the water is cold and dry (Figure 24.2). This may contribute to dehydration and bronchospasm. A decrease in core temperature is also associated with a reduction in airway protective mechanisms, with subsequent increased risk of aspiration. There is, however, no direct damage to the lung from exposure to cold, because of the effective heating and humidifying mechanism of the upper airway.

Page 347

Figure 24.2 Winter Swimming World Championships 2014 in Rovaniemi, Finland. Cold water exposure results in hyperventilation, with a resultant respiratory heat and water loss which may contribute to dehydration and bronchospasm

VW PICS/UIG VIA GETTY IMAGES

Other effects

Delayed nerve conduction and neuromuscular transmission cause numbness, uncoordinated movements and impaired cognition. These may persist for some time after the core temperature returns to normal.

Muscle stiffness and weakness associated with mild hypothermia and muscle cooling may lead to an increased risk of muscle tears. Adequate warm-up and stretching should be performed prior to muscular activity in cold conditions.

Excessive shivering may lead to poor voluntary muscular control, decreased efficiency and increased fatigue. Hypothermia may inhibit glycolysis and fat metabolism, affecting both speed and endurance. Renal function can be impaired due to decreased renal blood flow,[5] and coagulopathies can occur.[6]

MEASURING ENVIRONMENTAL AND BODY TEMPERATURES IN THE COLD

The cooling power of the environment is the result of air temperature and air movement or movement through air (e.g. as when skiing). These factors are combined into the wind chill index, which illustrates the cooling effect of temperature and wind on bare skin and predicts the associated danger of cold injury (Table 24.1).

Table 24.1 Wind chill: effect of increasing wind speed on degree of cooling at different ambient temperatures

Ambient temperature (°C)										
	4	−1	−7	−12	−18	−23	−29	−34	−40	−46
Wind speed (miles/h)	Wind chill (equivalent) temperature[a] (°C)									
5	2	−4	−12	−15	−21	−26	−32	−37	−43	−48
10	−1	−9	−15	−23	−29	−37	−34	−51	−57	−62
15	−4	−12	−21	−29	−34	−43	−51	−57	−65	−73
20	−7	−15	−23	−32	−37	−46	−54	−62	−71	−79
25	−9	−18	−26	−34	−43	−51	−59	−68	−76	−84
30	−12	−18	−29	−34	−46	−54	−62	−71	−79	−87
35	−12	−21	−29	−37	−46	−54	−62	−73	−82	−90
40	−12	−21	−29	−37	−48	−57	−65	−73	−82	−90
	Less danger			Increasing danger. Flesh may freeze within a minute			Great danger. Flesh 30 seconds may freeze within			

(a) Equivalent temperature is the environmental temperature that would have the same effect on bare skin in the absence of any wind (equivalent cooling power).

Note: It is a physical impossibility for wind to reduce dry tissue temperature below that of air temperature, it simply brings it closer to it. However, if the skin or clothing are wet, the wind will increase evaporative cooling which can reduce tissue temperature below that of air temperature.

The risk of frostbite is low in air temperatures above -7°C, irrespective of wind speed, and becomes pronounced when ambient temperature is below -25°C, even at low wind speeds. Page 348 Fluids on the skin will greatly accentuate the rate of cooling and increase the threat of cold injuries. When exercising in cold environments, a calculation can be made of the minimum clothing insulation required by workers (known as IREQ), which gives a guide to the protection required for a given cold stress. Thermal comfort can then be fine-tuned by adjusting clothing insulation or training sessions as the exposure proceeds.[7]

The critical body temperatures to measure for the avoidance, or quantification, of thermal injuries are T_{db} and extremity skin temperatures (T_{sk}). Extremity T_{sk} can be measured easily with thermistors or thermocouples secured to the skin with tape. In laboratory tests, as a precaution against cold injuries, participants are withdrawn from cold environments when an extremity temperature falls below 4°C, or below 8°C for more than 15 minutes.

Although both this and Chapter 23 on heat discuss measurement of deep body temperature, the concept is somewhat problematic. What we refer to as a 'core' temperature does not exist.[8] Various sites are used to estimate core temperature: tympanic membrane (via IR thermometers or thermistors); gastric (via radio pill); rectum (thermistor); oesophagus (thermistor); sublingual (thermistor); axilla (thermistor); and mid-stream urine (thermistor). Some of these techniques are better suited to a laboratory than a sports setting. Unfortunately, those that are easier to measure (ear, mouth, axilla) are often the most unreliable and likely to give false low readings in the cold. The clinician dealing with either a heat or a cold injury must take into consideration the reliability

of the apparatus at their disposal when deciding upon a course of action.

Various T_{sk} measures (e.g. insulated spine [T2] temperature) have been used to attempt to predict T_{db}. More recently monitors have used insulated auditory canal temperature to estimate T_{db}. While these monitors reflect T_{db} in warm, uniform, windless laboratory conditions, they are less accurate for individuals in natural cold environments. Even in ideal conditions they work best if the monitors and computational algorithms are calibrated for individual users, clothing, climate and exercise scenarios.

PRACTICE PEARL

An attempt to take a temperature, using whichever method, should not be conducted within 30 minutes of the ingestion of hot or cold food.

IMPACT OF COLD ON PERFORMANCE

This chapter focuses on the clinical aspect of cold exposure; for a detailed exposition of the impact of cold on performance, the reader is referred to the review of Castellani and Tipton (2015).[9] Sports with a particularly high risk of cold injury include endurance running, skiing, cycling, mountaineering, hiking, caving and water sports. Hypothermia is not generally an issue for fit, functioning and reasonably insulated athletes (see below). Cooling of the extremities is more likely, and results in discomfort and thereby distraction. This is important for sports requiring fine motor control and concentration. As noted, extremity T_{sk} is best maintained by insulation (both to the extremities and torso)[10] and the maintenance or slight increase in T_{db} to maintain skin blood flow and thereby the delivery of heat to the extremities.[11]

More profound cold exposure leading to cooling of the superficial nerves and muscles (usually in the limbs) can result in physical incapacitation. The conduction of action potentials is slowed (15 m/s per 10°C fall in local temperature) and their amplitude reduced. Below a muscle temperature of 27°C the contractile force and rate of force application is reduced and fatigue occurs earlier; maximum power output falls by 3 % per degree Celsius fall in muscle temperature.[12, 13] As a consequence, speed of movement, dexterity, strength and mechanical efficiency are all reduced with cooling. One consequence is that the energy cost of submaximal work increases, and time to fatigue decreases with cooling. The time taken for these changes to occur depends on the exact nature of the environment (air or water temperature, wind speed, etc).

COLD AIR AND WATER: MEDICAL RISKS, MITIGATION AND TREATMENT

The risks of operating in cold air and water environments include: hypothermia, freezing and non-freezing cold injuries, dehydration, exhaustion, drowning and cardiac arrest. Individual susceptibility to these conditions varies significantly due to a wide range of factors, including: age,

fitness, morphology, sex, ethnicity and predisposing medical conditions (Tables 24.2 and 24.4).

Table 24.2 Risk factors for hypothermia

Cold air/water temperature	Standardised risk to all
Air/water movement	Faster moving fluids increase convective heat loss
Age	Children and small adults cool faster than large adults due to their lower levels of subcutaneous fat and l
Body stature	Tall thin individuals cool faster than short stocky people
Body morphology	Body fat and unperfused muscle are good insulators
Gender	Females tend to have more subcutaneous fat than males
Fitness	High fitness enables higher heat production
Fatigue	Exhaustion and hypoglycaemia attenuate shivering and accentuate cooling
Intoxication	Drug or alcohol depressant effects on metabolism
Lack of appropriate clothing	Insulation without windproofing, or vice versa

Table 24.4 Predisposing factors for frostbite and non- freezing cold injury

Physiological	Medical
Ethnicity (Afro-Caribbean descent)	Hypotension
Age	Atherosclerosis
Sex (female)	Arteritis
Hypothermia	Raynaud's syndrome
Prior NFCI	Vasospastic disorders
Trauma	Anaemia
Erythrodermas	Sickle cell disease
Hyperhidrosis	Diabetes
Hypoxia	Shock
Smoking	Vasoconstrictors
Energy depletion	
Poor physical conditioning	

Dehydration is common in cold environments because thirst is blunted, water is not always easily available (frozen), and respiratory water loss can be high in cold dry environments. Dehydration can increase the likelihood of incurring a cold injury. Cold exposure can result in a cold-induced diuresis due to raised central venous pressure; this is prevented by moderate exercise in the cold.[14]

Snow blindness and sunburn may occur in cold environments and can happen in cloudy as well as in bright sunlight conditions. Snow blindness results in severe pain, swelling and reddening of the eye, with profuse weeping. Goggles and high-factor (25 + SPF) sunscreen should be considered for snow and ice work.

A cold burn injury occurs when tissue freezes very quickly (often instantly) when coming into contact with a very cold conductive surface, such as a metal rail or a tool. T_{sk} of 0°C can occur within 2–6 s when touching metal surfaces that are at or below −15°C.[15]

Touching surfaces at ambient temperatures below 0°C with bare hands is not recommended. Wearing gloves and avoiding other skin contact with cold surfaces provides protection.

PRACTICE PEARL

It is recommended that caffeine and other diuretics are avoided prior to physical activity in the cold, to reduce the risk of dehydration.

Hypothermia

Hypothermia exists when deep body temperature falls below 35°C. Once thought to be a major and likely hazard of cold exposure, hypothermia can now be downgraded as a risk factor in both cold air and water, largely because other problems tend to occur sooner and are more likely. Nevertheless, hypothermia remains a risk in a range of circumstances and should be briefly considered here. The risk factors for hypothermia are presented in Table 24.2.

Prevention of hypothermia in the cold can be achieved by utilising clothing with ventilation during work (to avoid sweat accumulation) and using insulated garments or seeking shelter during rest. Regular hot meals should be eaten and headgear worn. Provided the athlete is active and therefore generating heat and reasonably insulated, they are unlikely to become hypothermic. The problems tend to arise with a reduction in heat production due to exhaustion, hypoglycaemia or injury.

It can be very difficult to diagnose hypothermia, and even death, due to the significant reduction in vital signs and the adverse climatic conditions under which the medical examination is likely to take place. Some of the clinical features of hypothermia are presented in Table 24.3.

Table 24.3 Clinical features of hypothermia

Mild (32-35°C)	Moderate (28-31°C)	Severe (<28°C)
Cold extremities	Apathy, poor judgment	Inappropriate behaviour
Shivering	Reduced shivering	Total loss of shivering
Tachycardia	Weakness and drowsiness	Cardiac arrhythmias
Tachypnoea	Slurred speech and amnesia	Pulmonary oedema
Urinary urgency	Dehydration	Hypotension and bradycardia
Mild incoordination	Decreased coordination or clumsiness	Reduced level of consciousness
	Fatigue	Muscle rigidity

The management of hypothermia will depend on the severity of the condition and the facilities available or within easy reach. Outside of hospital, the following should be considered:[16]

- Lay casualty flat, give essential first aid, enquire about coexisting illness.
- Prevent further heat loss (blankets/sleeping bag)-cover head and leave airway clear. The major routes of heat loss in cold conditions are usually convection and evaporation, thus a heavy-duty plastic bag can provide cheap, effective protection.
- Insulate from the ground.

- If possible provide shelter from the wind and rain.
- Allow slow spontaneous rewarming to occur; rewarming too quickly can result in rewarming collapse.
- Maintain close observation of pulse and respiration.
- Obtain help as soon as possible and transport the casualty to hospital.
- If breathing is absent, becomes obstructed or stops, standard expired-air ventilation should be instituted.

Chest compressions should be started if:

- no carotid pulse is detectable after palpating for at least 1 minute (the pulse is slow and weak in hypothermia) AND
- cardiac arrest is observed or there is a reasonable possibility that a cardiac arrest occurred within the previous 2 hours AND
- there is a reasonable expectation that effective cardiopulmonary resuscitation (CPR) can be provided continuously until the casualty reaches more advanced life support–this is likely to mean being within 2 hours of a suitable hospital.[17]

The rates of expired-air ventilation and chest compression should be the same as for normothermic casualties. Hypothermia may cause stiffness of the chest wall.

Recent recommendations[18] state that hypothermic patients with risk factors for imminent cardiac arrest (temperature <28°C, ventricular arrhythmia, systolic blood pressure <90 mmHg) and those who have already arrested should be transferred directly to an extracorporeal life support (ECLS) centre. Patients in cardiac arrest should receive continuous CPR during transfer; mechanical CPR can be helpful in this regard if prolonged transport is required or terrain is difficult. Delayed or intermittent CPR may be appropriate in hypothermic arrest when continuous CPR is impossible.

Rewarming

Those with mild hypothermia can be given a warm, sweet drink and have external heat applied to speed the return of thermal comfort. Those suspected of suffering from severe hypothermia should be regarded as critically ill and handled as little and as gently as possible; the risk of ventricular fibrillation is increased in a cold myocardium. Profoundly cold individuals may survive several hours in a 'shut-down' state ('metabolic icebox')–hence the maxim 'no one is dead until they are warm and dead'. These patients must not be mistaken for being in asystole, as cardiopulmonary resuscitation may precipitate ventricular fibrillation.

External active rewarming (hot air or water-circulating blanket, hot packs, hot bath) is recommended in cases of mild hypothermia, but should be avoided in severe hypothermia. In cases of out-of-hospital moderate and severe hypothermia, passive rewarming is the safest way to rewarm (insulate and allow the casualty's metabolism to rewarm slowly, ~0.75-1.0°C per hour).[17, 19] ECLS, including cardiopulmonary bypass and extracorporeal blood warming and oxygenation, has revolutionised the management of hypothermic cardiac arrest, with survival rates significantly increased. Recent evidence suggests that ECLS is the treatment of choice in the patient with unstable circulation or cardiac arrest.[18] However, these treatments require highly monitored intensive care with experienced, skilled staff, otherwise active rewarming may be dangerous and counterproductive.

Cold injuries

It is the extremities (hands and feet) that are most affected (90% of frostbite cases) by cold injuries, due to their high surface-area-to-mass ratio, and the fact that their major source of heat, blood flow, is restricted by vasoconstriction. Cold injuries can be of the freezing variety (frostbite, freezing cold injury FCI) or non-freezing variety (non-freezing cold injury, NFCI). There are large variations in susceptibility to cold injury due, in part, to different predisposing factors (Table 24.4). These factors can be used as part of a screening test for those proposing to exercise in a cold environment (see below).

Frostbite

Human tissue freezes at around -0.55°C and, depending on the rate and depth of freezing, intracellular crystals may form (rapid cooling), causing direct mechanical disruption of the tissues. The more common slow cooling and freezing results in predominantly extracellular water crystallisation that increases plasma and interstitial fluid osmotic pressure. The resulting osmotic outflow of intracellular fluid raises intracellular osmotic pressure and can cause damage to capillary walls. On rewarming, the cell membrane may rupture giving rise to local swelling and skin blistering. The accumulation of escaped cellular fluid causes oedema, which, along with a local reduction in plasma volume and capillary sludging, can reduce local blood flow or cause circulatory occlusion in some contained tissue compartments. The result can be thrombosis, local hypoxia, the release of inflammatory mediators, and cell death or a gangrenous extremity (Fig. 24.3).[20]

Figure 24.3 Frostbite SHUTTERSTOCK/AVATAR_023

Non-freezing cold injury

'Non-freezing cold injury' (NFCI) is the term given to describe a prevalent, but relatively poorly understood condition that results from protracted exposure to low ambient thermal conditions, Examples include chilblains and trench foot. Continuous tissue exposure to temperatures just below 15°C for a period of around 36–48 hours may produce an injury similar to one resulting from a much shorter exposure (perhaps <6 hours) to temperatures <5°C. Immobility, posture, dehydration, low fitness, inadequate nutrition, constricting footwear, fatigue, stress or anxiety, concurrent illness or injury can all increase the likelihood of NFCI. The risk of cold injury varies significantly with race, with those of Afro-Caribbean descent being at higher risk.[21, 22]

The precise pathophysiology of NFCI has not been defined; it appears to be related to the neuro-endothelio-muscular walls of local blood vessels. The chronic sequelae of mild to moderate cold injury are: pain in the injured area, cold sensitivity (protracted cold vasoconstriction following a cold stimulus) and hyperhidrosis (local increased sweating). The last two of these accentuate local cooling and increase future risk of cold injury.[23]

CASE STUDY

Sir Ranulph Fiennes, polar explorer—frostbite and hypothermia

Sir Ranulph Fiennes is considered one of the greatest explorers of his generation. In 2000, he chopped off the tips of two fingers following an attempted solo walk to the North Pole. Upon returning, the pain (often severe in recovering limbs post-frostbite) in the fingers was so severe he undertook the **DIY** surgery. Then, in 2003, while attempting to walk across Antarctica in the winter, he suffered another episode of frostbite, to his other hand, after taking his mittens off to adjust a binding.

In the aptly named Frozen Otter Ultra event, Wisconsin, USA, the race winner lost both his great and second toes to frostbite. 'My feet were obviously frozen, I couldn't feel them and it was too cold to take my shoes off to check my feet',

In 2018, temperatures at the 9-day Yukon Arctic Ultra event dropped to −40°C. One italian competitor suffered severe frostbite of both his feet and hands after developing hypothermia and becoming confused. He had unhooked from the sled he was pulling after starting to become confused, leaving his GPS tracking device behind and wandering for a kilometre in deep snow.

To demonstrate that the risk is not confined to events in severe cold, in 2017, in an ocean race at Bondi Beach, Sydney, 25 swimmers required medical treatment. Outside ambient temperatures reached 30°C but the water temperature remained a lowly 15°C. The swim was shortened from 2.1 to 1.8 km, but three participants required hospitalisation. One finisher said, 'I didn't have recollection of where I was or who I was or what I just did'.

Conclusion

When covering events in cold conditions it is extremely important to monitor the temperatures, including wind chill factor or water temperature, and review whether an event is safe. Relying on participants to report symptoms is not enough, as recognition can be too late to prevent severe injury. Confusion is a known side-effect of hypothermia, and is an indication for immediate medical attention. When exercise stops, T_{db} can drop rapidly. To prevent complications athletes should be immediately provided shelter and removed to a warm environment.

Sources: references 37, 38

Preventing cold injuries

The following guidelines apply to all activities where hypothermia and cold injury have the potential to occur:

- Plan adequately and communicate plans to others.
- Avoid activity inappropriate for fitness level, and activity to exhaustion.
- Ensure adequate nutrition and hydration.
- Warm up prior to exposure and wear appropriate clothing for weather conditions:
  - Cover the head and extremities when the ambient temperature falls below 5°C. This should be mandatory below an ambient temperature of - 5°C or when high winds are expected. Mittens should replace gloves where possible below an ambient temperature of 0°C.

  - Footwear should not be laced tightly, socks should be changed if they become wet.
  - Prevent flushing of cold air/water beneath garments (i.e. have airtight/watertight seals).
  - Provide insulation by trapping a large volume of dry air close to the skin.
  - Enable adjustments in insulation to cater for times of increased or decreased metabolic heat production (e.g. opening vents or, ideally, allowing easy removal of layers).
  - Be windproof.
  - Wick moisture away from the body for comfort.
  - Be vapour permeable to prevent accumulation and condensation of moisture under the clothing, which, because of its high thermal capacity, will reduce clothing insulation.
- Cancel activity or seek shelter if appropriate. The International Ski Federation (FIS) and American College of Sports Medicine recommend considering cancelling an event if the ambient dry bulb temperature is below -20°C.[24]

TREATMENT OF COLD INJURIES AND SCREENING

The recommended treatments outlined in this chapter should not restrict the freedom of clinical decision making. The reader is encouraged to supplement their decision making by using guidelines, such as those produced by the US National Athletic Trainers' Association[25] and the American College of Sports Medicine.[26]

When treating FCI and NFCI, it is important to establish which is the dominant injury, as they often coexist; establishing this will determine the preferred method of rewarming. In all cases shelter and insulation should be sought because casualties with cold injury are at risk of hypothermia.

Frostbite

The management of frostbite has improved significantly over the last 10 years, there are clear management protocols available that are beyond the scope of this chapter, but the reader is referred to the review of Handford et al. (2014).[20] In brief, out of hospital care includes the following recommendations:[27]

- Remove to shelter.
- Provide warm fluids.
- Remove footwear (if feet injured) and replace wet socks.
- Rewarming in the field should only be attempted if there is no chance of refreezing.
- Warm the cold extremity by placing it under a companion's armpit for 10 minutes and then replace glove or boot (be aware of risk of swelling). If sensation returns add extra layers of clothing and continue; if sensation does not return seek medical attention.
- Do not rub affected part (possibility of mechanical damage).
- Do not use radiant heat from a fire or radiator; this can result in skin burns.

- Thawing frostbitten tissue requires pain management and access to a lot of warm water (whirlpool bath with added antiseptic solution maintained at 38°C for 15–30 min, possibly up to 60 min).
- Rewarming should continue until a red/purple colour appears and the extremity tissue becomes pliable.
- Topical aloe vera cream or gel (anti-prostaglandin agent) should then be applied to thawed tissue, before a loose, protective dressing is applied.
- Aspirin (75 mg) can be given for its rheologic effect, ibuprofen (12 mg/kg/day, divided into two daily doses, maximum of 2400 mg/day) for its prostaglandin effect.[20]

There is an ongoing, sparsely evidenced, debate about what to do with blisters. It has been recommended that there should be selective drainage of clear/cloudy blisters by needle aspiration (especially if restricting movement), with haemorrhagic blisters being left alone.[27] However, others suggest that all blisters are debrided in the hospital rather than in the field.[20]

Non-freezing cold injury

The evidence base for the recommended treatment of NFCI is weaker than for FCI. In contrast to those with FCI, it is recommended that patients with NFCI have their affected extremities rewarmed slowly, by exposure to warm air alone (no immersion). The early period after rewarming can be very painful in NFCI, even in those without obvious tissue damage. Historically, Page 353 amitriptyline (10–75 mg in a single dose at night) has been recommended as the drug of choice for the treatment of pain following NFCI. However, the evidence base for this treatment is weak (case-based observation). In the most severe cases, with tissue damage, twice-daily cleansing with a dilute antibacterial preparation is recommended. The areas of tissue damage should be photographed to record progress.[23]

With both FCI and NFCI, once rewarmed the affected extremities should be treated by exposure to air. Smoking should not be permitted.

Cold immersion

Cold water represents a greater threat than cold air because of its higher thermal conductivity. Skin temperature cools rapidly on immersion in cold water, and the deep body temperature of an individual immersed in cold water will cool about four times faster than when in air at the same temperature. For a detailed exposition of the physiology and pathophysiology associated with cold water immersion the reader should consult Golden and Tipton (2002).[28]

Athletes participating in long-distance, open-water swimming events might be at the greatest risk of hypothermia. The international swimming association (FINA) does not permit competition in water temperatures below 16°C, measured 1.4 m below the water surface.[29]

PRACTICE PEARL

Active external rewarming can cause 'core temperature afterdrop'. This can be minimised by using minimally invasive core rewarming before active external rewarming techniques.

Four stages of immersion associated with particular risk have been identified:

Stage 1. Initial responses (first 3–5 min). Cardio-respiratory responses called 'cold shock'[30] act as precursors to drowning and cardiac problems.

Stage 2. Short-term immersion (5–30 min). Neuromuscular dysfunction leading to physical incapacitation, caused by cooling of superficial nerves and muscle, can result in drowning.

Stage 3. Long-term immersion (30+ min). Hypothermia-will not occur earlier than this in adults even in coldest water temperatures. Hypothermia-induced unconsciousness results in drowning.

Stage 4. Post immersion. 'Circum rescue collapse' refers to a collapse in arterial blood pressure and cardiac failure occurring just before, during or just after rescue.[31]

These stages highlight the danger of drowning. Figure 24.4 presents the physiological pathways to drowning and possible mitigations.

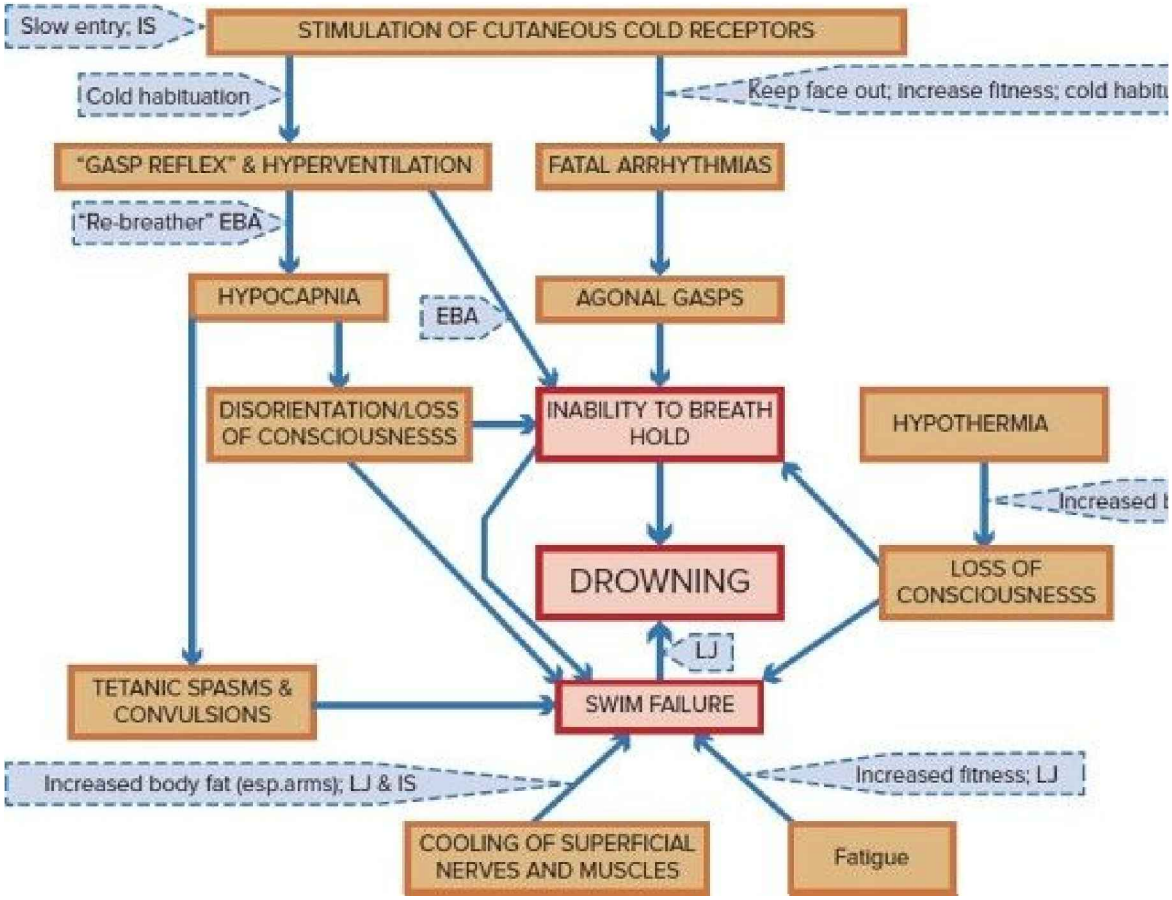


Figure 24.4 The physiological pathways to drowning following immersion or submersion in cold water, with possible interventions for partial mitigation (dashed). IS = immersion suit; LJ = lifejacket; EBA = emergency breathing aid

Recently, the possibility of sudden cardiac death on immersion in swimming events has been highlighted,[32] as has the possible underlying cause of 'autonomic conflict'[33] and ways of reducing this risk in open-water events (Table 24.5). See Chapter 26 (Underwater) for further discussion of the diagnosis and management of immersion pulmonary oedema.

Table 24.5 Approaches to reduce the risk of sudden cardiac death in open-water swimming events[34]

- Mandate a maximum wave/group size
- Regulate the start line/course width
- Time the gaps between wave starts
- Consider the number and visibility of buoys

- Consider the straight-line distance before requiring swimmers to make a turn—allowing swimmers to spre
- Ask swimmers to self-select into waves of appropriate ability, or ask weaker/novice swimmers to start at th
- Facilitate acclimatisation and anxiety reduction. Pre-race immersion: brief swimmers about the benefits of
- Increase the amount of cover in the first part of the swim (up to 400 m). This is where the greatest number

Treatment of immersion casualties

Any person suspected of aspirating water (abnormal lung sounds, severe cough, wheezing, blue lips and nailbeds, rapid shallow breathing, rapid pulse, frothy sputum/foamy material in the airway, depressed mental state or hypotension) should be evacuated to advanced medical care.

Both seawater and freshwater drowning represent a form of suffocation, the consequences of which depend on the length of the anoxic period and secondary damage. The risk of death or severe neurological impairment after hospital discharge is given as 'nearly 100%' when the duration of submersion exceeds 25 minutes.[35] Thus, interruption of the drowning process and the relief of hypoxia have the greatest impact on outcome. This includes: early tracheal intubation if indicated and the delivery of a high fraction of inspired oxygen at positive end expiratory pressure (5 cmH_2O) if available. Other objectives are restoration of cardiovascular stability, prevention of further heat loss and speedy evacuation to hospital.

Because cardiac arrest in drowning is a consequence of anoxia, basic life support should include ventilations and chest compressions. Ventricular fibrillation is rare in drowning (<10%), so use of an automated external defibrillator (AED) in the initial minutes of drowning should not interfere with oxygenation and ventilation. Otherwise AED use should be considered and is not contraindicated in a wet environment.[36]

Immersion hypothermia is usually acute, occurring rapidly due to the cooling power of water. Conscious casualties can be removed and rewarmed in a hot bath (39–40°C), Rewarming should cease before the casualty becomes too hot (i.e. appearance of sweat); over-warming can result in rewarming collapse. Unconscious casualties, whose airways are not under threat, should be carefully removed from the water horizontal and kept in this position during evacuation to hospital (see 'Hypothermia', above).

Health screening

Medical screening of athletes who enter or compete in cold environments may be appropriate. Factors to consider include (see also Table 24.4):

- state of health (e.g. fever/viral illness/cold/flu, diabetes mellitus, cardiovascular disease, gastroenteritis/diarrhoea)
- family history/genetic disorders
- peripheral vascular disorders (e.g. Raynaud's syndrome)

- hypertension
- asthma
- diabetes
- use of medication (e.g. vasoactive drugs)
- acute/chronic alcohol or drug abuse.

SUMMARY

- Physical activity in cold environments predisposes the human body to challenges that can result in injury.
- The guidelines set out by the American College of Sports Medicine currently state that if appropriate precautions are taken, physical activity in cold environments can continue. Guidelines are available for clinicians who are responsible for mass participation events.
- Clinicians should be aware of the signs and symptoms of injuries caused by cold exposure and know how to differentiate between FCI and NFCI.

REFERENCES

1. Folkow B, Neil E. *Circulation*. Oxford University Press, 1971.
2. Tipton MJ, Allsopp A, Balmi PJ et al. Hand immersion as a method of cooling and rewarming: a short review. *J R Nav Med Serv* 1993; 79: 125–31.
3. Burton AC, Edholm OG. *Man in a cold environment*. London: Edward Arnold, 1955.
4. Mekjavic IB, Bligh J. The pathophysiology of hypothermia. In: Oborne DJ, ed. *International reviews of ergonomics*. New York: Taylor & Francis, 1987: 201–18.
5. Yoshitomi Y, Kojima S, Ogi M et al. Acute renal failure in accidental hypothermia of cold water immersion. *Am J Kidney Dis* 1998; 31(5): 856–9.
6. Ulrich AS, Rathlev NK. Hypothermia and localized cold injuries. *Emerg Med Clin North Am* 2004; 22(2): 281–98.
7. Kuklane K, Gao C, Holmer I et al. Calculation of clothing insulation by serial and parallel methods: effects on clothing choice by IREQ and thermal responses in the cold. *Int J Occup Saf Ergon* 2007; 13(2): 103–16.
8. Taylor NAS, Tipton MJ, Kenny GP. Considerations for the measurement of core, skin and mean body temperatures. *J Therm Biol* 2014; 46: 72–101.
9. Castellani JW, Tipton MJ. Cold stress effects on exercise tolerance and exercise performance. *Compr Physiol* 2015; 6(1): 443–69.
10. Brajkovic D, Ducharme MB. Finger dexterity, skin temperature, and blood flow during auxiliary heating in the cold. *J Appl Physiol (1985)* 2003; 95(2): 758–70.
11. Eglin CM, Golden FStC, Tipton MJ. Cold sensitivity test for individuals with non-

freezing cold injury: the effect of prior exercise. *Extrem Physiol Med* 2013; 2: 16.

12. Douglas WW, Malcolm JL. The effect of localized cooling on conduction in cat nerves. *J Physiol* 1955; 130: 53–71.
13. Clarke SJ, Hellon RF, Lind AR. The duration of sustained contractions of the human forearm at different muscle temperatures. *J Physiol* 1958; 143: 454–73.
14. Rintamaki H, Makinen T, Oksa J et al. Water balance and physical performance in cold. *Arctic Med Res* 1995; 54(Suppl 2): 32–6.
15. Geng Q, Holmer I, Hartog DEA et al. Temperature limit values for touching cold surfaces with the fingertip. *Ann Occup Hyg* 2006; 50(8): 851–62. doi: 10.1093/annhyg/mel030.
16. Tipton MJ. Extreme temperature sport and exercise medicine. In: Whyte GP, Loosemore M, Williams C, eds. *ABC of Sports and Exercise Medicine*. 4th ed. Chichester, UK: BMJ Books, 2015: 67–75.
17. Handley AJ, Golden FStC, Keatinge WR et al. Report of the Working Party on Out of Hospital Management of Hypothermia. London: Medical Commission on Accident Prevention, Royal College of Surgeons, 1992.
18. Paal P, Gordon L, Strapazzon G et al. Accidental hypothermia: an update. *Scand J Trauma Resusc Emerg Med* 2016; 24: 111. doi: 10.1186/s13049-016-0303-7.
19. Nielson HK, Toft P, Koch J et al. Hypothermic patients admitted to an intensive care unit: a fifteen year survey. *Dan Med Bull* 1992; 39(2): 190–3.
20. Handford C, Buxton P, Russell K et al. Frostbite: a practical approach to hospital management. *Extrem Physiol Med* 2014; 3: 7. doi: 10.1186/2046-7648-3-7.
21. DeGroot DW, Castellani JW, Williams JO et al. Epidemiology of US Army cold weather injuries, 1980–1999. *Aviat Space Environ Med* 2003; 74(5): 564–70.
22. Maley MJ, House JR, Tipton MJ et al. Role of cyclooxygenase in the vascular responses to extremity cooling in Caucasian and African males. *Exp Physiol* 2017; 102(7): 854–65. doi: 10.1113/EP086186.
23. Ministry of Defence (UK). Joint services publication, 539. *Climatic Injuries in the Armed Forces: Prevention and Treatment*. London: HMSO, 2003.
24. Armstrong LE, Epstein Y, Greenleaf JE et al. American College of Sports Medicine position stand: heat and cold illnesses during distance running. *Med Sci Sports Exerc* 1996; 28(12): i-x.
25. Cappaert TA, Stone JA, Castellani JW et al. National Athletic Trainers' Association position statement: environmental cold injuries. *J Athl Train* 2008; 43(6): 640–58.
26. Castellani JW, Young AJ, Ducharme MB et al. American College of Sports Medicine position stand: prevention of cold injuries during exercise. *Med Sci Sports Exerc* 2006; 38(11): 2012–29.
27. McIntosh SE, Hamonko M, Freer L et al.; Wilderness Medical Society. Wilderness Medical Society practice guidelines for the prevention and treatment of frostbite.

Wilderness Environ Med 2011; 22(2): 156–66.

28. Golden FStC, Tipton MJ. *The essentials of sea survival*. Human Kinetics, 2002.
29. Federation Internationale de Natation. *Open water swimming manual*. Lausanne, Switzerland: FINA, 2006.
30. Tipton MJ. The initial responses to cold-water immersion in man. *Clin Sci (Lond)* 1989; 77: 581–8.
31. Golden FStC, Hervey GR, Tipton MJ. Circum-rescue collapse: collapse, sometimes fatal, associated with rescue of immersion victims. *J R Nav Med Serv* 1991; 77: 139–49.
32. Tipton MJ. Sudden cardiac death during open water swimming. *Br J Sports Med* 2013; 48(15): 1134–5.
33. Shattock M, Tipton MJ. 'Autonomic conflict': a different way to die during cold water immersion? *J Physiol* 2012; 590(14): 3219–30.
34. Tipton MJ, Bradford C. Moving in extreme environments: open water swimming in cold and warm water. *Extrem Physiol Med* 2014; 3: 12. http://www.extremephysiolmed.com/content/3/1/12.
35. Szpilman D, Bierens JJ, Handley AJ et al. Drowning. *N Engl J Med* 2012; 366: 2102–10.
36. Schmidt AC, Sempsrott JR, Hawkins SC et al. Wilderness Medical Society Practice Guidelines for the Prevention and Treatment of Drowning. *Wilderness Environ Med* 2016; 27(2): 236–51.
37. https://en.wikipedia.org/wiki/Ranulph_Fiennes
38. www.bbc.com/news/av/uk-24951702/sir-ranulph-fiennes-i-cut-my-fingertips-off-with-a-blade

Chapter 25

Altitude

with MICHAEL KOEHLE and YORCK OLAF SCHUMACHER

It was like I was very drunk. I couldn't walk without stumbling, and completely lost the ability to think or speak. It was a really strange feeling. I'd have some word in my mind, but I couldn't figure out how to bring it to my lips.

Dale Kruse, mountain climber, describing the effects of high-altitude cerebral oedema when climbing Mt Everest

As travel continues to get easier and cheaper, altitude sojourns for recreation or (hypoxic) training continue to grow in popularity. Alpinists cross peaks from their bucket lists; sporting teams and individual athletes look for higher ground to gain a competitive advantage; and active travellers enjoy spectacular recreation. Whether it be mountaineering in the Swiss Alps or training in high-altitude destinations like Flagstaff, Arizona, or in a simulated altitude tent closer to home, altitude exposure is now part of the mainstream sport and exercise medicine world.

The underlying principle of altitude training is that by exposing an individual to an environment that is low in available oxygen, the body will adapt and improve its efficiency at transporting and using limited oxygen. Endurance athletes in particular take advantage of exercising at high altitude to enhance performance once returning to sea level, or to acclimatise to competition at altitude. They employ a number of different altitude training strategies, such as 'live high, train high' or 'live high, train low', as discussed in this chapter.

Despite all the benefits of altitude training, exposing the body to extreme stress comes with risks. Clinicians must be aware of the potential dangers for every patient and help to mitigate the risk of altitude illness. The term 'high-altitude illness' refers to all conditions that can occur as a result of exposure to altitude, including acute mountain sickness, high-altitude pulmonary oedema and high-altitude cerebral oedema.

Reflecting the two sides of the altitude coin–risk and potential benefit-the chapter is split into two parts:

- medical concerns at altitude
- altitude training.

MEDICAL CONCERNS AT ALTITUDE

High-altitude illness

High-altitude illness usually occurs at altitudes above 3000 m (10 000 ft) and can cause significant morbidity. The life-threatening manifestations of high-altitude illness, high-altitude cerebral oedema and high-altitude pulmonary oedema occur in 0.1–4.0% of visitors to altitude.[1, 2] A larger proportion of travellers experience acute mountain sickness, which typically presents as headache, nausea, vomiting, dizziness, fatigue and insomnia. Although these milder symptoms are not life threatening, they can be severe enough to interfere with trip participation and enjoyment. Fortunately, altitude illness is preventable and proper pre-trip planning can reduce morbidity and mortality.

Acute mountain sickness can occur when a

Acute mountain sickness can occur when a person who is accustomed to being at a low altitude ascends to a higher altitude. It is the most common type of high-altitude illness and occurs in more than one-fourth of people travelling to above 3500 m (11 500 ft) and more than one-half of people travelling to above 6000 m (20 000 ft). Symptoms include headache, fatigue, poor appetite, nausea or vomiting, light-headedness and sleep disturbances. Symptoms usually occur 6–12 hours after ascent, and improve after 24–48 hours if there is no further ascent. In less than 1% of cases, symptoms can progress to high-altitude cerebral oedema.[3]

High-altitude pulmonary oedema

High-altitude pulmonary oedema (HAPO) is a potentially fatal accumulation of plasma and red blood cells in the lungs due to a breakdown in the pulmonary blood-gas barrier, which is triggered by hypobaric hypoxia. This breakdown develops due to maladaptive responses to the hypoxia encountered at higher altitudes and results in the accumulation of extravascular fluid in the alveolar spaces, ultimately impairing respiration.

High-altitude cerebral oedema

High-altitude cerebral oedema (HACO) is a potentially fatal condition that generally occurs in individuals with acute mountain sickness and/or high-altitude pulmonary oedema at elevations over 3000 m (10 000 ft).[4] It manifests as encephalopathic symptoms and signs, including ataxic gait, severe fatigue and lassitude, and progressive decline of mental function and consciousness. If HACO is suspected, evacuation and immediate descent are crucial.

Determinants of risk

The following reviews the determinants of risk for high-altitude illness, discussing key modifiable and non-modifiable risk factors.

CASE STUDY

Headache and dizziness while hiking above 2000 m in the Himalayas

A middle-aged male hiking to Gosainkunda Lake in the Nepal Himalayas trekked from 1950 m to 4380 m in one day. On the way, he had complained of headache and dizziness and had vomited twice. On arrival, his headache and dizziness became worse and he felt fatigued, retreating to his hotel room to rest. A fellow trekker found him barely conscious and summoned medical help.

On examination his lips were dry and chapped. He only moved his limbs and opened his eyes in response to pain. He was tachycardic and febrile. Bilateral coarse basal crackles were present and his peripheral oxygen saturation was 45%.

Diagnosis

He was diagnosed with HACO and probable HAPO.

Management

Oxygen and intravenous dexamethasone were administered. With difficulty, he was able to swallow acetazolamide, and he was also given sublingual nifedipine. His clinical status did not improve, and descent was required (Fig. 25.1). Due to the weather, time of day and geography, helicopter evacuation was impossible. A porter carried the patient down on foot, along with an accompanying medical escort.

Figure 25.1 Management of high-altitude illness when hiking at altitude above 2000 m in the Himalayas. (a) Patient being transferred to lower altitude (b) Close-up of barely responsive patient supplied with intranasal oxygen

COURTESY OF MICHAEL KOEHLE

Outcome

After descent of approximately 450 m to the nearest settlement (Lauribinayak), the oxygen was exhausted, but the man had improved substantially and started to mumble and then to talk. A military platoon had been contacted by radio and had hiked up, while the patient was brought down. The soldiers carried the patient a further 500 m down by stretcher overnight. The next day he was further evacuated down to 1920 m, and admitted to a regional health facility. He recovered completely.

Ascent rate

One of the most important determinants of an individual's risk of altitude illness is the itinerary.

PRACTICE PEARL

Rate of ascent is a strong predictor for acute mountain sickness. Those who ascend slowly, allowing for gradual acclimatisation, have a lower likelihood of developing acute mountain sickness.[2]

Sleeping altitude is monitored when assessing the rate of ascent, as large increases in sleeping altitude pose the greatest risk of altitude illness.

Various guidelines have been proposed for graded ascent, ranging from 300–600 m (1000–2000 ft) of ascent per night,[5, 6] when above 3000 m (10 000 ft). Additionally, at least one night at an intermediate altitude (1500–2500 m [5000–8000 ft]) on the way to very high altitude is recommended for acclimatisation.[6] No controlled studies have been conducted that demonstrate an ideal ascent rate. A recommended ascent rate of no more than approximately 500 m (1600 ft) per night should be followed.[7] Approximately every 1000 m (3200 ft), an additional rest day is recommended, where the traveller sleeps at the same altitude for two consecutive nights.

Daytime acclimatisation hikes to higher altitudes are permitted and encouraged in travellers who are not exhibiting signs and symptoms of altitude illness. This climb high, sleep low approach accelerates acclimatisation by intermittently exposing the individual to a higher dose of hypoxia.

Travellers with more rigid itineraries often ascend too quickly, or while symptomatic or sick, in order to meet external deadlines. Although only 40% of trekkers in the Nepal Himalayas are in organised groups, they account for 80% of medical evacuations.[8] Patients should be encouraged to have a flexible itinerary, with room for extra rest days to allow for illness or other setbacks.

Previous altitude history

Patients with a previous history of altitude illness are possibly at increased risk of recurrence;[2, 9]

however, recent research has cast doubt on the strength of that association.[9] Nevertheless, susceptible individuals should follow a more conservative itinerary, aiming for 300 m (1000 ft) increments in sleeping altitude. These individuals should also consider chemoprophylaxis (see below), especially if they are returning to an altitude at which they were previously ill.

The effect of recent previous altitude exposure is a matter of much debate. In laboratory models of deacclimatisation,[10] hypoxic ventilatory response seems to recede after only one week. However, observational studies suggest that altitude exposure in the previous two months provides a significant degree of protection from acute mountain sickness.[2]

The protection from high-altitude pulmonary oedema seems to be much shorter lasting. Re-entry high-altitude pulmonary oedema[11, 12] is a phenomenon whereby high-altitude residents develop pulmonary oedema after a brief trip to low altitude. These residents would presumably be well-acclimatised to their home altitude, but apparently do not retain any protection from high-altitude pulmonary oedema when they briefly descend. It therefore appears that previous altitude exposure may provide some protection from acute mountain sickness, but not from high-altitude pulmonary oedema.

Patient characteristics and previous medical history

Sex is not believed to be a risk factor for acute mountain sickness.[13, 14] However, there appears to be a slight overrepresentation of male patients with high-altitude pulmonary oedema.[1] Although early research suggested that older travellers might have some slight protection from acute mountain sickness, there is insufficient data using current definitions of altitude illness to confirm this finding.[15]

High-altitude pulmonary oedema has some unique medical risk factors. The pathophysiology of high-altitude pulmonary oedema involves increased pulmonary vascular pressures, possibly related to heterogeneous hypoxic pulmonary vasoconstriction. Therefore, conditions that increase pulmonary vascular pressure, such as unilateral pulmonary artery hypertension[16, 17] and primary pulmonary hypertension,[17] increase the risk of an individual developing high-altitude pulmonary oedema.

Asthma

Asthma is not a risk factor for high-altitude illness. Persons with asthma tend to have fewer symptoms while at moderate altitude. The improvement in clinical status is believed to be due to thinner air and a relative dearth of pollutants and lung irritants in the air.[18] However, at extreme altitude, airway heat loss may aggravate asthma. Before intense physical efforts, patients should medicate with bronchodilators (and possibly inhaled corticosteroids), especially if they have known exercise-induced bronchospasm.[19] Rapid ascent to an altitude of 3000 m (10 000 ft) or more should be avoided in those with moderate or severe asthma.[19]

Refractive eye surgery

Patients who have had refractive eye surgery may have visual difficulties while travelling at altitude, especially above 5000 m (16 400 ft). There are several reports of visual disturbances at high altitude in individuals who have had scalpel radial keratotomy.[20, 21] The more recent laser procedures (laser photorefractive keratectomy [laser PRK] and laser-assisted in situ keratomileusis [LASIK]) have resulted in fewer complications; however, mountaineers with LASIK can have symptoms such as blurring and dry eyes while travelling above 5000 m.[22]

PRACTICE PEARL

Patients with a previous history of refractive eye surgery should be cautioned about possible visual problems and should bring artificial tears for daily instillation while at moderate altitude and above. If visual blurring occurs, they should not ascend any further.

Oral contraceptive pill

The effectiveness of oral contraceptive pill regimens is not altered at altitude.[14] But mountain travellers often suffer diarrhoea or other conditions that require concurrent medication therapy and that may interfere with the efficacy of oral contraceptive pills.

PRACTICE PEARL

Women should be cautioned to use a second method of contraception when diarrhoea or the need for concurrent medication may affect the efficacy of oral contraceptive pills.

Theoretically, combination oral contraceptive pills have the potential of increasing the risk of thrombosis at altitude (especially when combined with dehydration, polycythaemia and stasis, which commonly occur at high altitude). To date, there have been no reports of deep vein thrombosis in this group.[14] At sea level, third-generation oral contraceptive pills (containing desogestrel or gestodene) are associated with a higher risk of thrombosis than second-generation oral contraceptive pills (relative risk 1.7);[23] consequently, second generation oral contraceptive pills may be preferable for travellers to altitude.

Pregnant women at altitude

There are at least three specific concerns for pregnant women at altitude. With travel at altitude, comprehensive medical care is often unavailable. Furthermore, medication options for acute mountain sickness prevention are more limited in pregnant women (e.g. sulphonamides, such as acetazolamide, are contraindicated in the first trimester and after 36 weeks of pregnancy). Pregnancy-specific conditions that may be affected by altitude include spontaneous abortion, pre-

eclampsia, gestational hypertension, placental abruption and intrauterine growth restriction. The data relevant to these conditions are limited and usually derived from studies of high-altitude residents (as opposed to travellers), who may have different risk profiles.

The Union Internationale des Associations d'Alpinisme (UIAA)[14] makes the following recommendations regarding pregnant women:

- Those at risk of spontaneous abortion, pre-eclampsia, intrauterine growth restriction or placental abruption should avoid high-altitude exposure.
- Pregnant women should allow 2–3 days for acclimatisation prior to exercising at altitude, waiting two weeks before performing strenuous exercise.
- Chronic hypertension, anaemia, smoking and cardiopulmonary disease are contraindications for travel to altitude after 20 weeks gestation.

General preventive measures

In all high-altitude endeavours, many general preventive measures can reduce the risk of high-altitude illness.

Exertion

Exertion is an independent risk factor for acute mountain sickness.[24] Because both exertion and cold can increase pulmonary vascular pressure, they are both believed to worsen HAPO.[25] Travellers should adopt a regular, even pace and avoid overexertion while at altitude. They should also be encouraged to bring appropriate clothing and equipment for the cold weather.

Hydration

Dehydration may also potentiate acute mountain sickness.[26] The air at altitude is dry, respiratory rate is higher and mouth breathing is more common. These factors increase insensible losses at altitude. Travellers should consume at least 3–4 L of water or clear, non-caffeinated, non-alcoholic beverages per day while trekking or climbing. On rest days, fluid requirements are slightly less. A good rule of thumb is to aim for the urine to be clear.

Infections

Upper respiratory tract infections are extremely common at altitude. There is some evidence that these infections may increase the risk of acute mountain sickness[27] and HAPO.[28] At altitude, upper respiratory tract infections may also increase the potential for dehydration (through increased insensible losses). Travellers should be counselled to modify their rate of ascent when they contract an upper respiratory tract infection, allowing more time for rest and acclimatisation. They should also be monitoring their fluid intake to avoid dehydration.

Diet

A high-carbohydrate diet is recommended for altitude travellers.[29] The benefit from this diet is related to an elevated respiratory quotient (VCO_2/VO_2) from the metabolism of carbohydrates over fats. Increasing carbon dioxide production leads to increased ventilation and improved arterial oxygen saturation.

One of the later manifestations of altitude acclimatisation is increased red blood cell production. Adequate iron stores are required to allow for the new haeme pigment production. Those who may have low iron stores (e.g. vegetarians and vegans, menstruating women) should consider iron supplementation to facilitate this process.[30]

Ultraviolet light

With ascent, ultraviolet light exposure increases by approximately 4% per 300 m (1000 ft).[6] By this formula, there is approximately 70% more ultraviolet radiation at Everest Base Camp than at sea level. This increased radiation is compounded by radiation reflected off snow, if it is present. This reflected radiation can cause sunburn in unlikely places, such as the underside of the nose or chin.

PRACTICE PEARL

Travellers should be advised of the increased risk of sunburn and snow blindness (ultraviolet keratitis) at altitude. They should bring appropriate sun-protective clothing, hats, sunblock and lip balm. Sunglasses with adequate face protection (glacier glasses or wraparound glasses are best) are essential for the prevention of snow blindness (Fig. 25.2).

Figure 25.2 Ultraviolet light exposure increases with altitude and this is compounded by radiation reflected off snow. Thus, porters working snowy peaks are at particular risk of ultraviolet keratitis (seen here after treatment in the clinic)

COURTESY OF DR CHRIS GOOCH

If travelling with guides or porters, the traveller should ensure that they are also adequately equipped for sun and cold protection. As many cases of snow blindness occur after the patient's sunglasses have been broken or lost, it is a good idea to bring an extra pair of sunglasses for the travelling group.

Chemoprophylaxis for particular conditions

Individuals who are at higher risk of altitude illness should consider taking medications for prophylaxis. These individuals are those with a previous history of an altitude illness, with an aggressive itinerary or with other risk factors mentioned above. Different medication regimens are used for prevention of acute mountain sickness and HACO from those used for HAPO.

Acute mountain sickness

Acetazolamide (a sulphonamide) is a medication that is legendary among climbers and trekkers. Acetazolamide is contraindicated in many travellers to altitude, including those with an allergy to sulphonamides and those with glucose-6-phosphate dehydrogenase deficiency. Pregnant and breastfeeding women should also avoid this medication. Furthermore, acetazolamide should not be taken in conjunction with salicylates, as there is an increased risk of central nervous system depression and metabolic acidosis.

PRACTICE PEARL

Several high-quality studies have demonstrated the efficacy of acetazolamide in preventing acute mountain sickness.[6, 31–33] Currently, the recommended dose for prevention is 125 mg orally twice daily, started prior to commencement of the ascent.[7]

Dexamethasone is an appropriate alternative for acute mountain sickness prophylaxis in those who cannot tolerate acetazolamide. The prophylactic dose is 8 mg daily (usually divided into two or four doses daily).[34] For prophylaxis, these medications need only be taken until the traveller reaches a stable altitude (and is asymptomatic at that altitude). Once descent has begun, these medications are not required.

Page 362

Some xenobiotics have been proposed for acute mountain sickness prophylaxis. Ginkgo biloba initially showed some promise in smaller studies, but two recent high-quality studies have shown no benefit over placebo.[32, 35] Both coca and garlic have been proposed as possible prophylactic therapies. There have been no published studies of either intervention. Coca can also increase the risk of acute coronary syndrome among users,[36] a devastating complication in a remote area. None of these alternative therapies can be recommended for the prevention of acute mountain sickness.

High-altitude pulmonary oedema

Several medications prevent recurrent HAPO (Table 25.1). There are no relative effectiveness studies of these four therapies. The decision of which medication to prescribe should be based on tolerance and mitigation of adverse events.

Table 25.1 Medications used to prevent pulmonary oedema and the level of evidence* of the study

Medication	Dose	Level of evidence
Nifedipine[37]	20 mg sustained-release preparation three times daily	1
Dexamethasone[38]	8 mg twice daily	2
Tadalafil[38]	10 mg twice daily	2
Salmeterol[39]	Two puffs twice daily	3

*Centre for Evidence-based Medicine (Oxford) system. See Chapter 2 in *Clinical Sports Medicine Volume 1: Injuries* for more on levels of evidence.

Poor sleep at high altitude

Visitors to high altitude often have poor sleep, marked by frequent arousals and periodic breathing.[40] The physiology of this phenomenon is detailed in the book *High Altitude* (Fig. 25.3).[41]

Sleep quality and periodicity improve with acclimatisation at moderate altitudes, but poor sleep may persist at extreme elevations.[40] Both acetazolamide and benzodiazepines have been used effectively to improve sleep quality at altitude.

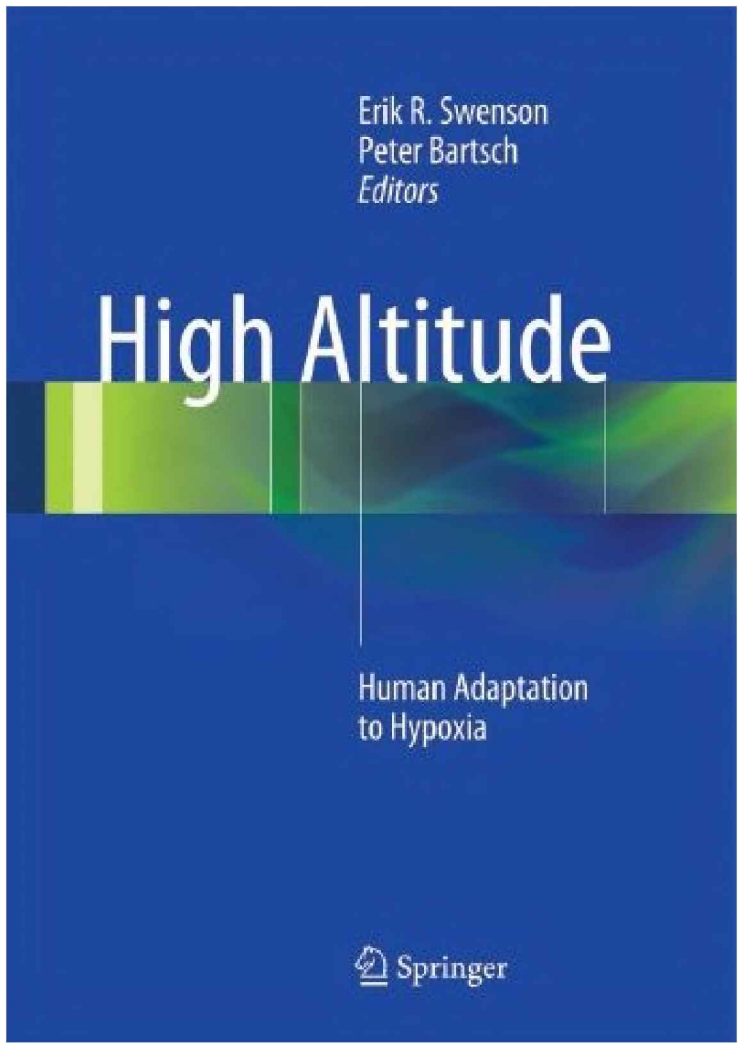


Figure 25.3 We recommend *High Altitude: Human Adaptation to Hypoxia* as a foundation for the reader interested in more detail on both the basic science and the clinical consequences of exposure to high altitude

SWENSON, ERIK R., BÄRTSCH, PETER (EDS.), *HIGH ALTITUDE - HUMAN ADAPTATION TO HYPOXIA,* 2014, SPRINGER-VERLAG NEWYORK, REPRODUCED WITH PERMISSION OF SNCSC

Acetazolamide reduces respiratory alkalosis and hence respiratory periodicity. It has long been used to improve sleep quality at high altitude.[42] The standard dose of acetazolamide for improving

sleep is 125 mg orally.

Temazepam (10 mg orally) improves both subjective[43, 44] and objective measures of sleep quality in travellers to altitude.[44] It is an appropriate alternative in patients unable to take acetazolamide.

ALTITUDE TRAINING

Following the dominance of altitude-acclimatised athletes during the 1968 Olympics in Mexico City, at 2400 m (8000 ft) above sea level, altitude training has become increasingly popular among elite athletes. In all endurance disciplines, most internationally successful endurance athletes now perform a substantial portion of their training at altitude. Historically populations originating from altitude have been more successful in endurance events compared to populations originating from sea level (e.g. Kenyan runners, mostly stemming from the Rift Valley area, situated at more than 2000 m (6500 ft)).

This section explores the underlying physiology of altitude training and addresses clinicians' frequently asked questions.

The clinical physiology of adaptation at altitude

Although the oxygen-poor environment of altitude can cause serious pathologies, it can also trigger adaptations that may benefit athlete performance. The main performance limiting factor in endurance sports is oxygen availability, which is reduced at altitude. When exposed to a low oxygen environment, the body tries to adapt and thus improve mechanisms that contribute to deliver oxygen to the working muscle. Athletes aim to take advantage of these adaptations to improve sea-level performance.

While a number of physiological processes play a role in the adaptation, the respiratory and more importantly the haematological adaptations are key to improved oxygen availability.

Respiratory adaptation

At altitude, in an environment with reduced oxygen per volume of air, an organism tries to keep the oxygen availability for its organs (expressed as the oxygen saturation in the blood) constant and thus increases the minute ventilation. This change is the so-called hypoxic ventilatory response (HVR). Whether or not this adaptation has a beneficial effect on exercise ventilation and thus performance at sea level is still unclear, as studies have provided conflicting results.

Some altitude-dwelling populations (Tibetans and Ethiopians) have, over their evolution, purely adapted through an improvement of their respiratory efficiency and do not show any relevant haematological adaptation, while others (Andeans) have an increased red cell mass.[45]

Haematological adaptation

The increase in total circulating haemoglobin is the most well-known mechanism triggered by the hypoxia at altitude. However, it is only the second step in the haematological adaptation cascade.

When arriving at altitude, the body immediately downregulates plasma volume (the liquid component of blood), which leads to an increased red cell concentration per volume of blood. This can be measured as an increased haemoglobin concentration-the increase can be as much as 20%). In practice this haemoconcentration manifests as diuresis in the first hours at altitude. The reduction in plasma volume will increase the density of red cells per volume of blood and thus improve oxygen delivery.[46]

The reduced oxygen tension in the blood then stimulates the production of new red cells through the increased release of erythropoietin (EPO) in the kidney. EPO inhibits the cell death of erythropoietic progenitor cells. There is a clear dose-response relationship between the duration and height of exposure to altitude and the increase in total red cell mass.[47]

Other adaptations

Although haematological adaptation is the most important contributor to performance gain, three other processes also play roles:[48, 49]

- angiogenesis, closely tied to erythropoiesis, increases
- energy metabolism is accelerated and subsequently improved through better glucose transport, leading to greater muscle efficiency, probably at a mitochondrial level
- pH regulation through better buffering and the ability to tolerate lactic acid production is optimised.[48, 49]

Putting altitude training into practice

Although these mechanisms contribute to improving the body's ability to process oxygen for aerobic metabolism, the challenging training environment also makes it more difficult to perform at the same intensity as at sea level. One of the challenges for altitude training is determining the right balance between training intensity and the stimulus of altitude exposure. If the training stimulus is too intense, the athlete will fatigue excessively and this will impair adaptation. On the other hand, if the training intensity at altitude is reduced too much, the athlete will suffer from detraining. This balance is further affected by the fact that sleep and recovery are also both impaired by the hypoxia of altitude.

To overcome this challenge, different models of altitude training have been developed, where the times of training and passive recovery are spent at different altitudes to resolve the above problem:

- *Live high, train high* The athlete lives and trains at (the same) altitude. The limitations in terms of recovery and training intensity mentioned above apply.
- *Live high, train low* The athlete lives at altitude but trains at (or near) sea level. This allows a more easily controllable training intensity with the beneficial passive effects of altitude.
- *Live low, train high* The athlete lives at sea level and trains at altitude to increase the intensity during training.

Training methods that use very short (minutes) exposures to severe hypoxia, such as intermittent hypoxic training through sprinting, have not been well evaluated. As the usefulness of these programs is unclear, they are not covered in this chapter. Page 364

The choice of appropriate altitude training methods depends on both training and logistical factors, which are likely to differ from athlete to athlete, and team to team.[50]

Altitude exposure—how much is enough?

One of the key factors to consider when planning altitude training is the appropriate duration and height of exposure. It is undisputed that the effects of hypoxia are continuous; that is, set in at relatively low altitude but become meaningful in terms of performance enhancement only at a certain duration and exposure height (Fig. 25.4).

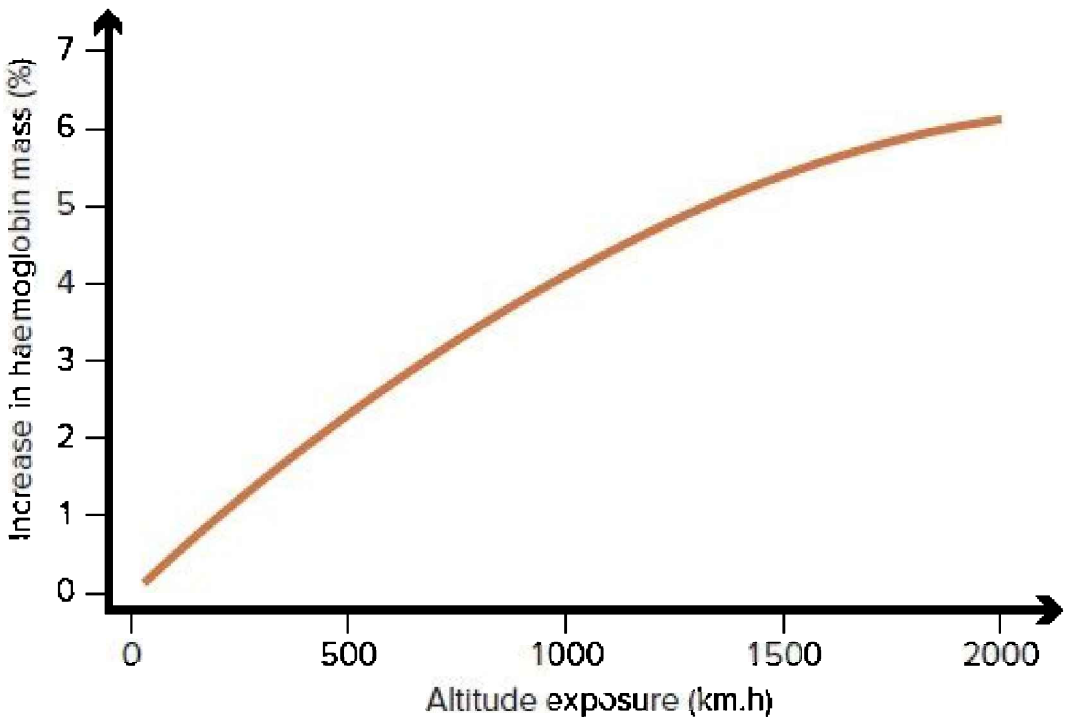


Figure 25.4 The correlation of altitude exposure (in km.h) and the increase in haemoglobin mass (in %) ADAPTED FROM GARVICAN-LEWIS ET, (2017).[51]

NEED TO KNOW

The unit commonly used to evaluate altitude exposure is 'kilometre hours' (km.h), calculated from the exposure height (in kilometres) multiplied by the exposure length (in hours). For example, an athlete exposed to altitude of 2000 m for 1 week has altitude exposure of 336 kmh

(2 km for 168 h).[51]

Meta-analysis has shown that haemoglobin mass (the key adaptation for performance increase) increases by about 1% per 100 h of exposure to relevant altitude. A meaningful increase of haemoglobin mass requires about 300–500 km.h.[47] It is clear that 300–500 km.h can be achieved by various means (i.e. higher exposure for a shorter time, or longer exposure to lower altitude). As mentioned above, the likelihood of adverse effects and potential pathologies at altitude increases with increasing altitude, and thus the decision as to how long and how high an athlete is to be exposed must be considered carefully. Practice-proven altitude models commonly use altitudes of 2000–2500 m (6500–8000 ft) with exposure times of 14–21 days, thus an exposure of 670–840 km.h.

Artificial altitude—does it work?

Athletes from many countries do not have ready access to high mountains required for natural training. Therefore, artificial environments of reduced oxygen availability have been developed.

Originating in Finland in the 1990s, many countries now have special facilities (houses or rooms) where athletes can stay in an artificial, altitude-like hypoxic environment while training under normal, normoxic conditions outside. Individual, commercially available solutions such as altitude tents with small hypoxia-generating generators also exist. Those artificial environments cannot mimic the difference in barometric pressure between such artificial environments and natural altitude, but the effects on the haematological and respiratory adaptation appear to be similar,[52] provided the duration and level of hypoxia are equivalent.

Timing when altitude training—when to go to altitude

The timing of altitude training in view of the general season planning and the major competitions is also key. While many factors related to training and race planning impact this decision, the choice of when to conduct an altitude training block should be guided by the likely time course of the key adaptations.

There is now a compelling body of evidence describing the timing of the effects of altitude on haematological adaptations and notably haemoglobin mass. After withdrawal of the hypoxic stimulus (i.e. return to sea level), haemoglobin mass increased by previous altitude exposure will likely decline over 3 weeks.[47] This needs to be considered when planning altitude training in relation to important competitions.

Page 365

To extend the altitude-induced increased haemoglobin mass beyond the end of altitude camps, sports scientists have evaluated athletes using intermittent hypoxic devices at sea level. However, the necessary duration of such intermittent hypoxic exposure with the aim of prolonging the beneficial effects of altitude are still being investigated. Note that haemoglobin mass increase is obviously not the only determinant of performance after altitude, and so other factors related to

training and tapering should be taken into consideration.

Potential interfering factors–what can go wrong?

Altitude training does not elicit the same effects for every athlete. While it was hypothesised that there are 'non-responders' to altitude training, athletes have also reported a varied and sometimes improving response over different altitude camps.[53, 54] It is therefore much more likely that the response to altitude and any beneficial adaptation depends less on innate, individual susceptibility than on many independent factors, just as in normal training. These factors should be assessed before going to altitude, and then again while training at altitude (Table 25.2). When such factors are not in place, beneficial adaptation will not occur (or only to a lesser degree).

Table 25.2 What to assess and perform before going to altitude and while at altitude

	Before	During 1
Nutrition	Educate on expected challenges related to altitude	Monitor nutrition, check with kitchen staff for appropriate menu options
Sleep	Educate on expected challenges related to altitude	Consider mild sleeping aids if conventional sleeping hygiene measures are not successful
Iron stores	Check ferritin about 3 months prior to altitude camp and start supplementation if ferritin is below 50 ng/mL	Consider routine supplementation for each athlete while at altitude[54]
Training intensity	Educate on expected challenges related to altitude, introduce RPE-based training monitoring system	Monitor RPE (rating of perceived exertion) closely, liaise with coaching staff

The best-known confounder for a sufficient haematological response to altitude is iron availability. Individuals with low iron availability will show no, or a reduced, increase in haemoglobin mass and thus most likely no, or a reduced, beneficial effect on their performance. Ferritin levels above 50 ng/mL elicit significantly better increase in haemoglobin mass compared to lower levels, even when those lower levels were still within the normal range for healthy adults.[55, 56]

In addition, sleep, the main source of recovery for the athlete, is often impaired at altitude. More frequent arousals and an increased prevalence of periodic breathing markedly reduce sleep quality and thus recovery.

Another factor that impairs altitude adaptation is chronic relative energy deficiency. This is of particular importance in endurance sports, where athletes strive to achieve low weight by dieting and sometimes starvation. The negative impact of such strategies on the erythropoietic system is likely amplified by hypoxia due to the higher basal metabolic rate at altitude. Illnesses and injuries also interfere with altitude adaptation.

As already outlined in the first half of this chapter, the environment of altitude is also challenging at many levels other than hypoxia. There is an increased risk of upper respiratory tract infections due to reduced humidity at altitude, causing dryness of the mucous membranes of the upper respiratory tract, which thus impairs their role in the first defence against viruses and bacteria. Immunity is further compromised by a much greater UV exposure at altitude compared to

sea level-this should be considered when planning long outdoor training sessions.[57]

Performance gains–what can the athlete expect?

From a purely physiological perspective, each gram of haemoglobin can bind 1.4 mL of oxygen. Optimal altitude adaptation typically will increase haemoglobin mass by about 1% per 100 h of exposure, thus 30–50 g in a trained athlete (or 3–5%, see above) during a typical altitude training camp. Thus, in theory, this would translate to an improvement of their maximal oxygen uptake (VO_2max) by about 120–200 mL.[58]

Page 366

Meta-analysis of altitude studies has confirmed an increase in performance of 1–7%, depending on the type and length of exposure and using different performance measures.[50] VO_2max is a likely contributor, with the results of the meta-analysis confirming the theoretical modelling. Given that a difference in performance of 1% is meaningful in elite sports settings, it is clear that such performance gains are beneficial for the athlete and make altitude training a valuable training tool.

Blood tests for measuring adaptation–are they useful?

The altitude-related increase in total red cell or haemoglobin mass is poorly reflected by measuring haemoglobin concentration in a full blood count, which is often used as a surrogate marker. This is due to the fact that shifts in plasma volume (see above) will markedly interfere with this measure. Thus, it is not useful to conduct blood tests while at altitude or after return to sea level to measure the efficiency of the exposure on haemoglobin mass.[59]

CASE STUDY

Advice for the athlete prior to altitude training

The case

A 25-year-old cyclist asks for your advice regarding an upcoming altitude camp (Fig. 25.5). She has finished her base training period, is nearly at race weight and is aiming to get an additional performance kick from altitude. She has tried it before but noted no marked improvement after a 2-week live high, train high camp at 1500 m.

Figure 25.5 Physiological principles and data regarding the relationship between altitude exposure and haemoglobin gains can be used to improve athlete performance SHUTTERSTOCK/DOLOMITE-SUMMITS.

Your advice

First, you educate the athlete about the main physiological adaptations and her expected time course. You highlight that her previous altitude training was at insufficient altitude to provide benefit (500 km.h). You advise her to go higher to bring her altitude exposure up to 800 km.h to augment her haemoglobin mass.

A blood test reveals a ferritin level of 24 ng/mL. While still within the normal range, there is good evidence that the haematological response will be improved if iron stores are full. Thus, you prescribe oral iron supplements (100 mg elemental iron/day) three weeks before the camp and throughout it. You further highlight the issues of changes in training load and the importance of recovery, sleep and nutrition.

Outcome

The athlete completed the camp at 2300 m, thus accumulating 772 km.h. She tolerated the camp well and did not have any major concerns or disruptions in training. When reviewing the power data from her first races upon returning to sea level, 10 days after altitude, she noticed a 15–20 W improvement in critical power, which is consistent with the theoretically expected performance gains.

REFERENCES

1. Schneider M, Bernasch D, Weymann J et al. Acute mountain sickness: influence of

susceptibility, preexposure, and ascent rate. *Med Sci Sports Exerc* 2002; 34(12): 1886–91.

2. Murdoch D. How fast is too fast? Attempts to define a recommended ascent rate to prevent acute mountain sickness. *Int Soc Mt Med Newsl* 1999; 9(1): 3–6.
3. Jin J. Acute mountain sickness. *JAMA* 2017 Nov 14; 318(18): 1840. doi: 10.1001/jama.2017.16077.
4. Schoene RB. Illnesses at high altitude. *Chest* 2008; 134: 402–16.
5. Hackett PH, Roach RC. High-altitude medicine. In: Auerbach PS, ed. *Wilderness medicine: management of wilderness and environmental emergencies*. 4th ed. St Louis, MO: Mosby, 2001: 1–37.
6. Basnyat B, Murdoch DR. High-altitude illness. *Lancet* 2003; 361(9373): 1967–74.
7. Luks AM, McIntosh SE, Grissom CK et al. Wilderness Medical Society consensus guidelines for the prevention and treatment of acute altitude illness. *Wilderness Environ Med* 2010; 21: 146–55.
8. Shlim D, Gallie J. The causes of death among trekkers in Nepal. *Int J Sports Med* 1992; 13(Suppl 1): S74–6.
9. MacInnis MJ, Lohse KR, Strong JK et al. Is previous history a reliable predictor for acute mountain sickness susceptibility? A meta-analysis of diagnostic accuracy. *Br J Sports Med* 2015; 49(2): 69–75.
10. Katayama K, Sato Y, Shima N et al. Enhanced chemosensitivity after intermittent hypoxic exposure does not affect exercise ventilation at sea level. *Eur J Appl Physiol* 2002; 87(2): 187–91.
11. Hultgren HN, Marticorena EA. High altitude pulmonary edema: epidemiologic observations in Peru. *Chest* 1978; 74(4): 372–6.
12. Scoggin CH, Hyers TM, Reeves JT et al. High-altitude pulmonary edema in the children and young adults of Leadville, Colorado. *N Engl J Med* 1977 Dec; 297(23): 1269–72.
13. Gaillard S, Dellasanta P, Loutan L et al. Awareness, prevalence, medication use, and risk factors of acute mountain sickness in tourists trekking around the Annapurnas in Nepal: a 12-year follow-up. *High Alt Med Biol* 2004; 5(4): 410–19. doi: 10.1089/ham.2004.5.410.
14. Jean D, Leal C, Kriemler S et al. Medical recommendations for women going to altitude. *High Alt Med Biol* 2005; 6(1): 22–31.
15. Honigman B, Theis MK, Koziol-McLain J et al. Acute mountain sickness in a general tourist population at moderate altitudes. *Ann Intern Med* 1993; 118(8): 587–92.
16. Hackett PH, Roach RC. High altitude cerebral edema. *High Alt Med Biol* 2004; 5(2): 136–46. doi: 10.1089/1527029041352054.
17. Naeije R, De Backer D, Vachiery JL et al. High-altitude pulmonary edema with primary pulmonary hypertension. *Chest* 1996; 110(1): 286–9.

18. Smith J. The use of high altitude treatment for childhood asthma. *Practitioner* 1981; 225(1361): 1663–6.
19. Cogo A, Fischer R, Schoene R. Respiratory diseases and high altitude. *High Alt Med Biol* 2004; 5(4): 435–44.
20. Mader TH, White LJ. Refractive changes at extreme altitude after radial keratotomy. *Am J Ophthalmol* 1995; 119(6): 733–7.
21. White LJ, Mader TH. Refractive changes with increasing altitude after radial keratotomy. *Am J Ophthalmol* 1993; 115: 821–3.
22. Dimmig JW, Tabin G. The ascent of Mount Everest following laser in situ keratomileusis. *J Refract Surg* 2003; 19(1): 48–51.
23. Kemmeren JM, Algra A, Grobbee DE. Third generation oral contraceptives and risk of venous thrombosis: meta-analysis. *BMJ* 2001; 323(7305): 131–4.
24. Roach RC, Maes D, Sandoval D et al. Exercise exacerbates acute mountain sickness at simulated high altitude. *Med Sci Sport Exerc* 1999; 31(Suppl): S182. http://content.wkhealth.com/linkback/openurl?sid=WKPTLP:landingpage&an=00005768-199905001-00813.
25. Reeves J, Wagner J, Zafren K. Seasonal variation in barometric pressure and temperature in Summit County: effect on altitude illness. In: Sutton J, Houston C, Coates G, eds. *Hypoxia and molecular medicine*. Burlington, VT: Queen City Printers, 1993: 275–81.
26. Cumbo TA, Basnyat B, Graham J et al. Acute mountain sickness, dehydration, and bicarbonate clearance: preliminary field data from the Nepal Himalaya. *Aviat Space Environ Med* 2002; 73(9): 898–901.
27. Murdoch DR. Symptoms of infection and altitude illness among hikers in the Mount Everest region of Nepal. *Aviat Space Environ Med* 1995; 66(2): 148–51.
28. Durmowicz AG, Noordeweir E, Nicholas R et al. Inflammatory processes may predispose children to high-altitude pulmonary edema. *J Pediatr* 1997; 130(5): 838–40.
29. Hansen JE, Hartley LH, Hogan RP, 3rd. Arterial oxygen increase by high-carbohydrate diet at altitude. *J Appl Physiol* 1972 Oct; 33(4): 441–5.
30. Hannon JP, Chinn KS, Shields JL. Effects of acute high-altitude exposure on body fluids. *Fed Proc* 1969; 28(3): 1178–84.
31. Dumont L, Mardirosoff C, Tramèr MR. Efficacy and harm of pharmacological prevention of acute mountain sickness: quantitative systematic review. *BMJ* 2000; 321(7256): 267–72. http://www.bmj.com/content/321/7256/267.
32. Gertsch JH, Basnyat B, Johnson EW et al. Randomised, double blind, placebo controlled comparison of ginkgo biloba and acetazolamide for prevention of acute mountain sickness among Himalayan trekkers: the Prevention of High Altitude Illness Trial (PHAIT). *BMJ* 2004; 328(7443): 797.

33. Carlsten C, Swenson ER, Ruoss S. A dose–response study of acetazolamide for acute mountain sickness prophylaxis in vacationing tourists at 12,000 feet (3630 m). *High Alt Med Biol* 2004; 5(1): 33–9. doi: 10.1089/152702904322963672.
34. Rock PB, Johnson TS, Larsen RF et al. Dexamethasone as prophylaxis for acute mountain sickness: effect of dose level. *Chest* 1989; 95(3): 568–73.
35. Chow T, Browne V, Heileson HL et al. Ginkgo biloba and acetazolamide prophylaxis for acute mountain sickness: a randomized, placebo-controlled trial. *Arch Intern Med* 2005; 165(3): 296–301.
36. Mittleman MA, Mintzer D, Maclure M et al. Triggering of myocardial infarction by cocaine. *Circulation* 1999; 99(21): 2737–41.
37. Oelz O, Maggiorini M, Ritter M et al. Prevention and treatment of high altitude pulmonary edema by a calcium channel blocker. *Int J Sports Med* 1992; 13 (Suppl) 1: S65–8. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/102/CN-00090102/frame.html.
38. Maggiorini M, Brunner-La Rocca HP, Peth S et al. Both tadalafil and dexamethasone may reduce the incidence of high-altitude pulmonary edema: a randomized trial. *Ann Intern Med* 2006; 145(7): 497–506.
39. Sartori C, Allemann Y, Duplain H et al. Salmeterol for the prevention of high-altitude pulmonary edema. *N Engl J Med* 2002; 346(21): 1631–6. http://www.nejm.org/doi/abs/10.1056/NEJMoa013183.
40. Weil JV. Sleep at high altitude. *High Alt Med Biol* 2004; 5(2): 180–9.
41. Swenson ER, Bärtsch P, eds. *High Altitude: Human Adaptation to Hypoxia*. New York: Springer Books, 2014.
42. Sutton JR, Houston CS, Mansell AL et al. Effect of acetazolamide on hypoxemia during sleep at high altitude. *N Engl J Med* 1979 Dec; 301(24): 1329–31.
43. Dubowitz G. Effect of temazepam on oxygen saturation and sleep quality at high altitude: randomised placebo controlled crossover trial. *BMJ* 1998; 316(7131): 587–9.
44. Nickol AH, Leverment J, Richards P et al. Temazepam at high altitude reduces periodic breathing without impairing next-day performance: a randomized cross-over double-blind study. *J Sleep Res* 2006; 15(4): 445–54.
45. Beall CM. Two routes to functional adaptation: Tibetan and Andean high-altitude natives. *Proc Natl Acad Sci U S A* 2007; 104(Suppl 1): 8655–60.
46. Beidleman BA, Staab JE, Muza SR et al. Quantitative model of hematologic and plasma volume responses after ascent and acclimation to moderate to high altitudes. *Am J Physiol Regul Integr Comp Physiol* 2017 Feb; 312(2): R265–72.
47. Gore CJ, Sharpe K, Garvican-Lewis LA et al. Altitude training and haemoglobin mass from the optimised carbon monoxide rebreathing method determined by a meta-analysis. *Br J Sports Med* 2013 Dec; 47 Suppl 1: i31–9.
48. Gore CJ, Clark SA, Saunders PU. Nonhematological mechanisms of improved sea-

level performance after hypoxic exposure. *Med Sci Sport Exerc* 2007 Sep; 39(9): 1600–9.

49. Bärtsch P, Saltin B. General introduction to altitude adaptation and mountain sickness. *Scand J Med Sci Sports* 2008 Jul; 18: 1–10.
50. Bonetti DL, Hopkins WG. Sea-level exercise performance following adaptation to hypoxia: a meta-analysis. *Sports Med* 2009; 39(2): 107–27.
51. Garvican-Lewis LA, Sharpe K, Gore CJ. Time for a new metric for hypoxic dose? *J Appl Physiol (1985)* published online 25 February 2016. doi: 10.1152/japplphysiol.00579.2015.
52. Mounier R, Brugniaux JV. Counterpoint: hypobaric hypoxia does not induce different responses from normobaric hypoxia. *J Appl Physiol* (2012) 112(10): 1784–6.
53. Friedmann B. Individual variation in the erythropoietic response to altitude training in elite junior swimmers. *Br J Sports Med* 2005 Mar; 39(3): 148–53.
54. Frese F, Friedmann-Bette B. Effects of repetitive training at low altitude on erythropoiesis in 400 and 800 m runners. *Int J Sports Med* 2010 Mar; 31(6): 382–8.
55. Govus AD, Garvican-Lewis LA, Abbiss CR et al. Pre-altitude serum ferritin levels and daily oral iron supplement dose mediate iron parameter and hemoglobin mass responses to altitude exposure. Connor JR, ed. *PLoS ONE* 2015 Aug; 10(8): e0135120.
56. Garvican-Lewis LA, Govus AD, Peeling P et al. Iron supplementation and altitude: decision making using a regression tree. *J Sports Sci Med* 2016; 15(1): 204.
57. Koehle MS, Cheng I, Sporer B. Canadian Academy of Sport and Exercise Medicine position statement: athletes at high altitude. *Clin J Sport Med* 2014 Mar; 24(2): 120–7.
58. Schmidt W, Prommer N. Impact of alterations in total hemoglobin mass on VO_2max. *Exerc Sport Sci Rev* 2010 Apr; 38(2): 68–75.
59. Lobigs LM, Sharpe K, Garvican-Lewis LA et al. The athlete's hematological response to hypoxia: a meta-analysis on the influence of altitude exposure on key biomarkers of erythropoiesis. *Am J Hematol* published online October 2017. doi: 10.1002/ajh.24941.

Chapter 26

Underwater

with JAMES O'DONOVAN and MICHAEL KOEHLE

If it were bends my joints would be hurting–not the middle of my thigh, that's what all the textbooks say ... Textbooks aren't always right!

Richard Pyle, experienced underwater diver, after suffering decompression sickness

Diving medicine (also known as undersea/hyperbaric medicine) focuses on the diagnosis, treatment and prevention of conditions that occur as a result of a human's exposure to the underwater environment. Diving is growing in popularity, with an estimated 25 million divers certified worldwide since 1967 and over one million new divers trained annually.[1]

Diving poses a wide set of physiological challenges and risks. Not only is the pressure of the underwater environment a stressor to the body, but diving often incorporates other challenges, such as cold (see Chapter 24), tides, currents and the patient's medical history. The sport and exercise medicine clinician may encounter these issues when a patient seeks guidance prior to diving, especially in the setting of a pre-existing medical condition.

METHODS OF DIVING

There are a number of different disciplines of diving that can expose an individual to risk. These include:

- scuba diving
- breath-hold/free diving
- umbilical (surface-supply) diving
- rebreather diving.

Scuba (self-contained underwater breathing apparatus) is the most common form of diving and is used in commercial and recreational as well as technical diving. Scuba divers carry their own

breathing gas, usually compressed air, allowing greater mobility than surface-supply diving and longer excursions underwater than breath-hold diving. The scuba apparatus is an open-circuit system, meaning that it discharges all the expired gases into the environment upon exhalation. The system consists of one or more diving cylinders containing breathing gas delivered at high pressure, supplied to the diver through a regulator. Although compressed air is by far the most common gas used, some divers will use specifically prepared mixed gases, such as nitrox, a mixture of nitrogen and oxygen, to increase the length of their dives.

Closed-circuit or semi-closed-circuit rebreather scuba systems allow recycling of exhaled gases. The volume of gas used is reduced compared to that of an open circuit; therefore, a smaller cylinder or cylinders may be used for an equivalent dive duration. Rebreathers extend the time spent underwater compared to open circuit for the same gas consumption. They produce fewer bubbles and less noise than scuba, which makes them attractive to covert military divers to reduce the risk of detection, scientific divers, to reduce disturbance of marine life, and media divers, to avoid bubble interference.

Surface-supplied (umbilical) diving is the method whereby the diver's breathing gas is supplied by an umbilical connection to the surface, either from the shore or from a diving support vessel. The primary advantages of conventional surface-supplied diving are lower risk of drowning and considerably larger breathing gas supply than scuba, allowing longer working periods. It is commonly used in saturation diving, where longer supply is required if going to greater depths, and in contaminated water, where divers are required to use helmets to protect from the environment.

THE PHYSIOLOGY OF DIVING

The physics of the hyperbaric environment, where the ambient pressure is greater than sea-level atmospheric pressure, imposes risks on divers. The Irish scientist Robert Boyle described the relationship such that, for gases at a given temperature, volume is inversely proportional to pressure. Applied to the diving environment, pressure increases by 1 atmosphere for every 10 m depth below the surface in sea water. An example of how pressure increases affect the lungs during diving according to Boyle's Law is shown in Figure 26.1.

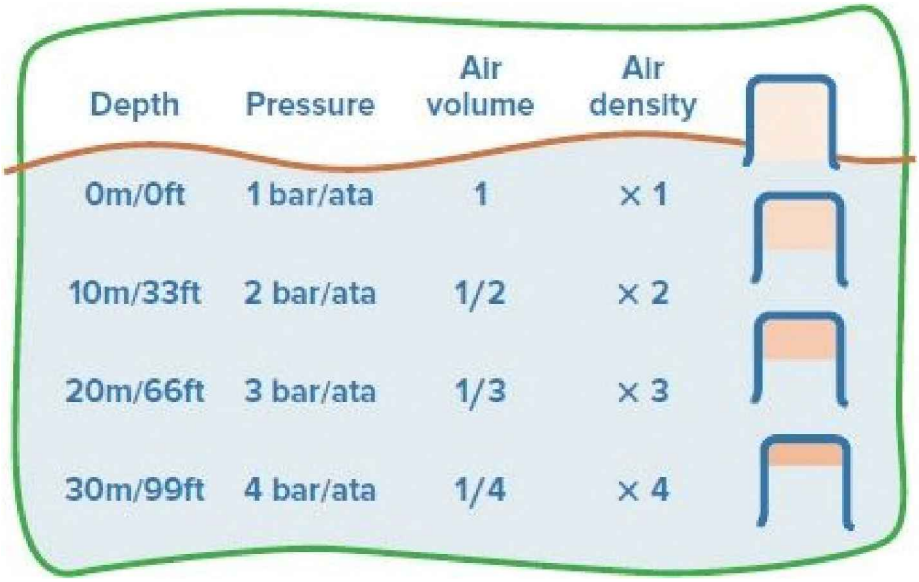


Figure 26.1 Atmospheric pressure with depth and effects on air volume

NEED TO KNOW

The average depth of the ocean is about 4 km. Given there is an increase of 1 atmosphere for every 10 m of depth, the pressure on the sea floor is about 400 atmospheres.

Another important law of physics, known as Dalton's Law, is that the total pressure of a gas is equal to the sum of the partial pressures of each of the individual gases in a mixture. Thus, the partial pressure of a gas is the product of the fractional concentration of that gas (%) and the surrounding ambient pressure. As one dives deeper, the concentration of oxygen in the air breathed by the diver remains the same but the partial pressure of oxygen increases as a function of the increasing ambient pressure. This is the same for all non-reacting gases, namely the other constituents of air, nitrogen and carbon dioxide. Thus, at significant depth, a diver can be exposed to very high partial pressures of nitrogen and oxygen, both of which can have medical consequences and are potentially toxic below certain depths.

THE PATHOPHYSIOLOGY OF DIVING

As a diver descends, the pressure inside the body's air spaces remains the same as it was on the surface, whereas the pressure of the surrounding water increases. On descent, the diver must equalise any pressure differentials between the ambient pressure and various spaces in the body (e.g. middle ear, sinuses). A sufficient pressure difference can cause a 'squeeze', the sensation of squeezing of the air space. Persistent and/or excessive pressure differentials can cause physical

damage (barotrauma).

The squeezes

The major manifestations of barotrauma include:

1. sinus or middle ear effects
2. arterial gas embolism
3. pneumothorax.

Specific barotrauma can occur at certain sites: ear, dentition, sinus, lung, mask and suit. It is vital that that a diver equalises the lower body cavity pressures to equate with the ambient external ambient pressures, to avoid the onset of a squeeze. One of the most common sites of barotrauma is the external, middle or inner ear. Middle ear barotrauma is the most common, being prevalent in 20–40% of divers,[2–4] and is due to insufficient equilibration of the middle ear. Squeezes of the inner ear, though much less common, can lead to varying degrees of conductive sensorineural hearing loss as well as vertigo. Sinuses (as air-filled cavities) are also prone, and this can result in pain, as well as epistaxis.

It is important to be aware that certain medical illnesses can predispose the diver to difficulty with equilibration. For example, an upper respiratory tract infection (URTI) or ear infection can cause congestion of the eustachian tubes, making it difficult to equalise the ears. Thus, significant congestion from causes such as an URTI can increase the risk of barotrauma for a diver.

Some equipment can also cause problems in this scenario. For example, a diving mask squeeze occurs over the eyes and nose. The main risk is rupture of the capillaries of the eyes and facial skin or orbital emphysema from higher pressures. This can be avoided by equalising the mask pressure with the ambient pressure through the nose. As such, goggles covering only the eyes are not suitable for deep diving as they cannot be equalised. A similar situation can occur with dry suits, which are used in cold-water diving. In these suits the amount of gas within the suit is regulated for buoyancy and comfort. If the volume of the gas in the suit gets too low during a dive, creases in the suit can cause marks on the skin (suit squeeze).

Page 369

Pulmonary barotrauma

Pulmonary barotrauma is caused by lung overpressure, usually caused by breath-holding on ascent. During ascent, the gas in the lungs expands as the ambient pressure decreases. Air that is trapped in regions or pockets cannot escape (because of breath-holding or airway obstruction) and continues to expand, leading to alveolar rupture (Fig. 26.2 demonstrates the mechanism leading to alveolar rupture and its subsequent effect on the body). As there are no nociceptive nerve endings in the lung, there is little warning to the diver as they overexpand. The damage caused by this alveolar rupture is termed pulmonary barotrauma and manifests clinically as two entities.

Page 370

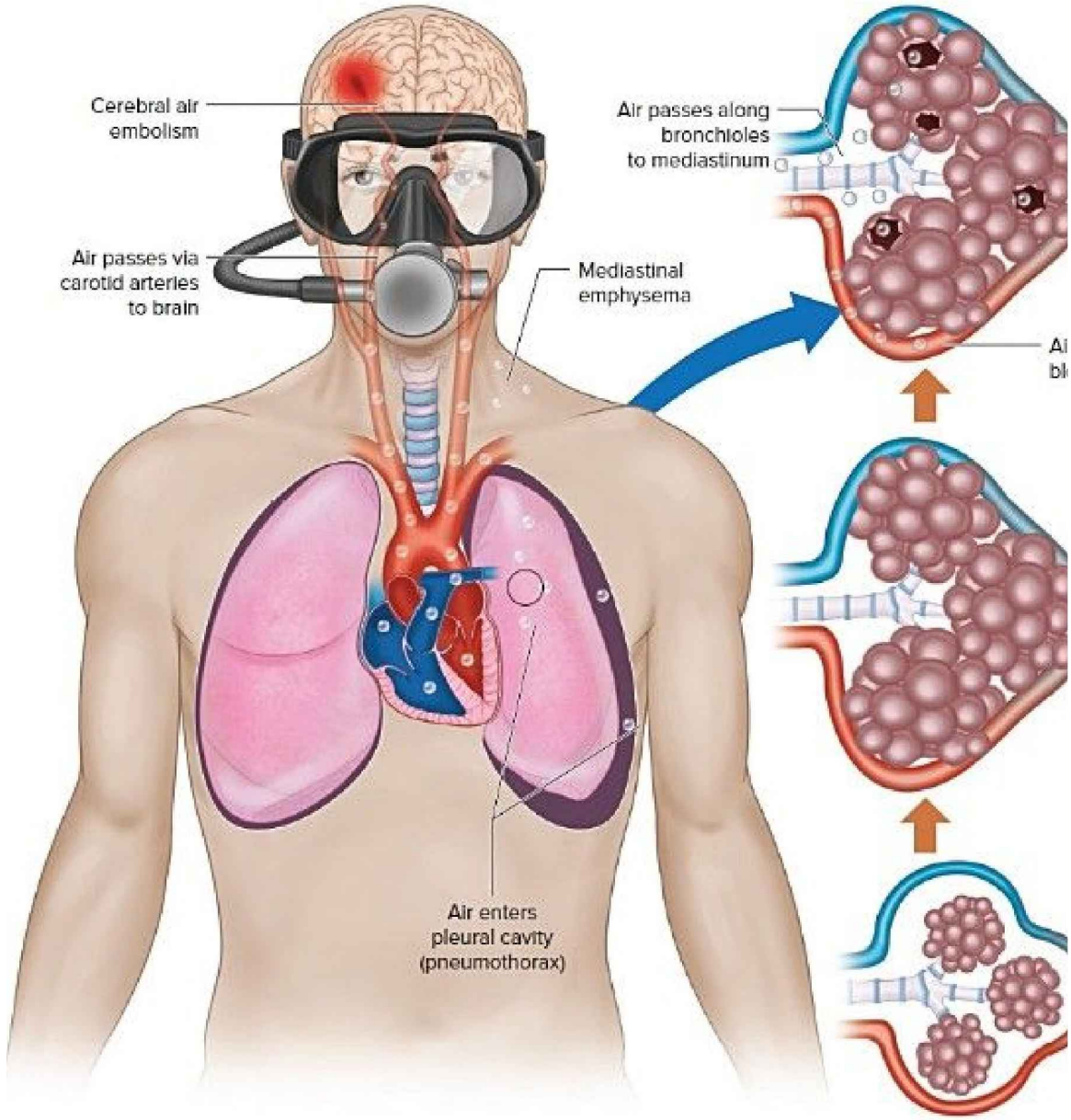


Figure 26.2 Pulmonary barotrauma. Different manifestations of pulmonary barotrauma ADAPTED WITH PERMISSION FROM WILDERNESS MEDICINE, 7TH ED., AUERBACH PS, FIGURE 71.1 COPYRIGHT ELSEVIER 2017

Arterial gas embolism

Pulmonary barotrauma on ascent more frequently leads to arterial gas embolism (AGE), or air embolism, in divers.[5] In contrast to pneumothorax, the intrapulmonary air expansion causing

alveolar rupture leads to introduction of the escaped gas into the arterial circulation. The resulting gas embolus causes sudden death in 5% of divers immediately secondary to cardiac arrest; however, 50% can have complete recovery. Clinical manifestations are usually abrupt and present immediately or within 10 minutes of the diver reaching the surface. The symptoms can be quite varied and depend on the tissue affected. Table 26.1 details the symptoms of arterial gas embolism and how common it is for them to present in the affected individual.

Table 26.1 Signs and symptoms of arterial gas embolism

Symptom	Percentage
Loss of consciousness	81
Pulmonary rales or wheezes	38
Blood in the ear (haemotympanum)	34
Decreased reflexes	34
Extremity weakness or paralysis	32
Chest pain	29
Irregular breathing or apnea	29
Vomiting	29
Coma without convulsions	26
Coughing blood (haemoptysis)	23
Sensory loss	21
Stupor and confusion	18
Vision changes	20
Cardiac arrest	16
Headache	16
Unilateral motor changes	16
Change in gait or ataxia	14
Conjunctivitis	14
Sluggishly reactive pupils	14
Vertigo	12
Coma with convulsions	11

ADAPTED FROM NEUMAN, (2003)[8]

The symptoms of AGE have significant overlap with decompression sickness (DCS) but are characterised by the rapid onset of symptoms (i.e. symptoms begin to present less than 10 minutes post return to ambient atmospheric pressures). The symptoms of DCS tend to build over a longer period. Although different pathological mechanisms, the two conditions are not mutually exclusive. For example, it is certainly possible to have DCS giving rise to venous bubbles that cross into the arterial system (via a patent foramen ovale) and then cause AGE.[6] The first-aid measures are the same initially, thus differentiation of these conditions clinically is not a priority. However, both conditions can be deadly, with AGE more concerning due to its sudden onset and targeting of the central nervous system and potential for cardiovascular collapse. It is important to be aware of the fundamental difference between AGE and DCS. Both entities involve bubble formation.

Decompression sickness is a disease that involves gas bubbles forming in tissues and venous blood, while AGE results from the introduction of gas bubbles directly into the arterial circulation. Although the pathologies and natural histories of DCS and AGE are different, the treatment of these conditions is recompression in both instances.[7]

Even for experienced clinicians, differentiating between the two entities can be challenging, and adequate training and experience are essential. The diagnosis is often made retrospectively, for insurance purposes or to assess treatment efficacy. The depth-time profiles are critical, as AGE can occur with any exposure, whereas DCS is unlikely in short, shallow dives.

Pneumothorax

Pneumothorax is the second form of pulmonary barotrauma, caused by the escaped gas invading the pleural space instead of the vasculature. This will often become a tension pneumothorax on ascent as the ambient pressure is reduced. This is a life-threatening situation and, therefore, a personal history of spontaneous pneumothorax is an absolute contraindication to diving. Lung rupture is commonly asymptomatic, and often one of the symptoms of a small pneumothorax is a voice change after a dive. This should raise a warning flag.

PRACTICE PEARL

A small pneumothorax may not be acutely serious; however, if undetected prior to a further diving attempt, the consequences can become severe.

Decompression sickness

Decompression sickness (DCS) is a condition arising from dissolved gases coming out of solution inside the body. Bubbles can occur anywhere in the bloodstream, particularly in the venous system, and are routed back to the heart and lungs and to the pulmonary filter. Oxygen is continuously used by the body and does not accumulate; however nitrogen molecules do. The accumulated nitrogen bubbles can expand and injure tissue or they have the potential to block vessels in many organs. A simple classification uses type 1 (simple) for symptoms involving only the skin, musculoskeletal system or lymphatic system, and type 2 for symptoms when other organs, such as the central nervous system, are involved. Type 2 is considered more serious and usually has worse outcomes.

There is much overlap between AGE and DCS and the two are not mutually exclusive. Clinical distinction between these entities is not crucial in the acute setting, as the initial treatments are the same. Although there is a perception that due to the sudden onset and targeting of the central nervous system, AGE is more serious, both can result in death and serious morbidity.

Type 1

Musculoskeletal pain syndromes are the most common symptoms of DCS, occurring in up to 80% of cases.[9] Pain in the joints and muscles (also known as 'the bends') primarily affects the limbs and not the axial skeleton. It frequently presents as a deep ache that is difficult to characterise and pinpoint. DCS primarily affects shoulders, elbows and hands in recreational divers. The cause is not completely understood, but it is thought to be related to blockage of specialised blood vessels in the fatty marrow of limb bones. If the condition is left untreated, it may result in the patient developing dysbaric osteonecrosis.

Cutaneous DCS commonly causes skin manifestations (Fig. 26.3), including itching and mild rashes, or as a distinct mottled, marbled and occasionally raised discolouration of the skin, a condition known as cutis marmorata that may presage the development of type 2 DCS.

https://www.sciencedirect.com. Due to rights and permissions restrictions, this content cannot be reproduced in a digital format. The content is available in the print edition at page 371.

Figure 26.3 Decompression sickness type 1—cutaneous presentation signs

REPRINTED FROM *THE LANCET,* VOL. 377, VANN RD, BUTLER FK, MITCHELL SJ, ET AL., DECOMPRESSION ILLNESS, PP 153–164, COPYRIGHT (2011), WITH PERMISSION FROM ELSEVIER

In addition, type 1 DCS is less commonly associated with obstruction of the lymphatic system, which can result in swelling and localised pain in the tissue surrounding the lymph nodes, such as in the armpits, groin or behind the ears.

Type 2

Neurological decompression syndromes are the most common form of DCS in sport divers. The spinal cord appears to be particularly vulnerable. Symptoms include abdominal, low back and lower extremity pain, weakness, and loss of feeling and function. Cerebral involvement is much more common than previously thought, while lesions in peripheral nerves may cause numbness, limb pain and weakness. Inner ear damage may affect balance or lead to tinnitus. Type 2 DCS is also known to cause cardiorespiratory symptoms such as chest tightness and shortness of breath.

Risk factors associated with decompression sickness

Although the occurrence of DCS is not easily predictable many predisposing factors are known. They can be considered environmental or individual. Table 26.2 lists the known risk factors in each category.

Table 26.2 Risk factors for decompression sickness

Environmental	Individual

Inadequate surface intervals	Dehydration, hangover
Repetitive exposures	Patent foramen ovale
Rate of ascent	Older age
Duration of exposure	Previous injury
Diving before going to altitude/flying	Higher body fat

Treatment of decompression sickness

Detailed management guidelines for DCS are beyond the scope of this chapter, but the principles are as follows. Treatment of DCS requires advanced certification and must only be prescribed by a specialist.

1. All cases are treated with 100% oxygen until hyperbaric oxygen therapy is available.
2. Fluids are administered for rehydration.
3. The patient is transported in the recovery position.
4. Recompression therapy: duration is dependent on severity of symptoms, dive history, type of recompression therapy used and patient's response to treatment. One of the more frequently used treatment schedules is the US Navy Table 6,[10] which provides hyperbaric oxygen therapy with a maximum pressure equivalent to 60 feet (18 m) of seawater for a total time under pressure of 288 minutes, of which 240 minutes are on oxygen and the balance are air breaks to minimise the possibility of oxygen toxicity.

Note: Readers wishing to gain a greater understanding of how to manage DCS are directed to consider courses such as those run by the Undersea and Hyperbaric Medicine Society.

Immersion pulmonary oedema

Immersion pulmonary oedema (IPO) is a rare but potentially life-threatening condition first reported in otherwise healthy scuba divers. Cases have also been described in swimmers and triathletes.[11] Dyspnoea, cough and haemoptysis were the most commonly reported symptoms, while loss of consciousness and cardiopulmonary arrest occurred infrequently. Onset of symptoms is rapid and exacerbated by exertion. IPO is believed to be caused by a combination of water immersion, cold and exertion, which act to increase cardiac output, elevating pulmonary artery pressure (P_{PA}). When P_{PA} is elevated beyond a certain point, capillary stress failure is likely to occur. Fluid is then forced from the capillary to the interstitial space and, at higher pressures, into the alveolar space of the lung. Increased hydrostatic pressure due to immersion causes a redistribution of blood from the periphery to the core. Cold causes peripheral vasoconstriction and blood is redistributed from peripheral to thoracic vessels resulting in increased preload and after-load. Cardiac output was found to increase significantly during cold-water immersion. Radiographic findings include Kerley B lines and airspace consolidation. When managing these

cases, treatment is conservative because hypoxaemia usually resolves within 12 hours, but it can also be treated with supplemental oxygen, for symptomatic relief. Most patients improve dramatically within the first 12 hours, but diuretics can be used if necessary.[12]

Internal carotid artery dissection

This is a rare occurrence after scuba diving and is often initially incorrectly diagnosed as arterial gas embolism. Although conceivably related to intravascular bubble-induced endothelial injury, its aetiology is a mystery. Symptoms include unilateral headache, with or without ipsilateral neck pain, and other neurological symptoms of intracranial origin. In all described cases, the condition was diagnosed after hyperbaric treatment for presumed AGE or DCS produced no improvement, or the condition worsened after hyperbaric treatment. The preferred diagnostic modality is magnetic resonance or conventional arteriography. Primary treatment of this condition entails anticoagulation aimed at preventing further thromboembolic complications. Most patients regain full function if appropriately treated.

MEDICAL CERTIFICATION OF FITNESS TO DIVE

It is advisable that prior to diving, one should be cleared medically. Many medical conditions are contraindications for diving and these need to be considered to ensure the safety of the individual diver and safety of members of the diving team. The median age of commercial divers is approximately 30 years of age and in recreational divers it is 40. Clinicians must be alert to the general health and fitness of a diver. A reasonable level of physical fitness is important to meet the demands of usual diving energy consumption, which is described as moderate to vigorous physical activity, as well as reserves to handle emergency situations. There are some medical conditions that are considered absolute contraindications for diving. Although some disparities exist between recreational and professional diving, and different parts of the world, these are generally accepted as absolute contraindications:

- epilepsy or seizure disorder
- history of spontaneous pneumothorax
- exertional angina, post myocardial infarction with left ventricular dysfunction, congestive heart failure or dependence on medication to control dysrhythmias.

Coronary artery disease

This is commonly encountered as the age profile of divers increases. Symptomatic coronary artery disease is an absolute contraindication; however, a history is not a disqualification. as long as sufficient time has elapsed post revascularisation procedure (such as stent insertion or cardiac bypass) to allow sufficient healing and recovery. Swimming against a 1 knot current will require 8 METs (metabolic equivalents), so 13 METs is the standard a candidate must reach on an exercise stress test with no evidence of ischaemia. Thus, after a period of stabilisation and healing (6–12 months is usually recommended), the individual should have a thorough cardiovascular evaluation prior to being cleared to dive. He or she should be free of chest pain and have normal

exercise tolerance, as evidenced by a normal stress ECG (13 METS), or stage 4 of the Bruce protocol.

Respiratory

Asthma has been previously considered an absolute contraindication due to the potential for air trapping and pulmonary over-inflation while diving.[13] Bronchospasm can develop in asthmatic patients rapidly and may cause airway obstruction underwater. Airway obstruction may be localised to the distal airway; with expansion of this distal airway, pulmonary barotrauma may occur. Another risk for asthmatic divers is the possibility of micro-aspiration of seawater, which could cause bronchospasm. The cold dry nature of compressed air can also act as a trigger for airway hyper-responsiveness.

Diving may be detrimental to the lung function of patients with asthma, with studies showing significant reductions in the forced expiratory volume in 1 second (FEV1), FEV 1/forced vital capacity (FVC) ratio and forced expiratory flows (FEF), in short- and long-term follow-up (6 years).[1 4] Despite the complications, asthmatic patients with normal lung function and well-controlled asthma should be able to successfully scuba dive. Table 26.3 summarises the factors that should be considered when recommending whether a person with asthma should take part in a scuba dive.

Table 26.3 Clinical assessment recommendations for asthmatic patients prior to scuba diving

A thorough history and physical examination by a trained physician
The patient's asthma should be well controlled (no current chest symptoms)
Normal spirometry: FEV1 ≥ 80%, FEV1/FVC ≥ 75%
Successful completion of a bronchial provocation challenge (exercise, dry air hyperpnea, mannitol, or hypertonic saline)
Cold-, exercise-, or emotion-induced asthmatic patients should not dive
Asthmatics requiring rescue medication within 48 h should not dive

REPRINTED BY PERMISSION FROM CLINICAL REVIEWS IN ALLERGY AND IMMUNOLOGY 50(1) 'SCUBA DIVING AND ASTHMA: CLINICAL RECOMMENDATIONS AND SAFETY', COOP ET AL. COPYRIGHT 2016, TABLE 1[15]

Diabetes

As with asthma, the traditional medical approach for type 1 diabetes mellitus was to manage this as a contraindication for diving, due to the risk of hypoglycaemic reaction underwater. However, well-controlled type 1 diabetes patients who are used to vigorous exercise, knowledgeable about their condition and who dive with prepared buddies, are deemed safe.[16] There are some restrictions if significant diabetic complications are present, such as retinopathy, neuropathy and peripheral vascular disease.

Other conditions for consideration in the medical exam

Conditions that must be considered also include headaches and migraine, in particular if they have focal neurological features such as scotomata or weakness, as they can be confused with AGE or DCS. Psychological readiness is important, in particular, history of anxiety and panic disorder, as

these may prompt a diver to make a rapid uncontrolled ascent that may precipitate pulmonary barotrauma.

Currently there is unanimity that women who are, or who may be, pregnant should forgo compressed air diving until after delivery. Animal studies have produced conflicting results in different species and laboratories, but the possibility of bubble formation in foetal or placental tissues leading to foetal insult is a concern. As diving is an avoidable risk for most women, the prudent choice is to avoid diving while pregnant. However, if diving is done before pregnancy is recognised, there is generally no indication for concern.

Generally, prescription medications should prompt an assessment by a diving physician. Non-prescription medications may have undesirable effects that can be intensified by increased partial pressures of breathing gases. For example, dimenhydrinate, which may be used to prevent motion sickness, has a sedating effect that potentiates the decreased mental performance caused by nitrogen narcosis.[17]

OTHER CONSIDERATIONS FOR THE DIVING ATHLETE

Diving often occurs at remote destinations that require flying prior to undertaking the dive. The participant and advising clinician should consider when it is safe to fly. Flying (even in pressurised aircraft) involves a sudden decrease in ambient pressure and can lead to the development of DCS during or after the flight. The recommended guidelines for flight[18] are:

Page 374

1. For single dives within no decompression limits, a minimum pre-flight surface interval of 12 hours is suggested.
2. For multiple dives per day or multiple days of diving, a minimum pre-flight surface interval of 18 hours is suggested.
3. For dives requiring decompression stops, divers should exercise extreme caution and a pre-flight surface interval substantially longer than 18 hours seems warranted.

CASE STUDY

43-year-old competitive triathlete–immersion pulmonary oedema

A 43-year-old woman experienced dyspnoea, chest tightness and cough after swimming 750 m of a half iron-distance triathlon. Symptoms began after 10 min of swimming in cold (19°C) fresh water. The patient completed the 1930 m swim, as well as the 90 km bicycle ride, but dropped out during the run. Paramedics treated her for a presumed diagnosis of hypothermia and addressed her low SPO2 with supplemental oxygen. One month prior, she experienced similar symptoms after 11 min of swimming in cold (22°C) fresh water, while competing in an iron-distance triathlon. Upon exiting the water, the patient was evaluated in the race medical tent, where her symptoms included chest tightness, dyspnoea, haemoptysis and rales. Medical staff reported her S_PO_2 as 76%.

Investigations

On admission to a local hospital, chest radiograph confirmed pulmonary oedema.

Diagnosis

Immersion pulmonary oedema.

Management

Once a loop diuretic (furosemide) and supplemental oxygen were administered the woman recovered fully. Additional episodes occurred in the following years on two occasions, after finishing iron-distance triathlons in Canada and France. Both episodes occurred in cold (<23°C) fresh water. The patient's medical history was unremarkable other than her having environmental allergies. A maximal exercise stress echocardiogram under the supervision of her cardiologist proved inconclusive. During each episode, she wore a wetsuit. She has completed multiple half and full iron-distance triathlons before and between these episodes.

Conclusion

Radiologically confirmed IPO has been reported among triathletes, military swimmers and divers. Although it can occur in all demographic groups, risk factors appear to include being female, aged >40 years, swimming in colder water and wearing a wetsuit.[19] IPO incidents are likely underreported in triathletes. Triathletes are often highly intrinsically motivated and may attempt to complete a race despite adverse events.[12]

The most important implications of this case are for race organisers and staff. Recognition and quick removal from immersion are crucial for patients with IPO (Fig. 26.4). Symptoms can begin quickly (<10 min into a race), even in relatively warm water. Race organisers should ensure that medical staff are educated on the field diagnosis and management of IPO. Organisers must equip their staff with equipment and training to immediately remove dyspnoeic, coughing swimmers from the water and to administer supplemental oxygen.[19]

Figure 26.4 It is important that race organisers and health professionals have the knowhow and the necessary simple equipment (diuretics and supplemental oxygen) to manage immersion pulmonary oedema

SHUTTERSTOCK/PAVEL1964

There is no clear consensus on the minimum pre-flight surface interval. However, it is accepted that the longer the interval between diving and flying, the lower the risk of DCS. The longer the pre-flight surface interval time, the more nitrogen expelled from the system. Unfortunately, even longer intervals can not fully preclude the risk of DCS developing. A recent study has suggested that bubbles were still found in some recreational divers after waiting 24 hours and suggested the 18-hour interval may need to be revised to 24 hours.[19]

SUMMARY

This chapter provides a brief overview of conditions that may present when exercising underwater. The clinician should have a basic understanding of common presentations for participants suffering illness

following an underwater episode. Further education, such as the courses run by the Undersea and Hyperbaric Medicine Society, is recommended for those wishing to specialise in this field.

REFERENCES

1. PADI. World corporate statistics 2017. https://www.padi.com/sites/default/files/documents/2017%20PADI%20WW%20Statistics.pdf.
2. Bayliss GJ. Aural barotrauma in naval divers. *Arch Otolaryngol* 1968; 88(2): 141–7.
3. Jansen S, Meyer MF, Boor M et al. Prevalence of barotrauma in recreational scuba divers after repetitive saltwater dives. *Otol Neurotol* 2016; 37(9): 1325–31.
4. Jansen S, Meyer MF, Boor M et al. Repetitive freshwater diving: risk factors and prevalence of barotrauma. *Undersea Hyperb Med* 2017; 44(5): 407–14.
5. Lafère P, Germonpré P, Balestra C. Pulmonary barotrauma in divers during emergency free ascent training: review of 124 cases. *Aviat Space Environ Med* 2009; 80(4): 371–5.
6. Koch AE, Kirsch H, Reuter M et al. Prevalence of patent foramen ovale (PFO) and MRI-lesions in mild neurological decompression sickness (type B-DCS/AGE). *Undersea Hyperb Med* 2008; 35(3): 197–205.
7. Gorman DF. Decompression sickness and arterial gas embolism in sports scuba divers. *Sports Med* 1989; 8(1): 32–42.
8. Neuman TS. Arterial gas embolism and pulmonary barotrauma. In: Brubakk AO, Neuman TS. *Bennett and Elliott's Physiology and Medicine of Diving*. 5th ed. Saunders Ltd, 2003: 568–71.
9. Ryles MT, Pilmanis AA. The initial signs and symptoms of altitude decompression sickness. *Aviat Space Environ Med* 1996; 67(10): 983–9.
10. Weaver LK. Monoplace hyperbaric chamber use of US Navy Table 6: a 20-year experience. *Undersea Hyperb Med* 2006; 33(2): 85–8.
11. Cialoni D, Pieri M, Balestra C et al. Flying after diving: should recommendations be reviewed? In-flight echocardiographic study in bubble-prone and bubble-resistant divers. *Diving Hyperb Med* 2015; 45(1): 10–15.
12. Koehle MS, Lepawsky M, McKenzie DC. Pulmonary oedema of immersion. *Sports Med* 2005; 35(3): 183–90.
13. Koehle M, Lloyd-Smith R, McKenzie D et al. Asthma and recreational SCUBA diving: a systematic review. *Sports Med* 2003; 33(2): 109–16.
14. Skogstad M, Thorsen E, Haldorsen T et al. Lung function over six years among professional divers. *Occup Environ Med* 2002; 59(9): 629–33.
15. Coop CA, Adams KE, Webb CN. SCUBA diving and asthma: clinical recommendations

and safety. *Clin Rev Allergy Immunol* 2016; 50(1): 18–22.

16. Bonomo M, Cairoli R, Verde G et al. Safety of recreational scuba diving in type 1 diabetic patients: the Deep Monitoring programme. *Diabetes Metab* 2009; 35(2): 101–7.
17. Taylor DM, O'Toole KS, Auble TE et al. The psychometric and cardiac effects of dimenhydrinate in the hyperbaric environment. *Pharmacotherapy* 2000; 20(9): 1051–4.
18. Cialoni D, Pieri M, Balestra C et al. Flying after diving: in-flight echocardiography after a scuba diving week. *Aviat Space Environ Med* 2014; 85(10): 993–8.
19. Carter EA, Koehle MS. Immersion pulmonary oedema in female triathletes. *Pulm Med* 2011; 2011: 261404.

Chapter 27

Physical activity and the built environment

with HAMISH REID and KAREN MILTON

Technology, urbanization, increasingly sedentary work environments and automobile-focused community design have engineered much physical activity out of daily life.

The Toronto Charter for Physical Activity[1]

Humans have become increasingly vulnerable to poor health behaviours since the industrial revolution. The environment in which we live governs the lifestyle choices we make, and modern environmental development has driven a global pandemic of physical inactivity,[2] as outlined in Ch apter 1.

Reversing physical inactivity relies on creating activity-permissive environments through a whole-of-system approach that employs evidence-based interventions and cultivates innovation. The 'Best investments for physical activity' (Fig. 27.1)[3] and the World Health Organization (WHO) Global Action Plan on Physical Activity 2018–2030 (GAPPA)[4] identify key action areas to increase population health through physical activity. While healthcare and health education are well represented in the GAPPA, clinicians need to understand the other important factors that influence people's behaviour. This public health lens provides a complementary perspective to the clinical lens, where the patient is in the office. The different perspectives provide different opportunities to intervene; for example, footpaths are important in the public health context, whereas specific brief advice (Chapters 3 and 4) is key in the clinical setting.

Infographicalised by THE UNIVERSITY OF EDINBURGH

Physical Activity

1 Communication and public education

Consistent public education, including use of mass and social media

7 Sport and recreation

Sport systems and programs that promote "sport for all" and encourage participation across the life span

Transport and the environment

Transport policies and systems that prioritise walking, cycling and public transport

6 Community-wide programs

Work with communities to provide appropriate local solutions, aiming to mobilise large numbers of people

Urban design an infrastructure

Provide safe and equit access for recreation physical activity across the life cours

5 Education

Make regular physical activity in schools and places of learning normal

Healthcare and health education

Ensure assessment and advice about physical activity is a routine part of healthcare services

ISPAH

www.ispah.org

We need action to achieve the goal of increase in participation by 2025

Work together to **make it happ**

Global Advocacy Council for Physical Activity (GAPA) the Advocacy Council of the International Society for Physical Activity and Health (ISPAH). NCD Prev Investments that Work for Physical Activity. Br J Sports Med 2012;46:8;70 9- 7 12

Figure 27.1 Best investments for physical activity HTTPS://BJSM.BMJ.COM/CONTENT/51/16/1227[6]

Urban design and infrastructure that promote activity are closely linked to action on transport and the environment. Good urban design influences the way people choose to travel–it encourages more active transport modes such as walking and cycling. In addition to promoting physical activity and clean air, good community and building design promotes social integration and community cohesion, and even improves quality of life.[5] The promotion of physical activity through environmental design also has other important benefits for economic and sustainable development, as summarised in the Bangkok Declaration, 2016,[5] and the GAPPA.

This chapter highlights good practice principles for town planning and building design, and the opportunities for healthcare professionals to promote such good practices. Healthy community design creates streets and public spaces that offer attractive places to live and empower people to live healthy lives.

Good design principles include:

- compact and mixed land use
- residential density
- connected street networks for walking, cycling and use of other wheeled transport
- provision of footpaths and safe crossings
- access to parks and open public spaces
- public transport links
- policies that create safe environments.

Schools and workplaces are ideal places to improve building design because children and adults are in those settings for long hours. Good building design can enable both purposeful and incidental physical activity, through actions such as promoting stair use (such as point-of-decision prompts or improvements to stairwells) and providing end-of-trip facilities for cyclists and other active commuters, as well as supportive indoor and outdoor spaces for active breaks.

There are vast resources available to guide and support the *Clinical Sports Medicine* reader to encourage advances in the built environment. This chapter is not meant to be comprehensive; our aim is to outline key examples of success stories and resources that may help replicate them. We also share trusted further reading resources.

COMMUNITY DESIGN

We share nine key elements that can serve to help and encourage physical activity:

- mixed land use
- residential density
- connected streets
- footpaths
- safe crossings
- speed limits
- cycling infrastructure
- public transport
- parks and open public spaces.

Mixed land use

Mixed land use involves the co-location of residential developments, shops, schools, employment opportunities, recreational facilities, services and public open spaces within proximity. Mixed land use makes it possible to walk or cycle to local destinations, therefore reducing reliance on personal motorised transport. Neighbourhoods that employ mixed land use have been associated with lower obesity rates, in contrast to sprawling communities with no access to local services.[7, 8] Mixed land use also increases perceived security and enhances the retail and economic development of the local area.[9]

Residential density

Residential density refers to the number of residential units per unit of land. In a recent study of 14 international cities, high residential density was one of the urban features most strongly associated with walking.[10] The association between residential density and physical activity is usually explained by the presence of greater mixed land use, whereby areas of greater residential density are associated with greater access to local shops and public transport services.

Connected streets

A connected street network means having frequent local street connections, aiding the directness of travel between destinations. Neighbourhoods with grid patterns are associated with greater connectivity and increased likelihood of walking for transport.[11]

Footpaths

Footpaths provide safe infrastructure for people to travel actively (e.g. walking, scootering, rollerblading, skateboarding) between destinations (Fig. 27.2). The presence of well-maintained footpaths is associated with walking for both recreation and for transport.[12] It is important that footpaths are well-maintained, well-lit and accessible to all, wide enough to accommodate their typical usage and kept free from obstacles such as parked cars.

Figure 27.2 Footpaths and cycleways, as shown here in Barangaroo, Sydney, as well as parks and open public spaces provide outdoor places for sport, active recreation and relaxation, as well as preserving areas of the natural environment, among advancing urban development

SHUTTERSTOCK / LEONID ANDRONOV

Safe crossings

Pedestrian safety through the provision of footpaths and safe crossings is a consistent predictor of physical activity.[13] Streets should connect with safe crossings along popular routes, to maximise the safety of pedestrians and other users while minimising diversions and unnecessary delays. Crossings should prioritise pedestrians over motorised traffic, ensuring short wait times and sufficient time to cross the road for people of all ages and abilities.

Speed limits

Reducing motor traffic speed in urban areas is increasingly being advocated as a holistic approach to addressing physical inactivity. Physical design measures such as speed humps, raised intersections and roadway narrowing are implemented to slow vehicle speeds and improve safety for pedestrians, cyclists and other road users. In urban areas in the UK where the speed limit has been reduced from 30 to 20 miles per hour, road fatalities have been significantly reduced–

particularly among children, who have a reduced ability, relative to adults, to judge the speed at which vehicles are travelling.[14, 15] Nearly half of road fatalities are 'vulnerable road users', which includes pedestrians, cyclists and motorcyclists.[16]

Cycling infrastructure

Cycling infrastructure can include on-road provision, such as cycle lanes (Fig. 27.3a) or cycle-friendly junctions (Fig. 27.3b), as well as off-road provision such as segregated paths (Fig. 27.3c). Key principles for the development of cycling infrastructure are accessibility, safety and connectivity. While there is no consensus on the best infrastructure to support cycling, increasing perceived safety is key to increasing cycling, particularly for transport purposes.[17] Amsterdam is a city that has invested heavily in cycling infrastructure, which has led to 36% of the population choosing cycling as their most frequent mode of transport on a typical day.[18]

Figure 27.3 Cycling infrastructure (a) Cycle lane (b) Cycle-friendly junction (c) Segregated path

(a) SHUTTERSTOCK/TUPUNGATO (b) GETTY IMAGES/JOHN KEEBLE (c) MODERNGOV.SOUTHWARK.GOV.UK

Public transport

Reliable public transport services that are easily accessible by foot should be provided across communities and should link residential areas with shops, schools, workplaces and other common destinations. Interestingly, providing diverse transport options may be more important than providing fewer options that have stops closer to people's homes. Therefore, if residents' needs can be met through the options provided, the likelihood they will walk to a stop may be increased.[10]

Parks and open public spaces

Parks and open public spaces provide outdoor places for sport, active recreation and relaxation, as well as preserving areas of the natural environment, among advancing urban development. Green and blue spaces (e.g. rivers or lakes) provide not only places for recreation but destinations to which people can travel. Therefore, green, blue and other open public spaces should be connected to residential areas by well-maintained footpaths, and be accessible by public transport. Distance

from homes to areas of green space is associated with green space usage,[19] and living in 'greener' areas is associated with increased physical activity.[20] Design features of green spaces are also an important determinant of physical activity. For example, outdoor gyms can have a positive impact on physical activity, particularly among older people.[21]

CASE STUDY

Bogotá, Colombia

Bogotá is recognised as a Latin American leader in the promotion of physical activity through changes in its built environment. Started in 1974, Ciclovía is an initiative in which the main streets of Bogotá are temporarily closed to motorised transport on Sundays and public holidays, providing approximately 76 miles of roadway exclusively for recreational activities. Every Sunday from 7 am until 2 pm, 1.7 million people, or a quarter of Bogotá's population,[22] use the car-free streets for walking, cycling and other forms of active recreation (Fig 27.4).[23] Since its creation, Ciclovía has been adopted in many other countries and continues to grow and gain support yearly.

Source: references 22, 23

Figure 27.4 Bogotá's Ciclovía, a Spanish term meaning 'bike way', is one of the world's most successful mass recreation initiatives

SHUTTERSTOCK/FOTO593

CASE STUDY

Complete Streets

Complete Streets is an advocacy movement that aims to implement policies and design approaches that ensure streets are planned, operated and maintained to meet the needs of all users of all ages and abilities, including cyclists, pedestrians, public transport users and motorists. While no two Complete Streets projects are identical, many share common features, such as bike lanes or protected cycle tracks, wider footpaths, dedicated bus lanes, improved and accessible public transit stations, landscaping and frequent safe crossings. The National Complete Streets Coalition is a program of the non-profit organisation Smart Growth America. Hundreds of Complete Streets policies have been implemented across communities in North America. An example of a 'complete street' is shown in Figu re 27.5.

Source: reference 62

Figure 27.5 The 'Complete Streets' program in Vancouver, Canada aims to design streets that are safe and provide comfortable access for pedestrians, cyclists and other transport users

SERGEI BOBYLEV\TASS VIA GETTY IMAGES

BUILDING DESIGN

The workplace

Rapid technological advancement has led to a proliferation of sedentary jobs. In the USA, jobs requiring moderate energy expenditure fell from 50% in the 1950s to under 20% in 2010.[24] In

Scotland, middle-aged office workers are more sedentary during the working week than people aged over 75 years.[25]

Since most work itself no longer demands physical activity, creative re-engineering of workplace structure and culture is required to make a difference. Such interventions are most successful if they employ a multisystem approach, are enjoyable, engage the least-active employees and specifically target physical activity.[26–28] Importantly for employers, activity-permissive workspaces do not compromise work performance[29–31] and can contribute to increased productivity and reduction in injuries and absenteeism.[32] Cultural change to promote physical activity in an organisation requires employee education and strong leadership.[33, 34] Methods include educational campaigns, physical activity programs and incentive schemes, and changes to the physical infrastructure of workplaces.

Page 382

Active travel

In contrast to downstream approaches that target the individual, upstream environmental approaches that reach a larger audience should be prioritised when addressing active commuting in the workplace.[35]

Walking

Walking initiatives may be the most effective physical activity interventions in the workplace.[26] Many successful initiatives utilise pedometers with education, which includes maps that show walking routes and distance to public transport. Interestingly, gamified walking interventions, such as Healingo Fit (see box), have shown promising results.[28]

Cycling

Regular cyclists form a minority of active commuters. However, favourable weather conditions and a permissive environment can significantly increase this proportion. Cycling to work schemes could increase physical activity levels among employees. Important features of such schemes include:

- easy access to the workplace, such as ramps into the building
- safe, covered bicycle storage
- showers
- space to dry and store clothes
- incentives and discount schemes
- maps that show cycling routes and connectivity
- clear signposting of cycle routes
- clear signposting within the building to relevant end-of-trip facilities, such as storage facilities and showers.

Infrastructure

Effective methods to increase stair usage in workplaces and other public buildings include:[36–42]

- placing point-of-decision prompts on or near stairwells, elevators and escalators to encourage individuals to use stairs
- building stairs close to access points
- designing staircases with a minimum number of turns
- positioning stairs so they are readily seen
- signposting stairs clearly throughout the building
- using transparent glazing
- installing magnetised fire doors that stay open
- making stairwells attractive, well-lit and well decorated.

Other modifications to infrastructure that can help to increase physical activity include:

- sit-stand desks
- flexible working spaces
- sports facilities in buildings (e.g. table tennis)
- connections to local walking and cycling networks

Pedometer-based walking intervention

Healingo Fit, a walking intervention implemented by a German automobile manufacturer, increased walking activity by 30%.[34] The intervention comprised a pedometer walking trial with gamification, providing four modules connected by a game framework in which participants were put in the role of a virtual traveller travelling from site to site. The four parts of the intervention were:

- step counts and goals
- quizzes aimed at increasing health and physical activity knowledge
- health goals selected from a list
- team and individual challenges.

These components were represented online as shown in the screenshots in Figure 27.6.

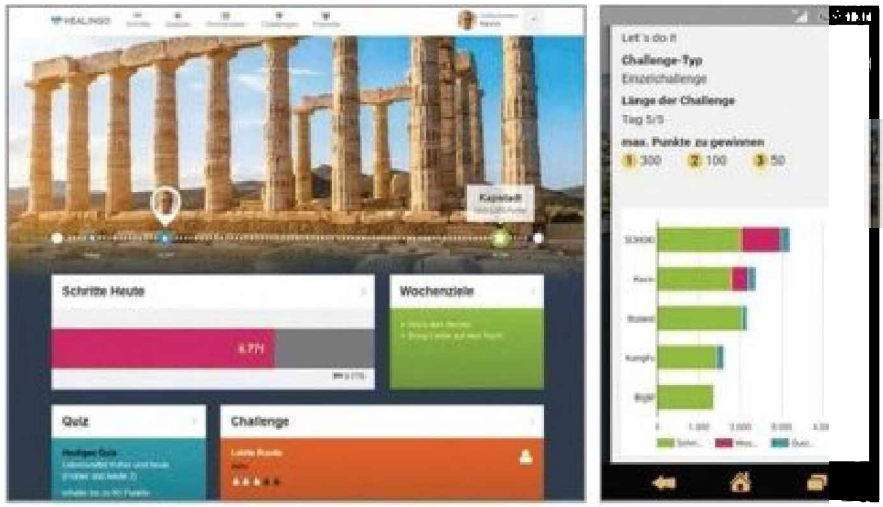


Figure 27.6 **Healingo Fit** desktop interface

DADACZYNSKI ET AL. 'PROMOTING PHYSICAL ACTIVITY IN WORKSITE SETTINGS: RESULTS OF A GERMAN PILOT STUDY OF THE ONLINE INTERVENTION HEALINGO FIT', BMC PUBLIC HEALTH (2017) 17:696 DOI 10.1186/S12889-017-4697-6 © THE AUTHOR(S). 2017 OPEN ACCESS

- walkways and cycle paths to connect sites; ideally these connect to and enhance existing travel networks
- safe and accessible parking spaces for bicycles, wheelchairs, strollers and other forms of wheeled transport
- off-site car parking with connected walkways.

Schools

As with the workplace, successful physical activity promotion within schools relies on whole-of-system intervention.[1, 3, 43, 44] Ideally, the initiative for change should come from within the education system, as demonstrated by the Finnish 'Schools on the Move' program. Utilising the 'Best investments' to promote physical activity in schools, this remarkable national program has a target of reaching over 90% of pupils nationwide.[45] Such intervention is necessary in a traditional school environment, where inactivity takes up to 70% of class time, including physical education lessons.[46]

Active travel

Local habits and community engagement are very important to redress the decline in active transport to school. For example, in Toronto, Canada, active travel to school declined from 42.5 to 53% in 11–13 year olds between 1986 and 2006.[47] Effective methods for promoting active travel to

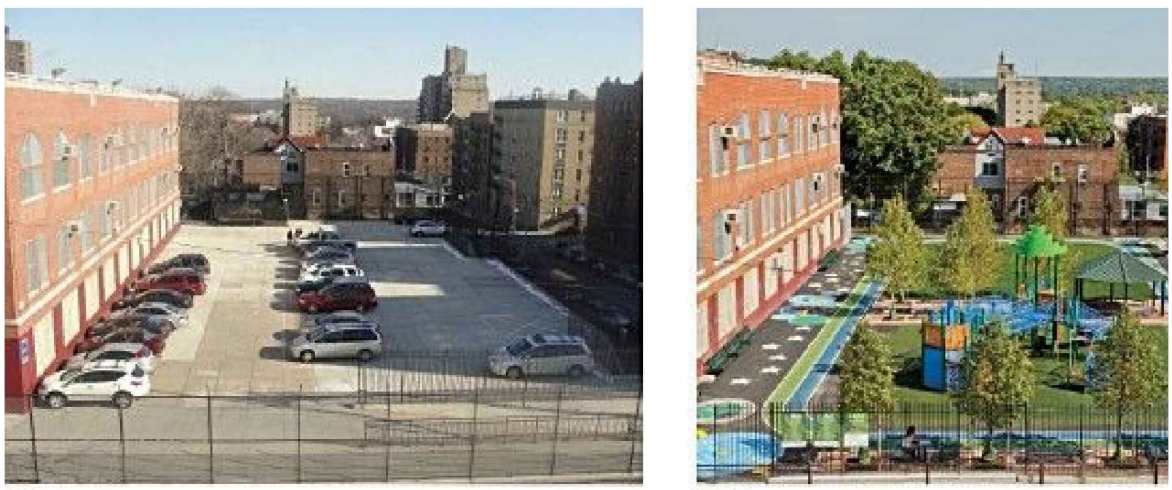
school include:

- defining and protecting safe routes, with initiatives such as 20 mph (32 km/h) zones and school crossing guards
- 'walking school buses' (groups of children walking to school with one or more adults) and 'bicycle trains' (cycling rather than walking together)
- bicycling and other wheeled transport policies and facilities, as per workplace initiatives above.

Infrastructure

The layout and design of a school substantially influences physical activity opportunities for pupils. And while active design principles should be considered when developing new infrastructure, there are many other actions that can be implemented to modify the existing environment:

- Simply marking playgrounds is a key intervention (Fig 27.7).[48] Creating multicolour zones, painting hopscotch, letters, squares, racetracks and clock faces all lead to sustained increases in physical activity.[49, 50]



(a) (b)

Figure 27.7 NYC Active Design team partnered with a local school and community in New York to transform their schoolyard (a) into a space (b) that promotes active play, increases physical activity and encourages social integration[55]

NANA TAIMOUR, COURTESY OF THE TRUST FOR PUBLIC LAND, NEW YORK

- Make play equipment available, such as goals, basketball hoops, balls and ropes.[50]
- Make play areas safe.[51]
- Build permanent play areas and sports facilities.[52]

- Transform indoor space:
  - Install springy gym floors in non-traditional spaces, such as school lobbies, canteens, hallways or classrooms, to create multifunctional space,
  - Re-deploy unused classrooms,
  - Convert unused or non-traditional space to physical activity areas (e.g. install a climbing wall in the foyer),
  - Build playgrounds indoors or on roofs when space is at a premium,
  - Use key principles of good stair design.
- Install roofing, to provide cover from inclement weather.
- Protect outside space and playing fields from development and destruction. Physical education lessons should be taken outside wherever possible.[53]
- Naturalise play spaces, particularly in urban areas, by introducing features such as grass and trees, to promote individual discovery and social interaction (Fig 27.7).[48, 54]
- Develop links to parks and local transport networks.[48]

Furniture

Programs such as the 'Moving School' initiative[56] demonstrate that the physical structure and arrangement of a classroom can improve physical activity, reduce sedentary behaviour, improve posture, reduce the prevalence of lower back pain and improve learning outcomes.[48, 55, 56] Activity-permissive classroom design reduces sitting time, increases energy expenditure and appears to increase students' attention.[57, 58] Simple principles rely on adequate teacher training[59] and include:

- giving children space to move
- using modular and moveable furniture, from desks to bookcases
- choosing child-specific dynamic seating
- permitting choice and providing children with options.

Community

Partnerships between schools and local communities can enable the use of school facilities outside of school hours. Community advocates can drive these partnerships, promoting shared-use agreements among communities and local government bodies.[60]

CLINICAL PRACTICE

Given physical activity's complexities, there is no single solution for increasing physical activity levels for the individual or the population as a whole. Healthcare and health education is only one of the 'Seven best investments for physical activity' (Fig. 27.1). Clinicians have many opportunities

to engage patients in the other six. The following outlines key actions for clinicians to implement in their daily clinical practice.

Clinical encounters

As emphasised in Chapter 3, clinicians should make assessment and counselling on physical activity part of their routine practice in all clinical encounters. These frequent opportunities should be used to ask patients specifically how the environment impacts upon their physical activity levels.

- Discuss key influencing factors, particularly focusing on identifiable environmental barriers and how they might be overcome.
- Utilise behaviour change tools and supports where necessary. Guidance on encouraging behaviour change can be found via the UK National Institute for Health and Care Excellence[59] and is discussed in Chapter 5.
- Be aware of physical activity guidelines and promote them. Ensure that posters of the physical activity guidelines are prominent in both your consulting rooms and the waiting room, for all to see.

Active travel

Clinicians, staff and patients all need to commute to the clinic. Clinicians should think about ways in which they can promote active travel, for all ages and abilities as appropriate.

- Provide adequate end-of-trip facilities to support active travel, particularly safe parking and storage for wheeled transport.

Neighbourhood school

An innovative program in Minnesota, USA, tested the impact of a 'neighbourhood school'.[44] The school was organised on the layout of a village square (Fig. 27.8), with the classroom in a hockey rink, and used sit-stand desks and mobile whiteboards and IT equipment. Children were allowed to move throughout the neighbourhood during lessons and reached higher daily physical activity levels than children in traditional classrooms—levels equivalent to those among children on their summer holidays.

Figure 27.8 Neighbourhood school in Minnesota LANNINGHAM-FOSTER L, FOSTER RC, MCCRADY SK, ET AL CHANGING THE SCHOOL ENVIRONMENT TO INCREASE PHYSICAL ACTIVITY IN CHILDREN. *OBESITY* (SILVER SPRING). 2008 AUG; 16(8): 1849–53

- Make information on local walking and cycling routes available for patients and staff.
- If possible, ensure the workplace is connected to local walking and cycling networks.

Page 385

Role modelling

Clinicians' health matters, and directly influences that of their patients. Importantly, clinicians' own physical activity practices influence their clinical attitudes towards physical activity and counselling practices.[61]

- Be a role model for patients and staff; act on the advice given to patients to be more active (see box). A recent survey revealed that of the physiotherapists who responded, only 38% met physical activity guidelines.[60]
- Identify and challenge the limiting factors in your own environment and use this experience to help talk to patients and to effect positive change in your own environment.
- Share your physical activity experience with staff, to encourage them to also become role models for a more active work environment.

Advocacy

Clinicians have an important and trusted voice. They should use their platform to lobby for change and represent their patients.

- Challenge developers and planners to consider active design principles.
- React to planning consultations and communicate with your colleagues to share ideas and strengthen partnerships for support.
- Check the contents of neighbourhood plans with the planning authorities and check that active design principles sit at the heart of their community plans for upcoming years.

How clinicians can stay active throughout the clinical day

- Walk to greet your patients
- Stand up when making phone calls
- Go outside if you have a break
- Get moving at lunch time, and encourage others to join you
- Have walking meetings
- Take breaks to move and stretch
- Use a sit-stand desk
- Use the stairs

REFERENCES

1. Global Advocacy Council for Physical Activity, International Society for Physical Activity and Health. The Toronto Charter for Physical Activity: A global call for action. *J Phys Act Health* 2010 Nov; 7 (Suppl 3): S370–85.
2. Kohl HW, Craig CL, Lambert EV et al. The pandemic of physical inactivity: global action for public health. *Lancet* 2012 Jul; 380(9838): 294–305.
3. Global Advocacy for Physical Activity (GAPA), the Advocacy Council of the International Society for Physical Activity and Health (ISPAH). Non communicable disease prevention: investments that work for physical activity. *Br J Sports Med* 2012 Aug; 46(10): 709–12.
4. World Health Organization (WHO). Global action plan on physical activity 2018–2030: more active people for a healthier world. Geneva, 2018. https://www.who.int/ncds/prevention/physical-activity/global-action-plan-2018-2030/en/.
5. ISPAH, International Society for Physical Activity and Health. The Bangkok Declaration on Physical Activity for Global Health and Sustainable Development. *Br J Sports Med* 2017 Oct; 51(19): 1389–91.
6. Schiphorst C, Murray A, Kelly P et al. Infographic. Best investments for physical activity. *Br J Sports Med* 2017; 51: 1227–8.

7. Frank L, Andersen M, Schmid T. Obesity relationships with community design, physical activity, and time spent in cars. *Am J Prev Med* 2004; 27(2): 87–96.
8. Wen L, Orr N, Millett C et al. Driving to work and overweight and obesity: findings from the 2003 New South Wales Health Survey Australia. *Int J Obes* 2006; 30: 782–6.
9. Healthy Spaces and Places. Design principles—Mixed land use. published online 2011. www.healthyplaces.org.au/site/mixed_land_use_-_full_text.php.
10. Sallis J, Cerin E, Conway T et al. Physical activity in relation to urban environments in 14 cities worldwide: a cross-sectional study. *Lancet* 2016; 387: 2207–17.
11. Koohsari M, Sugiyama T, Lamb E et al. Street connectivity and walking for transport: role of neighborhood destinations. *Prev Med* 2014; 66: 118–22.
12. Pikora T, Giles-Corti B, Knuiman M et al. Neighborhood environmental factors correlated with walking near home: using spaces. *Med Sci Sports Exerc* 2006; 38: 708e714.
13. Bracy N, Millstein R, Carlson J et al. Is the relationship between the built environment and physical activity moderated by perceptions of crime and safety? *Int J Behav Nutr Phys Act* 2014; 11(1): 24.
14. Grundy C, Steinbach R, Edwards P et al. Effect of 20 mph traffic speed zones on road injuries in London, 1986–2006: controlled interrupted time series analysis. *BMJ* 2009; 339: b4469.
15. Taylor M, Lynam D, Baruya A. The effects of drivers' speed on the frequency of road accidents. Wokingham, Berkshire, 2000.
16. World Health Organization (WHO). Road traffic injuries. 2018. Geneva, 2018. http://www.who.int/mediacentre/factsheets/fs358/en/.
17. Transport for London. International Cycling Infrastructure Best Practice Study. London, 2014. http://content.tfl.gov.uk/international-cycling-infrastructure-best-practice-study.pdf.
18. TNS Opinion & Social. Special Eurobarometer 22a—Quality of Transport. Brussels, 2014. http://ec.europa.eu/commfrontoffice/publicopinion/archives/ebs/ebs_422a_en.pdf.
19. Toftager M, Ekholm O, Schipperijn J et al. Distance to green space and physical activity: a Danish national representative survey. *J Phys Act Health* 2011; 8(6): 741–9.
20. Mytton O, Townsend N, Rutter H et al. Green space and physical activity: An observational study using Health Survey for England data. *Health Place* 2012; 18(5): 1034–41.
21. Cranney L, Phongsavan P, Kariuki M et al. Impact of an outdoor gym on park users' physical activity: a natural experiment. *Health Place* 2016; 37: 26–34.
22. Instituto Distrital de Recreacion y Deporte. Consulta Ciclovia. 2018. https://www.idrd.gov.co/SIM/Ciclovia/Consultas/ConsultaCiclovia.php.
23. Parra D, Gomez L, Pratt M et al. Policy and built environment changes in Bogota and

their importance in health promotion. *Indoor Built Environ* 2007; 16(4): 344–8.

24. Church TS, Thomas DM, Tudor-Locke C et al. Trends over 5 decades in US occupation-related physical activity and their associations with obesity. *PLoS ONE* 2011; 6(5): e19657.
25. Strain T, Kelly P, Mutrie N et al. Differences by age and sex in the sedentary time of adults in Scotland. *J Sports Sci* published online 16 June 2017. doi: 10.1080/02640414.2017.1339904.
26. Abraham C, Graham-Rowe E. Are worksite interventions effective in increasing physical activity? A systematic review and meta-analysis. *Health Psychol Rev* 2009 Mar; 3(1): 108–44.
27. Thomas L, Williams M. Promoting physical activity in the workplace: using pedometers to increase daily activity levels. *Health Promot J Austr* 2006 Aug; 17(2): 97–102.
28. Titze S, Martin BW, Seiler R et al. Effects of a lifestyle physical activity intervention on stages of change and energy expenditure in sedentary employees. *Psychol Sport Exerc* 2001 Apr; 2(2): 103–16.
29. Neuhaus M, Eakin EG, Straker L et al. Reducing occupational sedentary time: a systematic review and meta-analysis of evidence on activity-permissive workstations. *Obes Rev* 2014 Oct; 15(10): 822–38.
30. Engelen L, Dhillon HM, Chau JY et al. Do active design buildings change health behaviour and workplace perceptions? *Occup Med (Lond)* 2016 Jul; 66(5): 408–11.
31. National Institute for Health and Care Excellence (NICE). What works in motivating and changing employees' health behaviour. London, 2006.
32. van Dongen JM, Proper KI, van Wier MF et al. Systematic review on the financial return of worksite health promotion programmes aimed at improving nutrition and/or increasing physical activity. *Obes Rev* 2011; 12: 1031–49.
33. Davies CA, Spence JC, Vandelanotte C et al. Meta-analysis of internet-delivered interventions to increase physical activity levels. *Int J Behav Nutr Phys Act* 2012 Apr; 9(1): 52.
34. Dadaczynski K, Schiemann S, Backhaus O. Promoting physical activity in worksite settings: results of a German pilot study of the online intervention Healingo Fit. *BMC Public Health* 2017 Sep; 17(1): 696.
35. Stewart G, Anokye NK, Pokhrel S. What interventions increase commuter cycling? A systematic review. *BMJ Open* 2015 Aug; 5(8): e007945.
36. Kerr J, Eves F, Carroll D. Can posters prompt stair use in a worksite environment? *J Occup Health* 2001; 43(4): 205–7.
37. Eves FF, Webb OJ, Mutrie N. A workplace intervention to promote stair climbing: greater effects in the overweight. *Obesity (Silver Spring)* 2006 Dec; 14(12): 2210–16.
38. Soler RE, Leeks KD, Buchanan LR et al. Point-of-decision prompts to increase stair

use. *Am J Prev Med* 2010 Feb; 38(2): S292–300.

39. Sport England. *Active Design*. London, 2015.
40. US Green Building Council. *Design for active occupants*. 2013.
41. Bauman A, Milton K, Kariuki M et al. Is there sufficient evidence regarding signage-based stair use interventions? A sequential meta-analysis. *BMJ Open* 2017; 7(11): e012459.
42. Jennings CA, Yun L, Loitz CC et al. A systematic review of interventions to increase stair use. *Am J Prev Med* 2017; 52(1): 106–14.
43. McKay HA, Macdonald H, Nettlefold L, et al. Action Schools! BC implementation: From efficacy to effectiveness to scale-up, *Br J Sports Med* 2015; 49: 210-218.
44. Brittin J, Sorensen D, Trowbridge M et al. Physical activity design guidelines for school architecture. Adams MA, ed. *PLoS ONE* 2015 Jul; 10(7): e0132597.
45. Lanningham-Foster L, Foster RC, McCrady SK et al. Changing the school environment to increase physical activity in children. *Obesity (Silver Spring)* 2008 Aug; 16(8): 1849–53.
46. Blom A, Tammelin T, Laine K et al. Bright spots, physical activity investments that work: the Finnish Schools on the Move programme. *Br J Sports Med* published online 27 September 2017. doi: 10.1136/bjsports-2017-097711.
47. Nettlefold L, McKay HA, Warburton DER et al. The challenge of low physical activity during the school day: at recess, lunch and in physical education. *Br J Sports Med* 2011 Aug; 45(10): 813–19.
48. Buliung RN, Mitra R, Faulkner G. Active school transportation in the Greater Toronto Area, Canada: an exploration of trends in space and time (1986–2006). *Prev Med* 2009 Jun; 48(6): 507–12.
49. Stratton G, Mullan E. The effect of multicolor playground markings on children's physical activity level during recess. *Prev Med* 2005 Nov; 41(5–6): 828–33.
50. Ridgers N, Stratton G, Fairclough S et al. Long-term effects of playground markings and physical structures on children's recess physical activity levels. *Prev Med* 2007 May; 44(5): 393–7.
51. Farley TA, Meriwether RA, Baker ET et al. Safe play spaces to promote physical activity in inner-city children: results from a pilot study of an environmental intervention. *Am J Public Health* 2007 Sep; 97(9): 1625–31.
52. Nielsen G, Taylor R, Williams S et al. Permanent play facilities in school playgrounds as a determinant of children's activity. *J Phys Act Health* 2010 Jul; 7(4): 490–6.
53. Skala KA, Springer AE, Sharma SV et al. Environmental characteristics and student physical activity in PE class: findings from two large urban areas of Texas. *J Phys Act Health* 2012 May; 9(4): 481–91.
54. Nicaise V, Kahan D, Reuben K et al. Evaluation of a redesigned outdoor space on preschool children's physical activity during recess. *Pediatr Exerc Sci* 2012 Nov; 24(4):

507–18.

55. Garcia JM, Trowbridge MJ, Huang TT et al. Comparison of the effects of static and dynamic school furniture on physical activity and learning in children. *J Prim Prev* 2016 Dec; 37(6): 555–60.
56. Cardon G, De Clercq D, De Bourdeaudhuij I et al. Sitting habits in elementary schoolchildren: a traditional versus a 'moving school'. *Patient Educ Couns* 2004 Aug; 54(2): 133–42.
57. Minges KE, Chao AM, Irwin ML et al. Classroom standing desks and sedentary behavior: a systematic review. *Pediatrics* 2016 Feb; 137(2): e20153087.
58. Benden ME, Blake JJ, Wendel ML et al. The impact of stand-biased desks in classrooms on calorie expenditure in children. *Am J Public Health* 2011 Aug; 101(8): 1433–6.
59. National Institute for Health and Care Excellence, UK. 2014. https://www.nice.org.uk/guidance/ph49.
60. Lowe A, Littlewood C, McLean et al. Physiotherapy and physical activity: a cross-sectional survey exploring physical activity promotion, knowledge of physical activity guidelines and the physical activity habits of UK physiotherapists. *BMJ Open Sport & Exercise Medicine* 2017, 3(1), e000290. http://doi.org/10.1136/bmjsem-2017-000290. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5663264/.
61. Lobelo F, Duperly J, Frank E. Physical activity habits of doctors and medical students influence their counselling practices. *Br J Sports Med* 2009; 43: 89–92.
62. Keane Gruending, 'Making the shift: An autonomous vehicle future requires bigger thinking' *Vancouver Observer*, 9 November 2017, https://www.vancouverobserver.com/opinion/making-shift-autonomous-vehicle-future-requires-bigger-thinking?PAGE=0%2C0

PART D

Specific groups

Chapter 28

Childhood and adolescence

with CAROLYN BRODERICK and PAUL BLAZEY

Athletes need to enjoy their training. They don't enjoy going down the track with their coach making them do repetitions until they're exhausted. From enjoyment comes the will to win.
Arthur Lydiard, New Zealand runner and legendary athletics coach

Participation in youth (i.e. child and adolescent) sports is increasingly popular and widespread in Western culture. Children as young as 6 years of age initiate year-round training and specialisation in their sports, some training more than 20 hours per week and travelling with teams to compete at national and international levels.

Clinical Sports Medicine Volume 1: Injuries explores some specific physiological characteristics and the management of orthopaedic conditions in childhood and adolescence. This chapter aims to guide the clinician involved in the medical management of the young athlete at all levels of participation.

In this chapter, we will discuss:

- physiological characteristics of the young athlete
- changes in sports performance with age and maturation
- common paediatric medical presentations where a diagnosis needs to be made
- differential diagnoses of the child with dyspnoea on exertion or deteriorating exercise performance
- exercise prescription for children with a known life long condition
- contemporary principles for the management of concussion in the younger athlete.

CHARACTERISTICS OF THE YOUNGER ATHLETE

Engaging in sports activities at a young age has numerous health benefits but also carries risk of

injury. Health problems may appear for the first time due to increased participation and training intensity in sport. Some common conditions that may be diagnosed for the first time in the young athlete include type 1 diabetes, cardiac defects and asthma. Some of these conditions are covered in their own chapters in this volume, but this chapter focuses specifically on diagnosis and management in the young athlete.

CHANGES IN SPORTS PERFORMANCE WITH AGE AND MATURATION

At no time during the human lifespan does the body undergo as many changes as it does during childhood and adolescence.

Determinants of peak performance

Although some of the world's best sports performances have been achieved by athletes in their mid-teens (e.g. Alina Zagitova, Olympic gold medallist in figure skating at age 15; Simone Biles, world all-around gymnastics title at 16; Martina Hingis, Grand Slam tennis champion at 16) most of the physiological determinants of sports performance improve throughout childhood and adolescence and peak in the early 20s.

In elite youth sport among children under 12 years old, there is equal representation of those who mature early, at the normal time and late; but in most elite adolescent sports, there is a preponderance of athletes whose physical maturation is early or on time. There is a performance advantage of reaching maturation early in many sports and often those born early in the year (therefore more physically mature) tend to be over-represented in youth sports such as ice hockey, football and rugby.[1–3]

While advancing chronological age is linear, growth and maturation are not. The timing and tempo of puberty varies greatly between individuals of the same chronological age, and this confers a performance advantage on some children and adolescents in age-limited competition.

Aerobic capacity

Aerobic capacity is determined by central cardiac factors (heart rate and stroke volume) and peripheral factors (peripheral oxygen extraction and haemoglobin). Central and peripheral determinants increase with age and maturation, independent of training. Absolute aerobic capacity (expressed as L/min) increases with both age and maturation status. When expressed relative to body weight, aerobic capacity remains stable in boys and declines in girls from childhood to adolescence. The peak increase in VO_2 velocity (L/min) coincides with peak height velocity in both sexes at the same time as rapid increases in growth of the cardiorespiratory system.[4] Early and average maturing boys and girls have a higher absolute aerobic capacity than their late maturing peers.[5]

PRACTICE PEARL

Aerobic capacity increases with age and maturation but when expressed relative to body weight there is no increase in aerobic capacity with maturation.

Strength

Increases in strength are gradual in the pre-pubertal years and, as there is little difference in strength between boys and girls, mixed gender competitions in this age group are appropriate. Increases in strength accelerate in the pubertal years and peak strength velocity coincides with peak weight velocity in boys and girls. This usually occurs 6–12 months after peak height velocity. At sexual maturity males have on average 50% greater lower limb strength and twice the upper body strength of females.

Anaerobic capacity (power)

Anaerobic capacity is the ability to generate maximal power (peak power) over a few seconds and to sustain it over a short time frame (mean power). Change in anaerobic capacity with age and maturation are influenced by muscle size, enzymatic activity and stores of muscle glycogen.

Increases in anaerobic performance persist after sexual maturity. Peak anaerobic performance in women and men occurs in the early 20s and late 20s, respectively. Many of the world's best sprint performances have occurred around these ages. Nevertheless, exceptional performances can occur at any age. Usain Bolt set the 100 metres world record aged 22 and Merlene Ottey won an Olympic bronze medal at 40 years of age.

A difference between aerobic capacity and anaerobic capacity is that anaerobic capacity increases with age and maturation, even when expressed relative to body weight. This may be due to enhancement of peripheral factors such as glycolytic capacity, motor coordination and other neuromuscular control factors that continue after skeletal maturity.

CREATING A LEVEL PLAYING FIELD IN ADOLESCENT SPORT

Clinicians who have worked with a team of peri-pubertal children will be well aware that size mismatches can occur in sports competitions during these years (Fig. 28.1). Early maturation confers advantages in sports that require strength, power or aerobic fitness (i.e. most sports), but the difficulty in classifying sports competition by anything other than chronological age has meant that age-limited sport is ubiquitous. Classifying sports by pubertal stage or bone age has practical limitations, and some sports have used weight as a proxy for maturity and introduced weight-for-age competitions.

Figure 28.1 In response to mismatches in size among youth soccer teams of the same chronological age, arguments for improved youth competition classification systems in sport are increasing

SHUTTERSTOCK/MUZSY

Weight-for-age competitions

Despite parental concern regarding the risk of injury to a small, late-maturing child when competing against a larger, early-maturing competitor, there is a lack of evidence that significant size mismatch increases the risk of injury. Despite this, some contact sports (e.g. rugby union and league, combat sports) have introduced weight-for-age competitions in an attempt to equalise the opportunities for children and to minimise injury risk.

Page 390

Although the term 'growing pain' is widely known, there is currently no evidence that maturation and growth are associated with increased risk of musculoskeletal conditions.[6]

Early specialisation: good or bad?

The debate over early specialisation in a single sport has been ongoing for some time. Set against the ever-increasing rewards for finding the next Lionel Messi or LeBron James, the age at which professional teams from multiple sports recruit players has slowly reduced as many fear missing out on signing potential future stars.[7] Although large academies, such as the La Masia academy run by Barcelona FC, are well known for having vast scouting networks, smaller teams across many sports will also try to recruit young players, but may lack the same resources to support the young athlete or their parents.[8] Early identification and specialisation is based on a belief in the popular (but unproven) '10 000-hour rule'.[9] This drive to recruit earlier is associated with risk for the youth athlete.

Documented concerns include:

- social isolation[10]
- overdependence
- burnout
- manipulation
- overuse injury
- compromised growth and maturation.

The American Medical Society for Sports Medicine warns against early specialisation except in early-entry sports, such as gymnastics, swimming, diving and figure skating.[11]

The risks of early specialisation are multiple, from both a physical and psychological perspective, and the probability of reaching the elite level of competition in any sport remains low (Fig. 28.2). Current evidence suggests athletes reaching elite and sub-elite levels of performance specialise in their late teens, reaching higher levels of competition compared to those who specialise early.[12]

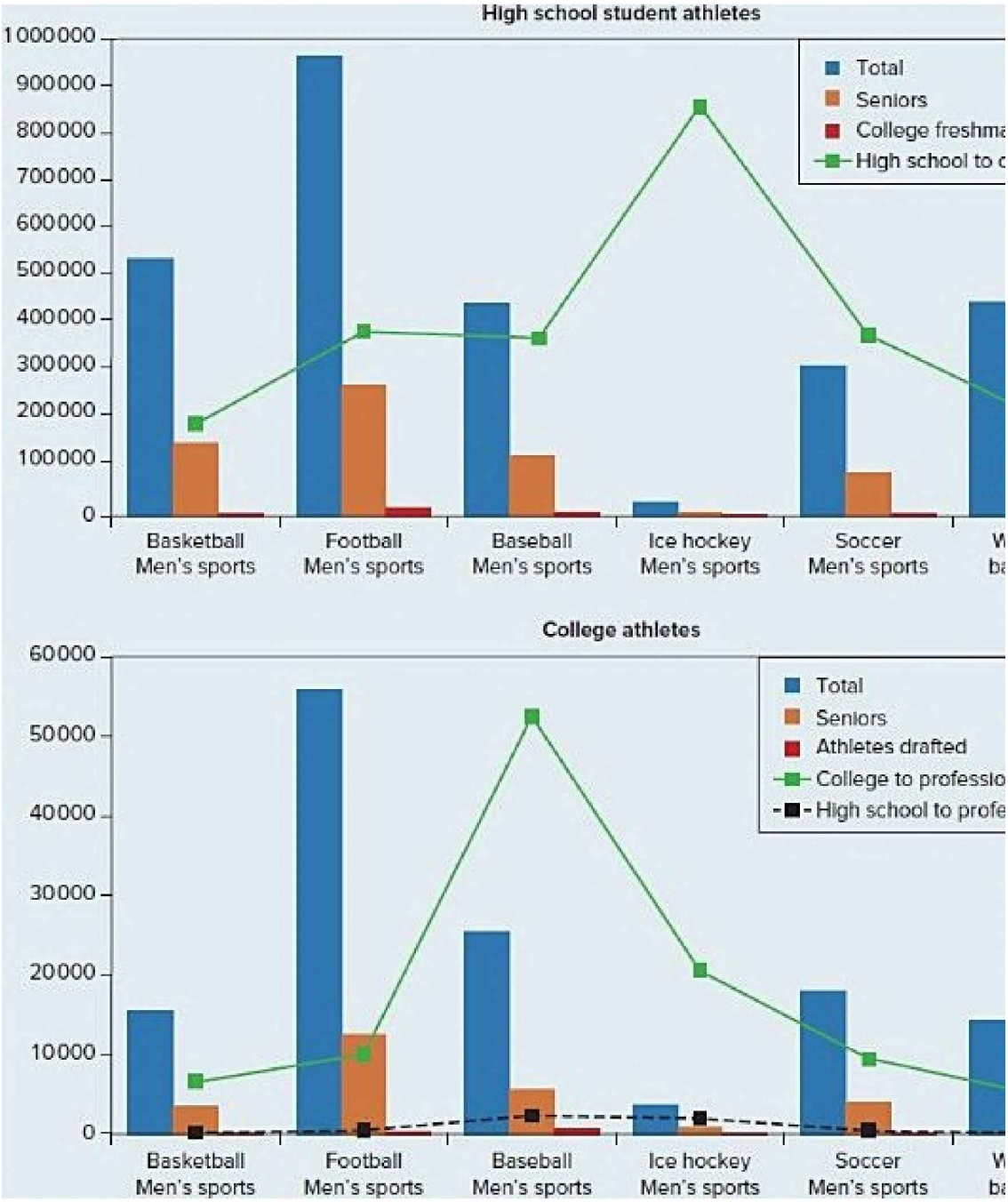


Figure 28.2 Number of US high-school and college athletes who reach professional sports across five of the most popular team games

Note: These percentages are based on estimated data and should be considered approximations of the

actual percentages.

ADAPTED FROM HTTP://WWW.NCAAPUBLICATIONS.COM/P-3957-A-CAREER-IN-PROFESSIONAL-ATHLETICS-A-GUIDE-FOR-MAKING-THE-TRANSITION.ASPX

Gregory et al. published guidelines in 2015 on early specialisation in sports and youth participation, as summarised below (for comprehensive guidelines see the International Olympic Committee consensus statement of 2015 on youth athletic development[3,13]).

- Youth should participate in free, unstructured play to improve motor skill development. Parents and educators should support the child to self-regulate their exposure to reduce the risk of overuse injuries.
- Opportunities for free, unstructured play during the growing years support the development of life-long musculoskeletal health benefits.
- Youth should be encouraged to participate in a variety of sports to identify sports they enjoy, before any later consideration of specialisation.
- Children who participate in more hours of sport per week than their age, or who spend more than 16 hours per week in intense training, and are specialised in sport activities should be closely monitored for indicators of burnout, overuse injury or potential decrements in performance due to overtraining.
- All youth (including inactive youth) can benefit from periodised strength and conditioning, to help them prepare for the demands of competitive sport participation.
- Youth who specialise in a single sport should plan periods of isolated and focused integrative neuromuscular training to enhance diverse motor skill development and reduce injury risk factors.

Clinicians working with youth should be aware of the heightened risk for harassment and abuse in this population. Recent scandals have brought this concern into the spotlight. For further reading see Chapter 37 on harassment and abuse.

Note: Integrative neuromuscular training comprises general (strength-building exercises) and specific (exercise targeted to motor control deficits) conditioning activities that are designed to enhance both health- and skill-related fitness in a socially supportive environment.

PAEDIATRIC EXERCISE MEDICINE

In this section we discuss the work-up of two common presenting complaints in the paediatric population:

- acute shortness of breath or dyspnoea in the younger athlete disproportionate to the amount of exercise being undertaken
- rapid fatigue and poor exercise tolerance in the child who exercises.

Dyspnoea on exertion in the younger athlete—what is the diagnosis?

In a referral-based paediatric sports medicine clinic, a common presentation is that of the child or

adolescent with inappropriate dyspnoea on exertion. In that setting, common causes in an otherwise healthy child include poor aerobic fitness, asthma and vocal cord dysfunction (VCD). See Table 28.1 for a summary of the differing clinical signs/symptoms. Dyspnoea on exertion may be a presentation of cardiac (congenital cardiac disease, cardiac arrhythmia), respiratory (spontaneous pneumothorax, cystic fibrosis), haematological (anaemia, leukaemia) or metabolic conditions, but these are less common and usually have other hallmark signs and symptoms.

Table 28.1 Differentiating between three common causes of dyspnoea on exertion based on spirometry and exercise testing

	Poor aerobic fitness	Exercise-induced bronchospasm	Vocal cord dysfunction
Timing of dyspnoea	Throughout exercise	At end or after exercise	With intense exercise
Auscultation	NAD	Expiratory wheeze	Inspiratory stridor
Aerobic Capacity	Low	Normal/High	Normal/High
Spirometry	NAD	> 10% fall in FEV1	NAD
Bronchodilator response	No	Yes	No
Flow-volume loops	NAD	Obstructive pattern expiration	Flattening inspiratory loop

FEV1 = forced expiratory volume in one second

History and clinical work-up

Important questions that must be included when taking a history from the younger athlete with dyspnoea on exertion (or their parent or guardian) include:

- length of symptoms
- timing of symptoms-after or during exercise? Do they resolve quickly on completing exercise? Are they present during training as well as competition?
- associated factors (e.g. chest pain, wheeze, cough, stridor, syncope, palpitations)
- underlying medical conditions–asthma, cardiac disease, gastro-oesophageal reflux disease (GORD), iron deficiency.

When performing the physical examination, the clinician should focus particularly on assessing pallor, resting pulse rate and rhythm, cardiac murmurs and wheeze.

Investigations

The following investigations should be considered:

- pre- and post-exercise spirometry (exercise-induced bronchospasm, ≥10% fall in FEV1 [forced expiratory volume in one second] with exercise)
- resting ECG if indicated
- chest radiography if symptoms are of recent onset

- FBC/FBE and iron studies if indicated
- exercise testing (to observe symptoms and assess VO_2, RER [respiratory exchange ratio], anaerobic threshold, breathing reserve and flow–volume loops)
- flexible laryngoscopy with exercise, to observe vocal cord movement and possible airway obstruction if vocal cord dysfunction is suspected.

For the diagnosis and management of asthma, see Chapter 11.

Vocal cord dysfunction—diagnosis and management

Vocal cord dysfunction (VCD) is discussed in detail in Chapter 11. The following focuses on how this condition can present in the young athlete. VCD can be associated with cough and subjective *'tightness'* (of the throat and chest).

Symptoms tend to occur during intense exercise, often during high-stress competition rather than daily training.

PRACTICE PEARL

A typical presentation of VCD is a high-achieving female adolescent athlete who has often been diagnosed with asthma but reports little or no response to bronchodilators.

VCD can coexist with exercise-induced bronchospasm (EIB) and is often associated with anxiety and GORD. In a study, 15% of military recruits with exercise-induced dyspnoea had VCD.[14]

Exercise testing can be a valuable aid to diagnosis if symptoms can be reproduced, especially if stridor is observed and there is flattening of the inspiratory portion of the flow-volume loop. The definitive diagnosis involves flexible laryngoscopy with exercise, where abnormal vocal cord movement can be observed and therapeutic breathing techniques can be shown to reverse the abnormal vocal cord movement in real time.

Management includes treating the underlying causes (e.g. GORD, anxiety) and performing breathing exercises (nasal breathing, pursed lip and diaphragmatic breathing) to counter vocal cord adduction. Speech pathologists and sports psychologists have a role to play in teaching breathing and relaxation techniques, respectively.

Other conditions causing dyspnoea on exertion include anaemia, congenital cardiac disease or arrhythmias and metabolic disorders.

Poor exercise tolerance and fatigue in the younger athlete

When approaching the child or adolescent with poor or deteriorating exercise tolerance, it is important to establish the main limiting symptom to guide the differential diagnosis. In addition to

dyspnoea (discussed above), common limiting symptoms are generalised fatigue, muscle pain or weakness. Metabolic myopathies, including mitochondrial myopathies, glycogen storage diseases (such as McArdle disease) and fatty acid oxidation defects can present as muscle fatigue or pain during exercise. Generalised fatigue with physical activity may be the main presenting complaint of the child with chronic fatigue syndrome (CFS), postural orthostatic tachycardia syndrome (POTS) or joint hypermobility syndrome (JHS). It may also be a feature of anaemia and metabolic disorders. A thorough clinical history that includes symptoms associated with exercise, previous illness, family history and current medications is essential. Physical examination is often unrewarding, but should include a full cardiorespiratory examination, strength testing and examination of mobility (joint range of motion) if the history suggests joint hypermobility syndrome.

Role of cardiopulmonary exercise testing

Exercise testing (with breath-by-breath gas analysis and continuous ECG monitoring) can be a valuable, non-invasive tool for evaluating the child with poor exercise tolerance (Fig. 28.3). Unlike adults, only about 20–40% of children achieve a plateau in VO_2 with increasing work rates on exercise testing, so the term VO_2peak is preferred to VO_2max, when referring to maximal aerobic capacity in children.[15], [16]

Figure 28.3 A young patient with mitochondrial myopathy undergoing exercise testing

COURTESY OF CAROLYN BRODERICK WITH CONSENT OF THE PATIENT'S LEGAL GUARDIAN

Children with mitochondrial myopathies have the following features on exercise testing:

- low aerobic capacity (VO_2peak)
- high respiratory exchange ratio (RER = CO_2 exhalation/ O_2 inhalation) for the level of workload and early anaerobic threshold (reflecting reliance on anaerobic metabolic pathways)
- elevated blood lactate with exercise
- low O_2 pulse (VO_2/HR) and high ventilatory equivalent (VE/VO_2) at peak exercise (reflecting central cardiorespiratory responses to compensate for poor muscle oxidative capacity).

There have been few studies on exercise capacity in children with chronic fatigue syndrome. A large study in adults found that adults with CFS had higher resting heart rate (HR), lower HR_{max} and a maximal workload and VO_2max that were almost 50% less than those of sedentary healthy controls.[17]

Page 394

EXERCISE PRESCRIPTION FOR CHILDREN WITH ESTABLISHED CHRONIC DISEASE

Exercise prescription is an integral component of the routine medical management of many chronic childhood diseases, and in some conditions (e.g. mitochondrial myopathies and joint hypermobility syndrome) it is the most effective or only effective treatment. In other chronic childhood diseases, it is an important adjunct treatment and may improve quality of life.[18] Many chronic childhood conditions are associated with inactivity, due to prolonged hospitalisation, pain or low energy levels. This has a significant negative impact on muscle strength, aerobic fitness and bone mineral density, but can potentially be reversed, or at least ameliorated, by an exercise program.[19] In some chronic childhood diseases, such as type 1 diabetes[20] and cystic fibrosis,[21] physical activity is associated with increased survival.

Type 1 diabetes

Physical activity in type 1 diabetes reduces cardiovascular risk factors and insulin requirements, and improves bone mineral density. It may improve survival.[20] While there is currently no evidence that aerobic exercise improves glycaemic control, it is associated with reduced insulin requirements,[18] and there is evidence that strength training may reduce HbA1c (the average amount of glucose bound to haemoglobin over the past 3 months), suggesting improved glycaemic control.[22] High-intensity interval training can reduce the risk of hypoglycaemia in both children and adults.[23]

Risks and considerations for the younger athlete with type 1 diabetes

Aerobic exercise of moderate intensity will usually lower blood glucose levels and increase the risk of both early and late hypoglycaemia. Conversely, short bouts of high-intensity exercise can result in increases in blood glucose mediated through catecholamine release. This observation can be used to minimise the risk of hypoglycaemia with exercise, by performing short bouts of high-intensity training after a more prolonged aerobic exercise session. For more information, readers can refer to Chapter 8.

Physical activity recommendations

Moderate intensity aerobic activity combined with at least two sessions of resistance training per week is recommended. Children should perform regular blood glucose measurements when commencing a new exercise regime, as it is likely to require a reduction in pre- and post-insulin doses. Check blood glucose before exercise to determine whether additional carbohydrate is required (if <5.6 mmol/L). In general, carbohydrate replacement is required for exercise sessions of more than 30 min duration. The rate of replacement will depend on the intensity of the exercise, but is generally in the order of 0.5–1 g/kg/h.

Insulin pumps have been shown to be beneficial for regular exercisers because they offer greater flexibility in terms of the timing of exercise, the ability to undertake spontaneous training sessions

and reduce the risk of hypoglycaemia. It is best to avoid exercising in extreme heat as the signs of heat-related illness can be similar to those of hypoglycaemia. Sports and situations in which an episode of hypoglycaemia could lead to serious consequences should be avoided (e.g. SCUBA diving, highspeed motor sports, outdoor rock climbing). Elite sports participation is possible with type 1 diabetes but requires good planning to maximise performance and to avoid hypoglycaemia. Elite athletes require a therapeutic use exemption (TUE) for the use of insulin.

Childhood cancer

Although childhood cancer is a heterogeneous group of diseases, many of the treatment options are common to different forms of cancer. Acute lymphocytic leukaemia (ALL) accounts for 30–40% of all childhood cancer, and the survival rates have improved greatly (>80%), but long-term disability often results. In Australia, 1 in 600 adults are survivors of childhood cancer, and more than 95% will develop at least one long-term complication. Exercise can be useful in the short-term management to improve fatigue and tolerance to chemotherapy, and to reduce the known long-term consequences of childhood cancer and its treatment, including metabolic disease, obesity, osteoporosis, recurrence of the original cancer and the development of second primary cancers. Despite this, survivors of childhood leukaemia have reduced levels of physical activity, particularly moderate to vigorous physical activity,[24] and reduced aerobic fitness compared with their healthy peers.[25]

The rationale for prescribing physical activity includes the short-term benefits of exercise in children undergoing treatment for cancer, such as reducing cancer-related fatigue, and improving aerobic fitness, strength, body composition and quality of life.[19, 26, 27] For more information about the benefits of physical activity in patients with cancer and its treatment, see Chapter 20.

Risks and considerations for the younger athlete with cancer

The main symptoms impacting a child's ability to take part in an exercise program include extreme fatigue (almost universal), nausea, poor aerobic capacity and strength, and low motivation for exercise. Other factors impacting on exercise include: low white cell count (WCC), with an associated increased risk of infection; low platelet count and tendency for bleeding/ bruising; anaemia, which will affect exercise tolerance; photosensitivity, impacting on outdoor exercise; and reduced bone density, which increases the risk of bony fractures with contact activities.

Central lines and port-a-caths may limit activity, particularly with overhead movement and swimming.

Physical activity recommendations

Moderate-intensity (Borg scale 11–14/20) aerobic exercise should be performed 5–7 days/week for 20–30 minutes, which can be split into multiple shorter sessions during treatment periods. Resistance training should be performed 1–3 sessions/week with 1–4 sets of 6–12 repetitions to

fatigue per muscle group.[28] Exercise should commence during the inpatient period, where possible, to ameliorate the decline in fitness, strength and body composition that occurs during prolonged hospital admissions.

Cystic fibrosis

Cystic fibrosis (CF) is the most common life-limiting autosomal recessive disorder in Caucasian populations. The life expectancy for children with cystic fibrosis has greatly increased over the past 30 years, with the average life expectancy now being almost 40 years.

The rationale for prescribing physical activity includes improving aerobic capacity (VO_2peak), which is an independent predictor of survival for those with CF.[21] Regular physical activity reduces the decline in lung function that occurs in children with CF, and both supervised and unsupervised aerobic and anaerobic exercise programs improve aerobic capacity, anaerobic capacity, quality of life and lung function in children with CF.[29, 30] Strength training alone improves muscle strength and respiratory muscle endurance in children with CF.[31]

Risks and considerations for the younger athlete with cystic fibrosis

Due to increased salt loss in sweat, children with CF need to be cautious when exercising in the heat or for prolonged periods. Replacement of electrolytes is necessary in these instances to prevent hyponatraemia and dehydration.

In children and adolescents with CF, sports performance can be impaired by the athlete's relative muscle weakness due to reduced muscle and body mass, impaired lung or cardiac function and reduced peripheral oxidative capacity. Uncontrolled coughing during exercise may cause brief periods of oxygen desaturation.

CF-related diabetes may also cause the metabolic complications discussed in the diabetes section above, with the most common concern being hypoglycaemia during or after exercise.

Physical activity recommendations

Exercise should be an important part of the routine medical management of children with CF. Different exercise modalities will target discrete aspects of the disease, leading to enhanced therapeutic benefit. Exercise should involve a combined aerobic and resistance training program, with the intensity to be determined by pre-training exercise evaluation. Exercise evaluation should assess lung function, cardiac function and baseline aerobic capacity.

Haemophilia

Until recently, children with haemophilia were discouraged from taking part in many forms of physical activity for fear of joint bleeds. The availability of safe prophylactic clotting factor in many parts of the world has now enabled children with haemophilia to lead more active lives. Unfortunately, because of the prohibitive cost of clotting factor concentrates, much of the world's population has limited or no access to prophylactic clotting factor.

The rationale for prescribing physical activity, in addition to the usual benefits outlined above, includes:

- an improvement in muscle strength and bone density, particularly around diseased joints
- reduced cardiovascular risk
- improvements in quality of life associated with normalisation of lifestyle.

Children with haemophilia have a tendency to obesity,[32] and obesity is associated with accelerated arthropathy.[33] There may also be a role for physical activity in the maintenance of joint health in haemophilia, although the evidence is still limited.[34]

Risks and considerations for the younger athlete with haemophilia

Page 396

The main risk of physical activity is bleeding episodes. Bleeds are most commonly joint bleeds, but can also include soft tissue or more serious intracranial or intra-abdominal bleeds. Recurrent bleeds into the same joint cause degenerative joint disease-known as haemophilic arthropathy. Although the transient increase in risk of bleeding with physical activity is moderate (3–4 times greater than the risk of bleeding at rest), the absolute risk of bleeding associated with physical activity is small due to the fact that even very active children spend only a small proportion of the day exercising.[35]

The risk of intracranial bleeding, although rare, would be considered by most to be an unacceptable risk and therefore sports in which there is a possibility of head trauma (e.g. boxing) are contraindicated.

Physical activity recommendations

Children with haemophilia should be encouraged to engage in regular physical activity. In sports involving contact or moderate risk of injury, children receiving prophylactic clotting factor should administer it prior to exercise. For every 1% increase in clotting factor level in the blood, the risk of bleeding is reduced by 2%.[35] While prophylactic clotting factor is the only evidence-based preventive measure to reduce bleeds in sport, protective equipment may reduce the risk of bleeding in certain sports (particularly contact sports).

REDRAWN WITH PERMISSION FROM McARDLE ET AL (2010)[41]

Mitochondrial myopathies

Mitochondrial myopathies (MM) occur due to mutations of nuclear or mitochondrial DNA (mtDNA). These mutations cause absence or reduced activity of proteins involved in the mitochondrial respiratory chain and hence decreased oxidative capacity and adenosine tri-phosphate (ATP) production. As a result of reduced peripheral oxygen extraction capacity, children with mitochondrial myopathies usually present with muscle weakness and severe exercise intolerance (see Fig. 28.4 for a normal response to longer duration physical activity). The exercise-related

symptoms in children with mitochondrial myopathies relate to reduced energy production (early fatigue) and the build-up of by-products of anaerobic metabolism (muscle pain and weakness). The rationale for exercise in MM is to:

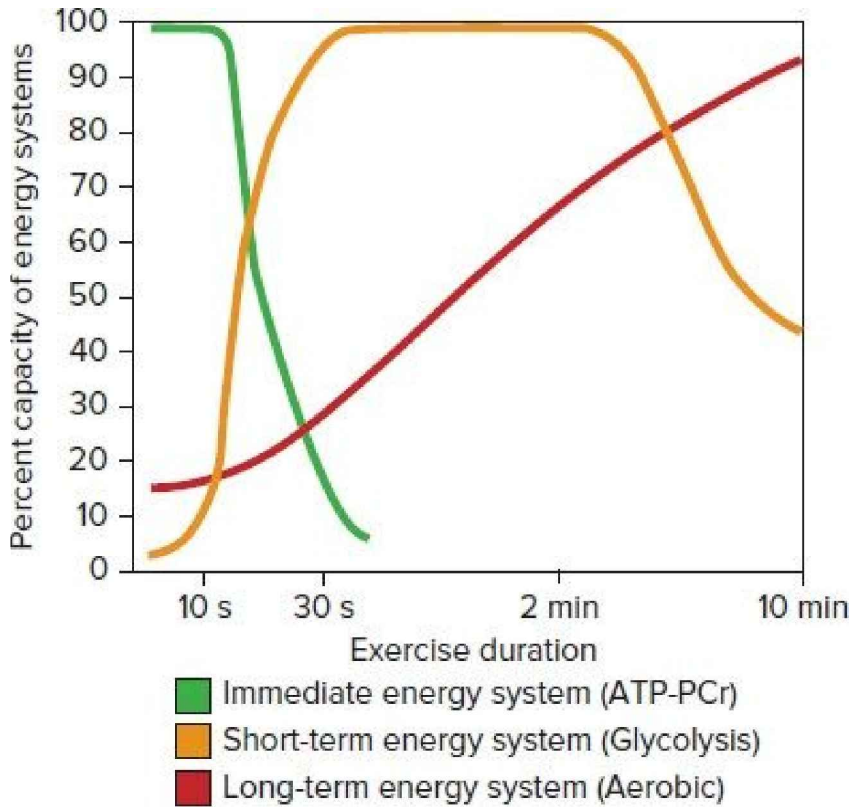


Figure 28.4 Energy systems, by physical activity of varying duration

- address deconditioning
- elicit a training-induced mitochondrial proliferation
- produce mitochondrial gene shifting (explained below).

Endurance training in healthy adults leads to mitochondrial proliferation and improved mitochondrial function. Children with mitochondrial myopathies have varying loads of mutant mtDNA, which determines their degree of exercise intolerance.[36] Oxidative capacity is inversely correlated with mutant mtDNA load. Aerobic training improves oxidative capacity in adults with MM.[37]

Early studies suggest that strength training may reduce the load of mutant mtDNA in mature muscle fibres by increasing the proportion of satellite cells (dormant myoblasts), which have low or undetectable levels of mutant mtDNA, through muscle regeneration following overload and injury.[38] This concept is known as gene shifting.

Risks and considerations for the younger athlete with mitochondrial myopathy

There has been some concern that the increase in mtDNA that occurs with aerobic training may favour mutated mtDNA over normal mtDNA, resulting in an increased mutant load. However, a small study that examined adults with MM who had repetitive bouts of training and detraining showed no evidence of this, suggesting that aerobic training is safe and does not increase mutant mtDNA loads.[39]

Physical activity recommendations

There is limited evidence to guide exercise prescription in children with MM. The best available evidence suggests that in an adult population with MM a combination of aerobic and resistance training three times a week of one hour duration improves function, muscle strength, muscle symptoms and aerobic capacity.[40]

McArdle disease

McArdle disease (glycogen storage disease, GSD V) is an autosomal recessive disorder which results in myophosphorylase deficiency and consequent failure of the muscle to convert glycogen to glucose in the early phase of exercise.

McArdle disease usually presents in the first two decades of life with exercise intolerance and muscle pain. The characteristic symptoms of muscle pain and weakness are more pronounced with intense exercise. If exercise continues the symptoms increase and may be followed by discolouration of the urine (myoglobinuria) associated with rhabdomyolysis.

The characteristic laboratory finding is an elevated creatine kinase (CK) level at rest and post-exercise. Children with McArdle disease have characteristic findings on exercise testing, including low aerobic capacity (VO_2peak) and muscle pain with exercise. They also exhibit a 'second-wind' phenomenon when they undergo exercise testing on a cycle ergometer with a fixed workload. The reduction in pain, heart rate and rating of perceived exertion (RPE) that occurs at the 6–10 minute mark is characteristic of McArdle disease. This phenomenon results from a switch to extramuscular fuel sources (glucose from hepatic glycogenolysis and free fatty acid oxidation).

Administering oral glucose (e.g. Poly-Joule® or Carb Plus) before exercise can prolong exercise by increasing the availability of glucose to the muscles.

Risks and considerations for the younger athlete with McArdle disease

Intense exercise, particularly exercise involving plyometrics or eccentric muscle loading, can be associated with rhabdomyolysis and brings with it the risk of putting the child into acute renal failure.

Physical activity recommendations

For the younger athlete with McArdle disease the recommendations for physical activity are:

- Perform low- to moderate-intensity aerobic exercise, 5 times per week, of 30–60 minutes duration.
- Avoid repetitive eccentric muscle contractions/plyometrics.
- Avoid bursts of high-intensity exercise.
- If exercising at a higher intensity, glucose load 5 minutes prior.
- Perform 10–15 minutes of a low-intensity warm-up specific to muscles being used, to take advantage of the second-wind phenomenon.

Juvenile idiopathic arthritis

Juvenile idiopathic arthritis (JIA) is the term used for the most common form of arthritis affecting children under the age of 16 years. It refers to an inflammatory arthritis of unknown origin (see Ch apter 15 for further discussion of rheumatological conditions). JIA may involve one joint or multiple joints. It may be associated with systemic features or be confined to joint symptoms including swelling, stiffness and pain.

Juvenile idiopathic arthritis has been classified into a number of different subtypes, which can inform the natural history and aid treatment decisions. The most common subtype is oligoarthritis, which involves less than five joints and accounts for approximately 50% of all cases of JIA. It usually presents before 5 years of age.

Physical activity in JIA protects against many of the common associated outcomes for those with this condition. Children with JIA have reduced levels of physical activity, particularly moderate to vigorous physical activity (MVPA), compared with their peers, with only one quarter reaching the World Health Organization daily physical activity guidelines of 1 hour of MVPA per day. This reduced activity persists even when they are in remission and off treatment.[42]

Children with JIA have reduced aerobic fitness compared with their healthy peers, and those with polyarticular disease also have impaired anaerobic capacity.[43, 44] JIA is associated with muscle weakness and low bone mass around affected joints, largely as a result of disuse.

Risks and considerations for the younger athlete with juvenile idiopathic arthritis

High-intensity aerobic training is well tolerated in children with JIA and does not exacerbate joint symptoms. However, a recent randomised controlled trial comparing high-intensity aerobic training with low-intensity, low-impact training found no difference in aerobic capacity or function between the groups and no significant improvement in aerobic capacity in either group. Compliance, however, was higher in the low-intensity group.[45]

Physical activity recommendations

While there is currently no strong evidence for the efficacy of exercise in improving quality of life and function in children with JIA, exercise programs do not exacerbate arthritis and they may have a role in improving muscle strength, aerobic fitness and lower limb bone mineral density. They may also have a role in improving quality of life and wellbeing. A combination of anaerobic, aerobic and resistance training is likely to be most beneficial to address the known deficits in physical function.

Joint hypermobility syndrome and other connective tissue diseases

Generalised joint hypermobility (GJH) is a common finding in adolescents, particularly females. In some sports where flexibility is advantageous (e.g. gymnastics), the majority of participants have evidence of GJH, as determined by a Beighton score of ≥4/9. In most instances there is a family history of hypermobility.

Joint hypermobility syndrome (JHS) refers to a subset of people with GJH who experience joint pain involving more than four joints for longer than three months. The rationale for physical activity in this population is to address fatigue and poor exercise tolerance, as both are commonly associated features. Children with JHS have reduced levels of physical activity and increased rates of overweight and obesity compared with their healthy peers. Exercise is aimed at improving joint stability, muscle strength and proprioception.[46, 47]

Risks and considerations for the younger athlete with joint hypermobility syndrome

Joint hypermobility syndrome is associated with increased risk of joint dislocations and other joint injuries. Knee injuries are five times more common in children with JHS participating in contact sports than their healthy peers.[48]

Physical activity recommendations

Children with JHS will benefit from a combination of aerobic and resistance exercise to improve fitness, muscle strength, joint pain and fatigue. The initial support of exercise professionals can support the identification and correction of altered movement patterns. Education and advice may encourage the adoption of postures that reduce joint stress and alleviate pain.

Contact and collision sports are not contraindicated and may support the strength and conditioning program prescription.[49]

Congenital coronary artery abnormalities

It is unlikely clinicians will encounter congential abnormalities such as tetralogy of Fallot or transposition of the great vessels. However, if there is suspicion or a confirmed diagnosis guidance from cardiologists should be sought to inform exercise prescription.

Atrial septal defects such as patent foramen ovale (PFO) are often asymptomatic but have led to complications for athletes during adulthood (see case study 'Kris Letang', in Chapter 14). It is believed PFO may be present in up to 25% of adults, but thanks to improved screening measures cardiac events are becoming less frequent.[50, 51]

For further discussion of congenital coronary artery abnormalities readers are referred to Chapt er 10.

CONCUSSION IN THE YOUNGER ATHLETE

Concussion was reviewed in detail in *Clinical Sports Medicine Volume 1: Injuries.* This section will focus on concussion diagnosis and management in children.

While the clinical signs of concussion do not appear to differ greatly between adults and children, the latter may have an increased incidence of concussion in certain sports, and their recovery may be prolonged, prompting the development of separate return-to-play guidelines for children.

Concussion in children, as in adults, presents challenges in terms of diagnosis and management. There are very few studies in child or adolescent populations on the incidence of concussion, the diagnostic accuracy of clinical tools or the management of concussion. There is currently no single diagnostic test to confirm concussion, so the diagnosis is based on clinical assessment, symptomatology and signs observed at the time of injury.

As most youth sporting competitions have no formal medical coverage, a substantial number of concussions go undiagnosed. Recent advances in community education in this area and publicity about possible long-term effects of recurrent concussive episodes[52–54] have increased the awareness of concussion in volunteers and organisers of youth sport. The Child SCAT5 is a specific instrument for clinicians to use in the assessment of child athletes (Fig. 28.5).[54]

Page 399

Patient details

Name: _____

DOB: _____

Address: _____

ID number: _____

Examiner: _____

Date of Injury: _____ Time: _____

WHAT IS THE CHILD SCAT5?

The Child SCAT5 is a standardized tool for evaluating concussions designed for use by physicians and licensed healthcare professionals[1].

If you are not a physician or licensed healthcare professional, please use the Concussion Recognition Tool 5 (CRT5). The Child SCAT5 is to be used for evaluating children aged 5 to 12 years. For athletes aged 13 years and older, please use the SCAT5.

Preseason Child SCAT5 baseline testing can be useful for interpreting post-injury test scores, but not required for that purpose. Detailed instructions for use of the Child SCAT5 are provided on page 7. Please read through these instructions carefully before testing the athlete. Brief verbal instructions for each test are given in italics. The only equipment required for the tester is a watch or timer.

This tool may be freely copied in its current form for distribution to individuals, teams, groups and organizations. It should not be altered in any way, re-branded or sold for commercial gain. Any revision, translation or reproduction in a digital form requires specific approval by the Concussion in Sport Group.

Recognise and Remove

A head impact by either a direct blow or indirect transmission of force can be associated with a serious and potentially fatal brain injury. If there are significant concerns, including any of the red flags listed in Box 1, then activation of emergency procedures and urgent transport to the nearest hospital should be arranged.

Key points

- Any athlete with suspected concussion should b FROM PLAY, medically assessed and mo deterioration. No athlete diagnosed with should be returned to play on the day of injur
- If the child is suspected of having a concussion personnel are not immediately available, the be referred to a medical facility for urgent as
- Concussion signs and symptoms evolve ove is important to consider repeat evaluation in ment of concussion.
- The diagnosis of a concussion is a clinica made by a medical professional. The Child SC NOT be used by itself to make, or exclude, th of concussion. An athlete may have a a conc if their Child SCAT5 is "normal".

Remember:

- The basic principles of first aid (danger, respo breathing, circulation) should be followed.
- Do not attempt to move the athlete (other than for airway management) unless trained to d
- Assessment for a spinal cord injury is a critic initial on-field assessment.
- Do not remove a helmet or any other equipr trained to do so safely.

Figure 28.5 The first page of the 8-page Child SCAT5 document, which clinicians can download free to assess the child with concussion

SPORT CONCUSSION ASSESSMENT TOOL - 5TH EDITION. BR J SPORTS MED 2017;51:851-858[54]

In elite adult sport, sideline assessment protocols and, in many instances, sideline video review enable high rates of identification and best-practice return-to-play protocols to be implemented. In youth sport, because most concussive episodes do not involve loss of consciousness, there are no well-validated sideline tools, the diagnosis may be missed and return-to-play protocols are therefore not followed.

Management of concussion in the younger athlete

Observational studies suggest that children and adolescents take longer to recover following concussion than adults, with the average recovery period being 10–14 days. As children's brains are undergoing development, and myelination is not complete, a different approach to concussion management is needed.

Children are usually advised to 'return to learn before return to sport'–that is, not returning to sport before they have returned to school. Many of the symptoms associated with concussion (e.g. poor concentration, fatigue and headache) affect a child's ability to learn.

The delay in return to sport, however, should not mean a delay in return to physical activity. While an initial period of rest of 24–48 hours may be indicated, studies suggest that returning to a low level of aerobic exercise within the first week following concussion reduces the risk of post-concussion syndrome in children and adolescents at 28 days.[55] Recent guidelines from the Australian Medical Association and the Australian Institute of Sport have recommended a conservative approach to return to play for children and adolescents, which defers commencing the graduated return-to-play protocol until asymptomatic for 14 days.[56] This advice, while not evidence based, reflects that caution is required.

PRACTICE PEARL

Clinicians involved in head injury assessment should maintain a high degree of suspicion and consider immediate removal from play for a youth athlete involved in a potentially concussive episode.

Second impact syndrome has been described in children. Although exceedingly rare, it can cause death. Return-to-play decisions are key to all age groups but where a child is involved caution remains paramount. If uncertainty exists, clinicians are encouraged to avoid unnecessary risk.

CASE STUDY

Mitochondrial myopathy

'AP', an 11-year-old girl, presented with a history of exercise intolerance beginning at the age of five. Dyspnoea and muscle fatigue limited her ability to exercise. Other symptoms included pallor, lethargy and vomiting with physical activity. AP needed to stop on the daily walk to school due to fatigue and leg pain. Her inability to keep up with her younger sibling while hiking led her parents to seek medical advice.

Investigations

Neurological, respiratory and cardiac examinations were unremarkable. AP exhibited a normal resting ECG, echocardiogram, 24-hour Holter monitor and respiratory function tests. Pathology tests including full blood count (FBC); urea, electrolytes and creatinine (UEC); and Liver function tests (LFT) were also

normal. She had a normal urine metabolic screen.

AP underwent exercise testing using a Bruce treadmill protocol. Table 28.2 depicts the results of her testing. AP's results provide a typical example of the physiological measures reproduced by this form of exercise testing.

Table 28.2 Laboratory results from AP s exercise testing

	Pred	Rest	VO_2max (or peak)	% predicted max
Time (min)		1:33	7:50	
Ex Time (min)			6:12	
Speed (KPH)			5.4	
Grade (%)			14.0	
Work - TM (Watts)	98	0	94	96
VO_2 WorkSlope (mL/min/watt			5.1	
Ventilation				
Vt BTPS (L)		0.32	0.77	
RR (br/min)		23.15	48.31	
VE BTPS (L/min)	86.0	7.50	37.30	43
BR(%)		91.30	56.70	
Vd/Vt - est		0.20	0.14	
O_2 Consumption				
VO_2 (mL/kg/min)	45.70	7.10	16.70	37
VO_2 (L/min)	1.31	0.20	0.48	37
VCO_2 (L/min)	1.59	0.19	0.77	49
RER		0.96	1.61	
V/Q				
VE/VO_2	46	37.0	78	169
VE/VCO_2	38	38.0	48	128
$PETO_2$ (mmHg)		108.0	128	
$PETCO_2$ (mmHg)		39.0	28	
SpO_2(%)		99.0	99	
Cardiac				
HR (BPM)	209	96	186	89
HRR (%)		54.3	11.2	
VO_2/HR (mL/beat)	6	2	3	41

COURTESY OF CAROLYN BRODERICK WITH CONSENT OF THE PATIENT'S LEGAL GUARDIAN

Diagnosis

AP exercised for 6 minutes and 12 seconds, stopping due to fatigue with an RPE of 9/10 and a peak heart rate of 186 (89% predicted maximum HR). Her VO_2 peak was 16.7 mL/kg/min (37% predicted VO_2peak). Resting lactate was 2.7 mmol/L (<2.0 mmol/L) and rose to 7.0 mmol/L with exercise. Her respiratory exchange ratio (VCO_2/VO_2) was 1.61 (an RER of > 1.0 is usually considered to indicate a maximal test in children). Her O_2 pulse (defined as VO_2/heart rate) was 3 mL/beat (41% of predicted)

and she had a high ventilatory equivalent for O_2 (VE/VO_2) of 78 (169% of predicted)—both hallmarks of mitochondrial myopathy.

Mitochondrial respiratory chain (MRC) enzymology from subsequent liver and muscle biopsies revealed deficiencies in complex I, **III** and IV activity in skeletal muscle.

AP had her heart rate monitored during her normal walk to school (Fig. 28.6). It oscillated between 180 and 200 bpm for most of the flat walk, an indicator of central attempts at compensation for her poor peripheral oxygen utilisation. These tests were enough to confirm a diagnosis of mitochondrial myopathy.

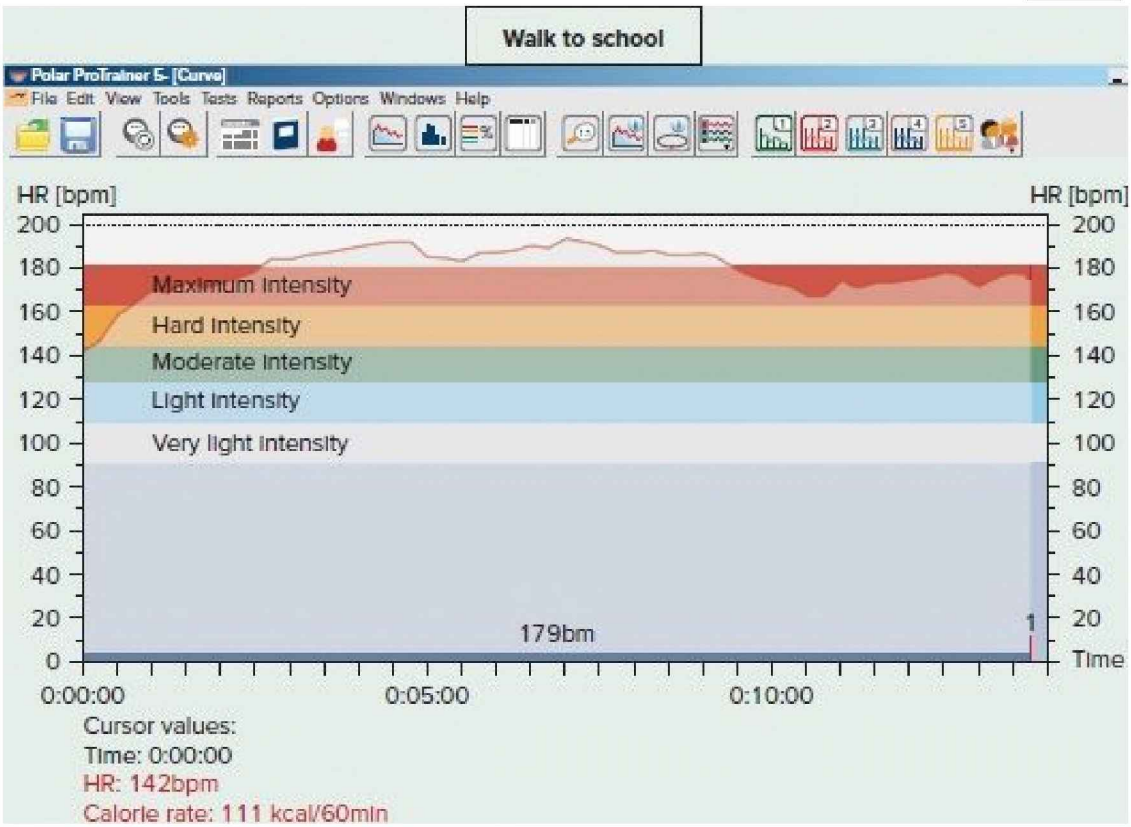


Figure 28.6 Heart-rate monitoring of AP when walking to school ADAPTED COURTESY OF CAROLYN BRODERICK

Management

In order to manage her mitochondrial myopathy, AP commenced a 12-week supervised exercise program involving a combination of aerobic and strengthening exercises. The exercise program facilitated her ability to walk to school without stopping. She was also able to return to her normal sporting activities (skiing, netball, cycling and dinghy sailing at national level).

SUMMARY

Young sport participants, including talented athletes, are children and adolescents with the needs of children and adolescents. Their goal is to 'grow up', to biologically grow and mature and behaviourally develop. – Robert Malina[5]

- Children should be given opportunities to enhance their athletic development through unstructured play.
- Physical activity in childhood and adolescence confers lifelong benefits on several of the bodies systems. These include enhanced bone and tendon health which may confer a preventive benefit against future musculoskeletal injury.
- Physical activity can be utilised in the management of many life-long conditions presenting in childhood and adolescence. This chapter considers several presentations of disease that can impact the physical activity of a child or adolescent patient.
- Many of the conditions extend into adulthood and therefore the information overlaps with other chapters within this book. To enhance awareness of long-term management and improve the adoption of lifelong healthy physical activity clinicians should consider the implications of each disease across the age span.

REFERENCES

1. Gladwell, M. *Outliers: The Story of Success*. New York: Little, Brown and Co. 2008.
2. Brown KA, Patel DR, Darmawan D. Participation in sports in relation to adolescent growth and development. *Translational Pediatrics*. 2017; 6(3): 150–159. doi:10.21037/tp.2017.04.03.
3. Bergeron MF, Mountjoy M, Armstrong N et al. International Olympic Committee Consensus Statement on Youth Athletic Development. *Br J Sports Med* 2015; 49(13): 843–51. doi: 10.1136/bjsports-2015-094962.
4. Geithner CA, Thomis MA, Eynde BV et al. Growth in peak aerobic power during adolescence. *Med Sci Sports Exerc* 2004; 36(9): 1616–24. doi: 10.1249/01.Mss.0000139807.72229.41.
5. Malina RM, Beunen G, Lefevre J et al. Maturity-associated variation in peak oxygen uptake in active adolescent boys and girls. *Ann Hum Biol* 1997; 24(1): 19–31.
6. Swain M, Kamper SJ, Maher CG et al. Relationship between growth, maturation and musculoskeletal conditions in adolescents: a systematic review. *Br J Sports Med* published online 20 March 2018. doi: 10.1136/bjsports-2017-098418.
7. ESPN. Real Madrid signs 7-year-old 'Leo'. 8 August 2011. http://www.espn.com/sports/soccer/news/_/id/6843531/real-madrid-signs-7-year-old-argentine-prospect-leonel-angel-coira.
8. Malina RM. Early sport specialization: roots, effectiveness, risks. *Curr Sports Med Rep*

2010; 9(6): 364–71. doi: 10.1249/JSR.0b013e3181fe3166.

9. Ericsson K, Krampe R. The role of deliberate practice in the acquisition of expert performance. *Psychol Rev* 1993; 100: 363–406.
10. Conn D. 'Football's biggest issue': the struggle facing boys released by academies. *The Guardian*, 6 October 2017. https://www.theguardian.com/football/2017/oct/06/football-biggest-issue-boys-rejected-academies.
11. DiFiori JP, Benjamin HJ, Brenner JS et al. Overuse injuries and burnout in youth sports: a position statement from the American Medical Society for Sports Medicine. *Br J Sports Med* 2014; 48(4): 287–8. doi: 10.1136/bjsports-2013-093299.
12. Moesch K, Elbe AM, Hauge MLT et al. Late specialization: the key to success in centimeters, grams, or seconds (cgs) sports. *Scand J Med Sci Sports* 2011; 21(6): e282–90. doi: 10.1111/j.1600-0838.2010.01280.x.
13. Gregory DM, Neeru J, John PD et al. Sports specialization, part II: alternative solutions to early sport specialization in youth athletes. *Sports Health* 2015; 8(1): 65–73. doi: 10.1177/1941738115614811.
14. Morris MJ, Deal LE, Bean DR et al. Vocal cord dysfunction in patients with exertional dyspnea. *Chest* 1999; 116(6): 1676–82. doi: 10.1378/chest.116.6.1676.
15. Armstrong N, Welsman J. Assessment and interpretation of aerobic fitness in children and adolescents. *Exerc Sport Sci Rev* 1994; 22: 435–76.
16. Barker AR, Williams CA, Jones AM et al. Establishing maximal oxygen uptake in young people during a ramp cycle test to exhaustion. *Br J Sports Med* 2011; 45(6): 498–503. doi: 10.1136/bjsm.2009.063180.
17. De Becker P, Roeykens J, Reynders M et al. Exercise capacity in chronic fatigue syndrome. *Arch Intern Med* 2000; 160(21): 3270–7.
18. D'Hooge R, Hellinckx T, Van Laethem C et al. Influence of combined aerobic and resistance training on metabolic control, cardiovascular fitness and quality of life in adolescents with type 1 diabetes: a randomized controlled trial. *Clin Rehabil* 2011; 25(4): 349–59. doi: 10.1177/0269215510386254.
19. Huang T-T, Ness KK. Exercise interventions in children with cancer: a review. *Int J Pediatr* 2011; 2011: 461512. doi: 10.1155/2011/461512.
20. Moy C, Songer T, Laporte R et al. Insulin-dependent diabetes mellitus, physical activity, and death. *Am J Epidemiol* 1993; 137(1): 74–81. doi: 10.1093/oxfordjournals.aje.a116604.
21. Nixon PA, Orenstein DM, Kelsey SF et al. The prognostic value of exercise testing in patients with cystic fibrosis. *N Engl J Med* 1992; 327(25): 1785–8. doi: 10.1056/nejm199212173272504.
22. Ramalho AC, de Lourdes Lima M, Nunes F et al. The effect of resistance versus aerobic training on metabolic control in patients with type-1 diabetes mellitus. *Diabetes Res Clin Pract* 2006; 72(3): 271–6. doi: 10.1016/j.diabres.2005.11.011.

23. Tonoli C, Heyman E, Roelands B et al. Effects of different types of acute and chronic (training) exercise on glycaemic control in type 1 diabetes mellitus: a meta-analysis. *Sports Med* 2012; 42(12): 1059–80. doi: 10.2165/11635380-000000000-00000.
24. Winter C, Muller C, Brandes M et al. Level of activity in children undergoing cancer treatment. *Pediatr Blood Cancer* 2009; 53(3): 438–43. doi: 10.1002/pbc.22055.
25. van Brussel M, Takken T, Lucia A et al. Is physical fitness decreased in survivors of childhood leukemia? A systematic review. *Leukemia* 2005; 19(1): 13–17. doi: 10.1038/sj.leu.2403547.
26. Battaglini CL, Hackney AC, Rey G et al. The effects of an exercise program in leukemia patients. *Integr Cancer Ther* 2009; 8(2): 130–8. doi: 10.1177/1534735409334266.
27. San Juan AF, Fleck SJ, Chamorro-Viña C et al. Effects of an intrahospital exercise program intervention for children with leukemia. *Med Sci Sports Exerc* 2007; 39(1): 13–21. doi: 10.1249/01.mss.0000240326.54147.fc.
28. Hayes S, Davies P, Parker T et al. Role of a mixed type, moderate intensity exercise programme after peripheral blood stem cell transplantation. *Br J Sports Med* 2004; 38(3): 304–9. doi: 10.1136/bjsm.2002.003632.
29. Klijn PHC, Oudshoorn A, van der Ent CK et al. Effects of anaerobic training in children with cystic fibrosis: a randomized controlled study. *Chest* 2004; 125(4): 1299–305. doi: 10.1378/chest.125.4.1299.
30. Hebestreit H, Kieser S, Junge S et al. Long-term effects of a partially supervised conditioning programme in cystic fibrosis. *Eur Respir J* 2010; 35(3): 578–83. doi: 10.1183/09031936.00062409.
31. Selvadurai HC, Blimkie CJ, Meyers N et al. Randomized controlled study of in-hospital exercise training programs in children with cystic fibrosis. *Pediatr Pulmonol* 2002; 33(3): 194–200. doi: 10.1002/ppul.10015.
32. Hofstede FG, Fijnvandraat K, Plug I et al. Obesity: a new disaster for haemophilic patients? A nationwide survey. *Haemophilia* 2008; 14(5): 1035–8. doi: 10.1111/j.1365-2516.2008.01806.x.
33. Soucie JM, Cianfrini C, Janco RL et al. Joint range-of-motion limitations among young males with hemophilia: prevalence and risk factors. *Blood* 2004; 103(7): 2467–73. doi: 10.1182/blood-2003-05-1457.
34. Parhampour B, Torkaman G, Hoorfar H et al. Effects of short-term resistance training and pulsed electromagnetic fields on bone metabolism and joint function in severe haemophilia A patients with osteoporosis: a randomized controlled trial. *Clin Rehabil* 2014; 28(5): 440–50. doi: 10.1177/0269215513505299.
35. Broderick CR, Herbert RD, Latimer J et al. Association between physical activity and risk of bleeding in children with hemophilia. *JAMA* 2012; 308(14): 1452–9. doi: 10.1001/jama.2012.12727.

36. Taivassalo T, Dysgaard Jensen T, Kennaway N et al. The spectrum of exercise tolerance in mitochondrial myopathies: a study of 40 patients. *Brain* 2003; 126(2): 413–23. doi: 10.1093/brain/awg028.
37. Jeppesen TD, Schwartz M, Olsen DB et al. Aerobic training is safe and improves exercise capacity in patients with mitochondrial myopathy. *Brain* 2006; 129(12): 3402–12. doi: 10.1093/brain/awl149.
38. Taivassalo T, Fu K, Johns T et al. Gene shifting: a novel therapy for mitochondrial myopathy. *Hum Mol Genet* 1999; 8: 1047–52. doi: 10.1093/hmg/8.6.1047.
39. Jeppesen TD, Dunø M, Schwartz M et al. Short- and long-term effects of endurance training in patients with mitochondrial myopathy. *Eur J Neurol* 2009; 16(12): 1336–9. doi: 10.1111/j.1468-1331.2009.02660.x.
40. Cejudo P, Bautista J, Montemayor T et al. Exercise training in mitochondrial myopathy: a randomized controlled trial. *Muscle Nerve* 2005; 32(3): 342–50. doi: 10.1002/mus.20368.
41. McArdle W, Katch F, Katch L. *Exercise Physiology: Energy, Nutrition, and Human Performance*. 7th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Wilkins Health, 2010.
42. Lelieveld OTHM, Armbrust W, van Leeuwen MA et al. Physical activity in adolescents with juvenile idiopathic arthritis. *Arthritis Care Res (Hoboken)* 2008; 59(10): 1379–84. doi: 10.1002/art.24102.
43. Lelieveld OTHM, van Brussel M, Takken T et al. Aerobic and anaerobic exercise capacity in adolescents with juvenile idiopathic arthritis. *Arthritis Care Res (Hoboken)* 2007; 57(6): 898–904. doi: 10.1002/art.22897.
44. van Brussel M, Lelieveld OTHM, van der Net J et al. Aerobic and anaerobic exercise capacity in children with juvenile idiopathic arthritis. *Arthritis Care Res (Hoboken)* 2007; 57(6): 891–7. doi: 10.1002/art.22893.
45. Singh-Grewal D, Schneiderman-Walker J, Wright V et al. The effects of vigorous exercise training on physical function in children with arthritis: a randomized, controlled, single-blinded trial. *Arthritis Care Res (Hoboken)* 2007; 57(7): 1202–10. doi: 10.1002/art.23008.
46. Scheper MC, Engelbert RHH, Rameckers EAA et al. Children with generalised joint hypermobility and musculoskeletal complaints: state of the art on diagnostics, clinical characteristics, and treatment. *Biomed Res Int* 2013; 2013: 121054. doi: 10.1155/2013/121054.
47. Pacey V, Tofts L, Adams R et al. Exercise in children with joint hypermobility syndrome and knee pain: a randomised controlled trial comparing exercise into hypermobile versus neutral knee extension. *Pediatric Rheumatology* 2013; 11: 30. doi: 10.1186/1546-0096-11-30.
48. Pacey V, Nicholson L, Adams R et al. Generalized joint hypermobility and risk of

lower limb joint injury during sport: a systematic review with meta-analysis. *Am J Sports Med* 2010; 38(7): 1487–97. doi: 10.1177/0363546510364838.

49. Murray KJ. Hypermobility disorders in children and adolescents. *Best Pract Res Clin Rheumatol* 2006; 20(2): 329–51. doi: 10.1016/j.berh.2005.12.003.
50. Atianzar K, Casterella P, Zhang M et al. Update on the management of patent foramen ovale in 2017: indication for closure and literature review. *US Cardiology Review* 2017; 11(2): 75–9. https://www.uscjournal.com/articles/update-management-patent-foramen-ovale-2017-indication-closure-and-literature-review.
51. American Heart Association. Patent Foramen Ovale (PFO). 2017. http://www.heart.org/HEARTORG/Conditions/More/CardiovascularConditionsofChildhood/Patent-Foramen-Ovale-PFO_UCM_469590_Article.jsp#.WswvG5dlA2w.
52. McCrory P, Meeuwisse W, Dvořák J et al. Consensus statement on concussion in sport—the 5th International Conference on Concussion in Sport held in Berlin, October 2016. *Br J Sports Med* 2017 Jun; 51(11): 838–47.
53. Concussion in Sport Group. Sport concussion assessment tool for children ages 5 to 12 years. *Br J Sports Med* published online 26 April 2017. doi: 10.1136/bjsports-2017-097492childscat5.
54. Davis GA, Purcell L, Schneider KJ et al. The Child Sport Concussion Assessment Tool 5th edition (Child SCAT5): background and rationale. *Br J Sports Med* 2017; 51: 859–61.
55. Grool AM, Aglipay M, Momoli F et al. Association between early participation in physical activity following acute concussion and persistent postconcussive symptoms in children and adolescents. *JAMA* 2016; 316(23): 2504–14. doi: 10.1001/jama.2016.17396.
56. Elkington L, Hughes D. Australian Institute of Sport and Australian Medical Association Concussion in Sport Position Statement. Australian Sports Commission, 2016.

Chapter 29

Female-specific considerations: anatomy, physiology, injuries and performance

with GENEVRA L STONE, MARGO MOUNTJOY and KATHRYN E ACKERMAN

My coach said I ran like a girl, I said if he could run a little faster he could too.
Mia Hamm, American soccer icon, Olympic gold medallist and FIFA Women's World Cup champion

The 2016 Summer Olympic Games marked the highest level of participation by female athletes in Olympic history, with women accounting for 45% of Olympians.[1] In this chapter, we discuss many of the ways in which females differ from males, and the implications for sport. Early physiology studies primarily enrolled male participants and thus differences observed in females were viewed as 'female specific'. As the sporting status of women equilibrates with men, it is important to view the following discussion not as concerning female-specific qualities but rather as sex differences relating to athletics.

PHYSICAL DIFFERENCES HEAD TO TOE

Bony growth in girls and boys occurs at similar rates until girls hit their (earlier) adolescent growth spurt. Peak height velocity occurs soon after the development of breast buds, which typically occurs between ages 10 and 12 years. A comparison of timing of height velocity in boys and girls can be seen in Figure 29.1. Population studies in the USA and Europe suggest a trend towards earlier breast development and height spurt, possibly correlated to environmental factors and/or increased adiposity. Conversely, pubertal delay is seen in girls who are physically very active.[2] The

rate of vertical growth typically decelerates with menarche (beginning of menstruation), at an average age of 12.8 years in the USA.[2]

https://www.sciencedirect.com. Due to rights and permissions restrictions, this content cannot be reproduced in a digital format. The content is available in the print edition at page 403.

Figure 29.1 American boys (solid line) reach peak height velocity (cm/year) later than girls (dashed line). The number 50 indicates that this is the 50th centile line

ADAPTED FROM *THE JOURNAL OF PEDIATRICS,* 107(3), TANNER JM, DAVIES PS. CLINICAL LONGITUDINAL STANDARDS FOR HEIGHT AND HEIGHT VELOCITY FOR NORTH AMERICAN CHILDREN, 317–29, 1985, WITH PERMISSION FROM ELSEVIER[3]

When fully developed, women have less lean body mass compared to men, reflecting relatively higher body fat composition and lower muscle mass. The average female body fat composition is 28.4%, versus the male equivalent of 15.2%.[4] From an evolutionary perspective, the greater percentage of body fat in females compared with males was necessary to support ovulation, gestation and lactation.[5] Oestrogen, the predominant sex hormone in females, maintains the body fat percentage, while the influence of androgens typically promotes muscle mass accumulation.[6]

The external reproductive organs are one of the obvious physiological differences between the sexes. Female breast development is the first visible stage of puberty, beginning between ages 9.0 and 13.4 years.[7] Breast size and shape is largely determined by genetic predisposition but may be affected by general weight loss or weight gain.

As females mature and reach their full height, their hips widen relative to their shoulders–an evolutionary adaptation to support childbirth.[8] The wider pelvis leads to an increased inward slant of the femur and to the knee sitting medial to the hip joint. The Q angle assesses the magnitude of an individual's hip width compared to her knee, by measuring the angle between an imaginary line drawn between the anterior superior iliac spine (ASIS) and the mid-point of the patella and true sagittal. The female Q angle is roughly three degrees greater than males (17° vs 14°), leading to an increased predisposition to a variety of knee pathologies.

Despite their mirrored existence in females and males, cardiopulmonary organs function slightly differently in the two sexes. When corrected for power, females' cardiac work is higher to meet the same physical demand. When exercising, women have higher measured cardiac index and heart rate, with increased peripheral oxygen extraction. These increased mechanisms counteract a higher basal vasodilatory state and lower stroke volume in females compared with men.[9] Additionally, a lower VO_2max relative to body size limits female endurance compared to males. The typical female VO_2max is 70–75% of that of the typical male.[10] Some of the disparity is due to the differences in body mass–females have less lean muscle–and some is due to the lower haemoglobin in females, leading to a relatively decreased oxygen carrying capacity. For the average female,

haemoglobin level is 10–14% below the average male.[11] Other cardiopulmonary differences between the sexes are included in Table 29.1.

Table 29.1 Sex differences in cardiopulmonary physiology[9,11,12]

Cardiopulmonary measure	Sex difference
Maximum cardiac output	Greater in men
VO_2max	Greater in men
Cardiac work	Greater in women
Cardiac index	Greater in women
Exercising heart rate	Greater in women
Haemoglobin level	Greater in men
Blood volume	Greater in men
HDL cholesterol level	Greater in women

BREAST ISSUES

Breasts can seem an impediment to exercise, particularly in large-breasted women and in those who do not wear appropriately supportive sports bras. The primarily fatty tissue of the breast is supported by Cooper's ligaments, which maintain the structural integrity and hold up the breast. However, the ligaments can stretch with increasing breast size (such as during pregnancy and lactation) and repeated bouncing motion (such as during running).[13] Because the muscle layers are deep, they do not provide much physical breast support. Breasts may become more tender and increase in size up to 40% during the premenstrual period.[14]

Up and down movement of the breasts may lead to pain and discomfort and can affect sports performance. If the breasts are not properly supported, the female athlete can develop strain and tension in her chest, upper back and neck muscle groups. This is more common in large-breasted women, where the weight on the chest requires the back muscles to work harder to keep the shoulders in the correct position during exercise. Furthermore, concern about breast bounce and fear of the potential discomfort during impact activity may lead to exercise avoidance in some females, particularly those who are large breasted.[15] In order to prevent overuse injuries related to breast motion, female athletes should wear a correctly fitted sports bra and receive breast education.

Sports bras should support the breasts from above (shoulder straps), below (chest strap) and the sides (fabric tension wrapping around the torso). The material should breathe and wick moisture, be comfortable and stretch while retaining its shape. The straps should be of non-stretch material and, ideally, crossed or Y-shaped at the back, to provide consistent vertical support, while the chest strap should have an elastic component.[16] There should be no seams or ridges in the nipple area, which could cause skin abrasions. The sports bra should be individually fitted and be comfortable both at rest and with vigorous activity.

When a female patient presents with complaints of neck and back pain in association with impact activity, it is important to assess mobility and movement of the thorax, including the ribs and thoracic vertebrae. If the pain appears due to an overuse injury related to exercise and posture, education, custom sports bra fitting and strengthening exercises (to decrease imbalanced muscle groups) are often sufficient to correct posture and to relieve pain. If the symptoms of overuse do not resolve, manual therapy can restore joint mobility and proper mechanics and aid in muscle strengthening.

Some large-breasted women may suffer from neck and back pain related to overuse during exercise despite a well-fitting sports bra, and these women may benefit from avoiding high-impact exercise (e.g. running) and participating in relatively low-impact exercise, such as cycling, aqua jogging and rowing. If the patient's breast volume is larger than 800 cc at normal weight or if the breasts have over 25% asymmetry (or at least 20 cc), the patient is a candidate for breast reduction mammoplasty, and referral to a plastic surgeon is appropriate if desired.[17]

Women with breast cancer (either undergoing treatment or after surgery) may need custom sports bras. A large proportion of women with breast cancer experience bra discomfort at the area of the chest band while they exercise.[18] Women being actively treated for breast cancer are susceptible to fluctuating tissue oedema, which requires attention to the current fit of a sports bra in use. After lumpectomy, women may have asymmetrical breast mass. As bras are designed for two breasts of similar size, the smaller (treated) breast may not adequately fill the bra cup, leading to greater motion during exercise and more breast pain. This can be addressed by a custom sports bra.

Breast trauma is not common, but a contusion may occur as a result of a direct blow from a ball, racquet, opponent or other cause. A contusion is associated with bleeding and swelling and should be treated with ice, analgesics and breast support. Occasionally, a deep haematoma will require aspiration. It is important to reassure the athlete that there is no evidence that trauma to the breast causes tumours or long-term risk. To prevent breast trauma during contact sports (e.g. martial arts, football), plastic chest guards or sports bras with padding or plastic inserts should be used.

Nipples are susceptible to friction injury. They contain smooth muscle fibres that respond to cold or tactile stimulation. When clothing rubs against nipples during prolonged activity, it can cause significant nipple irritation, commonly known as 'runner's' nipple'. This happens to both men and women. Risk factors include exercising in cold or wet weather, when the nipple is more prominent and harder, and cycling as a type of exercise. Nipple irritation can be prevented by using a layer of petroleum jelly or tape (including zinc oxide tape) between the nipple and the shirt in order to ease friction on the skin itself. For cyclists the use of appropriate clothing, especially a wind-breaking material over the chest, should help prevent nipple irritation.

GYNAECOLOGICAL INJURIES

Occasionally, the female genital organs are injured in association with exercise. Risks for injury include blunt trauma and repetitive impact. Traumatic impact can result in vulval contusions and

lacerations. The vulvar area is heavily vascularised and the vessels can be damaged by impact, which crush the vulvar tissues against the osseous planes. Contusions are more common in pre-pubescent females, who lack the adipose padding of the labia majora.[19] Most contusions can be treated with the application of ice, followed by sitz baths and pain control. Incision and drainage are recommended in more severe cases or cases in which the haematoma is actively expanding. Lacerations may need suturing with absorbable running or interrupted stitches if the wound does not clot with gentle pressure alone. The rich vascularity leads to relatively fast healing time of lacerations.

Hymenal injuries are rarely the result of unintentional injury. The presence of injury to the hymen suggests sexual abuse, and further evaluation for sexual abuse is necessary.[20]

Cyclists may experience urogenital symptoms as the result of extended time spent sitting on the bicycle. Stranguria, genital numbness and vulvar discomfort may be seen in over 25% of female cyclists after cycling. On physical exam, vulvar oedema is common. Additionally, for up to 48 hours after a long ride, up to 40% of cyclists may experience dyspareunia. Increasing age of cyclists is associated with increasing discomfort of the female genital organs.[21] Cycling-related urogenital symptoms tend to resolve without formal treatment within two days. Padding on the seat and in the shorts plays an important role in pain prevention.

PELVIC FLOOR COMPLICATIONS

Although more prevalent in older and parous females, urinary incontinence–the involuntary loss of urine–can affect the entire spectrum of female athletes. With more women participating in endurance sports and other high-impact activities, it has become evident that urinary incontinence affects some young and nonparous females. The two most common types are stress and urge incontinence, and female athletes may experience both.

Stress urinary incontinence (SUI) is the involuntary loss of a typically small amount of urine as a result of strain that increases intra-abdominal pressure, such as coughing or lifting a heavy object. Risk factors for SUI include parity, abdominal surgery, increasing age and professional sport.[22] Reported incidence of SUI in elite athletes ranges from 10% to 56%, with the highest rates in gymnasts.[23]

Urge incontinence is less common and involves larger amounts of urine leakage associated with a strong urge to void and inability to prevent voiding. There is no evidence that the rate of isolated urge incontinence is higher in female athletes compared with the general female population.

The initial treatment of incontinence involves exercises to improve pelvic floor strength, endurance and motor control. Exercises are also indicated following childbirth and for treatment of mild (stage 1 or 2) prolapse. These exercises strengthen the muscles of both the pelvic floor and the abdomen (transversus abdominis and diaphragm) by utilising a combination of sustained holds for endurance and quick alternations between contraction and relaxation for strength and timing. In order to succeed, the exercises must be done correctly and avoid compensation with strategies

such as the Valsalva manoeuvre. One week of effective pelvic floor muscle training can significantly reduce urinary leakage, particularly in cases of SUI.[23] Depending on the complexity of the individual's condition, consider referral to a physical therapist with additional training and practice in women's health.[24]

HYPERMOBILITY

Hypermobility refers to flexibility that stretches beyond normal. There are many causes of hypermobility, including unexplainable laxity in some joints, Ehlers–Danlos syndrome, Marfan syndrome and Stickler syndrome. Systemic syndromes, such as Ehlers–Danlos syndrome and Marfan syndrome, are associated with collagen or connective tissue defects. Athletes diagnosed with these syndromes may need multidisciplinary management that includes a rheumatologist and physical therapist, and referral for genetic testing is often warranted. Females are considered at higher risk than males, and estimates of prevalence in females range from 6% to 57%, with significant racial differences.[25] Younger age is also a risk factor as hypermobility is more common in childhood, and the severity of the mobility tends to decrease with increasing age. The exact prevalence of hypermobility in the general population is unknown due to a large number of untreated cases.[26]

Hypermobility has several advantages for athletes. In some sports, such as dance or figure skating, increased flexibility and large ranges of motion are required for success.[27] The prevalence of hypermobility in elite British female ballerinas has been reported to be 95%, suggesting that ballerinas may self-select into ballet due to their hypermobility (Fig. 29.2).[28] Athletes in other sports may benefit from wide ranges of motion, such as swimmers, hurdlers and gymnasts (Fig. 29.3).[27] However, hypermobility is not without its drawbacks in the realm of sport. Increased injury risk, such as joint subluxations and dislocations, is often cited as the biggest disadvantage for athletes with hypermobility, though the data are inconsistent.[27] Mobility has also been associated with higher levels of anxiety,[27] which may negatively affect athletic performance. This anxiety has not been specifically studied in athletes.

Figure 29.2 Female ballerinas may self-select into ballet due to their hypermobility INGRAM PUBLISHING

Figure 29.3 Gymnasts may benefit from the wide range of motion conferred by hypermobility

RUBBERBALL/ERIK ISAKSON/GETTY IMAGES

Hypermobility may be diagnosed using several methods. The Beighton scoring method[29] assesses hypermobility of the hands, elbows, lumbar spine and knees. The criteria for Beighton scoring are outlined in Table 29.2, and a score ≥4 is cause for diagnosis of hypermobility.

Table 29.2 Beighton scoring criteria for hypermobility[29]

Flexibility test	Hypermobility criteria
Passive dorsiflexion of each fifth finger	Past 90°
Passive dorsiflexion of each thumb	To flexor aspect of forearm
Hyperextension at each elbow	Past 10°
Hyperextension at each knee	Past 10°

Palm rest	Placed flat on floor with trunk flexed and knees extended

The Brighton scoring system can also be used to diagnose hypermobility.[30] A diagnosis is made with positive responses to two major criteria, one major criterion and two minor criteria, four minor criteria, or two minor criteria with an affected first-degree relative.

A non-invasive short questionnaire[32] has been developed to diagnose hypermobility. Positive answers to two or more questions indicate a diagnosis of hypermobility. The questionnaire's items are outlined in Table 29.3.

Table 29.3 Short questionnaire to diagnose hypermobility[32]

Can you now (or could you ever) place your hands flat on the floor without bending your knees?
Can you now (or could you ever) bend your thumb to touch your forearm?
As a child, did you amuse your friends by contorting your body into strange shapes or could you do splits?
As a child or teenager, did your shoulder or kneecap dislocate on more than one occasion?
Do you consider yourself double-jointed?

Joint hypermobility syndrome is the diagnosis of hypermobility accompanied by musculoskeletal complaints (e.g. muscle weakness; joint pain, dislocations and subluxations; easy bruising; ligament or tendon rupture) without systemic symptoms.[33] Pain may be related to improper joint alignment and impaired sensory feedback during activity.[34, 35] Joint hypermobility syndrome is best managed with an individualised care plan dependent on the severity of the condition. Educating hypermobility patients on effective symptom management techniques is critical.[36, 37] Hypermobility symptoms can be ameliorated by improving joint stability, proprioception, posture, strength and motor control.[38] Acute bouts of pain can be treated with non-steroidal anti-inflammatories, acetaminophen, ice, massage, electrotherapies, bracing or splinting, but these strategies are not recommended for long-term management.[36, 37] Children and adolescents with hypermobility participate in less physical activity than their peers,[39] and given the many benefits of regular physical activity, hypermobile children are encouraged to participate in the highest level of physical activity that is safe for their condition.

HAKIM AJ, GRAHAME R. A SIMPLE QUESTIONNAIRE TO DETECT HYPERMOBILITY: AN ADJUNCT TO THE ASSESSMENT OF PATIENTS WITH DIFFUSE MUSCULOSKELETAL PAIN. INTERNATIONAL JOURNAL OF CLINICAL PRACTICE 57(3):163-6, 2003 COPYRIGHT © 2003, JOHN WILEY AND SONS

PATELLOFEMORAL SYNDROME

Patellofemoral syndrome (PFS) is used to describe anterior knee pain resulting from a variety of aetiologies; it is discussed in detail in *Clinical Sports Medicine Volume 1: Injuries.* Female athletes are at higher risk of developing symptoms related to PFS than male athletes. Some authors report females

suffering a markedly higher prevalence (19.6% vs 7.4%),[40] while others report only a trend of more females experiencing PFS (15.3% vs 12.3%).[41] Among recreational runners, 62% of women experience PFS compared to 38% of men.

Females appear to experience increased patellofemoral loading compared to males, contributing to the increased risk of PFS.[42] Female recreational runners have higher peak knee extensor moments, higher patellofemoral contact force and higher patellofemoral contact pressure than their male counterparts.[43] Additional sex differences theorised to affect the higher incidence and prevalence of PFS in females are outlined in Table 29.4.

Table 29.4 Possible risk factors contributing to increased patellofemoral pain in females (outlined by Boling et al.[41])

Biomechanical factor	Females compared to males
Q angle	Increased static measures
Knee valgus angle	Increased dynamic measure
Hip internal rotation angle	Increased dynamic measure
Hip adduction moment	Increased dynamic measure
Knee valgus moment	Increased dynamic measure
Knee flexion angle	Decreased dynamic measure
Quadriceps strength	Weaker
Hip external rotation strength	Weaker
Hip extension strength	Weaker
Hip abductor strength	Weaker

Females seem to respond well to exercise therapy protocols, and individualised physical therapy plans for treatment are recommended.[44, 45] As previously discussed, hypermobility is more common in females than males and may be a risk factor for developing PFS.[4] [5] Identification of this condition may aid the physical therapist in developing an appropriate treatment plan.[45]

Page 408

ANTERIOR CRUCIATE LIGAMENT INJURIES

Anterior cruciate ligament (ACL) injuries are discussed in depth in *Clinical Sports Medicine Volume 1: Injuries,* but as females are at high risk for injuries to the ACL, some sex-specific facets will be reviewed here. After controlling for activity type, females are at a three- to eight-fold higher risk for ACL injuries than males.[46, 47] Female-specific risk factors for ACL injuries include smaller bones of the knee, larger Q angles and knee valgus.[48] Some have postulated that cycling of sex hormones (oestrogen, progesterone, relaxin) also plays a role, but the effects of these hormones throughout the menstrual cycle remain to be elucidated.

Systematic review has revealed that ACL injuries are more common during the pre-ovulatory

phase of the menstrual cycle, at which point oestradiol peaks.[49] There are some who debate the validity of this claim, on the basis of difficulty in determining menstrual cycle phase, particularly in an athletic setting, where clinical (amenorrhoea, oligomenorrhoea) and subclinical (luteal phase defect) menstrual dysfunction often occurs.[50] Hormonal fluctuation is proposed to affect ACL injury risk by changing neuromuscular control around the ACL.[49] Oral contraceptive use has many theorised benefits for preventing ACL injury, including improving balance of strength of the quadriceps and hamstrings and reducing torque at the knee.[49] These benefits, however, do not seem to confer a reduced risk of ACL injury, illustrating the complexity of the hormonal system.[51, 52] More work is needed with direct hormonal testing to determine phase of menstrual cycle during ACL injury and precise levels of hormones.

Adolescent girls are at particular risk for sustaining an ACL injury. Through puberty and growth spurts, it is more difficult for girls versus boys to add muscle bulk to accompany their longitudinal growth.[53] As such, adolescent female athletes must adopt specific training of leg muscles and agility to minimise ACL injury risk.[48, 53] Neuromuscular training programs seem to be most effective in preventing ACL injuries,[54, 55] though determining a 'best' prevention program is difficult.[56] Females benefit less than males from neuromuscular prevention programs, with a risk reduction of 52% compared to 85%.[56] Prolonged compliance with any prevention program is critical to its success and requires buy-in from both athlete and coach.

Risk of ACL tear varies among sports. Female athletes participating in gymnastics, soccer and basketball are at highest risk of ACL tear.[57, 58] These sports inherently require motions that place the athlete at risk of ACL tear, such as abrupt changes of direction.[48] While prevention programs are recommended for female athletes in many sports, especially considering their ancillary benefits (e.g. improved lower limb strength, vertical jump height, upper body strength, speed), female athletes participating in the high-risk sports are particularly recommended to diligently follow a prevention program.[59, 60]

ANAEMIA

Anaemia is particularly harmful to athletes, as it may decrease the capacity for physical activity (see also Chapter 19). As previously mentioned, healthy females have lower haemoglobin levels than males. Anaemia occurs when the lower haemoglobin crosses a threshold and becomes pathologic. For menstruating women, anaemia is present if the haemoglobin level is at or below 11.6–12.3 g/dL.[61] There are many causes of anaemia, including blood loss and insufficient vitamins and/ or minerals to produce sufficient haemoglobin. Iron is an important part of the haemoglobin protein, and iron deficiency is a frequent cause of anaemia in female athletes. Many types of anaemia can be treated with dietary supplements.

Among women of childbearing age, anaemia is a relatively common condition. One important component of its prevalence is blood loss during menstruation. In this population, iron deficiency is the most common cause of anaemia. The prevalence of iron deficiency among female adolescents

in the USA is estimated as high as 9–11%. Iron deficiency anaemia (IDA) in the same population is estimated at 2–5%.[62] These rates are roughly 10 times the rates seen in adolescent boys. A similar prevalence of IDA is reported in female athletes and non-athletes.[63, 64] However, recent studies examining the connection between iron sequestration and hepcidin, a protein that appears to rise with physical activity, imply that female athletes may experience more of a decline in iron absorption than female non-athletes.[65] Eating a vegetarian diet is an important risk factor for both IDA and anaemia caused by vitamin B_{12} deficiency.

The most common complaint in an anaemic athlete is poor athletic performance.[66] Other complaints include fatigue, weakness and dizziness. Iron deficiency impairs aerobic exercise, endurance capacity and energy efficiency. Patients with IDA may complain of pica, which is a craving for specific foods (often non-nutritive), such as ice chips. In severe IDA, nails may become brittle, with a spoon shape,[67] and the tongue may become smoother.[68]

The size of the red blood cells, measured by the mean corpuscular volume (MCV), can provide insight into the aetiology of the anaemia. Anaemia is classically defined according to the size and shape of the red blood cells. There are three types: microcytic (MCV <80 fL), normocytic (MCV 80–100 fL) and macrocytic (MCV >100 fL). Causes of microcytic anaemia pertinent to the female athlete include iron deficiency and thalassaemia. Normocytic anaemia may be caused by blood loss, haemolysis (red blood cell destruction), anaemia of chronic disease or endocrine causes. In the female athlete, severe macrocytic anaemia is likely caused by deficiency in vitamin B_{12} or folate.[69]

When undergoing evaluation for potential IDA, other lab values measured include ferritin and total iron binding capacity (TIBC). Ferritin is an intracellular protein that stores iron and releases it in a controlled fashion. The value is low in IDA; however, the value may be falsely elevated in cases of acute illness because it is an acute phase protein. Studies have demonstrated the inflammation in joints following physical activity may induce a rise in ferritin due to its acute phase protein properties.[70, 71] TIBC is an indirect measurement of transferrin, which is an iron transport protein contributing to the control of free iron levels. TIBC is elevated in IDA, presumably due to the body's attempts to maximise the little available iron.

When treating IDA, it important to note that the average female in childbearing years will need to absorb 1.4 mg of elemental iron daily to maintain a steady state. Average absorption for a female is around 10% of daily intake, and the absorption is heavily influenced by the nature of the diet.[72] Haeme iron (e.g. from red meat) is most readily absorbed. Absorption is augmented by vitamin C, which chelates the iron, making it more bioavailable. Tannins in coffee and tea significantly decrease iron absorption, as do phosphates in cola, and calcium in dairy products. In order to achieve maximal red blood cell production response to anaemia, greater iron intake is required than is provided by an ordinary diet; consequently, an iron supplement is often recommended. Depending on the severity of IDA, 150–300 mg of elemental iron should be consumed daily for 4–6 months. Such doses are best achieved with 50–65 mg tablets spread over the course of the day.[72] If the anaemia does not resolve with oral supplementation, intravenous administration of iron may

be necessary. If the anaemia aetiology is macrocytic, vitamin B_{12} and/ or folate supplementation is advised. In cases of vitamin B_{12} deficiency, daily oral supplementation of 1000 μg of vitamin B_{12} is recommended.[73] When folate deficiency is detected, 5 mg of oral folic acid should be given for 4 months.[74] Blood levels should be rechecked after 3 months to determine whether treatment is effective.

MENSTRUAL CYCLE

Menarche, the development of menses, typically occurs by the age of 15 years and is considered delayed (primary amenorrhoea) if there is no menstrual bleed by this age in the presence of secondary sexual characteristics.[75] It is common for girls to experience menstrual bleeding at irregular intervals for two to three years following menarche, but after this, it is considered unusual and should be evaluated.[76] Eumenorrhoea is the occurrence of menstrual cycles near the median for young adult women, 28 days ±7 days, during which menstruation, the follicular phase, ovulation and the luteal phase take place. After 2–7 days of menstruation, oestradiol increases throughout the follicular phase, leading to proliferation of the uterine lining. Mid-cycle, 24–36 hours after the luteinizing hormone (LH) surge, a dominant follicle releases an oocyte and the remainder of the follicle becomes the corpus luteum. The corpus luteum creates progesterone, which prepares the endometrial lining for implantation, maintaining the lining during the luteal or secretory phase. If no fertilisation takes place over the next two weeks, the corpus luteum involutes, accompanied by sharp decreases in oestradiol and especially progesterone. This leads to the instability of the endometrial lining and its shedding during menstruation.[77]

Except during the first 6–12 months after menarche, pregnancy and lactation, normal menstrual functioning is expected to occur and is healthy. As menopause nears, menstrual irregularity often develops, with natural menopause being diagnosed retrospectively after 12 months of amenorrhoea without a pathological aetiology.[78] The median age of menopause in industrialised countries is 50–52 years, with perimenopause beginning around age 47.5 years, but there is variation by race, other genetics, environment and lifestyle factors.[79] Menopause indicates cessation of ovulation, secondary to the decrease in ovarian follicles, resulting in reduction of oestradiol production. With the absence of the corpus luteum, progesterone secretion diminishes as well. Some effects of oestrogen and progesterone are shown in Table 29.5.

Table 29.5 Physiological effects of oestrogen and progesterone

Oestrogen	Progesterone
Cardiovascular	Increases insulin and promotes insulin re
• Antioxidant effects[80]	
• Increases HDL cholesterol[81]	
• Lowers LDL cholesterol[81]	
• Increases triglycerides[81]	
• Increases nitric oxide resulting in increased vascular flow-mediated arteriole dilation[80]	

• Reduces ischaemia, necrosis, apoptosis[80]	
Disease reduction[83] • Hypertension • Diabetes mellitus • Obesity • Vascular disease • Stroke	Lowers HDL cholesterol[82]
Substrate metabolism—increases fat metabolism[84]	Neuroprotective effects[82]
Development of female secondary sex characteristics	Increases body temperature[85]
Osteoprotective—inhibits osteoclast action	Increases central ventilatory drive[85]

Abnormal menstruation

Menstrual irregularity may refer to skipped periods, delayed cycles, irregular cycles or shortened cycles with breakthrough bleeding. Some patterns of menstrual irregularity are described in Table 29.6. Menorrhagia refers to heavy and or prolonged menstrual bleeding. It is common soon after menarche and prior to menopause. Causes include hormonal abnormalities leading to accumulation of the endometrial lining, sometimes even with a skipped menstrual bleed and then a heavier flow the next month; endometriosis; and fibroids. Menstrual cycles should be discussed at medical appointments, as menstrual abnormalities have various aetiologies that often need to be addressed. Additionally, menstrual dysfunction can affect both health and performance, either through perceived decrements or through increased likelihood of having iron deficiency.[86] Surveys indicate that 20–42% of athletes find that their menstruation affects their performance.[86, 87] Women with heavy menstrual bleeding were more likely to report that their menstrual cycles affected their training and performance.[86]

Page 410

Table 29.6 Types of menstrual dysfunction[88-90]

• Oligomenorrhoea—menstrual cycles longer than 35 days or fewer than 10 menses per year
• Amenorrhoea—no menstrual cycles for >90 days (secondary amenorrhoea)
• Primary amenorrhoea—no history of menstruation (pre-menarcheal) by age 15 years
• Anovulation—menstrual cycle without ovulation
• Dysmenorrhoea—cramping and lower abdominal pain associated with menstrual bleeding
• Luteal suppression—menstrual cycle with a luteal phase lasting fewer than 11 days or with a low concentration of progesterone
• Premenstrual dysphoric disorder (PMDD)—significant psychological changes (anxiety, depression) occurring with or immediately
• Heavy menstrual bleeding (HMB)—loss of >80 mL of blood per menstrual cycle (formerly known as menorrhagia)
• AUB—abnormal menstrual bleeding ◦ Coagulopathy (AUB-C)—HMB caused by systemic disorders (e.g. von Willebrand's disease) ◦ Ovulatory dysfunction (AUB-O)—AUB presenting as unpredictable timing of bleeding and variable flow ◦ Endometrial (AUB-E)—AUB, typically HMB, with normal menstrual periods and bleeding ◦ Iatrogenic (AUB-I)—AUB caused by medical intervention (e.g. OCPs, IUDs, anticoagulants) ◦ Not yet classified (AUB-N)—other disorders that may cause AUB

Menstrual cycle manipulation and contraception

Many types of contraception are available to females. Some of these contraceptives act through the administration of female sex hormones (oestrogen, progesterone or a combination) to alter the menstrual cycle to prevent pregnancy. Oral contraceptive pills (OCPs) deliver these hormones systemically, while certain intrauterine devices (IUDs) locally deliver the hormones to the uterus. Because the menstrual cycle can theoretically affect athletic performance (e.g. greater vasodilation with increased oestrogen, higher body temperature with high progesterone levels, discomfort and bloating in premenstrual phase as progesterone drops), female athletes sometimes prefer to manipulate their cycles to time certain phases of the cycle with training phases or competitions. This can be done using hormonal contraceptives.[91]

Combined oral contraceptive pills (COCs) are the most common form of contraception for females.[92] COCs prevent ovulation, thus blunting oestradiol secretion and progesterone production.[93] Other actions include disruption of gonadotropin-releasing hormone (GnRH) release, inhibition of the LH surge and suppression of follicle-stimulating hormone (FSH) secretion. OCPs can reduce premenstrual syndrome symptoms that may cause athlete discomfort during training and performance.[91] The effects of OCPs on other markers of performance are equivocal and are outlined in Table 29.7.

Page 411

Table 29.7 Possible changes to markers of performance due to oral contraceptive pill use. In all cases, there may be no effect on the performance marker[91, 94-96]

Performance marker	Possible changes with OCP use
VO_2max	Decrease
Ventilation	Increase; no performance changes
Substrate utilisation	Trend of carbohydrate sparing and increased fatty acid metabolism
Anaerobic capacity	Improvement during withdrawal phase
Anaerobic power	Improvement during withdrawal phase

Studies seem to agree that muscular strength is unaffected by OCPs despite possible androgenic effects of progestins.[91, 94, 97] Confusion over the effects of OCP use on athletic performance is caused by study differences: the type and dose of OCP, the determination of menstrual cycle phase, hormonal levels, and training status of study participants can all affect athletic performance and confound study conclusions. In general, the female athlete can select her OCP based on subjective preferences.

Delay of menses through extended OCP regimens is common among physically active females.[98] If an important competition is on the calendar, bleeding can be induced prior to the competition to allow the athlete to compete in the preferred post-bleed state.[91] The number of yearly menstrual cycles can be reduced by extended OCP regimens, and this confers many positive effects, such as

decreased bloating and dysmenorrhoea.[9]9 When engaging in menstrual cycle manipulation by changing OCP use, appropriate contraceptive measures should be employed as necessary.

The progesterone contained in OCPs can cause central rises in body temperature. During the hormonal dosing period of OCP use, women have been reported to have a resting and exercising temperature 0.31°C higher than during the hormone-free period.[100] Similar results have been observed when the women were exercising in a hot environment (30°C).[101] Additionally, exercising heart rate rises 6–8 beats per minute when on the hormonal period of an OCP regimen.[100], [101] These OCP-induced changes are not cause for concern for the female athlete, but their caregivers should be aware of the possible risks during exercise in extreme conditions.

Some IUDs contain levonorgestrel (LNg), a steroid belonging to the progestin family that shares similar actions with endogenous progesterone. Unlike OCPs, disruption of ovulation by LNg-releasing IUDs is variable and is not the primary pathway for contraception. Instead, LNg-releasing IUDs deliver LNg directly to the uterus and, through a series of reactions, prevent fertilisation and implantation.

LNg-releasing IUDs can change bleeding patterns and these patterns further change as duration of use increases. LNg-releasing IUDs can induce amenorrhoea or oligomenorrhoea, which would impart similar benefits to athletes as extended OCP regimens.[102] Users of LNg-releasing IUDs often experience a reduction in bleeding volume, which improves the athlete's comfort during training and competition and serves to reduce anaemia risk.[103] We are unaware of studies specifically investigating the effects of LNg-releasing IUDs on athletic performance.

Copper IUDs prevent pregnancy through natural spermicidal action and impairment of implantation. Soon after copper IUD insertion, some users reported heavier and more frequent bleeding, though these symptoms subsided in many as duration of use increased.[103] The specific effects of copper IUDs on athletic performance have not been studied. When choosing an IUD, an athlete should be counselled on the effects of each type and choose a type that fits her specific needs.

Contraceptive implants use various progestins to prevent pregnancy via a similar mechanism and have similar effects to the previously discussed LNg-releasing IUDs. However, because the implant is placed in the arm, the progestins are delivered systemically rather than locally. Implants reduce bleeding frequency and volume; however, implant users report being bothered more by the adverse effects of their contraception than their IUD-using counterparts.[103, 104] The exact athletic performance effects of the implant have not been studied.

Depo-medroxyprogesterone (DMPA) injections are a contraceptive method that require administration every three months and deliver medroxyprogesterone, a progestin, systemically. DMPA has deleterious effects on bone mineral density (BMD).[105] In a prospective study of physically active female military students, use of DMPA (median use: 6.3 months per year) was associated with BMD reductions at the spine, hip and calcaneus.[106] This indicates that DMPA can counteract the osteogenic effects of weight-bearing activity, and the risk of osteoporosis later in

life after use of DMPA as an adolescent is unknown.[105] We recommend female athletes try other forms of contraception before using DMPA.

FEMALE ATHLETE TRIAD

The female athlete triad (Triad) refers to the interrelationship of energy availability, menstrual function and bone density. It should be considered in relation to the broader syndrome of 'relative energy deficiency in sport' (RED-S). When the term 'female athlete triad' was first coined by the American College of Sports Medicine (ACSM) in 1992, it referred to the combination of disordered eating (with or without an eating disorder), amenorrhoea and osteoporosis.[107] With more research and clinical experience, the term evolved to represent three spectra (Fig. 29.4). An athlete may exist at different points along each of the three spectra and is at risk of worsening along all three if energy availability, menstrual health and bone health are not adequately addressed.[108]

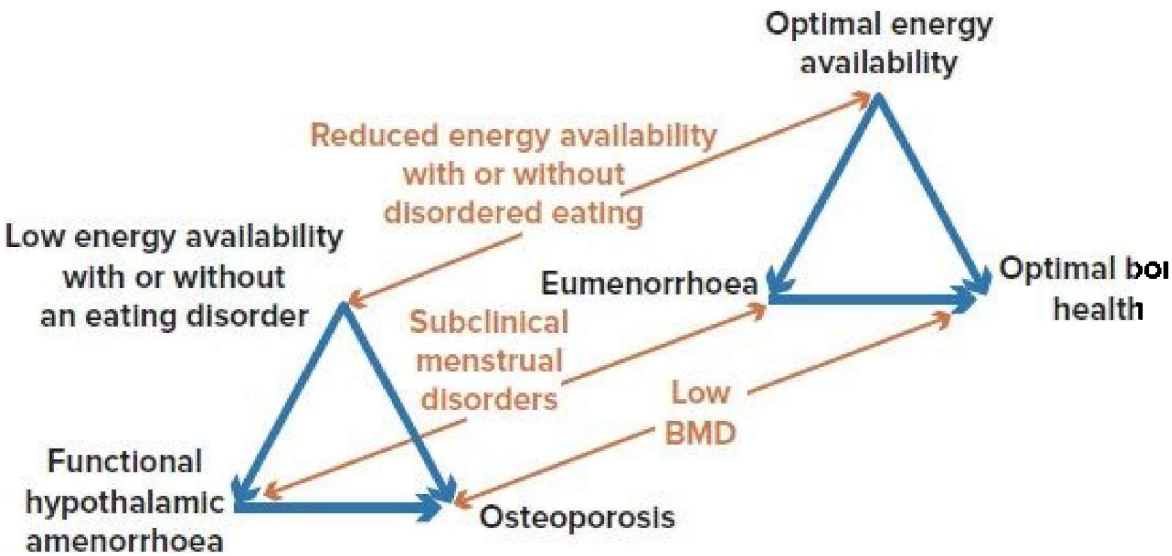


Figure 29.4 Female athlete triad spectra ADAPTED WITH PERMISSION FROM NATTIV A, LOUCKS AB, MANORE MM ET AL. AMERICAN COLLEGE OF SPORTS MEDICINE POSITION STAND: THE FEMALE ATHLETE TRIAD. MEDICINE & SCIENCE IN SPORTS & EXERCISE 2007; 39(10): 1867–82 © 2019 AMERICAN COLLEGE OF SPORTS MEDICINE HTTPS://JOURNALS.LWW.COM/ACSM-MSSE/FULLTEXT/2007/10000/THE_FEMALE_ATHLETE_TRIAD.26.ASPX[108]

Energy availability

Energy availability (EA) is the amount of energy remaining after exercise training for all other physiological functioning each day. It is often defined as dietary energy intake (EI) minus exercise energy expenditure (EEE), normalised to fat free mass (FFM), and is expressed as kcal/kg FFM per day.[109] All athletes are at risk of developing inadequate EA if they are not conscientious about proper fuelling for their athletic activity. Certain athletes are at heightened risk and include those

participating in leanness sports. Leanness sports are those in which leanness is thought to confer an athletic advantage (e.g. endurance sports, aesthetic sports, weight-class sports and anti-gravitation sports).[110]

Low EA may develop inadvertently or secondary to disordered eating (DE) or an eating disorder (ED). The prevalence of EDs in female athletes has been reported as high as 48%, with DE as high as 89.2%.[1]11 While both females and males are susceptible to EDs, female athletes, in particular, often struggle with physical performance versus physical appearance. The sports and non-sports cultures create a conflict for many women regarding the performing body versus the objectified body, food as fuel versus a guilty habit, and body type diversity in sport versus appearance prejudice.[112] Such struggles start early. One study of 527 girls aged 13–14 years divided participants by involvement in team sports or no sports participation and asked questions about body dissatisfaction and motivation for weight loss. The athletes had greater body dissatisfaction and greater motivation for weight loss despite all participants having a normal body mass index (BMI).[113] In a survey of 1000 female athletes (ages 15–30 years) presenting to a sports medicine clinic, using surrogate markers for low EA (self-reported ED/DE or positive results on ED screening tools), 47.3% of athletes screened positively for low EA.[114] This emphasises the importance of screening for low EA in sports teams and in clinical settings.

Menstrual function

With inadequate EA, the pulsatile secretion of gonadotropin releasing hormone (GnRH) from the hypothalamus is disrupted, causing irregular LH and FSH release from the pituitary, resulting in decreased oestradiol and progesterone secretion and menstrual irregularity including oligomenorrhoea and, more severely, amenorrhoea. Such resultant amenorrhoea is known as functional hypothalamic amenorrhoea (FHA).[115] FHA is an evolutionary adaptation to inadequate caloric availability, with the body conserving energy for the most vital processes and shifting fuel away from the reproductive system.[116] Interestingly, there may be many hormonal pathways signalling low EA to the hypothalamus to affect GnRH pulsatility. For example, the appetite regulating hormones leptin (anorexigenic), ghrelin (orexigenic) and peptide YY (anorexigenic) all impact the hypothalamic-pituitary-gonadal (HPG) axis and are modulated in low EA states. Studies in female athletes with low EA, amenorrhoeic athletes, and/or girls and women with anorexia nervosa have demonstrated decreases in leptin (likely an adaptive response to prevent further food restriction), increases in ghrelin (possibly to enhance food intake) and decreases in peptide YY (a potential marker of low EA and hypothesised to enhance ghrelin resistance).[117, 118] Adiponectin, an anorexic adipokine, may suppress GnRH and gonadotropin secretion and was lower in some, but not all, amenorrhoeic athletes compared to eumenorrhoeic athletes.[119, 120] Insulin enhances GnRH neuronal activity in the hypothalamus and aromatase activity in the ovary.[117] Insulin is decreased in low EA states and in amenorrhoeic athletes versus eumenorrhoeic athletes and controls, and insulin measures positively correlate with LH pulsatility.[117, 121, 122]

In those with anorexia nervosa and some athletes with amenorrhoea, growth hormone (GH) is elevated and insulin-like growth factor 1 (IGF-1) is decreased, suggesting a hepatic resistance to GH. IGF-1 increases GnRH secretion and GH correlated negatively with LH secretion.[117] Cortisol, an important hormone for energy intake, storage and mobilisation, is secreted in response to stress and glycogen depletion and has catabolic effects.[123] Cortisol measures have a U-shaped relationship with BMI and fat mass, with both extremely underweight and overweight states possibly activating the hypothalamic–pituitary–adrenal (HPA) axis.[124] Studies of severe caloric restriction and most studies of amenorrhoeic athletes have demonstrated increased cortisol levels with an inverse relationship between measures of cortisol secretion and LH pulsatile parameters. In animal models, high levels of cortisol inhibit GnRH secretion and gonadotropic response to GnRH; a corticotropin-releasing hormone (CRH) receptor antagonist mitigates negative effects of cortisol on LH pulsatility.[117]

The thyroid hormones triiodothyronine (T3) and thyroxine (T4) are important for metabolism, growth and reproductive function. Low levels of thyroid hormones are associated with disruption of menses and follicular development in animal studies.[125] T3 levels in women with anorexia nervosa and athletes with amenorrhoea are lower than in eumenorrhoeic women, but T4 and thyroid-stimulating hormone (TSH) levels have been more variable.[126] More work is needed to better understand how various hormones respond to low EA, interact with one another and collectively downregulate the HPG axis.

Many female athletes experience menstrual dysfunction (see above). Thus, it is important to investigate the aetiology of menstrual irregularity in athletes, with a particular suspicion for low EA. It is also important to note that specific EA thresholds leading to menstrual dysfunction may differ from one individual to another. In seminal work by Professor Anne Loucks and Dr JR Thuma, habitually sedentary, eumenorrhoeic young women aged 18–30 were studied under controlled laboratory conditions in two 5-day trials separated by two months.[127] The participants expended 15 kcal/kg FFM per day via supervised exercise and consumed calories resulting in an EA of 45 kcal/kg FFM per day in one trial, and either 10, 20 or 30 kcal/kg FFM per day in another trial. At an EA of 30 kcal/kg FFM per day, LH pulsatility was unaffected, but below this threshold, LH pulse frequency decreased and amplitude increased, with more extreme disruption noted in women with short luteal phases.[127]

When habitually sedentary, eumenorrhoeic young women aged 18–30 were studied using less-stringent field measurements (diet log) of EA, the probability of developing menstrual dysfunction was greater than 50% as EA dropped below 30 kcal/kg FFM per day.[128] There was a dose-response relationship between percentage decrease in EA from baseline (relative energy deficit) and frequency of menstrual dysfunction (luteal phase defects, anovulation and oligomenorrhoea), but there was no correlation between menstrual dysfunction and magnitude of energy deficiency.[129] No studies of measured low EA and amenorrhoea in adolescent athletes have been published. Thus, in a growing individual, it is plausible that energy needs could be even higher to prevent primary and secondary amenorrhoea.

Bone health

Bone health is the subject of Chapter 17. As outlined there, weight-bearing exercise in eumenorrhoeic athletes typically results in greater bone density compared to sedentary controls.[10 8] However, the osteogenic benefit of exercise is mitigated by low EA and menstrual dysfunction. Studies of adolescents and adults have demonstrated lower bone mineral density (BMD) as measured by dual-energy X-ray absorptiometry (DXA) in amenorrhoeic versus eumenorrhoeic athletes and controls.[130] DXA interpretation requires Z-scores for premenopausal women. A Z-score is a measure of BMD that indicates the standard deviation compared to a sex-, race- and age-matched control group. The ACSM considers a Z-score less than —1.0 of concern for a young weight-bearing female athlete.[108] In contrast, a T-score is to be used for postmenopausal women. A T-score is a measure of BMD that indicates the standard deviation compared to the mean for a young, healthy adult of the same race and sex.[131] See Table 29.9 for proper DXA interpretation in female athletes.

Adolescence, specifically, is a critical time for bone accrual. Girls who begin strenuous exercise during prepubescence typically gain twice as much bone mineral content (BMC) as those who initiate similar types of exercise after puberty, and in general, 90% of peak bone mass is accrued by age 18.[132, 133] Most of the hormones discussed above are critical for building and maintaining BMD. Oestrogen (oestradiol) is a bone anti-resorptive and important predictor of BMD. But appetite-regulating hormones, insulin, IGF-1, cortisol, T3 and other hormones disrupted by low EA are important for bone, as well. The changes in such hormones noted in female athletes with low EA and menstrual dysfunction correlate with worse BMD compared to eumenorrhoeic athletes.[134]

Amenorrhoeic athletes with FHA have lower BMD at various sites, as measured by DXA and computed tomography (CT), impaired bone architecture, as measured by peripheral quantitative CT (pQCT), impaired bone microarchitecture, as measured by high resolution pQCT (HRpQCT), and decreased estimates of bone strength, determined by finite elemental analysis.[130, 135, 136] In a study of 175 oligo-amenorrhoeic athletes, eumenorrhoeic athletes and eumenorrhoeic non-athletes aged 15–25 years, lifetime fracture risk was higher in the oligo-amenorrhoeic athletes compared to the eumenorrhoeic athletes and controls (47%, 25.7%, 12.5%, respectively), largely driven by stress fractures in the oligo-amenorrhoeic athletes (32% vs 5.9% and 0%, respectively).[136] When results of oligo-amenorrhoeic athletes were compared based on having <2 stress fractures or ≥2 stress fractures, those with >2 stress fractures had lower lumbar spine and whole body DXA results (mean Z-scores < –1.0 for lumbar spine and whole body). Those with ≥2 stress fractures also had worse bone microarchitecture at the non-weight-bearing radius and worse stiffness and failure load at the weight-bearing tibia.[136]

RELATIVE ENERGY DEFICIENCY IN SPORT

In 2014, the International Olympic Committee (IOC) introduced a new syndrome, relative energy deficiency in sport (RED-S), reflecting an evolution of the Triad concept.[137] Like Triad, low EA is the

underlying cause of RED-S. Because studies have demonstrated that low EA may result in many physiological and performance detriments, the RED-S models centre energy deficiency as a common cause for health and performance changes. The RED-S concept includes the Triad and also acknowledges that men, too, may be affected by low EA. Figures 29.3 and 29.4 describe the proposed health consequences and performance effects of RED-S.

Due to the relative infancy of RED-S, the proposed effects of low EA are not fully understood and the prevalence of RED-S is difficult to ascertain. However, there are strong relationships between low EA and many of the theorised effects, as described below.

Endocrine

Endocrine effects of low EA are pervasive and have been discussed in the context of menstrual function and bone health. Many of the endocrine changes occurring in RED-S remain to be elucidated. Significant evidence demonstrates that T3 levels are suppressed during low EA, suggesting T3 as a possible biomarker for athletes suspected of RED-S.[117, 126]

Metabolic

Various reports indicate that resting metabolic rate (RMR) can be lowered in the setting of inadequate EA in athletes and non-athletes.[139–142] In a 2015 study of female athletes, those with reduced EA had lowered RMR.[141] Athletes with menstrual dysfunction-a group with chronically low EA-also had lowered RMR.[141] The hypometabolic state is induced to preserve energy for other physiological processes.

Table 29.8 DXA measurements, sites and clinical meaning for female athletes of different age groups[108, 131]

Age	Site	Low bone mass	Osteopenia	Osteoporosis
Under 20	LS, TBLH	Z-score < -1		Z-score < —2 with significant fracture history or risk factors
20—menopause	LS, TH, FN	Z-score < -1		Z-score < —2 with significant fracture history or risk factors
Post-menopause	LS, TH, FN		T-score < -1	T-score ≤ -2.5

LS = lumbar spine; TBLH = total body less head; TH = total hip; FN = femoral neck

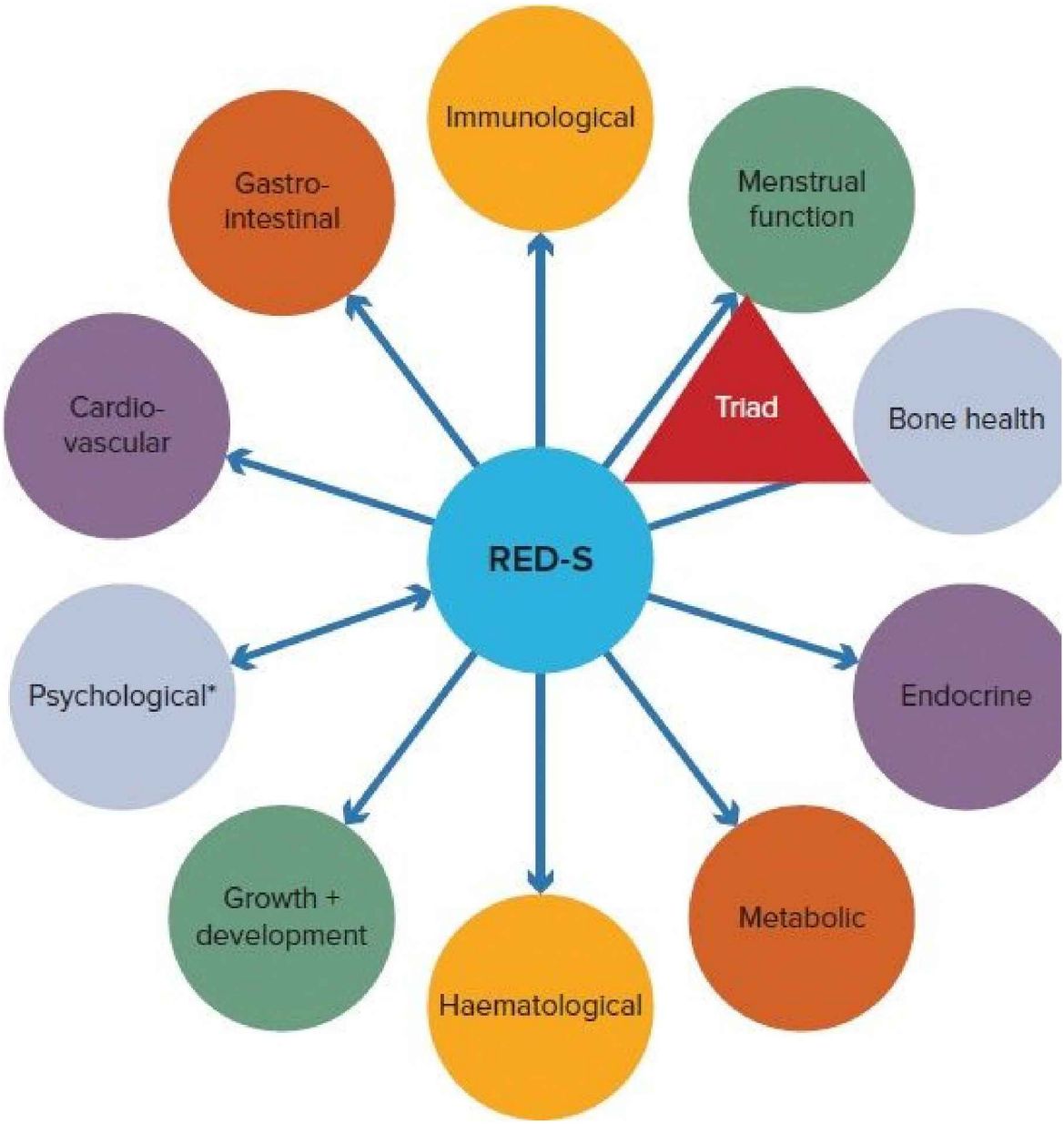
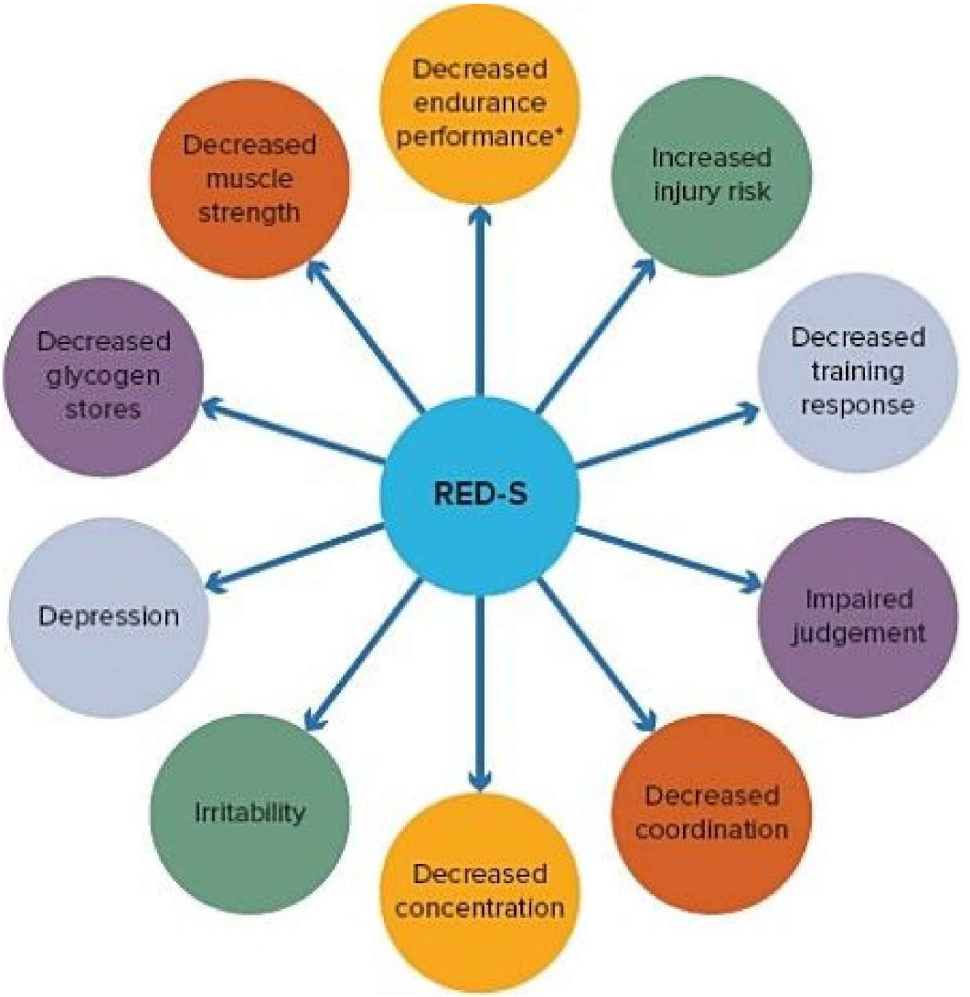


Figure 29.5 Health consequences of RED-S[137,138]

*Psychological consequences can either precede RED-S or be the result of RED-S



FIGURES 29.5 AN
REPRODUCED W
PERMISSION MO
SUNDGOT-BORG
L, ET AL. THE IOC
STATEMENT: BEY
FEMALE ATHLETI
RELATIVE ENERG
IN SPORT (RED-S
MED 2014;48(7):
491–7; ORIGINAL
CONSTANTINI NV
CONCERNS OF T
BOOK OF ABSTR
WORLD CONGRE
SPORTS MEDICIN
2002:151.

Figure 29.6 Potential performance effects of RED-S[137, 138]

*Aerobic and anaerobic performance

Haematological

Many athletes with reduced EA have iron deficiency and, as mentioned previously, females are particularly susceptible to iron deficiency due to blood loss during menstruation.[143] Estimates of the prevalence of iron deficiency in young female athletes range from 24% to 47%.[143] Iron deficiency can worsen the hypometabolic state associated with low EA, promote further progression of an energy deficiency by shifting adenosine triphosphate (ATP) production away from oxidative phosphorylation to anaerobic glycolytic pathways, impair reproductive function

and harm bone health.[144] Iron deficiency also reduces athletic performance by impairing adequate delivery of oxygen to muscles.

Growth and development

Patients with anorexia nervosa have demonstrated retardation of growth as a result of inadequate energy intake. Upon recovery and weight restoration, growth is often resumed, but attainment of predicted final height may not be achieved.[145] Yearly growth charts from an adolescent's paediatrician can be useful for identifying the presence, severity and duration of an energy deficiency or eating disorder.

Psychological

Psychological abnormalities can contribute to and result from low EA.[137] Eating disorders, such as anorexia nervosa, result in insufficient caloric intake.[146] Additionally, restrictive eating behaviours (e.g. disordered eating, restrictive diets such vegetarian, vegan, gluten-free) can result in psychological sequelae such as depression.[147]

Cardiovascular

Reduced EA may cause deleterious changes to the cardiovascular system. Athletes with FHA have unhealthy lipid profiles and endothelial dysfunction.[148, 149] These changes occur despite the beneficial effects of regular exercise on the cardiovascular system. Additionally, early development of cardiovascular disease has been reported in older premenopausal women with a history of FHA.[150] Bradycardia and hypotension are common in anorexia patients, and routine measurement of vital signs is recommended in athletes with suspected low EA.[151]

Gastrointestinal

Various forms of gastrointestinal (GI) dysfunction have been reported in anorexia nervosa patients. Types of GI dysfunction include delayed gastric motility, emptying and intestinal transit.[152] In a 2018 study that used surrogate markers of low EA, those with low EA were 1.5 times more likely to report GI complaints, such as constipation and stool leakage, than their adequate-EA counterparts.[114]

Immunological

High-level athletes and those with high training loads are at increased susceptibility to illness.[153] Among athletes preparing for the 2016 Summer Olympics, those with low EA were at increased odds of reporting upper respiratory infection, gastrointestinal distress, body aches or head-related symptoms.[154, 155] High-achieving athletes often live on the edge of illness, and monitoring their health and tailoring training and diet appropriately help to avoid the performance decrements associated with sickness.

Potential performance effects of relative energy deficiency in sport

The proposed effects on performance that accompany RED-S have not been studied closely in athletic populations. Decreased endurance performance has been observed in ovarian-suppressed (a marker of low EA) female swimmers compared to normally cycling swimmers.[156] As previously discussed, amenorrhoeic athletes are at higher risk of stress fracture than eumenorrhoeic athletes. Knee muscle strength is lower among amenorrhoeic athletes than eumenorrhoeic athletes; knee endurance strength was also diminished in the amenorrhoeic group.[157]

Screening and return to play for female athlete triad and relative energy deficiency in sport

In 2014, the Female Athlete Triad Coalition published guidelines for screening, care and assigning level of participation appropriate for female athletes with various Triad risk factors.[130] A point system was developed, and athletes are scored based on:

1. EA and history of DE/ED
2. BMI
3. age of menarche
4. number of menstrual cycles in past 12 months
5. BMD Z-score
6. stress reaction/fracture history.

Athletes are then assigned risk categories: low, moderate and high. The level of risk is tied to a level of clearance:

- full clearance
- provisional/limited clearance
- restricted from training or competition.

Clearance may be modified based on clinical judgment, athlete compliance and other factors.[130]

Page 417

The IOC also developed a clinical assessment tool (RED-S CAT) for sports participation in the context of RED-S.[158] Assessment of various risk factors leads to categorising athletes into three risk categories as well. This RED-S CAT uses Triad risk factors and other physiological and psychological impairments, but does not rely on a point system for clearance decisions.[158] Both the Triad screening tool and RED-S CAT rely significantly on clinical judgment. The primary focus of treatment for both Triad and RED-S is developing an interdisciplinary team and addressing the underlying low EA through medical management, nutritional knowledge, exercise modification and psychological support. Additional health and performance effects should also be addressed. Further work is needed to compare and modify the Triad and RED-S screening tools.

PREGNANCY

Throughout the nine months of pregnancy, the female body changes in order to foster foetal growth and in preparation for parturition. These changes are largely due to the hormonal effects of oestrogen and relaxin and they affect nearly every system, including cardiac, respiratory and musculoskeletal.

During pregnancy, up to one quarter of the maternal blood flow is directed to the uterus, and the maternal cardiovascular system adapts to meet the increased demand of both mother and foetus. Cardiac output rises throughout pregnancy, largely due to the increased levels of oestrogen, causing increased total blood volume (by 30–50%), which then increases pre-load and stroke volume.[159]

Progesterone's vasodilatory effects lead to a 15% decrease in systemic vascular resistance (SVR), leading to an initial drop in blood pressure during the first half of pregnancy.[160] In turn, the average heart rate increases (10–15 beats per minute) to compensate for the decreased SVR. The blood pressure returns to baseline at the end of the second trimester. The vasodilation in the venous system leads to compromised venous return and its downstream effects such as dependent oedema, varicose veins, haemorrhoids and increased risk of venous thromboembolism.[160]

The respiratory system responds both to the hormone changes of pregnancy and to the physical encumbrance of the uterus on the diaphragm. Beginning in the first trimester, increased progesterone levels act as a respiratory stimulant and lead to increased respiratory drive.[161] The tidal volume increases by roughly 40% and the respiratory rate does not change; thus, the minute ventilation rises by 30–50%.[162] The rise in minute ventilation is necessary to meet the increased oxygen consumption during pregnancy due to the metabolic demands of the mother, foetus and placenta. Additionally, as the foetus grows, the diaphragm is elevated by the enlarging uterus, which displaces the intra-abdominal contents upwards. The diaphragmatic elevation reduces the total lung capacity by 5% and the functional residual capacity (FRC) by 10–25% (greater decrease in FRC when supine compared with erect).[163]

The intensified respiratory drive and pressure of the intra-abdominal contents on the diaphragm along with the increased blood volume, anaemia and nasal congestion associated with pregnancy are frequently perceived by pregnant women as shortness of breath.[160] The increased baseline respiratory demands and decreased total lung capacity lead to less oxygen availability for aerobic exercise. Consequently, the perceived exertion increases and maximum exercise performance decreases in pregnancy.[164]

Joint laxity increases during pregnancy, largely in response to the hormone relaxin, which is secreted by the corpus luteum. Notable joint response is seen at the pubic symphysis as early as the tenth week of pregnancy, and the pubic symphysis continues to widen throughout the pregnancy in preparation for vaginal delivery.[165]

Pregnancy is often associated with musculoskeletal discomfort, commonly in the lower back. The gravid uterus creates an exaggerated lordosis, which places burden on the lower back, causing painful symptoms with occasional radiation down the posterior thighs. Lower back symptoms are more common in women with back pain preceding the pregnancy and in women of increased

maternal age. Despite the increase in back pain, there is not a higher prevalence of disc pathology in pregnant women.[166] Most lower back pain in pregnant women responds to symptomatic treatment.[166] Use of lumbar support binders has demonstrated reduced pain and improvement in activities of daily living.[167] Use of medication should be discussed with the patient's obstetrician.

Other musculoskeletal complaints with increased prevalence in pregnant women include carpal tunnel syndrome (CTS), de Quervain's tenosynovitis and leg cramps. CTS and de Quervain's tenosynovitis can be treated symptomatically with splinting, rest and ice, and both appear to resolve with the conclusion of pregnancy or the cessation of breastfeeding.[166] Pregnancy-associated leg cramps have an unknown aetiology, though it is theorised to relate to calcium deficiency. Oral calcium supplementation effectively reduces the frequency and severity of the symptoms.[168]

The pregnant woman who currently struggles, or has struggled, with an eating disorder is at risk of many pregnancy complications. These complications include hyperemesis gravidarum, anaemia, spontaneous abortion, preterm birth, caesarean section and postpartum haemorrhage.[169] Children born to mothers with an eating disorder history are more likely to have developmental disturbances and to develop anxiety, depression and substance abuse later in life.[170]

Exercise recommendations for pregnant women are similar to those for non-pregnant women, primarily consisting of aerobic and resistance training. Similar to non-pregnant women, exercise in pregnant women can lead to improved emotional and physical wellbeing. As an added benefit of exercise in pregnancy, consistent activity is associated with a decreased risk of gestational diabetes and approximately a 40% decreased risk of pre-eclampsia, when compared with inactivity.[171, 172] Exercising regularly when pregnant may decrease the risk of caesarean section and shorten the duration of labour in vaginal childbirth.[173] These benefits are most likely consequences of good abdominal and pelvic floor muscle tone.

In the past, concern over exercise during pregnancy focused on potential risks to the foetus; however, indirect evidence demonstrates that changes in foetal heart rate and transient hypoxic episodes during exercise have no lasting effects on foetal development.[164] Furthermore, birth weight appears to be unaffected by exercise in pregnant women who have an adequate caloric intake.[174] Pregnant women, however, should carefully choose the type and intensity of their exercise. If the pregnant woman experiences dyspnoea prior to physical activity, chest pain, dizziness, calf pain or swelling, leakage of amniotic fluid, preterm labour, vaginal bleeding or decreased foetal movement during exercise, she should stop exercising immediately.[175] All pregnant women should consult their obstetricians before beginning exercise programs. Absolute and relative contraindications to exercise in pregnancy are listed in Table 29.9.

Table 29.9 Contraindications for aerobic exercise in pregnancy [176]

Absolute	Relative

- Haemodynamically significant heart disease
- Restrictive lung disease
- Incompetent cervix or cerclage
- Multiple gestation at risk of premature labour
- Persistent second-trimester or third-trimester bleeding
- Placenta praevia after 26 weeks gestation
- Premature labour during current pregnancy
- Ruptured chorioamniotic membranes
- Pre-eclampsia or pregnancy-induced hypertension
- Severe anaemia
- Anaemia
- Unevaluated maternal cardiac arrhythmia
- Chronic bronchitis
- Poorly controlled type 1 diabetes
- Extreme morbid obesity
- Extreme underweight (body mass index < 12)
- History of extremely sedentary lifestyle
- Intrauterine growth restriction in current pregnancy
- Poorly controlled hypertension
- Orthopaedic limitations
- Poorly controlled seizure disorder
- Poorly controlled hyperthyroidism
- Heavy smoker

ARTAL R., EXERCISE IN PREGNANCY: GUIDELINES. CLINICAL OBSTETRICS AND GYNECOLOGY 2016; 59(3):639-44
COPYRIGHT © 2019 THE AUTHORS. PUBLISHED BY WOLTERS KLUWER HEALTH, INC. ON BEHALF OF THE INTERNATIONAL FEDERATION OF FERTILITY SOCIETIES. HTTPS://JOURNALS.LWW.COM/CLINICALOBGYN/ABSTRACT/2016/09000/EXERCISE_IN_PREGNANCY_____GUIDELINES.23.ASPX

Women with normal pregnancies who are currently physically active can continue exercising, and those with normal pregnancies who are not currently physically active can and should initiate exercising.[169, 175] A woman's aerobic fitness will be able to plateau or slightly improve during pregnancy if she continues to exercise as symptoms permit.[169] The ACSM recommends a minimum of 30 minutes of moderate intensity exercise 5 days per week for non-pregnant women.[177] Women who were not active prior to pregnancy should gradually increase the amount of activity, starting with as little as 5 minutes daily and increasing in 5-minute intervals as fitness allows until they reach 30 minutes.

Walking, swimming and stationary biking are all excellent aerobic options for the pregnant woman. Swimming does not increase lower extremity oedema, the action has minimal impact stress on the lower extremity joints and the water helps the body to stay cool. Women participating in any sport with an increased risk of falling (e.g. running) should be educated as to the changes in their centre of gravity and decreased balance due to the weight gain of pregnancy, and their ability to balance should be reassessed throughout the pregnancy. When participating in yoga, pregnant women should avoid excessive stretching due to relaxin's loosening effects on ligaments.

PRACTICE PEARL

During the third trimester, women should avoid activity in the supine position due to potential compression of the vena cava.

Sports that involve potential abdominal trauma should be avoided during pregnancy due to the threat of foetal harm. These activities include contact sports, such as rugby, soccer and hockey, downhill skiing and horseback riding. Scuba diving is absolutely contraindicated during pregnancy due to the disturbance of oxygen balance and the risk of decompression sickness.

Elite or amateur female athletes who become pregnant may wish to continue high-intensity exercise during pregnancy. There is a limited body of evidence on the effect of strenuous activity on the foetus. These small studies have demonstrated transient foetal cardiovascular changes during high-intensity exercise that do not appear to have lasting effects on the neonate.[171] When participating in exercise, women who monitor their heart rates as a guide to exertion should be aware that their heart rates in pregnancy will be 10–15 bpm higher than prior to pregnancy and their heart rate zones can be adjusted accordingly.

Light to moderate resistance training with free weights or weight machines appears to have no adverse effect on the foetus.[169] Women who wish to lift heavy weights should not use the Valsalva manoeuvre because it causes a rapid increase in blood pressure and intra-abdominal pressure, possibly decreasing blood flow to the foetus.[169] Additionally, the increased abdominal pressure may weaken or stretch the pelvic floor musculature, leading to a higher risk of incontinence or pelvic organ prolapse.[178]

Pregnant women should be aware of the importance of body temperature control and hydration while exercising. In general, the demands of exercise lead to heat generation. When exercising at a moderate intensity, the average non-pregnant woman has a temperature rise of 1.5°C during the first 30 minutes of exercise, then the core temperature plateaus if exercise continues for another 30 minutes.[179] The plateau reflects the steady state of heat production versus dissipation. If heat production outpaces dissipation, the core temperature continues to rise. Factors causing increased heat production include hot and humid climates and high-intensity exercise, and dehydration can lead to decreased dissipation. During pregnancy, the basal metabolic rate and, thus, baseline heat production are already increased before beginning exercise. Core temperatures rise additionally during exercise. Risk of heat exhaustion or potentially dangerously elevated maternal and foetal body temperatures can be reduced by maintaining proper hydration. Animal studies have demonstrated teratogenic effects when maternal core temperature rises more than 1.5°C early in gestation; however, there are no reports that hyperthermia due to exercise is teratogenic.[164]

Many of the physiological changes of pregnancy last for four to six weeks postpartum and may continue to affect a woman's ability to exercise. Women should be encouraged to return to activity gradually as tolerated. Physical activity may decrease the incidence of postpartum depression and fatigue, in addition to the cardiopulmonary benefits. There is no evidence that the composition or amount of breast milk is negatively affected by exercise.[167]

SUMMARY

- Women and girls have a legacy of achievement in sport.
- In this chapter we have highlighted the sex differences in anatomy, physiology and injury

that clinicians and other caregivers should be aware of when treating female athletes.

- A quality medical and training history should be taken whenever an athlete presents with an injury. Seemingly disconnected symptoms may be interrelated and contribute to an injury or a drop in performance.

REFERENCES

1. Marcason W. Female athlete triad or relative energy deficiency in sports (RED-S): is there a difference? *J Acad Nutr Diet* 2016; 116(4): 744.
2. Garibaldi L, Chemaitilly W. Physiology of puberty. In: Kliegman R, Stanton B, St Geme JW, 3rd, eds. *Nelson Textbook of Pediatrics*. 20th ed. Philadelphia, PA: Elsevier, 2016; 2: 2655.
3. Tanner JM, Davies PS. Clinical longitudinal standards for height and height velocity for North American children. *J Pediatr* 1985; 107(3): 317–29.
4. Campisi J, Finn KE, Bravo Y et al. Sex and age-related differences in perceived, desired and measured percentage body fat among adults. *J Hum Nutr Diet* 2015; 28(5): 486–92. doi: 10.1111/jhn.12252.
5. Puts DA. Beauty and the beast: mechanisms of sexual selection in humans. *Evolution and Human Behaviour* 2010; 31(3): 157–75.
6. O'Connell MD, Wu FC. Androgen effects on skeletal muscle: implications for the development and management of frailty. *Asian J Androl* 2014; 16(2): 203–12. doi: 10.4103/1008-682X.122581.
7. Marshall WA, Tanner JM. Variations in pattern of pubertal changes in girls. *Arch Dis Child* 1969; 44(235): 291.
8. Warrener AG, Lewton KL, Pontzer H et al. A wider pelvis does not increase locomotor cost in humans, with implications for the evolution of childbirth. *PloS ONE* 2015; 10(3): e0118903.
9. Wheatley CM, Snyder EM, Johnson BD et al. Sex differences in cardiovascular function during submaximal exercise in humans. *Springerplus* 2014; 3: 445. doi: 10.1186/2193-1801-3-445.
10. Kenney WL, Wilmore J, Costill D. *Physiology of sport and exercise*. 6th ed. Human Kinetics, 2015.
11. McArdle W, Katch F, Katch V. Measuring and evaluating human energy generating capacities during exercises. In: *Essentials of exercise physiology*. 3rd ed. Baltimore, MD: Lippincott Williams & Wilkins, 2006; 1: 223–59.
12. Lewis DA, Kamon E, Hodgson JL. Physiological differences between genders: implications for sports conditioning. *Sports Med* 1986; 3(5): 357–69.

13. Scurr JC, White JL, Hedger W. The effect of breast support on the kinematics of the breast during the running gait cycle. *J Sports Sci* 2010; 28(10): 1103–9. doi: 10.1080/02640414.2010.497542.
14. Hussain Z, Roberts N, Whitehouse G et al. Estimation of breast volume and its variation during the menstrual cycle using MRI and stereology. *Br J Radiol* 1999; 72(855): 236–45.
15. Scurr J, Brown N, Smith J et al. The influence of the breast on sport and exercise participation in school girls in the United Kingdom. *J Adolesc Health* 2016; 58(2): 167–73. doi: 10.1016/j.jadohealth.2015.10.005.
16. Bowles KA, Steele JR. Effects of strap cushions and strap orientation on comfort and sports bra performance. *Med Sci Sports Exerc* 2013; 45(6): 1113–19. doi: 10.1249/MSS.0b013e3182808a21.
17. Hansson E, Manjer J, Borren J et al. A feasible computer-based evaluation tool for reduction mammaplasty patients: indications for operation and monitoring of guidelines. *J Plast Reconstr Aesthet Surg* 2014; 67(7): 927–31. doi: 10.1016/j.bjps.2014.03.028.
18. Gho SA, Steele JR, Munro BJ. Is bra discomfort a barrier to exercise for breast cancer patients? *Support Care Cancer* 2010; 18(6): 735–41. doi: 10.1007/s00520-009-0707-2.
19. Hoffman BL, Schorge JO, Bradshaw KD et al. Benign disorders of the lower genital tract. In: *Williams Gynecology*. 3rd ed. New York: McGraw-Hill Education, 2016.
20. Bond GR, Dowd MD, Landsman I et al. Unintentional perineal injury in prepubescent girls: a multicenter, prospective report of 56 girls. *Pediatrics* 1995; 95(5): 628–31.
21. Hermans TJ, Wijn RP, Winkens B et al. Urogenital and sexual complaints in female club cyclists—a cross-sectional study. *J Sex Med* 2016; 13(1): 40–5. doi: 10.1016/j.jsxm.2015.11.004.
22. Annett S, Cassas K, Bryan S. Gender differences: considerations for the female endurance athlete. In: Miller TL, ed. *Endurance Sports Medicine: A Clinical Guide*. Switzerland: Springer, 2016: 55–70.
23. Bo K, Borgen JS. Prevalence of stress and urge urinary incontinence in elite athletes and controls. *Med Sci Sports Exerc* 2001; 33(11): 1797–802.
24. Kato T, Terashima T, Yamashita T et al. Effect of low-repetition jump training on bone mineral density in young women. *J Appl Physiol (1985)* 2006;100(3):839-43 doi: 10.1152/japplphysiol.00666.2005published Online First: Epub Date]|.
25. Remvig L, Jensen DV, Ward RC. Epidemiology of general joint hypermobility and basis for the proposed criteria for benign joint hypermobility syndrome: review of the literature. *J Rheumatol* 2007; 34(4): 804–9.
26. Grahame R. Hypermobility: an important but often neglected area within rheumatology. *Nat Clin Pract Rheumatol* 2008; 4(10): 522–4. doi: 10.1038/ncprheum0907.

27. Baeza-Velasco C, Gely-Nargeot MC, Pailhez G et al. Joint hypermobility and sport: a review of advantages and disadvantages. *Curr Sports Med Rep* 2013; 12(5): 291–5. doi: 10.1249/JSR.0b013e3182a4b933.
28. McCormack M, Briggs J, Hakim A et al. Joint laxity and the benign joint hypermobility syndrome in student and professional ballet dancers. *J Rheumatol* 2004; 31(1): 173–8.
29. Beighton P, Solomon L, Soskolne CL. Articular mobility in an African population. *Ann Rheum Dis* 1973; 32(5): 413–18.
30. Grahame R, Bird HA, Child A. The revised (Brighton 1998) criteria for the diagnosis of benign joint hypermobility syndrome (BJHS). *J Rheumatol* 2000; 27(7): 1777–9.
31. McKusick V. The Marfan syndrome. In: *Heritable Disorders of Connective Tissue*. 4th ed. St. Louis, MO: CV Mosby, 1972: 61–223.
32. Hakim AJ, Grahame R. A simple questionnaire to detect hypermobility: an adjunct to the assessment of patients with diffuse musculoskeletal pain. *Int J Clin Pract* 2003; 57(3): 163–6.
33. Mato H, Berde T, Hasson N et al. A review of symptoms associated with benign joint hypermobility syndrome in children. *Pediatric Rheumatology* 2008; 6(S1): P155.
34. Soep J. Rheumatic diseases. In: Hay W, Jr., Levin M, Deterding R et al., eds. *Current Diagnosis and Treatment: Pediatrics*. 21st ed. New York: McGraw-Hill, 2012.
35. Simpson MR. Benign joint hypermobility syndrome: evaluation, diagnosis and management. *J Am Osteopath Assoc* 2006; 106(9): 531–6.
36. Pacey V, Tofts L, Wesley A et al. Joint hypermobility syndrome: a review for clinicians. *J Paediatr Child Health* 2015; 51(4): 373–80. doi: 10.1111/jpc.12731.
37. Stone G, Foley CM, Geminiani E. Overuse injuries in young female athletes. In: Stein CJ, Ackerman KE, Stracciolini A, eds. *The Young Female Athlete*. Switzerland: Springer, 2016: 73–86.
38. Keer R, Simmonds J. Joint protection and physical rehabilitation of the adult with hypermobility syndrome. *Curr Opin Rheumatol* 2011; 23(2): 131–6. doi: 10.1097/BOR.0b013e328342d3af.
39. Schubert-Hjalmarsson E, Ohman A, Kyllerman M et al. Pain, balance, activity and participation in children with hypermobility syndrome. *Pediatr Phys Ther* 2012; 24(4): 339–44. doi: 10.1097/PEP.0b013e318268e0ef.
40. DeHaven KE, Lintner DM. Athletic injuries: comparison by age, sport and gender. *Am J Sports Med* 1986; 14(3): 218–24. doi: 10.1177/036354658601400307.
41. Boling M, Padua D, Marshall S et al. Gender differences in the incidence and prevalence of patellofemoral pain syndrome. *Scand J Med Sci Sports* 2010; 20(5): 725–30. doi: 10.1111/j.1600-0838.2009.00996.x.
42. Sinclair J, Taylor PJ. Sex variation in patellar tendon kinetics during running. *Human Movement* 2015; 16(2): 60–3.

43. Sinclair J, Selfe J. Sex differences in knee loading in recreational runners. *J Biomech* 2015; 48(10): 2171–5. doi: 10.1016/j.jbiomech.2015.05.016.
44. Lankhorst NE, van Middelkoop M, van Trier YD et al. Can we predict which patients with patellofemoral pain are more likely to benefit from exercise therapy? A secondary exploratory analysis of a randomised controlled trial. *J Orthop Sports Phys Ther* 2015; 45(3): 183–9. doi: 10.2519/jospt.2015.5583.
45. Keays SL, Mason M, Newcombe PA. Individualised physiotherapy in the treatment of patellofemoral pain. *Physiother Res Int* 2015; 20(1): 22–36. doi: 10.1002/pri.1593.
46. Prodromos CC, Han Y, Rogowski J et al. A meta-analysis of the incidence of anterior cruciate ligament tears as a function of gender, sport and a knee injury-reduction regimen. *Arthroscopy* 2007; 23(12): 1320–5. e6. doi: 10.1016/j.arthro.2007.07.003.
47. Toth AP, Cordasco FA. Anterior cruciate ligament injuries in the female athlete. *J Gend Specif Med* 2001; 4(4): 25–34.
48. Proffen BL, Murray MM. ACL injuries in the female athlete. In: Stein CJ, Ackerman KE, Stracciolini A, eds. *The Young Female Athlete*. Switzerland: Springer, 2016: 121–33.
49. Hewett TE, Zazulak BT, Myer GD. Effects of the menstrual cycle on anterior cruciate ligament injury risk: a systematic review. *Am J Sports Med* 2007; 35(4): 659–68. doi: 10 .1177/0363546506295699.
50. Vescovi JD. The menstrual cycle and anterior cruciate ligament injury risk: implications of menstrual cycle variability. *Sports Med* 2011; 41(2): 91–101. doi: 10.21 65/11538570-000000000-00000.
51. Lee H, Petrofsky JS, Yim J. Do oral contraceptives alter knee ligament damage with heavy exercise? *Tohoku J Exp Med* 2015; 237(1): 51–6. doi: 10.1620/tjem.237.51.
52. Lefevre N, Bohu Y, Klouche S et al. Anterior cruciate ligament tear during the menstrual cycle in female recreational skiers. *Orthop Traumatol Surg Res* 2013; 99(5): 571–5. doi: 10.1016/j.otsr.2013.02.005.
53. Myer GD, Ford KR, Hewett TE. Rationale and clinical techniques for anterior cruciate ligament injury prevention among female athletes. *J Athl Train* 2004; 39(4): 352–64.
54. Ramirez RN, Baldwin K, Franklin CC. Prevention of anterior cruciate ligament rupture in female athletes: a systematic review. *JBJS Rev* 2014; 2(9). doi: 10.2106/JBJS. RVW.M.00129.
55. Noyes FR, Barber-Westin SD. Neuromuscular retraining intervention programs: do they reduce noncontact anterior cruciate ligament injury rates in adolescent female athletes? *Arthroscopy* 2014; 30(2): 245–55. doi: 10.1016/j.arthro.2013.10.009.
56. Sadoghi P, von Keudell A, Vavken P. Effectiveness of anterior cruciate ligament injury prevention training programs. *J Bone Joint Surg Am* 2012; 94(9): 769–76. doi: 10. 2106/JBJS.K.00467.
57. Hootman JM, Dick R, Agel J. Epidemiology of collegiate injuries for 15 sports:

summary and recommendations for injury prevention initiatives. *J Athl Train* 2007; 42(2): 311–19.

58. Renstrom P, Ljungqvist A, Arendt E et al. Non-contact ACL injuries in female athletes: an International Olympic Committee current concepts statement. *Br J Sports Med* 2008; 42(6): 394–412. doi: 10.1136/bjsm.2008.048934.
59. Hewett TE, Stroupe AL, Nance TA et al. Plyometric training in female athletes: decreased impact forces and increased hamstring torques. *Am J Sports Med* 1996; 24(6): 765–73. doi: 10.1177/036354659602400611.
60. Myer GD, Ford KR, Palumbo JP et al. Neuromuscular training improves performance and lower-extremity biomechanics in female athletes. *J Strength Cond Res* 2005; 19(1): 51–60. doi: 10.1519/13643.1.
61. Primack B, Mahaniah K. Anaemia. In: South-Paul J, Matheny S, Lewis E, eds. *Current diagnosis & treatment in family medicine*. McGraw-Hill Professional, 2010.
62. Looker AC, Dallman PR, Carroll MD et al. Prevalence of iron deficiency in the United States. *JAMA* 1997; 277(12): 973–6.
63. Greydanus DE, Omar H, Pratt HD. The adolescent female athlete: current concepts and conundrums. *Pediatr Clin North Am* 2010; 57(3): 697–718. doi: 10.1016/j.pcl.2010.02.005.
64. Di Santolo M, Stel G, Banfi G et al. Anaemia and iron status in young fertile non-professional female athletes. *Eur J Appl Physiol* 2008; 102(6): 703–9. doi: 10.1007/s00421-007-0647-9.
65. McClung JP. Iron status and the female athlete. *J Trace Elem Med Biol* 2012; 26(2–3): 124–6. doi: 10.1016/j.jtemb.2012.03.006.
66. Risser WL, Lee EJ, Poindexter HB et al. Iron deficiency in female athletes: its prevalence and impact on performance. *Med Sci Sports Exerc* 1988; 20(2): 116–21.
67. Walker J, Baran R, Velez N et al. Koilonychia: an update on pathophysiology, differential diagnosis and clinical relevance. *J Eur Acad Dermatol Venereol* 2016; 30(11): 1985–91. doi: 10.1111/jdv.13610.
68. Osaki T, Ueta E, Arisawa K et al. The pathophysiology of glossal pain in patients with iron deficiency and anemia. *Am J Med Sci* 1999; 318(5): 324–9.
69. Shaskey DJ, Green GA. Sports haematology. *Sports Med* 2000; 29(1): 27–38.
70. Malczewska J, Blach W, Stupnicki R. The effects of physical exercise on the concentrations of ferritin and transferrin receptor in plasma of female judoists. *Int J Sports Med* 2000; 21(3): 175–9. doi: 10.1055/s-2000-299.
71. Nikolaidis MG, Michailidis Y, Mougios V. Variation of soluble transferrin receptor and ferritin concentrations in human serum during recovery from exercise. *Eur J Appl Physiol* 2003; 89(5): 500–2. doi: 10.1007/s00421-003-0839-x.
72. Adamson J. Iron deficiency and other hypoproliferative anemias. In: Longo DL, Fauci AS, Kasper DL et al., eds. *Harrison's principles of internal medicine*. 18th ed. New York:

McGraw-Hill Professional, 2012.

73. Hunt A, Harrington D, Robinson S. Vitamin B12 deficiency. *BMJ* 2014; 349: g5226. doi: 10.1136/bmj.g5226.
74. Devalia V, Hamilton MS, Molloy AM et al. Guidelines for the diagnosis and treatment of cobalamin and folate disorders. *Br J Haematol* 2014; 166(4): 496–513. doi: 10.1111/bjh.12959.
75. Eguiguren ML, Ackerman KE. The female athlete triad. In: Stein CJ, Ackerman KE, Stracciolini A, eds. *The Young Female Athlete*. Switzerland: Springer, 2016: 57–71.
76. Grey SH, Emans SJ. Abnormal vaginal bleeding in adolescents. *Pediatr Rev* 2007; 28(5): 175.
77. Mihm M, Gangooly S, Muttukrishna S. The normal menstrual cycle in women. *Anim Reprod Sci* 2011; 124(3–4): 229–36.
78. Sarri G, Davies M, Lumsden MA. Diagnosis and management of menopause: summary of NICE guidance. *BMJ* 2015; 351: h5746.
79. Gold EB. The timing of the age at which natural menopause occurs. *Obstet Gynecol Clin North Am* 2011; 38(3): 425–40. doi: 10.1016/j.ogc.2011.05.002.
80. Knowlton AA, Lee AR. Estrogen and the cardiovascular system. *Pharmacol Ther* 2012; 135(1): 54–70. doi: 10.1016/j.pharmthera.2012.03.007.
81. Barton M. Cholesterol and atherosclerosis: modulation by oestrogen. *Curr Opin Lipidol* 2013; 24(3): 214–20. doi: 10.1097/MOL.0b013e3283613a94.
82. Taraborrelli S. Physiology, production and action of progesterone. *Acta Obstet Gynecol Scand* 2015; 94 Suppl 161: 8–16. doi: 10.1111/aogs.12771.
83. dos Santos RL, da Silva FB, Ribeiro RF, Jr. et al. Sex hormones in the cardiovascular system. *Horm Mol Biol Clin Investig* 2014; 18(2): 89–103. doi: 10.1515/hmbci-2013-0048.
84. Oosthuyse T, Bosch AN. Oestrogen's regulation of fat metabolism during exercise and gender specific effects. *Curr Opin Pharmacol* 2012; 12(3): 363–71. doi: 10.1016/j.coph.2012.02.008.
85. Charkoudian N, Joyner MJ. Physiologic considerations for exercise performance in women. *Clin Chest Med* 2004; 25(2): 247–55. doi: 10.1016/j.ccm.2004.01.001.
86. Bruinvels G, Burden R, Brown N et al. The prevalence and impact of heavy menstrual bleeding (menorrhagia) in elite and non-elite athletes. *PLoS ONE* 2016; 11(2): e0149881. doi: 10.1371/journal.pone.0149881.
87. Sambanis M, Kofotolis N, Kalogeropoulou E et al. A study of the effects on the ovarian cycle of athletic training in different sports. *J Sports Med Phys Fitness* 2003; 43(3): 398–403.
88. Kasper D, Fauci A, Hauser S et al., eds. *Harrison's principles of internal medicine*. 19th ed. New York: McGraw-Hill Education, 2015.
89. Takemoto DM, Beharry MS. What's normal? accurately and efficiently assessing menstrual function. *Pediatr Ann* 2015; 44(9): e213–17. doi: 10.3928/00904481-2015091

0-08.

90. Munro MG, Critchley HO, Broder MS et al. FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding in nongravid women of reproductive age. *Int J Gynaecol Obstet* 2011; 113(1): 3–13. doi: 10.1016/j.ijgo.2010.11.011.
91. Constantini NW, Dubnov G, Lebrun CM. The menstrual cycle and sport performance. *Clin Sports Med* 2005; 24(2): e51–82, xiii–xiv.
92. Daniels K, Mosher WD. Contraceptive methods women have ever used: United States, 1982–2010. *Natl Health Stat Report* 2013 (62): 1–15.
93. Rivera R, Yacobson I, Grimes D. The mechanism of action of hormonal contraceptives and intrauterine contraceptive devices. *Am J Obstet Gynecol* 1999; 181(5 Pt 1): 1263–9.
94. Rechichi C, Dawson B, Goodman C. Athletic performance and the oral contraceptive. *Int J Sports Physiol Perform* 2009; 4(2): 151–62.
95. Vaiksaar S, Jurimae J, Maestu J et al. No effect of menstrual cycle phase and oral contraceptive use on endurance performance in rowers. *J Strength Cond Res* 2011; 25(6): 1571–8. doi: 10.1519/JSC.0b013e3181df7fd2.
96. Redman LM, Weatherby RP. Measuring performance during the menstrual cycle: a model using oral contraceptives. *Med Sci Sports Exerc* 2004; 36(1): 130–6. doi: 10.1249/01.MSS.0000106181.52102.99.
97. Nichols AW, Hetzler RK, Villanueva RJ et al. Effects of combination oral contraceptives on strength development in women athletes. *J Strength Cond Res* 2008; 22(5): 1625–32. doi: 10.1519/JSC.0b013e31817ae1f3.
98. Schaumberg MA, Emmerton LM, Jenkins DG et al. Use of oral contraceptives to manipulate menstruation in young, physically active women. *Int J Sports Physiol Perform* 2018; 13(1): 82–7. doi: 10.1123/ijspp.2016-0689.
99. Sillem M, Schneidereit R, Heithecker R et al. Use of an oral contraceptive containing drospirenone in an extended regimen. *Eur J Contracept Reprod Health Care* 2003; 8(3): 162–9.
100. Rogers SM, Baker MA. Thermoregulation during exercise in women who are taking oral contraceptives. *Eur J Appl Physiol Occup Physiol* 1997; 75(1): 34–8.
101. Martin JG, Buono MJ. Oral contraceptives elevate core temperature and heart rate during exercise in the heat. *Clin Physiol* 1997; 17(4): 401–8.
102. Hidalgo M, Bahamondes L, Perrotti M et al. Bleeding patterns and clinical performance of the levonorgestrel-releasing intrauterine system (Mirena) up to two years. *Contraception* 2002; 65(2): 129–32.
103. Diedrich JT, Desai S, Zhao Q et al. Association of short-term bleeding and cramping patterns with long-acting reversible contraceptive method satisfaction. *Am J Obstet Gynecol* 2015; 212(1): 50. e1–8. doi: 10.1016/j.ajog.2014.07.025.
104. Martin D, Sale C, Cooper SB et al. Period prevalence and perceived side effects of

hormonal contraceptive use and the menstrual cycle in elite athletes. *Int J Sports Physiol Perform* published online 27 July 2018. doi: 10.1123/ijspp.2017-0330.

105. US Food and Drug Administration (FDA). Depo-Provera (medroxyprogesterone acetate) prescribing information, 2010.
106. Nieves JW, Ruffing JA, Zion M et al. Eating disorders, menstrual dysfunction, weight change and DMPA use predict bone density change in college-aged women. *Bone* 2016; 84: 113–19. doi: 10.1016/j.bone.2015.12.054.
107. Yeager KK, Agostini R, Nattiv A et al. The female athlete triad: disordered eating, amenorrhea, osteoporosis. *Med Sci Sports Exerc* 1993; 25(7): 775–7.
108. Nattiv A, Loucks AB, Manore MM et al. American College of Sports Medicine position stand: the female athlete triad. *Med Sci Sports Exerc* 2007; 39(10): 1867–82. do i: 10.1249/mss.0b013e318149f111.
109. Loucks AB. Low energy availability in the marathon and other endurance sports. *Sports Med* 2007; 37(4–5): 348–52.
110. Ackerman KE, de Lourdes Eguiguren M, Barrack M. Risk biotypes and the female athlete triad. In: Vaamonde D, du Plessis SS, Agarwal A, eds. *Exercise and Human Reproduction: Induced Fertility Disorders and Possible Therapies*. New York: Springer, 2016: 209–28.
111. Gibbs J, Williams NI, De Souza MJ. Prevalence of individual and combined components of the female athlete triad. *Med Sci Sports Exerc* 2013; 45(5): 985–96.
112. Lunde C, Gattario KH. Performance or appearance? Young female sport participants' body negotiations. *Body Image* 2017; 21: 81–9. doi: 10.1016/j.bodyim.2017.03.001.
113. Koidou E, Papadopoulou S, Thoma F et al. Body dissatisfaction and body image of female athletes with normal body weight. *Clin Nutr ESPEN* 2016; 13: e63. doi: 10.1016/j.clnesp.2016.03.036.
114. Ackerman KE, Holtzman B, Cooper KM et al. Low energy availability surrogates correlate with health and performance consequences of relative energy deficiency in sport. *Br J Sports Med* published online 2 June 2018. doi: 10.1136/bjsports-2017-098958.
115. Gordon CM, Ackerman KE, Berga SL et al. Functional Hypothalamic Amenorrhea: an Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab* 2017; 102(5): 1413–39. doi: 10.1210/jc.2017-00131.
116. Jasienska G. Energy metabolism and the evolution of reproductive suppression in the human female. *Acta Biotheor* 2003; 51(1): 1–18.
117. Misra M. Neuroendocrine mechanisms in athletes. *Handb Clin Neurol* 2014; 124: 373–86. doi: 10.1016/B978-0-444-59602-4.00025-3.
118. Scheid JL, De Souza MJ. Menstrual irregularities and energy deficiency in physically active women: the role of ghrelin, PYY and adipocytokines. *Med Sport Sci* 2010; 55: 82–102. doi: 10.1159/000321974.

119. O'Donnell E, De Souza MJ. Increased serum adiponectin concentrations in amenorrheic physically active women are associated with impaired bone health but not with estrogen exposure. *Bone* 2011; 48(4): 760–7. doi: 10.1016/j.bone.2010.12.018.
120. Russell M, Stark J, Nayak S et al. Peptide YY in adolescent athletes with amenorrhea, eumenorrheic athletes and non-athletic controls. *Bone* 2009; 45(1): 104–9. doi: 10.1016/j.bone.2009.03.668.
121. Laughlin GA, Yen SS. Nutritional and endocrine-metabolic aberrations in amenorrheic athletes. *J Clin Endocrinol Metab* 1996; 81(12): 4301–9.
122. Rickenlund A, Thoren M, Carlstrom K et al. Diurnal profiles of testosterone and pituitary hormones suggest different mechanisms for menstrual disturbances in endurance athletes. *J Clin Endocrinol Metab* 2004; 89(2): 702–7. doi: 10.1210/jc.2003-030306.
123. Schaal K, Van Loan MD, Casazza GA. Reduced catecholamine response to exercise in amenorrheic athletes. *Med Sci Sports Exerc* 2011; 43(1): 34–43. doi: 10.1249/MSS.0b013e3181e91ece.
124. Schorr M, Lawson EA, Dichtel LE et al. Cortisol measures across the weight spectrum. *J Clin Endocrinol Metab* 2015; 100(9): 3313–21. doi: 10.1210/JC.2015-2078.
125. Martin B, Golden E, Carlson OD et al. Caloric restriction: impact upon pituitary function and reproduction. *Ageing Res Rev* 2008; 7(3): 209–24. doi: 10.1016/j.arr.2008.01.002.
126. Elliott-Sale KJ, Tenforde AS, Parziale AL et al. Endocrine effects of relative energy deficiency in sport. *Int J Sport Nutr Exerc Metab* 2018; 28(4): 335–49. doi: 10.1123/ijsnem.2018-0127.
127. Loucks AB, Thuma JR. Luteinizing hormone pulsatility is disrupted at a threshold of energy availability in regularly menstruating women. *J Clin Endocrinol Metab* 2003; 88(1): 297–311. doi: 10.1210/jc.2002-020369.
128. Lieberman JL, De Souza MJ, Wagstaff DA et al. Menstrual disruption with exercise is not linked to an energy availability threshold. *Med Sci Sports Exerc* 2018; 50(3): 551–61. doi: 10.1249/MSS.0000000000001451.
129. Williams NI, Leidy HJ, Hill BR et al. Magnitude of daily energy deficit predicts frequency but not severity of menstrual disturbances associated with exercise and caloric restriction. *Am J Physiol Endocrinol Metab* 2015; 308(1): E29–39. doi: 10.1152/ajpendo.00386.2013.
130. De Souza MJ, Nattiv A, Joy E et al. 2014 Female Athlete Triad Coalition Consensus Statement on Treatment and Return to Play of the Female Athlete Triad: 1st International Conference held in San Francisco, California, May 2012 and 2nd International Conference held in Indianapolis, Indiana, May 2013. *Br J Sports Med* 2014; 48(4): 289. doi: 10.1136/bjsports-2013-093218.
131. International Society for Clinical Densitometry. 2013 ISCD Combined Official

Positions. 2014.

132. Devlin MJ, Stetter CM, Lin HM et al. Peripubertal estrogen levels and physical activity affect femur geometry in young adult women. *Osteoporos Int* 2010; 21(4): 609–17. doi: 10.1007/s00198-009-0999-6.
133. Bachrach LK. Acquisition of optimal bone mass in childhood and adolescence. *Trends Endocrinol Metab* 2001; 12(1): 22–8.
134. Ackerman KE, Misra M. Neuroendocrine abnormalities in female athletes. In: Gordon CM, LeBoff M, eds. *The Female Athlete Triad—A Clinical Guide*. New York: Springer US, 2015: 85–109.
135. Ackerman KE, Misra M. Bone health and the female athlete triad in adolescent athletes. *Phys Sportsmed* 2011; 39(1): 131–41. doi: 10.3810/psm.2011.02.1871.
136. Ackerman KE, Cano Sokoloff N, de Nardo Maffazioli G et al. Fractures in relation to menstrual status and bone parameters in young athletes. *Med Sci Sports Exerc* 2015; 47(8): 1577–86. doi: 10.1249/MSS.0000000000000574.
137. Mountjoy M, Sundgot-Borgen J, Burke L et al. The IOC consensus statement: beyond the Female Athlete Triad— Relative Energy Deficiency in Sport (RED-S). *Br J Sports Med* 2014; 48(7): 491–7. doi: 10.1136/bjsports-2014-093502.
138. Constantini NW. Medical concerns of the dancer. Book of Abstracts. XXVII FIMS World Congress of Sports Medicine. Budapest, Hungary, 2002: 151.
139. De Souza MJ, Lee DK, VanHeest JL et al. Severity of energy-related menstrual disturbances increases in proportion to indices of energy conservation in exercising women. *Fertil Steril* 2007; 88(4): 971–5. doi: 10.1016/j.fertnstert.2006.11.171.
140. Koehler K, De Souza MJ, Williams NI. Less-than-expected weight loss in normal-weight women undergoing caloric restriction and exercise is accompanied by preservation of fat-free mass and metabolic adaptations. *Eur J Clin Nutr* 2017; 71(3): 365–71. doi: 10.1038/ejcn.2016.203.
141. Melin A, Tornberg AB, Skouby S et al. Energy availability and the female athlete triad in elite endurance athletes. *Scand J Med Sci Sports* 2015; 25(5): 610–22. doi: 10.1111/sms.12261.
142. Myerson M, Gutin B, Warren MP et al. Resting metabolic rate and energy balance in amenorrheic and eumenorrheic runners. *Med Sci Sports Exerc* 1991; 23(1): 15–22.
143. Rowland T. Iron deficiency in athletes: an update. *Am J Lifestyle Med* 2012; 6(4): 319–27.
144. Petkus DL, Murray-Kolb LE, De Souza MJ. The unexplored crossroads of the female athlete triad and iron deficiency: a narrative review. *Sports Med* published online 13 March 2017. doi: 10.1007/s40279-017-0706-2.
145. Modan-Moses D, Yaroslavsky A, Kochavi B et al. Linear growth and final height characteristics in adolescent females with anorexia nervosa. *PLoS ONE* 2012; 7(9): e45504. doi: 10.1371/journal.pone.0045504.

146. American Psychiatric Association (APA). *Diagnostic and statistical manual of mental disorders (DSM-5®)*. 5th ed. Arlington, VA: APA, 2013.
147. American Academy of Pediatrics. Committee on Sports Medicine and Fitness. Medical concerns in the female athlete. *Pediatrics* 2000; 106(3): 610–3.
148. Rickenlund A, Eriksson MJ, Schenck-Gustafsson K et al. Amenorrhea in female athletes is associated with endothelial dysfunction and unfavourable lipid profile. *J Clin Endocrinol Metab* 2005; 90(3): 1354–9. doi: 10.1210/jc.2004-1286.
149. Friday KE, Drinkwater BL, Bruemmer B et al. Elevated plasma low-density lipoprotein and high-density lipoprotein cholesterol levels in amenorrheic athletes: effects of endogenous hormone status and nutrient intake. *J Clin Endocrinol Metab* 1993; 77(6): 1605–9. doi: 10.1210/jcem.77.6.8263148.
150. O'Donnell E, Goodman JM, Harvey PJ. Clinical review: Cardiovascular consequences of ovarian disruption: a focus on functional hypothalamic amenorrhea in physically active women. *J Clin Endocrinol Metab* 2011; 96(12): 3638–48. doi: 10.1210/jc.2011-1223.
151. Sachs KV, Harnke B, Mehler PS et al. Cardiovascular complications of anorexia nervosa: a systematic review. *Int J Eat Disord* 2016; 49(3): 238–48. doi: 10.1002/eat.22481.
152. Norris ML, Harrison ME, Isserlin L et al. Gastrointestinal complications associated with anorexia nervosa: a systematic review. *Int J Eat Disord* 2016; 49(3): 216–37. doi: 10.1002/eat.22462.
153. Nieman DC, Pedersen BK. Exercise and immune function: recent developments. *Sports Med* 1999; 27(2): 73–80.
154. Drew M, Vlahovich N, Hughes D et al. Prevalence of illness, poor mental health and sleep quality and low energy availability prior to the 2016 Summer Olympic Games. *Br J Sports Med* 2018; 52(1): 47–53. doi: 10.1136/bjsports-2017-098208.
155. Drew MK, Vlahovich N, Hughes D et al. A multifactorial evaluation of illness risk factors in athletes preparing for the Summer Olympic Games. *J Sci Med Sport* 2017; 20(8): 745–50. doi: 10.1016/j.jsams.2017.02.010.
156. Vanheest JL, Rodgers CD, Mahoney CE et al. Ovarian suppression impairs sport performance in junior elite female swimmers. *Med Sci Sports Exerc* 2014; 46(1): 156–66. doi: 10.1249/MSS.0b013e3182a32b72.
157. Tornberg AB, Melin A, Koivula FM et al. Reduced neuromuscular performance in amenorrheic elite endurance athletes. *Med Sci Sports Exerc* 2017; 49(12): 2478–85. doi: 10.1249/MSS.0000000000001383.
158. Mountjoy M, Sundgot-Borgen J, Burke L et al. RED-S CAT. Relative energy deficiency in sport (RED-S) clinical assessment tool (CAT). *Br J Sports Med* 2015; 49(7): 421–3. doi: 10.1136/bjsports-2015-094873.
159. San-Frutos L, Engels V, Zapardiel I et al. Hemodynamic changes during pregnancy

and postpartum: a prospective study using thoracic electrical bioimpedance. *J Matern Fetal Neonatal Med* 2011; 24(11): 1333–40. doi: 10.3109/14767058.2011.556203.

160. Hill CC, Pickinpaugh J. Physiologic changes in pregnancy. *Surg Clin North Am* 2008; 88(2): 391–401, vii. doi: 10.1016/j.suc.2007.12.005.
161. Elkus R, Popovich J, Jr. Respiratory physiology in pregnancy. *Clin Chest Med* 1992; 13(4): 555–65.
162. Knuttgen HG, Emerson K, Jr. Physiological response to pregnancy at rest and during exercise. *J Appl Physiol* 1974; 36(5): 549–53.
163. Tan EK, Tan EL. Alterations in physiology and anatomy during pregnancy. *Best Pract Res Clin Obstet Gynaecol* 2013; 27(6): 791–802. doi: 10.1016/j.bpobgyn.2013.08.001.
164. Artal R, O'Toole M. Guidelines of the American College of Obstetricians and Gynecologists for exercise during pregnancy and the postpartum period. *Br J Sports Med* 2003; 37(1): 6–12; discussion 12.
165. Pires R, Labronici PJ, Giordano V et al. Intrapartum pubic symphysis disruption. *Ann Med Health Sci Res* 2015; 5(6): 476–9. doi: 10.4103/2141-9248.177980.
166. Heckman JD, Sassard R. Musculoskeletal considerations in pregnancy. *J Bone Joint Surg Am* 1994; 76(11): 1720–30.
167. Borg-Stein JP, Fogelman DJ, Ackerman KE. Exercise, sports participation, and musculoskeletal disorders of pregnancy and postpartum. *Semin Neurol* 2011; 31(4): 413–22. doi: 10.1055/s-0031-1293541.
168. Hammar M, Larsson L, Tegler L. Calcium treatment of leg cramps in pregnancy. Effect on clinical symptoms and total serum and ionised serum calcium concentrations. *Acta Obstet Gynecol Scand* 1981; 60(4): 345–7.
169. Bo K, Artal R, Barakat R et al. Exercise and pregnancy in recreational and elite athletes: 2016 evidence summary from the IOC expert group meeting, Lausanne. Part 1—exercise in women planning pregnancy and those who are pregnant. *Br J Sports Med* 2016; 50(10): 571–89. doi: 10.1136/bjsports-2016-096218.
170. Patel P, Wheatcroft R, Park RJ et al. The children of mothers with eating disorders. *Clin Child Fam Psychol Rev* 2002; 5(1): 1–19.
171. Hinman SK, Smith KB, Quillen DM et al. Exercise in pregnancy: a clinical review. *Sports Health* 2015; 7(6): 527–31. doi: 10.1177/1941738115599358.
172. Dempsey JC, Butler CL, Williams MA. No need for a pregnant pause: physical activity may reduce the occurrence of gestational diabetes mellitus and preeclampsia. *Exerc Sport Sci Rev* 2005; 33(3): 141–9.
173. Barakat R, Pelaez M, Lopez C et al. Exercise during pregnancy reduces the rate of caesarean and instrumental deliveries: results of a randomised controlled trial. *J Matern Fetal Neonatal Med* 2012; 25(11): 2372–6. doi: 10.3109/14767058.2012.696165.
174. Sternfeld B, Quesenberry CP, Jr., Eskenazi B et al. Exercise during pregnancy and pregnancy outcome. *Med Sci Sports Exerc* 1995; 27(5): 634–40.

175. Committee on Obstetric Practice. ACOG committee opinion. Exercise during pregnancy and the postpartum period. Number 267, January 2002. American College of Obstetricians and Gynecologists. *Int J Gynaecol Obstet* 2002; 77(1): 79–81.
176. Artal R. Exercise in pregnancy: guidelines. *Clin Obstet Gynecol* 2016; 59(3): 639–44. doi: 10.1097/GRF.0000000000000223.
177. Garber CE, Blissmer B, Deschenes MR et al. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. *Med Sci Sports Exerc* 2011; 43(7): 1334–59. doi: 10.1249/MSS.0b013e318213fefb.
178. Moore K, Dumoulin C, Bradley C et al. Adult conservative management. *Incontinence* 2013; 1101: 228.
179. Soultanakis HN, Artal R, Wiswell RA. Prolonged exercise in pregnancy: glucose homeostasis, ventilatory and cardiovascular responses. *Semin Perinatol* 1996; 20(4): 315–27.

Chapter 30

Transgender and intersex

with LIESEL GEERTSEMA, SIOBHAN STATUTA and SILVIA CAMPORESI

I know how I look like. I know how I sound. I know how I walk. I'm just gonna be me. I do me, and you do you.
Caster Semenya

The growing number of transgender and intersex athletes wanting to compete at amateur and elite levels raises complex biological, sociological and ethical issues to which there are no simple answers. Sex testing in women's sport has been controversial since its introduction in the 1930s. Much of the controversy is fuelled by rumours, misconceptions about motives, a poor understanding of the relevant science and preconceived ideas about fair play. In this chapter we share data, where they exist, and explore unresolved issues that are the subject of current debate. In complementing the previous chapter on women's health issues in sport, this chapter helps clinicians understand sex and gender more broadly, in the specific settings of transgender and intersex persons in sport. We will discuss:

- biology of normal sexual development
- the genetic basis for sex
- current definitions of transgender and intersex
- sex testing in sport and its clinical implications.

BIOLOGY OF NORMAL SEXUAL DEVELOPMENT

To understand sex testing and its effects, it is important to revisit the basics of normal sexual development. When an ovum and a sperm combine to form a zygote, the resulting sexual karyotype is usually XX or XY (the genotype or chromosomal sex). The Y chromosome contains the SRY (sex region of the Y) gene, which ultimately determines a baby's sex.

The default pathway in human development is for the zygote to develop ovaries, which produce oestrogen and progesterone, eventually leading to a female foetus with female genitalia (Fig 30.1).

However, in the presence of the SRY gene, testes develop. If the testes contain functional Leydig cells, the testes produce testosterone, which targets the cells of the external genitalia. The targeted cells only respond if they have functioning androgen receptors, as well as functional 5-alpha-reductase, to convert some of the testosterone into more-active dihydrotestosterone.

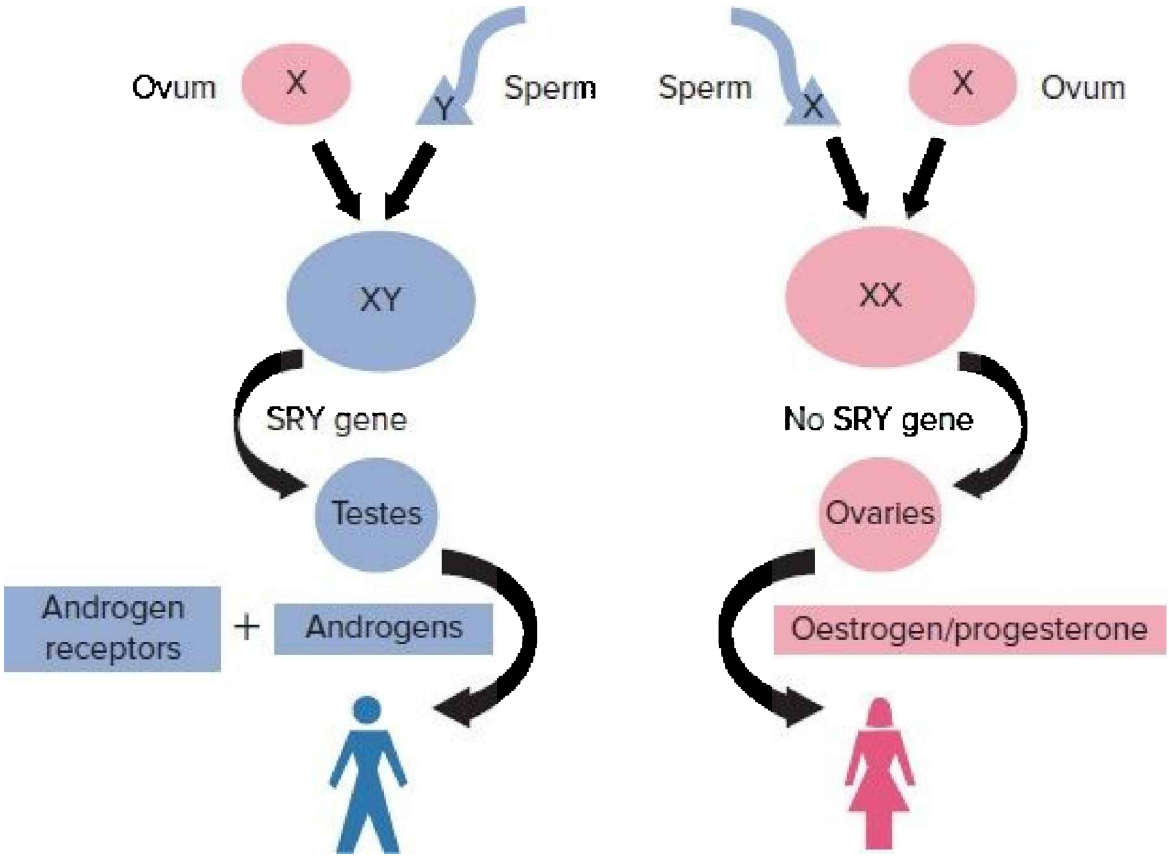


Figure 30.1 Normal pathways of male and female sexual development

If all of the above conditions are met, normal primary male sexual development occurs before birth (masculinisation) and around puberty (virilisation), resulting in a male phenotype or somatic sex. If anything goes awry with one of these steps, the baby (foetus) can revert back to the female pathway, resulting in a female phenotype. This explanation is somewhat simplistic, as none of the sex hormones are found exclusively in one sex (i.e. testosterone is not solely a male hormone). However, it represents the relative levels of these hormones and provides a foundation for a basic understanding.

BASIC CONCEPTS OF GENETICS AND SEX

In this section we discuss the basic concepts of genetics and sex, and how they influence one's

identity.

Sex versus gender

Sex refers to the 'biological and physiological characteristics that define men and women'.[1] While some biological characteristics are not mutually exclusive, as there are individuals who possess both sets, they tend to differentiate humans as males or females.

Gender refers to the 'socially constructed roles, behaviours, activities, and attributes that a given society considers appropriate for men and women'.[1] It is how individuals identify Page 422 themselves. For most individuals this would be male or female; however, additional gender types are increasingly being recognised. Some social media platforms now offer users the choice of more than 50 gender identities,[2] and an increasing number of countries are legally recognising a third (other) gender.[3, 4]

Sex characteristics (e.g. women menstruating) do not vary substantially between societies, while gender characteristics (e.g. who does most of the housework) may. While sex can be tested, gender cannot.

Chromosomal variants

Euploid human cells have 46 chromosomes, expressed as 46,XX or 46,XY. A cell can have an abnormal number of chromosomes (e.g. 45 or 47) due to deviations during cell division. When this involves the sex chromosomes at the fertilisation stage (during meiosis), it results in a number of possible abnormalities, which are reflected in all cells of the organism (e.g. 45,X, 47,XXX, 47,XXY, 47,XYY). When it involves cell division during the early stages of embryonic development (during mitosis), it results in a mosaic pattern-meaning that some cells have an aneuploid number while others display the normal complement of chromosomes. Examples include 45,X/46,XY and 46,XY/47,XXY mosaicism. The clinical manifestations of these chromosomal conditions are highly variable; some people have male genitalia, some have female and some indeterminate.

Gene variants

Gene translocations occur when two chromosomes exchange genetic material. Depending on the amount and type of the material exchanged, there may be an entire spectrum of outcomes, ranging from no clinical manifestations whatsoever, to the more diverse and extreme outcomes such as Down syndrome, various cancers and autism. When gene translocations involve the SRY gene, this can lead to the development of a phenotype (physical appearance) that is different from what would be expected with the associated genotype (chromosomes)–for example, the XX man or XY woman (Figs 30.2 and 30.3).

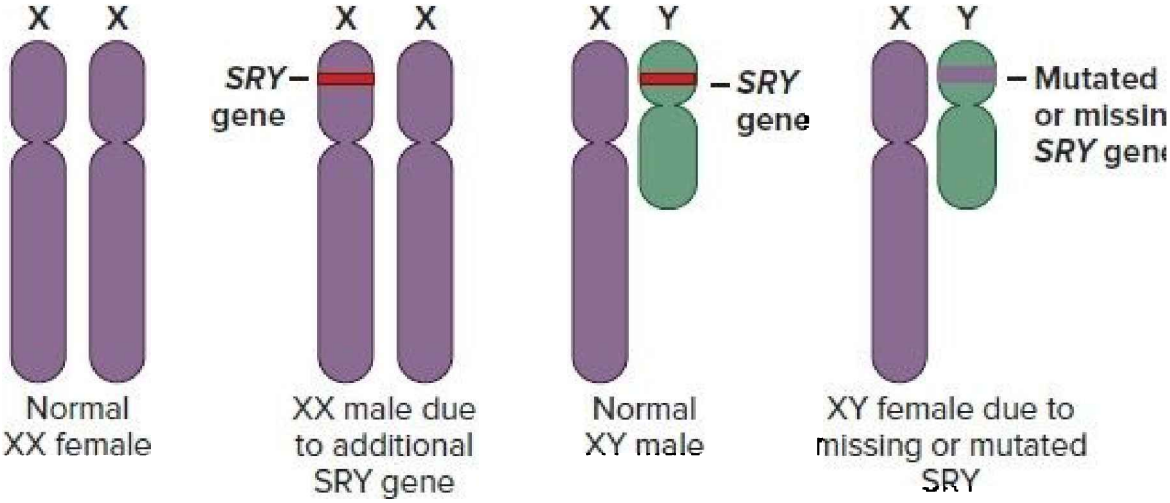


Figure 30.2 Examples of SRY gene abnormalities resulting in the XX man or XY woman

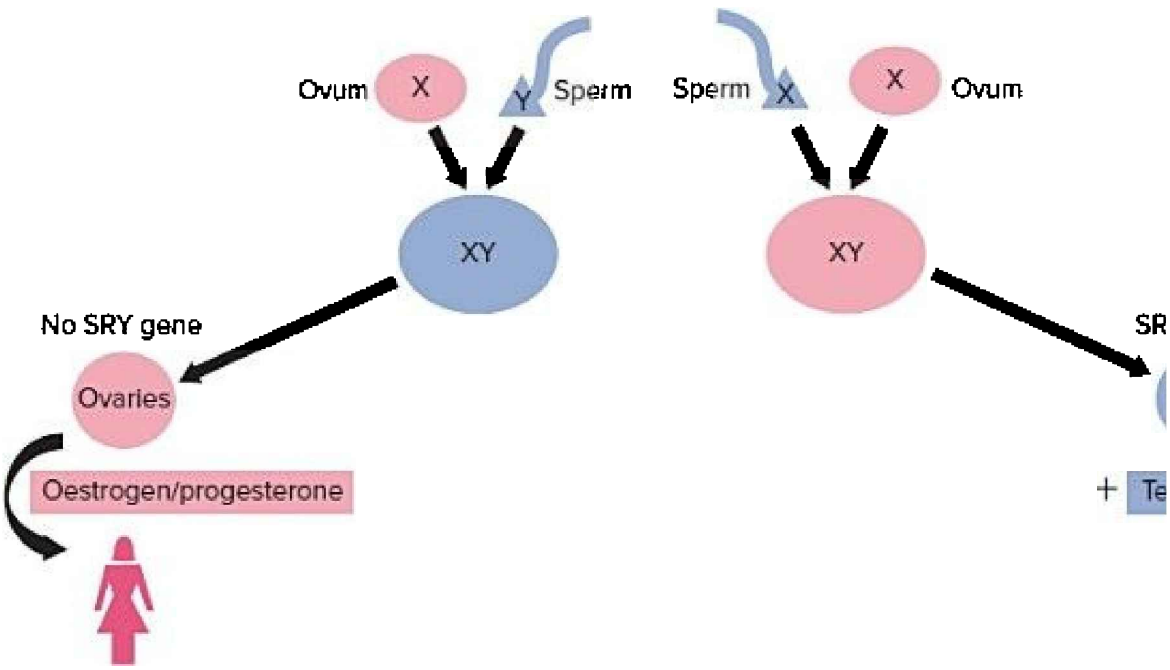


Figure 30.3 The presence or absence of the SRY gene can lead to the development of a phenotype that is different from what would be expected with the associated genotype

Androgens and their receptors

Hyperandrogenism strictly refers to high levels of androgen in men and women. However, in practice it is used almost exclusively in reference to women. There are many possible causes for hyperandrogenism, including polycystic ovary syndrome (PCOS), congenital adrenal hyperplasia,

tumours, pregnancy and androgen receptor abnormalities.

Androgen receptors may be partially insensitive to androgens (partial androgen insensitivity syndrome, PAIS) or completely insensitive (complete androgen insensitivity syndrome, CAIS). Depending on the underlying cause and the degree of receptor sensitivity, people with hyperandrogenism can have male or female genotypes and a variety of phenotypes. For example, it is possible to have an XY genotype, but have a normal female phenotype due to CAIS (Fig. 30.4). In this case, the individual would be unaware of their XY status as they would have been born as a 'girl' and developed as a woman, despite rudimentary (often internal) testes. Unless such an individual were to undergo a chromosome test and testosterone blood test, or investigate infertility or discover internal testes through imaging, they would never know that their genotype was XY.

Page 423

Page 424

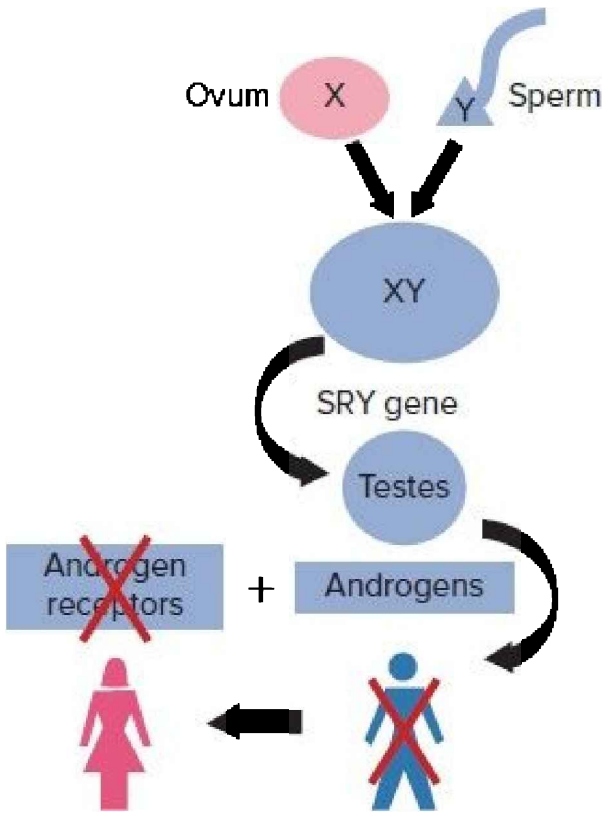


Figure 30.4 Male genotype with female phenotype due to complete androgen insensitivity syndrome (CAIS)

There are other abnormalities which can have similar effects, such as 5-alpha-reductase deficiency in an XY male genotype. Individuals with this condition are often born with testes, but can have normal male, ambiguous or normal female external genitalia. Many have a female appearance and are therefore raised as girls.

Defining intersex

'Intersex' is not a medical term. The Intersex Society of North America uses it to describe people who are born with reproductive or sexual anatomy that does not fit the classical definition of male or female.[5] However, the definitions of male and female are not clear across cultures. Traditional definitions of these terms are based on sexual anatomy, which is diverse, with no clear parameters of what constitutes 'normal' anatomical size or shape. The term intersex, as used in this context' also includes people who have a male genotype and a normal female phenotype, and vice versa. In other words, it also includes those people who are unaware of any ambiguity regarding their sex.

Sex is a spectrum

A broad spectrum of conditions lies between the two extremes of male and female, and can be classified as sex chromosome, gonadal and/or sex hormone deviations.[6] About 1.7% of people are affected by these conditions,[7] although incidence is unclear for several reasons:

- definitions are not clear
- there is a stigma attached to them in some cultures
- unless there is a medical concern that would trigger further investigation, individuals do not specifically look for these conditions.

Traditionally, the term 'disorders of sexual development' (DSD) has been used by clinicians to describe congenital conditions that result in an atypical sexual genotype or phenotype. However, this term is controversial, as not all of these forms lead to 'medical conditions', and DSD is alternatively being referred to as 'differences of sexual development' (DSD) (Fig. 30.5). Among individuals affected by various DSD diagnoses, survey data suggests the majority prefer the latter and appreciate flexible terminology.[8]

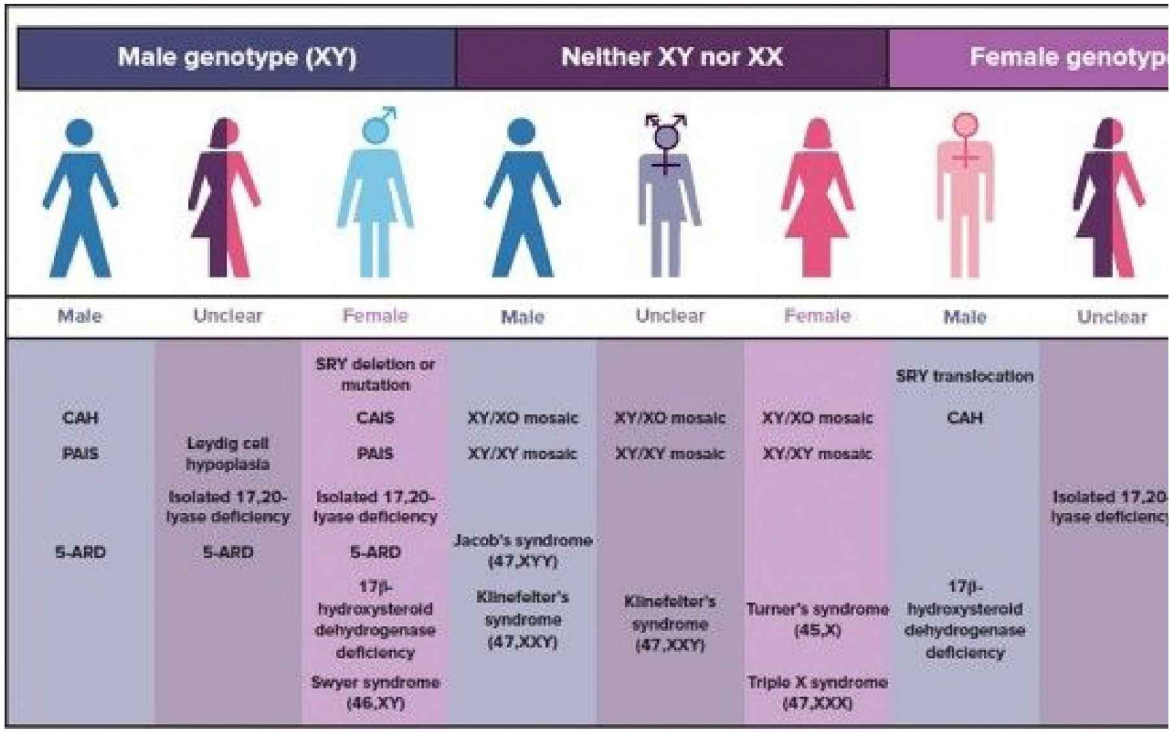


Figure 30.5 Differences of sexual development across the sex spectrum

Defining transgender

Transgender is often used to describe someone whose gender identity differs from their assigned sex at birth. Used very broadly, it can also include people whose gender identity is neither male nor female (terms include non-binary, pangender, bigender, genderfluid, agender). Intersex people may be transgender or not. For example, someone with a male genotype and female phenotype due to CAIS may identify as female having been assigned as 'female' at birth. This person would be intersex, but not transgender. However, this same individual may alternatively identify as male or non-binary and would, in that case, be transgender.

Page 425

PRACTICE PEARL

It is important to distinguish transgender from sexual orientation (e.g. bisexual, homosexual and lesbian). Transgender is about identity while sexual orientation is about attraction to others.

SEX TESTING IN SPORT

Sex testing in sport refers to the process of verifying the sex of athletes to determine their eligibility to compete in events that are limited to a single sex. Initially, sex testing in sport took the form of visual inspections, which was later followed by DNA analysis and testosterone testing.

Visual inspection

The first publicised sex test was during the 1936 Berlin Olympics, when Helen Stephens (the 100 m gold medallist) was required to undergo a sex test. Testing was not mandatory but could be done on demand and involved a physical genital inspection. Stephens passed the test.[9]

Ten years later, the International Association of Athletics Federations (IAAF) introduced a new regulation, which stated that women had to obtain a physician's letter verifying their sex in order to be eligible to compete in international women's events. The International Olympic Committee (IOC) introduced the same requirement at the 1948 London Olympics.[9] By 1966, sports authorities introduced a new type of visual inspection that was performed by a panel of doctors prior to major competitions.[10] These 'peek and poke parades' or 'nude parades' led to protests, and Page 426 visual inspections were consequently stopped in 1968. Dame Mary Peters, the 1972 Olympic pentathlon champion, described the nude parade as 'the most crude and degrading experience I have ever known in my life'.[11]

CASE STUDY

Foekje Dillema, The Netherlands, sprinter—banned from competition due to the results of a sex test

Foekje Dillema (1926–2007) (Fig. 30.6) was a relatively unknown Dutch sprinter who won both the 100 metres and 200 metres at a tournament in London in 1949. In the process, she set a new Dutch record.

Figure 30.6 Holland's Foekje Dillema finishes ahead of Great Britain's Sylvia Cheeseman in the WAAA International Match Women's 200 m at White City Stadium, August 1949. Foekje Dillema's national record of 24.1 seconds for the 200 m was erased after being banned from competition for life by the IAAF in 1950 BARRATTS/PA IMAGES VIA GETTY IMAGES

In 1950, Dillema was banned from competing for life by the Royal Dutch Athletics Federation due to the results of a sex test—for which results were never released and no records are currently available.[1,2]

Foekje returned to a small village in Friesland, battled depression and did not leave her house for a year, refusing to speak publicly about the situation.

Although Foekje had been designated female at birth, brought up as a girl and lived as a woman, a post-mortem chromosome test suggested that she may have had 46,XX/46,XY mosaicism. It remains unclear whether this would have provided any athletic advantage.

Chromosome testing

In 1967, the IAAF introduced the first chromosome test: the Barr body test.[9] This assessment involved taking a buccal smear, a relatively non-invasive method of collecting DNA samples for testing. A Barr body is present in a cell when there is an inactivated X chromosome. An X chromosome is inactivated in the presence of an active X chromosome. Therefore, Barr bodies are found in cells with XX but not XY karyotype. A positive test was supposed to confirm that an athlete was female and clear her for competition. However, the test would also have been positive in people with 47,XXY karyotype, and negative in those with 45,X karyotype.

By the time the Barr body test was introduced for sex testing in sport, it was already being

questioned by the medical community. Dr Murray Barr, who discovered the Barr body, pointed out that the test should not be used in isolation, and by 1987 he wrote to the Canadian Olympic Committee asking for the test to be abandoned as it had become an embarrassment to him.

DNA testing

In 1992, the Barr body test was abandoned and replaced by the polymerase chain reaction (PCR) test,[9] a test that amplifies sections of DNA and allows for identification of the SRY gene. A positive test in a female athlete excluded her from competition. However, gene translocations and mutations, as discussed above, complicate this test. The test would, for example, exclude individuals with a female genotype and a SRY gene translocation, while including those with a male genotype and a missing or mutated SRY gene.

Doctors and medical associations became increasingly opposed to genetic testing, arguing that there is no clear legal definition of sex, which is multidimensional and therefore cannot be easily determined through a single test.

CASE STUDY

Santhi Soundarajan, India, middle distance runner—banned from competition due to the results of a sex test

Santhi Soundarajan (Fig. 30.7) is an Indian middle-distance runner who has won 12 international medals, and was the first Tamil woman to win a medal at the Asian Games. Shortly after the 2006 Asian Games in Doha, she was mandated to undergo sex testing. Santhi recalled that she did not know the purpose of the test, or the outcome, because the doctors could not speak her native language. A few days later when watching the evening news, she learned that she had failed a sex test. Santhi was diagnosed with androgen insensitivity syndrome and was consequently stripped of her medal and barred from all competitions.

Figure 30.7 Santhi Soundarajan won the silver medal in the 800 metres at the 2006 Doha games, but was stripped of the medal after failing a sex test PHOTO BY IAN WALTON/GETTY IMAGES FOR DAGOC

Santhi was ostracised from her village and attempted suicide in 2007. In 2017, she filed a case against the Indian Olympic Association and the Indian Athletics Federation for abuse of human rights, which was rejected on the grounds that it was too late to accept it.[13]

Sources: references 13, 31, 32, 33, 34, 35

CASE STUDY

Mokgadi Caster Semenya, South Africa, world and Olympic champion 800 m runner—withdrawn from competition due to the results of a sex test

Mokgadi Caster Semenya (Fig. 30.8) is a two-time world and Olympic champion 800 m runner from South Africa. After winning the 800 metres at the 2009 World Championships, Semenya was forced to undergo sex testing and was withdrawn from international competition until the following year, when the IAAF cleared her to return to competition.
Although Semenya's test results were never formally released, her case left many concerned that women's sport would be threatened if athletes were allowed to compete with a testosterone advantage. The case has since prompted several rule changes in sex testing in women's sport.

Sources: references 36, 37, 38

Figure 30.8 Caster Semenya, world champion 800 m runner GETTY IMAGES/MARK KOLBE

The IOC finally abandoned routine sex testing in sport in 1999, prior to the 2000 Olympic Games in Sydney.[9]

On-demand multidisciplinary testing

Although routine sex testing was abandoned in 1999, sports authorities could still demand a sex test if required in individual cases.[9] These tests had become widespread across multiple disciplines and could include evaluation by gynaecologists, endocrinologists and psychologists. Two athletes, Santhi Soundarajan and Caster Semenya, (see case studies) made headlines when they failed these tests. This prompted the sports authorities to reconsider introducing sex testing, this time focusing on testosterone levels.

Testosterone levels

The IAAF Regulations Governing Eligibility of Females with Hyperandrogenism to Compete in Women's Competition came into force in May 2011, shortly followed by similar IOC policies. Although neither the IAAF nor IOC mention explicitly a relationship between Caster Semenya and the regulations, this is apparent, and an extensive body of critical literature has been written on the subject.[14]

These policies claimed that atypically high levels of endogenous testosterone in women create an unfair advantage and must be regulated. Women with features of hyperandrogenism had to demonstrate a serum testosterone level less than 10 nmol/L to be eligible to compete in the female category. This level was chosen because it represented the lower level for the normal male range and was significantly higher than the upper level for the normal female range. Athletes who had levels higher than 10 nmol/L could attain the required levels through either surgery or hormone therapy.[15] It is not clear how many athletes failed this test and underwent subsequent surgery or hormone therapy.

Dutee Chand, an Indian 100 m runner, was targeted by the regulations in July 2014 and disqualified from competing at the Commonwealth Games.[16] Chand refused both surgery and hormone therapy, and filed an appeal against the IAAF suspension in the Court of Arbitration for Sport (CAS). Her main arguments included discrimination based on sex and lack of sufficient evidence regarding the relationship between testosterone and athletic performance.

In July 2015, CAS made an interim award followed by two extensions, suspending the IAAF hyperandrogenism regulations and clearing Chand and other athletes with hyperandrogenism for competition, while the IAAF was given an opportunity to provide evidence to support its case.[17, 18] Some of the issues the CAS panel considered when evaluating the regulations are discussed here briefly.

- The regulations were not trying to distinguish between men and women, as high levels of testosterone do not automatically imply the person is male. Rather, the regulations were distinguishing between athletes (who were all legally women) with high levels of testosterone and those with normal levels. Therefore, if the athlete was found to have levels above 10 nmol/L, she would be barred from competition and unable to compete in any category. Importantly, this was counter to the fundamental Olympic principle of access to sport for all, without discrimination.

- The regulations excluded athletes based on conditions which were part of their unaltered, natural state.
- Excluded athletes would only be allowed to compete if they had undergone a medical intervention that was not medically indicated. Furthermore, it was intended to deprive each of a genetically determined performance advantage.
- Although it was generally accepted that male levels of testosterone provide a performance advantage, there was insufficient evidence to quantify that advantage. Current evidence suggests an advantage that does not reach the 3% difference that was requested by the Court of Arbitration for Sport for the reinstatement of the hyperandrogenism regulations. Nor does it reach the 10% accepted range of difference in performance between men and women.[19]

In April 2018, the IAAF issued new Eligibility Regulations for Female Classification (Athlete with DSD) for running events from 400 metres to the mile. The new regulations require any athlete who has a Difference of Sexual Development that results in their levels of serum testosterone being 5 nmol/L or above and who is androgen-sensitive to meet the following criteria. To be eligible to compete in international competition she must:[20]

a. be recognised at law either as female or as intersex (or equivalent)
b. reduce her blood testosterone level to below 5 nmol/L for a continuous period of at least 6 months (e.g. by use of hormonal contraceptives) and
c. thereafter maintain her blood testosterone level below 5 nmol/L continuously (i.e. whether she is in competition or out of competition) for so long as she wishes to remain eligible.

These new regulations came into effect in November 2018 and replaced the 2011 regulations, which no longer apply anywhere in the sport.

Androgen receptors

Androgen receptor (AR) function is taken into consideration when a multidisciplinary team assesses an athlete's eligibility to compete in a women's event. Recent research has highlighted a number of interesting findings regarding the AR gene:[21]

- Up to 40% of patients with CAIS and PAIS do not have any gene mutations. Therefore, an absence of an AR gene mutation does not exclude AIS as a diagnosis.
- There are already more than 300 AR gene coregulators and interacting proteins whose function has not been clearly characterised. This may explain why cases with identical genotypes have different phenotypes. Consequently, analysis of the AR gene in isolation may not predict androgen function.
- Somatic mosaicism may exist with the AR mutation being present only in genital tissue and not the blood, or vice versa. When determining the relationship between external genitalia and the performance benefits of testosterone, this may be an important consideration.
- Some AR mutations may lead to both loss-of-function effects (such as AIS) and gain-of-function

effects (such as prostate cancer). This raises the possibility that the presence of AIS does not necessarily reflect a loss of all AR functions.

Ongoing research seeks to address many other questions regarding testosterone and its impact on athletic outcomes, such as:

- What is the effect of endogenous versus exogenous testosterone?
- What is the difference in response to testosterone between men and women?
- How does one explain the success of elite-level female athletes with high levels of testosterone but complete androgen insensitivity?
- Why, within the limited evidence currently available, does there appear to be no association between performance and testosterone levels in male athletes?

RATIONALE FOR SEX TESTING IN SPORT

The initial rationale for sex testing was to exclude male impostors from female sport. While sex testing has never revealed a male impostor,[9] it has divulged the complexity of sex attribution. Consequently, the focus has shifted to the concept of 'fair play'. As such, one of the IOC's current recommendations is that rules should be in place for the protection of women in sport Page 429 and the principles of fair competition.

Women in sport

The earliest evidence of human participation in sport can be found in cave paintings dating back more than 15 000 years. Since then, there have been countless paintings discovered on walls, pot shards and other surfaces depicting men's participation in organised sport, preparing for war or fighting in battles.

Although there is some evidence of women's participation in athletic activities, such as the Herean Games and the women of Sparta, women had been banned from competing in the Olympics until relatively recently. Women were allowed to compete in the marathon for the first time in 1984, having previously been considered too weak for such an event. The 2012 Olympics in London was the first time that women were allowed to compete in every event at the Summer Olympics, and Beijing 2022 will be the first time that women will be allowed to compete in every event at the Winter Olympics.

Perceiving women as the inferior sex is flawed, because it inherently assumes that women are inferior to men and supports the misconception that any man can beat the best existing female athletes. The thought is that by systematically excluding women with natural and inborn advantages from the competition, women's sport is being held back and artificially kept at a level acceptable to society, where petite and feminine women are preferred over those who are fast and strong.

Women's sport is still young and needs to be protected and nurtured to thrive. Without female Olympians and sports role models, young girls across the globe could potentially miss out on the many benefits of physical activity and sports participation.

Where to draw the line?

This raises the question of *where* to draw the line between men and women. As highlighted in this chapter, sex is a spectrum, and if one wants to divide this spectrum into two categories, there must be a discrete or delineating point at which one category changes to the other.

Sex testing to date has attempted to draw the line next to the all-female woman (XX chromosomes, no SRY gene, normal levels of testosterone). However, it could also be drawn next to the all-male man, which would be consistent with basic biology in which the development of a female foetus is the default, unless all the requirements for a male foetus have been met. In other words, instead of excluding all people who are not all-female, only exclude those athletes who are all-male (XY, with a functioning

SRY gene, male gonads, male testosterone levels and functioning testosterone receptors). Or perhaps in the interest of fairness, we should abolish gender segregation to recognise natural potential,[22] which may then cater to the needs of all athletes.

Regardless of the resultant definition, this is commonly viewed as an artificial construct for the purposes of women's participation in sport. As it currently stands, only the most 'female' are considered cleared for sport and only the 'weakest' are allowed to compete.

Fair play

The premise of preserving the common good of 'fair play' for all is the main argument used to justify the abuse of the individual athlete's human rights. Many argue that there is no such thing as fair play in elite sport. Elite athletes train very hard, commit years of their life to their sport and develop exceptional mental fortitude to reach the Olympic podium. Yet, with exactly the same hard work and commitment, most of society will arguably never win an Olympic medal because they do not possess the required genetic composition, among other advantages.

It is the very prospect of watching humans perform seemingly impossible feats that draws us to elite sport. Even within elite sport there is no level playing field.[23] Articles have been written about the physical attributes and genetic advantages possessed by athletes such as Michael Phelps and Usain Bolt.[24, 25] An attempt at levelling the playing field for male swimmers and sprinters would mean the exclusion of these two athletes.

Sex testing has shifted from trying to exclude men from the women's competition to differentiating between those women with high (functioning) testosterone levels and those with normal levels. Although testosterone testing started as a means to distinguish between men and women, it has become clear (as with chromosomes and gene testing) that there is no definitive line. It has now become the only performance factor tested for in sport and used to exclude athletes-and only in women's sport. There is no such testing in men's sport. Nor is there an evaluation of any other trait associated with improved performance, such as lean body mass or VO_2max.

AN ISSUE OF HUMAN RIGHTS

The Universal Declaration of Human Rights[26] is a fundamental document in the development of human rights. It was proclaimed by the United Nations General Assembly in 1948 and is often invoked in treaties, constitutions and laws. It consists of 30 articles that affirm an individual's rights. Throughout the history of sex testing, athletes have suffered abuse of a number of the human rights identified in this document, such as:

Page 430

Sex testing versus doping control

There is an unfortunate association between sex testing and doping control for athletes—perhaps because both were introduced to the Olympics for the first time in 1968 and their justification lies somewhere in the field of 'fair play'.

Women who have failed sex tests have been sensationalised by the media and been perceived as cheats by those who do not understand the difference between exogenous and endogenous hormones or the complexities of the sex spectrum. And yet, even individuals who do understand the concepts may still consider these athletes to be 'inadvertent' cheats.

The overall impact on athletes is devastating. Not only do they have to deal with the discovery and stigma of a condition of which they were previously unaware, but they are also forced to deal with the stigma of being banned from competition and being labelled a cheat.

- discrimination based on sex (Article 2)
- enduring degrading treatment (Article 5)
- interference with privacy and attacks on honour and reputation (Article 12).

Athletes' rights as patients have also been violated–for example, undergoing medical tests without proper informed consent, and being encouraged to undergo medically unnecessary treatment or procedures.

Article 29 of the declaration states that:

> *. . . in the exercise of his rights and freedoms, everyone shall be subject only to such limitations as are determined by law solely for the purpose of securing due recognition and respect for the rights and freedoms of others and of meeting the just requirements of morality, public order and the general welfare in a democratic society.*

Although Article 29 appears to protect the integrity of an athlete, others interpret its meaning to strengthen their own actions against a single person. They claim this article provides justification for the violation of an individual athlete's human rights if it serves the 'common good'-that is, protecting other athletes' rights such as 'fair play'.

THE PARTICIPATION OF TRANSGENDER ATHLETES IN SPORT

A different sex issue concerns the participation of transgender athletes in sport. In 2003, the IOC released the Stockholm Consensus (see box), which outlined the regulations for the participation of

transgender athletes in the Olympics.

While sex reassignment surgery and gender changes are legal in many countries, some countries do not legally recognise these procedures and others prohibit them. There are also many inconsistencies across different international sport federations and associations-some require athletes to undergo surgery if they want to compete, while others do not.[28]

The IOC adjusted its regulations on sex reassignment and hyperandrogenism in November 2015 (see box), acknowledging these concerns and the potential violation of human rights. However, athletes are still required to have declared their female gender and maintain a testosterone level below 10 nmol/L.

2003 Stockholm Consensus on Sex Reassignment in Sports[27]

Individuals undergoing sex reassignment from male to female after puberty (and the converse) are eligible for participation in female or male competitions, respectively, under the following conditions:

- *Surgical anatomical changes have been completed including external genitalia changes and gonadectomy*
- *Legal recognition of their assigned sex has been conferred by the appropriate official authorities*
- *Hormonal therapy appropriate for the assigned sex has been administered in a verifiable manner and for a sufficient length of time to minimise gender-related advantages in sport competitions.*

In the opinion of the group, eligibility should begin no sooner than two years after gonadectomy.

International Olympic Committee transgender guidelines, 2015[29]

1. *Those who transition from female to male are eligible to compete in the male category without restriction.*
2. *Those who transition from male to female are eligible to compete in the female category under the following conditions:*

    2.1. *The athlete has declared that her gender identity is female. The declaration cannot be changed, for sporting purposes, for a minimum of four years.*

    2.2. *The athlete must demonstrate that her total testosterone level in serum has been below 10 nmol/L for at least 12 months prior to her first competition (with the requirement for any longer period to be based on a confidential case-by-case evaluation, considering whether or not 12 months is a sufficient length of time to minimize any advantage in women's competition).*

THE FUTURE OF SEX TESTING IN SPORT

Sex testing to date has focused on external genitalia, chromosomes, genes, testosterone levels and androgen receptors. At each level, it has become clear that although most people fall into the male or female categories, as we have classically defined them, there is a spectrum between these end points. Although society is increasingly accepting of this spectrum and making provisions for it, it remains a problem in sport because currently only two categories of participation exist.

The following outlines options for future developments in sex testing in sport.

1. Continue to try and fit the spectrum into two categories. This will require:
   a. a clear definition of the two categories
   b. a clear understanding of the differences between the categories and therefore the reasons for making the distinction
   c. identifying how to test for these differences in a way that is a true reflection of the differences and not an indirect indication of possible differences
   d. a clear pathway to categorise all currently known and future sexually ambiguous athletes into one of the two categories
   e. understanding that this division will always be unfair to some because it is arbitrary
   f. consideration of abandoning all testing until these issues have been addressed in a way that is justifiable.
2. Alternatively, create a third category, which will require much thought and many of the steps above.
3. Abolish the concept of categories and make sport accessible to all by changing the nature of sport so that it is not skewed towards one end of the spectrum. For example, more skills- or agility-based rather than power-based sport.

CLINICAL IMPLICATIONS OF SEX TESTING IN SPORT

Team clinicians usually do not get involved in sex testing. While this may be a relief to some, this also means that clinicians may not regularly consider the issue or formulate an approach to it. With greater acceptance of the sex spectrum and gender variety, it is likely that current and future generations of clinicians will have to deal with sex-related issues in athletes more frequently. There are four broad issues to consider:

- medical issues
- trust and sensitivity
- ethics of testing
- education.

Medical issues

Clinicians may encounter athletes with DSD when they present with primary amenorrhoea or

infertility. While there are many more likely causes for these symptoms, it is important to consider DSD in the differential diagnosis. Longer-term health complications may be associated with some of these conditions, requiring further work-up. For example, in the situation of rudimentary undescended testis, there is a higher incidence of testicular cancer.[30] Referral to an endocrinologist with experience in managing these conditions is essential.

Other needs to consider for these athletes may include psychological support and genetic counselling.

PRACTICE PEARL

The clinician's number one priority should always be the health of the athlete.

Trust and sensitivity

The clinician may be the one who initiates the process leading to the diagnosis of a DSD. Alternatively, the clinician may be the first individual in whom the athlete confides regarding their DSD. Either way, the clinician must approach the situation with knowledge, sensitivity and empathy. Confidentiality is paramount, in order to earn and keep the athlete's trust. A breach of confidentiality is not only indefensible medico-legally, but can also have devastating consequences for the athlete.

Clinicians may be pressured by other team members, management or the media to divulge information where sex issues are suspected. The entire clinical team must be prepared for this and make sure that no information is revealed deliberately or by implication.

The ethics of testing

Depending on the regulations, at any given time clinicians may be required to perform sex testing on athletes.

In the IOC regulations on female hyperandrogenism that were published prior to the 2012 London Olympics, the IOC Executive Board warns that sanctions may be imposed on the respective team physician if an investigated athlete is declared ineligible to compete due to functional hyperandrogenism. This means that clinicians need to assess or test Olympic athletes in their care and follow current regulations regarding hormone and other treatments. If clinicians have ethical objections, they need to excuse themselves from the team, or accept possible sanction in case of a positive finding. Either way, it is important for clinicians to be aware of current regulations and to make a balanced decision given available evidence.

But what if a clinician knows that an athlete has failed or will fail upcoming sex testing? If the athlete is part of a team and a failed test will lead to disqualification of the entire team, it is essential that clinicians know the correct procedure in terms of their responsibilities to the athlete versus the team, specifically with regards to confidentiality. A clinician's responsibilities will likely

be dependent on the content of signed contracts, and for this reason, clinicians should hold discussions with their teams well in advance of major competitions.

Education

One of a clinician's most important responsibilities is providing education to athletes and management teams. In the case of sex testing, clinicians must be able to explain the basics of sexual development, the concept of the sex spectrum and the shortcomings of sex. Clinicians need to help individuals understand that a failed sex test is not the same as a failed drugs test, and that athletes who test positive are not male impostors in women's sport. Rather, they are likely innocent people who are caught up in a complex situation for which there are currently more questions than answers.

Education of all concerned parties and expressing empathy towards others are the first steps towards finding a solution. Open discussion must take place between not only regulators and medical specialists, but also among gender scholars, psychologists, philosophers of sports and, perhaps more importantly, the athletes who have long been neglected in this debate.[6]

REFERENCES

1. World Health Organization. What do we mean by 'sex' and 'gender'? Geneva, 2017. https://web.archive.org/web/20170130022356/http://apps.who.int/gender/whatisgender/en/.
2. Bivens R, Haimson OL. Baking gender into social media design: how platforms shape categories for users and advertisers. *Social Media + Society* 2016; 2(4): 2056305116672486. doi: 10.1177/2056305116672486.
3. The Federal Constitutional Court, Germany. 'Civil status law must allow a third gender option'. Press Release No 95/2017 of 8 Nov 2017. 1 BvR 2019/16 https://www.bundesverfassungsgericht.de/SharedDocs/Pressemitteilungen/EN/2017/bvg17-095.html.
4. Vonberg J. Germany's top court tells lawmakers to recognize 'third gender'. 8 November 2017. https://www.cnn.com/2017/11/08/europe/germany-court-intersex-children/index.html.
5. Intersex Society of North America. What is intersex? 2008. http://www.isna.org/faq/what_is_intersex.
6. Camporesi S, Maugeri P. Unfair advantage and the myth of the level playing field in IAAF and IOC policies on hyperandrogenism: when is it fair to be a woman? In: Montanola S, Olivesi A, eds. *Gender Testing in Sport: Ethics, cases and controversies*. Routledge, 2016: 210.
7. Hull CL, Fausto-Sterling A. How sexually dimorphic are we? Review and synthesis.

Am J Hum Biol 2003; 15(1): 112–15; author reply 115–16. doi: 10.1002/ajhb.10122.

8. Johnson EK, Rosoklija I, Finlayson C et al. Attitudes towards 'disorders of sex development' nomenclature among affected individuals. *J Pediatr Urol* 2017; 13(6): 608.e1–8. doi: 10.1016/j.jpurol.2017.03.035.
9. Heggie V. Testing sex and gender in sports; reinventing, reimagining and reconstructing histories. *Endeavour* 2010; 34(4): 157–63. doi: 10.1016/j.endeavour.2010.09.005.
10. Lynch S. When men were men ... and so were the women. *The Guardian*, 7 August 2004.
11. Peters M. *Mary P: Autobiography*. Arrow Books, 1976.
12. Ballantyne KN, Kayser M, Grootegoed JA. Sex and gender issues in competitive sports: investigation of a historical case leads to a new viewpoint. *Br J Sports Med* 2012; 46(8): 614–17. doi: 10.1136/bjsm.2010.082552.
13. Mantri G. Human rights body rejects Santhi Soundarajan's complaint, claims it's too late to accept it. 16 February 2017. https://www.thenewsminute.com/article/human-rights-body-rejects-santhi-soundarajan-s-complaint-claims-it-s-too-late-accept-it,
14. Camporesi S. Ethics of regulating competition for women with hyperandrogenism. *Clin Sports Med* 2016; 35(2): 293–301. doi: 10.1016/j.csm.2015.10.003.
15. Karkazis K, Jordan-Young R, Davis G et al. Out of bounds? A critique of the new policies on hyperandrogenism in elite female athletes. *Am J Bioeth* 2012; 12(7): 3–16. doi: 10.1080/15265161.2012.680533.
16. Slater M. Sport & gender: a history of bad science & 'biological racism'. 28 July 2015. https://www.bbc.com/sport/athletics/29446276.
17. Viret M, Wisnosky E. CAS 2014/A/3759, Chand v. AFI & IAAF, Award of 24 July 2015. 2016. https://link.springer.com/chapter/10.1007%2F978-94-6265-129-6_12
18. CAS suspends the IAAF hyperandrogenism regulations until end of September 2017. Court of Arbitration for Sport 2017. http://www.tas-cas.org/fileadmin/user_upload/Media_Release_3759_July_2017.pdf.
19. Ospina Betancurt J, Zakynthinaki MS, Martinez-Patino MJ et al. Hyperandrogenic athletes: performance differences in elite-standard 200m and 800m finals. *J Sports Sci* published online 16 April 2018. doi: 10.1080/02640414.2018.1464620.
20. International Association of Athletics Federations (IAAF). *IAAF introduces new eligibility regulations for female classification*. Monaco: IAAF, 2018.
21. Gottlieb B, Beitel LK, Nadarajah A et al. The androgen receptor gene mutations database: 2012 update. *Hum Mutat* 2012; 33(5): 887–94. doi: 10.1002/humu.22046.
22. Foddy B, Savulescu J. Time to re-evaluate gender segregation in athletics? *Br J Sports Med* 2011; 45(15): 1184–8. doi: 10.1136/bjsm.2010.071639.
23. Sullivan CF. Gender verification and gender policies in elite sport: eligibility and

'fair play'. *J Sport Soc Issues* 2011; 35(4): 400–19. doi: 10.1177/0193723511426293.

24. Hadhazy A. What makes Michael Phelps so good? *Scientific American*, 18 August 2008. https://www.scientificamerican.com/article/what-makes-michael-phelps-so-good1/.
25. Thomas C. Built for speed: what makes Usain Bolt so fast? *The Telegraph*, 20 August 2016. https://www.telegraph.co.uk/usain-bolt-worlds-fastest-man/0/built-for-speed-what-makes-usain-bolt-so-fast/.
26. United Nations. The Universal Declaration of Human Rights. United Nations, 2015.
27. International Olympic Committee (IOC) Medical Commission. Statement of the Stockholm consensus on sex reassignment in sports. Stockholm, Sweden, 2003.
28. transathlete.com. Policies by organization. 2018. https://www.transathlete.com/policies-by-organization.
29. International Olympic Committee (IOC). IOC Consensus Meeting on Sex Reassignment and Hyperandrogenism November 2015. Lausanne, Switzerland, 2015.
30. Hutson JM, Balic A, Nation T et al. Cryptorchidism. *Semin Pediatr Surg* 2010; 19(3): 215–24. doi: 10.1053/j.sempedsurg.2010.04.001.

Chapter 31

Older people#

with DANIEL FRIEDMAN and KEN MADDEN*

I want people to know that you can reboot your body at any age.
Dr Charles Eugster (1919–2017), British record holder in the men's 95+ category 100 m and 200 m

Our older population is growing at an unprecedented rate. Half of the people who have ever lived beyond 65 years of age are inhabiting the planet today. Fifteen per cent of the planet's population is expected to be aged over 65 years by 2050.[1]

Physical inactivity increases with age,[2] and with increasing age there is also an elevated risk of developing chronic diseases, such as cardiovascular disease, cancer and diabetes.[3] There is a decline in many physiological systems, balance ability and cognitive performance, as well as a loss of muscle mass (sarcopenia), strength and endurance. Of people aged over 75 years in the UK, 30% report chronic musculoskeletal conditions, 32% report cardiovascular conditions and 13% report metabolic conditions.[4]

These increasing levels of physical inactivity and chronic disease create a vicious cycle. Disease and subsequent disability reduce levels of physical activity, which impairs functional independence and exacerbates disability. Regular physical activity can help older adults break this cycle.

Despite the fact that 'physical activity is medicine for older adults',[5] few older adults meet the recommended levels of physical activity. In the USA, more than one in four adults aged 50 years or older are completely sedentary.[6] Comprehensive public health action on physical activity in older adults is needed urgently. We must find effective ways to support older adults to increase their physical activity levels, by overcoming barriers to participation. This will reduce the burden of chronic disease and improve the quality of life for all.

In this chapter we explore:

- what constitutes an older person

- evidence for the physiological and psychological benefits of physical activity for older adults (healthy ageing)
- risks associated with physical activity for older adults
- exercise prescription for older adults
- potential interactions between physical activity and medications commonly used by older adults.

WHAT DEFINES AN OLDER PERSON?

Defining 'older person' by chronology is flawed because of increasing variability in health and functional status with increasing age. While most developed countries have accepted the chronological age of 65 as the definition of an older adult, equivalent to the approximate retirement ages in these countries, that cut-off is arbitrary. Socially constructed definitions of old age based on assigned roles within society are more important.

A more appropriate, universal definition of old age is one that considers functional limitation and a person's ability to live independently. For example, while some 70-year-olds may enjoy good physical and mental health and can perform all activities of daily living, others may be frail or require substantial support to meet their basic needs.

WHAT IS HEALTHY AGEING?

Healthy ageing is 'the process of developing and maintaining the functional ability that enables well-being in older age'.[11] 'Functional ability' describes the health-related attributes that enable older adults to be, and to do, what they value, which consists of an individual's intrinsic capacity and their environment.

Healthy ageing reflects the ongoing interaction between an individual and the environment they inhabit (Fig. 31.2), and can be thought of as the individual being able to do the things they value for as long as possible.

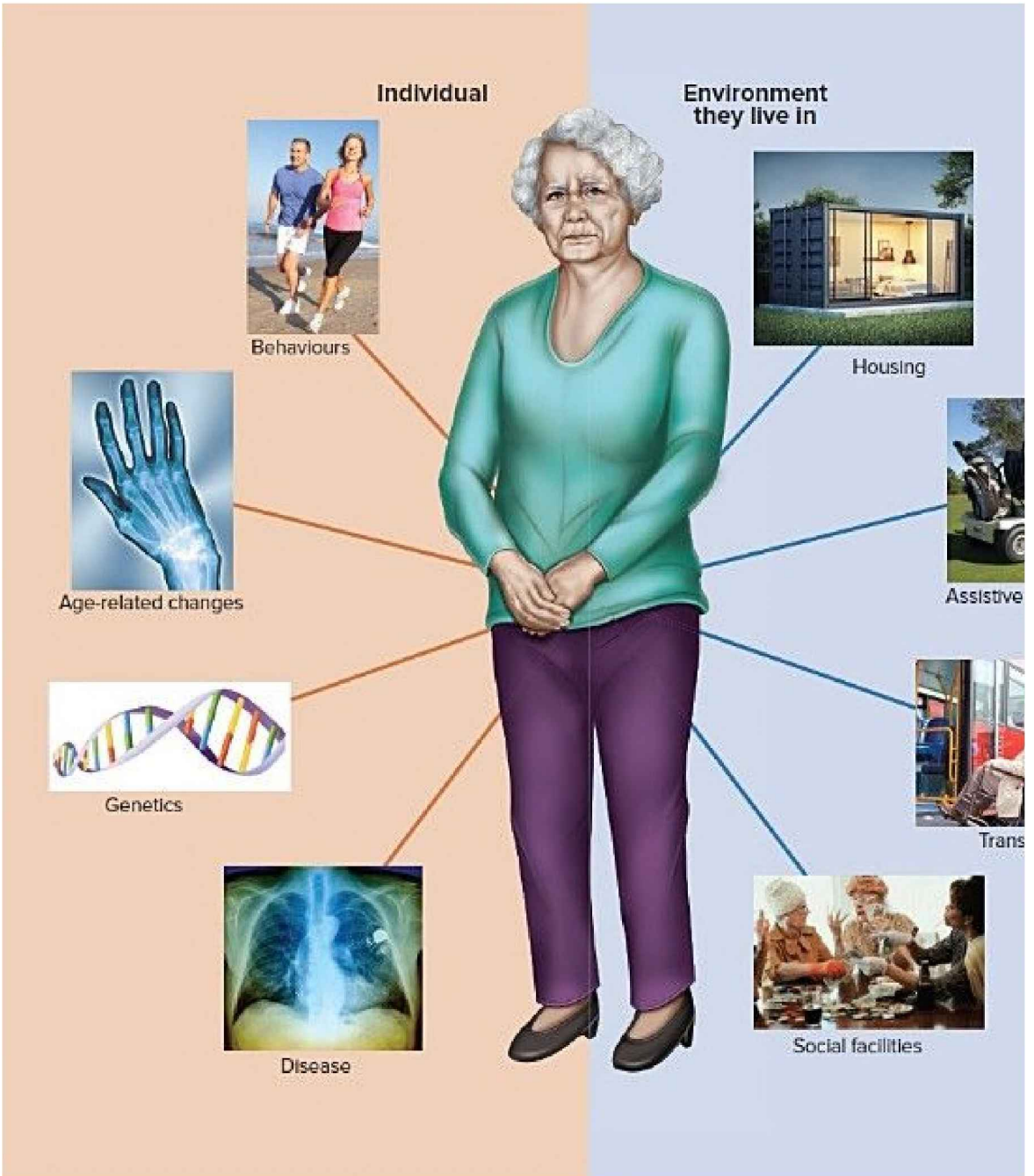


Figure 31.2 What influences health in older age?

ADAPTED FROM WHO, HEALTHY AGEING REPORT, 2015. BEHAVIOURS - MONKEY BUSINESS IMAGES/SHUTTERSTOCK.COM; AGE-RELATED - © SCIENCE PHOTO LIBRARY / ALAMY STOCK PHOTO; GENETICS - SHUTTERSTOCK / GRAPHICSRF; DISEASE - © SCIENCE PHOTO LIBRARY /

ALAMY STOCK PHOTO; SOCIAL FACILITIES - PURESTOCK/SUPERSTOCK; TRANSPORT - SHUTTERSTOCK/MONKEY BUSINESS IMAGES; ASSISTIVE TECHNOLOGIES - REALISTIC REFLECTIONS; HOUSING - SHUTTERSTOCK/P11IROM

Age is just a number (for some)

Greying (and possibly thinning) hair does not stop some older adults from engaging in regular physical activity, ranging from recreational walking and swimming, to more vigorous and often competitive activity (Fig. 31.1). In recent years, participants in endurance activities and other competitive sports are on average older than ever.[7]

The number of participants older than 50 years in the New York City marathon increased 119% from 1983 to 1999, and this was associated with faster completion times.[8,9] In a 2010 study of more than 900 000 marathon runners, one fourth of the runners in their mid-to late 60s outperformed half of the runners aged 20–54.[10] The 2018 Boston Marathon finishers included 764 men and women aged over 65 years; seven of them were octogenarians.

Figure 31.1 A combination of good genes, luck and consistent training can allow many people who fall into the chronologic older person category to function at a level often associated with a much younger age ITETRA IMAGES, LLC / ALAMY STOCK PHOTO

To enable all individuals to realise healthy ageing, we must:[11]

- change the way we think about ageing and older adults
- create age-friendly environments
- align health systems to the needs of older adults

- develop systems that support long-term and residential care
- use and develop new assistive technologies.

A word on frailty

Frailty is a geriatric syndrome that may be considered the opposite of healthy ageing and is characterised by multiple deficits to body systems. Frail people experience severe impairments in physical, mental and psychological functioning that restrict their ability to complete activities of daily living.

Frailty is usually diagnosed with the help of two classification systems:

- Rockwood scale–defines frailty as the accumulation of deficits, such as number of medications taken, number of diseases, frequency of medical interventions and other psychosocial indicators[12]
- Fried frailty phenotype-recognises frailty in people presenting with at least three of: unintentional weight loss; low physical activity levels; slow gait speed; exhaustion or weakness. [13]

BENEFITS OF PHYSICAL ACTIVITY IN OLDER PEOPLE

All older people can benefit from physical activity. In the presence of chronic conditions or disabilities, any physical activity is better than none, and any amount of physical activity provides at least some health benefit.[14]

Incidental physical activity, such as climbing stairs or housework, is associated with decreased cardiovascular disease incidence and reduced mortality in older adults.[15] An eight-year longitudinal study found that every additional 15 minutes of daily physical activity up to 100 minutes per day resulted in a further 4% decrease in all-cause mortality.[16]

NEED TO KNOW

Much age-related deterioration is the result of the effects of sedentary lifestyles and the development of medical conditions rather than of ageing itself.[7]

Here we discuss some of the benefits of regular physical activity for older adults, building on Cha pter 2.

The cardiovascular system

Physical activity interventions in older adults with coronary heart disease are associated with decreased morbidity, decreased mortality, reduced symptoms and reduced cardiac rehospitalisation.[17] These benefits may be explained by a number of mechanisms:[18]

- An increase in demand on the myocardium improves oxygen utilisation. Capillaries dilate and multiply to improve the delivery of oxygen and other nutrients to muscles. The myoglobin content of muscle is increased, improving the transfer of oxygen from the red blood cells to muscle cells. Inside the cell, the number of mitochondria increases, enhancing aerobic metabolism.
- Physical activity facilitates an increase in glycogen storage in skeletal muscle.
- Physical activity lowers resting heart rate, and the resultant increased diastolic time improves both coronary blood flow and cardiac output.
- Physical activity raises levels of high-density lipoproteins and lowers levels of low-density lipoproteins.
- Physical activity lowers blood pressure.

Notably, moderate physical activity may reduce stroke risk by up to 15%.[19]

The respiratory system

Ageing causes a reduction in respiratory muscle strength, which is often accompanied by a decrease in the elastic recoil of the lungs and chest wall compliance,[20] together predisposing older adults to respiratory infections.[21] In older adults with no history of respiratory disease, the more active the individual, regardless of level or duration of activity, the higher their respiratory muscle strength.[22]

Physical activity as part of a pulmonary rehabilitation program improves physical status and quality of life in older adults with chronic obstructive pulmonary disease.[23] Physical activity increases the older adult's tolerance for physical activity and enables them to reap the associated benefits of improved aerobic fitness.

Diabetes mellitus

Type 2 diabetes mellitus is highly prevalent among older adults. In combination with dietary modification, physical activity reduces the risk of developing type 2 diabetes across a wide age range. Physical activity is also an effective treatment of diabetes in older adults. Since muscle is the largest glucose sink in the human body, exercise improves blood glucose control in people with diabetes, by decreasing insulin resistance, thereby reducing the need for medication.[24, 25]

Osteoarthritis

Osteoarthritis of the knee and hip are major contributors to disability and chronic pain in older adults. Regular light-to moderate-intensity physical activity both prevents and treats knee osteoarthritis. Exercise regimens with strong evidence of benefit include those that focus on aerobic and lower extremity strength training.[26]

Cartilage loading in the form of regular moderate-intensity physical activity enhances glycosaminoglycan content in knee cartilage.[27] The cartilaginous matrix adapts to loading stresses by enhanced crosslinking analogous to osteoblastic activity in bones under moderate duress.[28]

Osteoporosis and prevention of fall-related fractures

With ageing comes decreased osteoblast activity, increased osteoclast activity, and diminished differentiation of bone marrow stem cells, due to a relative decline in trophic factors such as IGF-1.[29] Osteoporosis and bone health are discussed in Chapter 17.

Resistance training and physical activity of mixed loading impact are associated with gains in bone mass and reduced fracture risk in the elderly;[30] they also improve physical function and activities of daily living.

Osteoporosis is particularly important when considering that a third of people over 65 years of age fall at least once a year[31–33] and this increases to 42% for those over 70 years of age.[34–36] Ninety per cent of hip fractures are the result of falls;[37] 20% of these are fatal.[38] Physical activity in the form of strength and balance training reduces an older person's risk of falling,[39] and should be an integral part of every older person's physical activity routine. The Otago Exercise Programme (see box) is an evidence-based falls prevention program that is led by community-based physiotherapists.

Functional independence

After peaking in early adulthood, muscle mass, strength and endurance decline with age. Skeletal muscle mass and strength decline in a linear fashion, with up to 50% of mass being lost by the eighth decade of life[42]-a process referred to as sarcopenia. The progressive decline in musculoskeletal function is associated with slower walking speed, difficulties rising from a seated position and balancing.

Muscle strength and aerobic fitness have been strongly linked to functional independence. In older people without disabilities, aerobic training alone or combined with resistance training results in improved physical function. When older people engage in physical activity of sufficient intensity and frequency, the risk of functional limitation and disability reduces by up to 50%.[43]

Cognitive and psychological function

Physical activity not only improves physical and motor functions, but also cognitive ability, and reduces the risk of cognitive decline and dementia later in life.[45] Physical activity modifies metabolic, structural and functional dimensions of the brain and preserves cognitive performance. The psychological effects of physical activity are so profound that it has been considered a 'psychoactive drug' in the literature.[46]

However, the mechanisms by which physical activity reduces the risk of cognitive decline are still being explored. Observational studies support a dose-dependent neuroprotective relationship between physical activity and cognitive performance in older people; however, not all studies show significant effects.[47] Further research is needed to gain a deeper understanding of the relationship between different types of physical activity and cognitive function.

Otago Exercise Programme

The Otago Exercise Programme (OEP) is an example of a cost-effective home-based strength and balance program for reducing falls among community-dwelling older adults.[40] The manual (Fig. 31.3) is available for free online at http://ow.ly/ppQB30jwBsz.

Figure 31.3 The Otago Exercise Programme is an evidenced-based, home-based, individually tailored strength and balance retraining programme for fall prevention

WAVEBREAK MEDIA/SHUTTERSTOCK

The OEP uses muscle-strengthening and balance exercises delivered at home by physiotherapists. The exercises are completed on three days per week, increasing in intensity over time. Participants also go for a walk at least twice per week. A clinician visits the patient five times during the program at one-month intervals, and follows up every six months after the program has finished.

The OEP reduces the number of falls and injuries by up to 35%, particularly in individuals aged over 80 years.[41]

Physical activity also reduces anxiety in older people, especially in those recovering from illness. Physical activity can lessen depressive symptoms,[48] and perhaps even reduce the risk of developing depression.[49]

RISKS FOR PHYSICAL ACTIVITY IN OLDER PEOPLE

Despite the inherent risks of physical activity, global guidelines state that physical activity is generally safe for older adults,[14] and should be encouraged if there are no contraindications. The benefits that older adults gain from being physically active outweigh the risks of injury or exacerbation of an existing condition.[50]

Before any older person increases their levels of physical activity, appropriate pre-participation screening should be implemented to identify at-risk individuals who may require medical clearance (Chapter 3). According to the American College of Sports Medicine, the risk for acute physical activity-induced cardiovascular events is highest among sedentary older people who perform unaccustomed vigorous-intensity physical activity,[51] so necessary cardiac screening should be performed as appropriate.

Contraindications to physical activity in older people

The contraindications for physical activity are mostly the same for older people as they are for younger adults. The Swedish book *Physical Activity in the Prevention and Treatment of Disease* (FYSS)[52] states that common absolute contraindications include recent ECG changes or myocardial infarction, unstable angina, uncontrolled arrhythmia, total atrioventricular block and acute cardiac insufficiency.

Relative contraindications include, but are not limited to, cardiomyopathies, unrepaired severe cardiac valve disease and uncontrolled metabolic diseases. If a patient does not have any contraindications to physical activity, they can commence a physical activity program, as discussed below.

EXERCISE PRESCRIPTION IN OLDER PEOPLE

As we continue to enjoy greater longevity, clinicians will be challenged to provide appropriate medical care and advice to our ageing population. Older people, particularly those with chronic health conditions, have frequent contact with multiple clinicians, and so clinicians must be prepared to support their patients to realise healthy ageing through increased physical activity levels. Clinicians should have a sufficient understanding of exercise prescription for older people and recognise when referral to physiotherapists or exercise professionals is necessary.

The inactive older adult

For sedentary older people, the first goal of exercise prescription is simply to reduce their sitting time. An agreed physical activity plan (Chapter 3) should look to find engaging activities that reduce the amount of time spent watching television or being idle. Activities that are functional, task-specific, relevant to the individual and incorporated into daily activities are best to consider.

How fast does the Grim Reaper walk?

Walking speed is commonly used as an objective measure of physical capability in older people, as gait is influenced by muscle strength, joint limitations, coordination and proprioception. A 2011 study[44] analysed the walking speeds of 1705 men aged 70 and above, to assess the relationship between walking speed and mortality. In the 59 months of follow-up, a total of 266 deaths occurred.

- The mean walking speed was 3.2 km/h.

- A walking speed of 3.0 km/h was most predictive of mortality.
- Older men with a walking speed above 2.9 km/h were 20% less likely to die than those who had a slower walking speed.
- No men with walking speeds of 4.9 km/h or greater 'had contact with Death'.

Based on these results, the researchers concluded that the Grim Reaper's preferred walking speed underworking conditions is approximately 3 km/h, and anyone wanting to outrun the Grim Reaper should aim to walk at least 5 km/h (Fig. 31.4).

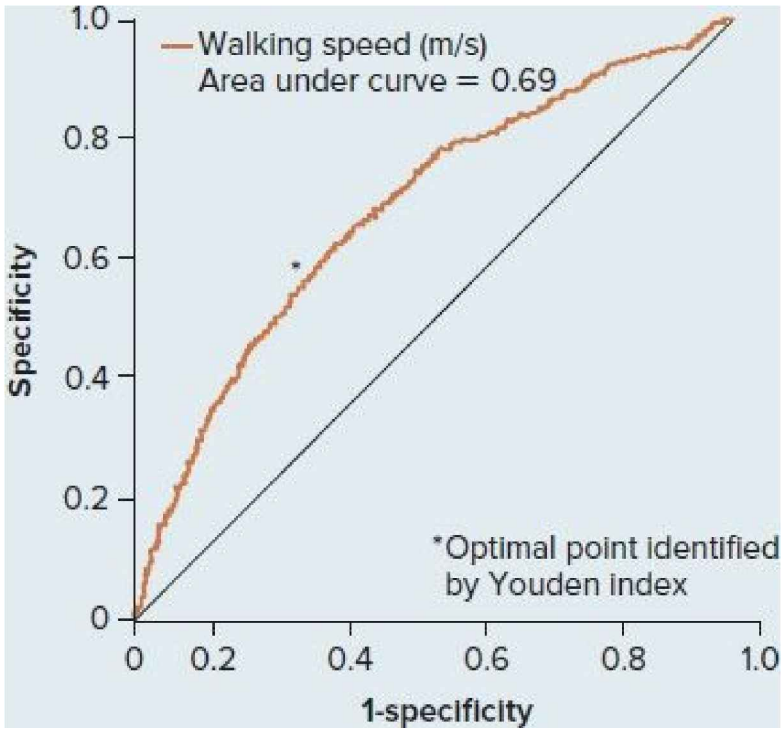


Figure 31.4 The *BMJ* Christmas edition publishes quirky science. It is factual. This 2011 report showed the receiver operating characteristics curve for mortality over five years in relation to walking speed. The conclusion was that walking above 5 km/h protected against death

STANAWAY ET AL (2011)[44]; TOMWANG/123RF

'Start low, go slow' applies to exercise prescription in this population, as it does in the general population (Chapter 4). The clinician should set easily attainable, realistic short-term goals and increase time spent performing moderate physical activity by no more than 5% per week. The eventual goal is to accumulate 30 minutes a day of moderately intense physical activity on most days of the week that includes a combination of aerobic, strength, balance and flexibility training.

Some older people may not be able to meet the recommended levels of physical activity due to chronic medical conditions or disability. If an older person cannot increase activity levels to meet

the recommendations, they should still be as active as physically possible, as a lack of physical activity can increase the level of frailty or worsen health conditions. Physical activity for older people who are frail should be tailored to meet the needs and abilities of each individual. Aerobic activities and vigorous physical activity can often be difficult for this group; low-intensity resistance activities that combine aerobic activities, such as 'chairobics', water-based programs ('aquacise') and sit-to-stand exercises, may be more appropriate.

PRACTICE PEARL

Practical suggestions to integrate physical activity into the daily routine include taking the stairs instead of the elevator or escalator, parking further away from the shops, and getting off public transport a stop early.

PRACTICE PEARL

It is never too late to start being physically active. Significant health benefits are seen even in those who only become physically active relatively late in life.[53]

World Health Organization physical activity recommendations for people 65 years and older

1. At least 150 min of moderate-intensity aerobic activity, or at least 75 min of vigorous-intensity aerobic activity, or an equivalent combination, per week.
2. Aerobic activity should be performed in bouts of at least 10 min duration.
3. For additional health benefits, up to 300 min of moderate-intensity or 150 min of vigorous-intensity aerobic activity, or an equivalent combination, per week.
4. People with poor mobility should do balance exercises on 3 or more days per week, to prevent falls.
5. Muscle-strengthening activities should be done on 2 or more days per week.
6. If older people are unable to do the recommended amounts of physical activity due to health conditions, they should be as physically active as they are able.[14]

The generally active older adult

The exercise prescription for older people should be multicomponent and include aerobic,

resistance, flexibility and balance training (Table 31.1).

Table 31.1 Physical activity guidelines for adults 65 years and over

Type	Time	Intensity	Frequency
Aerobic • Walking • Cycling • Swimming • Dancing	30–60 min/day or 150–300 min/week	Moderate to vigorous	≥ 5 days/week
Resistance • Calisthenics • Free weights • Stair climbing	One or more sets of 10–15 reps 8–10 major muscle groups 2–3 min rest in between sets	Moderate, 60–70% 1 repetition maximum	≥2 days/week, with 48 hours separating training sessions for the same muscle group
Balance • Balance exercises • Yoga • Pilates	≥ 10min	Challenge but not exceed functional capacity	≥3 days/week
Flexibility • Static and dynamic stretching • Yoga • Tai chi	10–30 seconds	To the point of tension, before discomfort	≥2 days/week

ADAPTED FROM WHO[14] and ACSM[51]

Aerobic

Aerobic activity should be performed at a moderate intensity, to a level at which the older adult notices an increase in heart rate and breathing (while still being able to speak in full sentences). Aerobic activities that may be particularly attractive to older people include cycling on a stationary bicycle, swimming, aquarobics, dancing and brisk walking.

Community-based group exercise programs that utilise social supports may be helpful in promoting aerobic and other forms of training to older people. Group-based exercise programs support participants to improve mobility, flexibility, upper and lower limb function, and overall quality of life.[55]

Resistance

When prescribing resistance exercise for older people, the clinician must tailor the exercise to the person's current functional ability. Importantly, older people must also learn the correct movement techniques, posture and breathing patterns for each exercise.

Proper breathing consists of exhaling during the eccentric phase (lowering of the weight for 4–6 seconds), working through the entire range of movement (or as much as is tolerated). The Valsalva manoeuvre should be avoided, particularly in older people, who are more prone to postural

hypotension and syncope than their younger peers.

Lifts should be separated by 2 seconds of rest. The goal is to perform one or two sets of 10–15 repetitions per set with 2–3 minutes of rest between sets. The patient should aim to lift a weight that is 60–70% of their one repetition maximum, or the most they can lift through a full range of motion.

While a single set of a particular lift may be sufficient to overload the muscles of older people who have only just begun to perform resistance training, multiple sets are recommended once they can tolerate a greater volume of exercise. Current guidelines state that resistance training should be performed on at least two days per week,[14] with multiple days of rest between sessions.

Balance

Activities that promote balance and coordination reduce the risk of falling and improve older people's ability to participate in recreational pursuits and realise healthy ageing. The primary goal when planning balance activities for older people is to challenge, but not exceed, their functional capabilities. This can be accomplished by providing balance activities that can be performed in diverse practice environments that simulate those encountered in daily life– such as changing levels on stairs, negotiating sedentary and moving obstacles, and moving at varied speeds.

A lifestyle approach to reducing falls through exercise

The Lifestyle integrated Functional Exercise (LiFE) programme, which involves integrating balance and lower limb strength training in habitual daily routines, provides an alternative to traditional exercise to consider, for fall prevention. The LiFE program helps to reduce the rate of falls by 30% compared with controls, and improves static and dynamic balance as well as ankle strength and function.[54]

Flexibility

Older people can improve their flexibility by stretching on a regular basis. Improvements in range of motion can be achieved by performing a variety of different exercises, including traditional static and dynamic stretching, dance, yoga, tai chi and aquatic exercise.

Special considerations for the active older adult

Due to age-related declines in temperature regulation, all older adults should be advised to take caution when being active in very warm or cold conditions (Chapters 23 and 24). Adequate fluid intake and avoiding physical activity in extreme temperatures should be emphasised.

For older adults with vision loss, ensure that their physical activity environment is well lit and free from clutter or tripping hazards. Any written prescriptions should be written or printed in larger type.

For older adults with sensory loss in their feet, manual support should be made available to

prevent a loss of balance, and prescribed activities should not include activities that require their eyes to be closed.

An older adult with a hearing impairment may also require support, particularly in group-based physical activity settings. When delivering instructions, it is important for the instructor to verify that the client is wearing their assistive devices and to speak slowly and clearly while facing them, so communication can be enhanced by lip reading, gestures and body language.

Exercise prescription for older adults with cognitive impairment should aim to minimise the likelihood of injury due to a loss of balance or engaging in risky, unaccustomed behaviours. The severity of an individual's cognitive impairment determines the level of supervision needed during each exercise session.

PRACTICE PEARL

For adults with cognitive impairment, fewer, simple exercises with more repetition can help minimise confusion and frustration.

HOW DO MEDICATION AND PHYSICAL ACTIVITY INTERACT IN OLDER PEOPLE?

Many older people have at least one chronic medical condition, and many have multiple chronic conditions for which medication is warranted. Certain physiological changes caused by physical activity can alter the pharmacokinetics and efficacy of some of these medications, and can result in unwanted adverse effects.

Much is still unknown regarding the interactions between medication and physical activity; however, clinicians must be aware that the potential for interactions exists, particularly for medications with narrow therapeutic windows and in patients who engage in intense physical activity. In this section we discuss the potential problems associated with common medications and physical activity, focusing on precautions that need to be considered in older people.

Medications affecting the renin-angiotensin system

Medications affecting the renin-angiotensin system, such as angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers, lower peripheral vascular resistance and are commonly used in the management of hypertension, heart failure and chronic kidney disease.

These medications are suitable for the hypertensive athlete as they do not limit maximal oxygen uptake; however, older people taking these medications may have an increased susceptibility to the effects of physical activity-related dehydration. Fluid losses combined with vasodilator effects can cause hypotension and dizziness.

Beta blockers

Beta blockers are used to treat hypertension, angina, heart failure, cardiac dysrhythmias, as well as tremor and migraine. They reduce cardiac rate and output, and attenuate the normal physiological response to physical activity. Older people who take beta blockers may have a restricted physical activity capacity, particularly in endurance events.

Adverse effects of beta blockers include postural hypotension, exacerbation of peripheral vascular disease, excessive tiredness, impotence and hyperkalaemia, as well as the potential for masking hypoglycaemic symptoms in people with diabetes taking older non-selective agents.

Diuretics

Thiazide diuretics are often recommended as a first-line therapy for hypertension. They are also used in the treatment of heart failure and fluid retention. Older adults who perform physical activity in warm to hot conditions and take diuretics are at risk of dehydration. Less common adverse effects include hyperglycaemia and increased uric acid levels, which can be sufficient to precipitate gout.

A combination of antihypertensive medication and vigorous physical activity with associated dehydration can decrease the intravascular volume and cause postural hypotension, which often manifests as lightheadedness or fainting.

By definition, diuretics lead to increased fluid excretion via the renal tract, and the diuresis occurs in relatively close proximity to oral administration. Older adults participating in exercise classes or being active outdoors may wish to delay taking their diuretic until after their activity, to avoid the need to urinate excessively.

Other cardiac drugs

Calcium channel blockers and nitrates are used to treat hypertension and angina, among other conditions. They may impair cardiac output when performing physical activity, and cause peripheral vasodilation, resulting in impaired performance. Peripheral venous pooling and the vasodilation can lead to postural hypotension, particularly during cool-down periods at the end of physical activity.

Non-steroidal anti-inflammatory drugs

Non-steroidal anti-inflammatory drugs (NSAIDs) are commonly used for the treatment of arthritis and musculoskeletal conditions in older people who are active. Adverse effects of these medications include hypertension, fluid retention, renal impairment, and the development of peptic ulceration and bleeding. The risk of bleeding is greatly increased when NSAIDs are prescribed in conjunction with warfarin. These drugs should be used cautiously in older people, and discontinued if the patient complains of adverse effects.

To minimise the risk of gastric irritation, NSAIDs should be taken with food or an acid-lowering medication. Topical anti-inflammatory medications may be a useful alternative.

Medications affecting the central nervous system

Medications such as benzodiazepines may affect fine motor skills, coordination, reaction time and thermoregulation-all of which can contribute to an increased risk of injury, particularly in contact

sports.

Although these medications are not recommended for older adults, many older adults who take these medications for sleep difficulties often reduce their need for them once physically active, as physical activity can improve sleep patterns.

Insulin and oral hypoglycaemic drugs

Physical activity can cause profound changes in glucose homeostasis and may lead to hypoglycaemia, necessitating close monitoring of glycaemic control and symptoms during any physical activity. Some symptoms of hypoglycaemia, such as sweating and fatigue, are similar to the physical sensations of normal exertion during activity, which can often make differentiation between the two difficult.

The dosages of insulin and oral hypoglycaemic drugs may need to be reduced prior to physical activity to avoid hypoglycaemia (Chapter 8).

REFERENCES

1. He W, Goodkind D, Kowal P. An Aging World: 2015 International Population Reports. March 2016. Report number P95-16–1. https://www.census.gov/library/publications/2016/demo/P95-16-1.html.
2. Hallal PC, Andersen LB, Bull FC et al. Global physical activity levels: surveillance progress, pitfalls, and prospects. *Lancet* 2012; 380(9838): 247–57.
3. World Health Organization (WHO). Global health risks: mortality and burden of disease attributable to selected major risks. Geneva, 2009.
4. General lifestyle survey overview—a report on the 2011 general lifestyle survey. 2013. https://www.ons.gov.uk/.peoplepopulationandcommunity/personalandhouseholdfinances/incomeandwealth/compendium/generallifestylesurvey/2013-03-07/chapter7generalhealthgenerallifestylesurveyoverviewareportonthe2011generallifestylesurvey.
5. Taylor D. Physical activity is medicine for older adults. *Postgrad Med J* 2014; 90: 26–32.
6. Watson KB, Carlson SA, Gunn JP et al. Physical inactivity among adults aged 50 years and older—United States, 2014. *MMWR Morb Mortal Wkly Rep* 2016; 65(36): 954–8.
7. Vopat BG, Klinge SA, McClure PK et al. The effects of fitness on the aging process. *J Am Acad Orthop Surg* 2014; 22: 576–85.
8. Jokl P, Sethi PM, Cooper AJ. Master's performance in the New York City Marathon 1983–1999. *Br J Sports Med* 2004; 38(4): 408–12.
9. Lepers R, Cattagni T. Do older athletes reach limits in their performance during marathon running? *Age (Dordr)* 2012; 34(3): 773–81.

10. Leyk D, Rüther T, Wunderlich M et al. Physical performance in middle age and old age: good news for our sedentary and aging society. *Dtsch Arztebl Int* 2010; 107(46): 809–16.
11. World Health Organization (WHO). World Report on Ageing and Health. Geneva, 2015.
12. Rockwood K, Song X, MacKnight C et al. A global clinical measure of fitness and frailty in elderly people. *CMAJ* 2005; 173(5): 489–95.
13. Fried LP, Tangen CM, Walston J et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001; 56(3): M146–57.
14. World Health Organization (WHO). Global Recommendations on Physical Activity for Health. Geneva, 2010.
15. Barengo NC, Antikainen R, Borodulin K et al. Leisure-time physical activity reduces total and cardiovascular mortality and cardiovascular disease incidence in older adults. *J Am Geriatr Soc* 2017; 65(3): 504–10.
16. Wen CP, Wai JPM, Tsai MK et al. Minimum amount of physical activity for reduced mortality and extended life expectancy: a prospective cohort study. *Lancet* 2011; 378(9798): 1244–53.
17. Jolliffe J, Rees K, Taylor RRS et al. Exercise-based rehabilitation for coronary heart disease. *Cochrane Database Syst Rev* 2001(1): CD001800.
18. Booth FW, Chakravarthy MV, Gordon SE et al. Waging war on physical inactivity: using modern molecular ammunition against an ancient enemy. *J Appl Physiol (1985)* 2002; 93(1): 3–30. doi: 10.1152/japplphysiol.00073.2002.
19. Diep L, Kwagyan J, Kurantsin-Mills J et al. Association of physical activity level and stroke outcomes in men and women: a meta-analysis. *J Womens Health (Larchmt)* 2010; 19(10): 1815–22.
20. Huang C-H, Yang G-G, Wu Y-T et al. Comparison of inspiratory muscle strength training effects between older subjects with and without chronic obstructive pulmonary disease. *J Formos Med Assoc* 2011; 110(8): 518–26.
21. Freitas FS, Ibiapina CC, Alvim CG et al. Relationship between cough strength and functional level in elderly. *Brazilian J Phys Ther* 2010; 14(6): 470–6.
22. Miranda APB, Gastaldi AC, de Souza HCD et al. The influence of physical fitness on respiratory muscle strength in the elderly. *Am J Sport Sci* 2015; 3(1): 6–12.
23. Lacasse Y, Brosseau L, Milne S et al. Pulmonary rehabilitation for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2002(3): CD003793.
24. Nylen ES, Kokkinos P, Myers J et al. Prognostic effect of exercise capacity on mortality in older adults with diabetes mellitus. *J Am Geriatr Soc* 2010; 58(10): 1850–4.
25. Ferriolli E, Pessanha FPAS, Marchesi JCLS. Diabetes and exercise in the elderly. In: *Diabetes and Physical Activity*. 2014: 122–9.
26. Esser S, Bailey A. Effects of exercise and physical activity on knee osteoarthritis.

Curr Pain Headache Rep 2011; 15(6): 423–30.

27. Roos EM, Dahlberg L. Positive effects of moderate exercise on glycosaminoglycan content in knee cartilage: a four-month, randomized, controlled trial in patients at risk of osteoarthritis. *Arthritis Rheum* 2005; 52(11): 3507–14.
28. Hallett MB, Andrish JT. Effects of exercise on articular cartilage. *Sports Med Arthrosc Rev* 1994; 2(1): 29–37.
29. Khosla S, Riggs BL. Pathophysiology of age-related bone loss and osteoporosis. *Endocrinol Metab Clin North Am* 2005; 34: 1015–30.
30. Marques EA, Mota J, Carvalho J. Exercise effects on bone mineral density in older adults: a meta-analysis of randomized controlled trials. *Age (Dordr)* 2012; 34(6): 1493–515.
31. Blake AJ, Morgan K, Bendall MJ et al. Falls by elderly people at home: prevalence and associated factors. *Age Ageing* 1988; 17(6): 365–72.
32. Prudham D, Evans JG. Factors associated with falls in the elderly: a community study. *Age Ageing* 1981; 10(3): 141–6.
33. Campbell AJ, Reinken J, Allan BC et al. Falls in old age: a study of frequency and related clinical factors. *Age Ageing* 1981; 10(4): 264–70.
34. Tinetti ME, Speechley M, Ginter SF. Risk factors for falls among elderly persons living in the community. *N Engl J Med* 1988; 319(26): 1701–7. doi: 10.1056/NEJM19881 2293192604.
35. Downton JH, Andrews K. Prevalence, characteristics and factors associated with falls among the elderly living at home. *Aging (Milano)* 1991; 3(3): 219–28.
36. Stalenhoef PA, Diederiks JPM, Knottnerus JA et al. A risk model for the prediction of recurrent falls in community-dwelling elderly: a prospective cohort study. *J Clin Epidemiol* 2002; 55(11): 1088–94.
37. Parkkari J, Kannus P, Palvanen M et al. Majority of hip fractures occur as a result of a fall and impact on the greater trochanter of the femur: a prospective controlled hip fracture study with 206 consecutive patients. *Calcif Tissue Int* 1999; 65(3): 183–7.
38. Peck WA, Riggs BL, Bell NH et al. Research directions in osteoporosis. *Am J Med* 1988; 84(2): 275–82.
39. Sherrington C, Whitney JC, Lord SR et al. Effective exercise for the prevention of falls: a systematic review and meta-analysis. *J Am Geriatr Soc* 2008; 56(12): 2234–43.
40. Davis JC, Robertson MC, Ashe MC et al. Does a home-based strength and balance programme in people aged ≥80 years provide the best value for money to prevent falls? A systematic review of economic evaluations of falls prevention interventions. *Br J Sports Med* 2010; 44: 80–9.
41. Robertson MC, Campbell AJ, Gardner MM et al. Preventing injuries in older people by preventing falls: a meta-analysis of individual-level data. *J Am Geriatr Soc* 2002; 50(5): 905–11.

42. Metter EJ, Conwit R, Tobin J et al. Age-associated loss of power and strength in the upper extremities in women and men. *J Gerontol A Biol Sci Med Sci* 1997; 52A(5): B267–76. doi: 10.1093/gerona/52A.5.B267.
43. Paterson DH, Warburton DE. Physical activity and functional limitations in older adults: a systematic review related to Canada's Physical Activity Guidelines. *Int J Behav Nutr Phys Act* 2010; 7: 38.
44. Stanaway FF, Gnjidic D, Blyth FM et al. How fast does the Grim Reaper walk? Receiver operating characteristics curve analysis in healthy men aged 70 and over. *BMJ* 2011;343(7837).
45. Gajewski PD, Falkenstein M. Physical activity and neurocognitive functioning in aging—a condensed updated review. *Eur Rev Aging Phys Act* 2016; 13(1): 1–7.
46. Viña J, Sanchis-Gomar F, Martinez-Bello V et al. Exercise acts as a drug; the pharmacological benefits of exercise. *Br J Pharmacol* 2012; 167: 1–12.
47. Kirk-Sanchez NJ, McGough EL. Physical exercise and cognitive performance in the elderly: current perspectives. *Clin Interv Aging* 2014; 9: 51–62.
48. Singh NA, Stavrinos TM, Scarbek Y et al. A randomized controlled trial of high versus low intensity weight training versus general practitioner care for clinical depression in older adults. *J Gerontol A Biol Sci Med Sci* 2005; 60(6): 768–76.
49. Salminen M, Isoaho R, Vahlberg T et al. Effects of a health advocacy, counselling, and activation programme on depressive symptoms in older coronary heart disease patients. *Int J Geriatr Psychiatry* 2005; 20(6): 552–8.
50. Warburton DER, Nicol CW, Bredin SSD. Health benefits of physical activity: the evidence. *CMAJ* 2006; 174(6): 801–9.
51. Chodzko-Zajko WJ, Proctor DN, Fiatarone Singh MA et al. American College of Sports Medicine position stand. Exercise and physical activity for older adults. *Med Sci Sports Exerc* 2009; 41(7): 1510–30.
52. Professional Associations for Physical Activity (Sweden). *Physical activity in the prevention and treatment of disease*. 2nd ed. Stockholm, Sweden: Swedish National Institute of Public Health, 2010.
53. Hamer M, Lavoie KL, Bacon SL. Taking up physical activity in later life and healthy ageing: the English longitudinal study of ageing. *Br J Sports Med* 2014; 48(3): 239–43.
54. Clemson L, Fiatarone Singh MA, Bundy A et al. Integration of balance and strength training into daily life activity to reduce rate of falls in older people (the LiFE study): randomised parallel trial. *BMJ* 2012; 345(7870).
55. Killingback C, Tsofliou F, Clark C. Older people's adherence to community-based group exercise programmes: a multiple-case study. *BMC Public Health* 2017; 17(1): 115.

#This chapter is dedicated to our great friend, champion of physical activity for older people, the late Professor A John Campbell.

*Thanks to 4th edition chapter authors Jack Taunton, Wendy Cook, Callista Haggis and Jacqueline Close

Chapter 32

The person with disability

with NICK WEBBORN and CHERI BLAUWET

When we're free to move, anything is possible.
Lauren Woolstencroft, Canadian alpine skier, eight-time Paralympic gold medallist

Participation and interest in sports for people with disabilities have increased exponentially over the last 70 years. Since the first formal competition in 1948, with only 16 competitors at the Stoke Mandeville Games, the Paralympic Games has become the third-biggest sporting event in the world. At the Rio 2016 Summer Paralympic Games, 4328 athletes from 159 countries competed in 22 sports in front of over two million spectators, and the International Paralympic Committee's (IPC) digital media activities engaged close to one billion people.

In this chapter we:

- provide a brief history of sport for people with disabilities
- discuss the importance of physical activity for the health of people with disabilities
- outline the classification system that promotes fair competition among persons with varied types of disabilities
- review the epidemiology of injury and illness at both the Summer and Winter Paralympic Games, and discuss important medical issues for Paralympic athletes
- discuss anti-doping in Paralympic sport
- highlight some key considerations for travelling with teams of athletes with disability.

SPORTS PARTICIPATION AMONG PEOPLE WITH DISABILITY

People with disabilities have participated in sport in at least a limited, unstructured way for more than 100 years. In 1944, Dr Ludwig Guttmann introduced sporting activity as part of the rehabilitation process for those with spinal cord injury at the Spinal Injuries Unit at Stoke

Mandeville Hospital in England. On the opening day of the 1948 Olympic Games in London, Guttmann arranged an archery contest between two spinal injury units on the lawns of the hospital. Thus began the Stoke Mandeville Games. Four years later a team of Dutch ex-servicemen joined the competition and the International Stoke Mandeville Games were founded.

Guttmann believed that 'by restoring activity in mind and body–by instilling self-respect, self-discipline, a competitive spirit and comradeship-sport develops mental attitudes that are essential for social reintegration'.[1] With time, athletics, swimming, table tennis and basketball increased the diversity of opportunities for people with disabilities. In 1960, the International Stoke Mandeville Games were held in Rome after the Olympic Games, and this launched the plan to hold these quadrennial games in the Olympic Games host city where possible. Between 1976 and 1980, opportunities for athletes with vision impairment, limb deficiencies and athletes with cerebral palsy were added to the program. Subsequently, athletes with a more diverse range of physical impairments and athletes with intellectual impairment were also included.

In 1985, the term 'Paralympic' was coined to describe a games 'parallel to the Olympics', and in 1989, the IPC was formed. Ever since, the games have taken the form of the modern Paralympic Games. Historically, different sports were organised by various international disability sport organisations, but as the movement progressed, many sports transitioned to be organised by their parallel International Federation (e.g. triathlon and cycling by the ITU and UCI, respectively) (Table 32.1).

Sport	Governing body	Paralympic Games I
Archery	World Archery*	1960–present
Para athletics	World Para Athletics	1960–present
Badminton	Badminton World Federation*	Starting 2020
Boccia	Boccia International Sports Federation	1984–present
Canoe	International Canoe Federation*	2016–present
Cycling	Union Cycliste Internationale*	1988–present
Equestrian	Fédération Équestre Internationale*	1996–present
Football 5-a-side	International Blind Sports Federation	2004–present
Goalball	International Blind Sports Federation	1980–present
Judo	International Blind Sports Federation	1988–present
Para powerlifting	World Para Powerlifting	1964–present
Rowing	World Rowing Federation*	2008–present
Shooting Para sport	World Shooting Para Sports	1976–present
Sitting volleyball	World Para Volley	1976–present
Para swimming	World Para Swimming	1960–present
Table tennis	International Table Tennis Federation*	1960–present
Taekwondo	World Taekwondo*	Starting 2020
Triathlon	International Triathlon Union*	2016–present
Wheelchair basketball	International Wheelchair Basketball Federation	1960–present
Wheelchair fencing	International Wheelchair & Amputee Sports Federation	1960–present
Wheelchair rugby	International Wheelchair Rugby Federation	2000–present
Wheelchair tennis	International Tennis Federation	1992–present

*integrated international federation

The IPC is the international representative body for elite sports for athletes with disabilities. Currently the majority of sport opportunities cater to athletes with physical disabilities; however, competition now also caters for those with visual disabilities and a cohort of elite athletes with intellectual disabilities.

Table 32.1 Sports of the 2020 Paralympic Games Page 444

Hearing-impaired athletes participate in the Deaflympics, organised by the international organisation Comité International des Sports des Sourds. The Special Olympics is an organisation for people with a full range of intellectual disability and focuses on participation at all ability levels, whereas the International Sports Federation for Persons with Intellectual Disability is a member of the IPC and is concerned with elite sport performance for athletes with intellectual disability meeting eligibility criteria and qualification standards.

PHYSICAL ACTIVITY FOR PEOPLE WITH DISABILITY

The potential health gains from regular physical activity (Chapter 2) that apply to all individuals apply equally to people with disabilities, but the ability to participate may be more challenging for a multitude of reasons–such as physiological restrictions associated with the disability, access to facilities and sociocultural factors. People with disabilities who are regularly physically active have lower healthcare costs and fewer visits to physicians and hospitals compared with their inactive counterparts.[2] In addition to the well-established musculoskeletal benefits of regular physical activity, people with disabilities can also gain psychological benefits, such as improvement in self-esteem.[3]

Prescribing exercise for people with disability

People with disabilities can take part in virtually every sport available, including high-risk sports such as mountain climbing, sub-aqua diving and skiing. In conventional sports (e.g. Page 445 swimming), often little or no modification is required, while in other sports (e.g. wheelchair basketball), specific adaptations may be required, such as sport-specific wheelchairs or prosthetics. Moreover, some sports have been specifically developed for certain disabilities (e.g. goalball for the visually impaired).

When helping a patient choose a sport or activity, it is important for the clinician to establish the patient's aims. If their aim is disease modification or health benefits generally, then one has to consider the difference between exercise and sport. Incorrectly, these terms are often used interchangeably. Sport is not always exercise, and exercise is not always sport. Sport implies competition and the physiological demands are determined by the discipline. Consider wheelchair sprint racing (anaerobic) in comparison to wheelchair road racing (aerobic), or pistol shooting (skill). Sport may also involve trauma, which is undesirable and can be particularly problematic in athletes with various medical conditions. For example, a high-risk crash in wheelchair racing may

result in fracture of the femur or proximal tibia in an athlete with osteoporotic lower limbs due to spinal cord injury.

The general principles of training discussed in Chapter 4, such as graded increase in duration, intensity and frequency of activity, apply equally to individuals both with and without a disability. However, additional considerations may be involved when selecting the mode of exercise that best matches an individual's disability and functional status. For example, an individual using a standard wheelchair may find it difficult to push with sufficient intensity to raise heart rate and blood pressure to the level required to reduce coronary risk factors and prevent type 2 diabetes. Thus, other modes of exercise, such as hand cycling, stationary hand cranking or swimming, may be needed to provide more intense and prolonged activity.

Providing a written exercise prescription for the individual with a disability parallels the process that would be implemented for any patient with an ongoing medical condition (Chapter 4), and includes determining the:

- patient's personal preference, to increase likelihood of participation and maintenance
- characteristics of the activity, such as physiological demands, coordination requirements and collision potential
- patient's medical conditions, cognitive ability and social skills
- availability and accessibility of facilities for training and competition
- availability of coaching and support staff
- availability and cost of equipment, such as specialist wheelchairs or prosthetic aids.

CLASSIFICATION TO DETERMINE ELIGIBILITY FOR PARTICIPATION

Classification is the process used to determine whether an athlete has an eligible impairment to compete in Paralympic sport, and subsequently, to group athletes into categories to ensure fair competition. The traditional system of classification for physical disabilities originated from a medical model of diagnosis based on certain impairments and severity of the individual's condition.

Physical activity guidelines for people with disability (WHO)

All people with disability should avoid inactivity. The World Health Organization (WHO) states that its Global Recommendations on Physical Activity for Health, excerpted below, can be applied to people with disability.[4]

- *Adults aged 18–64 should do at least 150 minutes of moderate-intensity aerobic physical activity throughout the week* [e.g. brisk walking, wheeling oneself in a wheelchair] *or do at least 75 minutes of vigorous-intensity aerobic physical activity* [e.g. jogging, wheelchair basketball] *throughout the week or an equivalent combination of moderate- and vigorous-intensity activity.*
- *Aerobic activity should be performed in bouts of at least 10 minutes duration.*
- *For additional health benefits, adults should increase their moderate-intensity aerobic physical*

activity to 300 minutes per week, or engage in 150 minutes of vigorous-intensity aerobic physical activity per week, or an equivalent combination of moderate- and vigorous-intensity activity.

- *Muscle-strengthening activities* [e.g. weight training, adapted yoga] *should be done involving major muscle groups on 2 or more days a week.*
- *Older adults* [aged 65 years and above], *with poor mobility, should perform physical activity to enhance balance and prevent falls on 3 or more days per week.*

Eligible impairment types in the Paralympic movement

- Hypertonia
- Ataxia
- Athetosis
- Impaired muscle power
- Impaired passive range of movement
- Leg length difference
- Limb deficiency
- Short stature
- Vision impairment
- Intellectual impairment

As the Paralympic movement has become more inclusive, so has the range of diagnoses and impairment types. The classification process has evolved into a more detailed study of the impact of the impairment on the individual's ability to perform the sport. The IPC now lists 10 eligible impairments (see box) for which there are minimum disability criteria for each sport. Each sport then has its own system of athlete evaluation and observation used to assign a sport class for competition. Each classification system must meet the common standards of the IPC's 2015 Athlete Classification Code.[5]

Team sports may use a system to enable athletes with different levels of ability to play together, meaning that individuals with tetraplegia, paraplegia or an amputation can all play alongside each other in the same team. In wheelchair basketball, for example, there is a points system that allocates points according to each athlete's degree of disability, from 1 point going up in half-point intervals to 4.5 points, creating eight classes. A higher classification number represents a greater ability to perform basketball-specific skills. During gameplay, coaches must then select players who contribute to a maximum of 14 points on the court at any one time.

Athletes with visual impairment and athletes with intellectual impairment each have their own system for classification (see boxes). The IPC has established three international research centres to lead on sport-specific classification research projects–one each for physical, visual and

intellectual impairment–recognising that classification is not necessarily linear and needs to become more sport specific. For example, for athletes with intellectual impairment, rapid decision making is more of a requirement in wheelchair basketball than it is in sprinting, while changes in ambient lighting can affect individuals with visual impairment differently depending on the sporting environment.

To be considered eligible to compete as an athlete with an intellectual impairment in elite Para sport, one must meet the eligibility criteria. These are based on World Health Organization (WHO) and American Association on Intellectual and Developmental Disabilities (AAIDD) research and guidance.

PRACTICE PEARL

When treating a patient with an intellectual disability, the clinician should seek informed consent from the patient's legal guardian, if necessary.

Classification schemes

1. Athletes with visual impairment
B1: Athletes have either a total absence of perception of light in both eyes or some perception of light but are unable to recognise the form of a hand at any distance and in any direction.

B2: Athletes have the ability to recognise the form of a hand to a visual acuity of 2/60 and/or a visual field of less than 5°.

B3: Athletes have a visual acuity of above 2/60 to a visual acuity of 6/60 and/or a visual field of more than 5° and less than 20°.

2. Athletes with intellectual impairment
To qualify as intellectually impaired, an athlete must have an impairment diagnosed before 18 years of age, with resultant:

1. IQ of 75 or lower
2. Significant behaviour limitations in conceptual, social and practical adaptive skills.

Traditional medical impairment types

- Amputation/limb deficiency
- Cerebral palsy
- Spinal cord related disability

- Intellectual impairment
- Visual impairment
- *Les Autres*—used to describe physical impairments that are not described by above types

Although the current system of classification is impairment based, an athlete's medical diagnosis or disability remains important for the clinician and treating team, for planning healthcare services at events and predicting potential complications. The majority of athletes will have 'traditional disability types', as listed in the box. Specific medical issues related to these impairment and disability types are discussed later in this chapter.

MEDICAL ISSUES IN SUMMER SPORT FOR PARA ATHLETES

Summer sports have been the staple of the Paralympic movement since its beginning. Athletes with all varieties of impairment compete in a full program of sports, as outlined in Table 32.1.

Given the size and scope of the summer Paralympic games program, a wide spectrum of medical services must be available to address both acute and chronic injury and illness in athletes with varied impairments.

Common summer sport injuries

Data from prior summer Paralympic games demonstrate a high incidence of pre-competition injury, suggesting that clinicians must be prepared to address injuries even prior to the start of competition.[7]

The likelihood of sport-related injury varies according to sport, with football 5-a-side (football for athletes with visual impairment) repeatedly showing the highest incidence of injury, likely due to injuries sustained during on-field collisions.[7, 8]

Overuse shoulder injuries

In comparison to Olympic athletes, Paralympic athletes experience a greater proportion of injuries to the upper extremities, particularly the shoulders.[7, 8] Athletes who use the upper limbs for both daily mobility as well as sport (i.e. wheelchair users) are at highest risk of injury and are predisposed to early-onset degenerative rotator cuff pathology, glenoid labral pathology and subsequent osteoarthritis. These pathologies may be due to the weight-bearing stress sustained by the shoulder during daily activities such as transfers, as well as scoliosis, poor seating position and muscle imbalance that results from pushing techniques–all potentially contributing to alterations in scapular stabilisation and abnormal patterns of movement.[9] Athletes in throwing disciplines (e.g. shot-put, discus and javelin) are also at particularly high risk of shoulder injury.[10]

As reducing the load on an injured shoulder in a wheelchair athlete involves loss of independence with activities of daily living, prevention is paramount and should include:

- progression of training loads

- equipment that is fitted correctly and well maintained
- strengthening and stabilisation of scapula and rotator cuff
- flexibility–focusing on potentially tight pectoralis and scalene muscles
- early reporting and assessment of injuries.

Common summer sport illnesses

The patterns of illness in Paralympic athletes at the summer games have been shown to mirror those of Olympic athletes, with a few important differences. Although respiratory illness is still shown to have the highest incidence per body system, Paralympic athletes experience a higher incidence of genitourinary illness and skin-related illness. Skin-related illness disproportionately impacts athletes with limb deficiency (likely due to issues at the stump-socket interface), as well as athletes with spinal cord injury (likely due to insensate areas).[11]

Genitourinary illness

Genitourinary illness disproportionately impacts athletes with spinal cord injury due to the presence of neurogenic bladder, resulting in poor storage and voiding function, with resultant need for self-catheterisation. Subtle clinical signs and symptoms may be the only indication of infection. In addition to classic symptoms of fever, dysuria and pelvic discomfort, reduced sporting performance, malaise, reduced appetite or 'feeling not quite right' can all be common presenting complaints.[12]

PRACTICE PEARL

Travelling clinicians should carry a supply of urine dipsticks to test for infection (leukocytes, nitrites and blood).

Prevention is again paramount; hydration, cranberry juice and aseptic catheter technique are all appropriate strategies. Many individuals with spinal cord injury have bacteriuria, and routine urinary dipstick or microscopy, culture and sensitivity testing is not recommended for these individuals. Likewise, routine antibiotic prophylaxis is not recommended in asymptomatic individuals, as this promotes the development of drug-resistant bacteria. Asymptomatic bacteriuria in spinal cord-injured athletes should not be treated. However, symptomatic athletes should have urine cultured and be treated with appropriate antibiotic therapy.[12]

Autonomic dysfunction

Athletes with spinal cord injury are at higher risk for certain conditions related to autonomic

dysfunction.[13]

Thermoregulation

Athletes may be vulnerable to heat injury due to a reduction in peripheral receptor and cooling mechanisms. Sweating may be impaired below the level of spinal injury. Athletes need to hydrate appropriately and acclimatise. Cooling and pre-cooling strategies offset the risk of heat illness and may translate into improved functional capacity.[14] Strategies include using misting fans on the bench, placing ice packs on the axillae and neck, and pre-cooling with ice slushy drinks or ice baths.

There is also an increased inability to maintain body temperature in a cold environment because of lack of sensory input and shivering response. Thus, adequate preventive measures, including appropriate clothing, are particularly important for the person with disabilities. For more information about exercising in the heat and the cold, refer to Chapters 23 and 24, respectively.

Autonomic dysreflexia

Athletes and clinicians must be aware of the potential presence of autonomic dysreflexia. Any nociceptive input below the level of the lesion can be the catalyst, such as a blocked catheter causing bladder distension, constipation, urinary calculi or ingrown toenails. The nociceptive stimulus results in inappropriate levels of noradrenalin (norepinephrine) secretion, resulting in hypertension, sweating, skin blotching above the level of the lesion and a pounding headache.

PRACTICE PEARL

Autonomic dysreflexia is a medical emergency that requires urgent attention to remove the nociceptive stimulus and reduce blood pressure with medication.

Some wheelchair athletes have found that when they are in the dysreflexic state while exercising, their rating of perceived exertion is reduced. Consequently, some athletes started to activate autonomic dysreflexia intentionally to improve their performance, which became known as 'boosting'. The problem of boosting first became evident at the Paralympic Games in Atlanta in 1996 and prompted the IPC to address boosting's ethical and health implications.[15] In 2004, the IPC banned boosting, and athletes most at risk of boosting have since had their blood pressure measured just prior to competition. Any athlete found to have a systolic blood pressure >180 mmHg after test and retest has not been allowed to compete on health grounds, and becomes subject to further investigation on whether boosting was intentionally induced. Not one athlete was found to have a reading over 180 mmHg at the Paralympic Games in Beijing in 2008, and only one was found at London in 2012. In 2016, the IPC medical committee revised its blood pressure threshold used to determine a dysreflexic state from 180 mmHg to 160 mmHg.[16]

Bone health

Any athlete with altered weight-bearing status may be susceptible to osteopenic or osteoporotic changes in their lower limbs and spine. This may result in fractures caused by minimal trauma or from impact collisions in sports such as wheelchair racing, basketball or quad rugby. In unilateral amputees, the affected limb may exhibit reduced bone mineral density.[17]

Clinicians must raise their index of suspicion for fractures in the wheelchair athlete. Even though the lower limbs may not be used for ambulation, fracture healing is important, as persistent deformity may result in increased difficulty with transferring to and from the chair and performing activities of daily living.

Energy needs

Para athletes have energy needs that differ from able-bodied athletes. Both male and female athletes with spinal cord injury demonstrate risk factors for low energy availability (LEA); however, the prevalence of LEA in Para athletes is incompletely characterised.[18] Characterising the effects of LEA on bone health in Para athletes requires consideration of baseline effects of each Page 449 individual's underlying disability, and more work is needed in this area.

Some important considerations regarding the energy needs of Para athletes are summarised here in brief.

- Male and female athletes with spinal cord injury may monitor or restrict body weight for sport and are at risk of nutrient deficiencies.[19, 20]
- Female athletes with a disability are at disproportionate risk for relative energy deficiency in sports (RED-S), dependent on sport and disability type.[18]
- The presence of central neurologic injury may result in alterations of the hypothalamic-pituitary axis and baseline menstrual function, regardless of energy status.[21-23]
- Athletes with central neurologic injury such as cerebral palsy, who demonstrate aberrant movement patterns that include dyskinesis or athetosis, may have higher energy expenditures than similar athletes without such non-purposeful movements.[24]
- Amputee athletes may have higher energy needs in the setting of prosthetic use and resultant gait asymmetry.[25]

MEDICAL ISSUES IN WINTER SPORT FOR PARA ATHLETES

In 1976, the first Winter Paralympic Games were held in Sweden, with only 53 athletes from 16 countries taking part in alpine and cross-country skiing for amputee and visually Page 450 impaired athletes. More recently, the 2018 Paralympic Winter Games, in PyeongChang, hosted 670 athletes competing across six sports: alpine skiing, biathlon, cross-country skiing, Para ice hockey, Para snowboard and wheelchair curling.

CASE STUDY

Dylan Alcott, Australia—wheelchair tennis and wheelchair basketball

I love having a disability and I want more people to feel like that.

Dylan Alcott (Fig. 32.1) is a wheelchair basketball and wheelchair tennis Paralympic champion who has become a household name in Australia for his efforts both on and off the court.

Figure 32.1 Alcott competing at the Australian Open in 2017 in wheelchair tennis—a sport that requires athletes to use their arms to accelerate, manoeuvre and swing their racquet, cumulatively placing great demands and stress on the shoulders

COURTESY OF DANIEL FRIEDMAN

Alcott became a paraplegic at just three days old, after undergoing surgery to remove a spinal cord tumour, and survived an ongoing battle during his first years of life.

As he grew up, Alcott was teased by other kids and frequently called 'the cripple' at school. As a consequence, he struggled throughout his childhood to come to terms with his disability. However, this all changed after he discovered Para sport at the age of 12—and he has not looked back since.

Not only did it get me fitter, but I also met people who were just like me, other people in wheelchairs who were smiling ... doing things that I didn't know if I could do. I didn't know any positive role models with disability [until then], so it was a real eye-opening experience for me.[26]

At 17 years of age, Alcott became the youngest wheelchair basketball gold medallist in history, at the 2008 Beijing Paralympics, going on to win two more gold medals at the 2016 Rio Paralympics, this time for wheelchair tennis. Since making the switch from basketball to tennis, Alcott has won four straight quad wheelchair singles titles at the Australian Open, 2015–2018, and a US Open quad championship title in 2015. In 2016, Alcott was awarded Paralympian of the Year and the Newcombe Medal.

As well as being a dual Paralympian, Alcott is an international speaker, radio broadcaster and disability advocate. He recently founded his own foundation (www.dylanalcottfoundation.com.au) to give people with a disability greater access to study and sport. In 2018, his foundation hosted its first major fundraiser, Ability Fest, an Australian music festival that aims to empower people of all abilities and backgrounds to experience live music.

Sources: references 30, 31, 32

Common winter sport injuries

Injury patterns have been monitored at the Winter Paralympic Games since 2002; however, the incidence of injury was only first documented at the Sochi 2014 Games.[27]

The incidence of injury was substantially greater at the Sochi Paralympic Winter Games compared to the Sochi Winter Olympic Games (IR 26.5 in Paralympic vs IR 7.8 in Olympic).[27] Additionally, the incidence of injury was much greater at the Sochi Winter Paralympic Games, compared to the London Summer Paralympic Games (IR 12.7), likely due to higher risk sports (particularly alpine ski and snowboard) in the Winter Games, as well as colder environmental conditions.

Acute injuries are common at the Winter Paralympic Games, accounting for 67% of all injuries–which is a different pattern to that observed in the summer Paralympic Games.[8, 27]

Sport-specific injuries

Typically, alpine events cater to the visually impaired, spinally injured or the limb-deficient athlete. Guide skiers are used for the visually impaired, and there are sitting and standing events for different physical impairments.

Ambulatory athletes are at risk of the usual skiing injuries, such as head injury or anterior cruciate ligament rupture. As small outriggers are used to control the ski in the sitting classes, forceful impact landing on the outrigger can cause wrist fracture or shoulder injury. The shoulder is the most common site of injury in sitting athletes. The cross-country events are associated with overuse injuries, and the sit-skier may experience shoulder and elbow problems.

Biathlon (skiing and shooting) can be performed by the visually impaired using a sighting mechanism that utilises an audible signal with increasing tone as the competitor points towards the centre of the target.

Para ice hockey is an adaptation of ice hockey. Competitors sit on the sled and skate by pushing two sticks, which are also used to strike the puck. A variety of disability groups participate in this team sport. Injuries occur by direct contact between players, use of the stick (intentionally or

accidentally), or by being hit by the puck. Athletes with spinal cord injury-induced low bone mass are susceptible to fracture in this sport. In 2002, several lower limb fractures were identified,[28] but changes in the protective wear and regulations regarding sled height have reduced the risk of lower limb fracture. Concussion remains a concern in this sport although accurate incidence data are lacking, partly through poor reporting.

Wheelchair curling was introduced to the Paralympic Winter Games in Torino in 2006 and is typically not associated with injury, although athletes may be susceptible to sports-related illness.

Common winter sport illnesses

The first systemic monitoring of illness in major Paralympic competition took place at the Sochi 2014 Paralympic Games.[29]

Although illness patterns are similar in comparison to the Olympic Games, the proportion of athletes impacted by illness is much higher at the Paralympic Games (17% in Paralympic vs 8% in Olympic).[29] This may be due to the impact of the athlete's disability on factors such as:

- immune function, which is reduced in athletes who are immunocompromised or on chronic glucocorticoids
- neurogenic bladder, resulting in higher risk of genitourinary illness
- reduced pulmonary function in athletes with quadriplegia or quadriparetic cerebral palsy
- increased age of athletes competing in the Winter Paralympic Games.

Little is known about the types or incidence of illness in non-elite winter Para athletes.

ANTI-DOPING ISSUES

Both the IOC and the IPC are signatories to the World Anti-Doping Code. Thus, the World Anti-Doping Agency (WADA) Prohibited List and the policies that guide testing are equally applicable to both Olympic and Paralympic athletes. In Para sport, it is more likely that athletes need to take prohibited medications in order to manage medical conditions. To take these medications, they must successfully complete a therapeutic use exemption (TUE) application process. A successful application has to meet the same international standard as for able-bodied athletes.

There are some differences to the urine sample collection process, which may vary according to disability. Athletes who use intermittent catheterisation are permitted to use their own catheter to collect the urine sample, and it is recommended that a sterile catheter is always used for doping control purposes in order to avoid potential contamination. For athletes who use a condom and leg bag drainage system, the contents of the leg bag must first be emptied, and a fresh sample of urine collected. This is to avoid the potential for inserting a 'clean' sample of urine into the leg bag prior to competition.

Athletes who are visually impaired may receive assistance to complete doping control forms and may select their own personal representative to accompany them in the sample collection process. The athlete's representative observes the doping control officer during the

sample collection process to ensure that there is no tampering with the sample. Athletes with an intellectual disability need to be accompanied by a representative who understands the doping control process.

The abuse of prohibited substances does not appear to be widespread in Para sport; however, concerning trends have been noted in certain high-risk sports such as powerlifting. Additionally, some controversy remains regarding TUE for certain prohibited substances that may be used at a higher rate in individuals with a disability, such as beta blockers.

Overall, because many Para athletes train in a resource-poor environment with suboptimal access to medical services, education and raising awareness regarding anti-doping rules and regulations remains a challenge.

TRAVEL WITH TEAMS

Travel with teams is discussed in Chapter 47 of *Clinical Sports Medicine Volume 1: Injuries.* Athletes with disability may have specific needs above and beyond the needs of able-bodied athletes.

CASE STUDY

Lauren Woolstencroft, Canada—Para alpine skiing

Lauren Woolstencroft (Fig. 32.2) is one of the most decorated Paralympians ever, having won 10 medals, including eight gold, across three Paralympic Games, as well as eight world championship titles and over 50 World Cup medals for alpine skiing. In 2006, the International Paralympic Committee named her Athlete of the Year and, in 2010, she became the first Canadian to win five gold medals at a single Paralympic Winter Games. Brianne Law, former Canadian Para Alpine Skiing director, described Woolstencroft as 'One of the greatest ambassadors the Paralympic movement has ever had'.

Figure 32.2 Lauren Woolstencroft competed with two leg prostheses and a modified ski pole tethered to her right hand. She skied in five Paralympic disciplines in the 2010 Winter Paralympic Games in Whistler, Canada, and won every event

GETTY IMAGES/EZRA SHAW

Lauren was born with bilateral fibular hemimelia and missing her left arm below the elbow. Hemimelia is a congenital condition that can indicate the absence of a longitudinal bone of the lower arm or leg (e.g. fibula, tibia, radius or ulna). Although in Lauren's case the cause is unknown, hemimelia may result from vascular insult to the foetus while in utero, amniotic band syndrome or maternal exposure to teratogens. At nine months of age, Lauren underwent a bilateral Syme's amputation to facilitate the fitting of prosthetic legs.

Lauren learned to tie shoelaces with one hand, learned to skip, to ride a bike, and was first introduced to skiing at four years of age—but did not become a competitive skier until she turned 14, spending her time competing in horseback riding instead. Woolstencroft skied wearing two lower-leg prosthetics, a left arm prosthetic to enhance balance control and used a normal ski pole in her fully operational right hand.

Her training program included support from alpine skiing specialist strength and conditioning coaches. The programs were written for specific winter sports disciplines and then adapted to individual requirements. Lauren was able to utilise resistance equipment for her left arm with the addition of strapping to allow an appropriate load to be applied to her upper arm and shoulder musculature.

Two years after starting to ski competitively, Woolstencroft competed in her first World Cup alpine skiing event and was soon named in the Canadian Para alpine team. Four years later, she was bound for her first Paralympics in Salt Lake City, Utah, in 2002. Looking back on her 12-year career, arguably no Canadian woman has ever dominated a sport the way Woolstencroft did alpine skiing.

The simple logistics of air travel for a team of wheelchair users, including boarding or disembarking an aircraft, take additional time and may require lifting and handling. Page 452 Toileting on board an aircraft often requires the use of a small-wheeled aisle chair and can be difficult for the non-ambulatory athlete, resulting in a purposeful reduction in fluid intake and resultant dehydration. This may be particularly detrimental for an athlete requiring long-haul travel to reach their competition, and places the athlete at higher risk for genitourinary illness such as urinary tract infection.

Transport at the destination needs to be accessible, both to and from the airport but also between the athlete's accommodation and the sports venues. The team clinician should aim to be familiar with the accessibility of toilets, rooms and sports facilities in advance of competition, as suboptimal access may impact the risk of injury and illness in this athlete cohort.

Prolonged sitting without the use of a pressure-relieving cushion may result in high pressure areas on the skin and resultant skin-related illness, particularly in athletes with reduced sensation due to neurologic injury. Athletes should strive to take pressure-relieving measures during the journey and check high pressure areas on arrival.

PRACTICE PEARL

The key to prevention of pressure ulcers is regular inspection of the skin after activity or travel, especially international or long-haul flying, looking for tell-tale red areas and abrasions.

The risk of deep vein thrombosis exists for all long-haul passengers, including Para athletes. Dependent oedema can be a particular problem among individuals with lower extremity paralysis, who do not have the capacity to use the active muscle pump, and compression stockings can be appropriate. Oedema may also be of concern for athletes with limb deficiency, wherein travel-related fluid shifts may result in changes to the size and/or shape of the residual limb and thus impact prosthetic fit.

REFERENCES

1. Webborn AD. Fifty years of competitive sport for athletes with disabilities: 1948–1998. *Br J Sports Med* 1999; 33(2): 138.
2. Shephard RJ. Benefits of sport and physical activity for the disabled: implications for the individual and for society. *Scand J Rehabil Med* 1991; 23(2): 51–9.
3. Nemček D. Self-esteem in people with physical disabilities: differences between active and inactive individuals. *Acta Facultatis Educationis Physicae Universitatis Comenianae* 2017; 57(1): 34–47.
4. World Health Organization (WHO). Global Recommendations on Physical Activity for Health. Geneva, 2010.
5. International Paralympic Committee (IPC). IPC Athlete Classification Code. Bonn, Germany, 2015.
6. International Paralympic Committee (IPC). International Standard for Eligible Impairments Bonn, Germany, 2016.
7. Derman W, Runciman P, Schwellnus M et al. High precompetition injury rate dominates the injury profile at the Rio 2016 Summer Paralympic Games: a prospective cohort study of 51 198 athlete days. *Br J Sports Med* 2018; 52(1): 24–31. doi: 10.1136/bjsports-2017-098039.
8. Willick SE, Webborn N, Emery C et al. The epidemiology of injuries at the London 2012 Paralympic Games. *Br J Sports Med* 2013; 47(7): 426–32. doi: 10.1136/bjsports-2013-092374.
9. Heyward OW, Vegter RJK, de Groot S et al. Shoulder complaints in wheelchair athletes: a systematic review. *PLoS ONE* 2017; 12(11): e0188410. doi: 10.1371/journal.pone.0188410.
10. Blauwet CA, Cushman D, Emery C et al. Risk of injuries in Paralympic track and field

differs by impairment and event discipline: a prospective cohort study at the London 2012 Paralympic Games. *Am J Sports Med* 2016; 44(6): 1455–62. doi: 10.1177/0363546516629949.

11. Derman W, Schwellnus MP, Jordaan E et al. Sport, sex and age increase risk of illness at the Rio 2016 Summer Paralympic Games: a prospective cohort study of 51 198 athlete days. *Br J Sports Med* 2018; 52(1): 17–23. doi: 10.1136/bjsports-2017-097962.
12. Compton S, Trease L, Cunningham C et al. Australian Institute of Sport and the Australian Paralympic Committee position statement: urinary tract infection in spinal cord injured athletes. *Br J Sports Med* 2015; 49(19): 1236–40. doi: 10.1136/bjsports-2014-094527.
13. Hou S, Rabchevsky AG. Autonomic consequences of spinal cord injury. *Compr Physiol* 2014; 4(4): 1419–53. doi: 10.1002/cphy.c130045.
14. Webborn N, Price MJ, Castle PC et al. Effects of two cooling strategies on thermoregulatory responses of tetraplegic athletes during repeated intermittent exercise in the heat. *J Appl Physiol (1985)* 2005; 98(6): 2101–7.
15. Mazzeo F, Santamaria S, Iavarone A. 'Boosting' in Paralympic athletes with spinal cord injury: doping without drugs. *Funct Neurol* 2015; 30(2): 91–8. doi: 10.11138/FNeur/2015.30.2.091.
16. International Paralympic Committee (IPC). The IPC tightens rules to clamp down on boosting. 2016. https://www.paralympic.org/news/ipc-tightens-rules-clamp-down-boosting.
17. Sherk VD, Bemben MG, Bemben DA. BMD and bone geometry in transtibial and transfemoral amputees. *J Bone Miner Res* 2008; 23(9): 1449–57. doi: 10.1359/jbmr.080402.
18. Blauwet CA, Brook EM, Tenforde AS et al. Low energy availability, menstrual dysfunction, and low bone mineral density in individuals with a disability: implications for the Para athlete population. *Sports Med* 2017; 47(9): 1697–708. doi: 10.1007/s40279-017-0696-0.
19. Krempien JL, Barr SI. Risk of nutrient inadequacies in elite Canadian athletes with spinal cord injury. *Int J Sport Nutr Exerc Metab* 2011; 21(5): 417–25.
20. Krempien JL, Barr SI. Eating attitudes and behaviours in elite Canadian athletes with a spinal cord injury. *Eat Behav* 2012; 13(1): 36–41. doi: 10.1016/j.eatbeh.2011.11.005.
21. Ripley DL, Harrison-Felix C, Sendroy-Terrill M et al. The impact of female reproductive function on outcomes after traumatic brain injury. *Arch Phys Med Rehabil* 2008; 89(6): 1090–6. doi: 10.1016/j.apmr.2007.10.038.
22. Colantonio A, Mar W, Escobar M et al. Women's health outcomes after traumatic brain injury. *J Womens Health (Larchmt)* 2010; 19(6): 1109–16. doi: 10.1089/jwh.2009.1740.
23. Ranganathan P, Kumar RG, Davis K et al. Longitudinal sex and stress hormone

profiles among reproductive age and post-menopausal women after severe TBI: a case series analysis. *Brain Inj* 2016; 30(4): 452–61. doi: 10.3109/02699052.2016.1144081.

24. Crosland J, Boyd C. Cerebral palsy and acquired brain injuries. In: Broad E, ed. *Sports Nutrition for Paralympic Athletes*. Boca Raton, FL: CRC Press, 2014: 91–105.
25. Gonzalez EG, Corcoran PJ, Reyes RL. Energy expenditure in below-knee amputees: correlation with stump length. *Arch Phys Med Rehabil* 1974; 55(3): 111–19.
26. Day L. Dylan Alcott wants to make disability sexy. 14 February 2018. http://www.abc.net.au/news/2018-02-14/dylan-alcott-defies-disability-for-fourth-australian-open-win/9415392.
27. Derman W, Schwellnus MP, Jordaan E et al. High incidence of injury at the Sochi 2014 Winter Paralympic Games: a prospective cohort study of 6564 athlete days. *Br J Sports Med* 2016; 50(17): 1069–74. doi: 10.1136/bjsports-2016-096214.
28. Webborn N, Willick S, Reeser JC. Injuries among disabled athletes during the 2002 Winter Paralympic Games. *Med Sci Sports Exerc* 2006; 38(5): 811–15. doi: 10.1249/01.mss.0000218120.05244.da.
29. Derman W, Schwellnus MP, Jordaan E et al. The incidence and patterns of illness at the Sochi 2014 Winter Paralympic Games: a prospective cohort study of 6564 athlete days. *Br J Sports Med* 2016; 50(17): 1064–8. doi: 10.1136/bjsports-2016-096215.
30. https://www.abc.net.au/news/2018-02-14/dylan-alcott-defies-disability-for-fourth-australian-open-win/9415392
31. https://www.abc.net.au/news/2018-04-07/melbournes-first-ability-fest-the-music-festival-for-everyone/9630116
32. https://dylanalcottfoundation.com.au/about-dylan/

PART E

Performance and ethics

Chapter 33

Nutrition for performance

by JAMES MORTON and GRAEME CLOSE

Nutrition is massively important if you want to train at your best.
Geraint Thomas, 2018 Tour de France Champion

Sport nutrition is one of the most rapidly growing subdisciplines of sport science and medicine, and its importance is becoming increasingly recognised across multiple sports. Many sport governing bodies, national institutes, Olympic sports and professional sports teams now employ sport nutrition practitioners on a full-time or consultancy basis, and they are considered an integral part of the wider sports medicine team. In North America and Australia, the accredited career path for the sport nutritionist arises from formal training in dietetics and hence the sport dietitians will have relevant clinical training. Alternatively, in the United Kingdom, sport nutritionists can gain formal accreditation (with the Sport and Exercise Nutrition Register, SENr) through a non-dietetics pathway that is often grounded in sport science. Regardless of career entry, all sport nutritionists and dietitians (or 'performance nutritionists' as they are often called) should work towards a common objective:

> *To provide evidence-based, sport- and athlete-specific nutrition interventions that aim to optimise performance, training adaptations, body composition and recovery as well as ensuring athlete health and wellbeing at all times.*

The sport nutritionist has a variety of roles and responsibilities (Table 33.1) and should work closely with various members of the athlete support staff, such as team physician, sport scientists, strength and conditioning coaches, physiotherapists (and soft tissue therapists), psychologists, chefs and, of course, the technical coaching staff themselves. Effective and clear communication between all team members is essential to ensure a high-quality and, above all, consistent multidisciplinary service provision.

Table 33.1 Typical responsibilities of the sport nutritionist working in elite sport

General
• Devise an evidence-based nutrition philosophy emphasising a 'food first' approach, and communicate to all key stakeholders
• Devise, implement and monitor an evidence-based, safe and legal sports supplement policy
• Devise, implement and monitor training day nutrition and hydration strategies for both food and supplements
• Devise, implement and monitor competition day nutrition and hydration strategies for both food and supplements
• Devise, implement and monitor nutrition and hydration strategies for travelling
• Monitor body composition and develop and implement strategies to ensure optimal but safe values
Individual athlete
• Undertake one-on-one athlete consultations and devise and implement athlete-specific nutrition, hydration and supplement strategies to optimise performance, training adaptations and recovery
• Devise and implement athlete-specific nutrition, hydration and supplement strategies to achieve optimal and safe body composition
• Devise and implement athlete-specific nutrition, hydration and supplement strategies for injured athletes
• Liaise with athlete's parents, guardians, houseparents or partners (where appropriate) to ensure effective nutrition support
• Enhance general health of the athlete
Educational
• Develop group and individual strategies to ensure continual athlete and staff education on sport nutrition-related issues
• Develop and implement shopping and cooking education programs for athletes, partners, houseparents and staff
• Educate staff within the wider athlete support team and run internal continuing professional development (CPD) programs
Personal
• Gain appropriate academic and professional qualifications
• Ensure continual critical evaluation of classic and contemporary sport nutrition topics and, if possible, engage in academic research
• Understand the culture of the sport
• Implement and adhere to an ethical code of conduct
• Develop professional, practical and technical skills through ongoing CPD and reflective practice
• Keep accurate and professional notes

In this chapter we provide the sports clinician with a contemporary review of the theoretical and practical basis of performance nutrition. We begin by providing a brief overview of energy storage and metabolism, to allow the reader to consider the energetic demands of their particular sport. We then outline a series of assessments that may help the sports clinician perform a nutrition assessment of the athlete. The macronutrient (carbohydrates, protein and fats), micronutrient (vitamins and minerals) and fluid requirements for performance are then discussed, as well as some evidence-based supplements that can enhance physical performance and training adaptations. Finally, we outline some special nutrition considerations that sports clinicians may encounter when working with elite athletes, before closing by discussing emerging themes within nutrition periodisation.

OVERVIEW OF EXERCISE METABOLISM

Prior to intervening with a nutrition strategy, it is vital that clinicians possess a sound

understanding of exercise metabolism, so that appropriate consideration can be given to both energy storage and substrate utilisation during exercise. Although a detailed understanding of such processes is beyond the scope of the present text (readers should consult MacLaren and Morton[1]), it is pertinent to at least provide a brief overview here (Table 33.2).

Table 33.2 Overview of energy storage within key tissues of the human body (values are representative of a 75 kg male)

Substrate	Amount (kg)	Energy (kcal)
Carbohydrate		
Plasma glucose	0.02	78
Liver glycogen	0.1	388
Muscle glycogen	0.4	1 550
Total	**0.52**	**2 000**
Fat		
Plasma free fatty acids	0.0004	4
Plasma triglycerides	0.004	39
Adipose tissue	10	83 333
Intramuscular triglycerides	0.3	2616
Total	**10.3**	**86 000**

Energy-yielding processes have typically been described as aerobic (i.e. energy is produced with the utilisation of oxygen) or anaerobic (i.e. energy is produced without the use of oxygen). In its simplest terms, the 100-metre sprinter relies predominantly on anaerobic metabolism, whereas the marathon runner relies on aerobic metabolism. However, there are many sporting events Page 455 that exist on the continuum between these two extremes and that require appropriate development of both the anaerobic and aerobic energy-producing pathways in order to maximise performance during competition (Fig. 33.1).

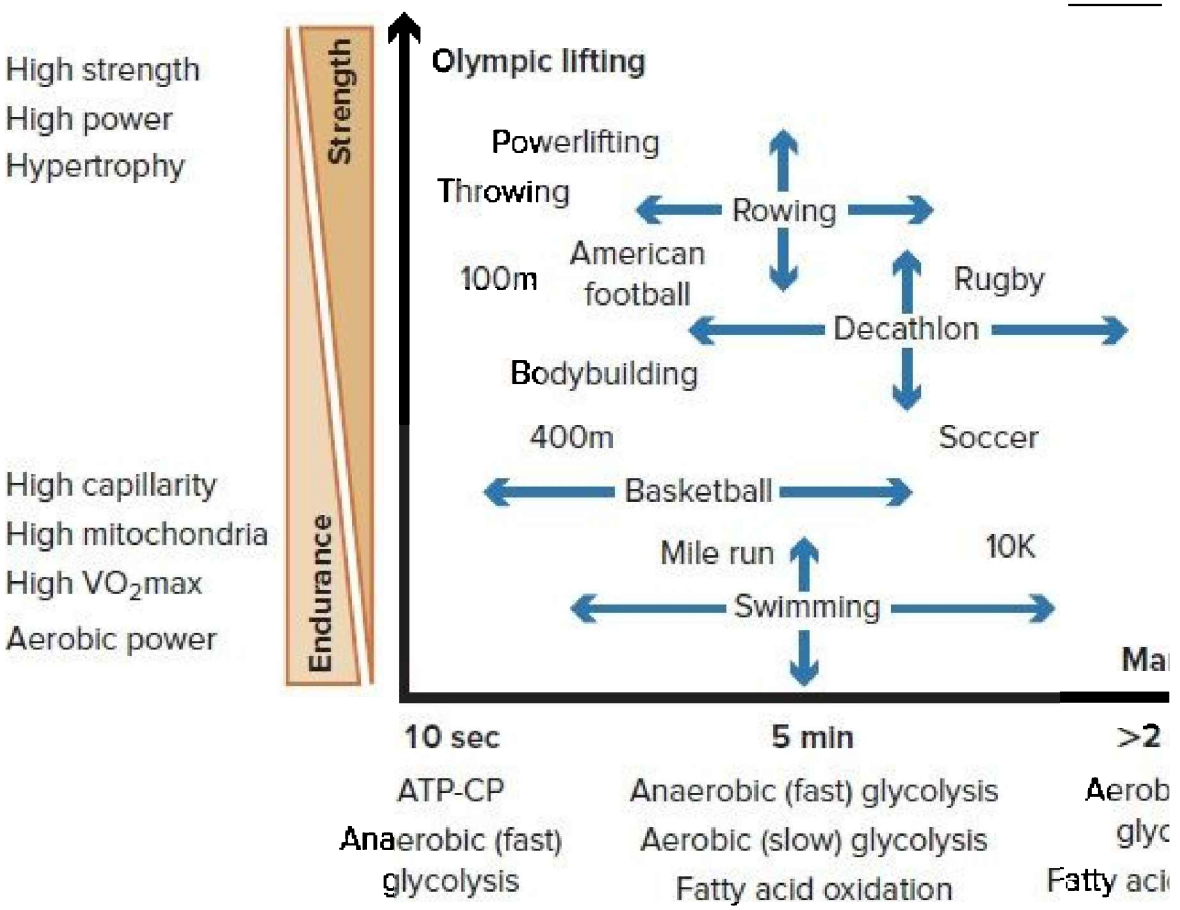


Figure 33.1 Overview of predominant energy systems fuelling energy production during common sporting activities

ADAPTED WITH PERMISSION FROM NADER GA. CONCURRENT STRENGTH AND ENDURANCE TRAINING: FROM MOLECULES TO MAN. MEDICINE & SCIENCE IN SPORTS & EXERCISE 2006;38(11):1965-70 © 2019 AMERICAN COLLEGE OF SPORTS MEDICINE. HTTPS://JOURNALS.LWW.COM/ACSM-MSSE/FULLTEXT/2006/11000/CONCURRENT_STRENGTH_AND_ENDURANCE_TRAINING FROM.13.ASPX[2]

Although carbohydrates (CHO) supply the major energy source for moderate- to high-intensity exercise >70% VO_2max,[3] the absolute amount of CHO that can be stored is typically limited to around 500 g (100 g and 400 g in liver and muscle, respectively) and is effectively depleted by the end of 2 hours of exercise (Table 33.2). In contrast, the supply of fat sources within the body is much more plentiful, but lipids can typically only supply energy for low- to moderate-intensity

exercise (i.e. <60% VO_2max). For many sporting activities (e.g. team sports, marathon running, cycling), it is therefore commonly advised that athletes begin competition with adequate CHO stores, so as to maintain high-intensity performance (this is discussed later in the chapter).

Practical considerations

1. Energy for physical activity is largely dependent on the aerobic and anaerobic metabolism of carbohydrate and the aerobic metabolism of lipids.
2. Carbohydrates supply the majority of energy during moderate- to high-intensity activity and in sporting events <2 hours.
3. The contribution of fat becomes more important during submaximal and prolonged activity.
4. Whereas the availability of fat is usually not limiting to performance, CHO stores can become depleted within 2 hours of commencing intense exercise.
5. Many of the most popular sporting activities are CHO-dependent during competitive situations.

ASSESSING THE ATHLETE

The first step in formulating an individualised nutrition plan is to conduct an assessment of the athlete from a variety of perspectives (Fig. 33.2). Such an athlete assessment is usually conducted by a multidisciplinary team and takes into account the athlete's specific training and competition goals within the current microcycle, mesocycle or macrocycle. While an objective and critical evaluation of the methods outlined below is beyond the scope of the present chapter, assessment of such parameters will allow both a sport- and athlete-specific performance nutrition plan to be developed.

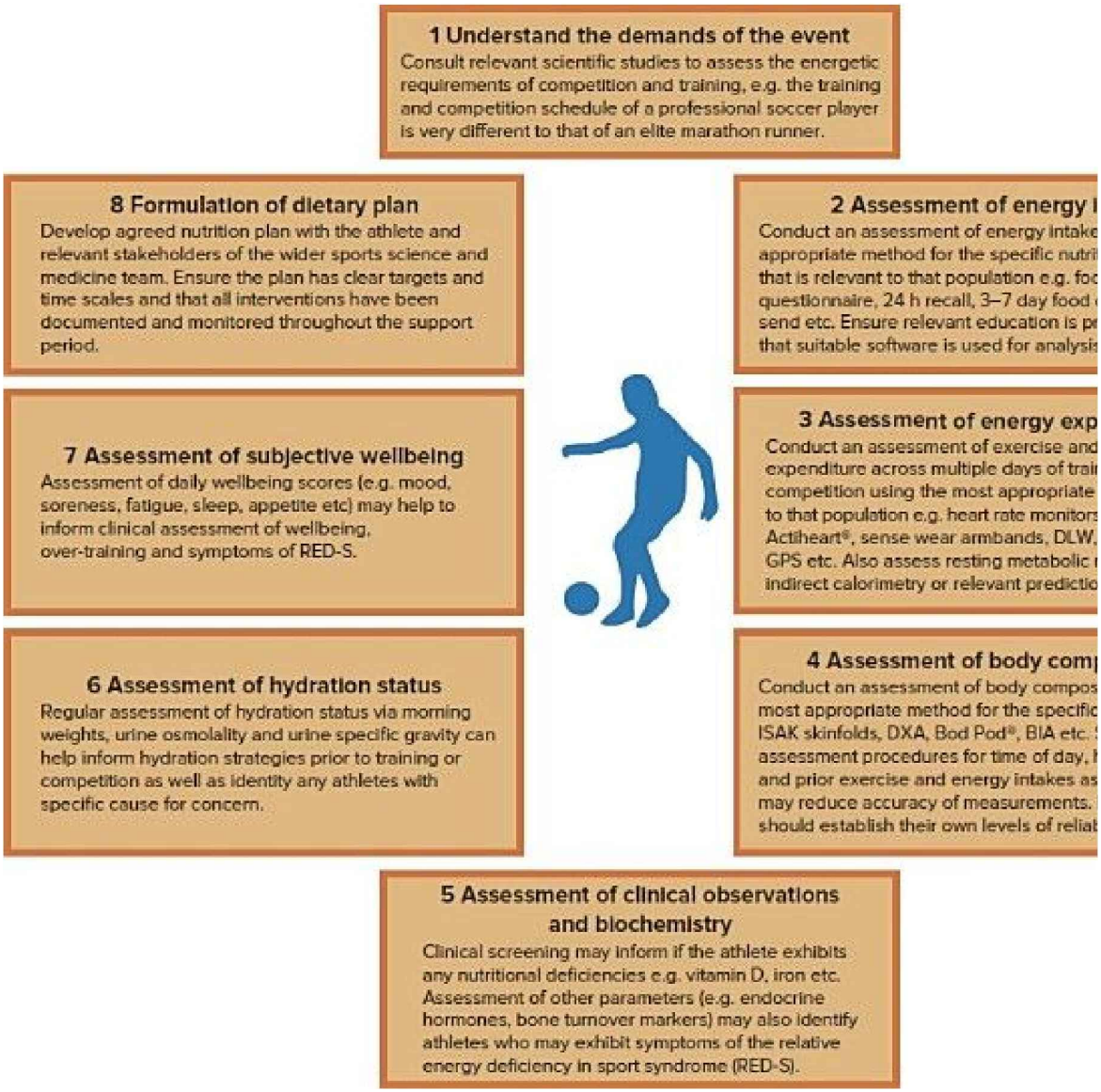


Figure 33.2 Overview of athlete assessments that could be undertaken prior to devising an individualised performance nutrition plan

Assessment of energy intake

In order to make informed decisions on an athlete's diet and devise individually tailored nutrition plans, an initial assessment of habitual dietary intake should be made. Despite the assessment of energy intake being an everyday task for sport nutritionists, it is often described as one of the most difficult of all physiological measures. Broadly speaking, dietary assessment methods are classified

as 'retrospective' (e.g. 24-hour recall, food frequency questionnaires, diet histories) or 'prospective' (e.g. food diaries with or without weighed inventory, duplicate portions and, most recently, 'snap-n-send', using mobile phones).

The food diary is often considered the gold standard approach, although in practical terms, the choice of method is dependent on the population being measured[4] and should reflect what the clinician is trying to assess. For example, the chosen approach to assess total energy intake in highly motivated cyclists could be very different to the appropriate approach to assess calcium deficiencies in elite youth football players. An athlete's diet may also change significantly day-to-day, dependent on the training goal[5, 6] and, hence, this should also be taken into account when performing dietary analysis.

There is, of course, the compromise between recording data from enough days to represent the typical variation of nutritional habits during the athlete's week while not overburdening the athlete.[7] A summary of the common dietary assessment methods, their advantages and disadvantages, is displayed in Table 33.3.

Table 33.3 Overview of common dietary assessment methods

Page 458

Method	Advantages	Disadvantages	Recommended use
		Retrospective methods	
24-hour recall Semi-structured interview where the athlete is asked to describe the last 24 hours of eating. Most accurate when performed using the multiple-pass or triple-pass method	• Clinician interaction with the athlete to tease out extra details and use time wisely to build rapport • Immediate feedback possible • Can be fast, with low burden on the athlete • Removes temptation to change regular diet • Allows 'why' to be asked as well as 'what'	• Skilled interviewer required • Limited to one day, which may not be a typical day • Can be time-consuming if using multiple-pass method,* which increases accuracy[8] • Requires honesty from the athlete	• Requires memory of what was consumed in the last 24 hours • Assessing a particular day of interest (e.g. game day) • Looking to identify a specific problem
Diet history Semi-structured conversation with open questions regarding typical nutrition intake, allergies, intolerances, dislikes and general nutrition knowledge, including supplement awareness	• Allows a lot of general information to be collected • Some immediate feedback can be given if needed • Allows for the different days of the week to be discussed	• Can be superficial, not allowing specific details to be established • Requires honesty, which can be difficult in an initial conversation • Requires good memory, food	• Often a great initial conversation with an athlete to allow a bespoke education package to be tailored

		knowledge and a trained interviewer	
Food frequency questionnaire Involves giving the athlete a questionnaire with a list of foods, to establish the frequency of consumption. Often, they are specific to a particular situation (e.g. to assess antioxidant intake)	• Rapid to complete with low athlete burden • Can identify nutrient deficiencies • Can be self-completed, which is time efficient for the nutritionist working with teams	• Questionnaires must be validated • Does not allow nutrition periodisation or timing of food intake to be assessed • Requires honesty from the athlete • Requires good nutrition knowledge in the athlete	• Good for identifying deficiencies in a nutrient or food group
	Prospective methods		
Food diary with weighed inventory Written record of everything eaten over a 3–7 day period, including weight of the food	• Allows dietary intake to be assessed over several days to assess nutrition periodisation • Allows accurate portion sizes to be reported	• Food intake may change as the athletes know they are being assessed • Some meals are impossible to weigh (e.g. pre-bought stir-fry) • Extremely inconvenient to take scales everywhere and weigh all food • Can be seen as a major burden to athletes	• Research trials • Highly motivated athletes looking for precise information
	Prospective methods		
Food diary without weighed inventory Written record of everything eaten over a 3–7 day period including estimate of portion sizes	• Allows intake to be assessed over several days to assess nutrition periodisation • Less burden estimating portion sizes, which can increase compliance • Less likely to change normal eating patterns compared with weighed intake	• Can be seen as a burden to athletes • Food intake may change as they know they are being assessed • Portion sizes can be difficult to estimate	• Highly motivated athletes looking for specific feedback • Limited time with an athlete to perform multiple 24-hour recalls

Food diary using mobile phoneapp Use of a mobile phone to document everything eaten over a 3–7 day period, including an estimate of portion size or exact portion size if using barcode scanning techniques	• Allows intake to be assessed over several days to assess nutrition periodisation • Phone is a convenient tool to record data, as most athletes take their phone everywhere with them • Usual meals are easy to add into the app to make it more time efficient • Barcode scanning allows pre-bought food to be added quickly and accurately • Athlete can get immediate feedback from the app • Can be shared with nutritionist to give daily feedback	• Can be seen as a burden to athletes • Requires estimate of portion sizes • Can change eating behaviour • Can be time-consuming if cooking fresh with lots of ingredients	• Athletes with poor nutrition knowledge, to help with education • Highly motivated athletes who want detailed advice • Less motivated athletes who need some tracking to promote behaviour change
Snap-n-send Picture taken of all food consumed for a given period and sent to the nutritionist	• Easy for the athlete to take pictures of food using camera phone • If performed properly it is easy to document all food	• Does not provide immediate education • Sometimes hard for nutritionist to see what the food is and evaluate portion size • Requires honesty, to take pictures of perceived 'unhealthy' foods • Time-consuming for the nutritionist to analyse • Requires pictures of uneaten food to be sent as well	• Research studies • Athletes who may not be willing to write a record or use a food diary with app

*The multiple-pass method is a technique to improve the accuracy of a 24-hour recall. In sport nutrition, often a triple-pass method is employed. This involves the athlete initially being asked to

recall all of the food and drink consumed for the day, without interruption; during the second pass the nutritionist then explores this recall in more detail, enquiring about time of day the food was eaten and quantities; and then in the final pass, the recall reviewed prompting for any omission and clarifying any issues that may have arisen.

A major problem with all of the above techniques is under-reporting (e.g. athletes may under-report by approximately 30%), which can either be deliberate or due to inaccurate data collection. In studies in our laboratory we have measured energy expenditure (EE) using doubly labelled water (DLW) and compared this to estimated energy intake (EI) using food diaries in rugby players[9] and jockeys.[10] Despite high motivation from the athletes, there were large discrepancies in the EE and EI (8 and 5 MJ, respectively), likely a result of unintentional under-reporting. Alternatively, we reported reliable data when using a combination of food diaries, 24-hour recalls and snap-n-send in elite premiership soccer players.[6] As such, the ability of the clinician to tease out dietary intakes, as well as the level of athlete education, may affect the quality of the assessment undertaken. Once dietary data has been collected, it is then important to analyse the reported intakes using appropriate databases.

While there are now numerous software packages available to do this (e.g. Microdiet®, Nutritics®, My Fitness Pal®), errors may also arise from foods not being accurately recorded in the database, elimination of key ingredients (e.g. sauces) and even poor labelling of the products. The clinician should therefore work closely with skilled assessors in order to make accurate inferences on the athlete's typical nutritional intakes.

Assessment of energy expenditure

Having assessed energy intake, there is then the requirement to consider the daily energy expenditure required for the specific athlete within their sport and also in relation to the specific training goal. To this end, the clinician should ensure they have a basic understanding of the metabolic and energetic requirements of both competition and training.

The assessment of total energy expenditure (TEE) comprises resting metabolic rate (RMR), the thermic effect of exercise, non-exercise activity thermogenesis (NEAT) and the thermic effect of food. These components of TEE can be measured individually or collectively, where the gold standard measure of TEE in free-living individuals is DLW (Fig. 33.3).

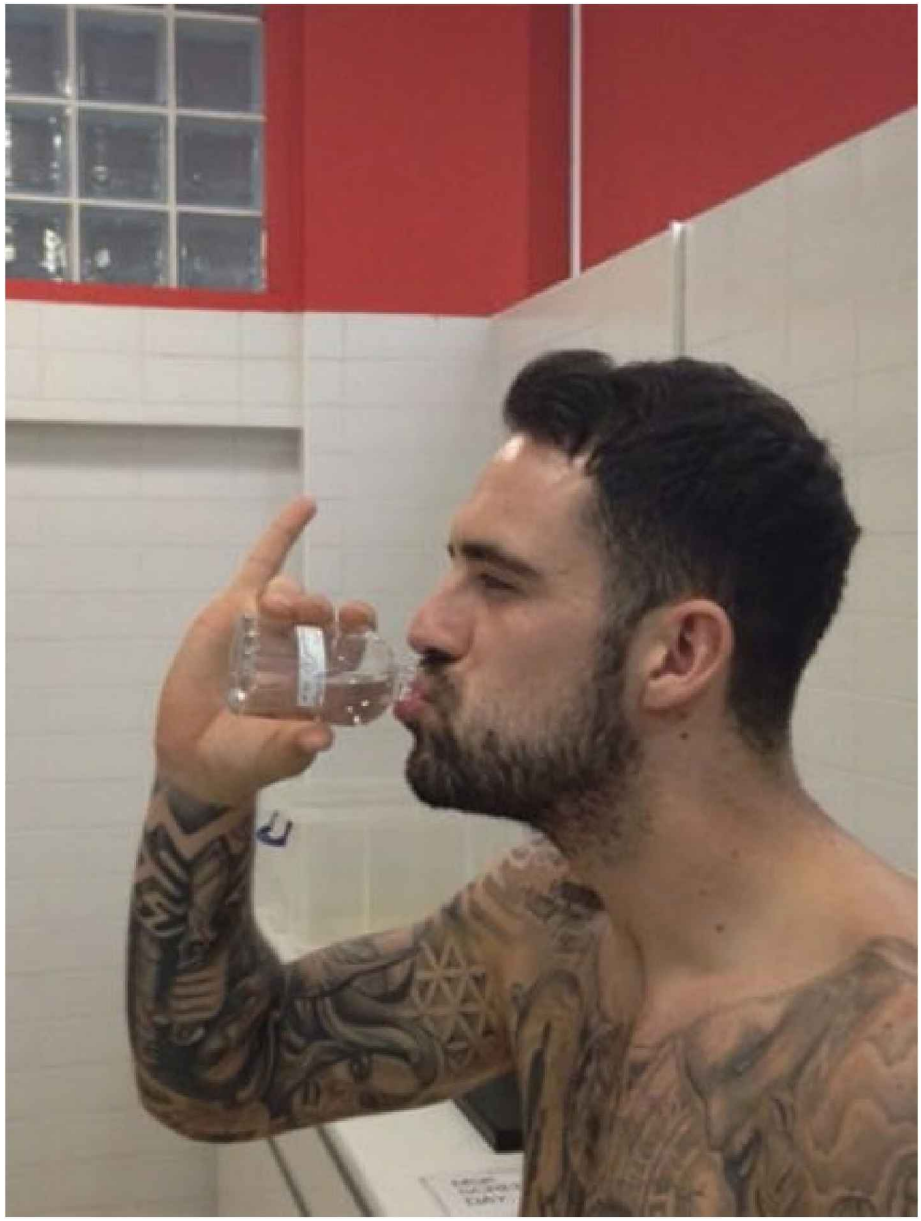


Figure 33.3 A professional football player drinking DLW for the assessment of energy expenditure
JAMES MORTON

DLW is usually reserved for research studies, given the expense (approximately £1000 [A41800] per person) combined with the fact that it cannot measure day-to-day variability, which is typically of interest in the applied sports setting. For example, using SenseWear® arm bands, we observed elite rugby players' mean TEE was 3600 kcal per day, with a range of 3200–5200 kcal per day.[5]

Despite the practical limitations of DLW, we have utilised DLW to assess TEE in elite rugby and

football players and also in jockeys,[6, 9, 10] where values of >5000, 3000–4000 and <3000 kcal per day were observed, respectively. The use of DLW in these studies also demonstrated large individual variations despite similar training loads (in some cases, >1500 kcal per day), thus highlighting the role of NEAT in contributing to TEE.

Where it is not practical to assess TEE using DLW, a variety of other assessment tools can be used to help make inferences on energetic requirements (Table 33.4). Additionally, in endurance sports such as cycling, energy expenditure during exercise can be estimated using power meters. In such situations, it is common for elite cyclists to expend between 2000 and 5000 kcal during exercise alone, thereby likely increasing daily TEE to >7000 kcal in some instances (e.g. a stage of the Tour de France).

Table 33.4 Overview of common methods to assess energy expenditure

Method	Advantages	Disadvantages	Recommended use
Doubly labelled water Athlete drinks small amount of DLW and collects urine over a 7–14 day period to assess CO_2 production, which is later analysed and converted to a calorific value.	• Gold standard providing accurate data • Nothing worn so suitable for contact sports • Minimal burden to the athlete	• Expensive, so rarely used in sport • Cannot assess day-to-day variability • Requires frequent urine collection • Requires highly skilled laboratory staff for the analysis	• Research studies • Understanding general energy demands of a sport
SenseWear armband Portable multisensor biaxial device that is worn around upper arm, measuring both step count and skin temperature, as well as being programmed for anthropometric data	• Relatively cheap • Once purchased can be used frequently over the year • Can detect day-to-day variability • Minimally invasive • Battery lasts up to 14 days	• Cannot be worn during contact sports • Has been reported to affect sleep in some athletes	• Free-living athletes especially those not involved in contact sports
Heart rate monitor using chest strap and watch Chest strap that accurately measures heart rate and uses this to estimate energy expenditure. Some can be programmed to input anthropometric data to increase accuracy	• Cheap to purchase and can be used daily • Can detect day-to-day variability • Good reliability compared with more expensive equipment • Can be worn during most contact sports	• Some athletes do not like the chest strap • Validity of the device is lacking compared with more advanced technology	• Where an estimate of energy expenditure is useful rather than precise information • When trying to understand day-to-day variation in energy expenditure
Acti-Heart® Chest-worn device that measures heart rate and interbeat interval, and has an internal accelerometer to measure physical activity via chest movements	• Good validity compared with DLW in athletes • Can detect day-to-day variability • Once purchased can be used multiple times	• Expensive to purchase • Needs to be charged every 3–4 days • Not suitable for sports that involve forward rotation	• Research trials where DLW is not possible • To influence behaviour and give a rough idea of TEE
Commercial wrist-worn activity tracker	• Cheap to purchase • Wrist straps can be	• Poor reliability compared with DLW	• To influence behaviour and give a rough idea

Watch-like device that has inbuilt accelerometer to track movement (and some have heart rate monitoring) alongside ability to add anthropometric data	worn daily with no discomfort • Gives immediate data, which can influence behaviour	• Often straps need to be removed during contact sports • Wrist-based heart rate monitoring lacks accuracy compared with chest-based	of TEE

Body composition

Assessing body composition is one of the fundamental roles of the sport nutritionist. Although some sports have a requirement to compete at a given absolute body mass, often we are more concerned with the composition of the athlete's mass–that is, gaining increased lean mass and reducing fat mass. There are many techniques available to assess body composition, including hydrostatic weighing, dual-energy X-ray absorptiometry (DXA) scans, air-displacement plethysmography (e.g. Bod Pod®), bioelectrical impedance and the assessment of skinfold thickness.

Body composition analysis involves segmenting the body into different compartments (often two or three compartments). The two-compartment model involves dividing the body into fat mass and fat-free mass, whereas the three-compartment model involves fat mass, bone mineral mass and fat-free plus bone-mineral-free mass. It should be noted that none of the models directly measure muscle mass, despite some research papers claiming to have measured muscle mass using three-compartment model techniques. It is now common practice for elite athletes to be assessed via DXA scans for a three-compartment assessment, or skinfold thickness for a two-compartment model. The remainder of this section will therefore focus on these two techniques.

For a comprehensive review of the DXA technique and its application, the reader is referred to Bazzocchi et al.[11] Briefly, the technique works on the basis of high- and low-energy X-ray photons passed through the body via a pencil or fan beam (Fig. 33.4). A typical scan takes 3–5 minutes to perform, although the athlete does need to be precisely set up on the bed and then the scan requires analysis by a trained technician, making the total assessment time approximately 15 minutes. The energy of the beams is attenuated differently by different tissue, and this is used to calculate body composition. DXA scans were not developed to assess body fat, rather it is a technique to assess the clinical risk of osteoporosis; however, it is now widely used in both research and applied practice to measure body fat.

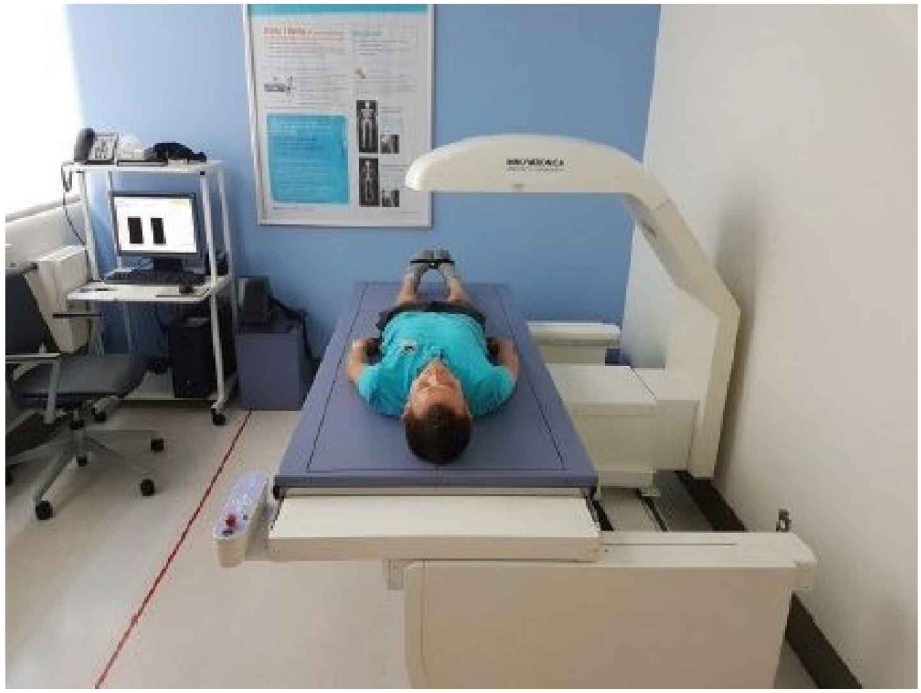


Figure 33.4 A patient undergoing a DXA scan

There are a number of issues that must be considered prior to using a DXA scanner to assess the body composition of athletes. Firstly, despite the dose of radiation delivered during measurement being extremely low (approximately 2–10 μSv), the technique is controlled by radiation protection authorities and it is crucial that the regulations of specific countries are checked prior to scanning.

Perhaps more importantly, there is recent evidence to suggest that unless scanning conditions are tightly standardised, the data collected may not be as accurate as first suggested. It is crucial that the pre-scan nutrition intake of the athlete is controlled,[12] that the athlete arrives for the scan euhydrated[13, 14] and having followed similar exercise as for previous scans.[15, 16] When combined with the expense of scanning, the fact that most sports teams need to visit a hospital or university to get their athletes scanned (thus disrupting training), along with the time taken to perform the exams, a growing number of teams are reconsidering the use of DXA scans as their method of choice for body composition assessments.

Skinfold assessment is the most widely used two-compartment model and perhaps the simplest of all the techniques. The technique involves the measurement of subcutaneous adipose tissue using skinfold callipers. (It is important that the callipers are high quality, such as Harpenden Skinfold Calipers, and are regularly calibrated.) The major criticism of this technique stems from the inaccuracies that arise when converting the obtained measures into a percentage body fat, along with inter- and intra-tester variability.

To combat all of these issues the International Society for the Advancement of

Kinanthropometry (ISAK) was established to provide an educational and training resource to standardise the technique of trained kinanthropometry practitioners,[17] and it is strongly suggested that individuals performing skinfold assessments are ISAK accredited, to ensure consistent measurements. It has also been suggested by ISAK and others that data should be reported as a sum of 8 ISAK skinfold sites (bicep, tricep, subscapular, abdomen, supraspinale, iliac crest, mid-thigh and medial calf), rather than converting to a percentage value using a prediction equation. If a prediction equation must be used (sometimes coaches insist on this), it is crucial to ensure that the selected equation (of which there are more than 100) is sport-specific, (e.g. using the Reilly equation for soccer players).[18]

The use of 'sum of 8' skinfold (SKF) sites is still somewhat new and as a consequence coaches often have no frame of reference to determine what is acceptable. With this in mind, we present an overview of skinfold ranges as lower, middle and upper ranges (Table 33.5). The ranges presented here are not from published literature, but rather have been established through personal communications with peers working in the sports cited.

It is also important to highlight that all athletes are different and some may perform exceptionally well in their given sport despite not conforming to what we have suggested as acceptable skinfold assessments. Finally, we also acknowledge that the ranges cited should be treated with some degree of sensitivity by the nutritionist, sport physician and coaching staff, to ensure that disordered eating is not promoted.

Table 33.5 Overview of ISAK sum of 8 sites skinfold ranges in a variety of sports. Ranges suggested are based on typical values measured in elite sport, although it must be stressed that attributing performance to skinfold measures is difficult

Page 463

	Males			Females		
	Lower	*Middle*	*Upper*	*Lower*	*Middle*	*Upper*
Rugby						
Backs	40–45	45–60	60–75	55–60	60–70	70–80
Forwards	40–55	55–70	70–90	65–70	70–80	80–95
7s	45–50	50–65	65–75	–	–	–
Footballers	40–45	45–55	55–65	60–65	65–75	75–85
Road cyclists	30–35	35–40	40–50	–	–	–
Distance runners	30–40	40–45	45–55	40–55	55–70	70–85
Cricketers						
Bowlers	55–60	60–70	70–80	75–80	80–100	100–120
Batters	70–80	80–100	100–120	90–100	100–120	120–140
Combat athletes	35–40	40–55	55–65	45–50	50–65	65+
Tennis players	40–45	45–55	55–65	50–55	55–65	65+

DATA COMPILED FROM PERSONAL COMMUNICATIONS WITH PEERS WORKING IN ELITE PERFORMANCE

Practical considerations

1. An assessment of energy intake, energy expenditure and body composition is a suitable starting point from which to formulate an individual performance nutrition plan.
2. There is no gold standard method for assessing energy intake and therefore the selected method will be dictated by the circumstances. Most methods have been suggested to under-report total energy intake, and this should be accounted for when developing dietary plans.
3. There can be significant individual differences in TEE, even within the same team, and this needs to be accounted for in dietary plans.
4. If using DXA to assess body composition, it is crucial that the pre-screening conditions are standardised, including time since last meal, hydration status and previous exercise. If these cannot be controlled or if more routine analysis is required, skinfold analysis should be performed.
5. When measuring body composition using skinfold thickness, use the ISAK method and an ISAK-accredited practitioner, and report the values as the sum of eight skinfold sites.

MACRONUTRIENT AND MICRONUTRIENT REQUIREMENTS FOR PERFORMANCE

Carbohydrate

Given the effects of exercise intensity, duration and training status on muscle glycogen utilisation, it follows that glycogen depletion (in both muscle and liver) is a major cause of fatigue in both endurance and high-intensity (intermittent) type activities. As such, traditional nutrition advice for these types of activities (whether for competition or training sessions) is to ensure sufficient daily carbohydrate (CHO) intake before, during and after the activity, so as to promote both performance and recovery.

Carbohydrate and the glycaemic index

Although CHOs have been traditionally considered as simple or complex (on the basis of their chemical structure), it is more appropriate to categorise CHO-containing foods on the basis of their glycaemic index (GI). The GI is a numerical scale that ranks CHO foods on their ability to raise circulating glucose concentrations. Glucose or white bread is the reference food and is given a numerical value of 100. Foods categorised as high GI (HGI), moderate GI (MGI) and low GI (LGI) are typically considered as those with scores of >70, 55–70 and <55, respectively. A full database of GI values was published in 2008.[19]

Considering the differential effects of HGI and LGI foods on both the post-prandial and metabolic responses during exercise, it is important to appreciate the application of the GI concept. For example, LGI foods in the hours before exercise may confer a metabolic advantage as they increase lipid oxidation, maintain more stable plasma glucose concentrations and spare muscle glycogen

utilisation during exercise.[20] As such, these food sources are useful choices to include in the pre-competition or pre-training meal.

Alternatively, because of their capacity to rapidly elevate blood glucose, HGI carbohydrates are superior to LGI in the post-exercise recovery period, in order to promote muscle glycogen resynthesis.[21] In the practical setting, it is therefore prudent to vary the GI of the available CHO foods according to the immediate goal, while also accounting for individual preferences.

Muscle glycogen and CHO loading

The basic principles of CHO loading were developed in the late 1960s, when it was identified that a period of exhaustive exercise followed by several days of high dietary CHO intake induces a super-compensation effect so that glycogen storage is augmented.[22, 23] A less extreme form of CHO loading was developed in the 1980s, when Sherman et al.[24] observed that a simple exercise taper in conjunction with several days of increased dietary CHO intake was also sufficient to increase glycogen storage.

It is now generally accepted that trained athletes can increase glycogen storage in both type I and II fibres within 24–48 hours of increased CHO intake.[25] In relation to practical application, it is also accepted that high-glycaemic foods are superior to low-glycaemic foods[21] in augmenting glycogen storage and that dietary intakes of 8–12 g/kg per day are required to truly maximise glycogen storage.[26]

The general consensus from the wealth of studies undertaken in the last 40 years is that CHO loading can improve performance and capacity, especially when the exercise is greater than 90 minutes in duration.[27] The enhanced performance effect is likely *initially* mediated by a delay in the time point at which energy availability becomes limiting to the maintenance of the desired workload, which, in the case of *race pace,* is dependent on sustained and high rates of CHO oxidation.[28, 29] In reviewing the literature, Hawley et al.[27] cited that CHO loading can improve exercise capacity by approximately 20%, and time trial performance can increase by 2–3%.

In addition to providing substrate availability for adenosine triphosphate (ATP) production, it is now recognised that glycogen availability can directly modulate contractile function. Research from Ørtenblad and colleagues[30] has shown a preferential utilisation of the intra-myofibrillar storage pool of glycogen during exercise, in a manner that also correlates with impaired Ca^{2+} release from the sarcoplasmic reticulum. Such impaired excitation-contraction coupling is likely to be of particular importance during those situations where higher power outputs and sprint finishes are required in the very late and finishing stages of races.

Pre-exercise CHO availability

Whereas the 1960s and 1970s focused on CHO loading studies, research in the next two decades examined the effects of pre-exercise feeding as well as consuming additional CHO during exercise. Pre-exercise feeding (i.e. 3–4 hours before competition) is not only advantageous, as it can lead to

further elevations in muscle glycogen content,[20] but can also restore liver glycogen content, which is usually reduced after an overnight fast. The latter is particularly important given that liver glycogen content is related to exercise capacity.[31]

Sherman et al.[32] observed that time trial performance after 90 minutes of steady-state exercise at 70% VO_2max was greater when 150 g of CHO was consumed before exercise compared with 75 g of CHO, both of which had a greater effect than no meal. The enhanced performance effect was associated with maintenance of blood glucose concentration late during exercise, which is important because liver glucose production and muscle glucose uptake and oxidation become more important when muscle glycogen concentrations begin to decline. In a further study, the same authors also observed that performance can be further increased when CHO is ingested during exercise in addition to a pre-exercise meal.[33] As such, current CHO guidelines for pre-exercise feeding advise an intake of 1–4 g/kg body mass, 3–4 hours prior to exercise.[26]

CHO feeding during exercise

In addition to high endogenous pre-exercise muscle glycogen stores, it is widely accepted that exogenous CHO feeding during exercise also improves physical, cognitive and technical elements of performance.[34] Whereas it was generally accepted that exogenous CHO oxidation rates were thought to be limited at approximately 1 g/min due to saturation of intestinal glucose transporters, it is now known that exogenous CHO oxidation rates can increase to 1.8 g/min with the addition of sucrose or fructose to the CHO blend.[35]

When taken together, it is currently thought that CHO feeding during exercise may therefore augment exercise performance via multiple mechanisms, including muscle glycogen sparing,[36] liver glycogen sparing[37] and maintenance of plasma glucose and CHO oxidation rates.[38] However, despite the proposed mechanisms, it is important to acknowledge that exercise duration, intensity, nutritional status prior to exercise, CHO intake rate and the CHO type/blend consumed during exercise will all have an impact upon the efficacy of these mechanisms, fuel metabolism and performance.

It is noteworthy that exogenous CHO feeding during exercise also improves performance[39] when exercise duration is <60 minutes (i.e. glycogen availability is not limiting), an effect that is not apparent when glucose is directly infused to the bloodstream during exercise.[40] Such data suggest that CHO feeding may also improve exercise performance via non-metabolic effects through direct actions on the central nervous system.[41]

The last decade of research has resulted in a growing body of literature demonstrating that simply 'rinsing' CHO in the oral cavity (for 10-second periods every 5–10 minutes during exercise) is ergogenic to performance,[42] an effect that is independent of sweetness[43] and that is especially apparent in the absence of a pre-exercise CHO meal,[44] or when pre-exercise muscle glycogen is low.[45]

The conventional approach to CHO fuelling during exercise is to consume 6–8% CHO beverages, although relying solely on this approach does not allow for flexibility in terms of individual variations in body mass or actual fluid requirements given variations in ambient conditions. As such, many athletes rely on a CHO fuelling approach that is based on a combination of solids (e.g. bars), semi-solids (e.g. gels) and fluids (e.g. sports drinks), so as to collectively meet their personalised exogenous CHO targets, typically in the region of 30–90 g/h, depending on exercise duration.

Nevertheless, although there is little difference in exogenous CHO oxidation rates (albeit in fluid matched conditions) between the aforementioned sources,[46, 47] many athletes experience gastrointestinal discomfort when attempting to hit these targets, possibly related to extreme differences in osmolality between commercially available CHO gels,[48] as well as the presence of fibre, fat and protein in energy bars.[49] As such, it is now advised that athletes should clearly practise their approach to in-competition fuelling during those training sessions of similar intensity and duration to competition. As a general rule of thumb, it is suggested that 30–60 g/h of CHO (glucose polymers) is consumed during events lasting up to 60–90 minutes, whereas in events >2.5 hours, 60–90 g/h (glucose/fructose blends) is the recommended rate.[26]

CHO as an aid for recovery

Given the importance of CHO as the main energy source for moderate- to high-intensity exercise, we emphasise that adequate CHO intake in the post-exercise recovery period is essential. To maximise short-term glycogen resynthesis, it is typically advised to consume 1.2 g/kg per hour for several hours post-exercise.[26] Delaying CHO intake by 2 hours can reduce glycogen resynthesis rates,[50] so care should be taken to ensure athletes have access to CHO-rich foods and drinks within 30 minutes post-exercise.

The precise amount of CHO to be consumed is dependent on the timing of when the athlete is due to compete or train again. For example, a Tour de France cyclist would have approximately 18 hours to fully restore muscle glycogen stores between stages, whereas an elite team sport athlete may have 7 days before the next game. In the latter situation, it is unlikely that the training loads undertaken between games would require such high daily CHO intakes.[6]

Summary of CHO requirements for athletes

Traditional guidelines for CHO intakes for athletes were representative of a one-size-fits-all approach, where high daily CHO intakes (e.g. 8 g/kg) were advised. However, it is now recognised that CHO intake (in terms of timing, quantity and type) should vary according to daily training demands and the competition schedule of the particular week or month. Furthermore, growing evidence demonstrates that completing and recovering from repeated training sessions with consistently high levels of CHO availability can actually attenuate the magnitude of oxidative adaptations of skeletal muscle.[51] Clearly, the role of CHO has moved beyond that of a simple energy

store, and sport scientists now recognise the importance of glycogen as a signalling molecule regulating training adaptations rather than just having an energy provision role.

Based on the concept of a periodised approach to CHO intakes, we present an overview of suggested CHO intake in the context of a typical team sport athlete (e.g. soccer, rugby, Australian rules football) during a typical week in which consecutive games are separated by seven days (Table 33.6). Note that an elite endurance athlete's CHO requirements may range from 3–12 g/kg per day, dependent on the training and competition loads. Clearly, the clinician and performance nutrition team must possess a sound understanding of the energetic requirements of the sport in question, as well as the athlete-specific training goals. Ultimately, CHO guidelines should be considered as a 'fuel for the work required' approach, where CHO is adjusted day by day and meal by meal, dependent on the training and competition goals. Further details of how to Page 466 periodise CHO intake are provided by Impey et al.[52] and discussed later in the chapter.

Table 33.6 Strategy to periodise CHO intake during the weekly schedule of a team sport athlete

Specific situation	Suggested CHO intake	Comments
Day before game	6–8 g/kg	HGI CHO foods and drinks to augment glycogen stores for competition on the proceeding day.
Breakfast on match day	1–3 g/kg	L/MGI CHO foods and drinks consumed. For a 3 pm kick-off, this meal should be consumed between 8 am and 9 am.
Pre-match meal	1–3 g/kg	L/MGI CHO foods and drinks consumed. This meal should be consumed 3–4 h prior to kick-off. For midday kick-off, this meal would effectively be breakfast.
During match	30–60 g/h	HGI CHO in the form of 6% CHO drinks or sports gels. Players could take advantage of breaks in play to consume small but regular CHO intake to avoid gut discomfort. Additionally, the half-time break should be used for refuelling according to the player's preferred approach. Players should practise fuelling strategies during training, in order to develop individually suited strategies.
Post-match	1.2 g/kg/h	HGI CHO foods and drinks consumed for several hours post-match so as to promote glycogen resynthesis.
Day after game	6–8 g/kg	HGI CHO foods and drinks consumed so as to promote glycogen resynthesis.
General training day	3–6 g/kg	Combination of L/MGI and HGI CHO foods and drinks consumed to ensure adequate CHO availability for training and recovery purposes, depending on the specific energy demands of the particular training day as well as individual training goals. For players wishing to lose body fat, <4 g/kg would prove beneficial (in conjunction with increased protein intake, e.g. 2 g/kg), and L/MGI choices should be emphasised.

HGI = high glycaemic index; L/MGI = low/moderate glycaemic index

Protein

Protein is often considered essential for athletes involved in weight training in order to promote muscle growth. In reality, however, proteins have a variety of functions that extend far beyond the mere requirement to build muscle. Proteins not only give our muscles the basic structure they need

to perform, but also provide the building blocks to make the many thousands of enzymes that are required in order to provide energy from the breakdown of carbohydrate and fat.

In the fasted state, the stress of intense exercise causes our muscle protein stores to actually break down (referred to as 'protein degradation'), which, of course, can be detrimental to training adaptation as it leads to negative protein balance. However, in the presence of adequate protein feeding, the combined effects of exercise and protein ingestion result in the formation of new proteins (referred to as 'protein synthesis') such that a positive protein balance occurs.[53, 54]

It is these repeated changes in protein turnover (in favour of protein synthesis to yield a positive protein balance) in response to every exercise session that ultimately form the molecular basis of how our muscles adapt and recondition to the demands of heavy training.[55] These transient changes in protein synthesis eventually lead to the upregulation of specific proteins (e.g. myofibrillar and/or mitochondrial) such that we can better withstand the physical demands associated with the next exercise bout.

Essential and non-essential amino acids

In order for optimal training adaptation to occur (i.e. to facilitate protein synthesis), it is essential that protein be ingested in close proximity to the exercise stimulus. As such, protein-rich foods and supplements contain the key amino acids that are used as the building blocks to make new proteins in our muscles. There are 20 amino acids that are required to form new proteins (Table 33.7), nine of which are described as *essential* (i.e. they must be obtained from the diet) and 11 of which are known as *non-essential* (i.e. the body can make these amino acids).

Table 33.7 Overview of essential and non-essential amino acids

Essential	Non-essential
Histidine	Alanine
Isoleucine	Arginine
Leucine	Asparagine
Lysine	Aspartate
Methionine	Cysteine
Phenylalanine	Glutamate
Threonine	Glutamine
Tryptophan	Glycine
Valine	Proline
	Serine
	Tyrosine

The amino acids leucine, valine and isoleucine are collectively known as the branched amino acids (BCAAs) and are especially required to facilitate muscle protein synthesis. Of all the BCAAs, leucine has been identified as particularly important for muscle protein synthesis as it can also act in a signalling role to instruct the molecular machinery to initiate protein synthesis

pathways.

Protein requirements for athletes

Daily protein requirements for athletes are now considered to be 2 × RDA (recommended daily allowance) and range between 1.6 and 2.0 g/kg per day. As such, a 75 kg athlete would need 120–150 g per day. Additionally, athletes may need to exceed this intake, to 2-2.5 g/kg, during heavy training periods that are designed to reduce body fat but preserve muscle mass.[56]

On the basis of recent dietary surveys, it appears that professional team sport athletes[5, 57] are readily meeting such protein requirements. In professional soccer players from the English Premier League, daily protein was consistent across a 7-day in-season training period and reported to be in the region of 2-2.5 g/kg per day.[58]

Perhaps more important than total daily protein intake, however, is the pattern of ingestion of protein throughout the day. In this regard, it is now recommended that 0.4 g/kg boluses be consumed every 3–4 hours.[59]

In the context of exercise, it is also advised that protein is consumed in the post-exercise period so as to promote recovery and remodelling of muscle fibres. Although it was previously suggested that 20 g post-exercise was sufficient,[60] more recent data suggest that 30–40 g is likely optimal in those instances where athletes are performing whole-body training, as is the case for most elite athletes.[61]

Furthermore, because of its high leucine content and rapid digestion, whey protein supplements are superior to casein and soy-based supplements for activating muscle protein synthesis.[62, 63] Liquid forms of protein have also been shown to induce a more rapid rise in plasma amino acids than solid foods and, as such, may not only be a convenient form of provision but also a superior strategy in the post-exercise period.[64]

Finally, it is now also advised that protein be consumed prior to the overnight sleep period (0.4–0.5 g/kg) so as to provide a supply of amino acids to muscle in the overnight period that may also stimulate recovery and training adaptation.[65, 66] Unlike at main meals, professional team sport athletes have reported an intake of only 0.1 g/kg body mass at this time point, thus highlighting an important time for improved nutritional choices that may potentially improve training adaptation.[58]

Fat

Fat has historically been viewed in a negative light (see Chapter 6) and, as such, many athletes believe they should eliminate all fats from their diets. However, although excessive intake of fat may be problematic for general health and weight control (as is over-consumption of any macronutrient), too little dietary fat is also a problem for optimal health.

The body needs an adequate intake of essential fatty acids (such as omega-3 and omega-6 fatty acids), as well as the fat-soluble vitamins (A, D, E and K). It should also be noted that fats are

required during exercise as an energy source, especially when carbohydrate stores become depleted, such as when the exercise is greater than 60–90 minutes, which can occur in both training and in the late stages of team sport and endurance events.

Types of dietary fat

Fats are generally classified as saturated or unsaturated, based on their chemical structure. Unsaturated fats can then be further subdivided into monounsaturated fatty acids (MUFA) or polyunsaturated fatty acids (PUFA). It is important to acknowledge that, despite some foods being described as saturated or unsaturated fats, all fats contain a mixture of fatty acids and are simply classified according to the majority fat source they contain. Traditionally, saturated fats have been classed as 'bad fats', to be consumed in moderation, whereas unsaturated fats have been classed as 'good fats', although emerging evidence would suggest that this classification might also be over-simplified.

A major problem with the notion of removing saturated fats from the diet is the issue of what to replace them with. Studies have clearly demonstrated that reducing saturated fat intake will be of no benefit and can even cause more harm if the saturated fats are replaced with refined carbohydrates.[67] In contrast, replacing some saturated fats with unsaturated fats, including foods such as salmon, nuts, avocados and seeds, has been shown to improve markers of health. An additional problem in attempting to remove saturated fat from the diet is that all food that contains fat contains all three natural fats: saturated; monounsaturated and polyunsaturated. It is impossible to consume unsaturated fat without saturated fat, or vice versa, in natural food.

Page 468

Moreover, individual saturated fatty acids have differing effects on blood lipid levels, depending upon their composition. For example, lauric acid (found in high concentrations in coconut oil), despite being a saturated fatty acid, actually decreases the total-to-HDL cholesterol ratio, due to an increase in HDL cholesterol.

Therefore, with regards to saturated fats and health, it may be unwise to advise athletes regarding the types of fatty acids and better simply to give advice regarding the types of food to eat.[68]

PRACTICE PEARL

The simple message to the athlete is to choose 'natural' fats and avoid processed ones, especially trans fats (e.g. margarine, pastry, confectionery products), which should without question be eliminated from athletes' diets. Trans fats increase LDL cholesterol and lower HDL, and are a risk factor for cardiovascular disease.[69]

A further class of PUFAs are the essential fatty acids (EFAs). Just as with essential amino acids, the body cannot make its own EFAs, and these must be obtained through the diet to achieve optimal health. The EFAs are classified as omega-3 (n-3) and omega-6 (n-6) fatty acids. Generally,

athletes consume sufficient omega-6, but diets often lack omega-3. The main dietary source of omega-3 is oily fish (mackerel, salmon, tuna, herring) and therefore athletes should be encouraged to eat wild oily fish on a regular basis or consider a high-quality fish oil supplement (see below).

Efficacy of high-fat diets for athletes

Given that it is well documented that performance in prolonged endurance events is limited by endogenous carbohydrate stores, many exercise scientists have become interested in strategies which could increase lipid oxidation thereby sparing glycogen utilisation. One such strategy is *fat adaptation,* a nutritional approach in which athletes consume a high-fat (and low-CHO) diet for a period of up to 2 weeks, during which they perform their normal intensity and volume of training followed by 1–3 days of a high-CHO diet and a taper in training volume.[70] Five days of fat adaptation increases lipid oxidation and reduces CHO oxidation during exercise undertaken on both days 6 and 7 despite CHO restoration on day 6.

While the restoration of muscle glycogen is of obvious benefit, it is remarkable that lipid oxidation is still enhanced under these conditions, considering that high glycogen availability usually enhances glycogen utilisation. The increased reliance on lipid oxidation induces a sparing of muscle glycogen utilisation but does not affect plasma glucose utilisation. In terms of reducing CHO oxidation rates, available data suggest the enzyme pyruvate dehydrogenase (PDH) as a major control point. Fat adaptation reduces PDH activity at rest as well as during both sub maximal and supramaximal exercise.[71]

The suitability of high-fat diets for high-intensity performance is therefore questionable, as this attenuation of PDH activity is problematic during periods of high-intensity exercise (when high CHO oxidation rates are required), such as sprinting. It is therefore likely that sustained periods of high-fat diets are not beneficial for athletes involved in CHO-dependent sports, though short periods of high-fat/low-CHO diets may be beneficial for weight loss.

The effects of 3 weeks of a ketogenic diet have been evaluated in a cohort of Olympic-level race walkers.[72] When compared with both a high-CHO diet or a periodised CHO diet, the ketogenic diet impaired economy and negated the training effects induced by 3 weeks of intensified training. Additionally, high-fat diets may also reduce muscle protein synthesis.[73]

When taken together, such data suggest that high dietary fat intake (beyond that occurring within 20–25% of typical daily energy intake) is unlikely to provide any performance benefits in those athletes where CHO metabolism predominates during competition (e.g. team sport athletes and endurance athletes). Nonetheless, it is possible that high-fat diets may prove beneficial for ultra-endurance athletes, and further research is required.

Fluid

Given the intense energy demands of training and competition, metabolic heat production can increase core and muscle temperature to >39°C.[74] Sweat losses of 2 L have been observed during both team sport match play and training,[75] even when ambient temperature is < 10°C. For

a 75 kg athlete, this sweat loss equates to >2% dehydration and, if appropriate fluid is not consumed, performance could be impaired. Dehydration of this magnitude reduces repeated sprint capacity,[76] as well as soccer dribbling performance.[77] Potential mechanisms underpinning dehydration-induced decrements in physical and mental performance include increased core temperature, cardiovascular strain, muscle glycogen utilisation and impaired brain function.[78]

From observations of athletes during training and competition, sweat loss and dehydration appears to be lower in cool (< 10°C) compared with warm environments (25–35°C).[79] To compensate for the warmer conditions, however, athletes voluntarily consume significantly more fluid during training. The development of fatigue during competition is also more pronounced during high ambient temperatures.[76]

In addition to fluid loss *per se,* sweat contains electrolytes, such as sodium, chloride, potassium, calcium and magnesium. Loss of sodium is the most significant for athletes (given its role in promoting fluid retention), and athletes can lose 2–13 g during training or competition.[75, 79] The importance of high salt losses is also underscored by observations linking them to exercise-related muscle cramps,[80] and for this reason it is important to identify athletes who are 'salty' sweaters, so as to develop individually tailored hydration strategies.

Practical assessment of hydration status

In developing individualised hydration strategies, it is important to perform regular estimates of pre-exercise hydration status, in order to identify those athletes who may need particular attention. Within the setting of training grounds or on competition days, assessments of pre-exercise urine osmolality and colour provide reasonably inexpensive and informative measures. Osmolality values <700 mOsmol/kg are suggestive of euhydration, as is a urine colour that is pale yellow (note that excessive vitamin B intake can also promote urine colour changes).

Urine indices of hydration are sensitive to changes in posture, food intake and body water content and, for these reasons, a urine sample passed on waking is often advised as the criterion sample. However, values indicative of dehydration at this time (e.g. 7 am) may not mean the athlete is dehydrated on commencing training or competition at 10.30 am, assuming that appropriate fluid has been consumed on waking and with breakfast. Where practical, athletes should therefore be assessed at both the former and latter time points, so as to identify initially those individuals who are causes for concern and to verify that any subsequent hydration strategies implemented are effective to ensure euhydration prior to competition.

Soccer players studied prior to an evening kick-off have exhibited pre-game osmolality values >900 mOsmol/kg, despite the fact that they would have had the morning and afternoon to hydrate.[75] Such values are indicative of 2% dehydration and effectively mean that players are commencing the game dehydrated, thereby running the risk of impaired physical and mental performance.

Fluid requirements for athletes

It is difficult to provide fixed prescriptive fluid recommendations for all athletes, due to differences in workload, heat acclimatisation, training status and variations in ambient temperatures. Nevertheless, in order to offset the negative effects of dehydration on performance, the American College of Sports Medicine advises fluid ingestion at a rate that limits body mass loss to *<2%* of pre-exercise values.[81]

Alternate guidelines have suggested that merely drinking to thirst is sufficient to offset the negative effects of dehydration,[82] although this has recently been questioned given that dehydration impairs cycling performance in hot conditions independent of thirst.[83] Regardless of the precise amount, athletes should not drink quantities that would result in an increase in mass during exercise, as this can lead to water intoxication, a condition known as hyponatraemia (a serum sodium concentration <135 mmol/L), which in extreme cases is fatal.[84]

It is recommended that 5–7 mL/kg of fluid is consumed at least 3–4 hours prior to exercise.[81] Additionally, if the individual does not produce urine or the urine remains dark coloured, a further 3–5 mL/kg could be consumed about 2 hours before commencing the exercise. Drinking within this time schedule should allow for fluid absorption and enable urine output to return to normal levels. Consumption of sports drinks at this time, as opposed to water, is beneficial given that they not only contain electrolytes but also additional CHO. For training days, fluid should be consumed on waking (before travelling to training) and with breakfast.

In order to promote a drinking strategy that prevents weight losses >2–3%, athletes should routinely weigh themselves nude before and after exercise to ascertain whether their habitual drinking patterns are effective. Athletes should have individually labelled drink bottles, so that support staff can monitor habitual fluid intake, and any urine passed during exercise should be accounted for when calculating sweat loss.

Cold beverages (10°C, as opposed to 37 or 50°C) are beneficial to attenuate the rise in body temperature during exercise,[85] and sports drinks are considered superior to water due to Page 470 the provision of electrolytes and CHO. Sports drinks should be in the range of 2–8% CHO, as both high CHO concentration and osmolality can delay gastric emptying.[86]

It is important that athletes practise with different fluid intake strategies during training so as to develop individually suited approaches that maximise gastric emptying, fluid absorption and CHO delivery, yet are suited for taste and do not cause gastrointestinal discomfort during exercise.

Finally, there is usually no need for aggressive rehydration strategies post-training, unless there is a subsequent training session within several hours and ambient temperature is high. Nevertheless, those athletes identified as salty sweaters may benefit from the addition of sodium to drinks or foods, or the provision of salty snacks, so as to promote fluid retention. It is important to consider that the majority of commercially available sports drinks do not have the sodium concentration required (40–60 mmol/L) to be an effective rehydration solution, and more specific oral rehydration formulations should be considered,[87] especially for those identified as salty sweaters. As a general rule of thumb, replacing weight losses by 150% using electrolyte-containing solutions is considered appropriate to promote rehydration (e.g. 1.5 L of fluid for every 1 kg weight

loss).

Micronutrients

Micronutrients are compounds that are required in small quantities (<1 g) to maintain normal physiological function. Although micronutrients do not directly supply energy for human performance, they play essential roles in many metabolic pathways.

Broadly speaking, micronutrients can be divided into vitamins and minerals. While it is accepted that deficiency in most micronutrients can adversely affect health and performance, it is also known that some micronutrients taken in excess can be equally harmful to health.

In reality, the vast majority of micronutrients will be obtained comfortably in an athlete's diet and, in our experience, it is unusual to detect micronutrient deficiencies (with the exception of vitamin D). Factors that could contribute to micronutrient deficiencies include:

- eliminating food groups from diets, either due to food dislikes, allergies or moral reasons–given the growing trend for dairy-free and vegan diets this is becoming a concern
- low-calorie diets, often utilised when attempting to reduce body fat, typically seen in weight-sensitive sports
- very low fat diets, which could affect the fat-soluble vitamins
- a lack of variety in the diet, sometimes seen in younger athletes
- lack of sunlight exposure (including constant use of sunscreen or protective clothing), resulting in vitamin D deficiency.

Unless the athlete fits into one of the scenarios above, it is highly unlikely that they will be deficient in any micronutrients. The first course of action if an athlete (or coach) is concerned about micronutrient intake is to complete a detailed food diary and have this analysed by a suitably qualified dietician or sport nutritionist. If there is cause for concern following dietary analysis, subsequent blood analysis may be required.

Caution should be taken using companies that claim to measure micronutrient deficiencies for athletes and then promote the use of their own expensive mega-dose supplements to correct these 'deficiencies'. Furthermore, we would discourage the use of self-assessment allergy tests, which often result in false positives and can result in foods being eliminated from the diet unnecessarily.

The major vitamins and minerals, their physiological role, typical food sources and recommended nutrient intake (RNI) are summarised in Tables 33.8 and 33.9.

Table 33.8 Major fat- and water-soluble vitamins, their physiological role, typical food sources and recommended nutrient intake (RNI) for non-pregnant adults. It is important to note that RNI varies for different countries Page 471

Vitamin	Physiological role	Food source	Recommended nutrient intake (per day)
		Fat-soluble vitamins	
A	Antioxidant. Eye function, cell growth and division	Oily fish, liver, egg yolk, milk, butter, carrots and apricots	700 µg for males 600 µg for females

D	Facilitates the utilisation of calcium, cell differentiation, immunity, skin cell development and muscle function	Oily fish, eggs and fortified foods	No DRV* because of sun-related synthesis. Safe upper limit set at 4000 IU
E	Major fat-soluble antioxidant. Growth and development	Almonds, peanuts, shrimp, sunflower seeds, corn oil	No DRV, but 4 mg for males and 3 mg for females considered adequate
K	Essential for blood clotting and formation of some proteins	Broccoli, cabbage, liver, cauliflower, spinach	No DRV, but 1 µg/kg body weight considered adequate
	Water-soluble vitamins		
C	Major water-soluble antioxidant. Iron absorption. Important in skin, gum and blood vessel health	Asparagus, grapefruit, limes, oranges, lemons, broccoli, bean sprouts	40 mg
B_1 (thiamin)	Important in carbohydrate and amino acid metabolism (energy)	Almonds, liver, peanuts, whole grain bread and cereals, green peas	1.4 mg for males 1.0 mg for females
B_2 (riboflavin)	Important in carbohydrate metabolism (energy)	Asparagus, broccoli, spinach, banana, mushrooms, tuna, dairy products	No DRV, but 1.1 mg for females and 1.3 mg for males prevent deficiencies
B_3(niacin)	Important in carbohydrate, fat and amino acid metabolism (energy)	Liver, meat and fish, milk, eggs, avocados, tomatoes, legumes, carrots	17 mg for males 13 mg for females
B_5 (pantothenic acid	Needed to synthesise coenzyme A and important in carbohydrate, fat and amino acid metabolism (energy)	Chicken, beef, potatoes, tomatoes, liver, egg yolk, broccoli, whole grains	No DRV, but 3 mg considered safe
B_6 (pyridoxine)	Haemoglobin formation and important in carbohydrate metabolism (energy)	Banana, fish, spinach, tuna, egg yolk, chicken	1.4 mg for males 1.2 mg for females
B_{12} (cobalamin)	Haemoglobin formation and prevention of anaemia. Carbohydrate metabolism (energy). Plays role in nervous system	Beef, dairy products, chicken, egg yolk, tuna	1.5 µg
Folic acid	Cell division and important in the production of some proteins	Meat, liver, green leafy vegetables, legumes, fruit	200 µg
Biotin	Important in carbohydrate, fat and amino acid metabolism (energy)	Egg yolk, liver, kidney, meat	No DRV, but 10–200 µg considered safe and adequate

DRV = dietary reference value (UK)

COMPILED BASED ON DATA TAKEN FROM EXPERT GROUP ON VITAMIN AND MINERALS[88]

Table 33.9 Common minerals that athletes may be deficient in, their physiological role, typical food sources and RNI

Page 472

Mineral	Physiological role	Food source	RNI for non-pregnant adults (per day)
	Water-soluble vitamins		
Calcium	Important in muscle contraction and transmission of nerve	All dairy products, including milk, cheese and yoghurt. Small	700 mg

	impulses. Involved in developing strong bones	fish with bones (e.g. sardines), beans and broccoli	
Iron	Important in the transport of oxygen	Red meat, liver, broccoli, spinach, fortified cereals, eggs, dried fruits, nuts and seeds	8.7 mg for males 14.8 mg for females
Magnesium	Muscle contraction and transmission of nerve impulses	Meats and dairy, vegetables and potatoes, bread and cereals, nuts (brazil, almonds and cashews), mushrooms	300 mg for males 270 mg for females
Zinc	Assists immune function and is an antioxidant. Helps protein digestion and assists in some energy pathways	Liver, kidney, red meat, seafood, poultry, milk, whole grain, leafy and root vegetables	5.5–9.5 mg for males 4–7 mg for females

COMPILED BASED ON DATA TAKEN FROM EXPERT GROUP ON VITAMIN AND MINERALS[88]

Vitamin D

Vitamin D is a unique vitamin given that it is difficult to achieve sufficient intake through diet alone.[89] The vast majority of vitamin D comes from dermal synthesis following appropriate UV exposure and therefore athletes can often be deficient, especially during the winter months or if sunscreen is applied in the summer months.[90]

Vitamin D deficiencies have been reported to impair muscle function and recovery[91] as well as compromising immune health,[92] and it is therefore essential that athletes who are deficient are identified and treated accordingly. The current adequate concentration defined by the US Institute of Medicine (IoM) and the European Food Safety Authority (EFSA) is 50 nmol/L, although that has been highly debated, with some authors suggesting that it is too conservative[93] and that athletes may benefit from optimal serum concentrations that may be around 75–125 nmol/L.

It is important, however, to highlight that there is evidence that athletes can have too much supplemental vitamin D,[94] therefore if a deficiency is observed, 2000–4000 IU per day of vitamin D_3 is suggested, which will correct the deficiency without risking overdose (note, 4000 IU is the current safe upper limit set by the EFSA and US IoM).

Calcium

Calcium is a difficult micronutrient to assess because there are no serum markers of acute calcium intake. Given the fundamental role of calcium as a signal for skeletal muscle and cardiac contraction, it is not surprising that serum calcium concentration is tightly regulated regardless of acute calcium intake.

The largest store of calcium in an athlete's body is in their skeleton, and this store is utilised as an immediate supply of calcium when dietary intake is inadequate, thus maintaining blood calcium homeostasis. The consequence of this mobilisation of calcium is demineralisation of bone tissue through the action of parathyroid hormone.

The major food sources of calcium are dairy products, and, given increasing numbers of vegan or

dairy-free athletes for presumed health reasons, the assessment of calcium intake is particularly important. Calcium may also be lost through sweat, and particular attention should therefore be given to athletes who utilise sweating techniques to make weight or those training or competing in hot environments.

If supplements are to be used, calcium carbonate and calcium citrate are well absorbed. It has been suggested that calcium absorption begins to hit a plateau at ~500 mg, therefore intake should be spread throughout the day rather than in one bolus dose.[95] Practically, there may therefore be benefits to consuming 500 mg prior to exercise in food or supplements to promote bone health although this suggestion requires further research.

Iron

Iron deficiency is one of the most common dietary deficiencies in athletes[96] and, even without anaemia, can have major effects on aerobic performance.[97] Optimal iron status is often discussed in elite sporting environments, although it appears that research to guide such a status is lacking, with iron supplements failing to enhance performance in non-deficient athletes.[98]

There are many reasons why athletes may suffer from low iron status, including red cell haemolysis, gastrointestinal bleeding, sweating, inflammation, menstruation and inadequate dietary intake.[99] The current recommended daily intake of iron is 14.8 mg for females and 8.7 mg for males. Where possible iron should be consumed from highly bioavailable sources, including meat and seafood, and taken alongside iron enhancing foods containing vitamin C; foods that impair iron absorption such as tea and coffee should be avoided.

If a deficiency has been identified, iron-fortified foods or iron supplements may be considered, following consultation with a dietician or sport physician. These supplements should be the most bioavailable forms, including iron sulphate, iron gluconate and iron fumarate. Where possible regular testing of athletes to detect iron deficiencies is advised.

SUPPLEMENTS FOR PERFORMANCE

Although most sport nutritionists now follow a ‘food first’ approach, dietary supplements are extremely common, with widespread use reported in elite athletes.[100] Broadly speaking, supplements can be divided into four main categories:

- supplements claimed to increase muscle mass
- supplements claimed to decrease fat mass
- supplements claimed to increase performance or recovery
- supplements claimed to improve health or decrease illness.

Within each of these categories, there are numerous products, many of which suffer from a lack

of well-controlled research to guide their use. In reality, the vast majority of these supplements are at best placebos and have little genuine effect although there are some exceptions.

It is beyond the scope of this chapter to cover all supplements, and the reader is therefore referred to the A–Z of sports supplements published in the *British Journal of Sports Medicine* [95], as well as a recent consensus statement published by the International Olympic Committee (IOC).[100, 101] Table 33.10 presents the main non-prohibited supplements commonly used by athletes. Supplements that may improve athletic performance but are prohibited are not covered.

Table 33.10 Summary of common non-prohibited supplements used by athletes, their ergogenic claims as well as the key literature to support their use Page 474

Supplement	Ergogenic claims	Reasons not to take	Common dose	Key reference
		Increase lean muscle mass		
Whey protein	Protein is essential for muscle protein synthesis and some struggle to achieve their target intake from food alone.	If sufficient protein is consumed in the diet at the correct times protein supplements are unnecessary.	0.4 g of protein per kg muscle mass attempting to achieve 2 g/kg of muscle mass per day. Note, 2 g/kg is total daily intake not supplement intake.	61, 102
Casein protein	Being a slow releasing protein, suggested when taken pre-bed can increase muscle protein synthesis overnight	Whey has been shown to be better when taken regularly and casein has never been compared to whey when taken pre-bed.	40 g approximately 1 hour pre-sleep	62, 103
Branched chain amino acids (BCAAs)	Prevent central fatigue, increase lean mass	Little evidence to support central fatigue hypothesis. Little evidence to support increase in lean mass if consuming adequate dietary protein.	5 g taken 2–3 times per day	104
Beta-hydroxy-beta-methylbutyrate(HMB)	A derivative of leucine that can increase muscle mass and strength through its anti-catabolic properties, reduce post-exercise muscle damage/soreness.	Limited evidence of effects in trained individuals. Recent studies showing huge benefits have recently been questioned.	3 g per day	105, 106
Creatine	Improve speed, strength, power and high-intensity exercise capacity.	Increased mass, which may not be wanted in some sports. Has been suggested to increase cramping, although no evidence to support this.	5 g, 4 times per day for 4–5 days, followed by 3 g/day or 3 g/day for 30 days	107
Zinc monomethionine aspartate (ZMA)	Claimed to increase muscle strength by increasing anabolic hormone synthesis. Also claimed that given pre-bed could improve sleep.	Only 1 paper has ever shown a benefit of ZMA on muscle strength. No obvious mechanism by which it could help in non-deficient athletes. No data to support the sleep claim.	Typically: 30 mg zinc (aspartate and monomethionine), 450 mg magnesium aspartate, 10.5 mg B_6	108
D-aspartic acid	Increase testosterone by up to 40%.	No evidence that modest increases in testosterone have any ergogenic benefits in athletes.	2000–3000 mg taken daily	109–111
Conjugated linoleic acid (CLA)	CLAs are essential fatty acids reported to promote loss of	Limited studies in athletes. Most positive data are from animal studies.	1.4–6.8 g/day	

Page 475

	body fat and increase lean muscle mass.			112
Green tea extract	Research has suggested that fat oxidation is increased by approximately 15% during exercise, as well as improving insulin sensitivity. Could be beneficial for prolonged endurance exercise.	Inconsistent research findings and suggestions of poor bioavailability. Poor correlation between acute fat oxidation and long-term loss of body fat.	Approximately 400 mg	113
	Increase performance/recovery			
Caffeine	Prolong endurance performance, increase lipid oxidation, increase mental alertness.	Some athletes naive to caffeine may get adverse effects including nausea, headache and tremors at high dose. Ergogenic effect can be gained from drinking coffee, removing the need to supplement.	2–4 mg/kg body mass, taken 10–60 minutes pre-exercise dependent on the form of the caffeine (gum, liquid or tablet)	107, 114
Beta alanine	Increases muscle carnosine, which is the main intracellular buffer of hydrogen ions, thus improving high-intensity exercise.	Some athletes will experience skin tingling, which may cause distress.	3–6 g per day. Must be taken daily for about 4 weeks before benefits are noticed.	115
Sodium bicarbonate	Potent extracellular buffer minimising the deleterious effects of acidosis through increasing blood bicarbonate concentrations thus improving high-intensity exercise.	Effective doses can cause gastrointestinal problems, sometimes quite severe.	200–300 mg per kg body mass	116, 117
Nitrate	Most researched form is beetroot juice, which is high in nitrate. Nitrate is converted to nitrite and ultimately nitric oxide. Increasing nitric oxide has been shown to lower the oxygen cost of submaximal exercise, which can improve aerobic exercise performance.	Most of the evidence is in less-trained athletes and after following a nitrate-depleted diet. Some athletes do not tolerate the taste especially well, which is important given that benefits are seen through days of supplementation. Can be gained through the diet (e.g. rhubarb, beetroot).	8.4 mmol nitrate (approximately 2 'shots' of commercially available beetroot juice) taken 1–7 days pre-exercise	118, 119
Carnitine	Increased muscle carnitine increases the enzyme CPT1, which is the rate-limiting step in fatty acid oxidation. Chronic supplementation could therefore increase fat oxidation during low-intensity activity, aiding performance and reducing body fat.	To be effective it must be taken for 6 months alongside high GI carbohydrates.	2 g of l-carnitine-l-tartrate taken with 80 g high GI carbs twice per day for 24 weeks	Page 476 120, 121
Polyphenols (e.g. cherry juice)	Taken in the days leading up to exercise, has been shown to reduce some markers of 'oxidative stress', attenuate muscle soreness and improve sleep.	Most of the evidence involves athletes who previously followed a polyphenol-depleted diet. Most markers of oxidative stress are inappropriate measures (e.g. total antioxidant capacity or TBARS), making conclusions difficult to establish.	Varies depending upon the polyphenol; for example, 2 × 30 mL servings of cherry juice, giving approximately 40 mg of anthocyanins	122, 123
Antioxidants (e.g. vitamins Cand E)	Claimed to reduce exercise-induced free radical production thus reducing muscle soreness	Suggestions that some adaptations to exercise are redox sensitive and therefore antioxidant supplements could	Varies dependent on antioxidant. Vitamin C is typically 500–	124–127

	and attenuating the loss of muscle function. Vitamin C has also been linked with reducing the severity and duration of a cold through non-antioxidant mechanisms.	impair improvements with training, although this suggestion seems difficult to explain from a mechanistic point of view. High-quality research has demonstrated vitamin C is not effective for preventing or treating a viral illness.	1000 mg, Vitamin E 200–800 IU	
Electrolytes	Given that sodium is lost in sweat, it seems prudent to replace this in the fluid replacement strategy, to maximise hydration and absorption of fluid through the gut.	Some drinks can taste salty, which may reduce athlete's desire to drink them.	40–60 mM sodium solutions needed, although many commercially available are much lower	128, 129
Probiotics	Shown to reduce the likelihood of URTIs. Suggested to improve general gastrointestinal function as well as reduce exercise-induced gut damage.	Evidence is still lacking as to the best strains and doses of probiotics that are most efficacious for different health outcomes in different populations.	>20 billion CFUs taken daily. Multispecies strains including those from lactobacillus and bifidobacterium species are the most widely studied.	Page 477 130
Zinc acetate	Recent systematic review and meta-analysis suggested that sucking on zinc acetate lozenges can reduce duration of common cold symptoms by 16 hours and symptoms of URTI by 44% through local effects in the pharyngeal region.	The RDAfor zinc is 9.5 mg and long-term high-dose zinc is toxic. Therefore, if being used, it should not be for more than 7 days and only if symptoms of a cold are present.	During illness 75 mg of elemental zinc per day, given equally spaced throughout the day. Must be zinc acetate. Note 10 mg zinc requires 34 mg zinc acetate.	127
Vitamin D	Correction of a deficiency is claimed to improve bone health, muscle function and immune function.	High-dose supplementation could result in problems such as hypercalcaemia and kidney stones.	Requires individual consultation with a clinician	89, 131
Fish oil	Increasing omega-3 intake, particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), suggested to reduce inflammation and even promote muscle protein synthesis.	Large doses needed, which can repeat on some people giving fishy taste in mouth. Can be expensive, and evidence is still not conclusive in terms of its benefits.	1–3 g per day of EPA/DHA	132, 133
Bovine colostrum	Rich in immune and growth factors. Claimed to increase lean mass, improve immune function and promote gut health.	Claimed by WADA that there is potential for elevated IGF-1 levels and thus a positive drug test, although the science behind this claim is lacking. Limited evidence that it can increase lean mass.	Various doses used, usually 10–20 g per day	134
Glutamine	Suggested to have numerous benefits, including increased anabolic activity, recovery from exercise-induced muscle damage and immune function, although evidence is lacking. There is emerging evidence for a role in attenuating exercise-induced gut damage.	Currently, only large doses have been shown to attenuate markers of gut damage, although this has not necessarily related to reduced GI symptoms.	10–40 g, 1–2 hours pre-exercise	Page 478 135
Calcium	Emerging evidence that athletes lose calcium in sweat and therefore replacing this could	1 g of calcium can easily be achieved in a normal diet and therefore supplements may not be needed.	1 g pre-exercise	95, 136

	reduce loss of bone mass.			
Collagen	Recent evidence that collagen supplements given pre-exercise could improve collagen synthesis thus preventing tendon/ligament injuries and promoting tissue repair.	Needs to be taken pre-exercise with vitamin C, and research is still emerging rather than conclusive.	15 g, 1 hour pre-exercise	137, 138
Turmeric (curcumin)	Emerging research suggesting turmeric has anti-inflammatory properties, potentially reducing post-exercise muscle soreness, as well as supplementation having the potential to facilitate tendon healing.	Has poor bioavailability, although suggested this can be improved through addition of piperine. Most of the research is in animal models or *in vitro,* rather than *in vivo.*	2.5–5 g turmeric root, twice per day	139–141

A common misconception is that supplements are essential, with many believing that sport nutrition is as simple as getting the supplements correct. However, supplements are 'supplements, not a substitute' and have little benefit if an athlete's diet is inadequate. Once an athlete's diet has been addressed, there are some instances where a targeted supplement plan may be of use, but this should only be prescribed by qualified individuals who are up to date with the current sport-specific anti-doping regulations. This is particularly important given that in 2012 it was suggested that 44% of UK anti-doping offences were supplement-related, while in Australia there is one violation per month related to supplements.

Practical considerations

1. CHO loading can occur within the 24–36 hours prior to competition and would require 8–12 g/kg per day.
2. Daily CHO guidelines for athletes exist on a sliding scale of 3–12 g/kg depending on training loads, training goals and competition requirements.
3. Pre-competition meals should be consumed 3–4 hours before exercise and consist of 1–3 g/kg.
4. CHO during exercise should be in the range of 30–90 g/h depending on exercise duration and intensity.
5. To rapidly replenish muscle glycogen stores, post-exercise CHO intakes should be 1.2 g/kg per hour for 3–4 hours.
6. CHO intakes should be periodised across the weekly microcycle in accordance with the fuel for the work required approach.
7. Daily protein intakes should range from 1.6–2.2 g/kg with equal portions of 0.4 g/kg consumed every 3–4 hours.
8. Post-exercise protein feeding of 30–40 g will maximally stimulate muscle protein synthesis and recovery.
9. During times of muscle hypertrophy and/or energy restriction (where the goal is to maintain lean tissue but reduce fat mass), daily protein intake could range from 2–3 g/kg per day.

10. Protein intake before sleep (e.g. 0.4–0.5 g/kg) can also help potentiate muscle mass growth and strength gains.
11. Although high-fat diets can improve fat oxidation during exercise, this approach is unlikely to increase performance given that it can reduce the ability to utilise CHO during high-intensity exercise.
12. Daily intake of fat (emphasising choices such as oily fish, nuts, seeds) equating to 20–25% of total daily energy intake is likely sufficient to achieve intake of essential fatty acids.
13. Consuming 5–7 mL/kg of fluid (especially electrolyte solutions) is likely sufficient to ensure hydration prior to exercise.
14. Fluid should be consumed during exercise (electrolyte solutions are superior to plain water) to prevent body mass losses >2% of body mass.
15. Post-exercise fluid intake (equivalent to 150% of body mass losses) will help promote rehydration.
16. Monitoring of morning body mass to limit daily changes to < 1% of body mass provides a crude measure of hydration status alongside urine osmolality (<700) or specific gravity (< 1.020).
17. It is unusual for athletes to present with micronutrient deficiencies, with the exception of vitamin D. If vitamin D supplementation is required, no more than 4000 IU per day of vitamin D_3 should be given.
18. Weight-making athletes, athletes eliminating food groups, athletes on low-calorie diets or very low fat diets, and those who are fussy eaters may be susceptible to micronutrient deficiencies.
19. Athletes who engage in regular sweating (e.g. jockeys) may require additional calcium, as may weight-sensitive athletes.

Athletes inadvertently ingest supplements containing prohibited ingredients in one of two ways:

Page 479

1. The product intentionally contains a prohibited substance, which is stated on the label, but the athlete is not aware of the status of this ingredient. A common example of this is supplements containing methylhexaneamine as a 'fat burner'.
2. Poor manufacturing processes result in cross-contamination. In this situation, something as innocuous as vitamin C could be contaminated with methylhexaneamine, resulting in an anti-doping violation.

If an athlete does decide to use a supplement, only those from companies that have their products independently batch tested by a recognised body such as Informed Sport or NSF should be used. Athletes should also be aware that although a product has been tested this does not guarantee that the product is drug free, and that batch testing programs are at best risk minimisation rather than risk elimination. However, to date, there have been no reported cases of a supplement that is on the Informed Sport register ever resulting in a positive test for an athlete.

An athlete must remember that they are 100% responsible for what is in their body and therefore it is essential that the final decision whether to take supplements must lie with the

athlete, rather than a sporting organisation making supplementation compulsory. The Sport and Exercise Nutrition Register (SENr) has proposed a flow chart to help guide the decision whether or not to use a supplement (Fig. 33.5).

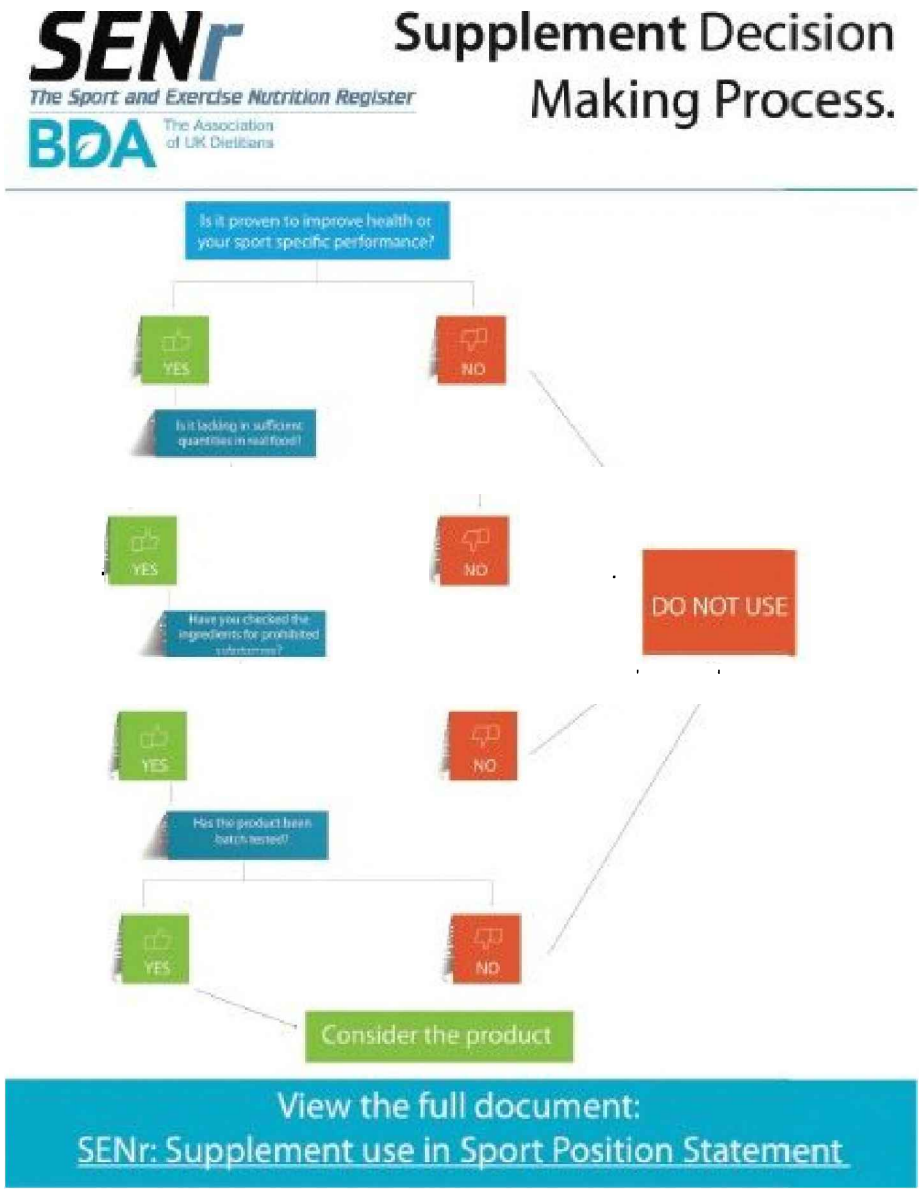


Figure 33.5 Supplement decision-making flow chart proposed by SENr

THE SPORT AND EXERCISE NUTRITION REGISTER (UK), BDA

SPECIAL CONSIDERATIONS

There are many special considerations that the sport nutritionist may face, though it is beyond the scope of this chapter to discuss them all in detail. Rather, some of the most common considerations are summarised in Table 33.11, along with the recommended action required.

Table 33.11 Specia considerations for the sport nutritionist

Page 480

Situation	Potential concerns	Actions	Key reference
Vegan athlete	• Low total energy intake • Low protein intake • B_{12} deficiency • Low iron intake • Low calcium • Low vitamin D • EPA/DHA deficiency • Low muscle creatine • Low muscle carnosine	• Check why the athlete has become vegan. Provide education about increased risk of nutrition deficiencies. • Perform full dietary review and provide advice to ensure energy and protein intake is sufficient. • Consider B_{12} supplement and marine algae for EPA/DHA. • Assess iron, calcium and vitamin D intake. • Consider creatine and beta alanine supplementation. • Discuss with physician whether blood tests are required.	142
Injured athlete	• Loss of lean muscle mass • Increase in body fat • Increased inflammation • Can we promote faster recovery? • Micronutrient deficiencies	• Increase protein intake to 2.5 g/kg and consider supplements such as creatine (if not on it). • Perform immediate dietary review to ensure intake and expenditure are adjusted accordingly and begin regular body composition assessments. • Consider omega-3 supplements to reduce inflammation. • Consider collagen supplements, if bone, ligament or tendon injury. • Consider calcium and vitamin D supplements, if bone injury. • Avoid alcohol intake. • Promote more than ever a good intake of fruit and vegetables.	137, 138, 143
Travelling athlete	• Becoming ill during travel or upon arrival • Lack of appropriate food at the destination • Danger of meat contamination at the destination (e.g. some places in South America) • Danger of drinking tap water or eating foods washed in tap water	• Promote hand sanitisation and encourage athlete to take own alcohol gel with them. • Plan ahead and try to contact the airline to provide athlete-specific food. • Prepare and take food for the flight, so not reliant on food provided by the airline. • Stay hydrated during travel—take water with you. Consider taking electrolyte tablets on board the flight. • Check local hygiene issues including meat contamination and safety of drinking water. • Take food with you to eat on arrival and in the hotel. • Avoid buffets where possible and avoid vegetables that have been washed in water. Choose fruit that needs to be peeled, such as bananas.	144
Athlete with	• Diagnosed allergies are extremely serious and can be life	• If an athlete has a diagnosed allergy, ALL members of the support team must be made	145

Page 481

allergies	threatening. • Undiagnosed allergies may exist that have yet to be identified but could be causing serious problems. • Athlete could suffer from IBS and ignore this, but could benefit from a low FODMAP* diet. • Athlete may have self-diagnosed allergy that is a false positive and be eliminating food groups unnecessarily.	aware, as well as other team members, and education should be provided about the consequences of this. • Food must be labelled accurately with allergens clearly highlighted. Items free from allergens must be provided. • If an athlete presents with IBS symptoms, provide support and appropriate referral. They may benefit from a FODMAP consultation. • If an athlete states they have an allergy/intolerance, check how this was diagnosed and if it was using a self-test kit. Consider sending for a more appropriate diagnosis. Provide advice about the problems with eliminating food groups unnecessarily.	
Athletes with disordered eating	• Athletes in weight-sensitive sports may be susceptible to eating disorders, although they are not always confined to such sports. Female athletes are especially susceptible. • Eating disorders could result in low energy availability and a variety of physical and mental health problems. • Athletes may have low energy availability without disordered eating, which can have detrimental health consequences.	• Be aware of signs of eating disorders and ensure that you are up to date with training in this field. • Provide appropriate education in high-risk sports, in an attempt to prevent them from occurring. • Consider screening for eating disorders in sports where there is a high risk. • If there is a suspicion of an eating disorder, speak to the appropriate medical personnel in the organisation. • Athletes with eating disorders will need screening from the team physician prior to returning to play. • Remember that sport nutritionists are often not qualified to deal with eating disorders, but it is essential that they know how to refer and support the athlete appropriately. • Identify athletes that have low energy availability and provide appropriate support.	146–148
Athlete with minor illness	• Performance impaired from an upper respiratory tract infection • Potential to spread the illness through the team • Reduced appetite • Dehydration	• If cleared fit to train by the physician, consider zinc acetate lozenges (Table 33.10) and 500 mg vitamin C. • Consider electrolytes to promote hydration. • Consider using smoothies if appetite is suppressed, to ensure adequate nutrition intake. • Increase awareness of hand sanitisation throughout the entire team.	149

*FODMAP = FERMENTABLE OLIGO-, DI-, MONO-SACCHARIDES AND POLYOLS

It is important to note here that some of these special considerations can fall outside the scope of practice of the sport nutritionist or dietitian and, as in all professions, it is crucial to recognise the situation and make an appropriate referral. For example, sport nutritionists are usually not qualified to handle eating disorders or dietary allergies; however, they should be able to guide their athlete towards appropriate support.

A growing number of athletes are choosing to eliminate major foods groups from their diet for perceived health and performance benefits; for example, as part of gluten-free, dairy-free, vegetarian or vegan diets. While the sport nutritionist must respect an athlete's belief, such as choosing to eliminate meat for ethical reasons, it is also crucial that the nutritionist educates and

helps to dispel myths that may have led to such dietary decisions. It is crucial that, with all of these special considerations, the sport nutritionist works within a multidisciplinary team and seeks appropriate support from other members of the team.

Practical considerations

1. Supplements carry a significant risk of contamination and therefore any supplement provided to athletes must be independently screened by an accredited laboratory (e.g. Informed Sport, NSF).
2. Athletes should have the final say when it comes to taking supplements. No athlete should ever be forced to take supplements against their wishes.
3. The majority of supplements are at best placebos, and nutritionists should therefore assess the need for supplementation through a thorough review of the most relevant literature.
4. There are a handful of supplements with proven benefits and these could be recommended in a sport-specific context following a comprehensive review of the risks.

NUTRITION PERIODISATION

In practice, the delivery of a nutrition service often manifests itself as a periodised approach to practice, in recognition that an athlete's nutrition requirements are not static and will change according to training goals and phase of the competitive calendar. Moreover, whereas team sport athletes may partake in up to 40 games per season (and, on occasion, three games per week), an endurance athlete may aim to peak for only 2–3 races per year. Similarly, a combat athlete may also compete 1–6 times per annum, during which time they are likely to have to make weight for each contest. For the Olympic athlete, the training and nutrition plan is likely to be part of a 4-year performance plan, in order to peak for the Olympic Games.

The concept of nutrition periodisation is therefore gaining increased popularity among clinicians, in recognition that nutrition plays a significant role in modulating aspects of training adaptation, in addition to the well-documented effects on competitive performance. To this end, nutrition periodisation could be defined as:

> *the deliberate manipulation of macronutrient, micronutrient and energy availability, alongside targeted use of supplements and ergogenic aids, across the microcycle, macrocycle and mesocycle, in order to modulate training adaptations, body composition and competitive performance.*

CHO periodisation

As previously discussed, the principle of promoting high CHO availability before, during and after exercise is the foundation on which traditional sport nutrition guidelines are based. Although this is essential for promoting maximal competition performance and ensuring adequate recovery,

accumulating data now suggest that restricting CHO before, during and in recovery from endurance-based exercise augments the cell signalling and gene expression responses associated with oxidative adaptations in human skeletal muscle.

Both acute and training-based studies have collectively observed that the reduction of endogenous and/or exogenous CHO promotes mitochondrial enzyme activity and protein content, increases both whole-body[150] and intramuscular[151] lipid metabolism and can improve both exercise capacity[152] and performance.[153] This approach to CHO periodisation has been termed 'train low/compete high', a model that promotes CHO-restricted training for augmenting adaptation, but ensures high CHO availability during competition, to promote maximal performance.

Despite the clear rationale of the train-low paradigm, there are a number of potential limitations to this type of training that can make it difficult for exercise physiologists and nutritionists to best periodise this type of training in an elite athlete's training schedule. Reduced CHO availability impairs acute training intensity[150, 151] and, hence, if performed long term, may actually lead to a detraining effect.

Additionally, given the role of CHO in preventing immunosuppression, it is possible that repeated high-intensity training under conditions of low CHO increases susceptibility to illness and infection.[154] Restriction of CHO availability has also been shown to increase muscle protein breakdown,[155] an effect that if performed chronically may lead to muscle mass loss, Page 483 especially in conditions of both calorie and CHO restriction.

Practical considerations

1. There are many special considerations that may present to a sport nutritionist, and it is crucial that these are handled by the most appropriate professional. Often this requires the sport nutritionist to identify the problem and then refer to other medical staff.
2. Many athletes can suffer from eating disorders, and it is crucial to screen for this, especially in high-risk sports (i.e. weight-class sports).
3. Many athletes eliminate food groups for perceived health benefits. These athletes should be identified and given appropriate support.
4. There are a growing number of home-test allergy assessments that lead many athletes to believe they have allergies. Education must be provided regarding the appropriateness of such tests.
5. Athletes with minor illnesses often look to the nutritionist for advice. Some benefit may be gained from zinc acetate lozenges and vitamin C.

Finally, data also demonstrate a reduced ability to oxidise exogenous CHO following regular training with low CHO, which could lead to a negative effect on competition performance.[156] Taking the above limitations into account, it is important to recognise that training with low CHO

availability should be carefully periodised in an athlete's training program.

In practice, this approach could represent an amalgamation of train-low paradigms and is perhaps best communicated by the principle of 'fuel for the work required'.[53] Indeed, athletes could strategically reduce CHO availability prior to completing predetermined training workloads that can be readily performed with reduced CHO availability, thereby inducing a 'work-efficient' approach to training. Alternatively, when the goals of the training session are to complete the highest workload possible over more prolonged durations, then adequate CHO should be provided in the 24-hour period prior to and during the specific training session.

Careful day-to-day periodisation in a meal-by-meal manner (as opposed to chronic periods of CHO restriction) is likely to maintain metabolic flexibility and still allow for the completion of high-intensity and prolonged duration workloads on heavy training days (e.g. interval type workouts undertaken above lactate threshold). Intuitively, train-low sessions may be best left to those training sessions that are not CHO dependent and in which the intensity and duration of the session is not likely to be compromised by reduced CHO availability (e.g. steady-state type training sessions performed at intensities below the lactate threshold).

Page 484

Clearly, more studies are required to investigate the optimal practical approach for integrating periods of the train-low method into an elite athlete's training program. Examples of a periodised approach to CHO intake across the weekly microcycle are presented for a professional road cyclist and team sport athlete in Figures 33.6a and b, respectively.

CHO feeding schedule

Training session	Pre-training meal	During training	Post-training meal	E
Day 1 4–6 hours high-intensity session consisting of multiple intervals > lactate threshold	High	High	High	
Day 2 3–5 hours low-intensity steady-state session at intensity < lactate threshold	Low	Low	High	
Day 3 3 hours high-intensity session consisting of multiple intervals > lactate threshold	High	Medium	High	
Day 4 <1 hour recovery session at intensity < lactate threshold	Low	Low	High	

(a)

Figure 33.6 **(a)** Theoretical overview of the fuel for the work required model. The model is presented for an elite endurance athlete (e.g. road cyclist) who trains once per day on four consecutive days, where each session commences at 10 am every day. In this example, the athlete has four main feeding points and the CHO content of each time point is colour coded according to a red, amber or green (RAG) rating that represents low, medium and high CHO intake. Note that we have not prescribed specific CHO quantities and have deliberately chosen a RAG rating so as to highlight the necessity for flexibility in relation to athlete history, training status and specific training goals etc. Rather, the model is simply presented to illustrate how train-low paradigms can be amalgamated to adjust CHO availability day by day and meal by meal, according to the demands of the specific training session across the 4-day training block. In this example, high CHO intake is advised before, during and after the training session on **day 1** (e.g. train high) but reduced in the evening meal to facilitate sleep low and train low for a lower intensity session on **day 2** (i.e. likely commenced with reduced muscle glycogen and withholding or reducing CHO content of the pre-training meal). Following completion of the second training session, high CHO availability is prescribed for the remainder of **day 2**, so as to promote glycogen storage in preparation for a higher absolute workload and intensity on **day 3**. Given that **day 4** is a designated recovery day of much lower duration and intensity, CHO intake is then reduced in the evening of **day 3** and breakfast of **day 4**, but then increased throughout the remainder of 1–2hoursoflow-intensityMediumday 4 in order to prepare for another 4-day training block. The model should be adjusted according to the number of feeding points and training sessions that are to be undertaken on each day (e.g. a marathon runner would have a different CHO periodisation model from a cyclist)

CHO feeding schedule

Training session	Breakfast	Lunch	Dinner	Ev
Monday Day off following game	High	High	High	
Tuesday 1–2 hours of high-intensity field training followed by weight training	High	High	Medium	
Wednesday 1–2 hours of low-intensity field training followed by weight training	Medium	Medium	Low	
Thursday Day off	Low	Low	Low	
Friday 1 hour field training followed by power-based weight training	Medium	Medium	Medium	
Saturday 30 min light training	High (load for game)	High (load for game)	High (load for game)	(lo
Sunday Game day	High	High	High	

(b)

(b) Theoretical overview of the fuel for the work required model presented for an elite team sport player (e.g. rugby player) who trains twice per day on 5 days with 2 rest days per week. The athlete performs field-based training in the morning followed by resistance training after lunch. In this example, the athlete has four main feeding points. High CHO intake is advised at breakfast, lunch, dinner and evening snack on **Monday** (game day +1) to assist with recovery. **Tuesday** is the high-intensity training day and therefore high CHO is prescribed at breakfast and lunch but reduced in the evening meal to prepare for a lower intensity session on Wednesday. On **Wednesday** medium CHO intake is prescribed at breakfast and lunch to fuel the lower intensity morning session and post-lunch weights, but is then reduced in the evening to prepare for a rest day. **Thursday** is a rest day and therefore CHO is low all day. **Friday** is game day −2 and therefore CHO is increased to fuel the training sessions plus to begin the CHO load in preparation for game day. **Saturday** (game day −1) is a high-CHO day at every meal, to load muscle glycogen for game day. **Sunday** (game day) is a high-CHO breakfast and lunch, to continue to load muscle and liver glycogen, and then high CHO at dinner and evening snack, to replace muscle glycogen. The model should be adjusted according to the number of feeding points and training sessions as well as

the athlete's personal preferences

Energy periodisation

The relative energy deficiency in sport syndrome (RED-S) was developed[157] in recognition that low energy availability also induces negative effects in male athletes (Chapter 29). As such, RED-S extends beyond the female athlete triad and can affect multiple aspects of physical and mental wellbeing (Figs 33.7a and b). Energy availability is calculated as follows and essentially refers to the energy available to support body functions once the cost of exercise has been accounted for:

Energy availability = (Total energy intake–Exercise energy expenditure)/Lean body mass

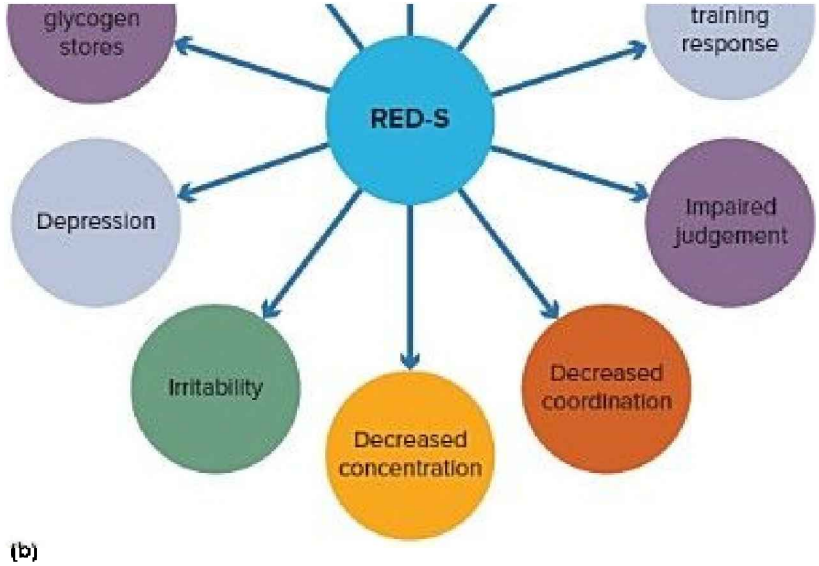


Figure 33.7 (a) Physiological and psychological consequences of RED-S (b) Performance consequences of RED-S REPRODUCED WITH PERMISSION MOUNTJOY M, SUNDGOT-BORGEN J, BURKE L, ET AL. THE IOC CONSENSUS STATEMENT: BEYOND THE FEMALE ATHLETE TRIAD-RELATIVE ENERGY DEFICIENCY IN SPORT (RED-S). BR J SPORTS MED 2014;48(7):491–7; ORIGINAL CONCEPT: CONSTANTINI NW. MEDICAL CONCERNS OF THE DANCER. BOOK OF ABSTRACTS. FIMS WORLD CONGRESS OF SPORTS MEDICINE BUDAPEST, 2002:151.

When energy availability is chronically <30 kcal/kg lean body mass, athletes are susceptible to exhibiting many of the symptoms outlined in Figures 33.7a and 33.7b. The IOC has also introduced a clinical assessment tool to screen athletes for RED-S, as well as monitor their return to play, to re-introduce athletes to training and competition once they have been diagnosed with RED-S.[157] While the identification of 30 kcal/kg has been recognised as a level of critical energy availability, it is not to say that athletes should never be below this value. Indeed, for those athletes involved in weight-sensitive sports, there is the need to manipulate body composition to peak for performance. Rather, energy availability should be periodised to help offset the negative consequences associated with chronically low levels of energy availability and yet achieve peak performance. As a case example, the reader is referred to a 10-year case study of an elite female middle-distance runner.[158]

Wider periodisation

The principles of periodisation, of course, extend beyond that of CHO and energy availability, and should be focused around the athlete's annual performance plan. As a theoretical example, Figure 3 3.8 displays a professional road cyclist's periodised plan taking into account the requirement to peak for races in July, August and September while also supporting prior altitude training camps and targeted phases to optimise body composition.

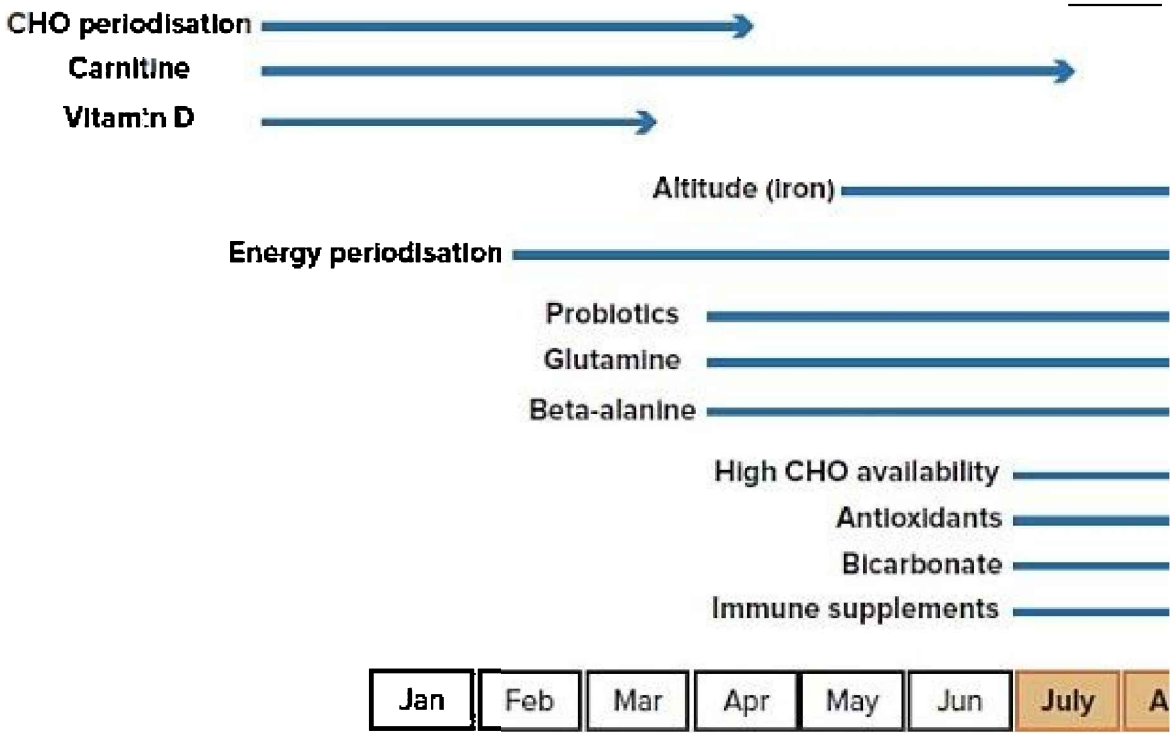


Figure 33.8 Example of a periodised nutrition plan for an elite road cyclist aiming to peak in two grand tours undertaken in July, August and September. In this example, CHO, energy and supplements are strategically introduced and phased in, to achieve peak performance effects

Practical considerations

1. Nutrition requirements are not static, owing to changing training and competition goals.
2. CHO and energy availability can be periodised to augment training adaptations and promote weight loss, respectively.
3. Chronically low energy availability (i.e. <30 kcal/kg lean muscle mass) can induce negative physical and mental consequences of RED-S that can impair performance.
4. Principles of nutrition periodisation should also consider supplements and ergogenic aids so as to achieve peak performance when necessary.

SUMMARY

The role of nutrition in modulating training adaptations, body composition, recovery, immune function and, of course, performance is becoming increasingly recognised in high-performance sport. While many sports employ full-time or part-time sport nutritionists, many aspects of the nutrition service are often delivered by other members of the sports performance team, such as the sports physician. Accordingly, the material presented in this chapter provides an overview of the key issues that clinicians are likely to face in their current practice. As always, we encourage the clinician to refer to appropriate specialists for more detailed guidance on specific issues.

REFERENCES

1. MacLaren DPM, Morton JP. *Biochemistry for Sport and Exercise Metabolism*. London: John Wiley & Sons, 2012.
2. Nader GA. Concurrent strength and endurance training: from molecules to man. *Med Sci Sports Exerc* 2006; 38(11): 1965–70.
3. van Loon LJ, Greenhaff PL, Constantin-Teodosiu D et al. The effects of increasing exercise intensity on muscle fuel utilisation in humans. *J Physiol* 2001; 536(Pt 1): 295–304.
4. Magkos F, Yannakoulia M. Methodology of dietary assessment in athletes: concepts and pitfalls. *Curr Opin Clin Nutr Metab Care* 2003; 6(5): 539–49.
5. Bradley WJ, Cavanagh B, Douglas W et al. Energy intake and expenditure assessed 'in-season' in an elite European rugby union squad. *Eur J Sport Sci* 2015; 15(6): 469–79.
6. Anderson L, Orme P, Naughton RJ et al. Energy intake and expenditure of professional soccer players of the English Premier League: evidence of carbohydrate periodisation. *Int J Sport Nutr Exerc Metab* 2017; 27(3): 228–38.
7. Livingstone MB, Robson PJ, Wallace JM. Issues in dietary intake assessment of children and adolescents. *Br J Nutr* 2004; 92 Suppl 2: S213–22.
8. Conway JM, Ingwersen LA, Vinyard BT et al. Effectiveness of the US Department of Agriculture 5-step multiple-pass method in assessing food intake in obese and nonobese women. *Am J Clin Nutr* 2003; 77(5): 1171–8.
9. Morehen JC, Bradley WJ, Clarke J et al. The assessment of total energy expenditure during a 14-day 'in-season' period of professional rugby league players using the doubly labelled water method. *Int J Sport Nutr Exerc Metab* 2016: 26(5): 464–72.
10. Wilson G, Lucas D, Hambly C et al. Energy expenditure in professional flat jockeys using doubly labelled water during the racing season: implications for body weight management. *Eur J Sport Sci* 2018; 18(2): 235–42.
11. Bazzocchi A, Ponti F, Albisinni U et al. DXA: technical aspects and application. *Eur J Radiol* 2016; 85(8): 1481–92.

12. Bone JL, Ross ML, Tomcik KA et al. Manipulation of muscle creatine and glycogen changes dual X-ray absorptiometry estimates of body composition. *Med Sci Sports Exerc* 2017; 49(5): 1029–35.
13. Nana A, Slater GJ, Hopkins WG et al. Importance of standardized DXA protocol for assessing physique changes in athletes. *Int J Sport Nutr Exerc Metab* 2016; 26(3): 259–67.
14. Nana A, Slater GJ, Stewart AD et al. Methodology review: using dual-energy X-ray absorptiometry (DXA) for the assessment of body composition in athletes and active people. *Int J Sport Nutr Exerc Metab* 2015; 25(2): 198–215.
15. Nana A, Slater GJ, Hopkins WG et al. Effects of exercise sessions on DXA measurements of body composition in active people. *Med Sci Sports Exerc* 2013; 45(1): 178–85.
16. Nana A, Slater GR, Hopkins WG et al. Effects of daily activities on DXA measurements of body composition in active people. *Med Sci Sports Exerc* 2012; 44(1): 180–9.
17. Stewart A, Marfell-Jones M. *International Standards for Anthropometric Assessment*. Lower Hutt, New Zealand: International Society for the Advancement of Kinanthropometry, 2011.
18. Reilly T, George K, Marfell-Jones M et al. How well do skinfold equations predict per cent body fat in elite soccer players? *Int J Sports Med* 2009; 30(8): 607–13.
19. Atkinson FS, Foster-Powell K, Brand-Miller JC. International tables of glycemic index and glycemic load values: 2008. *Diabetes Care* 2008; 31(12): 2281–3.
20. Wee SL, Williams C, Tsintzas K et al. Ingestion of a high-glycemic index meal increases muscle glycogen storage at rest but augments its utilization during subsequent exercise. *J Appl Physiol (1985)* 2005; 99(2): 707–14.
21. Burke LM, Collier GR, Hargreaves M. Muscle glycogen storage after prolonged exercise: effect of the glycemic index of carbohydrate feedings. *J Appl Physiol (1985)* 1993; 75(2): 1019–23.
22. Bergstrom J, Hermansen L, Hultman E et al. Diet, muscle glycogen and physical performance. *Acta Physiol Scand* 1967; 71(2): 140–50.
23. Bergstrom J, Hultman E. The effect of exercise on muscle glycogen and electrolytes in normals. *Scand J Clin Lab Invest* 1966; 18(1): 16–20.
24. Sherman WM, Costill DL, Fink WJ et al. Effect of exercise-diet manipulation on muscle glycogen and its subsequent utilization during performance. *Int J Sports Med* 1981; 2(2): 114–18.
25. Bussau VA, Fairchild TJ, Rao A et al. Carbohydrate loading in human muscle: an improved 1 day protocol. *Eur J Appl Physiol* 2002; 87(3): 290–5.
26. Thomas DT, Erdman KA, Burke LM. American College of Sports Medicine Joint Position Statement. Nutrition and Athletic Performance. *Med Sci Sports Exerc* 2016;

48(3): 543–68.

27. Hawley JA, Schabort EJ, Noakes TD et al. Carbohydrate-loading and exercise performance: an update. *Sports Med* 1997; 24(2): 73–81.
28. O'Brien MJ, Viguie CA, Mazzeo RS et al. Carbohydrate dependence during marathon running. *Med Sci Sports Exerc* 1993; 25(9): 1009–17.
29. Leckey JJ, Burke LM, Morton JP et al. Altering fatty acid availability does not impair prolonged, continuous running to fatigue: evidence for carbohydrate dependence. *J Appl Physiol (1985)* 2016; 120(2): 107–13.
30. Ørtenblad N, Nielsen J, Saltin B et al. Role of glycogen availability in sarcoplasmic reticulum Ca^{2+} kinetics in human skeletal muscle. *J Physiol* 2011; 589(Pt 3): 711–25.
31. Casey A, Mann R, Bannister K et al. Effect of carbohydrate ingestion on glycogen resynthesis in human liver and skeletal muscle, measured by (13)C MRS. *Am J Physiol Endocrinol Metab* 2000; 278(1): E65–75.
32. Sherman WM, Peden MC, Wright DA. Carbohydrate feedings 1 h before exercise improves cycling performance. *Am J Clin Nutr* 1991; 54(5): 866–70.
33. Wright DA, Sherman WM, Dernbach AR. Carbohydrate feedings before, during, or in combination improve cycling endurance performance. *J Appl Physiol (1985)* 1991; 71(3): 1082–8.
34. Stellingwerff T, Cox GR. Systematic review: carbohydrate supplementation on exercise performance or capacity of varying durations. *Appl Physiol Nutr Metab* 2014; 39(9): 998–1011.
35. Jeukendrup A. A step towards personalized sports nutrition: carbohydrate intake during exercise. *Sports Med* 2014; 44 Suppl 1: S25–33.
36. Stellingwerff T, Boon H, Gijsen AP et al. Carbohydrate supplementation during prolonged cycling exercise spares muscle glycogen but does not affect intramyocellular lipid use. *Pflugers Arch* 2007; 454(4): 635–47.
37. Gonzalez JT, Fuchs CJ, Smith FE et al. Ingestion of glucose or sucrose prevents liver but not muscle glycogen depletion during prolonged endurance-type exercise in trained cyclists. *Am J Physiol Endocrinol Metab* 2015; 309(12): E1032–9.
38. Coyle EF, Coggan AR, Hemmert MK et al. Muscle glycogen utilization during prolonged strenuous exercise when fed carbohydrate. *J Appl Physiol (1985)* 1986; 61(1): 165–72.
39. Jeukendrup A, Brouns F, Wagenmakers AJ et al. Carbohydrate-electrolyte feedings improve 1 h time trial cycling performance. *Int J Sports Med* 1997; 18(2): 125–9.
40. Carter JM, Jeukendrup AE, Mann CH et al. The effect of glucose infusion on glucose kinetics during a 1-h time trial. *Med Sci Sports Exerc* 2004; 36(9): 1543–50.
41. Carter JM, Jeukendrup AE, Jones DA. The effect of carbohydrate mouth rinse on 1-h cycle time trial performance. *Med Sci Sports Exerc* 2004; 36(12): 2107–11.
42. Burke LM, Maughan RJ. The governor has a sweet tooth—mouth sensing of

nutrients to enhance sports performance. *Eur J Sport Sci* 2015; 15(1): 29–40.

43. Chambers ES, Bridge MW, Jones DA. Carbohydrate sensing in the human mouth: effects on exercise performance and brain activity. *J Physiol* 2009; 587(Pt 8): 1779–94.
44. Lane SC, Bird SR, Burke LM et al. Effect of a carbohydrate mouth rinse on simulated cycling time-trial performance commenced in a fed or fasted state. *Appl Physiol Nutr Metab* 2013; 38(2): 134–9.
45. Kasper AM, Cocking S, Cockayne M et al. Carbohydrate mouth rinse and caffeine improves high-intensity interval running capacity when carbohydrate restricted. *Eur J Sport Sci* 2016; 16(5): 560–8.
46. Pfeiffer B, Stellingwerff T, Zaltas E et al. CHO oxidation from a CHO gel compared with a drink during exercise. *Med Sci Sports Exerc* 2010; 42(11): 2038–45.
47. Pfeiffer B, Stellingwerff T, Zaltas E et al. Oxidation of solid versus liquid CHO sources during exercise. *Med Sci Sports Exerc* 2010; 42(11): 2030–7.
48. Zhang X, O'Kennedy N, Morton JP. Extreme variation of nutritional composition and osmolality of commercially available carbohydrate energy gels. *Int J Sport Nutr Exerc Metab* 2015; 25(5): 504–9.
49. Pfeiffer B, Stellingwerff T, Hodgson AB et al. Nutritional intake and gastrointestinal problems during competitive endurance events. *Med Sci Sports Exerc* 2012; 44(2): 344–51.
50. Ivy JL, Katz AL, Cutler CL et al. Muscle glycogen synthesis after exercise: effect of time of carbohydrate ingestion. *J Appl Physiol (1985)* 1988; 64(4): 1480–5.
51. Bartlett JD, Hawley JA, Morton JP. Carbohydrate availability and exercise training adaptation: too much of a good thing? *Eur J Sport Sci* 2015; 15(1): 3–12.
52. Impey SG, Hearris MA, Hammond KM et al. Fuel for the work required: a theoretical framework for carbohydrate periodization and the glycogen threshold hypothesis. *Sports Med* published online 16 February 2018. doi: 10.1007/s40279-018-0867-7.
53. Tipton KD, Ferrando AA, Phillips SM et al. Postexercise net protein synthesis in human muscle from orally administered amino acids. *Am J Physiol* 1999; 276(4 Pt 1): E628–34.
54. Levenhagen DK, Carr C, Carlson MG et al. Postexercise protein intake enhances whole-body and leg protein accretion in humans. *Med Sci Sports Exerc* 2002; 34(5): 828–37.
55. Pedersen DJ, Lessard SJ, Coffey VG et al. High rates of muscle glycogen resynthesis after exhaustive exercise when carbohydrate is coingested with caffeine. *J Appl Physiol (1985)* 2008; 105(1): 7–13.
56. Mettler S, Mitchell N, Tipton KD. Increased protein intake reduces lean body mass loss during weight loss in athletes. *Med Sci Sports Exerc* 2010; 42(2): 326–37.
57. Bradley WJ, Cavanagh BP, Douglas W et al. Quantification of training load, energy intake and physiological adaptations during a rugby preseason: a case study from

an elite European rugby union squad. *J Strength Cond Res* 2015; 29(2): 534–44.

58. Anderson L, Naughton RJ, Close GL et al. Daily distribution of macronutrient intakes of professional soccer players from the English Premier League. *Int J Sport Nutr Exerc Metab* 2017; 27(6): 491–8.
59. Morton RW, Murphy KT, McKellar SR et al. A systematic review, meta-analysis and meta-regression of the effect of protein supplementation on resistance training-induced gains in muscle mass and strength in healthy adults. *Br J Sports Med* 2018; 52(6): 376–84.
60. Moore DR, Robinson MJ, Fry JL et al. Ingested protein dose response of muscle and albumin protein synthesis after resistance exercise in young men. *Am J Clin Nutr* 2009; 89(1): 161–8.
61. Macnaughton LS, Wardle SL, Witard OC et al. The response of muscle protein synthesis following whole-body resistance exercise is greater following 40 g than 20 g of ingested whey protein. *Physiol Rep* 2016; 4(15): e12893. doi: 10.14814/phy2.12893.
62. Tang JE, Moore DR, Kujbida GW et al. Ingestion of whey hydrolysate, casein, or soy protein isolate: effects on mixed muscle protein synthesis at rest and following resistance exercise in young men. *J Appl Physiol (1985)* 2009; 107(3): 987–92.
63. Phillips SM, Tang JE, Moore DR. The role of milk- and soy-based protein in support of muscle protein synthesis and muscle protein accretion in young and elderly persons. *J Am Coll Nutr* 2009; 28(4): 343–54.
64. Burke LM, Winter JA, Cameron-Smith D et al. Effect of intake of different dietary protein sources on plasma amino acid profiles at rest and after exercise. *Int J Sport Nutr Exerc Metab* 2012; 22(6): 452–62.
65. Trommelen J, Kouw IWK, Holwerda AM et al. Presleep dietary protein-derived amino acids are incorporated in myofibrillar protein during postexercise overnight recovery. *Am J Physiol Endocrinol Metab* published online 23 May 2017. doi: 10.1152/ajpendo.00273.2016.
66. Snijders T, Res PT, Smeets JS et al. Protein ingestion before sleep increases muscle mass and strength gains during prolonged resistance-type exercise training in healthy young men. *J Nutr* 2015; 145(6): 1178–84.
67. Hu FB. Are refined carbohydrates worse than saturated fat? *Am J Clin Nutr* 2010; 91(6): 1541–2.
68. Astrup A, Dyerberg J, Elwood P et al. The role of reducing intakes of saturated fat in the prevention of cardiovascular disease: where does the evidence stand in 2010? *Am J Clin Nutr* 2011; 93(4): 684–8.
69. Mozaffarian D, Katan MB, Ascherio A et al. Trans fatty acids and cardiovascular disease. *N Engl J Med* 2006; 354(15): 1601–13.
70. Yeo WK, Carey AL, Burke L et al. Fat adaptation in well-trained athletes: effects on

cell metabolism. *Appl Physiol Nutr Metab* 2011; 36(1): 12–22.

71. Stellingwerff T, Spriet LL, Watt MJ et al. Decreased PDH activation and glycogenolysis during exercise following fat adaptation with carbohydrate restoration. *Am J Physiol Endocrinol Metab* 2006; 290(2): E380–8.
72. Burke LM, Ross ML, Garvican-Lewis LA et al. Low carbohydrate, high fat diet impairs exercise economy and negates the performance benefit from intensified training in elite race walkers. *J Physiol* 2017; 595(9): 2785–807.
73. Hammond KM, Impey SG, Currell K et al. Postexercise high-fat feeding suppresses p70S6K1 activity in human skeletal muscle. *Med Sci Sports Exerc* 2016; 48(11): 2108–17.
74. Mohr M, Krustrup P, Nybo L et al. Muscle temperature and sprint performance during soccer matches—beneficial effect of re-warm-up at half-time. *Scand J Med Sci Sports* 2004; 14(3): 156–62.
75. Maughan RJ, Watson P, Evans GH et al. Water balance and salt losses in competitive football. *Int J Sport Nutr Exerc Metab* 2007; 17(6): 583–94.
76. Mohr M, Mujika I, Santisteban J et al. Examination of fatigue development in elite soccer in a hot environment: a multi-experimental approach. *Scand J Med Sci Sports* 2010; 20 Suppl 3: 125–32.
77. McGregor SJ, Nicholas CW, Lakomy HK et al. The influence of intermittent high-intensity shuttle running and fluid ingestion on the performance of a soccer skill. *J Sports Sci* 1999; 17(11): 895–903.
78. Gonzalez-Alonso J. Hyperthermia impairs brain, heart and muscle function in exercising humans. *Sports Med* 2007; 37(4–5): 371–3.
79. Kurdak SS, Shirreffs SM, Maughan RJ et al. Hydration and sweating responses to hot-weather football competition. *Scand J Med Sci Sports* 2010; 20 Suppl 3: 133–9.
80. Bergeron MF. Heat cramps: fluid and electrolyte challenges during tennis in the heat. *J Sci Med Sport* 2003 Mar; 6(1): 19–27.
81. Sawka MN, Burke LM, Eichner ER et al. American College of Sports Medicine position stand. Exercise and fluid replacement. *Med Sci Sports Exerc* 2007; 39(2): 377–90.
82. Noakes TD. Is drinking to thirst optimum? *Ann Nutr Metab* 2010; 57 Suppl 2: 9–17.
83. Adams JD, Sekiguchi Y, Suh HG et al. Dehydration impairs cycling performance, independently of thirst: a blinded study. *Med Sci Sports Exerc* published online 5 March 2018. doi: 10.1249/MSS.0000000000001597.
84. Almond CS, Shin AY, Fortescue EB et al. Hyponatremia among runners in the Boston Marathon. *N Engl J Med* 2005; 352(15): 1550–6.
85. Lee JK, Shirreffs SM. The influence of drink temperature on thermoregulatory responses during prolonged exercise in a moderate environment. *J Sports Sci* 2007; 25(9): 975–85.

86. Vist GE, Maughan RJ. The effect of osmolality and carbohydrate content on the rate of gastric emptying of liquids in man. *J Physiol* 1995; 486(Pt 2): 523–31.
87. Maughan RJ, Watson P, Cordery PA et al. A randomized trial to assess the potential of different beverages to affect hydration status: development of a beverage hydration index. *Am J Clin Nutr* 2016; 103(3): 717–23.
88. Expert Group on Vitamins and Minerals (UK). *Safe Upper Levels for Vitamins and Minerals*. 2003. https://cot.food.gov.uk/committee/committee-on-toxicity/cotreports/cotjointreps/evmreport
89. Owens DJ, Allison R, Close GL. Vitamin D and the athlete: current perspectives and new challenges. *Sports Med* 2018; 48(Suppl 1): 3–16.
90. Close GL, Russell J, Cobley JN et al. Assessment of vitamin D concentration in non-supplemented professional athletes and healthy adults during the winter months in the UK: implications for skeletal muscle function. *J Sports Sci* 2013; 31(4): 344–53.
91. Owens DJ, Sharples AP, Polydorou I et al. A systems-based investigation into vitamin D and skeletal muscle repair, regeneration and hypertrophy. *Am J Physiol Endocrinol Metab* 2015; 309(12): E1019–31.
92. He CS, Handzlik M, Fraser WD et al. Influence of vitamin D status on respiratory infection incidence and immune function during 4 months of winter training in endurance sport athletes. *Exerc Immunol Rev* 2013; 19: 86–101.
93. Zittermann A. Vitamin D in preventive medicine: are we ignoring the evidence? *Br J Nutr* 2003; 89(5): 552–72.
94. Owens DJ, Tang JC, Bradley WJ et al. Efficacy of high-dose vitamin D supplements for elite athletes. *Med Sci Sports Exerc* 2017; 49(2): 349–56.
95. Burke LM, Castell LM, Stear SJ et al. BJSM reviews: A-Z of nutritional supplements: dietary supplements, sports nutrition foods and ergogenic aids for health and performance, Part 7. *Br J Sports Med* 2010; 44(5): 389–91.
96. Clenin G, Cordes M, Huber A et al. Iron deficiency in sports— definition, influence on performance and therapy. *Swiss Med Wkly* 2015; 145:w14196.
97. DellaValle DM, Haas JD. Impact of iron depletion without anemia on performance in trained endurance athletes at the beginning of a training season: a study of female collegiate rowers. *Int J Sport Nutr Exerc Metab* 2011; 21(6): 501–6.
98. Tsalis G, Nikolaidis MG, Mougios V. Effects of iron intake through food or supplement on iron status and performance of healthy adolescent swimmers during a training season. *Int J Sports Med* 2004; 25(4): 306–13.
99. Peeling P, Dawson B, Goodman C et al. Athletic induced iron deficiency: new insights into the role of inflammation, cytokines and hormones. *Eur J Appl Physiol* 2008; 103(4): 381–91.
100. International Olympic Committee Expert Group on Dietary Supplements in Athletes. International Olympic Committee Expert Group Statement on Dietary Supplements

in Athletes. *Int J Sport Nutr Exerc Metab* published online 1 March 2018. doi: 10.1123/ijsnem.2018-0055.

101. Peeling P, Binnie MJ, Goods PSR et al. Evidence-based supplements for the enhancement of athletic performance. *Int J Sport Nutr Exerc Metab* published online 21 February 2018. doi: 10.1123/ijsnem.2017-0343.
102. Phillips SM. The science of muscle hypertrophy: making dietary protein count. *Proc Nutr Soc* 2011; 70(1): 100–3.
103. Res PT, Groen B, Pennings B et al. Protein ingestion before sleep improves postexercise overnight recovery. *Med Sci Sports Exerc* 2012; 44(8): 1560–9.
104. Blomstrand E. Amino acids and central fatigue. *Amino Acids* 2001; 20(1): 25–34.
105. Zanchi NE, Gerlinger-Romero F, Guimaraes-Ferreira L et al. HMB supplementation: clinical and athletic performance-related effects and mechanisms of action. *Amino Acids* 2011; 40(4): 1015–25.
106. Phillips SM, Aragon AA, Arciero PJ et al. Changes in body composition and performance with supplemental HMB-FA+ATP. *J Strength Cond Res* 2017; 31(5): e71–2.
107. Tarnopolsky MA. Caffeine and creatine use in sport. *Ann Nutr Metab* 2010; 57 Suppl 2: 1–8.
108. Brilla LR, Conte V. Effects of a novel zinc-magnesium formulation on hormones and strength. *J Exerc Physiol Online* 2000; 3(4): 26–36.
109. West DW, Kujbida GW, Moore DR et al. Resistance exercise-induced increases in putative anabolic hormones do not enhance muscle protein synthesis or intracellular signalling in young men. *J Physiol* 2009; 587(Pt 21): 5239–47.
110. Topo E, Soricelli A, D'Aniello A et al. The role and molecular mechanism of D-aspartic acid in the release and synthesis of LH and testosterone in humans and rats. *Reprod Biol Endocrinol* 2009; 7:120.
111. Willoughby DS, Leutholtz B. D-aspartic acid supplementation combined with 28 days of heavy resistance training has no effect on body composition, muscle strength and serum hormones associated with the hypothalamo–pituitary–gonadal axis in resistance-trained men. *Nutr Res* 2013; 33(10): 803–10.
112. Schoeller DA, Watras AC, Whigham LD. A meta-analysis of the effects of conjugated linoleic acid on fat-free mass in humans. *Appl Physiol Nutr Metab* 2009; 34(5): 975–8.
113. Venables MC, Hulston CJ, Cox HR et al. Green tea extract ingestion, fat oxidation and glucose tolerance in healthy humans. *Am J Clin Nutr* 2008; 87(3): 778–84.
114. Trexler ET, Smith-Ryan AE, Roelofs EJ et al. Effects of coffee and caffeine anhydrous on strength and sprint performance. *Eur J Sport Sci* 2016; 16(6): 702–10.
115. Hobson RM, Saunders B, Ball G et al. Effects of beta-alanine supplementation on exercise performance: a meta-analysis. *Amino Acids* 2012; 43(1): 25–37.
116. McNaughton LR, Siegler J, Midgley A. Ergogenic effects of sodium bicarbonate. *Curr Sports Med Rep* 2008; 7(4): 230–6.

117. McNaughton L, Dalton B, Palmer G. Sodium bicarbonate can be used as an ergogenic aid in high-intensity, competitive cycle ergometry of 1 h duration. *Eur J Appl Physiol Occup Physiol* 1999; 80(1): 64–9.
118. Jones AM. Dietary nitrate supplementation and exercise performance. *Sports Med* 2014; 44 Suppl 1: S35–45.
119. Wylie LJ, Kelly J, Bailey SJ et al. Beetroot juice and exercise: pharmacodynamic and dose-response relationships. *J Appl Physiol (1985)* 2013; 115(3): 325–36.
120. Wall BT, Stephens FB, Constantin-Teodosiu D et al. Chronic oral ingestion of L-carnitine and carbohydrate increases muscle carnitine content and alters muscle fuel metabolism during exercise in humans. *J Physiol* 2011; 589(Pt 4): 963–73.
121. Stephens FB, Wall BT, Marimuthu K et al. Skeletal muscle carnitine loading increases energy expenditure, modulates fuel metabolism gene networks and prevents body fat accumulation in humans. *J Physiol* 2013; 591(18): 4655–66.
122. Bell PG, Walshe IH, Davison GW et al. Recovery facilitation with Montmorency cherries following high-intensity, metabolically challenging exercise. *Appl Physiol Nutr Metab* 2015; 40(4): 414–23.
123. Bell PG, Walshe IH, Davison GW et al. Montmorency cherries reduce the oxidative stress and inflammatory responses to repeated days high-intensity stochastic cycling. *Nutrients* 2014; 6(2): 829–43.
124. Cobley JN, McHardy H, Morton JP et al. Influence of vitamin C and vitamin E on redox signalling: implications for exercise adaptations. *Free Radic Biol Med* 2015; 84: 65–76.
125. Close GL, Ashton T, McArdle A et al. The emerging role of free radicals in delayed onset muscle soreness and contraction-induced muscle injury. *Comp Biochem Physiol A Mol Integr Physiol* 2005; 142(3): 257–66.
126. Gomez-Cabrera MC, Ristow M, Vina J. Antioxidant supplements in exercise: worse than useless? *Am J Physiol Endocrinol Metab* 2012; 302(4): E476–7; author reply E478–9.
127. Hemila H, Fitzgerald JT, Petrus EJ et al. Zinc acetate lozenges may improve the recovery rate of common cold patients: an individual patient data meta-analysis. *Open Forum Infect Dis* 2017; 4(2):ofx059.
128. Shirreffs SM, Maughan RJ. Volume repletion after exercise-induced volume depletion in humans: replacement of water and sodium losses. *Am J Physiol* 1998; 274(5 Pt 2): F868–75.
129. Maughan RJ, Shirreffs SM. Dehydration and rehydration in competative (sic) sport. *Scand J Med Sci Sports* 2010; 20 Suppl 3: 40–7.
130. Walsh NP, Gleeson M, Pyne DB et al. Position Statement. Part two: Maintaining immune health. *Exerc Immunol Rev* 2011; 17: 64–103.
131. Willis KS, Peterson NJ, Larson-Meyer DE. Should we be concerned about the vitamin D status of athletes? *Int J Sport Nutr Exerc Metab* 2008; 18(2): 204–24.

132. Jouris KB, McDaniel JL, Weiss EP. The effect of omega-3 fatty acid supplementation on the inflammatory response to eccentric strength exercise. *J Sports Sci Med* 2011; 10(3): 432–8.
133. Smith GI, Atherton P, Reeds DN et al. Dietary omega-3 fatty acid supplementation increases the rate of muscle protein synthesis in older adults: a randomized controlled trial. *Am J Clin Nutr* 2011; 93(2): 402–12.
134. Shing CM, Hunter DC, Stevenson LM. Bovine colostrum supplementation and exercise performance: potential mechanisms. *Sports Med* 2009; 39(12): 1033–54.
135. Pugh JN, Sage S, Hutson M et al. Glutamine supplementation reduces markers of intestinal permeability during running in the heat in a dose-dependent manner. *Eur J Appl Physiol* 2017; 117(12): 2569–77.
136. Haakonssen EC, Ross ML, Knight EJ et al. The effects of a calcium-rich pre-exercise meal on biomarkers of calcium homeostasis in competitive female cyclists: a randomised crossover trial. *PLoS One* 2015; 10(5):e0123302.
137. Baar K. Minimizing injury and maximizing return to play: lessons from engineered ligaments. *Sports Med* 2017; 47(Suppl 1): 5–11.
138. Shaw G, Lee-Barthel A, Ross ML et al. Vitamin C-enriched gelatin supplementation before intermittent activity augments collagen synthesis. *Am J Clin Nutr* 2017; 105(1): 136–43.
139. Nicol LM, Rowlands DS, Fazakerly R et al. Curcumin supplementation likely attenuates delayed onset muscle soreness (DOMS). *Eur J Appl Physiol* 2015; 115(8): 1769–77.
140. Buhrmann C, Mobasheri A, Busch F et al. Curcumin modulates nuclear factor kappaB (NF-kappaB)-mediated inflammation in human tenocytes in vitro: role of the phosphatidylinositol 3-kinase/Akt pathway. *J Biol Chem* 2011; 286(32): 28556–66.
141. Jiang D, Gao P, Lin H et al. Curcumin improves tendon healing in rats: a histological, biochemical and functional evaluation. *Connect Tissue Res* 2016; 57(1): 20–7.
142. Rogerson D. Vegan diets: practical advice for athletes and exercisers. *J Int Soc Sports Nutr* 2017;14:36.
143. Tipton KD. Nutritional support for exercise-induced injuries. *Sports Med* 2015; 45 Suppl 1: S93–104.
144. Reilly T, Waterhouse J, Burke LM et al.; International Association of Athletics Federations. Nutrition for travel. *J Sports Sci* 2007; 25 Suppl 1: S125–34.
145. Lis DM, Stellingwerff T, Kitic CM et al. Low FODMAP: a preliminary strategy to reduce gastrointestinal distress in athletes. *Med Sci Sports Exerc* 2018; 50(1): 116–23.
146. Joy E, Kussman A, Nattiv A. 2016 update on eating disorders in athletes: a comprehensive narrative review with a focus on clinical assessment and management. *Br J Sports Med* 2016; 50(3): 154–62.
147. Loucks AB, Kiens B, Wright HH. Energy availability in athletes. *J Sports Sci* 2011; 29

Suppl 1: S7–15.

148. Loucks AB, Stachenfeld NS, DiPietro L. The female athlete triad: do female athletes need to take special care to avoid low energy availability? *Med Sci Sports Exerc* 2006; 38(10): 1694–700.
149. Hemila H. Zinc lozenges may shorten the duration of colds: a systematic review. *Open Respir Med* J 2011; 5: 51–58.
150. Yeo WK, Paton CD, Garnham AP et al. Skeletal muscle adaptation and performance responses to once a day versus twice every second day endurance training regimens. *J Appl Physiol (1985)* 2008; 105(5): 1462–70.
151. Hulston CJ, Venables MC, Mann CH et al. Training with low muscle glycogen enhances fat metabolism in well-trained cyclists. *Med Sci Sports Exerc* 2010; 42(11): 2046–55.
152. Hansen AK, Fischer CP, Plomgaard P et al. Skeletal muscle adaptation: training twice every second day vs. training once daily. *J Appl Physiol (1985)* 2005; 98(1): 93–9.
153. Marquet LA, Brisswalter J, Louis J et al. Enhanced endurance performance by periodization of carbohydrate intake: 'sleep low' strategy. *Med Sci Sports Exerc* 2016; 48(4): 663–72.
154. Gleeson M, Nieman DC, Pedersen BK. Exercise, nutrition and immune function. *J Sports Sci* 2004; 22(1): 115–25.
155. Howarth KR, Phillips SM, MacDonald MJ et al. Effect of glycogen availability on human skeletal muscle protein turnover during exercise and recovery. *J Appl Physiol (1985)* 2010; 109(2): 431–8.
156. Cox GR, Clark SA, Cox AJ et al. Daily training with high carbohydrate availability increases exogenous carbohydrate oxidation during endurance cycling. *J Appl Physiol (1985)* 2010; 109(1): 126–34.
157. Mountjoy M, Sundgot-Borgen J, Burke L et al. The IOC consensus statement: beyond the Female Athlete Triad—Relative Energy Deficiency in Sport (RED-S). *Br J Sports Med* 2014; 48(7): 491–7.
158. Stellingwerff T. Case study: body composition periodization in an Olympic-level female middle-distance runner over a 9-year career. *Int J Sport Nutr Exerc Metab* published online 15 November 2017. doi: 10.1123/ijsnem.2017-0312.

Chapter 34

Drugs and the athlete

"One day I'm a normal person with a normal life," he said. "The next I'm standing on a street corner in Madrid with a secret phone and a hole in my arm and I'm bleeding all over, hoping I don't get arrested. It was completely crazy. But it seemed like the only way at the time."

Tyler Hamilton, *The Secret Race*, 2012

The use of performance-enhancing drugs is probably *the* major problem facing sport today. Despite intense efforts by sporting bodies and the medical profession to eliminate the problem, drug taking to assist sports performance remains widespread (Table 34.1).

Table 34.1 WADA testing—Olympic sports, 2016

Sport	No. of samples	AAFs	%AAF
Aquatics	15 174	145	1.0
Athletics	31 433	373	1.2
Basketball	5 079	51	1.0
Boxing	4 769	97	2.0
Canoe	4 196	71	1.7
Cycling	23 132	252	1.1
Football	33 227	168	0.5
Gymnastics	2 123	18	0.8
Handball	3 889	16	0.4
Judo	4 272	49	1.1
Rowing	4 930	30	0.6
Rugby	7 366	75	1.0
Shooting	1 811	8	0.4
Taekwondo	1 716	25	1.5
Tennis	4 544	33	0.7
Triathlon	3 665	34	0.9
Volleyball	4 199	31	0.7

Weightlifting	8 834	167	1.9
Wrestling	5 069	135	2.7

AAF = adverse analytical finding (+ve test)
2016 Anti-Doping Testing Figures by Sport, Table 1 page 6 https://www.wada-ama.org/sites/default/files/resources/files/2016_anti-doping_testing_figures.pdf

The World Anti-Doping Agency (WADA) is responsible for producing and maintaining the World Anti-Doping Code, containing the Prohibited List of Substances, which lists those substances and methods that are banned either at all times or in competition only. Doping is defined as the occurrence of one or more of the anti-doping rule violations set forth in Article 2.1 through Article 2.10 of the Code. Substances will be added to the list if they satisfy any two of the following three criteria:

1. they have the potential to enhance performance
2. they have the potential to be detrimental to health
3. they violate the spirit of sport.

The list is reviewed annually and an updated list commences on 1 January each year. The list that took effect on 1 January 2018 contains five classes *of substances* that are prohibited both in and out of competition, another four classes of substances prohibited in competition only, three *methods* prohibited in and out of competition and another group of substances prohibited in particular sports (for edited extracts of the Prohibited List, see boxes in this chapter).

In addition, WADA monitors certain other substances (in 2018, stimulants and narcotics) to detect patterns of misuse; this may lead to these substances being added to the Prohibited List in the future.

World Anti-Doping Code The Prohibited List (as at 1 January 2018)[2]

Substances and methods prohibited at all times (in and out of competition)

S0. Non-approved substances

S1. Anabolic agents

S2. Peptide hormones, growth factors, related substances and mimetics

S3. Beta-2 agonists

S4. Hormone and metabolic modulators

S5. Diuretics and masking agents

Prohibited methods (in and out of competition)

M1. Manipulation of blood and blood components

M2. Chemical and physical manipulation
M3. Gene doping

Prohibited classes of substances (in competition only)

S6. Stimulants

S7. Narcotics

S8. Cannabinoids

S9. Glucocorticosteroids

Substances prohibited in particular sports
P1. Beta-blockers

Note that The Prohibited List is updated annually and is available online: World Anti-Doping Agency (WADA)
https://www.wada-ama.org/en/what-we-do/the-prohibited-list.
The official text of the Prohibited List shall be maintained by WADA and shall be published in English and French. In the event of any conflict between the English and French versions, the English version shall prevail.

Athletes may have illnesses or conditions that require them to take banned medications. In these cases the athlete may apply for a therapeutic use exemption (TUE) from their national anti-doping organisation or their international federation for authority to use the substance. WADA does not grant TUEs but may consider appeals related to the granting or denying of a TUE.

A summary of the prohibited classes of drugs, their medical usage, effect on performance and adverse effects is shown in Table 34.2.

Table 34.2 Prohibited drugs and their effects

Type of drug (examples)	Medical usage	Effect on performance	Adverse effects
Anabolic steroids			
Methandrostenolone, stanozolol, nandrolone	Hypogonadism, severe osteoporosis, breast carcinoma	Increased muscle bulk, increased muscle strength, possibly improving anticatabolic effect, recovery	Acne, baldness, gynaecomastia, decreased sperm production, testes size and sex drive, increased aggression, liver abnormalities, hypertension, hypercholesterolaemia
Peptide hormones, growth factors and related substances			
Erythropoietin (EPO)	Anaemia secondary to chronic renal disease	Increased endurance	Increased blood viscosity, myocardial infarction
Human growth hormone (hGH)	Dwarfism, short stature	Anecdotal evidence only	Allergic reactions, diabetogenic effect, acromegaly
Insulin-like growth factor-1 (IGF-1)	Dwarfism, diabetes mellitus type 2	Anecdotal evidence only	Acromegaly, organomegaly, hypoglycaemia
Human chorionic gonadotrophin (hCG)	Hypogonadism	May increase endogenous production of steroids	Gynaecomastia
Adrenocorticotropic hormone	Steroid-responsive	Euphoria	As in corticosteroids

(ACTH)	conditions		
Beta-2 agonists			
Salbutamol, terbutaline	Asthma, exercise-induced bronchospasm	Possible anabolic effects	Tachycardia, tremor, palpitations
Hormone and metabolic modulators			
Aromatase inhibitors (anastrozole, aminoglutethimide)	Breast cancer	Used to counter gynaecomastia	Joint aches, stiffness
Selective oestrogen receptor modulators (SERMs) (tamoxifen)	Breast cancer, osteoporosis	Males: used with AAS to prevent gynaecomastia Females: muscle bulk (anecdotal evidence)	Females: masculinisation Deep venous thrombosis
Clomiphene, cyclofenil	Anovulatory infertility	Increases gonadotrophin-releasing hormone (GnRH) and endogenous testosterone (anecdotal evidence)	Bloating, stomach pains, blurred vision, headaches, nausea and dizziness
Insulin	Diabetes	Anecdotal evidence only	Hypoglycaemia
Diuretics and other masking agents			
Frusemide, hydrochlorothiazide, chlorothiazide	Hypertension, oedema, congestive cardiac failure	Rapid weight loss, decreases concentration of drugs in urine	Electrolyte imbalance, dehydration, muscle cramps
Stimulants			
Amphetamines (dexamphetamine, dimethylamphetamine)	Narcolepsy, ADHD	May delay fatigue, increased alertness	Anxiety, insomnia, dizziness, euphoria, headache, nausea, vomiting, confusion, psychosis, hypertension, addiction
Ephedra	Dietary supplements for weight loss	Large doses improve cycling performance Additive effect with caffeine	Hypertension, arrythmias, seizure, cerebrovascular accident
Cocaine	Nasal anaesthetic	Increased alertness	Impaired hand—eye coordination, aggression, cardiac and cerebral abnormalities
Narcotics			
Pethidine, morphine	Moderate to severe pain	No evidence of improved performance, may be able to compete with injury	Nausea, vomiting, dizziness, respiratory depression, addiction
Cannabinoids			
Marijuana, hashish	Palliative care, chronic pain	Negative effect	Impaired psychomotor skills, altered perception of time, impaired concentration
Glucocorticosteroids			
Prednisolone	Widely used anti-inflammatory Severe asthma	Euphoria Some evidence of performance enhancement	Cushingoid symptoms
Enhancement of oxygen transfer			
Blood doping Artificial oxygen carriers (haemoglobin oxygen carriers, perfluorochemicals)	Nil Rapid blood volume expansion following acute blood loss	Improves endurance Improved endurance (no evidence)	Transfusion reaction, increased blood viscosity

SUBSTANCES AND METHODS PROHIBITED AT ALL TIMES (IN AND OUT OF COMPETITION)

Non-approved substances

Any pharmacological substance which is not addressed by any of the subsequent sections of the Prohibited List and with no current approval by any governmental regulatory health authority for human therapeutic use (i.e. drugs under pre-clinical or clinical development or discontinued) is prohibited at all times.

S1: Anabolic agents Refer to www.wada-ama.org/en/what-we-do/the-prohibited-list

Anabolic agents are prohibited.

1. Anabolic androgenic steroids (AAS)
   (a) Exogenous AAS including: 1-androstenediol, 1 -androstenedione, 1 -androsterone, 1 -testosterone, 4-hydroxytestosterone, bolandiol, bolasterone, calusterone, clostebol, danazol, dehydrochlormethyltestosterone, desoxymethyltestosterone, drostanolone, ethylestrenol, fluoxymesterone, formebolone, furazabol, gestrinone, mestanolone, mesterolone, metandienone, metenolone, methandriol, methasterone, methyldienolone, methyl-1 -testosterone, methylnortestosterone, methyltestosterone, metribolone, mibolerone, norboletone, norclostebol, norethandrolone, oxabolone, oxandrolone, oxymesterone, oxymetholone, prostanozol, quinbolone, stanozolol, stenbolone, tetrahydrogestrinone, trenbolone, and other substances with a similar chemical structure or similar biological effect(s).
   (b) Endogenous AAS including 19-norandrostenediol, 19-norandrostenedione, androstanolone, androstenediol, androstenedione, boldenone, boldione, nandrolone, prasterone (dehydroepiandrosterone, DHEA), testosterone, and their metabolites and isomers.
2. Other anabolic agents

   Including, but not limited to: clenbuterol, selective androgen receptor modulators (SARMs, e.g. andarine, LGD-4033, ostarine and RAD140), tibolone, zeranol and zilpaterol.

AAS = anabolic androgenic steroids; ADHD = attention deficit hyperactivity disorder

Anabolic agents

Anabolic androgenic steroids

Androgens are steroid hormones that are secreted primarily by the testes but also by the adrenal

glands and ovaries. Testosterone is the principal androgen responsible for the development of the primary sexual characteristics in utero and during the neonatal period. It is also responsible for the development of the pubertal secondary sexual characteristics and contributes to the increase in height and amount of skeletal muscle at that time. Testosterone promotes aggressive behaviour, which is possibly due to direct stimulation of brain receptors. It also plays a role in sexual orientation.

Anabolic androgenic steroid (AAS) hormones are derivatives of testosterone. The structure of the testosterone molecule can be adjusted to maximise either the androgenic or anabolic effect. Athletes generally abuse those agents that have maximum anabolic effect while minimising the androgenic effect. A large number of different AAS hormones have been synthesised.

Examples of prohibited AASs are shown in the box above. The exogenous ones are synthetic analogues of testosterone and the endogenous ones are naturally occurring and are involved in the metabolic pathways of testosterone.

The clinical uses of anabolic steroids are limited. They may be used as hormone replacement for primary and secondary hypogonadism, Klinefelter's syndrome and, occasionally, delayed puberty. They have also been used to treat disturbances of nitrogen balance and muscular development and several other non-endocrine diseases, including several forms of anaemia, hereditary angioneurotic oedema and breast carcinoma. Steroids increase lean body mass in patients with chronic obstructive pulmonary disease and HIV, and they may have a role in the treatment of muscular dystrophy and several dermatological diseases.[3]

The use of AASs in certain sports, particularly power sports such as weightlifting, power lifting,[4] sprinting and throwing, is widespread, as is their use by bodybuilders.[5] The use of AASs in footballers varies in the different codes. There would appear to be a high incidence of use in players of American football, with a lower incidence in players of other football codes.

While the incidence of AAS use is highest in elite athletes, there is a disturbingly high incidence among recreational and high school athletes.[6–9] This may be related to a desire to increase sporting performance or to improve body image. In 1987, the first US national study of AAS use at a high school level found that 6.6% of male seniors had used the drugs; 38% of those users had commenced before turning 16 years of age.[6] Subsequent studies have confirmed that 4–6% (range 3–12%) of US high school boys have used AASs at some time, as have 1–2% of US high school girls.[10]

A worldwide review of the literature in 2014 suggested that 3.3% of the world's population have used anabolic steroids at least once, most of whom were male (around 6.4% of males and 1.6% of females). The biggest users were in the Middle East, followed by South America, Europe, North America, Oceania, Africa and Asia. Use was highest among recreational sportspeople, followed by athletes, prisoners, drug users, high school students and non-athletes. The researchers concluded that millions of individuals across the world, many of whom have no athletic ambitions, are using AASs to increase and improve their physical strength and appearance.[11]

AASs are taken orally or by intramuscular injection. More recently, transdermal patches, buccal tablets, nasal sprays, gels and creams are being used as the delivery mechanism.[12]

AASs are usually used in a cyclical manner, with periods of heavy use, generally lasting 6–12 weeks, alternating with drug-free periods lasting 1–12 months. The aim of the drug-free periods is to reduce the adverse effects of the drugs; whether this is the case remains unknown.

AAS users follow a 'pyramid' regimen, which commences with a low daily dose and gradually increases to a high dose then back down to a lower dose, and/or a 'stacking' regimen, in which several different types of anabolic steroids, oral and/or injectable, are taken simultaneously. The purpose behind the stacking regimen is to achieve receptor saturation with a lower total androgen dose than would be required if only one compound were used. Users hope that this regimen may reduce the incidence of adverse effects. Commonly, a combination known as 'pyramid stacking' is used. The dosages taken by AAS users vary, but those wishing to bulk up frequently use dosages 10–100 times the physiological dose.

Different AASs are used at different times of the training program depending on the phase of activity being performed. Certain AASs are regarded by their users (e.g. bodybuilders) as more appropriate for specific aims, such as increased muscle definition. AAS users may use other drugs (e.g. diuretics, anti-oestrogens, human chorionic gonadotrophin, hCG, and anti-acne medications) to counteract the common adverse effects of AASs.

Most AASs are obtained via a black market that exists through gymnasiums, health centres and increasingly on the internet. Information (and misinformation) is readily available in pamphlets, niche-market magazines and, of course, the internet.

Testosterone precursors (e.g. dehydroepiandrosterone, DHEA) and designer steroids (e.g. tetrahydrogestrinone, THG) have recently received considerable publicity (see below).

Effect on performance

Anabolic steroids have a threefold effect.

1. *Anabolic effect.* This is due to the induction of protein synthesis in skeletal muscle cells. AASs attach to specific cytoplasmic receptors in muscle cells, and this complex then activates the nucleus to synthesise ribosomal and messenger RNA and initiate the process of protein synthesis. This anabolic effect continues during steroid treatment. An additional anabolic effect may occur indirectly through increased levels of endogenous growth hormone associated with AAS administration.
2. *Anticatabolic effect.* This is mediated in two ways. AASs may reverse the catabolic effects of glucocorticosteroids released at times of training stress, and they may improve the utilisation of ingested protein, thereby increasing nitrogen retention. This effect depends on adequate protein intake. Athletes in heavy training, especially weight training, are in a catabolic state. This is associated with the release of glucocorticosteroids and increased nitrogen utilisation. When intense training is combined with insufficient recovery time or inadequate protein intake, a chronic catabolic state may develop. This can be associated with impaired training and competition performance and the development of overuse injuries. Anabolic steroids may reverse this catabolic state and permit an increased training load.

AAS use appears to increase muscle size and muscle strength but only when certain conditions are met. For anabolic steroids to be effective in increasing muscle size and strength, the athlete taking the steroids must perform intense weight training and have an adequate protein intake. If these conditions are met, an increase in muscle size and strength will result.

3. *Enhancement of aggressive behaviour.* Increased aggression may encourage a greater training intensity and may also be advantageous during competition in sports such as weightlifting and contact sports. However, there may also be negative psychological effects, as discussed below.

There is considerable evidence that testosterone administration combined with weight training leads to an increase in lean body mass and a decrease in body fat.[13–15] This effect appears to be dose related. The change in muscle mass with testosterone use is due to muscle fibre hypertrophy and increases in myonuclear number.[16]

Studies have demonstrated a 5–20% increase in baseline strength, depending on the drugs and dose used as well as the administration period.[3]

While the majority of anabolic steroid use has been by athletes in power events, there is anecdotal evidence of a positive effect of anabolic steroids on endurance exercise. Firstly, the anticatabolic effect may improve recovery from heavy training, thus reducing the likelihood of injury and allowing the athlete to undertake greater volume and intensity of training. Secondly, anabolic steroids have a stimulatory effect on bone marrow, which may result in an increased production of red blood cells, thus improving the oxygen-carrying capacity of the blood.

Long-term treatment of certain anaemias with AASs has shown an increase in haemoglobin concentrations, but the majority of studies have failed to show any improvement in endurance performance with AAS.[3]

The above effects of anabolic steroids occur in both males and females. AASs are thought to have a more dramatic effect on strength and power in female athletes than in male. In some sport events, female athletes with high or very high androgen levels (whether of endogenous or exogenous origin) have an estimated competitive benefit of 2–5% over those with androgen levels within the normal female range.[17]

Adverse effects

Adverse effects of anabolic steroid usage (Table 34.3) are extremely common and can be particularly significant in women.

The majority of adverse effects are reversible on cessation of the drug(s). However, a number of serious adverse effects have been reported with anabolic steroid use, in some cases leading to death. The mortality rate among elite power lifters suspected of steroid abuse was significantly higher (12.9%) than that of a control population (3.1%).[18] In a review of 19 deaths associated with AAS use, a mechanical cardiovascular cause of death (bilateral pulmonary embolism from deep venous thrombus of lower extremities) was found in only one case. In numerous cases, a common

finding was a left ventricular hypertrophy, frequently associated with fibrosis and myocytolysis.[19] Another study investigating the deaths of 34 known users of the drugs concluded that AAS use was associated with an increased risk of violent death from impulsive, aggressive behaviour or depressive symptoms.[20]

An additional health risk associated with the use of AASs is that of infection associated with needle sharing.[3] HIV, hepatitis B and C, and abscesses have been documented among anabolic steroid injectors who share needles,[21] and one study found that 25% of adolescent AAS users shared needles.[21]

As yet, the long-term effects of prolonged anabolic steroid use are unknown. However, as athletes who abuse these compounds often administer doses as high as 100 times the usual therapeutic dose, there must be serious concerns for adverse effects and toxicity. As well as this, a number of violent crimes (including domestic violence) that have resulted in death have been attributed to 'roid rage'. A list of the common and less common adverse effects of anabolic steroid use is shown in Table 34.3.

Page 495

Table 34.3 Adverse effects of anabolic steroids

Common	Less common
Both sexes	
Acne	Peliosis hepatis
Alopecia	Hepatoma/hepatocarcinoma
Abnormal liver enzymes	Wilms' tumour
Lowered HDL level	Coronary artery disease
Raised LDL level	Tendon ruptures
Elevated triglyceride level	Psychosis
Hypertension	Acute schizophrenia
Reduced humoral immunity	? Addiction
Irritability	? Leukaemia
Aggression	
Mood swings	
Changes in libido	
? Addiction	
Males	
Decreased sperm production	? Cancer of the prostate
Decreased testicle size	
Decreased FSH, LH	
Gynaecomastia	
Females	
Menstrual irregularities	Deepening of voice
	Male pattern baldness
	Hirsutism
	Clitoromegaly
	Breast shrinkage

Adolescents	
Increased facial/body hair	Phallic enlargement
Acne	Male pattern baldness
Premature closure of epiphyses	Deepening of voice
	Abnormal psychosocial maturation

FSH = follicle stimulating hormone; HDL = high-density lipoprotein; LDL = low-density lipoprotein; LH = luteinising hormone; ? = possible effects (not absolute evidence)

Toxicity in both sexes

1. *Liver.* As many as 80% of individuals using those androgens that have a 17-methyl substitution on the steroid molecule have developed liver disorders, including hyperbilirubinaemia and elevated liver enzyme levels.[22] These changes can be reversed with cessation of the drug. However, continued administration can lead to biliary obstruction and jaundice. This may take up to three months to reverse when steroid use is ceased. The responsible steroid compounds are mainly oral and include stanozolol and oxymethalone. Intermittent administration of these compounds has been shown to lower the incidence of these symptoms. The carbon-17 esters such as testosterone and nandrolone are not associated with these liver problems, as these substances are administered by injection and bypass the liver. The use of anabolic steroids to treat various medical illnesses has been occasionally associated with the development of other liver abnormalities, such as peliosis hepatis (blood-filled cysts in the liver),[23, 24] as well as benign and malignant hepatic tumours.[25, 26]
2. *Tumours.* There have been occasional cases of tumours reported in athletes using anabolic steroids. These include Wilms' tumour, carcinoma of the prostate and leukaemia. It is not possible to prove a direct relationship between the development of these tumours and anabolic steroid usage.
3. *Lipids.* Changes in lipid profiles are commonly seen with anabolic steroid usage.[27–30] Lowered levels of high-density lipoprotein (HDL) cholesterol and raised levels of low-density lipoprotein (LDL) cholesterol are seen. A lowered HDL/LDL ratio is a risk factor for the development of coronary heart disease, but as yet there is no convincing evidence of an increased incidence of coronary heart disease in anabolic steroid users.[31] These lipid changes appear to be reversed on cessation of the drug(s).[32]
4. *Hypertension.* Raised blood pressure is commonly seen in association with anabolic steroid usage,[29, 33] although the changes are not consistent. The increase in blood pressure also usually reverts to normal on cessation of use. The elevation in blood pressure may be secondary to sodium and water retention.
5. *Cardiac.* Isolated cases of myocardial infarction[34, 35] and cerebrovascular accident[34–36] have been reported in association with anabolic steroid use. Long-term use is associated with left

ventricular (LV) dysfunction.[37] Healthy athletes abusing AASs may exhibit LV hypertrophy with both systolic and diastolic myocardial dysfunction and focal areas of delayed gadolinium enhancement (DGE) at cardiac magnetic resonance (CMR), with non-ischaemic distribution.[38] AASs have direct toxicity on myocardial structures, with increased collagen deposition, fibrosis and intimal hyperplasia of the intramural coronary vessels with chronic ischaemic damage and microcirculation alterations.[39]

There is serious concern about the possible long-term sequelae of anabolic steroid use, in particular, the possibility of an increased incidence of coronary artery disease, in the light of the persistent findings of elevated blood pressure, decreased HDL levels and increased LDL levels. Whether or not these transient effects are negated by the return to normal values in times of steroid abstinence remains to be seen.

6. *Immunity.* There is evidence that humoral immunity is reduced with steroid use. Lowered levels of IgG, IgM and IgA have been noted. The clinical significance of these changes is uncertain.
7. *Skin.* Skin changes are common with anabolic steroid usage and are related to excessive sebum production.[40, 41] These changes include acne, rosacea, sebaceous cysts, furunculosis, folliculitis and increased body and facial hair. Care should be taken with the treatment of severe acne with either tetracyclines or isotretinoin as these drugs may aggravate pre-existing liver damage.
8. *Psychological.* Mild psychological effects, such as irritability, mood swings, changes in libido and increased aggression, are common with anabolic steroid usage.[42, 43] AAS use directly causes significant disturbances in personality profile.[44] Another study showed that AAS users reported being significantly less in control of their aggression than did controls.[45]

AASs also show mood destabilising effects, with long-term use inducing depression and short-term hypomania; withdrawal/discontinuation may be accompanied by depression. The effects of AASs on anxiety behaviour are unclear and studies are inconsistent. AASs are also linked to psychotic behaviour.[46]

Violent behaviour may occur in susceptible individuals, and psychiatric abnormalities such as acute schizophrenia and transient psychoses are not uncommon.[47] Anabolic steroids may also become both psychologically and physically addictive.[48] Withdrawal may lead to depression, fatigue, decreased sex drive, insomnia and anorexia.

Toxicity in males

A reduction in testicular size and sperm volume appears to be common with anabolic steroid use, due to a negative feedback effect resulting in decreased pituitary production of follicle stimulating hormone (FSH) and luteinising hormone (LH).[49] Testicular volume is reduced on average by 20%, and sperm production is severely reduced and commonly ceases altogether.[50] The popular usage of human chorionic gonadotrophin (hCG) in conjunction with anabolic steroids to avoid testicular atrophy does not appear to be effective, although it has been suggested that clomiphene may successfully restore AAS-induced pituitary–gonadal dysfunction.[51]

These adverse effects appear to be reversible on cessation of anabolic steroids. However, decreased sperm production may take three months to return to normal.

Ironically, one of the adverse effects of anabolic steroid usage is feminisation. This occurs as a result of peripheral conversion of AAS to oestrogens. Plasma oestradiol levels rise considerably with anabolic steroid usage. This feminisation manifests itself as gynaecomastia (development of breast tissue in males). Bodybuilders use tamoxifen to counteract this oestrogen effect and, as a result, increase the androgenic adverse effects, but there is no evidence for its effectiveness.[52]

Toxicity in females

In female athletes, menstrual irregularities frequently occur with anabolic steroid use. Other symptoms can include deepening of the voice, male pattern baldness, hirsutism, altered libido, uterine atrophy and an enlarged clitoris.[53] These changes may be irreversible. Anabolic steroids taken in pregnancy can cause foetal abnormalities or miscarriage.

Toxicity in adolescents

Anabolic steroid usage during adolescence in both sexes is commonly associated with acne, increased facial and body hair and premature closing of the epiphyseal plates.[54, 55] Other changes that may be seen during adolescence include phallic enlargement, male pattern baldness, deepening of the voice and abnormal psychosocial maturation.

Testosterone precursors

It has been suggested that testosterone precursors or prohormones, such as androstenedione ('andro') and dehydroepiandrosterone (DHEA), may have an ergogenic effect by increasing testosterone levels.

Androstenedione

Androstenedione is a relatively weak steroid available in many over-the-counter nutritional supplements. It is an immediate precursor to testosterone, as well as oestradiol and oestrone. Its anabolic activity is one-fifth to one-tenth that of testosterone. Although some studies have shown that androstenedione use will lead to increased testosterone levels, there is no evidence that it will significantly increase strength or lean body mass.[12] Adverse effects include gynaecomastia and increased risk of cardiovascular disease secondary to increased levels of oestrogen and a significant reduction of HDL cholesterol.

Dehydroepiandrosterone

Dehydroepiandrosterone (DHEA) is also a testosterone precursor and secreted by the adrenal gland.[56] It has been promoted to increase muscle mass and weight loss. Its use was publicised by the US baseballer, Mark McGwire, who admitted to using DHEA during the season

in which he set the home run scoring record. DHEA does not enhance serum testosterone concentration or increase strength.[57] Although there is some evidence of a weight-loss effect in rats, the only human study into the effectiveness of DHEA in weight loss failed to show any benefit.[58] Due to the potential for androgenic effects, DHEA is not recommended for young children and women.[12]

Designer steroids

In order to try to evade detection, athletes who continue to dope are resorting to a far more dangerous form of drug-the designer steroid.[59] These steroids are manufactured to closely resemble known compounds, but with sufficient chemical diversity to ensure that their detection by WADA-accredited laboratories is more difficult. A worrying feature of the use of these compounds is that no data are available to evaluate either their efficacy or safety.

Many such drugs are now being made in clandestine ways (as demonstrated by the recent BALCO case) and then passed on to athletes, who become the guinea pigs determining the potential of the substances as doping agents. Methods for the detection of these new compounds are being developed using emerging techniques, such as gas chromatography or liquid chromatography attached to a variety of mass spectrometry instruments.[59]

The first designer steroids were: norbolethone, in 2002; tetrahydrogestrinone, in 2003; and 'madol' (17-methyl-5-androst-2-ene-17-ol), in 2004.[60] Tetrahydrogestrinone (THG) was discovered when a track and field coach gave the contents of a used syringe to drug testing authorities. The drug was subsequently analysed and its chemical structure determined. A test to detect the presence of THG was developed, and past urine samples of a number of elite track athletes were analysed and found to be positive.[61]

THG was created with the dual purpose of imparting anabolic steroid effects to athletes and allowing those athletes to avoid detection by standard doping control drug testing. The primary reason THG went undetected in urine samples was that it tends to break down when prepared for analysis by the standard anabolic steroid screen.[62] Once it was suspected that the steroid was disintegrating during standard testing, a more sensitive assay process was used.

THG has been shown to be chemically and pharmacologically related to the anabolic steroids gestrinone and trenbolone, specifically listed on the WADA Prohibited List. *In vitro* studies have suggested that THG may be a potent anabolic agent, although the *in vivo* potency will depend upon the steroid's circulating half-life and its binding to sex hormone-binding globulin.[63]

The athlete biological passport

The athlete biological passport (ABP) was first introduced in 2009 to detect haematological abnormalities associated with erythropoietin (EPO) use and blood doping (see below). In 2014, an additional ABP, the steroidal module, was introduced. The steroidal module collects information on markers of steroid doping. The module aims to identify endogenous AAS when administered

exogenously and other anabolic agents, such as selective androgen receptor modulators (SARMS), categorised under section S1.2 of the Prohibited List. The steroidal module is also an effective means to identify samples that may have been tampered with or exchanged with the urine of another person.

The following markers are considered within the ABP steroidal module (the 'steroid profile'): testosterone (T), epitestosterone (E); androsterone (A); etiocholanolone (Etio); 5α-androstane-3α,17β-diol (5αAdiol); and 5β-androstane-3α,17β-diol (5βAdiol); as well as the following ratios: testosterone to epitestosterone (T/E); androsterone to testosterone (A/T); androsterone to etiocholanolone (A/ Etio); 5α-androstane-3α,17β-diol to 5β-androstane-3α,17β-diol (5αAdiol/5βAdiol); and 5α-androstane-3α,17β-diol to epitestosterone (5αAdiol/E).

Clenbuterol

Clenbuterol, which is considered both an anabolic agent and a beta-2 agonist, has been used as an ergogenic aid, but there is no scientific evidence in humans to support the animal studies that showed increased lean mass.[64] Adverse effects include tremor and tachycardia. There are anecdotal reports of sudden death in two bodybuilders.[64] In 2010 and 2011, unexplainable doping cases of clenbuterol in groups of table tennis and soccer players led to investigations of the origin of these findings, which was thought to be meat contaminated with clenbuterol. Clenbuterol has been evidently misused as a growth promoter in cattle feeding in selected countries, and meat originating from those farms can contain traces of clenbuterol, leading to doping offences or even poisonings. It could be shown that travelling to and staying in China and Mexico was connected with a high risk of inadvertent doping with clenbuterol.[65, 66]

Peptide hormones, growth factors, related substances and mimetics

Erythropoietin-stimulating agents

Erythropoietin (EPO) is a naturally occurring hormone secreted by the kidney. It stimulates the bone marrow and increases red blood cell production. This leads to an increase in red blood cell mass, haemoglobin and haematocrit. Its main therapeutic use has been in patients with anaemia due to conditions such as chronic renal failure, cancer chemotherapy or HIV (patients on zidovudine) and also for surgical patients, to minimise the need for blood transfusions.[67]

S2: Peptide hormones, growth factors, related substances and mimetics[2] Refer to www.wada-ama.org/en/what-we-do/the-prohibited-list

The following substances, and other substances with similar chemical structure or similar biological

effect(s), are prohibited:

1. Erythropoietins (EPO) and agents affecting erythropoiesis, including, but not limited to:

    1.1 Erythropoietin-receptor agonists, e.g. darbepoetins (dEPO), erythropoietins (EPO), EPO based constructs [EPO-Fc, methoxy polyethylene glycol-epoetin beta (CERA)], EPO-mimetic agents and their constructs (e.g. CNTO-530, peginesatide).

    1.2 Hypoxia-inducible factor (HIF) activating agents, e.g. argon, cobalt, molidustat, roxadustat (FG-4592), xenon.

    1.3 GATA inhibitors, e.g. K-11706.

    1.4 TGF-beta (TGF-β) inhibitors, e.g. luspatercept, sotatercept.

    1.5 Innate repair receptor agonists, e.g. asialo EPO, carbamylated EPO (CEPO).

2. Peptide hormones and hormone modulators

    2.1 Chorionic gonadotrophin (CG) and luteinising hormone (LH) and their releasing factors, e.g. buserelin, deslorelin, gonadorelin, goserelin, leuprorelin, nafarelin and triptorelin, in males

    2.2 Corticotrophins and their releasing factors, e.g. corticorelin.

    2.3 Growth hormone (GH), its fragments and releasing factors, including, but not limited to: growth hormone fragments, e.g. AOD-9604 and hGH 176-191; growth hormone releasing hormone (GHRH) and its analogues, e.g. CJC-1293, CJC-1295, sermorelin and tesamorelin; growth hormone secretagogues (GHS), e.g. ghrelin and ghrelin mimetics, e.g. anamorelin, ipamorelin and tabimorelin; GH-releasing peptides (GHRPs), e.g. alexamorelin, GHRP-1, GHRP-2 (pralmorelin), GHRP-3, GHRP-4, GHRP-5, GHRP-6 and hexarelin.

3. Growth factors and growth factor modulators including, but not limited to: fibroblast growth factors (FGFs), hepatocyte growth factor (HGF), insulin-like growth factor-1 (IGF-1) and its analogues, mechano growth factors (MGFs), platelet-derived growth factor (PDGF), thymosin-β4 and its derivatives, e.g. TB-500, vascular-endothelial growth factor (VEGF).

Additional growth factors or growth factor modulators affecting muscle, tendon or ligament protein synthesis/ degradation, vascularisation, energy utilisation, regenerative capacity or fibre type switching.

Recombinant erythropoietins are produced by transfection of the erythropoietin gene into mammalian cells in culture or activation of the gene in human cells.[68] The first recombinant erythropoietins that were commercially available were epoetin alfa and eopoetin beta, which were released in 1989 and 1990, respectively.

The use of EPO and related substances has been widespread in certain sports, such as distance running and road cycling. The Lance Armstrong case highlighted the extent of the problem among Tour de France riders.

As EPO causes an increased red cell mass, an extra oxygen-carrying capacity is created, which permits an increase in energy production by aerobic oxidation of glucose and free fatty acids.[69, 70] This is the most efficient means of energy production and limits anaerobic production, which is inefficient and leads to fatigue. Aerobic oxidation is the most important energy source for endurance athletes. EPO provides the benefits of blood doping without the risk of blood transfusion.

EPO has been shown to increase haemoglobin levels by 11%[71] and improve VO_2max (7%)[72] and exercise tolerance (17% increased time for run to exhaustion).[73]

The main side effect of EPO is hyperviscosity of the blood due to a raised haematocrit. This raises the risk of myocardial infarction and cerebrovascular accident, the risk being increased with dehydrating endurance exercise.[74] The unexplained deaths of 18 otherwise healthy cyclists between 1997 and 2000 has been linked to EPO, but there is no concrete evidence to support this theory.[67] Less serious adverse effects of EPO use include fever, nausea, headache, anxiety and lethargy. Seizures have been reported in 2–3% of patients in the first 90 days of therapy.[67]

Since detection of EPO became possible, athletes have been using related products such as darbepoetins or those which indirectly stimulate EPO production, such as CERA, peginesatide (Hematide™) and roxadustat (FG-4592), which are much more difficult to detect. As a result indirect tests to detect their use have been introduced.

Page 499

The main form of indirect testing is the athlete biological passport (ABP), which has two forms: the haematological form, to detect use of EPO-like substances; and the steroid form (mentioned above), to detect otherwise undetectable steroids. The principle behind the ABP is the monitoring of selected biological parameters over time that may indirectly reveal effects of doping on the body. This approach allows anti-doping organisations to generate individual, longitudinal profiles for each athlete and to look for any fluctuations that may indicate the use of performance-enhancing drugs or methods. The longitudinal profile for each athlete is generated based on statistical tools that utilise data from an athlete's previous samples to predict the likely individual limits or reference range for future samples. If any data from a sample falls outside of the athlete's reference range, this abnormal value may be an indication of doping or a pathological condition. This data can also be used to conduct targeted, conventional anti-doping tests on athletes with abnormal profiles. ABP data can also be used as corroborating evidence of doping during an anti-doping rule violation case.[75]

The haematological form uses the blood parameters: haemoglobin, haematocrit, red blood cell count, reticulocyte number, reticulocyte percentage, mean corpuscular volume, mean corpuscular haemoglobin, mean corpuscular haemoglobin concentration, red cell distribution width, immature reticulocyte fraction and both the OFF-score (calculated from the haemoglobin concentration and the reticulocyte percentage) and the abnormal blood profile score (ABPS).

Some sports have introduced safety cut-offs for haematocrit levels (e.g. 50%), as an indirect means of restricting the use of EPO.[76] This is unsatisfactory due to the wide variations in normal haematocrit levels and the number of factors that can affect the value.[77] Athletes may then

manipulate their drug intake to ensure that they are just below the allowed limit.

Human chorionic gonadotrophin

Human chorionic gonadotrophin (hCG) is produced by the placenta and is a glycoprotein hormone produced in large amounts during pregnancy and also by certain types of tumours. It has a very similar structure to LH and has the same biological activity, except that it has a much longer half-life. This hormone mainly stimulates sex steroid hormone biosynthesis in the gonads. Thus, in the female, hCG can substitute for the ovulatory surge of LH and ovulation and also maintain the corpus luteum for the production of progesterone, mainly in pregnancy. In the male, hCG can replace LH in stimulation of the interstitial cells within the testes to produce testosterone.

The therapeutic uses of hCG are limited. It can be used to stimulate ovulation in females and has been used to induce puberty in adolescent males who have delayed sexual development. It is mainly abused by male athletes as it increases the endogenous production of both testosterone and epitestosterone without increasing the urinary testosterone-to-epitestosterone ratio above normal levels. Its other main use is to attempt to maintain testicular volume in the male athlete using anabolic steroids, which inhibit pituitary LH and FSH secretion, leading to loss of testicular volume. However, as it is FSH that maintains testicular volume, using hCG is unlikely to be effective. In the female athlete it is unlikely to give any benefit.

The main side effect of hCG is gynaecomastia, probably from raised oestrogen secretion from the testes. The drug combination of hCG and anabolic steroids causes headaches, depression and oedema.

hCG and LH were prohibited in all athletes, but following problems with elevated hCG levels in females who were either currently pregnant or had recently miscarried, since 2006 they are prohibited in male athletes only. An elevated level of hCG in the male is a doping offence unless it can be shown to be due to a physiological or (very rarely) a pathological condition such as a tumour.

Corticotrophins

Adrenocorticotropic hormone (ACTH) is also known as corticotrophin or adrenocorticotrophin and is secreted by the anterior pituitary gland. Its main effect is on the adrenal cortex. Three major steroid hormones are produced in the adrenal cortex. These are:

1. aldosterone (mineral corticoid)
2. cortisol (glucocorticoid effect)
3. DHEA (androgenic effect) (see above).

ACTH stimulates secretory activity in those cells that produce cortisol and androgens. It is abused in order to increase the secretion of the adrenal androgens, which are moderately active male sex hormones. These are converted to testosterone in extra-adrenal tissues, which accounts for much of their androgenic activity. ACTH abuse also increases cortisol levels and this in turn

stimulates gluconeogenesis, which raises blood glucose levels. This is achieved by mobilisation of amino acids, mainly from muscle, for conversion to glucose in the liver and also by decreasing glucose utilisation by the cells. Thus, the ergogenic effect of ACTH is negligible as its catabolic effects cancel out its anabolic effects. In fact, ACTH has no ergogenic benefit and is detrimental to performance. It is because of a belief in increased performance within the athletic Page 500 community that it is placed on the Prohibited List.

Human growth hormone

Human growth hormone (hGH) is a polypeptide hormone produced by the anterior pituitary. It is also called somatotrophic hormone and somatotrophin. It is essential for normal growth and development.

Growth hormone exerts its effect on all cells in the body. It is anabolic in nature and causes an increased rate of protein synthesis and concurrent reduction in protein catabolism. It produces mobilisation and increased use of fatty acids for energy, and thus increases lean tissue mass and decreases fat mass. It causes a decreased rate of glucose utilisation. Growth hormone also produces accelerated growth. In the skeletally immature, stature is increased and prolonged treatment results in gigantism. When the epiphyses are closed, linear growth ceases and hGH produces acromegaly.

Another important action of hGH is the stimulation of the insulin-like growth factor-1 (IGF-1) in the liver, which synergises with hGH to produce many of its effects. Exercise stimulates the production of hGH fivefold to tenfold, whereas starvation decreases its production.[78]

hGH is species-specific and bovine and porcine hormones have no effect in humans. Since 1985 recombinant hGH has been produced. Prior to this hGH was derived from cadavers, and this led to several cases of Creutzfeldt–Jakob disease in the recipients.

The medical use of hGH is limited to the treatment of 'dwarfism' and replacement therapy in growth-deficient children. It may have a role for children with Turner's syndrome and for people with chronic renal insufficiency. It is only available in the injectable form.

Athletes use hGH because of its alleged anabolic effects, that is, increased muscle mass and decreased fat mass.[79] Use of hGH in athletes was first described by Dan Duchaine in the *Underground Steroid Handbook,* published in 1982. In 1988, Ben Johnson's coach admitted that he had given his athletes hGH in addition to anabolic steroids. In that year also, a large quantity of GH was found in a team car at the Tour de France.

In 1989, the IOC added hGH to its list of banned substances despite not having a test that could detect its use. At the 1998 World Swimming Championships, Yuan Yuan, a Chinese swimmer, was stopped on entry into Perth with a suitcase full of GH that had been exported to China for therapeutic reasons. Six months before the Sydney Olympic Games, 1575 vials of GH were stolen from an importer's warehouse in Sydney. More recently, Victor Conte, the owner of the Bay Area Laboratory Co-Operative (BALCO), claimed that he had supplied GH to many high profile American athletes, including Tim Montgomery and Marion Jones.[80]

The effect of GH on physical performance in healthy adults has not been studied rigorously. Most of the studies available have evaluated the effects in small groups of subjects and almost exclusively in men. Liu and colleagues[81] have undertaken a systematic review of the effects of GH on various measures of athletic performance, such as muscle strength and endurance. Twenty-seven studies, comprising a total of 303 physically fit participants with a mean age of 27 years and mean body mass index (BMI) of 24 kg/m^2, were considered suitable for analysis. Participants from seven studies received GH as only one injection, but 20 of the studies used GH treatment for an average of 20 days with average daily dose of 36 μg/kg. Change in strength was evaluated in two studies, and exercise capacity outcomes were measured in six studies. The authors concluded that claims that GH enhances physical performance are not supported by the scientific literature.

However, these studies included very small sample sizes and used doses of hGH that are probably considerably less than those used by athletes. No studies have evaluated the use of a combination of hGH and AAS, a common practice among athletes. In an Australian study,[82] GH significantly reduced fat mass, increased lean body mass through an increase in extracellular water and increased body cell mass in men when co-administered with testosterone. It also significantly increased sprint capacity in men and women combined, alone and with testosterone. Further studies must be done before we can finally determine whether hGH has an anabolic effect.

Adverse reactions are well documented and include gigantism in the younger athlete, acromegaly in the adult athlete, hypothyroidism, hypercholesterolaemia, ischaemic heart disease, congestive cardiac failure, cardiomyopathy, myopathies, arthritis, diabetes mellitus, impotence, osteoporosis, menstrual irregularities and Creutzfeldt–Jakob disease. Although recombinant hGH has no risk of Creutzfeldt–Jakob disease, black market sources of hGH are often derived from cadavers.

A number of different attempts to detect hGH use have been trialled. The current test is the isoform differential immunoassays (the isoforms test), first introduced as a research-scale test at the 2004 Summer Olympic Games in Athens, Greece, and later applied at the 2006 Winter Olympic Games in Torino, Italy. Following a process of assay development and validation into a new technical platform (tube-based chemiluminescence technique), which is suitable for the production of commercial kits, the currently applied test kits were first used during the 2008 European Football Championship in Austria and Switzerland, as well as during the 2008 Summer Olympic Games in Beijing. Currently, all WADA-accredited laboratories test for hGH using the isoforms test.[83]

Insulin-like growth factors

Growth hormone effects on the growth of bones and cartilage and on protein metabolism are brought about indirectly by stimulation of the liver and other tissue to release somatomedins (growth factors). The principal somatomedin is insulin-like growth factor-1 (IGF-1/somatomedin C). IGF-1 results in an increase in glucose and amino acid uptake and inhibits apoptosis (programmed cell death). It enhances lipolysis indirectly by insulin suppression and it may be

linked to carcinogenesis (increased IGF-1 receptors have been found in tumours of the lung and breast, and in Wilms' tumour of the kidney).

Clinical applications are limited but include some types of dwarfism and growth problems in children and in people with diabetes mellitus type 2, and it may have a role in kidney disease, catabolic states, osteoporosis, atherosclerosis and osteoarthritis.

IGF-1 is typically used to enhance the anabolic effects of concurrent GH and/or anabolic steroid use. Prevalence of its use as a performance-enhancing drug was reported to be 16% of patients admitted to a Swedish addiction clinic; over 6% (including IGF-1 and MGF) in a UK survey disseminated via online weightlifting forums to participants of needle exchange programs, and 7% in a poll of weightlifters from the USA.[84]

IGF-1 has effects on carbohydrate, lipid and protein metabolism, and some of these actions could prove beneficial to competitive athletes. No studies have demonstrated a positive effect of IGF-1 on physical performance in healthy individuals, but this has not yet been studied in appropriately designed trials.[85]

In addition, supplementation of IGF-1 appears to be associated with moderate-to-severe hypoglycaemia, decreased growth hormone secretion, a shift from lipid to carbohydrate oxidation for energy and a general disruption of the insulin/glucagon system.[86] In the clinical trials, the commonest short-term adverse effects are oedema, headache, arthralgia, jaw pain and hypoglycaemia.[87] A common adverse effect is erythema and lipohypertrophy at the injection site.

Beta-2 agonists

The prevalence of asthma is higher in elite athletes than in the general population. The risk of developing asthmatic symptoms is the highest in endurance athletes and swimmers. Asthma seems particularly widespread in winter sport athletes such as cross-country skiers. Asthmatic athletes commonly use inhaled beta-2 agonists to prevent and treat asthmatic symptoms.

When given systemically by tablet or injection, beta-2 agonists may have anabolic effects, and their use is therefore prohibited. Only salbutamol and salmeterol by inhalation are permitted. There are limits placed on the amount of these substances that are permitted in the urine. The levels are set to detect oral use. Normal use of inhaled salbutamol (Ventolin®) should result in levels in the urine well below the upper limit permitted, although it has been suggested that dehydration of greater than 2% may result in levels above the permitted level.[88]

In 17 of 19 randomised placebo-controlled trials in non-asthmatic competitive athletes, performance-enhancing effects of the inhaled beta-2 agonists formoterol, salbutamol, salmeterol and terbutaline could not be proved. This is particularly true for endurance performance, anaerobic power and strength performance. In three of four studies, even supratherapeutic doses of salbutamol (800–1200 μg) had no ergogenic effect.[89]

S3: Beta-2 agonists[2]

Refer to www.wada-ama.org/en/what-we-do/the-prohibited-list

All selective and non-selective beta-2 agonists, including all optical isomers, are prohibited.

Including, but not limited to:

- fenoterol, formoterol, higenamine, indacaterol, olodaterol, procaterol, reproterol, salbutamol, salmeterol, terbutaline, tulobuterol, vilanterol. Except:
- Inhaled salbutamol: maximum 1600 micrograms over 24 hours in divided doses not to exceed 800 micrograms over 12 hours starting from any dose; Inhaled formoterol: maximum delivered dose of 54 micrograms over 24 hours;
- Inhaled salmeterol: maximum 200 micrograms over 24 hours.

The presence in urine of salbutamol in excess of 1000 ng/mL or formoterol in excess of 40 ng/mL is not consistent with therapeutic use of the substance and will be considered as an *Adverse Analytical Finding (AAF)* unless the *Athlete* proves, through a controlled pharmacokinetic study, that the abnormal result was the consequence of a therapeutic dose (by inhalation) up to the maximum dose indicated above.

Adverse effects include nervousness, tremor, tachycardia, palpitation, headache, nausea, vomiting and sweating. These are minimised when the drugs are given by inhalation.

Hormone and metabolic modulators

Aromatase inhibitors lower the amount of oestrogen in the body, whereas drugs such as the selective oestrogen receptor modulators (SERMs) block the oestrogen receptors.

The anti-oestrogen drugs such as tamoxifen and clomiphene are used by both male and female athletes for different reasons. Male athletes primarily use tamoxifen in conjunction with AASs to prevent the development of gynaecomastia. Tamoxifen also increases testosterone levels in males and is advertised as a body fat reducer. In females, there is evidence that tamoxifen is used as an ergogenic agent, particularly by body builders.[90] By blocking the oestrogen receptors in a woman's body, tamoxifen leaves testosterone unopposed. This could lead to masculinisation.

Tamoxifen has a number of harmful effects in females. It has been shown to increase the risk of venous thromboembolic events. As it is related to diethylstilboestrol (DES), women who become pregnant while taking the drug may be at increased risk of giving birth to a child with congenital defects.

Insulins

Insulin is a small hormone produced in the pancreas, whose main role is in carbohydrate metabolism. Insulin is anabolic in nature, causing cell growth, increasing both glucose and amino acid uptake by cells and increasing protein synthesis. It also decreases protein catabolism. Insulin also increases lipogenesis by promoting fatty acid synthesis and storage in adipose tissue. The main clinical use for insulin is for treating people with diabetes mellitus type 1.

The first suggestions of insulin as an anabolic agent were published in two bodybuilding magazines in 1996. The most graphic account of doping with insulin came from Victor Conte, of the

Bay Area Laboratory Co-operative, who alleged that he personally provided Marion Jones and other athletes with a number of performance enhancing concoctions that included a number of peptide hormones including insulin, erythropoietin and hGH.[91] He described how insulin was used after strenuous weight-training sessions during the off-season. Three units of the fast-acting insulin lispro were injected immediately after the workout sessions, while the athlete consumed a glucose and protein drink, with the purpose of replenishing glycogen and adenosine triphosphate (ATP) quickly and promoting protein synthesis and muscle growth.

Although there is a paucity of data on the use of insulin as a performance-enhancing drug, it appears to be commonly abused because it is inexpensive and readily available in most settings.[84] Athletic use of insulin is mainly found in the power sports–weightlifting and bodybuilding. In one report, as many as 25% of AAS users concurrently use insulin.[92] Its prevalence was reported to be just below 10% among recreational and professional bodybuilders in Iran[93] and among recreational weightlifters in the UK.[94] The IOC banned its use in 1998 for those without diabetes.

The anabolic properties of insulin used in the hypoinsulinemic state (diabetic) are well recognised; however, the concept of a hyperinsulinemia-induced anabolic state is much less well supported.[95] Physiological hyperinsulinemia reportedly stimulates amino acid transport Page 503 in human skeletal muscle. Although insulin inhibits protein breakdown, stimulation of bulk protein synthesis during hyperinsulinemia is observed only when concomitant hyperaminoacidemia occurs.[96] The use of insulin in this situation is potentially very dangerous. Unrecognised hypoglycaemic attacks can cause permanent neurological deficit and even death.[95]

S4: Hormone and metabolic modulators
Refer to www.wada-ama.org/en/what-we-do/the-prohibited-list

The following hormone and metabolic modulators are prohibited:

1. Aromatase inhibitors including, but not limited to: 4-androstene-3,6,17 trione (6-oxo); aminoglutethimide; anastrozole; androsta-1,4,6-triene-3,17-dione (androstatrienedione); androsta-3,5-diene-7,17-dione (arimistane); exemestane; formestane; letrozole; testolactone.
2. Selective oestrogen receptor modulators (SERMs) including, but not limited to: raloxifene; tamoxifen; toremifene.
3. Other anti-oestrogenic substances including, but not limited to: clomifene; cyclofenil; fulvestrant.
4. Agents modifying myostatin function(s) including, but not limited, to: myostatin inhibitors.
5. Metabolic modulators:

    5.1 Activators of the AMP-activated protein kinase (AMPK), e.g. AICAR, SR9009; and peroxisome proliferator activated receptor δ (PPARδ) agonists, e.g. 2-(2-methyl-4-((4-methyl-2-(4-(trifluoromethyl) phenyl)thiazol-5-yl)methylthio)phenoxy) acetic acid (GW1516, GW501516)

5.2 Insulins and insulin-mimetics

5.3 Meldonium

5.4 Trimetazidine.

Blood tests can be used to measure insulin levels, and measurements of plasma C-peptide and proinsulin levels will help distinguish endogenous from exogenous hyperinsulinemia. Specific assays can detect a variety of insulins, including human insulin, animal insulin and insulin analogues.[84]

Meldonium

Meldonium (Midronate™) came to prominence when the Russian tennis player Maria Sharapova tested positive to the substance at the 2016 Australian Open and was subsequently banned for 2 years, which was later reduced to 15 months on appeal. Meldonium is manufactured in Latvia and is only available in the Baltic countries and in Russia.

In 2015 WADA became aware that a large number of athletes were using meldonium and spent a year monitoring its use before announcing in September 2015 that it would be added to the banned list on 1 January 2016. Sharapova claimed that she had been taking the drug for 10 years for medical reasons and had been unaware that it had been added to the banned list.

Meldonium is used in the treatment of ischaemia, as it is thought to increase blood flow. The increased blood flow could potentially be performance enhancing, although there is no scientific evidence available.

Diuretics and other masking agents

Diuretics

Clinically, diuretics are used in the treatment of hypertension, fluid retention and congestive cardiac failure. Adverse effects from their use include dehydration, hypotension, muscle cramps and electrolyte disturbances. Athletes use diuretics in order to lose weight rapidly prior to competition in sports where weight limits are set. These sports include boxing, wrestling, weightlifting, judo and lightweight rowing; diuretics are also used by jockeys. The use of diuretics may be combined with other dehydration techniques, such as use of a sauna, exercise in hot conditions and food and water restrictions. These practices may result in rapid dehydration and electrolyte imbalances, which may be harmful to the athlete, particularly if practised on a regular basis. Diuretics are also used to aid the excretion or dilute the presence of illegal substances in the urine.

Masking agents

Probenecid is a drug used clinically to increase the uptake of penicillin administered intramuscularly. It is used by athletes to accelerate the excretion of prohibited substances. Plasma volume expanders such as hydroxyethyl starch (HES) dilute the concentration of haemoglobin and erythrocytes. Glycerol is no longer on the Prohibited List.

PROHIBITED METHODS

Blood doping

Blood doping is the administration of blood or red blood cells to an athlete to increase the red blood cell mass. This may be autologous (infusion with the athlete's own blood) or homologous (infusion with appropriately cross-matched donated blood).

Page 504

S5: Diuretics and masking agents[2]

Refer to www.wada-ama.org/en/what-we-do/the-prohibited-list

The following diuretics and masking agents are prohibited, as are other substances with a similar chemical structure or similar biological effect(s).

Including, but not limited to:

- Desmopressin; probenecid; plasma expanders, e.g. intravenous administration of albumin, dextran, hydroxyethyl starch and mannitol.
- Acetazolamide; amiloride; bumetanide; canrenone; chlortalidone; etacrynic acid; furosemide; indapamide; metolazone; spironolactone; thiazides, e.g. bendroflumethiazide, chlorothiazide and hydrochlorothiazide; triamterene and vaptans, e.g. tolvaptan.

Except:

- Drospirenone; pamabrom; and ophthalmic use of carbonic anhydrase inhibitors (e.g. dorzolamide, brinzolamide);
- Local administration of felypressin in dental anaesthesia.

The detection in an Athlete's Sample at all times or In-Competition, as applicable, of any quantity of the following substances subject to threshold limits: formoterol, salbutamol, cathine, ephedrine, methylephedrine and pseudoephedrine, in conjunction with a diuretic or masking agent, will be considered as an Adverse Analytical Finding (AAF) unless the Athlete has an approved Therapeutic Use Exemption (TUE) for that substance in addition to the one granted for the diuretic or masking agent.

M1: Manipulation of blood and blood components[2]

Refer to www.wada-ama.org/en/what-we-do/the-prohibited-list

The following are prohibited:

1. The administration or reintroduction of any quantity of autologous, allogenic (homologous) or heterologous blood or red blood cell products of any origin into the circulatory system.
2. Artificially enhancing the uptake, transport or delivery of oxygen. Including, but not limited to: perfluorochemicals; efaproxiral (RSR13)and modified haemoglobin products, e.g. haemoglobin-based blood substitutes and microencapsulated haemoglobin products, excluding supplemental oxygen by inhalation.
3. Any form of intravascular manipulation of the blood or blood components by physical or chemical means.

The usual method of blood doping is to withdraw one to four units of an athlete's own blood 4–6 weeks prior to competition. This allows time for the red blood cell count to return to normal prior to reinfusing the blood a day or two before competition. The aim of this procedure is to increase the red blood cell mass and therefore increase the oxygen-carrying capacity of the blood. Improved endurance may occur as a result of blood doping.[97, 98]

Blood doping has been prohibited since 1984 but its use dropped dramatically when recombinant EPO became available in 1987.[99] Recently, with the advent of testing for EPO, blood doping has again become popular. The American cyclist Tyler Hamilton was one of the first athletes to be found guilty of blood doping, in 2004. Since then, many elite cyclists including Lance Armstrong have admitted to blood doping.

Adverse effects do occur with blood doping, as they do with any transfusion, especially if donated blood is used. Allergic reactions may occur and there is an increased risk of blood-borne diseases such as hepatitis B and C and HIV. In addition, blood doping has been reported to increase the blood viscosity significantly, and this may lead to some serious health risks due to sludging of blood, particularly in the cerebral circulation.

A test for homologous blood transfusions (HBT) was implemented at the 2004 Summer Olympic Games in Athens. No reliable method exists to detect autologous blood doping, so WADA relies on the athlete biological passport (ABP), mentioned previously.

Artificial oxygen carriers

Artificial oxygen carriers or 'blood substitutes' are being developed to serve as a temporary replacement for transfused red blood cells in the prevention of ischaemic tissue damage and hypovolemic shock. Two main types are available: haemoglobin oxygen carriers (HBOCs) and perfluorocarbons (PFCs).

Haemoglobin oxygen carriers

HBOCs have been developed as haemoglobin substitutes in recent years for use when a rapid expansion of blood volume is needed in acute blood loss following severe injury, surgery or severe haemolytic anaemia when human blood is unavailable, time necessary to undertake a proper cross-match is short or the risk of blood infection is high.[100] Due to an apparent increase in myocardial

infarction associated with their use, HBOCs have not been approved for general medical use.

Perfluorocarbon emulsions

PFCs, a group of synthetic compounds similar to Teflon™, are hydrocarbons to which fluorine atoms have been added. They are extremely inert, inexpensive to produce and are made up in a sponge-like emulsion containing very small particles, 0.2 μm in diameter, that can deliver oxygen to the tissues through very small blood vessels. They are capable of physically dissolving large amounts of oxygen in plasma.[100] The first generation PFCs (e.g. Fluosol-DA) proved unsatisfactory, but the second generation products (Oxygent™, Oxyfluor™), using improved technology and containing higher concentrations of the active agent in the emulsion, show promise.

As yet, no study has investigated the performance-enhancing effects of PFCs; however, they have been found to improve oxygen delivery to the tissue under many conditions.

Detection

It would be futile to analyse urine samples in search of PFCs and most HBOCs since they are not processed by the kidney and/or the urinary excretion is too low and variable. The presence of an artificial oxygen carrier in the blood can be detected as long as the sample is taken soon after competition.[101]

M2: Chemical and physical manipulation[2]

Refer to www.wada-ama.org/en/what-we-do/the-prohibited-list

The following are prohibited:

1. *Tampering* or *Attempting to Tamper,* to alter the integrity and validity of *Samples* collected during *Doping Control.* Including, but not limited to: Urine substitution and/or adulteration, e.g. proteases.
2. Intravenous infusions and/or injections of more than a total of 100 mL per 12 hour period except for those legitimately received in the course of hospital treatments, surgical procedures or clinical diagnostic investigations.

Chemical and physical manipulation

The allowed volume and timing of intravenous infusions was increased in 2018 from infusions of no more than 50 mL per 6-hour period to no more than a total of 100 mL per 12-hour period.

Chemical and physical manipulation is the use of substances and/or methods that alter, attempt to alter or may reasonably be expected to alter the integrity and validity of urine samples used in doping controls. These include, without limitation:

- catheterisation
- sample substitution and/or tampering.

The success or failure of the use of a prohibited substance or method is not material. It is sufficient that the said substance or procedure was used or attempted for the infraction to be considered as consummated.

WADA has prohibited procedures that interfere with the content or collection of urine samples used for drug testing, such as the use of catheters to substitute urine. There have been a number of cases of athletes who have been disqualified from competition when they have been caught substituting urine from a coach, relative or fellow athlete in order to avoid having their own urine tested. This use of surrogate urine is prohibited, and there have been examples where the athlete has subsequently been caught out because the surrogate urine has contained a prohibited substance that was being used by a friend or relative at the time of the test.

Current testing procedures are structured in such a way that the risk of substituting surrogate urine is minimal. The athlete is accompanied by a chaperone (of the same gender) so that the urine sample is provided under direct observation and the chance of substituting alternative urine is virtually impossible. However, athletes still use ingenious methods to avoid detection.

Gene doping

Gene doping or gene transfer technology to improve athletic performance is a serious threat to the integrity of elite sport. The principle of gene therapy is based on the delivery to a cell of a therapeutic gene that may compensate for an absent or abnormal gene. In general, DNA is used as the genetic material. This genetic material encodes for a therapeutic protein and needs to be delivered to the cell nucleus to be active.

M3: Gene doping[2]

Refer to www.wada-ama.org/en/what-we-do/the-prohibited-list

The following, with the potential to enhance sport performance, are prohibited:

1. The use of polymers of nucleic acids or nucleic acid analogues.
2. The use of gene editing agents designed to alter genome sequences and/or the transcriptional or epigenetic regulation of gene expression.
3. The use of normal or genetically modified cells.

Gene delivery

To facilitate the introduction of a gene into the cells of the recipient, a delivery vehicle is required. These delivery systems can be either biologic or physical. The use of a biologic vector is the most common delivery mode for gene therapy. Viral vectors such as retroviruses, adenoviruses and

adeno-associated viruses (AAVs) are commonly used, as they function to integrate into host cells and use those cells to replicate their own genetic material. In gene therapy, these viruses are modified to reduce the potential for viral infection while carrying the ability to be delivered to specific cells for expression.

Plasmid DNA (pDNA) is an alternative biologic vector but differs from viral vectors in that it is synthetic and may be grown in bacteria, then purified. Although more inefficient than viral vectors, pDNA has the advantage of avoiding a possible immune response.

Plasmid delivery can also be improved by combining the plasmid with lipid vesicles that aid penetration of the cell membrane. These plasmid/liposome complexes can be enhanced by the addition of proteins to target specific cell surface receptors, essentially creating an artificial virus.

In comparison to gene delivery with viral vectors, plasmid DNA is very inefficient, but this efficiency can be markedly increased by modifying the means of delivery to add a physical component. The application of a series of electrical pulses following intramuscular injection *(in vivo* electroporation) can increase the efficiency of plasmid DNA delivery over 1000-fold and genetically modify the majority of the target muscle fibres. Other methods of physically enhancing plasmid-based gene delivery include ultrasound, laser and magnetic particles.

Page 506

Gene therapy and gene doping

The fundamental difference, physically, biochemically and ethically, between gene therapy and gene doping is that the goal of gene doping is not to replace an absent or dysfunctional protein in an unhealthy individual but rather to artificially alter gene expression in an otherwise healthy individual. The evolution of gene therapy from a strictly medical tool to a performance-enhancement mechanism has significant ramifications both in the competitive sports world and in the general population.

What makes a gene a good candidate for doping? Obviously, the targets for gene doping would depend on the desired effect. Overexpression or underexpression of the gene product should enhance traits that are desirable for peak athletic performance.

For endurance sports, such as long-distance running or swimming, genes that bolster oxygen production or usage and delay fatigue would be the likely candidates. For sports in which strength or agility provide the competitive advantage, genes involved in muscle mass stimulation and injury recovery are the more likely targets.

Genes for endurance

1. *Erythropoietin (EPO).* EPO is a hormone produced in response to decreased oxygen levels in the blood that signals the body to increase haemoglobin production. EPO-stimulating agents have long been a part of performance-enhancing doping.[102] Overexpression of EPO by gene doping would increase endogenous haemoglobin production and thereby oxygen distribution to muscles.
2. *Peroxisome proliferator-activated receptor delta* (PPAR-δ). PPAR-δ and its family of hormones are

involved in changing type I (fast twitch) skeletal muscle fibres to type II (slow twitch) muscle fibres. Upregulation of this gene could produce an increase in the number of type II muscle fibres, desired for endurance sports, even in the absence of endurance training. The WADA 2011 Prohibited List banned PPAR- δ agonists (e.g. GW1516) and PPAR-d-adenosine monophosphate-activated protein kinase axis agonists (e.g. AICAR), the only genes that were specifically mentioned under the gene doping section.

3. *Phosphoenolpyruvate carboxykinase (PEPCK).* The role of PEPCK in skeletal muscle is somewhat unclear, but overexpression in mice increases endurance and longevity and leads to decreased body fat.[103]
4. *Vascular endothelial growth factor.* This growth factor is instrumental in the development of new blood vessels and also appears to be important in some injury healing molecular pathways.

Genes for strength

1. *Insulin-like growth factor-1 (IGF-1).* IGF-1 is the primary target of growth hormone action. Increased gene expression leads to increased muscle mass and power. In addition to promoting muscle hypertrophy, IGF-1 also hastens muscle repair.[104]
2. *Myostatin.* Unlike many other candidate genes for gene doping, myostatin would be targeted to promote decreased expression of this gene. Myostatin is a negative regulator of muscle growth and by impeding its actions, increased muscle mass would be expected.[105]

Genes for tissue repair/other

1. *Bone morphogenetic protein (BMP).* The BMP family of growth factors enhance bone repair and would theoretically shorten recovery time from injury. In the absence of an injury, these growth factors have the potential to increase bone, cartilage or tendon strength in an effort to stave off potential career-ending injuries.[106]
2. *Endorphins.* Endorphins are important components of pain management, fatigue delay and endurance. Genes that increase endorphins would increase pain threshold both acutely during competition, by reducing lactic acid–related pain, and chronically, by dulling the effects of prior injury. These effects make genes related to endorphin production, expression and release reasonable targets for gene doping.[105]

Animal studies

Examples of potential areas for gene doping to improve athletic performance are EPO for endurance performance and IGF-1 for muscle strength. An adenovirus was used to deliver the EPO gene in mice and monkeys, and this boosted the haematocrit from 49% to 81% in the mice and from 40% to 70% in the monkeys. The effects lasted over a year in the mice and for 12 weeks in the monkeys.[107] Mice injected with the IGF-1 gene showed a 15% increase in muscle bulk.[108]

However, in addition to shedding light on the potential enhancement effects of gene doping in humans, animal studies have also uncovered concerns that may directly affect human subjects.[105] It is perhaps unsurprising that artificially overexpressing genes to promote athletic prowess may lead to unwanted side effects.

Some studies reported an increase in hyperactivity, aggressiveness and other behavioural sequelae in treated mice. Overexpression of EPO in macaques has been reported to increase blood viscosity, with effects on cardiac functioning.[103] Clearly, although animal models may demonstrate the promise of gene doping, the perils of this procedure cannot be ignored because its use is contemplated in humans.

Risks of gene doping

The risks associated with gene therapy in a regulated, controlled setting are still being defined.[105] Results of gene therapy trials performed in the 1990s indicated both a substantial variability in response to vectors and a nonlinear relationship between vector dose and toxicity.

The death of an 18-year-old volunteer in a pilot study of gene therapy was attributed to systemic inflammatory response syndrome caused by an immune response to the adenoviral vector used.[109] Therefore, the risks associated with taking a new procedure and illegally abusing it in otherwise healthy individuals are real and concerning. The most significant risks are associated with both the unregulated delivery of the gene therapy by dopers and the effects of this doping on a cellular and functional level in the athlete.

The illicit production and administration of gene doping products would compound these risks. The safety, quality and contents of a gene doping product would be unregulated and the secretive nature of doping in general may hinder appropriate medical follow-up if needed.

The risks secondary to altered gene expression include:

1. an immune response to a viral vector
2. an autoimmune response to a recombinant protein
3. insertional mutagenesis
4. lack of expression control and the sequelae related to an artificial overproduction of a protein in a healthy subject.

The immune response to a viral vector can be mild, such as a fever or inflammation, but could also be overwhelming and fatal. If a protein produced differs from that which is endogenously produced, autoimmune responses are possible.[105]

The prospect of insertional mutagenesis is concerning in that the vector could insert itself into the host genome and disrupt oncogenes, leading to tumour development. In some cases, the risk of germline integration or permanent, heritable genetic changes being introduced adds another serious ethical consideration to gene doping.

EPO overexpression leads to increased blood viscosity, which can increase the risk for heart

failure or stroke. Overexpression of a growth factor, such as IGF-1, can cause cardiac hypertrophy and stimulate growth of cancerous cells. Increasing muscle mass by manipulating myostatin, IGF-1 or other factors is also likely to put extra stress on supporting bones and tendons, which could actually increase the risk of injury.

Detection

Detecting gene doping will be very difficult. To be successful, doping detection needs to be accessible, fast and reliable; For example, if a gene doping product is produced by introducing genes to make more proteins endogenously, how can it be distinguished from the naturally produced protein? Can evidence of gene doping be reliably assessed using body fluids?

Studies have shown that gene therapy with IGF-1, while increasing the detectable levels in muscle cells, did not show an increase in circulating IGF-1 levels in the blood.[110] A muscle biopsy, although more sensitive, is not practical.

Detection strategies can be categorised into direct (evidence of doping agent) and indirect (evidence of consequences of gene doping).[105]

Direct approach

Direct detection of gene doping would involve identification of the vector used or a recombinant protein that differs from naturally occurring protein.[105] Vectors have been identified in blood after gene therapy, but the window of opportunity for detection seems to be short, which poses obvious limitations.[106] There is some evidence that some proteins produced by gene therapy undergo slightly different post-translational modification, which opens up possible detection.

Some genes may be regulated by promoters that need to be activated. Detection of activating substances such as rapamycin, tetracycline and antiprogestins would indicate gene doping but may also be present for therapeutic reasons.[110] Although direct evidence of gene doping may be preferred, especially if legally challenged, the technical limitations of these processes may not make it may mean they are not the most likely solution for gene doping detection.

In 2016, prior to the Rio Olympic Games, WADA reported that an Australian team of researchers led by Anna Baoutina at the National Measurement Institute (NMI) in Sydney had devised a test to detect a transgene, an extra copy of a gene injected to enhance performance.[111]

Indirect approach

Indirect detection of gene doping would involve identification of the consequences of the procedure on the athlete. Various fields of study are being investigated as a potential 'biologic profile' to distinguish normal standards from those indicating gene doping. For example, transcriptomics, or the profiling of gene expression, measures changes in the concentration of messenger RNA for thousands of genes.

Proteomics, or protein profiling, evaluates the set of proteins expressed from the genome and

provides qualitative and quantitative analysis of their variants. Metabolomics, or the profiling of non-protein low-molecular-weight metabolites, can also provide a possible measure of gene-doping activities.[112]

Although these are promising approaches, the development of normal standards, individual passports and variability parameters is expected to be costly, time consuming and open to legal interpretation if a gene doping charge is made. As illustrated in the testosterone metabolism studies, natural genetic variation in the population can lead to extremely variable enzyme activity under normal circumstances and may provide enough reasonable doubt to discount a suspected case of gene doping.[105]

SUBSTANCES AND METHODS PROHIBITED IN-COMPETITION

Stimulants

The stimulants are a broad group of substances and include central nervous system stimulants, sympathomimetic agents and cocaine. Until 2004, all stimulants were on the Prohibited List. In 2004, bupropion, caffeine, phenylephrine, phenylpropanolamine, pipradrol, pseudoephedrine and synephrine were removed from the Prohibited List and placed on the Monitoring Program. Pseudoephedrine was reintroduced on the banned list in 2010, due to evidence of abuse in some sports and scientific proof of its performance-enhancing effects at certain doses.

The major stimulants remaining on the banned list are the amphetamines, cocaine, ephedrine and modafinil.

S6: Stimulants[2]

Refer to www.wada-ama.org/en/what-we-do/the-prohibited-list

All stimulants, including all optical isomers, e.g. d- and l- where relevant, are prohibited.

Stimulants include:

a: Non-specified stimulants: adrafinil, amfepramone, amphetamine, amphetaminil, amiphenazole, benfluorex, benzylpiperazine, bromantan, clobenzorex, cocaine, cropopamide, crotetamide, fencamine, fenetylline, fenfluramine, fenproporex, fonturacetam, furfenorex, lisdexamfetamine, mefenorex, mephentermine, mesocarb, methamphetamine(D-), p-methylamphetamine, modafinil, norflenfluramine, phendimetrazine, phentermine, prenylamine, prolintane.

A stimulant not expressly listed in this section is a specified substance.

b: Specified stimulants: 1,3-dimethylbutylamine; 4-methylhexan-2-amine (methylhexaneamine), benzfetamine, cathine,** cathinone and its analogues, e.g. mephedrone, methedrone and α-pyrrolidinovalerophenone; dimethylamphetamine; ephedrine,*** epinephrine (adrenaline),**** etamivan, etilamfetamine, etilefrine, fenbutrazate, fencamfamine, heptaminol, hydroxyamfetamine (parahydroxyamphetamine), isometheptene, levmethamfetamine, meclofenoxate, methylenedioxymethamphetamine; methylephedrine,*** methylhexaneamine (dimethylpentylamine), methylphenidate, nikethamide, norfenefrine, octopamine, oxilofrine,

pemoline, pentetrazol, phenethylamine and its derivatives, phenmetrazine, phenpromethamine, propylhexedrine, pseudoephedrine,***** selegiline, sibutramine, strychnine, tenamfetamine (methylenedioxyamphetamine), tuaminoheptane, and other substances with a similar chemical structure or similar biological effect(s).

Except:

- Clonidine;
- Imidazole derivatives for topical/ophthalmic use and those stimulants included in the 2018 Monitoring Program.*

*Bupropion, caffeine, nicotine, phenylephrine, phenylpropanolamine, pipradrol and synephrine: These substances are included in the 2018 Monitoring Program and are not considered Prohibited Substances.

**Cathine: Prohibited when its concentration in urine is greater than 5 micrograms per millilitre.

*** Ephedrine and methylephedrine: Prohibited when the concentration of either in urine is greater than 10 micrograms per millilitre.

****Epinephrine (adrenaline): Not prohibited in local administration, e.g. nasal, ophthalmologic or co-administration with local anaesthetic agents.

*****Pseudoephedrine: Prohibited when its concentration in urine is greater than 150 micrograms per millilitre.

Amphetamines

Amphetamines were first used clinically in the 1930s for their stimulatory effects in the treatment of narcolepsy. Their clinical use nowadays is restricted to the treatment of narcolepsy and childhood hyperactive syndromes, such as attention deficit hyperactivity disorder (ADHD).[113] They have been widely used in sport to delay fatigue and increase alertness, although their use appears to have diminished in recent years, possibly due to adverse publicity regarding adverse effects. There is some evidence that the use of amphetamines may enhance speed, power, endurance and concentration.

The benefits of amphetamine use must be weighed against the adverse effects. Acute behavioural adverse effects are common with the use of amphetamines. These include central nervous system excitation as demonstrated by irritability, insomnia, restlessness, dizziness or tremor. Occasionally, more severe effects such as confusion, paranoia, delirium and uncontrolled aggression may occur. Systemic adverse effects include hypertension, angina, vomiting, abdominal pain and occasional cerebral haemorrhage.

Some deaths of athletes have resulted, even when 'normal' doses of amphetamines have been used, when undertaking maximal physical activity. Chronic use of amphetamines is associated with central nervous system-related symptoms such as uncontrolled involuntary movements. Amphetamines are addictive and withdrawal is associated with fatigue, lethargy and depression.

There has been considerable controversy over the granting of TUEs for amphetamines on the basis of required treatment for ADHD. The granting of TUEs in ADHD is mostly confined to children. The previous requirements involved requiring children to cease their ADHD treatment on weekends or other occasions to allow them to compete, but this was considered unreasonable, after

expert advice deemed it to have negative effects on symptom control. Currently, the granting of TUEs for children with ADHD is well documented and accepted.

The use of stimulants in the treatment of adult-onset ADHD remains controversial, primarily because recognition of the clinical entity itself is relatively recent. It appears that with the release of new non-stimulating medications (e.g. atomoxetine) for adult ADHD the problem of no alternative treatment may be solved.

Ephedra and pseudoephedrine

Ephedra is a shrub that grows mainly in desert or arid regions and is native to Northern China and Inner Mongolia. Different species vary in the amount of ephedrine alkaloids-the content of which produces the pharmacological effects of ephedra. The most common alkaloid is ephedrine, which generally constitutes 40–90% of the alkaloid content. This is the major ephedra alkaloid found in over-the-counter supplements. Pseudoephedrine is the next most common alkaloid and is less potent. It is produced synthetically and is used in many over-the-counter and prescription medications as a nasal decongestant. Norephedrine and norpseudoephedrine are minor alkaloid components.

The main use of ephedra, especially in the USA, is in dietary supplements. A review of case reports showed that 60% of users of ephedra-containing supplements were women and that the major reasons for its use were weight loss (59%), improved athletic performance (16%) and increased energy (6%).[114] There is some physiological basis for the use of ephedra as a weight-loss medication and some data showing a modest increase in weight loss, although only over a 6-month period.[115]

The performance-enhancing effects of ephedrine and pseudoephedrine have been extensively studied. Normal dosages of both substances do not appear to enhance performance.[116] Large doses of pseudoephedrine enhance cycling performance,[117] and the combination of ephedrine and caffeine has been shown to enhance performance[118] and carry the most risk.

Following an increasing number of reports of adverse events, including hypertension, arrhythmias, myocardial infarction, seizure, cerebrovascular accidents and death, the US Food and Drug Administration made it illegal for manufacturers to sell dietary supplements containing ephedrine.

Similarly, phenylpropanolamine, another commonly used dietary supplement, was voluntarily withdrawn from the market after its use was found to be an independent risk factor for haemorrhagic stroke in females.

Until the end of 2003, pseudoephedrine was prohibited in sports when a threshold value of 25 μg/mL of urine was exceeded. The threshold level for pseudoephedrine was initially set to 10 μg/mL, then increased to 25 mcg/ mL in 2000. From January 2004, the presence of this drug in doping control urine samples and its use in sports were no longer prohibited. Hence, pseudoephedrine represents an interesting case of the possible effect of lifting a ban on a drug, the ergogenic properties of which are controversially discussed.[119]

Following the lifting of the ban, the use of pseudoephedrine was monitored by WADA, and its incidence in testing samples increased dramatically, especially among cyclists. While only 0.2% of specimens measured between 2001 and 2003 yielded pseudoephedrine levels greater than 25 mcg/mL, 3.9% of all samples analysed in 2007–2008 were found to contain more than the formerly existing threshold value.[119]

These data suggest that the misuse of the stimulating agent pseudoephedrine was rather limited as long as the substance was prohibited and that lifting the ban resulted in much more frequent use aiming for performance enhancement. Consequently, a new threshold value for urinary pseudoephedrine of 150 mcg/mL was introduced in January 2010.

Cocaine

Cocaine is more a community drug problem rather than a drug for performance enhancement. It emerged in the 1960s to become a major health problem. Recently, the introduction of crack, a purer form of cocaine, has increased the risks associated with its use.

Cocaine has a minimal performance-enhancing effect because of the brief duration of its action. Decreased fatigue has been noticed and cocaine use causes increased activity and talkativeness. The main feeling produced by cocaine is one of euphoria and a sense of wellbeing. The mood elevation appears similar to that produced by amphetamines but is far more transient. The feeling of euphoria is usually followed soon after by a feeling of dysphoria and craving. This may be overcome by another dose of cocaine. Tachyphylaxis occurs following repeated use.

The positive effects on athletic performance are minimal and may be associated with heightened arousal and increased alertness with low doses. Detrimental effects on performance are reported more frequently and include impaired hand-eye coordination, distorted sense of time and inappropriate aggression.

The adverse effects of cocaine are numerous and include:

- serious cardiovascular problems, such as myocardial infarction and cardiac arrhythmia
- cerebral haemorrhage
- convulsions
- similar behavioural changes to amphetamine users.

The normal clinical use of cocaine is restricted to its use as a topical anaesthetic agent in eye and nose surgery, but it cannot be used in sport as a topical anaesthetic. Its use is illegal in most countries and possession of cocaine can carry heavy penalties.

Modafinil

In the 2003 World Track and Field Championships, Kelli White was disqualified after her victories in the 100-metre and 200-metre sprints when she tested positive for the presence of modafinil, which she claimed she was taking for the treatment of narcolepsy. At the time modafinil was not

specifically listed on the Prohibited List, but the International Association of Athletics Federations (IAAF) considered that modafinil fell under the category 'and related substances' to stimulants and recommended that she be stripped of her medals.

Modafinil is not a classic psychostimulant and it is not clear whether it is a performance-enhancing agent.[120] Those who are prescribed modafinil in the treatment of narcolepsy should apply for a TUE, which requires the diagnosis of narcolepsy to be confirmed by one of the accepted methods (e.g. sleep studies in an accredited institution).

S7: Narcotics[2]

Refer to www.wada-ama.org/en/what- we-do/the-prohibited-list

The following narcotics are prohibited in competition: buprenorphine, dextromoramide, diamorphine (heroin), fentanyl and its derivatives, hydromorphone, methadone, morphine, nicomorphine, oxycodone, oxymorphone, pentazocine, pethidine.

Narcotics

Narcotics are derivatives of the opium poppy and include morphine, pethidine and diamorphine (heroin). They are commonly used in the management of moderate to severe pain. As well as their analgesic effect, narcotics may cause mood disturbances, drowsiness, mental clouding, constipation, nausea and vomiting. In high doses they may cause respiratory depression, hypotension, muscle rigidity and addiction, and they have significant withdrawal effects.

Narcotics have no ergogenic effect but have the potential to mask pain and permit athletes to compete with musculoskeletal injuries. For this reason, they are included on the list of prohibited substances.

Codeine, dextromethorphan, dextropropoxyphene, dihydrocodeine, diphenoxylate, ethylmorphine, pholcodine, propoxyphene and tramadol are permitted.

Cannabinoids

The products of the cannabis plant, such as marijuana, hashish, hash oil, sinsemilla and others, are considered to be the most popular illicit drug in the world. The most important compounds contained in the plant are the cannabinoids, of which the psychoactive substance delta-9- tetrahydrocannabinol (THC) is the most significant compound. The rate of absorption of THC by the lungs is very high. Maximal blood concentrations are obtained after 3–8 minutes, the onset of action on the central nervous system is observed in approximately 20 minutes and the peak effect in 2–4 hours. Duration of action for psychoactive effects is 4–6 hours.

S8: Cannabinoids[2]

Refer to www.wada-ama.org/en/what-we-do/the-prohibited-list

The following cannabinoids are prohibited:

- Natural cannabinoids, e.g. cannabis, hashish and marijuana,
- Synthetic cannabinoids e.g. Δ9-tetrahydrocannabinol (THC) and other cannabimimetics.

Except:

- Cannabidiol.

For occasional users cannabinoid metabolites can be detected in urine up to 5–7 days after the exposure. In chronic users they may be detected as long as 30 days after the last exposure.

From 1989, cannabis has been included on the list of drugs subject to certain restrictions. A concentration in the urine of carboxy-THC greater than 15 ng/mL has been used as the threshold, to allow for the possible effect of passive smoking. In the 1998 Nagano Winter Olympics, snowboarder Ross Rebagliati tested positive for cannabinoids, and was suspended. This decision was eventually overturned, largely on the basis that marijuana was not on the list of banned substances, and Rebagliati was reinstated.

Cannabinoids have a negative effect on sports performance through impairment of psychomotor skills and concentration, as well as altered perception of time. They may also have a negative effect on exercise performance.[121] The well-recognised 'amotivational' syndrome associated with long-term marijuana use may be particularly damaging to a sporting career.

Glucocorticosteroids

Glucocorticosteroids (GCs) exert many beneficial actions in exercising humans. GCs increase the availability of metabolic substrates for muscle energy needs (increased lipolysis and plasma free fatty acids [FFA], increased glycogen synthesis) and maintain normal vascular integrity and responsiveness during exercise. In addition, GCs prevent an overreaction of the immune system as a result of exercise-induced muscle damage (immunosuppressive and anti-inflammatory effects).

S9: Glucocorticosteroids[2]

Refer to www.wada-ama.org/en/what-we-do/the-prohibited-list

All glucocorticosteroids are prohibited in competition when administered by oral, intravenous, intramuscular or rectal routes.

Including but not limited to:

- betamethasone, budesonide, cortisone, deflazacort, dexamethasone, fluticasone, hydrocortisone; methylprednisolone, prednisolone, prednisone, triamcinolone.

Cortisol also prepares the organism for the next bout of exercise, explaining why, when an acute bout of endurance exercise is stopped, cortisol levels may return to pre-exercise values with a

delay (<2 hours post-exercise).[122]

These physiologic properties of GCs suggest that they could enhance performance and this explains why they are in such widespread use in the sporting world. Indeed, the expected effects of the use and abuse of GCs are numerous: neurostimulatory effects at cerebral GC receptors could attenuate central impressions of fatigue, and anti-inflammatory and analgesic effects could inhibit sensations of muscle pain on effort and raise the fatigue threshold. The metabolic effects of these compounds consolidate glycogen reserves in muscle tissue and accelerate lipolysis and glycolysis mechanisms induced by catecholamines and growth hormone, thereby leading to more efficient use of energy sources by the muscles in the course of exercise.[122]

Research reveals inconsistencies regarding the ergogenic effect of GC administrations in humans. These inconsistencies may be attributed to:

1. the GC administration dosage, route and mode (acute or short-term)
2. the type, duration and intensity (submaximal, maximal) of exercise tested
3. the participants (highly trained or professional vs recreationally trained)
4. the differences in diet, such as whether or not experiments are food controlled and whether or not subjects fasted
5. GC intake coupled or not with intensive training.[122]

After short-term prednisolone administration (60 mg for 7 days), Arlettaz and colleagues[123] found a significant improvement in performance (154% compared with placebo), measured by time to exhaustion at 70–75% VO_2max in healthy, recreationally trained men.

To determine whether the effects of GC treatment could be extrapolated to elite athletes, Collomp and colleagues[124] investigated in a further study the influence of short-term prednisolone administration (60 mg for 7 days) combined with a standardised training program (2 hours per day) on performance measured by time to exhaustion at 70–75% VO_2max. Compared with the placebo condition, strenuous training associated with the GC treatment resulted in a marked improvement in endurance performance (average increase of about 80%, compared with an average increase of 54% in their previous study without training).

The health risks of using GCs are well characterised. Long-term GC use may lead to complications, notably on bone tissue (osteoporosis), metabolism (insulin resistance) and the cardiovascular system (hypertension and atherosclerosis).

While the inclusion of corticosteroids on the WADA Prohibited List is controversial, there would appear to be sufficient evidence of performance enhancement and health risk to justify their presence. Some[122, 125] would argue that systemic use of GCs should be prohibited at all times (in and out of competition) and not just in competition, as in the current WADA legislation.[2]

SUBSTANCES PROHIBITED IN PARTICULAR SPORTS

Beta blockers

Beta blockers are drugs commonly used in the treatment of hypertension, angina, arrhythmia, migraine, anxiety, tremor and following myocardial infarction. Their anxiolytic and anti-tremor effects resulted in their use in the sports of shooting and archery, where steadiness of hand and arm is important.

Beta blockers do not show any other positive effect on performance; in fact, they may have negative effects on both anaerobic and aerobic endurance. Adverse effects may include fatigue, depression, nightmares, bronchospasm and sexual dysfunction. Alternative treatments to beta blockers are available for most of the clinical conditions mentioned.

POSITIVE TESTS

Positive tests or, as they are known, AAFs (adverse analytical findings) can come from any of the classes of substances. The AAFs divided by substance class for 2016 are shown in Table 34.4. Anabolic agents, peptide hormones, stimulants and diuretics make up 85% of AAFs.

Table 34.4 WADA testing–AAFs for each drug class, 2016[126]

	Substance group	Occurrences	% of AAFs
S1	Anabolic agents	1804	43
S4	Hormone and metabolic modulators	721	17
S6	Stimulants	568	13
S5	Diuretics and other masking agents	499	12
S9	Glucocorticosteroids	184	4
S3	Beta- 2 agonists	172	4
S8	Cannabinoids	110	3
S2	Peptide hormones, growth factors and related substances	109	3
S7	Narcotics	49	1
P2	Beta blockers	14	0.3
M2	Chemical and physical manipulation	4	0.1
P1	Alcohol	0	**0**
M1	Enhancement of oxygen transfer	0	0

WORLD ANTI-DOPING AGENCY (WADA). 2016 ANTI-DOPING TESTING FIGURES. HTTPS://WWW.WADA-AMA.ORG/SITES/DEFAULT/FILES/RESOURCES/FILES/2016_ANTI-DOPING_TESTING_FIGURES.PDF.

P1: Beta-blockers[2]

Refer to www.wada-ama.org/en/what-we-do/the-prohibited-list

Unless otherwise specified, beta-blockers are prohibited in competition only, in the following sports:

- Archery* (FGITA, IPC)
- Automobile (FIA)

- Billiards and snooker (WCBS)
- Darts (WDF)
- Golf (IGF)
- Shooting* (ISSF, IPC)
- Skiing/snowboarding (FIS) in ski jumping, freestyle aerials/halfpipe and snowboard halfpipe/big air
- Underwater sports (CMAS) in constant-weight apnoea with or without fins, dynamic apnoea with and without fins, free immersion apnoea, Jump Blue apnoea, spearfishing, static apnoea, target shooting and variable weight apnoea.

*Also prohibited Out-of-Competition

Including, but not limited to: acebutolol, alprenolol, atenolol, betaxolol, bisoprolol, bunolol, carteolol, carvedilol, celiprolol esmolol, labetalol, levobunolol, metipranolol, metoprolol, nadolol, oxprenolol, pindolol, propranolol, sotalol, timolol.

THERAPEUTIC USE OF A PROHIBITED SUBSTANCE

Athletes may have illnesses or conditions that require them to take particular medications. If the medication an athlete is required to take for an illness or condition happens to be on the Prohibited List, a therapeutic use exemption, or TUE, may give that athlete the authorisation to take the needed medicine.

The criteria that must be fulfilled to grant 'therapeutic use' are:

- the athlete would experience significant health problems without taking the prohibited substance or method
- the therapeutic use of the substance would not produce significant enhancement of performance and
- there is no reasonable therapeutic alternative to the use of the otherwise prohibited substance or method.

WADA has issued an International Standard for the granting of TUEs. The standard states that all international federations and national anti-doping organisations must have a process in place whereby athletes with documented medical conditions can request a TUE and have such a request appropriately dealt with by a panel of independent physicians, called a therapeutic use exemption committee (TUEC).

Those athletes wishing to take a prohibited substance can begin treatment only after receiving the authorisation notice from the relevant organisation. TUEs are granted for a specific medication with a defined dosage and specific length of time.

It has been suggested that the TUE system has been abused by athletes and teams wishing to gain an advantage. Both Alberto Salazar's distance running group in the USA and the UK Sky cycling team of Brad Wiggins have been accused of abusing the TUE process.

PERMITTED SUBSTANCES

The drug groups that are permitted by WADA are:

- antibiotics
- antidepressants
- antidiarrheals
- antihistamines
- antihypertensives (excluding beta blockers)
- antinauseants
- aspirin (ASA), paracetamol (acetaminophen), codeine, dextropropoxyphene
- eye medications
- NSAIDs
- oral contraceptives
- skin creams and ointments
- sleeping tablets.

DELETED DRUGS

As mentioned above, a number of drugs have been removed from the Prohibited List over the past few years and are now being monitored by WADA to detect possible patterns of misuse. The most controversial omission is caffeine.

Caffeine

Caffeine is the most commonly used drug in the world. It occurs naturally in more than 60 plants and is contained in coffee, tea, chocolate, cola and various beverages. Until 2004, caffeine was on the Prohibited List, with urine levels above 12 μg/mL deemed illegal. This was thought to be the equivalent of 6–8 cups of coffee. A typical cup of brewed coffee contains about 100 mg of caffeine, the same amount as an Australian No Doz® tablet. Interestingly, an American No Doz tablet contains 200 mg of caffeine. For many years athletes in various sports have been using caffeine in doses below the banned level.

There is clear evidence that caffeine is an ergogenic aid for a variety of sports, although studies involving elite athletes and field situations are lacking. Further research is needed to define the range of caffeine protocols and sports activities that show evidence of performance enhancement, as well as the benefits or harm to other issues underpinning recovery after exercise or preparation for an event.[127]

Newer evidence suggests, at least in endurance sports, that the maximal benefits of caffeine are seen at small to moderate caffeine doses (2–3 mg/kg body mass), which are well within the normal daily caffeine intakes of the general population. This makes the recent decision to remove caffeine from the list of prohibited substances in sports a pragmatic choice.

To date, there is little evidence that this change has increased the use or misuse of caffeine by

athletes, at least within the levels of elite and sub-elite sport, where anti-doping codes apply. Caffeine use may also enhance the performance of sport in recreational athletes, but it is inappropriate and unnecessary for use by young adults.[127]

Alcohol

Alcohol was removed from the Prohibited List at the start of 2018. WADA stated that the intent of this change was not to compromise the integrity or safety of any sport where alcohol use is a concern, but rather to endorse a different means of enforcing bans on alcohol use in those sports. The four international federations (air sports, archery, automobile and powerboating) affected by this change were alerted sufficiently in advance to amend their rules and put in place protocols to test for alcohol use and appropriately sanction athletes who do not abide by the rules of their sport.

NON-INTENTIONAL DOPING IN SPORTS

When an athlete tests positive for a banned substance, they frequently deny the claim and allege circumstances other than intentional doping. Typical defences include that their drink had been spiked, passive inhalation of drug smoke or inadvertently taking a nutritional supplement or food that contained a prohibited substance.

Studies have shown that it is possible that an individual could produce detectable levels of cannabinoids in urine samples only after extremely severe conditions of passive exposure to marijuana smoke.[128, 129] Similarly, only individuals exposed to passive cocaine smoke under extremely harsh conditions would show cocaine metabolites in a urine sample.

Research has indicated that food containing poppy seed[130] and herbal coca tea[131, 132] can both produce levels of morphine and cocaine metabolites above the allowed limit. Studies have also shown that it is possible to yield positive test results for anabolic agents after consumption of meat originating from animals treated with those agents.[133]

A number of studies have shown that there are a significant number of 'nutritional supplements' that contain substances other than those described on the label, and that a number of these are prohibited substances, such as prohormones or anabolic steroids.[134]

The IOC has reported that 14.8% of some 650 products sampled contained levels of banned substances sufficient to result in a positive urine sample. None of the substances carried warnings or product information on the contents.[135] Athletes should be wary of ingesting these supplements.

Biotransformation products of permitted substances can also cause an athlete to test positive. One example is the permitted analgesic codeine, which is metabolised to morphine at levels above the threshold.

DRUG TESTING

Drug testing has become commonplace in both amateur and professional sport. The clinician providing services to the team or individual must be familiar with the list of prohibited substances and the drug testing procedure itself. The athlete is entitled to have a representative present to confirm that the correct testing procedures have taken place. Often the representative is the team clinician.

Testing procedure

1. Athlete selection

An athlete can be selected for testing anywhere, any time, and is subject to both random and targeted selection methods.

The role of the doping control officer (DCO) is to organise and manage the sample collection session. The role of the chaperone is to notify, accompany and witness the athlete providing a sample. The DCO can also perform all the duties of a chaperone.

DCOs and chaperones ensure that sample collection occurs in strict accordance with the relevant procedures, so all athletes are treated in a fair and equitable manner.

2. Notification

The DCO or chaperone notifies the athlete for sample collection, generally in person or less frequently by telephone, written notice or by a third party. Once notified of selection for testing, the athlete must remain in direct observation of the DCO or chaperone until the DCO is satisfied that the sample collection procedure is complete. Any attempt to evade notification may result in an anti-doping rule violation and a ban from sport.

3. Reporting to the doping control station

For no-advance notice testing, including in-competition testing, the athlete is required to report to the doping control station immediately unless they request a delay in reporting for valid reasons.

4. Selecting a collection vessel

The athlete is given a choice of individually sealed collection vessels and selects one, after verifying that the equipment is intact and has not been tampered with. The athlete will maintain control of the collection vessel at all times.

5. Providing the sample

Urine sample provision

Only a chaperone (or DCO) of the same gender is permitted in the area of privacy when the athlete

provides the sample. If the athlete is under 18 years of age, they may request a representative be present. The chaperone (or DCO) will directly witness the urine sample leaving the athlete's body and going into the collection vessel.

The athlete is responsible for controlling their sample and keeping it in view of the DCO or chaperone until it is sealed in a sample collection kit. If the sample provided is less than the required volume, the athlete is required to temporarily seal it and provide further volume.

Blood sample provision

The athlete selects the blood collection equipment and checks that it is intact and has not been tampered with. A blood collection official collects the sample in the presence of a DCO and, if applicable, the athlete's representative. In some instances the athlete may be required to wait two hours after training or competition before the blood is drawn. The athlete is advised not to do any strenuous exercise using that arm for a minimum of 30 minutes, to minimise bruising at the puncture site.

6. Selection of the sample collection kit

The athlete selects an individually sealed sample collection kit that is intact and has not been tampered with, opens the kit and confirms that the sample code numbers on the bottles, the lids and the containers all match. All sample collection kit numbers will be recorded on the doping control test form.

7. Splitting and sealing the sample

Urine

The athlete pours a measured amount of the urine into each of the 'A' and 'B' labelled bottles and then secures the kits. The athlete is asked to leave a small amount of urine in the collection vessel, so the DCO can measure the specific gravity. Then the athlete seals both the A and B bottles. The DCO will verify that the bottles are sealed properly.

Blood

The athlete places and secures the blood samples in the relevant labelled containers and secures the kits.

8. Measuring specific gravity

The DCO checks the specific gravity of the residual urine left in the collection vessel and records the value on the doping control test form. The athlete should avoid over hydrating; this can happen if he or she drinks too much fluid. If the sample is too diluted and does not meet the required specific gravity, the athlete will be required to provide additional urine samples, as directed by the

DCO.

9. Final paperwork

The athlete's personal information is recorded on the doping control test form, including contact details, and he or she is then asked to provide information on prescription and non-prescription medications, vitamins, herbal products, food supplements and any other substances used within the previous seven days. These are recorded on the doping control test form.

It is essential to declare any substance used in the last seven days, including any substances for which a current and valid therapeutic use exemption has been obtained. Not declaring use may affect results management and have adverse consequences. The athlete is invited to note comments and concerns about how the session was conducted on the form.

At the conclusion of the session, the athlete checks that all the information recorded is correct and signs the doping control paperwork. The paperwork must also be signed by the parties present, including the DCO and, if applicable, the chaperone, the athlete's representative and blood collection official. The DCO will provide a copy of the doping control paperwork to the athlete. The copy of the doping control paperwork that the laboratory receives does not contain any information that could identify the athlete.

10. Securing and transporting the sample

The secure sample(s) and the laboratory copy of the doping control test form are sent to the laboratory for analysis. There is a strict chain of custody regarding transportation, storage and opening of the sample. The laboratory will inspect the samples upon arrival to ensure there is no evidence of tampering. All urine and blood samples are sent to a WADA-accredited laboratory for analysis, or storage for future analysis.

The analytical procedure

The laboratory will analyse the A sample (urine) or blood sample for the presence of substances on the WADA Prohibited List. The national anti-doping agency can store samples in its deep-freeze facility for up to 10 years, and retrospectively analyse the samples to detect prohibited substances and methods and enforce sanctions against athletes.

Results management

If the doping agency is advised by a WADA-accredited laboratory that the athlete's A sample has recorded an adverse analytical finding, which is the presence of a prohibited substance or its metabolites or markers, or evidence of use of a prohibited method on the WADA Prohibited List, the athlete will be notified.

If the A sample, whether urine or blood (where an A and B sample were collected), returns an adverse analytical finding, the athlete has the right to have the B sample analysed to confirm the result.

Athlete's rights

The athlete has the right to:

- have a representative present
- have an interpreter, if available
- ask for additional information about the sample collection process
- request modifications, if they have a disability
- request a delay in reporting to the doping control station for valid reasons such as:
  - for in-competition testing:
    - to perform a warm-down
    - to compete in further competitions
    - to fulfil media commitments
    - to participate in a victory ceremony
    - to obtain necessary medical treatment
    - to obtain photo identification
    - to locate a representative and/or interpreter
    - for any other reasonable circumstances as approved by the DCO
  - for out-of-competition testing:
    - to locate a representative
    - to complete a training session
    - to receive necessary medical treatment
    - to obtain photo identification
    - for any other reasonable circumstances as approved by the DCO.

Page 516

Athlete's responsibilities

The athlete has the responsibility to:

- remain within direct observation of the DCO or chaperone at all times from the point of notification until the completion of the sample collection procedure
- produce appropriate identification
- comply with the directions of the DCO and chaperone during the sample collection session.

THE ROLE OF THE TEAM CLINICIAN

The team clinician has an extremely important role to play in the prevention and management of doping problems. The primary role of the team clinician should be education of team members. This should involve regular briefings, especially prior to the season. Topics covered should include:

- the Prohibited List (available at https://www.wada-ama.org/sites/default/files/prohibited_list_2018_en.pdf)

- prescription drugs:
  - athletes must inform clinicians that they are subject to drug testing and ensure that the clinician confirms that the medication being prescribed does not contain any banned substance
  - if the clinician is uncertain, suggest contacting the national anti-doping agency for confirmation
- inadvertent doping:
  - check the contents of all medications, especially over-the-counter substances and supplements
  - if uncertain, contact the national anti-doping agency for confirmation
- drug testing protocols:
  - especially reinforce the importance of listing all medications including supplements
- travel:
  - be aware while travelling in foreign countries that drugs with the same or similar brand names in one country may have a different composition in another country
  - always ensure that athletes take their own regular medications with them.

REFERENCES

1. World Anti-Doping Agency (WADA). 2016 Anti-Doping Testing Figures. Sport Report pp. 6-9. https://www.wada-ama.org/sites/default/files/resources/files/2016_anti-doping_testing_figures.pdf
2. World Anti-Doping Agency (WADA). The World Anti-Doping Code. International Standard. Prohibited List January 2018. https://www.wada-ama.org/sites/default/files/prohibited_list_2018_en.pdf.
3. Hartgens F, Kuipers H. Effects of androgenic-anabolic steroids in athletes. *Sports Med* 2004; 34(8): 513–54.
4. Yesalis CE, 3rd, Herrick RT, Buckley WE et al. Self-reported use of anabolic-androgenic steroids by elite power lifters. *Phys Sportsmed* 1988; 16(12): 91–8.
5. Lindstrom M, Nilsson AL, Katzman PL et al. Use of anabolic-androgenic steroids among body builders—frequency and attitudes. *J Intern Med* 1990; 227: 407–11.
6. Buckley WE, Yesalis CE, 3rd, Friedl KE et al. Estimated prevalence of anabolic-androgenic steroid use among male high school seniors. *JAMA* 1988; 260: 3441–5.
7. Corbin CB, Feyrer-Melk SA, Phelps C et al. Anabolic steroids: a study of high school athletes. *Pediatr Exerc Sci* 1994; 6: 149–58.
8. Melia P, Pipe A, Greenberg L. The use of anabolic-androgenic steroids by Canadian

students. *Clin J Sport Med* 1996; 6: 9–14.

9. Terney R, McLain LG. The use of anabolic steroids in high school students. *Am J Dis Child* 1990; 144: 99–103.
10. Thiblin I, Petersson A. Pharmacoepidemiology of anabolic androgenic steroids: a review. *Fundam Clin Pharmacol* 2005; 19: 27–44.
11. Sagoe D, Molde H, Andreassen CS et al. The global epidemiology of anabolic-androgenic steroid use: a meta-analysis and meta-regression analysis. *Ann Epidemiol* 2014; 24(5): 383–98.
12. Yesalis CE, Bahrke MS. Anabolic-androgenic steroids and related substances. *Curr Sports Med Rep* 2002; 4: 246–52.
13. Bhasin S, Storer TW, Berman N et al. The effects of supraphysiological doses of testosterone on muscle size and strength in normal men. *N Engl J Med* 1996; 335: 1–7.
14. Forbes GB, Porta CR, Herr BE et al. Sequence of changes in body composition induced by testosterone and reversal of changes after drug is stopped. *JAMA* 1992; 267: 397–9.
15. Giorgi A, Weatherby RP, Murphy PW. Muscular strength, body composition and health responses to the use of testosterone enanthate: a double blind study. *J Sci Med Sport* 1999; 2: 341–55.
16. Sinha-Hikim I, Artaza J, Woodhouse L et al. Testosterone-induced increase in muscle size in healthy young men is associated with muscle fiber hypertrophy. *Am J Physiol Endocrinol Metab* 2002; 283: E154–64.
17. Bermon S. Androgens and athletic performance of elite female athletes. *Curr Opin Endocrinol Diabetes Obes* 2017; 24(3): 246–51.
18. Parssinen M, Kujala U, Vartiainen E et al. Increased premature mortality of competitive power lifters suspected to have used anabolic agents. *Int J Sports Med* 2000; 21: 225–7.
19. Frati P, Busardo FP, Cipolloni L et al. Anabolic androgenic steroid (AAS) related deaths: autoptic, histopathological and toxicological findings. *Curr Neuropharmacol* 2015; 13(1): 146–59.
20. Thiblin I, Lindquist O, Rais J. Cause and manner of death among users of anabolic androgenic steroids. *J Forensic Sci* 2000; 45: 16–23.
21. Rich JD, Dickinson BP, Feller A et al. The infectious complications of anabolic-androgenic steroid injection. *Int J Sports Med* 1999; 20: 563–6.
22. Ishak KG, Zimmerman HJ. Hepatotoxic effects of the anabolic/androgenic steroids. *Semin Liver Dis* 1987; 7(3): 230–6.
23. Bagheri SA, Boyer JL. Peliosis hepatis associated with androgenic-anabolic steroid therapy: a severe form of hepatic injury. *Ann Intern Med* 1971; 81: 610–18.
24. Cabasso A. Peliosis hepatis in a young adult bodybuilder. *Med Sci Sports Exerc* 1994; 26(1): 2–4.

25. Creagh TM, Rubin A, Evans DJ. Hepatic tumours induced by anabolic steroids in an athlete. *J Clin Pathol* 1988; 41: 441–3.
26. Klava A, Super P, Aldridge M et al. Body builder's liver. *J R Soc Med* 1994; 87: 43–4.
27. Cohen LI, Hartford CG, Rogers GG. Lipoprotein (a) and cholesterol in body builders using anabolic androgenic steroids. *Med Sci Sports Exerc* 1996; 28(2): 176–9.
28. Ebenbichler CF, Sturm W, Ganzer H et al. Flow-mediated endothelium-dependent vasodilatation is impaired in male body builders taking anabolic-androgenic steroids. *Atherosclerosis* 2001; 158: 483–90.
29. Kuipers H, Wijnen JA, Hartgens F et al. Influence of anabolic steroids on body composition, blood pressure, lipid profile and liver functions in body builders. *Int J Sports Med* 1991; 12: 413–18.
30. Achar S, Rostamian A, Narayan SM. Cardiac and metabolic effects of anabolic-androgenic steroid abuse on lipids, blood pressure, left ventricular dimensions and rhythm. *Am J Cardiol* 2010; 106(6): 893–901.
31. Melchert RB, Welder AA. Cardiovascular effects of androgenic-anabolic steroids. *Med Sci Sports Exerc* 1995; 27(9): 1252–62.
32. Hartgens F, Kuipers H. Body composition, cardiovascular risk factors and liver function in long-term androgenic-anabolic steroids using body builders three months after drug withdrawal. *Int J Sports Med* 1996; 17: 429–33.
33. Riebe D, Fernhall B, Thompson PD. The blood pressure response to exercise in anabolic steroid users. *Med Sci Sports Exerc* 1992; 24(6): 633–7.
34. Ferenchick GS, Adelman S. Myocardial infarction associated with anabolic steroid use in a previously healthy 37-year-old weight lifter. *Am Heart J* 1992; 124(2): 507–8.
35. Sullivan ML, Martinez CM, Gennis P et al. The cardiac toxicity of anabolic steroids. *Prog Cardiovasc Dis* 1998; 41: 1–15.
36. Mochizuki RM, Richter KJ. Cardiomyopathy and cerebrovascular accident associated with anabolic-androgenic steroid use. *Phys Sportsmed* 1988; 18(11): 109–14.
37. Baggish AL, Weiner RB, Kanayama G et al. Long-term anabolic-androgenic steroid use is associated with left ventricular dysfunction. *Circ Heart Fail* 2010; 3(4): 472–6.
38. D'Andrea A, Limongelli G, Morello A et al. Anabolic-androgenic steroids and athlete's heart: when big is not beautiful ...! *Int J Cardiol* 2016; 20(3): 486–8.
39. Carbone A, D'Andrea A, Riegler L et al. Cardiac damage in athlete's heart: when the 'supernormal' heart fails! *World J Cardiol* 2017; 9(6): 470–80.
40. Kiraly CL. Androgenic-anabolic steroid effects on serum and skin surface lipids, on red cells and on liver enzymes. *Int J Sports Med* 1988; 9: 249–52.
41. Walker J, Adams B. Cutaneous manifestations of anabolic-androgenic steroid use in athletes. *Int J Dermatol* 2009; 48(10): 1044–8.
42. Bahrke MS, Yesalis CE, 3rd, Wright JE. Psychological and behavioural effects of endogenous testosterone levels and anabolic-androgenic steroids among males.

Sports Med 1990; 10(5): 303–37.

43. Trenton AJ, Currier GW. Behavior manifestations of anabolic steroid use. *CNS Drugs* 2005; 19(7): 571–95.
44. Cooper CJ, Noakes T, Dunne T et al. A high prevalence of personality traits in chronic users of anabolic-androgenic steroid users. *Br J Sports Med* 1996; 30: 246–50.
45. Midgley SJ, Heather N, Davies JB. Levels of aggression among a group of anabolic-androgenic steroid users. *Med Sci Law* 2001; 41: 309–14.
46. Piacentino D, Kotzalidis GD, Del Casale A et al. Anabolic-androgenic steroid use and psychopathology in athletes. A systematic review. *Curr Neuropharmacol* 2015; 13(1): 101–21.
47. Lubell A. Does steroid abuse cause—or excuse—violence? *Phys Sportsmed* 1989; 17(2): 176–85.
48. Kashkin KB, Kleber HD. Hooked on hormones? An anabolic steroid addiction hypothesis. *JAMA* 1989; 262(22): 3166–70.
49. Jarow JP, Lipshultz LI. Anabolic steroid-induced hypogonadotropic hypogonadism. *Am J Sports Med* 1990; 18(4): 429–31.
50. Christou MA, Christou PA, Markozannes G et al. Effects of anabolic androgenic steroids on the reproductive system of athletes and recreational users: a systematic review and meta-analysis. *Sports Med* 2017; 47(9): 1869–83.
51. Tan RS, Vasudevan D. Use of clomiphene citrate to reverse premature andropause secondary to steroid abuse. *Fertil Steril* 2003; 79: 203–5.
52. Friedl KE, Yesalis CE. Self-treatment of gynecomastia in bodybuilders who use anabolic steroids. *Phys Sportsmed* 1989; 17(3): 67–79.
53. Huang G, Basaria S. Do anabolic-androgenic steroids have performance-enhancing effects in female athletes? *Mol Cell Endocrinol* 2018; 464: 56–64.
54. Rogol AD, Yesalis CE, 3rd. Clinical review 31: anabolic-androgenic steroids and athletes: what are the issues? *J Clin Endocrinol Metab* 1992; 74(3): 465–9.
55. Wilson JD. Androgen abuse by athletes. *Endocr Rev* 1988; 9(2): 181–99.
56. Corrigan B. DHEA and sport. *Clin J Sport Med* 2002; 12: 236–41.
57. Brown GA, Vukovich MD, Reifenrath TA et al. Effects of anabolic precursors on serum testosterone concentrations and adaptations to resistance training in young men. *Int J Sport Nutr Exerc Metab* 2001; 10: 340–59.
58. Welle S, Jozefowicz R, Statt M. Failure of dehydroepiandrosterone to influence energy and protein metabolism in humans. *J Clin Endocrinol Metab* 1990; 71: 1259–64.
59. Kazlauskas R. Designer steroids. *Handb Exp Pharmacol* 2010; 195: 155–85.
60. Van Eenoo P, Delbeke FT. Metabolism and excretion of anabolic steroids in doping control—new steroids and new insights. *J Steroid Biochem Mol Biol* 2006; 101: 161–78.
61. Caitlin DH, Sekera MH, Ahrens BH et al. Tetrahydrogestrinone discovery, synthesis

and detection in urine. *Rapid Commun Mass Spectrom* 2004; 18: 1245–9.

62. Malvey TC, Armsey TD. Tetrahydrogestrinone: the discovery of a designer steroid. *Curr Sports Med Rep* 2005; 4: 227–30.
63. Death AK, McGrath KCY, Kazlauskas R et al. Tetrahydrogestrinone is a potent androgen and progestin. *J Clin Endocrinol Metab* 2004; 89: 2498–500.
64. Prather ID, Brown DE, North P et al. Clenbuterol: a substitute for anabolic steroids? *Med Sci Sports Exerc* 1995; 27(8): 1118–21.
65. Guddat S, Fußhöller G, Geyer H et al. Clenbuterol—regional food contamination a possible source for inadvertent doping in sports. *Drug Test Anal* 2012; 4(6): 534–8.
66. Thevis M, Geyer L, Geyer H et al. Adverse analytical findings with clenbuterol among U-17 soccer players attributed to food contamination issues. *Drug Test Anal* 2013; 5(5): 372–6.
67. Scott J, Phillips GC. Erythropoietin in sports: a new look at an old problem. *Curr Sports Med Rep* 2005; 4: 224–6.
68. Franz SE. Erythropoiesis-stimulating agents: development, detection and dangers. *Drug Test Anal* 2009; 1: 245–9.
69. Audran M, Gareau R, Matecki S et al. Effects of erythropoietin administration in training athletes and possible indirect detection in doping control. *Med Sci Sports Exerc* 1999; 31(5): 639–45.
70. Ekblom B. Blood doping and erythropoietin. The effects of variation in hemoglobin concentration and other related factors on physical performance. *Am J Sports Med* 1996; 24(6): S40–2.
71. Berglund B, Ekblom B. Effect of recombinant erythropoietin treatment on blood pressure and some hematological parameters in healthy men. *J Intern Med* 1991; 229: 125–30.
72. Birkeland KI, Stray-Gundersen J, Hemmersbach P et al. Effect of rhEPO administration on serum levels of sTfR and cycling performance. *Med Sci Sports Exerc* 2000; 32: 1238–43.
73. Ekblom B, Berglund B. Effect of erythropoietin administration on maximal aerobic power. *Scand J Med Sci Sports* 1991; 1: 88–93.
74. Lippi G, Franchini M, Salvagno GL et al. Biochemistry, physiology and complications of blood doping: facts and speculation. *Crit Rev Clin Lab Sci* 2006; 43: 349–91.
75. World Anti-Doping Agency (WADA). Athlete biological passport operating guidelines. Version 6.0, January 2017. https://www.wada-ama.org/sites/default/files/resources/files/guidelines_abp_v6_2017_jan_en_final.pdf.
76. O'Toole ML, Douglas PS, Douglas W et al. Hematocrits of triathletes: is monitoring useful? *Med Sci Sports Exerc* 1999; 31(3): 372–7.
77. Schumacher YO, Schmid A, Lenz T et al. Blood testing in sports: hematological profile of a convicted athlete. *Clin J Sport Med* 2001; 11: 115–17.

78. Dean H. Does exogenous growth hormone improve athletic performance? *Clin J Sport Med* 2002; 12: 250–3.
79. Crist DM, Peake GT, Egan PA et al. Body composition response to exogenous GH during training in highly conditioned adults. *J Appl Physiol (1985)* 1988; 65(2): 579–84.
80. Holt RIG, Erotokritou-Mulligan I, Sönksen PH. The history of doping and growth hormone abuse in sport. *Growth Horm IGF Res* 2009; 19(4): 320–6.
81. Liu H, Bravata DM, Olkin I et al. Systematic review: the effects of growth hormone on athletic performance. *Ann Intern Med* 2008; 148(10): 747–58.
82. Meinhardt U, Nelson AE, Hansen JL et al. The effects of growth hormone on body composition and physical performance in recreational athletes: a randomized trial. *Ann Intern Med* 2010; 152(9): 568–77.
83. World Anti-Doping Agency (WADA). Human growth hormone (hGH) testing. 2017. ht tps://www.wada-ama.org/en/questions-answers/human-growth-hormone-hgh-tes ting.
84. Anderson LJ, Tamayose JM, Garcia JM. Use of growth hormone, IGF-I and insulin for anabolic purpose: pharmacological basis, methods of detection and adverse effects. *Mol Cell Endocrinol* 2018; 464: 65–74.
85. Guha N, Dashwood A, Thomas NJ et al. IGF-I abuse in sport. *Curr Drug Abuse Rev* 2009; 2(3): 263–72.
86. Adams G. Insulin-like growth factor in muscle growth and its potential abuse by athletes. *Br J Sports Med* 2000; 34: 412–13.
87. Kemp SF, Fowlkes JL, Thrailkill KM. Efficacy and safety of mecasermin rinfabate. *Expert Opin Biol Ther* 2006; 6: 533–8.
88. Dickinson J, Hu J, Chester N et al. Impact of ethnicity, gender and dehydration on the urinary excretion of inhaled salbutamol with respect to doping control. *Clin J Sport Med* 2014; 24(6): 482–9. doi: 10.1097/jsm.0000000000000072 [published online first: 13 February 2014].
89. Kindermann W. Do inhaled beta(2)-agonists have an ergogenic potential in non-asthmatic competitive athletes? *Sports Med* 2007; 37(2): 95–102.
90. Seeheusen DA, Glorioso JE. Tamoxifen as an ergogenic agent in women body builders. A case report. *Clin J Sport Med* 2002; 12: 313–14.
91. Erotokritou-Mulligan I, Holt RIG. Insulin-like growth factor I and insulin and their abuse in sport. *Endocrinol Metab Clin North Am* 2010; 39: 33–43.
92. Rich JD, Dickinson BP, Merriman MA et al. Insulin use by bodybuilders. *JAMA* 1998; 279: 161–3.
93. Haerinejad MJ, Ostovar A, Farzaneh MR et al. The prevalence and characteristics of performance-enhancing drug use among bodybuilding athletes in the south of Iran, Bushehr. *Asian J Sports Med* 2016; 7(3): e35018.
94. Chandler M, McVeigh J. Steroids and image enhancing drugs 2013 survey results.

Liverpool, UK: LJMU Centre for Public Health, 2014.

95. Evans PJ, Lynch RM. Insulin as a drug of abuse in body building. *Br J Sports Med* 2003; 37: 356–7.
96. Banadonna RC, Saccomani MP, Cobelli C et al. Effect of insulin on system A amino acid transport in human skeletal muscle. *J Clin Invest* 1993; 91: 514–21.
97. Jones M, Pedoe DST. Blood doping—a literature review. *Br J Sports Med* 1989; 23(2): 84–8.
98. Sawka MN, Joyner MJ, Miles DS et al. American College of Sports Medicine position stand. The use of blood doping as an ergogenic aid. *Med Sci Sports Exerc* 1996; 28(6): i–viii.
99. Leigh-Smith S. Blood boosting. *Br J Sports Med* 2004; 38: 99–101.
100. Corrigan B. Beyond EPO. *Clin J Sport Med* 2002; 12: 242–4.
101. Schumacher YO, Ashenden M. Doping with artificial oxygen carriers. *Sports Med* 2004; 34(3): 141–50.
102. Varlet-Marie E, Audran M, Ashenden M et al. Modification of gene expression: help to detect doping with erythropoiesis-stimulating agents. *Am J Hematol* 2009; 84(11): 755–9.
103. Azzazy HME, Mansour MMH, Christenson RH. Gene doping: of mice and men. *Clin Biochem* 2009; 42: 435–41.
104. Harridge SDR, Velloso CP. IGF-1 and GH: potential use in gene doping. *Growth Horm IGF Res* 2009; 19: 378–82.
105. McKanna TA, Toriello HV. Gene doping: the hype and the harm. *Pediatr Clin North Am* 2010; 57(3): 719–27.
106. Wells DJ. Gene doping: possibilities and practicalities. *Med Sport Sci* 2009; 54: 166–75.
107. Svensson E, Black H, Dugger D et al. Long-term erythropoietin expression in rodents and non-human primates following intramuscular ingestion of a replication-defective adenoviral vector. *Hum Gene Ther* 1997; 8: 1797–806.
108. Barton-Davis E, Shoturma D, Musaro A et al. Viral mediated expression of insulin like growth factor I blocks the ageing-related loss of skeletal muscle function. *Proc Natl Acad Sci U S A* 1998; 95: 15603–7.
109. Raper SE, Chirmule N, Lee FS et al. Fatal systemic inflammatory response syndrome in an ornithine transcarbamylase deficient patient following adenoviral gene transfer. *Mol Genet Metab* 2003; 80: 148–58.
110. Wells DJ. Gene doping: the hype and the reality. *Br J Pharmacol* 2008; 154: 623–31.
111. https://www.theaustralian.com.au/sport/olympics-aussie-teams-gene-drug-test-may-be-ready-for-rio/news-story/f2523f0b4e9acce8134874735360f096
112. Baoutina A, Alexander IE, Rasko JEJ et al. Developing strategies for detection of gene doping. *J Gene Med* 2008; 10: 3–20.

113. Hickey G, Fricker P. Attention deficit hyperactivity disorder, CNS stimulants and sport. *Sports Med* 1999; 27(1): 11–21.
114. Geiger JD. Adverse effects associated with supplements containing ephedra alkaloids. *Clin J Sport Med* 2002; 12: 263.
115. Shekelle P, Hardy MA, Morton S et al. Efficacy and safety of ephedra and ephedrine for weight loss and athletic performance: a meta-analysis. *JAMA* 2003; 289: 1537–45.
116. Bohn AM, Khodaee M, Schwenk TL. Ephedrine and other stimulants as ergogenic aids. *Curr Sports Med Rep* 2003; 2: 220–5.
117. Pritchard-Peschek KR, Jenkins DG, Osborne MA et al. Pseudoephedrine ingestion and cycling time-trial performance. *Int J Sport Nutr Exerc Metab* 2010; 20(2): 132–8.
118. Bell DG, Jacobs I, Zamecnik J. Effects of caffeine, ephedrine and their combination on time to exhaustion during high intensity exercise. *Eur J Appl Physiol* 1996; 81: 428–33.
119. Thevis M, Sigmund G, Geyer H et al. Stimulants and doping in sport. *Endocrinol Metab Clin North Am* 2010; 39(1): 89–105.
120. Kaufman KR, Gerner R. Modafinil in sports: ethical considerations. *Br J Sports Med* 2005; 39(4): 241–4.
121. Renaud AM, Cormier Y. Acute effects of marihuana smoking on maximal exercise performance. *Med Sci Sports Exerc* 1986; 18(6): 685–9.
122. Duclos M, Gouarne C, Bonnemaison D. Acute and chronic effects of exercise on tissue sensitivity to glucocorticoids. *J Appl Physiol (1985)* 2003; 94: 869–75.
123. Arlettaz A, Portier H, Lecoq AM et al. Effects of short-term prednisolone intake during submaximal exercise. *Med Sci Sports Exerc* 2007; 39(9): 1672–8.
124. Collomp K, Arlettaz A, Portier H et al. Short-term glucocorticoid intake combined with intense training on performance and hormonal responses. *Br J Sports Med* 2008; 42(12): 983–8.
125. Duclos M. Evidence on ergogenic action of glucocorticoids as a doping agent risk. *Phys Sportsmed* 2010; 38(3): 121–7.
126. World Anti-Doping Agency (WADA). 2016 Anti-Doping Testing Figures. https://www.wada-ama.org/sites/default/files/resources/files/2016_anti-doping_testing_figures.pdf.
127. Burke LM. Caffeine and sports performance. *Appl Physiol Nutr Metab* 2008; 33(6): 1319–34.
128. Herrmann ES, Cone EJ, Mitchell JM, et al. Non-smoker exposure to secondhand cannabis smoke II: Effect of room ventilation on the physiological, subjective, and behavioral/cognitive effects. *Drug Alcohol Depend*. 2015;151:194–20.
129. Cone EJ, Bigelow GE, Herrmann ES, et al. Non-smoker exposure to secondhand cannabis smoke. I. Urine screening and confirmation results. *J Anal Toxicol*. 2014;39(1):1–12.

130. elSohly HN, elSohly MA, Stanford DF. Poppy seed ingestion and opiates urinalysis: a closer look. *J Anal Toxicol* 1990; 14: 308–10.
131. Jackson GF, Saady JJ, Poklis A. Urinary excretion of benzoylecgonine following ingestion of health Inca tea. *Forensic Sci Int* 1991; 49(1): 57–64.
132. Jenkins AJ, Llosa T, Montoya I et al. Identification and quantitation of alkaloids in coca tea. *Forensic Sci Int* 1996; 77: 179–86.
133. Kicman AT, Cowan DA, Myhre L et al. Effect on sports drug tests of ingesting meat from steroid (methenolone)-treated livestock. *Clin Chem* 1994; 40(11 Pt 1): 2084–7.
134. Yonamine M, Garcia PR, Moreau RLM. Non-intentional doping in sports. *Sports Med* 2004; 34(11): 697–704.
135. Geyer H, Parr MK, Mareck U et al. Analysis of non-hormonal nutritional supplements for anabolic-androgenic steroids—results of an international study. *Int J Sports Med* 2004; 25: 124–9.

Chapter 35

Genetics in exercise and sport

with WILLIAM GIBSON and DANIEL GAMU

Though the ACTN3 gene does appear to influence sprinting ability, making a sports decision based on it is like deciding what a puzzle depicts when you've only seen one of the pieces. You need that piece to complete the puzzle, but you certainly can't see a meaningful picture without more pieces.

David Epstein, *The Sports Gene* (2013)

Dedicated training has long been known to improve athletic performance. But why do some individuals consistently outperform others who have undertaken comparable training regimens? The degree to which an individual's genetic makeup can predict their future performance, and even their ability to respond to athletic training, has excited much debate. Although often framed as a nature versus nurture debate, the *interaction* between an athlete's genetic make-up (i.e. nature) and their environment (i.e. nurture–training, nutrition etc.) may also have a significant effect on their athletic performance, susceptibility to sports-related injury and speed of recovery.

While studies measuring genetic variation between athletes may appear to find specific genetic predictors of athletic performance,[1] these associations may not always hold up when more stringent genome-wide significance levels are demanded.[2] A detailed understanding of the 'genetic architecture' of sport performance and recovery requires identification of the full spectrum of genetic contributors (including not only common polymorphisms, but also rare DNA variants) that influence athletic parameters such as strength, endurance, recovery time and coordination.

In the study of rare diseases, pinpointing the causal relationship between DNA variants and disease phenotypes is assisted by the fact that an individual patient's rare disease often has a single genetic determinant–such that comparisons between affected persons can find different rare variants in the same gene. This strategy for monogenic disease traits cannot be used with non-

disease phenotypes like athletic performance, because these human phenotypes are polygenic. In other words, each athlete's phenotype is influenced by multiple DNA variants, both rare and common. In this chapter we will explore:

- important concepts and terminology needed to interpret genetic studies on sport performance and related injuries
- methods of testing the association between genetic variation and health outcomes
- implications of genomics for exercise and sport.

INTRODUCTORY GENETICS: IMPORTANT CONCEPTS AND TERMINOLOGY

Genome

An individual's genome is made up of strings of the chemical nucleotide bases adenine (A), thymine (T), cytosine (C) and guanine (G). Two complementary strands of these bases wind around each other in a double helix, which is then wrapped like a spool of thread around proteins called 'histones'. The packaging of DNA with these proteins and other molecules, like RNA, is called 'chromatin'. Within the cell's nucleus, chromatin is further packaged into units called 'chromosomes' (Fig. 35.1), of which humans have 23 pairs (22 pairs of autosomes and 1 pair of sex chromosomes). In addition to the DNA found in the nuclear compartment, the energy-processing mitochondria (mt) have their own small genome (mtDNA).

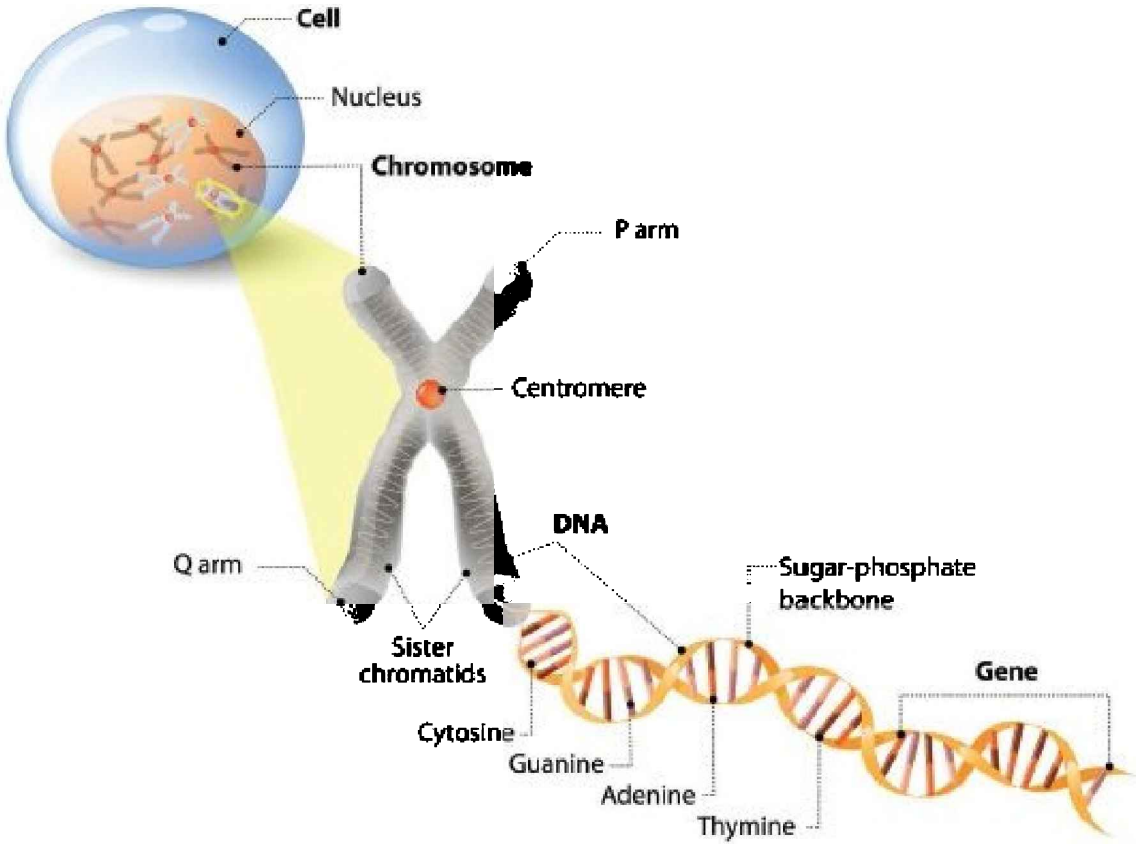


Figure 35.1 The many levels of DNA packaging, from double-stranded DNA helix to chromosome

DESIGNUA/SHUTTERSTOCK

Genes

Genes are discrete stretches of DNA that produce some functional product, such as a tRNA, a non-coding microRNA, a messenger RNA and its encoded protein, or some other biologically active molecule. Most human genes have different versions that coexist naturally in different human populations, which are termed 'alleles'. An allele is a variant of a gene, in which more than one sequence is possible for that specific gene.

Page 518

Because chromosomes come in pairs that are inherited from each parent, an individual can simultaneously have more than one version, or allele, of the same gene. If an individual has identical copies of the same allele, that person is homozygous for a specific gene, whereas individuals who possess different copies on each of their two chromosomes, are said to be heterozygous. A person's genome is the composite of all of the nuclear and mitochondrial genes, including the intervening DNA within and between those genes, as well as the middle parts (centromeres) and end parts (telomeres) of the chromosomes.

Genotype versus phenotype

Much like the study of rare and common diseases, an objective of exercise genomics is to identify relationships between specific genes (and DNA variants therein) and one or more measurable performance attributes. However, careful consideration should be given to measuring and defining genetic and physical characteristics.

The term 'genotype' refers to an individual's genetic characteristics, whereas 'phenotype' refers to their physical characteristics. Both genotype and phenotype can be defined at varying degrees of resolution. For example, genotype can be defined broadly as someone's continental ancestry (e.g. West African descent), or very specifically (e.g. R577R/R577X heterozygote for a common DNA variant in the *ACTN3* gene).

Similarly, phenotype can be defined relatively generally (e.g. the ectomorph/mesomorph/endomorph somatotypes of days past),[3] or very specifically (e.g. ultrarapid metaboliser of codeine).[4] The degree to which a genotype-phenotype association exists, and even the ability to find one, depends heavily on the methodology used to measure it. For example, although body mass index (BMI) is commonly used to define body fatness, dual-energy X-ray absorptiometry or computed tomography imaging provide a more detailed analysis of body composition, even allowing regional fat deposition to be calculated. Pairing high-resolution phenotyping techniques with high-resolution genotyping will improve our ability to find robust and useful associations between physical traits and genetic variants.

Single nucleotide polymorphisms

As with phenotyping, the degree to which an individual's genetic makeup is described can vary greatly in its level of detail. Although disputed in accuracy and significance by genomics experts for years, humans are widely quoted as being 99.9% identical to one another. This variability in the genetic code can include single base pair substitutions (i.e. single nucleotide polymorphism, SNP, or rare variants), small insertions and deletions called 'indels', large insertions and deletions called 'copy number variants', or any other complex rearrangements of DNA, such as translocations or inversions. Once non-SNP variation is taken into account, the estimate of genetic identity between two randomly selected people of the same sex drops to approximately 99.5% at the nucleotide level.[5] If we assume this to be true, in a 6.9–7 billion base-pair diploid genome, the difference between any two randomly selected humans of the same sex is likely to be upwards of 35 million base pairs.

To categorically define SNPs, rare variants or other changes in the genome of an individual or group, there needs to be a reference point from which deviations can be observed. At any specific site in the genome, the most commonly observed sequence of bases (e.g. ATGCCG) is considered to be the major allele. Any change in nucleotide sequence from the reference sequence is then considered to be a DNA variant, or minor allele. For the example reference sequence above, ATACCG would be considered a variant because it contains an 'A' in the third position from the left instead of the commonly found 'G'.

Rare variants or polymorphisms are defined by their frequency in a population. If 55% of people

had 'ATGCCG' and the remaining 45% had 'ATACCG', the 'G' variant would be the major allele and the 'A' variant would be the minor allele. The part of the genome where these alleles were found would then be annotated to have a G/A single nucleotide polymorphism, or SNP (pronounced 'snip'). If 99.55% of the population possessed ATGCCG and only 0.05% had ATACCG, then the 'A' variant would be considered rare, and possibly even termed a 'mutation'-but only if it resulted in a disease outcome.

Debate exists as to whether the term mutation should only describe rare DNA variants having major negative effects on physical characteristics (i.e. pathogenic mutations), or possibly also be employed to describe a new variant that has occurred for the first time in a specific generation but not the preceding one (i.e. *de novo* mutation). When a DNA variant is 100% associated with pathology, as is the case in rare diseases, one can call the variant a mutation. However, in some literature the word mutation is still used to describe a rare variant that occurs in less than 1% of the population (regardless of whether it does anything to the phenotype).

PRACTICE PEARL

Even if someone possesses a rare variant that enhances athleticism, that variant alone may not guarantee the presence of a highly athletic phenotype.

Mendelian traits

Because DNA is passed from parent to child, phenotypes can be passed down to successive generations. A Mendelian trait or phenotype is one that obeys Gregor Mendel's laws of inheritance (e.g. dominant, recessive, X-linked) (Fig. 35.2). Mendelian traits are transmitted with a relatively high frequency to immediate family members, in the order of 25–50%.

Autosomal Recessive

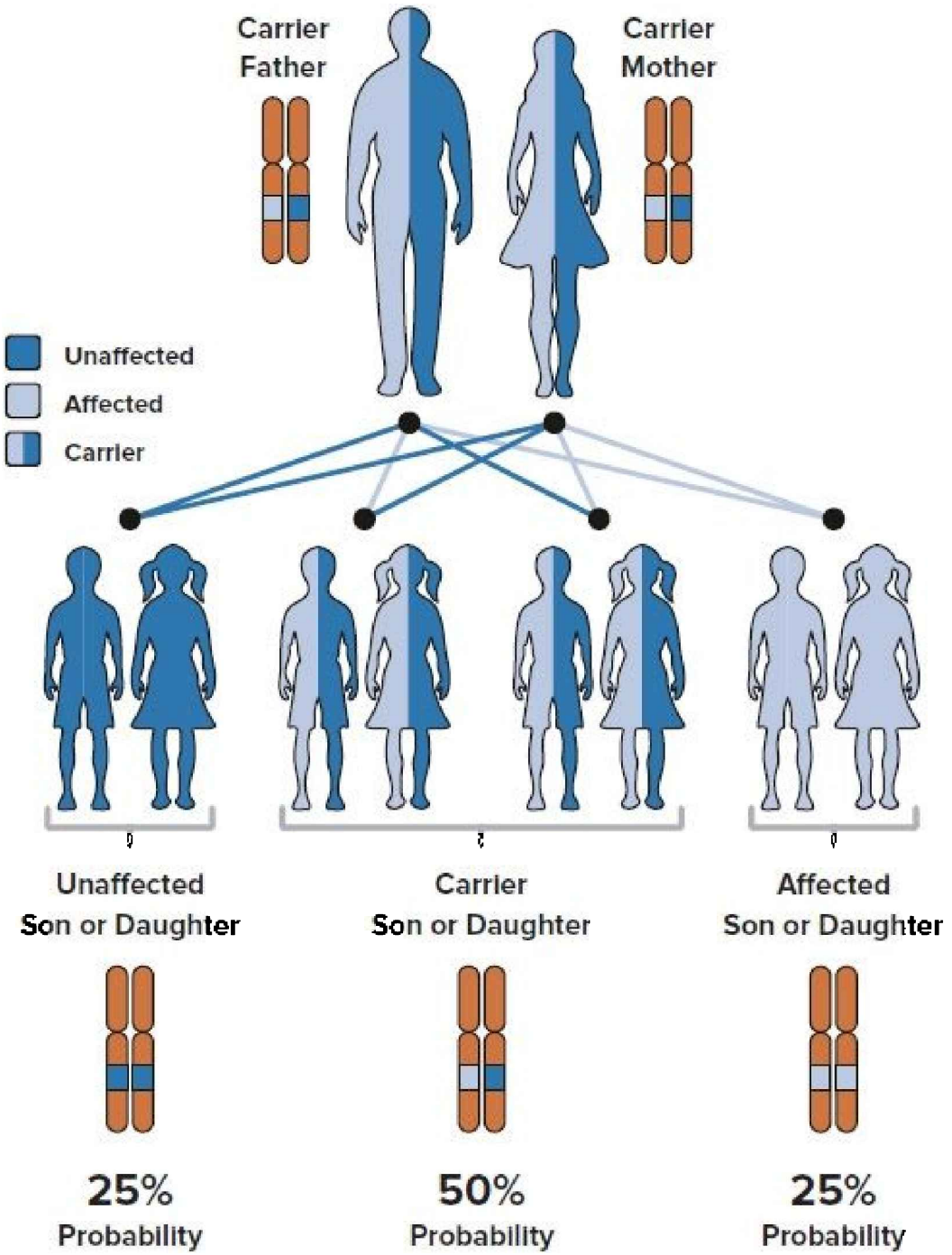


Figure 35.2 Pedigrees illustrating patterns of Mendelian inheritance

SHUTTERSTOCK/UDAIX

Dominant traits are passed directly from parent to child, and the causative disease allele need only to be present in one parent (i.e. a single 'healthy' allele on the other chromosome cannot compensate for the presence of the disease allele). All siblings and offspring of an individual with a dominant trait have a 50% chance of inheriting that exact allele, and therefore manifesting the same phenotype.

Recessive traits, on the other hand, are those inherited from two parents who themselves are unaffected (i.e. carriers of the recessive allele). A special case exists for sex-linked or X-linked recessive traits, in which 50% of a carrier's male offspring may be affected. A carrier will also have a 25% risk of transmitting the allele to each offspring (when males and females are considered together).

For traits that display a Mendelian pattern of inheritance, there is a high degree of correlation between the physical characteristic and the susceptibility allele. Although many genetic diseases obey Mendelian inheritance, it is important to note that most complex physical traits, like those associated with athletic performance, will not.

Complex traits

Complex traits like athletic performance have polygenic and multifactorial contributions. Unlike rare genetic diseases that typically have a single-gene cause, complex traits are influenced by both genetic and environmental factors (e.g. diet, intrauterine environment, physical activity).

Examples of complex traits often encountered in sports science include body mass, maximal aerobic capacity (VO_2max), cardiac output, stride length, grip strength and visuospatial coordination. Using the example of VO_2max, it is easy to see how a multitude of factors, both genetic and environmental, contribute to its outcome. Whereas VO_2max can be improved through dedicated endurance training, it is also determined by cardio-respiratory and musculoskeletal factors, each of which themselves may have a host of genetic determinants.

PRACTICE PEARL

Most individuals are likely to have a combination of multiple genetic and environmental factors that contribute to their athletic capabilities.

Genetic mapping

The process of assigning physical traits to specific genes or locations on chromosomes is referred to as 'genetic mapping'. It is important to distinguish here the difference between a gene (described above) and a DNA marker. DNA markers, also referred to as genetic markers or sequence tags, are used as convenient reference points to describe the location of genes relative to each other. They establish a point of reference, much like a physical landmark would on a map. DNA

markers do not need to produce a biological product; they are simply known locations within the genome. SNPs are commonly used as DNA markers in genetic mapping, because millions of them have been identified at millions of different sites.

A locus is a location within the genome that is associated with a physical trait. It may contain a gene, DNA marker, or even a non-coding DNA sequence. A locus can be thought of as a genetic 'neighbourhood' known to contain the gene(s) responsible for a specific trait, even if their precise location is not yet known. Once there is enough data to associate a trait with a specific region in the genome, that locus is then defined by the physical traits by which it governs (e.g. one of the many loci for human height).[6]

IDENTIFYING RISK USING CANDIDATE GENE AND GENOME–WIDE APPROACHES

Just as in the study of rare diseases, sports geneticists are interested in linking genetic variation with physical variation. In epidemiology, an association study is a tool to measure the degree to which one factor can explain the risk of developing a particular disease. Such a risk factor could be environmental (e.g. sugar consumption) or genetic (e.g. a specific SNP), and the outcome under study could be the risk of developing a disease (e.g. diabetes) or the 'risk' of an improved health outcome (e.g. high-performance athleticism).

Glossary of key terminology

Allele: The DNA sequence at a defined region of the genome, either rare or common.
Candidate gene association study (CGAS): A type of hypothesis-driven case-control study whereby the frequency of variants in a pre-selected gene or genes are examined to determine the frequency of their appearance in the cases (e.g. athletes) compared to the controls (e.g. sedentary people). Although inexpensive and relatively easy to do, CGASs fell out of favour in the early 2000s because of their high false-discovery rate.
***De novo mutation*:** A new mutation appearing for the first time within a lineage. While this mutation may be present in an individual's genome, his or her biological parents will not have it. De *novo* mutations themselves are heritable and can be passed down to successive generations from the individual carrying it. Not all de *novo* mutations will affect the phenotype.
DNA marker: A sequence of DNA with a known location used as a reference point to describe the location of other genes or variants. **Genome:** The total of all DNA within an organism. In humans this constitutes the sum of bases pairs on each of the 23 pairs of chromosomes. Compared to females, males have a smaller genome because of their smaller Y chromosome.
Genome-wide association study (GWAS): The main method of determining associations between common human genotypes and phenotypes. GWASs use microarray technology to genotype millions of preselected single nucleotide polymorphisms across the genomes of up to hundreds of thousands of unrelated individuals on whom relevant phenotypic traits have been measured.
Genotype: The specific allele(s) of an individual. **Indel:** A genetic variant resulting from the removal or addition of base pairs at a defined location within the genome (e.g. CAAAAG vs CAG). Indels may be common or rare at a specific site.
Locus: A defined genetic address within the genome wherein a gene may be known or hypothesised to reside (plural = loci).
Mitochondrial genome (mtDNA): This energy producing organelle contains its own mini genome

comprised of 16 569 base pairs and 13 protein-coding genes. Most of the proteins found in cellular mitochondria are actually transcribed from nuclear genes, and subsequently imported into the mitochondria.
Pathogenic mutation: A DNA variant that results in a disease. Dominant pathogenic mutations need only be present on one chromosome to result in a phenotype, whereas recessive ones must be present on both chromosomes to produce a phenotype.
Phenotype: The measured physical manifestation of an individual's allele(s). It can include the presence of a disease, or a quantifiable non-disease trait like running speed or strength.
Polymorphism: A DNA variant that is typically present in more than 1 % of individuals, and described as common.
Rare DNA variant: A DNA variant that is typically present in fewer that 1 % of individuals, and described as uncommon.
Single nucleotide polymorphism (SNP): A singular switch in the genetic alphabet at a specific location within an individual's genome (e.g. A vs G). SNPs are common in a population.

There are two main methods of testing the association between genetic variation and health outcomes: the candidate gene approach and the genome-wide approach. Both approaches have been used to test-correlate genotypes and phenotypes. These correlations may be strong, weak or absent.

Rare genetic diseases typically result in very strong genotype-phenotype correlations, because the affected gene product is usually critical for normal biological function. For example, individuals with mutations in various components of the muscular contractile protein myosin have gross abnormalities in their hearts and skeletal muscles.[7, 8] A rare variant in the gene for myostatin, a potent inhibitor of muscle development and size,[9] is associated with high muscle mass from a young age.[10] This skeletal muscle phenotype might be considered advantageous for power-related sports like weightlifting, and some preliminary evidence suggests that certain SNPs in and near the myostatin gene may be associated with an improved response to resistance training, at Page 522 least among African Americans.[11] However, detailed phenotyping of myostatin-deficient mice identified functional declines in grip strength and endurance that were worse in the mutant mice compared with non-mutant controls, suggesting complex downstream consequences of myostatin deficiency.[12]

Candidate gene approach

In a candidate gene association study (CGAS), a gene or genes are preselected for study, and the frequency by which common or rare variants in these genes co-occur with a trait are examined. These genes are preselected based on the *a priori* hypothesis that they are relevant to the phenotype under study. CGASs are often used as a first step in assessing a possible genotype-phenotype association, because fewer SNPs need to be genotyped, making them less expensive and relatively easy to do.

Unfortunately, CGAS designs are highly vulnerable to false-positive results, such that most CGAS results are not replicated when larger validation studies are attempted.[13] There are a number of reasons for the high false-discovery rate of CGASs, which are reviewed elsewhere.[14] It is difficult to

control for and remove all sources of bias in a CGAS. Population genetic substructure, or the differences in ancestral composition that exist among various populations, is one such confounding factor in genetic association studies that may lead to spurious genotype-phenotype relationships.[15]

Because genotype-phenotype correlations are likely to be rather weak for non-disease traits, such correlations will be more difficult to detect if one or only a few genes are interrogated in a study. For example, polymorphisms in the *MC1R* gene are often seen in individuals who have red hair and green eyes, but variation at this locus does not assure that someone will always develop these traits, because *MC1R* is not the sole determinant of hair and eye colour.[16] Given the multitude of biological and environmental factors involved in athletic performance traits, it is not surprising that associations between DNA variants and athletic outcomes are not easily proven and replicated.

The aforementioned *ACTN* R577X polymorphism causes the loss of the protein a-actinin-3, a protein typically found in fast-twitch skeletal muscle fibres. To study a possible association between variation in the *ACTN3* genotype and performance, a CGAS would use elite-level athletes (the cases) and the general public (the controls). Using this design, a higher frequency of the R577X genotype has been found in elite-level sprinters, suggesting this variant is beneficial for generating forceful muscle contractions during high-velocity activity.[17]

The above example demonstrates correlation between the R577X genotype and performance, but not true causation. Although a genotype-phenotype association may be found using elite athletes (the cases) and the general public (the controls), this should not be taken as direct mechanistic evidence of that variant causing enhanced performance. Elite-level athletes have a multitude of physiological adaptations resulting from their intensive training programs that aid in performance. Cellular and organismal modelling of individual SNPs is required to truly validate any causal links. Although detailed animal phenotyping studies have been done to validate causation between *ACTN3* deficiency and enhanced athletic performance,[18] this will not be the case for every variant flagged by human genetic studies.

Genome-wide approach

A genome-wide association study (GWAS) examines DNA markers across all chromosomes, which may involve genotyping thousands to millions of SNPs, in addition to measuring some physical trait (e.g. VO_2max). Due to the large number of people who require genotyping, and the costs of measuring the trait of interest at high resolution, GWASs are much more expensive than CGASs.

Because CGASs make prior assumptions that a gene or variant is involved in disease susceptibility, or 'susceptibility' to high-performance athleticism, CGASs are said to be hypothesis-driven. GWASs, on the other hand, are often described as being 'hypothesis-free'. However, this is a misnomer because they do test a hypothesis: whether there is genomic variation that is both functional and common enough to flag a population-attributable risk. In other words, a GWAS tests the hypothesis that an association exists somewhere within the genome.[19]

Although GWASs have succeeded in predicting biological traits that have a high genetic contribution,[6, 20] the strength of the effect of each genetic variant on these traits is low, and the proportion of the trait that is explainable by adding up all of the genetic factors is typically small.

In a study of the association between more than 300 000 SNPs and training-induced improvements in VO_2max, not one SNP reached a genome-wide level of statistical significance.[21] This is partly due to the fact that the threshold for an association to be considered statistically significant in a GWAS is very conservative (with p-values in the order of 5×10^{-8}, as opposed to the more 'traditional' p-value of 0.05). Due to the sheer number of SNPs genotyped, the number of comparisons is several orders of magnitude greater than the number performed in most epidemiological studies.[22, 23] Claims of such associations should be weighed very carefully and replicated in large independent populations before they are considered valid.[24]

Predicting elite athleticism and disease

Very few SNPs have been identified that result in a high probability of predicting elite athleticism independent of other genetic or environmental factors. Figure 35.3 illustrates the postulated relationship between genetic variation at multiple loci and high-performance athleticism or disease.

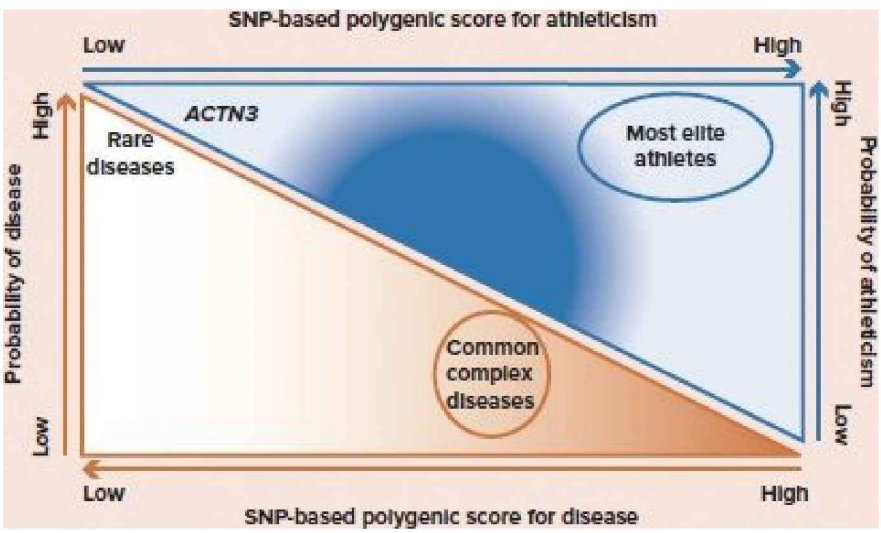


Figure 35.3 Relationship between genetic variation at multiple loci (SNP-based polygenic score) and high-performance athleticism (grey/blue) or disease (orange).

A greater colour density refers to a relatively higher proportion of individuals in a population. A low polygenic score represents variation in only one (monogenic) or a few alleles, whereas a high score refers to additive effects of variation in multiple alleles, each of which individually has a small quantitative effect

It is debatable where the ACTN3 R577R/R577X variant should appear in the figure, as most elite athletes are likely to have a combination of multiple genetic (i.e. have a high polygenic score) and environmental factors that contribute to their athletic capabilities.

The top left corner of the orange triangle in the figure describes the small proportion of the population who have a rare monogenic disease, while the bottom left corner of the orange triangle describes the small proportion of the population who have low probability of disease because they have no rare disease alleles and few common disease alleles.

The bottom right corner of the orange triangle describes the large proportion of the population who have significant genetic risk scores for common complex diseases and a high lifetime probability of disease.

The top right corner of the blue triangle describes the small proportion of the population who have high innate athletic ability attributable to multiple common alleles that additively improve phenotypic factors that enhance athleticism (e.g. VO_2max) and who also pursue dedicated training.

The bottom corner of the blue triangle describes the small proportion of the population who have high innate athletic ability but a low probability of athleticism because they train poorly or not at all, and the top left corner of the blue triangle describes the small proportion of the population who may have high innate athletic ability attributable to a single monogenic cause.

It is expected that most people's athletic phenotype will be in the 'middle' of the blue triangle, such that they have several genetic variants that enhance their athletic ability, but that their observed performance will depend strongly on non-genetic factors such as training regimen.

IMPLICATIONS OF GENOMICS IN SPORT: CAUTIONS AND CONSIDERATIONS

While exercise genomics continues to hold promise, studies of genetic variation and sport have not yet generated enough quality evidence to provide actionable information to athletes.[2S] A number of recommendations have been made to lead the field in a paradigm shift, with the hopes of generating studies that are highly powered and replicable.

For reasons described above, the use of the CGAS for discovering genotype-phenotype relationships is advised against in favour of the GWAS.[25 26] Despite their benefits, GWASs are often underpowered for the study of performance traits, in part because of the specialised athletic population they examine. Sample sizes for successful GWASs can be in the order of hundreds of thousands of participants[6, 20] this is a near insurmountable number for any single research group to achieve.

Services that provide genetic testing

Conceptually, the use of genomic data could aid coaches, athletes and clinicians in developing personalised training and rehabilitation programs, identify individuals likely to respond optimally (or suboptimally) to specific training regimens, or even flag those at risk of having a severely negative reaction to exercise (e.g. sudden cardiac death).

In the age of personalised medicine, a number of direct-to-consumer genetic testing products are marketed as providing actionable health and wellness information based on an individual's genotype. These claims are not supported by the current state of exercise genomics literature,[27] and so are fraught with a number of ethical issues.[28] A consensus statement has been released by leaders in the field, explicitly advising against the use of such testing,

particularly in youth athletics, as it holds no utility in talent identification or in maximising training results.[28]

PRACTICE PEARL

Clinicians should advise against the use of direct-to-consumer genetic testing for talent identification, and for decision making regarding sport training regimens, unless more robust evidence becomes available.

Gene doping in sports

Drug doping with performance-enhancing pharmaceuticals remains a persistent threat to clean competition, especially because novel, difficult-to-detect agents continue to be developed. But have we reached a point where doping with performance-enhancing genes is likely to occur? Although gene therapy has enabled treatment of several rare genetic diseases by correcting their primary genetic defect,[29] gene doping in sport is likely to be decades away. In a gene therapy trial, the healthy genetic material is first inserted into a cellular vehicle (such as stem cells, or a viral or non-viral vector).[29] Once inside the vehicle, the healthy DNA is then injected into the patient locally or systemically, after which it can be translated into a protein to exert the desired biological effect. In theory, gene doping might allow athletes to increase endogenous production of proteins that enhance strength, endurance or muscular repair. If stable levels of expression could be achieved, there would no longer be a need to administer exogenous agents to maintain the (now-enhanced) performance.[30] This type of gene doping has been suggested as a way for athletes to gain a competitive edge.

Despite the fact that a number of candidate proteins have been suggested to have the potential for abuse by athletes,[30, 31] gene doping is banned[32] and has yet to be documented as having occurred. Methods for detecting erythropoietin (EPO) gene doping are being developed.[33] Although functional erythrocytosis mutations in the *EPO* gene can be as small as a single nucleotide,[34] editing of endogenous sequences might be more difficult to detect than a fully-integrated cDNA vector would be.

Given the large number of genes that contribute to sport performance, the possibility that exogenous delivery of one or a small number of genes might enhance sport performance at the elite level seems unlikely. However, exogenous delivery of one or a small number of genes might well boost healing at the site of an injury, once the pathways relevant to injury recovery are better understood. As better means of human gene therapy and gene editing are developed, these technologies may become better suited to enhancing recovery from sports-related injuries, which may be a more broadly applicable use of these techniques.

CASE STUDY

Eero Mäntyranta, Finland—the ‘gold medal mutation’

Eero Mäntyranta (1937–2013) (Fig. 35.4) was a record-breaking Finnish gold medal cross-country skier, who competed in four Winter Olympics between 1960 and 1972, winning seven medals overall. In the 1964 Winter Olympics 15 km cross-country skiing race, Mäntyranta finished 40 seconds ahead of the next competitor—a margin of victory never before or since equalled in that event at the Olympics–while the next five finishers were within 20 seconds of one another. In the 30 km race, he won by over a minute.

Figure 35.4 Finnish athlete Eero Mäntyranta had a rare variant in his erythropoietin receptor (EPOR) gene, which David Epstein describes as a ‘gold medal mutation’, in his book *The Sports Gene*

PHOTO COURTESY DAVID EPSTEIN

Although Mäntyranta’s training regime was not radically different to his competitors, he did possess a distinct genetic advantage. Mäntyranta had a rare variant in his erythropoietin receptor (EPOR) gene, which David Epstein describes as a ‘gold medal mutation’, in his book *The Sports Gene*. EPOR functions to bind EPO, an endogenous hormone secreted by the kidneys that stimulates the production of red blood cells—a process known as erythropoiesis. With a rare variant in his EPOR gene that made it seem like EPO was always bound to its receptors (EPOR), Mäntyranta was able to naturally produce abnormally high numbers of red blood cells. When tested throughout his career, his haematocrit was as high as 60–65% (normal being 45–52% in males, in volume percentage of red blood cells in blood) and his haemoglobin was above 200 g/L (normal 138–172 g/L).

The Mäntyranta EPOR gene finding was a major discovery in the early 1990s. Primary familial and congenital polycythaemia was found to be passed down through the Mäntyranta family in an autosomal dominant fashion, meaning that only a single copy of the mutant gene was required for a family member to have the condition.

Page 525

Mäntyranta’s gold medal mutation is exceedingly rare; however, anyone can boost his or her red blood cells simply by taking exogenous EPO, referred to as ‘blood doping’—a practice which has been banned since the early 1990s. Endurance athletes have since looked to other ways to naturally increase erythropoiesis without exogenous substances, such as training at high altitude (Chapter 25).

REFERENCES

1. Ahmetov II, Fedotovskaya ON. Current progress in sports genomics. *Adv Clin Chem* 2015; 70: 247–314. doi: 10.1016/bs.acc.2015.03.003.
2. Rankinen T, Fuku N, Wolfarth B et al. No evidence of a common DNA variant profile specific to world class endurance athletes. *PLoS* ONE 2016; 11(1): e0147330. doi: 10.1371/journal.pone.0147330.
3. Sheldon WH. *The Varieties of Human Physique: An Introduction to Constitutional Psychology*. New York: Harper, 1940.
4. Madadi P, Ross CJ, Hayden MR et al. Pharmacogenetics of neonatal opioid toxicity following maternal use of codeine during breastfeeding: a case-control study. *Clin Pharmacol Ther* 2009; 85(1): 31–5. doi: 10.1038/clpt.2008.157.
5. Levy S, Sutton G, Ng PC et al. The diploid genome sequence of an individual human. *PLoS Biol* 2007; 5(10): e254. doi: 10.1371/journal.pbio.0050254.
6. Wood AR, Esko T, Yang J et al. Defining the role of common variation in the genomic and biological architecture of adult human height. *Nat Genet* 2014; 46(11): 1173–86. doi: 10.1038/ng.3097.
7. Fananapazir L, Dalakas MC, Cyran F et al. Missense mutations in the beta-myosin heavy-chain gene cause central core disease in hypertrophic cardiomyopathy. *Proc Natl Acad Sci U S A* 1993; 90(9): 3993–7.
8. Poetter K, Jiang H, Hassanzadeh S et al. Mutations in either the essential or regulatory light chains of myosin are associated with a rare myopathy in human heart and skeletal muscle. *Nat Genet* 1996; 13(1): 63–9. doi: 10.1038/ng0596-63.
9. McPherron AC, Lawler AM, Lee SJ. Regulation of skeletal muscle mass in mice by a new TGF-beta superfamily member. *Nature* 1997; 387(6628): 83–90. doi: 10.1038/387083a0.
10. Schuelke M, Wagner KR, Stolz LE et al. Myostatin mutation associated with gross muscle hypertrophy in a child. *N Engl J Med* 2004; 350(26): 2682–8. doi: 10.1056/NEJMoa040933.
11. Kostek MA, Angelopoulos TJ, Clarkson PM et al. Myostatin and follistatin polymorphisms interact with muscle phenotypes and ethnicity. *Med Sci Sports Exerc* 2009; 41(5): 1063–71. doi: 10.1249/MSS.0b013e3181930337.
12. Guo W, Miller AD, Pencina K et al. Joint dysfunction and functional decline in middle age myostatin null mice. *Bone* 2016; 83: 141–8. doi: 10.1016/j.bone.2015.11.003.
13. Ioannidis JP, Tarone R, McLaughlin JK. The false-positive to false-negative ratio in epidemiologic studies. *Epidemiology* 2011; 22(4): 450–6. doi: 10.1097/EDE.0b013e31821

b506e.

14. Attia J, Ioannidis JP, Thakkinstian A et al. How to use an article about genetic association: B: are the results of the study valid? *JAMA* 2009; 301(2): 191–7. doi: 10.1001/jama.2008.946.
15. Marchini J, Cardon LR, Phillips MS et al. The effects of human population structure on large genetic association studies. *Nat Genet* 2004; 36(5): 512–17. doi: 10.1038/ng1337.
16. Sulem P, Gudbjartsson DF, Stacey SN et al. Genetic determinants of hair, eye and skin pigmentation in Europeans. *Nat Genet* 2007; 39(12): 1443–52. doi: 10.1038/ng.2007.13.
17. Yang N, MacArthur DG, Gulbin JP et al. ACTN3 genotype is associated with human elite athletic performance. *Am J Hum Genet* 2003; 73(3): 627–31. doi: 10.1086/377590.
18. Lee FX, Houweling PJ, North KN et al. How does alpha-actinin-3 deficiency alter muscle function? Mechanistic insights into ACTN3, the 'gene for speed'. *Biochim Biophys Acta* 2016; 1863(4): 686–93. doi: 10.1016/j.bbamcr.2016.01.013.
19. Hoggart CJ, Clark TG, De Iorio M et al. Genome-wide significance for dense SNP and resequencing data. *Genet Epidemiol* 2008; 32(2): 179–85. doi: 10.1002/gepi.20292.
20. Locke AE, Kahali B, Berndt SI et al. Genetic studies of body mass index yield new insights for obesity biology. *Nature* 2015; 518(7538): 197–206. doi: 10.1038/nature14177.
21. Bouchard C, Sarzynski MA, Rice TK et al. Genomic predictors of the maximal O_2 uptake response to standardized exercise training programs. *J Appl Physiol (1985)* 2011; 110(5): 1160–70. doi: 10.1152/japplphysiol.00973.2010.
22. Ioannidis JP. Non-replication and inconsistency in the genome-wide association setting. *Hum Hered* 2007; 64(4): 203–13. doi: 10.1159/000103512.
23. McCarthy MI, Abecasis GR, Cardon LR et al. Genome-wide association studies for complex traits: consensus, uncertainty and challenges. *Nat Rev Genet* 2008; 9(5): 356–69. doi: 10.1038/nrg2344.
24. NCI-NHGRI Working Group on Replication in Association Studies, Chanock SJ, Manolio T et al. Replicating genotype-phenotype associations. *Nature* 2007; 447(7145): 655–60. doi: 10.1038/447655a.
25. Bouchard C. Exercise genomics—a paradigm shift is needed: a commentary. *Br J Sports Med* 2015; 49(23): 1492–6. doi: 10.1136/bjsports-2015-095294.
26. Eynon N, Voisin S, Lucia A et al. Preface: genomics and biology of exercise is undergoing a paradigm shift. *BMC Genomics* 2017; 18(Suppl 8): 825. doi: 10.1186/s12864-017-4184-6.
27. Vlahovich N, Hughes DC, Griffiths LR et al. Genetic testing for exercise prescription and injury prevention: AIS-Athlome consortium-FIMS joint statement. *BMC Genomics* 2017; 18(Suppl 8): 818. doi: 10.1186/s12864-017-4185-5.

28. Webborn N, Williams A, McNamee M et al. Direct-to-consumer genetic testing for predicting sports performance and talent identification: consensus statement. *Br J Sports Med* 2015; 49(23): 1486–91. doi: 10.1136/bjsports-2015-095343.
29. Naldini L. Gene therapy returns to centre stage. *Nature* 2015; 526(7573): 351–60. doi: 10.1038/nature15818.
30. Fischetto G, Bermon S. From gene engineering to gene modulation and manipulation: can we prevent or detect gene doping in sports? *Sports Med* 2013; 43(10): 965–77. doi: 10.1007/s40279-013-0075-4.
31. van der Gronde T, de Hon O, Haisma HJ et al. Gene doping: an overview and current implications for athletes. *Br J Sports Med* 2013; 47(11): 670–8. doi: 10.1136/bjsports-2012-091288.
32. World Anti-Doping Agency (WADA). Gene doping. https://www.wada-ama.org/en/gene-doping, accessed 31 March 2018.
33. Neuberger EW, Jurkiewicz M, Moser DA et al. Detection of EPO gene doping in blood. *Drug Test Anal* 2012; 4(11): 859–69. doi: 10.1002/dta.1347.
34. Zmajkovic J, Lundberg P, Nienhold R et al. A gain-of-function mutation in EPO in familial erythrocytosis. *N Engl J Med* 2018; 378(10): 924–30. doi: 10.1056/NEJMoa1709064.

Chapter 36

Medico-legal issues

by HAYDEN OPIE

[Michael Owen, knocked unconscious in a World Cup warm-up game, pleaded not to be taken off.] Owen later admitted, "I might have told them I was OK, but I didn't feel OK."... The last person to heed in the heat of a contest is the performer. Adrenaline overrules common sense.

Rob Hughes, Chief Sports Correspondent, *The Times*

Legal and regulatory issues specific to the practice of sports medicine are not especially new. They have been considered by commentators for the past 30 to 40 years at least.[1–4] Examination of liability for physical harm to athletes caused by deficient medical care, in particular the management of injuries, occurred increasingly within the context of general works on sports medicine.[5, 6]

Where the attending clinician was engaged by a club or other sports organisation to treat athletes, the potential for a misplaced sense of obligation was recognised early on, as well as the question of whether the club or other organisation should incur liability in addition to the clinician.[7, 8] Later, the expansion of anti-doping regimes and of human rights law brought substantial changes to the legal and regulatory environment in which sports medicine is practised.[9–11]

This chapter introduces readers to today's complex sports medico-legal environment and provides explanations of key concepts and issues. It is important that clinicians maintain a relevant understanding of the field and are active in shaping the laws and regulations specific to sports medicine, with the aims of making that environment sensitive to the needs of clinicians and of achieving higher standards of care and more rewarding careers.

Every clinician pursues his or her career within a legal and regulatory framework. Qualifying for practice; the ongoing obligation to be licensed; controls over the prescription, dispensing and administration of pharmaceuticals; and the necessity to comply with professional and ethical

standards or risk disciplinary measures; are some of the legal and regulatory controls encountered by all clinicians.

Conducting business will also involve legal issues pertaining to partnerships, employees, insurance, owning or leasing consulting rooms and taxation. Much of what is required of clinicians in those respects may be routine or, in the case of business matters, delegated to practice managers. This chapter does not explore that legal and regulatory framework, although reference is made to it occasionally.

This chapter focuses on the legal and regulatory issues that are specific to sports medicine. These include:

- the standard of health care expected of sports clinicians
- the difficulties arising from the tripartite relationship of athlete, clinician and sports organisation
- the relationship between medical research, game rule change and legal liability, with special reference to neck injuries and concussion
- drugs and anti-doping
- the emergence of human rights law, with attention to single-sex sports and the sex status of athletes, pregnant athletes and athletes with disabilities, including infectious diseases.

Wherever human activity occurs it produces similar problems requiring legal solutions. That applies to the practice of sports medicine particularly. However, there are numerous legal systems worldwide, built upon different cultural, historical, political and social foundations. While globalisation has a 'converging' effect on the law, especially for international activities like sport and sports medicine, differing legal approaches and solutions may apply depending on the legal jurisdiction in which a problem arises.

To produce a detailed statement of the law as it affects sports medicine for every legal system is not an achievable task for a single book chapter. Also, it is assumed that non-lawyer readers will prefer general rather than detailed discussion of the legal and regulatory issues and their implications. These considerations have guided the preparation of this chapter.

Aspects of sports medicine having legal dimensions are identified and considered in general and non-technical terms, with the aim of offering both a conceptual and practically useful guide for clinicians. This chapter is a point of first reference. When making general observations and statements in this chapter, it has not been possible to account for the range of local rules and variations that exist. In many cases where references are provided, they have been selected as typical or interesting examples of general approaches or rules found in legal systems and are not intended to form a comprehensive statement of applicable sources. The reader with a specific inquiry about the law in a place, or needing legal advice on some eventuality, should consult a legal professional practising locally.

THE PRACTICE OF SPORTS MEDICINE

As the two volumes of *Brukner & Khan's Clinical Sports Medicine* demonstrate, sports medicine has become an established field of medical knowledge and practice. It continues to develop. There is a wide range of complex issues involved in the healthcare of those who participate in sport. In some places sports medicine is a recognised medical specialty, with its own formalities for qualification and certification, whereas elsewhere it is pursued as part of a general medical practice that might incorporate the care of athletes in an individual or team environment.

This chapter is directed primarily to the 'sports clinician', which is a term intended to incorporate medical doctors, medical practitioners and physicians working in sport or with athletes, and to those who are in general training or the process of formal sports medicine qualification and certification. Also, in various ways, the chapter will be relevant to the work of others who are responsible for aspects of the health of sport participants, including soft tissue therapists, nutritionists, physiotherapists, physical therapists and trainers.

The well-established roles of the sports clinician in diagnosis, advice and treatment are of central importance. As well, the sports clinician can expect involvement with injury prevention and performance improvement in both practice and theory. The context will often shape the nature of care to be delivered. Presence at a sports event or travel with a team may require proficiency in first aid and cardiopulmonary resuscitation. Team environments have the potential to produce conflicting notions of responsibility. The different grades at which sport is played may be accompanied by varying levels of medical resourcing and expectations of the objectives of care. Elite and professional athletes may seek immediate or at least rapid return to competition whereas other athletes may be best treated conservatively.

The sports clinician's care of an athlete may be part of a wider effort. This is usually encountered in professional and elite team sport settings, where the sports clinician is expected to lead a team of health professionals, including physiotherapists/physical therapists, soft tissue therapists, nutritionists and trainers. In turn, these health professionals will work with team managers, coaches, sports scientists, and specialist strength and skills coaches. The relationships between them have legal and ethical dimensions that will be considered later.

Recent years have witnessed the emergence of full-or part-time non-clinical roles to which sports clinicians bring expert knowledge and skill. These roles often entail the development and implementation of various health-related policies that leagues and other sports governing bodies are expected to follow. The topics covered by these policies include anti-doping, climate, infectious diseases, injury reporting, concussion management, emergency care, game rule revision and pregnancy. Decision-making responsibilities may be given to sports clinicians in pre-contractual medical examinations of professional players, disputes over whether an athlete has sustained a career-ending injury, and the grant of therapeutic use exemptions for otherwise prohibited substances and methods under the World Anti-Doping Code. The news media offer roles for sports clinicians as regular or occasional print and electronic commentators to explain the nature of sports injuries, analyse injury lists and offer real-time assessment of the cause and implications of injuries for readers and viewers.

At the top end of sport, especially professional team sport, the sports clinician has become part

of the sporting entertainment; a celebrity in his or her own right. Sought after by clubs anxious to maintain low injury rates and quick recovery times, clinicians and other health professionals can build reputations (and financial rewards) on the back of the unexpectedly rapid recovery of star players.[12] The kudos of team clinician status for a famous club may be a potent marketing tool for a medical practice.[13] Appointments to senior medical roles are of themselves newsworthy events.[14] It will be seen that there are risks to this notoriety. There are occasions when certain sports clinicians and their evildoings are the compelling focus of international attention, with former US gymnastics team doctor Larry Nassar arguably the most infamous of all.[15]

LEGAL AND REGULATORY SYSTEMS

As mentioned above, there are numerous legal systems worldwide. One way of categorising these systems is to align them with the nation states that exercise legal authority over their respective territories and citizens. In turn, many nation states are further subdivided into regional units, which may have their own legal authority, with the nation's constitution allocating powers between the central and regional governments. Moreover, legal systems are often divided into two main types: civil law and common law.

Civil law systems adopt extensive legal codes made by legislatures (often called congresses or parliaments), which aim to set out the law in detail, whereas common law systems have, historically at least, relied on successive decisions of courts to develop legal principles, which future courts follow through a system of precedent. There has been a tendency for these two types of system to converge. Detailed laws made by legislatures (or their delegates) form a rapidly growing, if not predominant, part of the law in common law countries, whereas the rulings of courts on the interpretation of codes are becoming a larger part of civil law systems, where the courts endeavour to be consistent but without applying rules of precedent.

There are three other relevant, significant influences. First, international treaties or conventions agreed between nation states may establish important international legal standards or rules. For example, the Universal Declaration of Human Rights (including its progeny) and the International Convention Against Doping in Sport are the foundations for many legal and regulatory requirements that affect sports medicine. The role of human rights law is particularly evident in medical issues attaching to separate sports competitions for women and men, the status of intersex and transgender athletes, participation by pregnant women and athletes with congenital conditions, infectious diseases and other disabilities, and therapeutic use exemptions under the World Anti-Doping Code.

Second, the rules and regulations of international sports federations are believed by some commentators to form the basis of a global sports law (sometimes referred to as *lex sportiva)* that may have a degree of practical, if not theoretical, independence from national legal systems. *Lex sportiva* is interpreted and developed through the rulings of the Switzerland-based Court of Arbitration for Sport (CAS), which is an arbitral tribunal rather than a court.

Third, ethical standards mandated by sports medicine bodies may play a role in shaping legal outcomes in individual cases and can be identified as the precursors for significant legal

developments. Foremost among those standards is the Code of Ethics of the International Federation of Sports Medicine (FIMS).[16] However, the code offers these cautionary words on the relationship between law and the ethics of sports medicine:

> Ethics in sports medicine should also be distinguished from law as it relates to sport. One refers to morality, the other to a set of enforceable social rules [note omitted]. Although it is desirable that the law be grounded in moral principles and that matters of moral importance should be given legal backing in many instances, not everything that is illegal is immoral and similarly, not every immoral behaviour is against the law. Thus, when speaking of ethics in sports medicine, one is not concerned with etiquette or law, but with basic morality [clause 2].[16]

As these legal systems and influences interact and react, complexities and tensions may result. For instance, it is difficult to tread a path between the liberties and freedoms protected by human rights law and the inherently invasive nature of anti-doping rules. Furthermore, sports will usually need to maintain uniform international practices for their activities but they may be confronted by some potentially conflicting national legal systems grounded in different philosophies.

It is within this broad and complex legal and regulatory context that sports medicine is practised around the globe.

THE SPORTS CLINICIAN/ATHLETE RELATIONSHIP

Central to any consideration of the legal and regulatory aspects of sports medicine is the relationship between the attending sports clinician and an athlete. This is an example of the doctor/patient relationship, which is one of the oldest and most significant among the professions and it holds a special place in most legal systems. There is a large body of ethics and law that applies, but this section concentrates on, in general terms, the creation of the sports clinician/athlete relationship and the main implications that follow.

Creation

Whenever a sports clinician undertakes the care of an athlete the relationship exists. There is usually little formality associated with the relationship's creation, although the athlete may initially provide a medical history to assist the clinician. Also, very little, if anything, is said between the athlete and sports clinician about the terms of the relationship, other than the fees expected to be paid for the service. The occasion for providing care may exist because the athlete consults or is referred to the clinician's practice, a sports club requests the clinician to provide healthcare services to its players or the clinician may happen to be present when emergency assistance is needed.

The legal dimensions of the sports clinician/athlete relationship are influenced by the circumstances in which the care is undertaken. The clinician may be working as an independent contractor (in the sense of being in practice alone or in partnership) or as an employee of a club, school, clinic or other healthcare organisation. The care may be paid or voluntary,

planned or rendered in an emergency.

There are other circumstances where a sports clinician and an athlete may come into contact in a medical setting but a full doctor/patient relationship may not arise. These include pre-contractual medical assessments of potential team athletes and examinations for the purpose of insurance claims. These circumstances give rise to limited obligations on sports clinicians, which will be considered below.

Implications

Three main implications follow from the creation of the sports clinician/athlete relationship. They relate to the legal authority of the clinician to care for the athlete, the standard of medical skill expected and the obligations of confidence and trust.

Legal authority to provide care

Local laws

At the outset, the sports clinician must possess current authority to practise medicine in the place where the care is provided. This is determined by the general laws and regulations of the local health and professional authorities. Where advanced qualifications or special conditions are stipulated they must be satisfied. There may also be controls on the possession and prescription of pharmaceuticals. Criminal and disciplinary penalties usually apply to any breach of these laws and regulations. Compliance with these requirements should be routine for local clinicians.

However, the clinician who is not licensed to practise medicine locally must be wary of those requirements, particularly sports clinicians who are travelling with teams. If called upon to administer care in a serious medical emergency, there is unlikely to be concern because the necessity of the occasion excuses any technical breach of the local law. Of course, once local emergency care is in attendance the clinician should either hand over or assist under direction. Where a team member requires hospitalisation, prescription pharmaceuticals or pathology or radiology services, the travelling team clinician will have little practical alternative other than to call in local healthcare providers.

In other circumstances, the team sports clinician may be tempted to provide care to team and entourage members without holding the necessary local licences. Not only does this risk criminal prosecution locally and potentially invalidate the clinician's legal liability insurance coverage, it may constitute a disciplinary issue for the clinician in his or her place of registration and create an adverse impression in the event of any litigation alleging professional malpractice.

Clinicians should also acquaint themselves with, as well as comply with, local laws and procedures before carrying pharmaceuticals and items such as syringes onto aeroplanes and across legal borders. What may be lawful in one place is not necessarily so in another, with disruptive and serious consequences such as arrest and seizure of important equipment, like a clinician's medical bag.

If intending an extended stay in a place where the clinician is not licensed, it is wise to obtain

temporary registration. An increasingly common response to these difficulties is for the organisers of major sports events to negotiate exemptions from local licensing requirements for visiting health professionals, provided they confine their medical care to team members, as occurred in the arrangements for the 2018 Commonwealth Games on the Gold Coast in Queensland.

Consent

An important general principle is that medical treatment cannot be administered without the athlete's authorisation, often referred to as 'consent'. Touching or threatened touching without consent is unlawful and may constitute the criminal offence of assault, as well as a violation of the civil right to bodily integrity, which can lead to a claim for monetary compensation (damages).

Consent may be given expressly: either orally or in writing. To acquiesce in minor treatment, such as bandaging or application of antiseptic or ice, amounts to implied consent. Before surgery it is common practice to seek written consent. The athlete must be aware that he or she is giving consent and possess sufficient knowledge of the proposed procedure to make the consent valid.

The legal test for how much knowledge is required may vary between legal systems, but in many common law systems it is enough for the athlete to be informed of the basic nature of the treatment. An athlete who is told that he or she is receiving an injection of vitamins to address a deficiency is not consenting to an injection of anabolic steroids as part of a secret doping program. (The clinician's obligation to provide sufficient information for athletes to make informed choices is considered in the next section.) Thus, an allegation of assault or a claim of violation of bodily integrity will succeed only where there has been no consent at all (in the sense that the basic nature of the treatment has not been made known and agreed to) or the treatment has exceeded the consent given. Once given, consent may be withdrawn, whereupon treatment should not occur or cease if commenced.

The above legal principles are broadly reflected in the FIMS Code of Ethics:

> The sports medicine physician will inform the athlete about the treatment, the use of medication and the possible consequences in an understandable way and proceed to request his or her permission for the treatment [clause 4].[16]

Emergencies that are life threatening or constitute a serious risk to health pose some different issues. Often the athlete will indicate a desire for an attending clinician to proceed even though this may be given abruptly or hardly at all, if he or she is distressed by pain or otherwise disabled. An athlete may suspect a spinal injury and ask not to be moved. Such requests should be respected until specialist care arrives, although avoiding imminent threats from other sources such as fire may justify proceeding without express consent. Where an athlete is not able to give express consent due to, say, unconsciousness, applying first aid and more advanced treatment to save life or preserve health from serious risk is permissible.

Obtaining consent for the treatment of children raises special and complex issues. Children do not reach full legal capacity until they attain the age of majority (adulthood). This age varies between nations and their regions, but 18 years is the most common age in Western nations. From

the age of majority, a person may consent to medical treatment provided they are otherwise of full capacity. In the case of young children, parents can consent to medical care on behalf of their child.

As a child matures, it may attain the legal capacity to consent to medical care before reaching the age of majority and even against the wishes of its parents. The relevant age and circumstances vary between legal systems (as within the European Union[17]) and may be set by legislation (as in New South Wales, at 14 years or upwards[18]) or by common law. In the USA, the 'mature minor' common law doctrine recognises adolescent children as legally competent to make decisions about medical treatment, based on factors such as age, maturity, intelligence and the risks,[19, 20] while in the UK[21] and Australia[22] the common law provides that a child under 16 years may consent once he or she is capable of full understanding of the treatment proposed.

A cautious approach when dealing with apparently mature children would entail obtaining the consent of both the child and a parent or legal guardian. If this is not forthcoming, advice should be sought from local lawyers and ethical committees. When treating immature children, the consent of a parent or legal guardian should always be obtained.

Emergency care is delivered to children according to the principles for emergencies outlined above, but may be complicated where a parent refuses permission, perhaps on religious grounds. Legal systems often make provision for the delivery of life-saving emergency care in the face of parental opposition; reference should be made to local laws.

Standard of medical skill expected

The second main implication arising from the sports clinician/athlete relationship is that the clinician is under a legal duty to exercise medical skill in rendering healthcare. According to the FIMS Code of Ethics (clause 4), the 'athlete can expect a physician to exercise professional skill at all times'.[16] These legal and ethical responsibilities are embodied in the term 'duty of care'. The standard of that care, that is, the level of medical skill required to be exercised by the clinician, will now be considered.

If there is a contract between the clinician and the athlete, the terms of the contract will set the standard. However, it is rare for anything to be said expressly about the standard in contractual arrangements, and it is left to the law to imply a standard. In some legal systems the implied contractual standard of medical care coexists with a similar standard arising from the relationship of clinician and athlete; so, the standard has its foundations in both the contract and the relationship. This relationship standard will also apply where there is no contract between the athlete and clinician, as with voluntary care or where the care is organised and paid for by another person or organisation, such as a sports club.

Good Samaritans

An exception may apply if the clinician voluntarily goes to the aid of an injured or ill person in a serious emergency and the clinician is not performing in a role in which giving such aid is part of their responsibilities, such as a duty clinician at a sports stadium or a designated emergency carer.

In such circumstances, some legal systems confer an immunity from legal responsibility for these 'good Samaritans', but the immunity may not extend to deliberate acts in bad faith or grossly deficient treatment.[23–25]

Negligence

The legal obligation of the clinician to exercise medical skill is described by terms like 'due care and skill', 'prudent care', 'ordinary care and skill' and 'reasonable care'. It is an alleged failure to exercise that degree of skill (a breach of the duty of care) that is the most common cause of litigation between clinicians and patients. 'Negligence' and the wider term 'malpractice' encompass any such failure.

Whether a clinician has been negligent is usually regarded as a question of fact to be determined by a court, allowing for the circumstances of the case. This determination is made within a legal framework often involving two intertwined considerations: a risk analysis and reference to the skills to be expected of the clinician involved. On the evidence, the court will determine the standard of care that ought to have been exercised and then assess whether the clinician's conduct met or fell short of that standard. Any shortfall, no matter how small, will constitute a breach of the duty of care.

The risks are those that can be foreseen by an objective or independent clinician, sometimes referred to as the 'reasonable' clinician. The action, if any, to be taken regarding a foreseeable risk will depend on factors including its probability of materialising, the extent of the likely harm if it does materialise and the benefits, costs and difficulty involved. For example, a surgical procedure aiming to extend an athlete's career by a short duration may be contraindicated if it has a small chance of success and carries a substantially increased long-term prospect of osteoarthritis.

The practice of medicine is a profession employing skills not possessed by ordinary people. The performance of any clinician is judged by reference to the standards of the profession, not those of ordinary people. This is often referred to as a 'special skill',[26] but that does not mean a 'specialty' as that term is widely understood in the health professions. The skills expected will include the knowledge, judgment and technique of the ordinary, competent clinician.

The standard required by the law is not the highest possible, and the skill to be expected is judged according to the knowledge and professional standards applying at the time the injury is sustained, not according to subsequent advances in medical science or with the benefit of hindsight. However, a breach of the standard is not excused by a claim that the clinician did his or her best or was inexperienced, if there is a failure to meet the standard of ordinary competency. As a guide, this is the standard of medical skill that many legal systems would require of a clinician who occasionally treats a patient injured in sport or who might volunteer services to a local community or school sports team.

Sports medicine as a specialty

The position is different where specialist sports medicine skills are involved. Here the standard of care expected is higher. The law recognises that within professions there may be specialties. This

means that the work of a specialist will not be judged by the standard of the ordinary, competent clinician. Instead, the standard is that to be expected of the ordinary, competent clinician having those specialist medical skills who, in the present context, is referred to as a 'sports clinician', 'sports physician' or similar title.

The establishment of recognised postgraduate qualifications in sports medicine, the formation of associations or colleges of specialist sports clinicians, the opportunity to be licensed in some places as a sports clinician and the creation of a substantial body of research and literature on sports medicine topics have all served to increasingly identify sports medicine as a specialty in the eyes of the law and health profession regulators. A consequence of these developments is that the standard of medical skill expected of the sports clinician will be that of the ordinary, competent sports clinician, not a general clinician. That standard may be informed by the curricula, practical training and membership requirements of specialist colleges, including ongoing education and certification.[27]

Clinicians will be judged by this higher sports medicine standard if they possess applicable specialist training or certification. It will also likely apply to those clinicians who are appointed to professional or other elite teams or who otherwise regularly care for athletes. Even if clinicians do not possess specialist training or certification, by referring to themselves as 'sports clinicians' or as conducting a 'sports medicine practice' those clinicians *profess* specialist skills and must therefore comply with the higher specialist standard. Should an athlete require care in other fields of medicine, like cardiology or orthopaedic surgery, the applicable standard of care will be that expected of specialists in those fields.

Difficulties

Determining the standard of care by which sports clinicians are to be judged is not without difficulty; a difficulty arising in medical litigation in general. Some legal systems accept geographic variations in the standard of care (a factor in decline with improved electronic communications), as well as differences between responsible bodies of medical opinion among the clinician's peers.[28] In England, for example, a court accepted medical evidence that for rehabilitation from reconstruction of a ruptured anterior cruciate ligament 'no one protocol had ever been developed and numerous different ones exist'.[29] Sometimes courts will accept compliance with standard medical practice as sufficient to prove that the clinician exercised due care and skill, whereas courts in other legal systems will reserve the decision to themselves but be guided by medical practice. In other cases, especially those concerned with giving advice, medical practice may not be the only factor to consider (see below).

Proof in legal disputes is usually on a balance of probabilities, which entails a different approach to scientific proof, with the consequence that there can be discordance between legal and medical views in 'cause and effect' cases particularly. Parties to medical litigation may shop around for expert medical witnesses willing to provide favourable reports; a practice which has prompted some legal systems to provide experts independent of the parties to advise the court.

Negligence and incident types

The usual legal rule is that athletes must shoulder responsibility for the ordinary risks of injury inherent in sports participation. The loss is said to lie where it falls. However, injury attributable to negligent medical care is not an ordinary risk, and an injured athlete may endeavour to shift the loss to the clinician (and hence to an insurer) by taking legal action. If a sports clinician is accused in that respect it will most likely be because one of the following types of incident has occurred.

1. *An injury is undetected, undiagnosed or otherwise overlooked leading to prolonged disability.* For example, where foreign objects (glass and gravel) entered a rally car driver's hand fractured in a road crash but were overlooked at the time of surgery and not removed for some years.
2. *An injury or condition is not identified or communicated and subsequent participation in sport exposes the athlete to harm inflicted by opponents or caused by the demands of participation.* For example, not detecting a neck injury sustained during an ice hockey match that, in a later match, was converted into serious paralysis by an opponent's legitimate tackle.[31] Also, due to omissions in follow-up and poor communication by clinicians, a 16-year-old entrant to an elite football academy was permitted to train and play notwithstanding that a routine electrocardiogram revealed abnormal cardiac function, with the result that cardiac arrest occurred during a competitive match causing catastrophic brain damage.[32]
3. *An injury suffered during participation in sport is aggravated by an inappropriate emergency response.* For example, an attending doctor failed to supervise moving a schoolboy American football player who had a suspected spinal injury, thereby causing quadriplegia.[33] Also, the failure at a professional boxing match to have present at ringside resuscitation equipment and clinicians who knew how to use it, which would have avoided or limited brain damage to a boxer who had sustained a brain haemorrhage during the match[34] (although here fault lay with the sanctioning body rather than the clinicians).
4. *The treatment recommended and undertaken is inappropriate for the condition or injury from which the athlete is suffering.* For example, a First Division footballer in England sustained a partial tear of the posterior cruciate ligament of his right knee in training and was recommended to undergo knee reconstruction surgery, whereas conservative treatment with a knee brace for 4–6 weeks together with continuing physiotherapy was appropriate.[35]
5. *Surgery is not conducted in accordance with appropriate professional standards, with consequential lack of success and, possibly, additional harm.* For example, knee reconstruction surgery to repair a partial tear in an athlete's posterior cruciate ligament was undertaken negligently, with the consequence that he had to undergo further surgery to try to make good the damage and, eventually, a tibial osteotomy.[35] This ended his career as a promising First Division footballer in England. Also, a 19-year-old Canadian ice hockey player, who had been drafted by an NHL team, underwent surgery to repair an acute inferior dislocation of the shoulder only to have the surgeon 'make a serious mistake by leaving metal anchors or screws standing proud (sticking up from the bone)', which ultimately produced career-ending damage to his shoulder.[36]

6. *Deficient post-surgical care may result in unnecessary complications.* For example, infections, which are a recognised complication of surgery, may be exacerbated by delayed treatment, as where the failure by a team clinician over two days to detect *Staphylococcus aureus* infection resulted in greater septic arthritis and consequential cartilage damage to the knee of an academy professional footballer in England than would have occurred had intervention been timely.[37] However, the court in that case concluded that the extent of damage already caused to the footballer's knee by earlier injury, in combination with the initial infection before it could be reasonably detected, would have precluded a professional career in any event.
7. *A new injury may be caused by treatment.* For example, burns can result from the use of ice or electrophysical agents such as ultrasounds and thermal modalities. According to one legal report, an athlete sustained third-degree burns from the incorrect application of ice.[38]
8. *A program of rehabilitation is either inappropriate or incorrectly applied, with consequential lack of success and, possibly, additional harm.* For example, following successful surgery to repair a rupture of the anterior cruciate ligament and a tear of the posterior horn of the lateral meniscus of the left knee of an academy professional footballer in England, it was alleged that the player was progressed to jogging and running by the academy's head physiotherapist before he had recovered sufficient strength in his left quadriceps, leading to complications that ended his professional career. The court, however, held that the rehabilitation protocol followed was 'in principle perfectly acceptable' and the evidence did not prove a breach of the protocol.[37]

Among these types of incident, three phases of medical care may be observed: (1) diagnosis, (2) providing information and advice and (3) treatment. In practice, a failure in (1) or (2) may cascade into a failure in the next phase, or deficient treatment can occur independently of the other phases.

Providing information and advice

In deciding whether a sports clinician's diagnosis or treatment is negligent, a court will apply the principles mentioned above, which place substantial reliance on medical practice and opinion. However, in a growing number of legal systems, the standard of care for the provision of information and advice by a sports clinician must incorporate not only medical practice and opinion as to what should be communicated to an athlete (particularly risks of treatment), but also what the athlete may need to know. There has been a rejection of the approach of 'doctor knows best', in favour of what some legal systems refer to as an individual's autonomy over his or her body and related rights of informed consent or informed decision making. This legal position is reflected in the FIMS Code of Ethics:

> A basic ethical principle in health care is that of respect for autonomy. An essential component of autonomy is knowledge. Failure to obtain informed consent is to undermine the athlete's autonomy. Similarly, failure to give them necessary information

violates the right of the athlete to make autonomous choices [clause 3].[16]

In general terms, if a sports clinician has not informed an athlete of a risk of treatment, that risk materialises and the athlete would not have undergone the treatment had he or she known of the risk, the clinician incurs legal liability for the added harm. Similar considerations apply to not informing an athlete of the risks of sports participation either before recovery from injury is complete or when suffering from a risky health condition such as Marfan syndrome.

The FIMS Code of Ethics (clause 3) states, further, that the 'overriding ethical concern is to provide information to the best of one's ability that is necessary for the patient to decide and act autonomously'.[16] The information and advice should be material, meaning that it is significant for the decision-making process. Pieces of material information and advice may have varying degrees of importance and perhaps point in different directions. The decision will usually involve a weighing-up process, including a risk analysis.

However, there are differences between legal systems in the tests for the level of information and advice required. These tests range from providing what a reasonable sports clinician would regard as customary or appropriate, to what the reasonable person in the athlete's position would regard as significant, through to what the individual athlete under care subjectively requires given his or her questions and circumstances.

Some legal systems recognise a 'therapeutic privilege', which permits a clinician to withhold information about the risks of treatment if the athlete's mental condition would render knowledge of the risks counterproductive to the athlete's health and safety by deterring consent to essential medical care. The reader with a specific inquiry about the law in a place, or needing legal advice on some eventuality, should consult a legal professional who is practising locally.

Providing information and advice to an athlete about important decisions is one of the most challenging tasks faced by sports clinicians. This will include decisions about: (1) whether to undergo major treatment for an injury or condition and, if so, the timing and type of treatment; (2) the timing of return to sports participation following injury or illness; and (3) whether retirement from a professional career (or more generally from a sport) is advisable because of the risk of further injury or the activation of a dangerous medical condition such as abnormal cardiac function.[32]

Aside from the medical risks and benefits of any proposed action, the sports clinician should take into account the athlete's personal circumstances, which might indicate that more detail about risks is needed than usually provided. Those circumstances might include the athlete's age and maturity, ability to understand and make rational choices, sporting milestones that the athlete might be aiming to achieve (including games played, championships and bonuses), likely remaining duration of sporting career (the prospect of a long career may suggest a conservative approach to recovery from injury), other life milestones (including weddings, birth of children and qualification periods for leave or superannuation) and the athlete's concerns and expressed desire for information. Important or difficult decisions might warrant the involvement of close relatives (parents for a young athlete) and the athlete's trusted advisors. Decisions are best made in a calm

environment, not in the heat of competition. Overall, the information and advice should be accurate, understandable and appropriate for the athlete's personal circumstances and the purpose of making an informed decision.

Sometimes a sports clinician is the conveyor of unwelcome news, as when a recently discovered congenital defect dashes the dream of a professional career in a major sport,[32] or that an Page 535 injury is not sufficiently recovered to warrant return to play. Clinicians may have worked with athletes for lengthy periods and have become close. It is especially important under such conditions for the clinician's advice to be dispassionate and not compromised by the clinician developing 'fan syndrome'.[39] The athlete will not be thankful for advice that ultimately proves misguided, notwithstanding it was what he or she wished to hear at the time.

While the decision must remain the athlete's and not the clinician's, the bare tendering of information and clinical options may be of limited assistance to an athlete who has not been in such a position before. The sports clinician is likely to be a 'repeat player', with significant experience on which to draw, such as the options taken by other athletes in a similar position, the outcomes and even the clinician's assessment of the degree of success. However, for the clinician to advocate one path as if he or she were in the athlete's shoes is inappropriate, at least for the reason of the power imbalance, but there is a place for wise counsel carefully delivered. There is no bright line between the two. Good record keeping, second medical opinions and the sports clinician seeking advice from more experienced colleagues are useful practical measures in many cases.

Legal responsibility for negligent advice may extend to doping cases where an athlete has relied on incorrect information from a sports clinician, including whether a substance is banned (see below).

Confidentiality and trust

The third main implication arising from the sports clinician/athlete relationship is that the clinician is under legal obligations of confidence and trust. The FIMS Code of Ethics (clause 4) states that the 'basis of the relationship between the physician and the athlete should be that of absolute confidence and mutual respect. . . The athlete's right to privacy must be protected'.[16]

As a general principle, personal health information about an athlete received by a sports clinician through the professional relationship with the athlete must be held in confidence. This confidentiality will extend beyond information received direct from the athlete to include information obtained from other health professionals. A breach of ethical rules about confidentiality will usually amount to professional misconduct and involve the risk of disciplinary action by the local authorities.

Any contract existing between the athlete and sports clinician, the law of confidence, privacy law, health information protection legislation[40] and general data protection laws[41] may impose further obligations on sports clinicians, the breach of which could result in compensation payments, fines and other penalties. Ancillary obligations may exist requiring the sports clinician to maintain both the physical and electronic security of an athlete's health information.

The obligation of confidence is not absolute. There are exceptions, including the following. The athlete may authorise disclosure. This might occur expressly, such as when the athlete requests that a health report be given to the manager of a professional team interested in employing the athlete. The authority may be given by implication where, say, it is necessary for the clinician to obtain essential X-rays or pathology reports, or to refer the athlete to a medical colleague and provide a treatment history. Legislation may authorise disclosure, for example where certain injuries or illnesses must be reported to public health authorities or potential health fraud is under investigation.

Trust is an essential element in the sports clinician/ athlete relationship. It will not exist if the athlete believes that the clinician will improperly pass on his or her personal health information to others. Trust also involves honesty and the underlying expectation that the clinician will act in the best interest of the athlete and not of someone else, including the clinician's own interest. The FIMS Code of Ethics notes that 'Truthfulness is important in health care ethics [clause 3]'[16] and 'Advice given and action taken should always be in the athlete's best interest [clause 4]'.[16] The law requires that the clinician must be frank and honest with the athlete. For example, to discover an injury and not inform the athlete would in almost all cases be a dereliction of duty, as would overservicing in the provision of medical care.

Health records are usually created and therefore owned by the physician. In some places, the clinician may be able to deny the athlete the right to inspect and copy the records, although the clinician must provide a summary to enable another clinician to render treatment. However, in other countries specific legislation affords the athlete access to his or her records.[42, 43]

Conversely, the clinician must be able to trust the athlete to provide complete and honest information about the athlete's medical condition and to cooperate with treatment, if the healthcare is to succeed.

THE SPORTS TEAM CLINICIAN

National sports organisations, professional clubs and leading community sports associations and educational institutions commonly engage sports clinicians and other health professionals to provide medical care for the players on their teams. A key role for the clinician is to have the players fit and ready to play and, where teams compete at the highest levels, an inability to do so may have financial implications. Such a sports body (in this section called 'the team') will usually engage the clinician as an employee or an independent contractor. This creates a tripartite relationship between the team, the clinician and the athlete.

Providing medical care and managing conflict of interest

The tripartite relationship may present the risk of conflict of interest for the clinician. For example, if team management desperately require a star player to be available after injury, there will be expectations of the clinician to ensure that occurs. On the other hand, premature return may expose the athlete to the risk of an aggravated injury. Any dilemma may be complicated by pressure from the athlete to return to play (see below).[44] However, both the ethics of sports

medicine and the law stipulate that the health of the athlete is the clinician's priority. The FIMS Code of Ethics[16] gives various indications of that position:

> Always make the health of the athlete a priority [clause 1].
>
> The physician's duty to the athlete must be his/her first concern and contractual and other responsibilities are of secondary importance [clause 3].
>
> It is the responsibility of the sports medicine physician to determine whether the injured athletes should continue training or participate in competition. The outcome of the competition or the coaches should not influence the decision, but solely the possible risks and consequences to the health of the athlete [clause 8].
>
> In all cases, priority must be given to the athlete's health and safety. The outcome of the competition must never influence such decisions. To enable the sports medicine physician to undertake this ethical obligation the sports medicine physician must insist on professional autonomy and responsibility for all medical decisions concerning the health, safety and legitimate interest of the athlete. No third party should influence these decisions [clause 11].

The established legal position, as reflected in commentaries,[45, 46] is summarised in these terms: 'the team physician's judgment should be governed only by medical considerations, not the team's need for the services of the player or the athlete's strong desire to play'.[47] 'It is ... negligent not to have primary regard to the well-being and long-term health of the patient-player.'[48]

In honouring these ethical and legal obligations, the clinician must demonstrate resolve in the face of pressure and, sometimes, public criticism.[49] It is not unnatural for a younger clinician to relate to the athletes (or seek to do so), while an older clinician who has been with a team for some years will become more familiar with management as players come and go. Whatever the position, the clinician should aim to maintain an appropriate degree of 'distance' to ensure that sound professional judgment is not compromised. Such a path is more likely to see the sports clinician earn the respect of those concerned.

Trust and confidence

As mentioned above, the clinician's obligation of confidence regarding an athlete's personal health information is not absolute. The tripartite relationship in which the team clinician operates, of necessity, will require passing on some of an athlete's health information to coaches and management, including the fact of injury, planned treatment and whether a long-term or career-ending disability is foreseen. The FIMS Code of Ethics states:

> When serving as a team physician, the sports medicine physician assumes the responsibility to athletes as well as team administrators and coaches. It is essential that each athlete is informed of that responsibility and authorizes disclosure of otherwise confidential medical information, but solely to the specific responsible persons and for the expressed purpose of determining the fitness of the athlete for participation [clause

4].[16]

It is commonplace for professional player contracts and team agreements to authorise clinicians (both the athlete's personal clinician and team clinicians) to pass personal health information to specified people, such as team coaches and managers. One possible response of players is to not tell clinicians of an injury, or its full extent, or to only reveal the injury if the clinician will not pass on that information. It is important medically for the clinician to be informed so appropriate treatment may proceed, but the clinician should not be expected to dishonour obligations to the team. This potentially difficult dilemma is best addressed through good communication of respective responsibilities and a cooperative and supportive team environment.

Information about an athlete's physical capabilities as well as their injuries has become both sophisticated and commercially valuable. Aside from the authorised disclosures identified above, sports clinicians who have access to this health information may be involved in briefing the news media. Again, the FIMS Code of Ethics offers guidance:

> In view of the strong public and media interest in the health of athletes, the physician should decide with the athlete what information can be released for public distribution [clause 4].[16]

As well as the athlete's interests, as identified by FIMS, leagues and other sport controlling bodies may insist on some disclosure of the injury status of players to satisfy the news media and fans generally, but also for participants in increasingly popular fantasy leagues and betting markets. The nature and extent of such disclosure is usually governed by contractual terms in major professional sports. On the other hand, teams may not wish to disclose too much information for competitive sporting reasons.

The growing use of wearable technology to gather biometric and biomechanical data of elite athletes presents medico-legal issues that are relatively unexplored.[50] That data could provide a powerful diagnostic tool, but also be used in contract negotiations where the longevity of a player is in contention. Those issues, as well as who owns and controls the data and its security, are certain to generate debate and commercial negotiation.[51]

In addition to the obligation of confidence that a sports clinician owes to the athlete, the clinician must be careful also not to reveal information about the status of an athlete's health (or team tactics) because to do so will breach the clinician's contract with the team and, in some jurisdictions, constitute the criminal offence of dealing in 'inside information', if linked to gambling.[52]

A breach of the clinician's obligation to provide information and advice to enable an athlete to make an informed decision (discussed above) may also involve a breach of the obligation of trust. This is perhaps more likely to occur in a team setting where the clinician's judgment is compromised by a conflict of interest. In a court case involving American football, a team clinician was found to have acted fraudulently when he 'consciously failed to make full, meaningful

disclosure to [the footballer]... respecting the magnitude of the risk he took in continuing to play a violent contact sport with a profoundly damaged left knee'.[53] A deficiency of trust in team doctors is evident in calls for independent doctors to hold crucial decision-making powers about whether a player should be removed from play on account of injury.

Vicarious liability

In many legal systems, the relationship between an employer and employee gives rise to a vicarious liability. That means the employer will be liable for at least some wrongful acts committed by the employee in the course of his or her employment notwithstanding that the employer may not have been at fault personally. For example, the partners in a medical clinic will be vicariously liable for the negligence of non-partner clinicians or other staff members, such as nurses, who are their employees.

One rationale for this rule is that employers profit from their employees' work and should be responsible for the losses. Another is that employers are more likely to be insured and able to pay the injured person's damages. That the employer is vicariously liable will not necessarily relieve the employee of personal responsibility and, under some legal systems, the employer may be entitled to reimbursement from the employee if the employer must pay compensation.

Professional teams in large leagues often employ clinicians on a full-time basis to head a medical department including physiotherapists, physical therapists, trainers and soft tissue therapists. When first appointed, leading clinicians may bring their preferred supporting health professionals to the team. In those circumstances, the clinician and support staff will usually be regarded as employees for which the team may be vicariously liable.

Where an external medical practice is engaged to provide medical services to the team, the clinicians allotted to treat the players may nonetheless be considered as employees of the team for vicarious liability purposes if they are sufficiently 'embedded' in the team's organisation as official team clinicians.[31] On the other hand, a team may not be vicariously liable for the negligence of external consulting specialists, even though the specialist is a person of 'first choice' to treat, say, knee injuries; usually the consulting specialist's responsibilities will be confined to the athlete.[54]

For the sports clinician, a very important practical consideration is insurance coverage. The losses potentially incurred by a leading professional player who can prove career-ending medical negligence are immense. Teams are more likely to be better placed than sports clinicians to obtain the necessary coverage. So, the existence of appropriate insurance arrangements should be a matter of careful investigation and negotiation for any clinician (employee or external) who treats elite professional athletes.

Other roles

Sports clinicians may perform other roles bringing them into contact with team athletes but where the normal clinician/patient relationship does not apply. These circumstances include medical examinations for pre-contractual or insurance claim purposes. Here the athlete is not the clinician's patient, but there is a legal obligation to take care not to injure the athlete during the course of the examination and a strong ethical, if not legal, obligation to inform the athlete of any

significant conditions discovered of which the athlete might be unaware; for example, indications of cancer.

MANAGING RISKY SPORTS

As stated above, the usual legal rule is that athletes must shoulder responsibility for the ordinary risks of injury inherent in sports participation. Those risks can be severe: resulting in, for example, paralysis, brain injury or death in a small minority of cases. It has been a long-established view that the social and health-giving benefits of sports participation greatly outweigh the cost of injuries that do occur, so the toll has been tolerated, if not accepted. However, as more is learned medically and scientifically about the mechanisms of injury, the occurrence of overuse injury, as opposed to traumatic injury, and the cumulative effect of repeated small injuries, there are increased calls to make sports safer. That task will be borne largely by sports governing bodies and those who employ professional athletes, as well as by lawmakers, but sports clinicians will play an important role too.

The FIMS Code of Ethics states:

> If the physician considers that a certain sport entails major risks he should try to eliminate the risk by exerting pressure on the athletes as well as on the relevant decision makers. Injury prevention should receive the highest priority [clause 8].[16]

In relatively recent times, medico-legal attention has been directed to neck injuries causing paralysis (especially in rugby union) and blows to the head alleged to cause degenerative brain damage (especially in American football). It is likely that other types of injuries, such as knee osteoarthritis,[55, 56] will attract medico-legal attention in the future, at least to provide former professional players with improved welfare benefits.

Neck injuries

In the 1980s and 1990s in particular, sports clinicians and medical researchers recorded the occurrence of cervical spine injuries in rugby union during scrummaging.[57–59] Calls were made for rule changes to minimise the risk of such injuries, which were eventually implemented, but not before the sport was confronted by numerous legal claims.[60–62]

Those claims included one in the highest Australian court, in which it was argued there was an obligation on the international governing body for the sport to change the rules to remove unnecessary risks. The claim was unsuccessful for voluntary adult amateur players, who were said to accept the risks of a ‘notoriously dangerous game’. A detailed understanding of the nature of specific risks was not necessary before a risk was ‘accepted’. However, the court left the door open for claims by professional players alleging an unsafe workplace and by children participating in compulsory school sport.[63]

Commentary on the decision suggested that had the court allowed the claim it would have encouraged sport governing bodies to become more proactive in terms of conducting research into

injuries, devising ways to avoid injuries and making rule changes.[64] In any event, the rule changes made in rugby union appear to have had some success in reducing the incidence of cervical spine injuries.[65]

Head injuries—concussion

Traumatic injury to the head is a known risk of a substantial number of sports: fractures and lacerations as well as damage to eyes, teeth and hearing. Such injuries may or may not be suffered in company with the athlete being what is described in the vernacular as 'knocked out'. The history of sport is littered with examples of players who have received blows to the head causing complete loss of consciousness, or impaired consciousness, and then returned to play almost immediately or without what is by today's standards regarded as sufficient time for the brain to recover. Some high-profile incidents have attracted praise for the player's 'courage', while more-informed commentators expressed concern over the risk to the player of a further hit while impaired.[66]

Progressively more has been learned about how a blow to the head affects the brain, and the appropriate medical response. This growing knowledge has altered the way in which athletes are tested for concussion and when it is considered safe to return to participation. However, there has been no greater impetus for change than the class action by former players in the USA's National Football League (NFL), which was settled in early 2017 at a potential cost to the NFL of over US$ 1 billion.[67] Not only was the action huge (there are over 20 000 eligible former players),[68] but it spawned game rule changes,[69] research[70] and significant legislation in the USA to protect children from concussion when participating in sport.[71–73] The class action and its consequences have attracted worldwide attention, accompanied by a sense of urgency to develop appropriate responses.

Other sports are confronting the prospect of litigation.[74] From a medico-legal perspective, it is likely that a large proportion of any legal claims will allege deficient medical care of concussed players that can be traced to deterioration of brain function in later life. The success of those claims will depend in part on the expected standard of care (reflecting appropriate medical practice at the time of concussion) and whether a causal link is established between how the concussion was contemporaneously managed and later loss of brain function in each individual case. Complex questions will arise, on which local legal advice should be obtained.

The NFL class action and aftermath have also highlighted issues that were left open or arguably unsatisfactorily resolved in the neck injury litigation in rugby union; namely, the protection of children (subsequently addressed through extensive legislation across individual US states), and the obligation of sporting bodies and clubs to provide professional players with safe workplaces. The class action included claims that the NFL and clubs had failed in their legal obligations by not educating and warning players about the emerging knowledge of dangerous health effects of repeated blows to the head and by fraudulently concealing the harm sustained by some players.[74]

Although, in 2000, the international governing body of rugby union was found by the highest

appeal court in Australia not to owe a legal duty to players to adopt rule changes aimed at making that sport safer (subject to possible exceptions), there is evidence from the reaction to the 'concussion crisis' that high-level governing bodies internationally in some contact and collision sports have embraced the mantra of rule change for safety.

Important in this regard has been a series of international conferences on concussion in sport; the first occurring in Vienna in 2001.[75] These conferences have become meetings of the Concussion in Sport Group, which is constituted by medical researchers and other experts on concussion in sport. The fifth conference, held in Berlin in 2016, issued a Consensus Statement on Concussion in Sport, which is:

> designed to build on the principles outlined in the previous statements . . . and to develop further conceptual understanding of sport-related concussion (SRC) using an expert consensus-based approach. This document is developed for physicians and healthcare providers who are involved in athlete care, whether at a recreational, elite or professional level. While agreement exists on the principal messages conveyed by this document, the authors acknowledge that the science of SRC is evolving and therefore individual management and return-to-play decisions remain in the realm of clinical judgement.[76]

The consensus statement identifies many issues, some in significant detail, including a definition of SRC, diagnosis of SRC at the sideline and more thorough diagnostic evaluation away from the playing area, decisions to remove an athlete from play, treatment options involving rest, rehabilitation and follow-up, and return to play. Although the consensus statement states that it is 'not intended as a clinical practice guideline or legal standard of care', it is likely to be regarded by courts at the very least as helpful in identifying issues and behaviour to be considered in setting the standard of medical skill expected of the sports clinician when treating an athlete who may have sustained a concussion. The consensus statement also addresses various ways in which concussion might be prevented, including screening, education of players and rule change. It calls for more research.

The general nature of the consensus statement invites specific elucidation in sports with greater risk of participants sustaining concussion. Officials from 10 such contact and collision sports (American football, Australian rules football, basketball, cricket, equestrian sports, soccer, ice hockey, rugby league, rugby union and skiing), together with some multisport governing bodies, met in Dublin, Ireland, in July 2017 for that purpose. A report of their deliberations recognised that:

> Due to their different settings and rules, individual sports need to adapt concussion guidelines according to their specific regulatory environment. At the same time, consistent application of the Berlin Consensus Statement's themes across sporting codes is likely to facilitate superior and uniform diagnosis and management, improve concussion education and highlight collaborative research opportunities.[77]

The resulting joint position statement is, again, likely to be regarded by courts as influential in

setting the standard of medical skill expected of the sports clinician when treating an athlete who may have sustained a concussion, at least in the sports participating in this process.

One degenerative condition of the brain claimed to arise from repeated minor blows to the head (of which an NFL player or a boxer may receive many hundreds during a career) is chronic traumatic encephalopathy (CTE), sometimes referred to in boxing as 'dementia pugilistica'. Whether there is a link between sport and CTE is disputed in scientific circles. However, the law does not require the same degree of proof for civil claims (a balance of probabilities usually suffices), and so it is difficult to avoid the conclusion that the settlement of the claim in the NFL class action was based at least in part on the prospect of a court accepting a causal link between SRC and CTE.

This brief consideration of concussion in sport demonstrates some of the ways in which the sports clinician may become involved in assisting to shape the medico-legal environment in which sports medicine is practised.

DRUGS IN SPORT

The use of drugs in the context of sport is one of the most legally complex and tightly regulated aspects of sports medicine. Not only must the sports clinician know which substances and doping methods are prohibited in order to avoid any inadvertent breach of the rules by an athlete under treatment, the clinician must be cautious of circumstances where his or her own behaviour may become the subject of investigation and prosecution.

The FIMS Code of Ethics states that the:

> . . . sports medicine physician should oppose and in practice refrain from using methods to improve performance artificially such as those prohibited by the International Olympic Committee ... it is contrary to medical ethics to condone doping in any form [clause 12].[16]

For sports and organisations that are affiliated with the Olympic Movement, compliance with the World Anti-Doping Code (WADC) is mandatory.[78] This means that a large majority of professional and elite athletes worldwide are subject to Code-compliant anti-doping policies issued by their sports. Some non-Olympic sports have been encouraged by national governments to follow the WADC, while others, notably the major leagues in the USA, have adopted anti-doping policies that, to varying degrees, take different paths to that of the WADC.[79, 80] National governments support the WADC by becoming parties to the UNESCO International Convention against Doping in Sport.[81] The convention is the second most ratified of all UNESCO treaties.[82]

There have been three editions of the WADC, taking effect on 1 January in 2004, 2009 and 2015, respectively. A fourth edition is scheduled to come into force on 1 January 2021. The World Anti-Doping Agency (WADA) has a range of roles and responsibilities under the WADC, including managing the process by which new editions of the WADC are developed, adopting new editions, monitoring compliance with the WADC, accrediting testing laboratories and promoting anti-doping research and education.[83] WADA is constituted under Swiss law as a foundation, but is

headquartered in Montreal, Canada. It is governed by a foundation board that consists of equal numbers of representatives from sport and government. The presidency is rotated between the sport and government sectors.

Anti-doping rules and testing have evolved rapidly over the past 60 years, and noteworthy developments, apart from the establishment of WADA in 1999, have included the harmonisation of the rules worldwide and the emergence of national anti-doping organisations.[84, 85] The WADC is much analysed by legal commentators, especially the offences, known as 'anti-doping rule violations' (ADRVs) and the penalties.[86–88] The WADC operates in conjunction with six international standards issued by WADA, which regulate particular aspects of the anti-doping effort. They apply to prohibited substances and methods, testing and investigations, laboratories, therapeutic use exemptions (TUEs), protection of privacy and personal information and compliance with the WADC by sports and other organisations.

Part One of the WADC deals with doping control. It defines the offence of doping (arts 1–2), provides for the collection of samples for testing and analysis, as well as results notification (arts 5–7), sets minimum standards for fairness in disciplinary hearings (art. 8), stipulates penalties (arts 10–12) and regulates appeal rights (art. 13).

Article 2 of the WADC creates 10 ADRVs, which, in shortened form, prohibit:

1. presence
2. use or attempted use
3. avoiding sample collection
4. whereabouts [athlete location reporting] failures
5. tampering or attempted tampering with doping control
6. possession
7. trafficking
8. administration
9. complicity
10. prohibited association.

Some of these ADRVs are particularly relevant to sports clinicians, either because the clinician is implicated in an athlete's commission of an ADRV or because the clinician commits an ADRV as an 'athlete support person' or in some other capacity.

Prohibited substances and methods appear in an annual list, which forms one of the six international standards. To be included in the Prohibited List, a substance or method must meet any two of three criteria identified in art. 4.3.1: performance-enhancement, risk to health, and violation of the 'spirit of sport' as defined in the introduction to the WADC. Some prohibited substances (stimulants, narcotics, cannabinoids and glucocorticoids) are banned during competition only. WADC art. 2 explicitly provides that athletes and athlete support personnel such as team clinicians are responsible for knowing which substances and methods are on the Prohibited List.

WADC art. 2.1 creates the ADRV of 'presence of a prohibited substance or its metabolites or markers in an athlete's sample'. Presence is determined by the outcome of laboratory tests of urine or blood samples donated by the athlete. (Further information about the Prohibited List and testing processes is provided in Chapter 34.) It is the presence of the prohibited substance in the donated sample that activates the ADRV. It is not necessary to show that the athlete intended to break the anti-doping rule or that he or she was negligent, at fault or knowingly used the substance (art. 2.1.1). This absence of the need to prove a 'guilty mind' has led to art. 2.1 being described as a 'strict-liability' offence.[89, 90] However, 'absolute liability' is more accurate, because once the presence of the substance is identified via a laboratory test, no excuse will avoid the ADRV.

WADC art. 2.2 creates the ADRV of 'use or attempted use by an athlete of a prohibited substance or a prohibited method'. This ADRV is not usually proven by a laboratory test, although it can be. Instead, other reliable means are used, including admissions, documentary evidence, witness statements, longitudinal profiling (using, for example, the athlete biological passport[91]) and surveillance. Use of a prohibited substance occurs the moment the substance enters the athlete's body. Again, to establish use of a prohibited substance or prohibited method, it is not necessary for the prosecution to prove a guilty mind on the athlete's part. However, proof of an athlete's intent to use the substance or method is necessary to establish the attempted-use ADRV.

From time to time, sports clinicians are alleged to have played a significant but unintended role in the commission by athletes of either the presence or use ADRV, or of similar offences under earlier anti-doping rules. These incidents have included prescribing or supplying a pharmaceutical that either was or contained a prohibited substance,[92, 93] failing to check or checking incorrectly a pharmaceutical obtained by an athlete over the counter that the athlete declared to a treating sports clinician for approval,[94] and providing incorrect advice of the clearance time for a substance prohibited only in competition.[95] Reliance on the sports clinician will not save the athlete from a finding that he or she committed an ADRV, although in some limited cases it may reduce a period of ineligibility.[96] The consequences for athletes can be dire, including the loss of Olympic gold medals.[92, 94] Aside from reputational damage to the sports clinician, in some legal systems the athlete may be able to sue the clinician for negligent advice, seeking compensation for the economic losses flowing from a period of suspension and reputational damage. Where an athlete has suffered physical harm from using a prohibited substance recommended or supplied by a sports clinician, there may also be scope for compensation.[97]

A sports clinician working for a team or forming part of the entourage of an individual athlete may be subject to the terms of the WADC as 'athlete support personnel'.[98] This will require the agreement of the clinician, which is commonly obtained via team contractual arrangements or the terms of entry to events as part of an athlete's entourage. Even without these official connections, a sports clinician may come within the scope of the WADC and commit an ADRV by engaging in certain forms of conduct.

The FIMS Position Statement on Doping in Sport says:

> In addition to the ethical and health consequences surrounding doping, recognition is made of potential legal implications. The distribution of many banned substances (e.g. anabolic steroids), if not for a medically justified reason, is illegal in many countries. Encouraging or assisting athletes to use such substances or methods is unethical and, therefore, equally forbidden.[9]9

Four ADRVs are particularly relevant, namely, possession (art. 2.6.2), trafficking (art. 2.7), administration (art. 2.8) and complicity (art. 2.9). These ADRVs can be committed by sports clinicians who are active participants in doping by athletes.[100] A notable example is the prosecution by the US Anti-Doping Agency (USADA) of Dr Geert Leinders, who was the Rabobank professional cycling team chief doctor from 1996 to 2009. In January 2015, a panel of the American Arbitration Association found Dr Leinders guilty on charges of having committed all four of those types of ADRVs and imposed a life ban from involvement with sport.[101] The terms 'possession', 'trafficking' and 'administration' are given wide meanings in Appendix One to the WADC. Under these ADRVs, exceptions are provided for actions out-of-competition related to substances not prohibited out-of-competition, TUEs and other acceptable justifications such as medical emergencies.

For the sports clinician who is an active participant in doping by athletes, not only is there the prospect of committing an ADRV and receiving a penalty such as a lifetime ban from sport,[102] there is also the prospect of disciplinary action resulting in disqualification from practice[103, 104] and criminal responsibility, carrying imprisonment in some jurisdictions.[105–107]

WADC art. 2.10 prohibits athletes and other people subject to the WADC from associating with athlete support personnel who are disqualified under the WADC or found guilty under an equivalent criminal, disciplinary or professional process because of involvement with doping. Article 2.10 was introduced into the third edition of the WADC to discourage athletes from continuing professional relationships with such persons. Once warned of the clinician's status, an athlete must boycott the clinician to avoid committing an ADRV.[108]

Some athletes require prohibited substances or prohibited methods for bona fide medical reasons. A medical condition or illness is usually considered to be a disability, and unequal treatment on the ground of disability is a contravention of human rights law.[109, 110] Although an anti-doping rule that no athlete may use a certain substance appears at face value to apply equally to all, it is discriminatory because the rule sets a requirement of no use, which a person with the relevant health condition needing the prohibited substance or method cannot satisfy because of the disability. The problem presented by this dilemma has been resolved by the creation of therapeutic use exemptions (TUEs), which provide a reasonable way of accommodating people with disabilities. TUEs are conferred under art. 4.4 of the WADC and in accordance with the International Standard for Therapeutic Use Exemptions. Conduct consistent with the terms of an applicable TUE is not a violation of the WADC. TUEs are considered further in Chapter 3 4.

As stated above, some substances are prohibited in competition only. This is a long-established practice, dating from the beginning of anti-doping testing. Those substances include so-called illicit or recreational drugs, such as amphetamines, cocaine, heroin and marijuana. If an athlete consumes them out of competition, the ADRV of use under WADC art. 2.2 is not committed. However, should their residue be detected in an in-competition test, the ADRV of presence under WADC art. 2.1 is committed. Consumption of the drugs on competition day constitutes both ADRVs. Whether this situation should continue remains a matter of debate. However, it draws attention to a significant difference in approach between adherents to the WADC and those sports that either do not adhere to the WADC or would prefer to proceed differently.

The WADC model is in large measure based on a punitive methodology, with more broadly worded ADRVs, increased penalties and larger enforcement budgets over time. An alternative approach employs a stronger health and welfare focus, in that athletes who are detected using prohibited substances may be referred to counselling and other forms of treatment in conjunction with moderated penalties compared with the WADC. This alternative is employed by the US major leagues, which do not adopt the WADC model, and in some Australian leagues that have illicit drugs policies to cover out-of-competition use in addition to WADC-compliant anti-doping policies.[80, 1] These alternative approaches are collectively bargained between players and their leagues.[80, 1]

MEDICO-LEGAL ASPECTS OF HUMAN RIGHTS IN SPORT

The emergence of human rights law over the past 50 to 60 years has expanded the range of legal considerations that impinge on the practice of sports medicine. This section briefly considers some of the significant developments.

The second paragraph of the Charter of the United Nations features a statement reaffirming 'faith in fundamental human rights, in the dignity and worth of the human person, [and] in the equal rights of men and women'.[112] The usual starting point for discussion of this topic is the Universal Declaration of Human Rights, which was proclaimed by the United Nations General Assembly in 1948. The declaration was strongly influenced by the experiences of the First and Second World Wars and has been supplemented in the meantime by numerous international treaties, including the Convention on the Elimination of All Forms of Discrimination against Women (CEDAW), the Convention on the Rights of Persons with Disabilities and the European Convention on Human Rights.

One theme of these international documents is that of outlawing discrimination on the grounds of a person's sex and, in some cases, disability. Once adopted by a nation state, a treaty may have immediate legal force within the state, or the further step of enacting specific legislation to give effect to the treaty may be required. Not all treaties have been adopted by all nation states, while some states have taken the additional step of developing their own pronouncements, such as the Canadian Charter of Rights and Freedoms and the New Zealand Bill of Rights. In the context of sport, the UNESCO International Charter of Physical Education and Sport states:

> Every human being has a fundamental right to physical education, physical activity and

> sport without discrimination on the basis of ethnicity, gender, sexual orientation, language, religion, political or other opinion, national or social origin, property or any other basis.[113]

The Olympic Charter, in its fundamental principles, makes a similar provision, although it refers to a person's sex rather than gender.[114]

While the principle of human rights is widely accepted in international law and, specifically, in sport, the application and observance of it in practice are quite often the objects of difference and debate.

Sex, gender and pregnancy

The essential principle of CEDAW is to eliminate discrimination against women and ensure equality of opportunity. For example, art. 10(g) provides that in education women should have the 'same opportunities to participate actively in sports and physical education' as men. In those nation states where CEDAW (or something like it) has been adopted into local law, women have equal rights regarding playing opportunities and access to sports facilities.

Single-sex sports

A feature of many sports is that there are separate competitions for women and men. As a general approach, this is not inconsistent with the principle of equality of opportunity. The physical differences between the average or generic male and female are recognised as meriting separate competitions, for without separation there are not equal opportunities for sporting success as between the two groups. For some sports physical differences are not material: women and men compete together in equestrian events, lawn bowls, darts and, as jockeys, in thoroughbred horse racing.

Significant medico-legal issues may arise in the implementation of the essential CEDAW principle. Some nation states permit separate competitions for men and women only where the 'strength, stamina or physique' of competitors is relevant to the outcome.[115–117] For children, this approach means that until around the age of puberty boys and girls compete in combined competitions. Little has been said about the meaning of the expression 'strength, stamina or physique', but one tribunal suggested the following.

> Strength can be regarded as the state or quality of being strong or powerful. More specifically, . . . the word can be said to represent the amount of force (or torque) a muscle group can exert against a resistance in one maximal effort. Stamina denotes resistance to fatigue, illness and hardship. The concept embraces endurance, that is to say, the ability of the body to sustain prolonged exercise. Physique means the structure, form, constitution, strength or appearance of the body.[118]

The knowledge of sports clinicians can guide courts on the meaning of this expression or similar

concepts, and especially in how it applies to growing children and to specific sports.

Intersex and transgender

People who are physically intersex or transgender present very challenging and often high-profile issues for sports. That is especially so if the athlete seeks to participate in women's competitions where they might be regarded as having an advantage. That context will be the focus of the brief analysis in this section, and reference should be made to the more detailed analysis contained in Ch apter 30.

Medical understanding of the nature and causes of these two conditions has grown, and social attitudes towards intersex and transgender people have evolved in some nations to become less discriminatory and more inclusive. An element of fluidity in the notions of sex and gender is increasingly claimed, and the binary divide, while sustained for most people, is now perceived as less rigid.

An intersex person may have been identified at birth as a baby girl and raised and socialised as female. She will be regarded by the legal system governing her personal status (in this case, the country of birth) as female and is eligible for participation in women's sports competitions. Mass sex testing at major sports events is no longer employed, but some international sports governing bodies reserve the right to investigate 'suspicious' cases and engage in more limited screening. As explained in Chapter 30, some, but not all, intersex conditions are claimed to provide performance advantages associated with male characteristics.

In recent years, attention has focused on hyperandrogenism-the natural production of testosterone by a woman at levels regarded as above normal. In 2011, the International Association of Athletics Federations (IAAF) made rules that rendered ineligible any woman who was hyperandrogenic to the specified degree; the rules did not purport to claim that she was a man. Symmetry with anti-doping rules that prohibited the administration of testosterone exogenously was suggested. However, the rules were successfully challenged before CAS in 2015 for lacking an appropriate scientific foundation.[119] In April 2018, new rules for female eligibility with respect to hyperandrogenism were announced by the IAAF, and promptly subjected to criticism.[120] This led to a further challenge with CAS,[121] which failed. CAS is situated within the Swiss city of Lausanne and therefore falls under Swiss Law. An appeal against the CAS decision was subsequently lodged with the Swiss Federal Tribunal (Supreme Court), and at the time of publishing remains ongoing.[122] The future of such rules remains unclear in the current context.

A growing number of legal systems offer recognition for people who are transgender, enabling them to obtain the legal status of the sex/gender with which they associate. Recognition may be subject to conditions (such as divorce, in nations that do not permit same-sex marriage) and the requirement of surgical intervention. The International Olympic Committee has issued guidelines for the participation of transgender people in sports competition, which include requirements governing testosterone levels that do not necessarily hinge on surgical intervention.[123]

The rules of sports governing bodies that might apply to participation by intersex and

transgender athletes must operate within the framework of the applicable local legal system. Those frameworks adopt widely varying positions, ranging from outlawing discrimination against intersex and transgender people in a wide range of walks of life (including sport), to offering no protection. The former extreme would likely bring down the IAAF hyperandrogenism rules. One solution is for local laws to afford sufficient flexibility to accommodate a position ultimately reached by a sport's governing body without causing confusion and conflict, although some legal systems may not necessarily agree with the sport's position and would be unwilling to grant such flexibility.

Pregnancy

The objective of eliminating discrimination against women extends to those who are pregnant or might become pregnant.[124] Many legal issues are raised by a pregnant woman's participation in sport that cannot be covered here;[125] but to exclude her from sports participation may breach human rights law.[126] The potential benefits and risks of sport and physical activity for a pregnant woman were considered in Chapter 29. The important task for the sports clinician who is caring for a pregnant athlete is to be sure that she is aware of the risks and benefits of sports participation to her and her unborn child, so that she may make an informed decision. It is suggested that clinicians refer to the legal rules and approaches discussed above regarding the provision of information and advice.

Disability

The purpose of the Convention on the Rights of Persons with Disabilities 'is to promote, protect and ensure the full and equal enjoyment of all human rights and fundamental freedoms by all persons with disabilities and to promote respect for their inherent dignity'. Article 30 paragraph 5 (a) obliges state parties 'to encourage and promote the participation, to the fullest extent possible, of persons with disabilities in mainstream sporting activities at all levels'. As with CEDAW, this convention has been adopted by many nation states and implemented through legislation.[110] The International Paralympic Games, held in conjunction with the Olympic Games, have contributed to increased awareness of disabled athletes and advanced the purpose of the convention.

The term 'disability' includes both physical and mental conditions, those which are permanent or passing, and illnesses. Exclusion or less favourable treatment of a person with a disability is unlawful where the convention or similar legislation applies. The US Supreme Court once famously ruled that professional golfer Casey Martin could ride on a golf cart while his opponents walked because he suffered from a circulatory disorder in his legs.[127] Some exceptions are usually recognised. These may include instances where it is not reasonable to require the disabled person's needs to be accommodated if the person is to participate or the disabled person is unable to perform the tasks expected when participating in the sport (perhaps thereby representing a danger to other participants or themselves). Local legal advice should be sought on the extent of any exceptions.

The sports clinician plays an important role in medico-legal issues concerning disabled athletes. Arguably the most important function concerns the provision of information and advice to an athlete who has a condition that indicates he or she should retire from the sport or at least forgo a demanding professional or elite career. Legal liability for negligent advice in these circumstances has been discussed above.

The same clinician may also be called upon to participate in a decision about whether the athlete should be excluded from the competition in cases where the athlete (after taking account of the proffered advice) makes an informed decision to continue playing. Should the clinician respect and support the athlete's decision while perhaps disagreeing with it, or recommend to the team that the athlete be excluded? Whose interests are protected—the athlete's or the team's? Teams will not wish to see a player die on the field of play from cardiac arrest or similar in front of television cameras. In those circumstances, the preferable path would be for the clinician to recommend obtaining another opinion regarding any exclusion decision.

Exclusion from playing sport of an athlete with an infectious disease, such as chickenpox, does not offend anti-discrimination law, because of the higher interest of public health involved.[128] Managing more serious illnesses, such as HIV and hepatitis, presents complex legal problems on which local legal advice should be taken.[129, 130]

Finally, sports clinicians are involved in the process of grading athletes for the purposes of Paralympic competition categories.

SUMMARY

The preceding pages introduce some of the key concepts and issues in an increasingly complex sports medico-legal environment. It is hoped that sports clinicians will be active players in developing legal and regulatory models that advance the cause of athlete health and welfare and meet the needs of the profession.

REFERENCES

1. Weistart J, Lowell C. *The law of sports*. Charlottesville, VA: Michie Company, 1979: 984–96.
2. Barnes J. *Sports and the law in Canada*. Toronto: Butterworths, 1983: 332–5.
3. Kelly G. *Sport and the law: An Australian perspective*. Sydney: Law Book Co, 1987: 172–6.
4. Grayson E. *Sport and the law*. London: Butterworths, 1988: 218–36.
5. Opie H. Legal requirements. In: Zuluaga M et al. *Sports Physiotherapy*. Melbourne: Churchill Livingstone, 1995: 739–59.
6. Grayson E. Sports medicine and the law. In: Payne S, ed. *Medicine, sport and the law*. Oxford: Blackwell Scientific, 1990: 3–50.
7. Pitt M. Malpractice on the sidelines: developing a standard of care for team sports

physicians. *COMM/ENT, J Comm Entertain Law* 1980; 2: 579–600.

8. King J. The duty and standard of care for team physicians. *Houston Law Rev* 1981; 18: 657–705.
9. Grayson E. *Ethics, Injuries and the law in sports medicine*. Oxford: Butterworth Heinemann, 1999.
10. Opie H. Medico-legal issues in sport: the view from the grandstand. *Sydney Law Rev* 2001; 23: 375–404.
11. Mitten M. Emerging legal issues in sports medicine: a synthesis, summary and analysis. *St John's Law Rev* 2002; 76: 5–86.
12. Stebbings P. Shanghai SIPG's million-euro Brazilian 'miracle doctor'. *Agence France Presse*, 30 March 2018. https://au.news.yahoo.com/shanghai-sipgs-million-euro-brazilian-miracle-doctor-39676897.html, accessed 30 June 2018.
13. Matheson G. Can team physicians buy credibility? *Phys Sportsmed* 2001; 29(12): 3.
14. Pavitt M. UCI announce appointment of Bigard as medical director. *Inside the Games*, 10 April 2018. https://www.insidethegames.biz/articles/1063770/uci-announce-appointment-of-bigard-as-medical-director, accessed 30 June 2018.
15. Palmer D. Nassar sentenced to another 40 to 125 years for abuse of gymnasts. *Inside the Games*, 6 February 2018. https://www.insidethegames.biz/articles/1061146/nassar-sentenced-to-another-40-to-125-years-for-abuse-of-gymnasts, accessed 30 June 2018.
16. International Federation of Sports Medicine (FIMS). Code of Ethics. http://www.fims.org/about/code-ethics/, accessed 30 June 2018.
17. European Union Agency for Fundamental Rights. Age at which children can consent to medical treatments, including diagnosis and surgery, without parental consent. 14 November 2017. http://fra.europa.eu/en/publications-and-resources/data-and-maps/minag?dataSource=MINAG_en_62756&media=png&width=740&topic=group05&question=MINAG_HE01&plot=MAP&subset=NONE&subsetValue=NONE&answer=MINAG_HE01&year=2017, accessed 30 June 2018.
18. *Minors (Property and Contracts) Act 1979* (NSW), s. 49(2).
19. Schlam L, Wood J. Informed consent to the medical treatment of minors: law and practice. *Health Matrix: Journal of Law-Medicine* 2000; 10:141.
20. Hill J. Medical decision making by and on behalf of adolescents: reconsidering first principles. *Journal of Health Care & Policy* 2012; 15:37.
21. *Gillick v West Norfolk and Wisbech Area Health Authority* [1986] AC 112 (House of Lords, UK).
22. *Secretary, Department of Health and Community Services v JWB (Marion's Case)* (1992) 175 CLR 218 (High Court of Australia).
23. *Health and Safety Code*, §1799.102 (2009) (California, USA).

24. *Good Samaritan Act, 2001*, SO 2001, c. 2 (Ontario, Canada).
25. *Civil Liability Act 2002* (NSW), Pt 8.
26. *Bolam v Friern Hospital Management Committee* [1957] 1 WLR 582 (McNair J, Queen's Bench, England).
27. Australasian College of Sport and Exercise Physicians. Training program. https://www.acsep.org.au/page/about/education-and-training, accessed 30 June 2018.
28. *Wrongs Act 1958* (Vic.), s. 59.
29. *Hall v Thomas* [2014] EWHC 1625 (High Court Queen's Bench Division, England and Wales), at para. 16.
30. *Geysen v Australian Capital Territory* [2006] ACTSC 21 (Supreme Court, Australian Capital Territory).
31. *Robitaille v Vancouver Hockey Club Ltd* (1981) 124 DLR (3d) 228 (Court of Appeal, British Columbia, Canada).
32. *Hamed v Mills* [2015] EWHC 298 (High Court Queen's Bench Division, England and Wales).
33. *Welch v Dunsmuir Joint Union High School District* 326 P2d 633 (1958) (Court of Appeal Third District, California, USA).
34. *Watson v British Boxing Board of Control* [2001] QB 1134 (Court of Appeal, England and Wales).
35. *Appleton v El Safty* [2007] EWHC 631 (High Court Queen's Bench Division, England and Wales).
36. *Morrow v Outerbridge* [2009] BCSC 433 (Supreme Court, British Columbia, Canada).
37. *Hall v Thomas* [2014] EWHC 1625 (High Court Queen's Bench Division, England and Wales).
38. McKimmie D, Macnamara J. Physiotherapists and medical negligence. *Plaintiff* (1998) April: 24–5.
39. Opie, H. The team/doctor/athlete legal relationship. *Sports Train Med Rehab* 1991; 2: 287.
40. *Standards for Privacy of Individually Identifiable Health Information* ('Privacy Rules') issued under the *Health Insurance Portability and Accountability Act of 1996* (USA), Public Law 104–191.
41. Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data (General Data Protection Regulation), in force 25 May 2018.
42. *Access to Health Records Act 1990* (UK).
43. *Health Information Privacy Code* issued under the *Privacy Act 1993* (NZ).
44. Anderson L, Jackson S. Competing loyalties in sports medicine: threats to medical

professionalism in elite, commercial sport. *Int Rev Soc Sport* 2012; 48(2): 238–56.

45. Keim T. Physicians for professional sports teams: health care under the pressure of economic and commercial interests. *Seton Hall J Sport Law* 1999; 9(1): 196–225.
46. Polsky S. Winning medicine: professional sports team doctors' conflicts of interest. *J Contemp Health L & Pol'y* 1998; 14(2): 503–29.
47. Mitten M, Davis T, Smith R et al. *Sports law and regulation*. 4th ed. New York: Wolters Kluwer, 2017: 923.
48. Barnes J. *The law of hockey*. Toronto, Canada: LexisNexis, 2010: 258.
49. Reuters. Chelsea's former doctor Eva Carneiro settles case against Jose Mourinho. ABC News Online, 8 June 2016. http://www.abc.net.au/news/2016-06-08/former-chelsea-doctor-eva-carneiro-settles-against-jose-mourinho/7488772?section=sport.
50. Osborne B. Legal and ethical implications of athletes' biometric data collection in professional sport. *Marquette Sports L J* 2017; 28(1): 37–84.
51. Kim WS, Nelson P. Wearable technology fits into professional sport. Data Security Law Blog, 14 May 2018. https://www.jdsupra.com/legalnews/wearable-technology-fits-into-39987/, accessed 30 June 2018.
52. *Crimes Act 1900* (NSW), s. 193Q(2).
53. *Krueger v San Francisco Forty Niners* 234 Cal Rptr 579, 584 (1987) (Court of Appeal First District, California, USA).
54. *West Bromwich Albion Football Club Limited v El-Safty* [2006] EWCA Civ 1299 (Court of Appeal, England and Wales).
55. FIFPro. Alarming number of ex-pros suffer knee damage. 5 April 2018. https://www.fifpro.org/news/alarming-number-of-ex-pros-suffer-knee-damage/en/.
56. Fernandes GS, Parekh SM, Moses J et al. Prevalence of knee pain, radiographic osteoarthritis and arthroplasty in retired professional footballers compared with men in the general population: a cross-sectional study. *Br J Sports Med* 2018; 52(10): 678–83.
57. Burry HC, Gowland H. Cervical injury in rugby football—a New Zealand survey. *Br J Sports Med* 1981; 15(1): 56–9.
58. Kew T, Noakes TD, Kettles AN et al. A retrospective study of spinal cord injuries in Cape Province rugby players, 1963–1989. *S Afr Med J* 1991; 80: 127–33.
59. Rotem T, Lawson JS, Wilson SF et al. Severe cervical spinal cord injuries related to rugby union and league football in New South Wales 1984–1996. *Med J Aust* 1998; 168(8): 379–81.
60. *Watson v Haines* (1987) Aust Torts Reports 80-094 (Supreme Court of New South Wales).
61. *Van Oppen v Clerk to the Bedford Charity Trustees* [1989] 3 All ER 389 (Court of Appeal, England and Wales).

62. *Hamstra v British Columbia Rugby Union* (1995) 123 DLR (4th) 693 (Court of Appeal, British Columbia, Canada).
63. *Agar v Hyde* (2000) 201 CLR 552 (High Court of Australia).
64. Opie H. The sport administrator's charter: *Agar v Hyde*. *Torts Law J* 2001; 9(2): 131–51.
65. Reboursiere E, Bohu Y, Retière D et al. Impact of the national prevention policy and scrum law changes on the incidence of rugby-related catastrophic cervical spine injuries in French rugby union. *Br J Sports Med* 2018; 52(10): 674–7.
66. Grayson E. *Ethics, injuries and the law in sports medicine*. Oxford: Butterworth Heinemann, 1999: 99–101.
67. Belson K. First NFL concussion payments are approved, but some may miss out. *New York Times*, 4 August 2017. https://www.nytimes.com/2017/08/04/sports/football/nfl-concussion-settlement-player-registration.html, accessed 30 June 2018.
68. NFL Concussion Settlement. https://www.nflconcussionsettlement.com/, accessed 30 June 2018.
69. Barca J. The NFL's new targeting rule will save football. *Forbes*, 31 March 2018. https://www.forbes.com/sites/jerrybarca/2018/03/31/the-nfls-new-targeting-rule-will-save-football/#68e49e377d57, accessed 30 June 2018.
70. Football Players Health Study at Harvard University. 2017. Petrie-Flom Center for Health Law Policy, Biotechnology and Bioethics. http://petrieflom.law.harvard.edu/research/fphs, accessed 30 June 2018.
71. Kim S, Connaughton DP, Spengler J et al. Legislative efforts to reduce concussions in youth sports: an analysis of state concussion statutes. *J Legal Aspects Sport* 2017; 27(2): 162–86.
72. Lau C. Leaders and laggards: tackling state legislative responses to the youth sports concussion epidemic. *Fordham L Rev* 2017; 85(6): 2879–913.
73. Shen F. Are youth sports concussion statutes working? *Duquesne L Rev* 2018; 56(1): 7–33.
74. Greenhow A, Gowthorp L. Head injuries and concussion issues. In: Schulenkorf N, Frawley S, eds. *Critical issues in global sport management*. Abingdon, UK: Routledge, 2017: 93–111.
75. Aubry M, Cantu R, Dvorak J et al. Summary and agreement statement of the 1st International Symposium on Concussion in Sport, Vienna 2001. *Clin J Sport Med* 2002; 12: 6–11.
76. McCrory P, Meeuwisse W, Dvorak J et al. Consensus statement on concussion in sport—the 5th International Conference on Concussion in Sport, held in Berlin, October 2016. *Br J Sports Med* 2017; 51(11): 838–47.
77. Patricios J, Ardern C, Hislop M et al. Implementation of the 2017 Berlin Concussion in Sport Group Consensus Statement in contact and collision sports: a joint position statement from 11 national and international sports organisations. *Br J Sports Med*

2018; 52: 635–41.

78. International Olympic Committee (IOC). Olympic Charter—in force as from 15 September 2017, rule 43. https://stillmed.olympic.org/media/Document%20Library/OlympicOrg/General/EN-Olympic-Charter.pdf#_ga=2.178935524.1759902822.1538638177-159776511.1538035184.
79. Major League Baseball's Joint Drug Prevention and Treatment Program. http://www.mlb.com/pa/pdf/jda.pdf, accessed 30 June 2018.
80. Mitten M, Davis T, Smith R et al. *Sports law and regulation*. 4th ed. New York: Wolters Kluwer, 2017: 511–19.
81. International Convention against Doping in Sport, signed 19 October 2005, 2419 UNTS 201 (entered into force 1 February 2007).
82. United Nations Educational, Scientific and Cultural Organization (UNESCO). International Convention against Doping in Sport. http://www.unesco.org/new/en/social-and-human-sciences/themes/anti-doping/international-convention-against-doping-in-sport/, accessed 30 June 2018.
83. World Anti-Doping Agency (WADA). The World Anti-Doping Code (WADC) 2015 with 2018 amendments, art. 20.7. https://www.wada-ama.org/sites/default/files/resources/files/wada_antidoping_code_2018_english_final.pdf.
84. Mitten M, Opie H. 'Sports law': implications for the development of international, comparative and national law and global dispute resolution. *Tulane Law Rev* 2010; 85: 269, 274–83.
85. Kamber M. Development of the role of national anti-doping organisations in the fight against doping: from past to future. *Forensic Sci Int* 2011; 213: 3.
86. David P. *A Guide to the World Anti-Doping Code*. 3rd ed. Cambridge: Cambridge University Press, 2017.
87. Flint C, Lewis A, Taylor J. The fight against doping in sport: the regulatory framework. In: Lewis A, Taylor J, eds. *Sport: Law and Practice*. 3rd ed. Haywards Heath, UK: Bloomsbury Professional, 2014: 135–204.
88. Flint C, Lewis A, Taylor J. Bringing and defending anti-doping cases. In: Lewis A, Taylor J, eds. *Sport: Law and Practice*. 3rd ed. Haywards Heath, UK: Bloomsbury Professional, 2014: 412–660.
89. World Anti-Doping Agency (WADA). The World Anti-Doping Code (WADC) 2015 with 2018 amendments, comment to art. 2.1.1. https://www.wada-ama.org/sites/default/files/resources/files/wada_anti-doping_code_2018_english_final.pdf.
90. David P. *A guide to the World Anti-Doping Code*. 3rd ed. Cambridge: Cambridge University Press, 2017: 46–50, 182–3.
91. Viret M. *Evidence in anti-doping at the intersection of science and law*. The Hague, Netherlands: Asser Press, 2016: 727–78.
92. *Raducan v International Olympic Committee* CAS OG/00/011, 28 September 2000 (Court

of Arbitration for Sport).

93. *International Ski Federation v Johaug* CAS 2017/A/5015, 21 August 2017 (Court of Arbitration for Sport).
94. Tibballs G. *Great sporting scandals*. London: Robson Books, 2003: 173–5.
95. *Aloyan v International Olympic Committee* CAS 2017/A/4927, 16 June 2017 (Court of Arbitration for Sport).
96. World Anti-Doping Agency (WADA). The World Anti-Doping Code (WADC) 2015 with 2018 amendments, arts 10.4 and 10.5 and comment to art. 10.4. https://www.wada-ama.org/sites/default/files/resources/files/wada_anti-doping_code_2018_english_final.pdf.
97. Vines P. Doping as tort: liability of sports supervisors and the problem of consent. In: Hass U, Healey D, eds. *Doping in sport and the law*. Oxford: Hart Publishing, 2016: 189–203.
98. World Anti-Doping Agency (WADA). The World Anti-Doping Code (WADC) 2015 with 2018 amendments, Appendix One. https://www.wada-ama.org/sites/default/files/resources/files/wada_anti-doping_code_2018_english_final.pdf.
99. International Federation of Sports Medicine. Position Statement on Drugs in Sport. http://www.fims.org/files/4414/2056/2561/PS13-Statement-on-Doping-in-Sport.pdf, accessed 30 June 2018.
100. *Gibilisco v Comitato Olimpico Nazionale Italiano (CONI)* CAS 2007/A/1426, 9 May 2008 (Court of Arbitration for Sport).
101. *United States Anti-Doping Agency v Leinders* AAA No 77-20-1300-0604, 15 January 2015 (American Arbitration Association).
102. World Anti-Doping Agency (WADA). The World Anti-Doping Code (WADC) 2015 with 2018 amendments, art 10. https://www.wada-ama.org/sites/default/files/resources/files/wada_anti-doping_code_2018_english_final.pdf.
103. *Medical Board of Australia v Singh* [2017] WASAT 33 (State Administrative Tribunal, Western Australia).
104. Butler N. British doctor who boasted about doping 150 athletes struck off medical register. *Inside the Games*, 9 March 2018.
105. Reuters. Juventus doctor jailed in doping case. *Eurosport*, 26 November 2004.
106. Juventus doctor wins doping appeal. *UEFA.com*, 14 December 2005.
107. Tremlett G. Doping doctor Eufemiano Fuentes given one-year prison sentence. *The Guardian*, 30 April 2013.
108. Haas U. Revising the World Anti-Doping Code. In: Hass U, Healey D, eds. *Doping in sport and the law*. Oxford: Hart Publishing, 2016: 19, 29–31.
109. *Canadian Charter of Rights and Freedoms*, 1982, s. 15(1).
110. *Disability Discrimination Act 1992* (Cth) (Australia).

111. Harcourt P, Unglik H, Cook J. A strategy to reduce illicit drug use is effective in elite Australian football. *Br J Sports Med* 2012; 46(13): 943–5.
112. Charter of the United Nations. 1945. https://treaties.un.org/doc/publication/ctc/uncharter.pdf, accessed 29 June 2018.
113. International Charter of Physical Education and Sport (adopted by the UNESCO General Conference at its thirty-eighth session, Paris, 18 November 2015), art. 1.1.
114. International Olympic Committee (IOC). Fundamental Principles of Olympism. Olympic Charter—in force as from 15 September 2017: 11–12. https://stillmed.olympic.org/media/Document%20Library/OlympicOrg/General/EN-Olympic-Charter.pdf#_ga=2.178935524.1759902822.1538638177-159776511.1538035184.
115. *Sex Discrimination Act 1984* (Cth), s. 42 (Australia).
116. *Human Rights Act 1993* (NZ), s. 49(1).
117. *Equality Act 2010* (UK), s. 195.
118. *Jernakoff v Western Australian Softball Association Inc* (1999) EOC ¶92-981 at 79 231 (Equal Opportunity Tribunal, Western Australia).
119. *Chand v Athletics Federation of India* CAS 2014/A/3759, 24 July 2015 (Court of Arbitration for Sport).
120. Koh B, Adair D, Elphick L. Not by gender, not by sex, but by testosterone saith the IAAF: international athletics and the new female eligibility regulations. *Law In Sport*, 25 May 2018.
121. Caster Semenya challenges the IAAF eligibility regulations for female classification at the Court of Arbitration for Sport. Media release. Court of Arbitration for Sport, 19 June 2018.
122. Imray G. 'IAAF won't drug me:' Caster Semenya appeals testosterone ruling. The Associated Press, 29 May 2019. https://www.cbc.ca/sports/olympics/trackandfield/semenya-appeal-court-of-arbitration-for-sport-1.5154607.
123. International Olympic Committee (IOC). IOC Consensus Meeting on Sex Reassignment and Hyperandrogenism. November 2015. https://stillmed.olympic.org/Documents/Commissions_PDFfiles/Medical_commission/2015-11_ioc_consensus_meeting_on_sex_reassignment_and_hyperandrogenism-en.pdf, accessed 30 June 2018.
124. *Human Rights Code 1990*, s. 10(2) (Ontario, Canada).
125. Werren J. Law, pregnancy and sport: what are the repercussions when a pregnant lady plays? *J Law Med* 2006; 14(1): 45–63.
126. *Gardner v All Australia Netball Association Ltd* (2003) 197 ALR 28 (Federal Magistrates Court, Australia).
127. *PGA Tour Inc v Martin* 532 US 661 (2001) (USA).
128. *Human Rights Act 1993* (NZ), s. 49(3).

129. Magnusson R, Opie H. HIV and hepatitis in sport: a legal framework for resolving hard cases. *Monash Uni L Rev* 1994; 20(2): 214–70.
130. Mitten M. AIDS and athletics. *Seton Hall J Sport Law* 1993; 3(1): 5–40.

Chapter 37

Harassment and abuse

with MARGO MOUNTJOY and JENNY SHUTE

You used that position of trust that you had in the most vile way to abuse children. You violated the oath that you took, which is to do no harm, and you harmed them selfishly.

Judge Rosemarie Aquilinar, in the trial of Larry Nassar

On 22 November 2017, Dr Larry Nassar, former team physician for the US Olympic gymnastics team, admitted to using his position to sexually abuse underage girls. More than 250 victims reported assaults. In the words of one of his victims, '. . . Larry is disgusting. Larry is a MONSTER and not a doctor'.[1] Attorney John Manley identified three institutions that 'miserably failed' to protect children under their care: USA Gymnastics, the US Olympic Committee and Michigan State University.[2]

This tragic case of sexual abuse in sport clearly demonstrates the necessity for clinicians to not only be aware of their own professional boundaries and codes of conduct, but also be proficient in the prevention, identification and treatment/management of disclosures of harassment and abuse. Most postgraduate sport medicine training programs do not include athlete safeguarding in their curriculum as a required competency. The objectives of this chapter are thus designed to fill this gap in education. Readers will gain an understanding of the following relevant topics in athlete safeguarding:

- what is harassment and abuse in sport
- types of harassment and abuse (non-accidental violence)
- delivery mechanisms of harassment and abuse
- the scientific base underpinning the field of harassment and abuse in sport
- the consequences of harassment and abuse for athletes, the entourage and sport
- prevention principles of harassment and abuse

- clinical management of allegations of harassment and abuse.

WHAT IS HARASSMENT AND ABUSE IN SPORT?

Harassment and abuse in sport is rooted in failed leadership where there is an abuse of power within an organisational culture with inadequate athlete protection policies and attitudes of passive indifference, denial or silence.[3] All forms of harassment and abuse arise when there is an actual or perceived inequality of power and trust in the relationship between the individuals concerned. The International Olympic Committee (IOC) has developed a conceptual model to demonstrate the cultural context, the forms of harassment and abuse, the mechanisms and the impacts.

To facilitate an understanding of the terminology of the field, in its consensus statement on harassment and abuse in sport the IOC adopted agreed definitions (see box below).

Two more terms in frequent use in the field are 'violence' and 'safeguarding'. The range of the various forms of physical, sexual and psychological abuse in sport is often referred to as 'non-accidental violence', or simply 'violence', to be consistent with the terminology used by other advocacy agencies in the field of safeguarding, including UNICEF and Safe Sport International.[5] In some countries, 'safeguarding' is the term used to refer to all aspects of the prevention of harassment and abuse in sport. The full term used by the IOC is 'safeguarding athletes from harassment and abuse'.[6]

TYPES OF HARASSMENT AND ABUSE (NON-ACCIDENTAL VIOLENCE)

As illustrated in Figure 37.1, there are four main types of harassment and abuse, each of which may take place separately or in combination, and each of which may occur once, repeatedly, or continuously.[4]

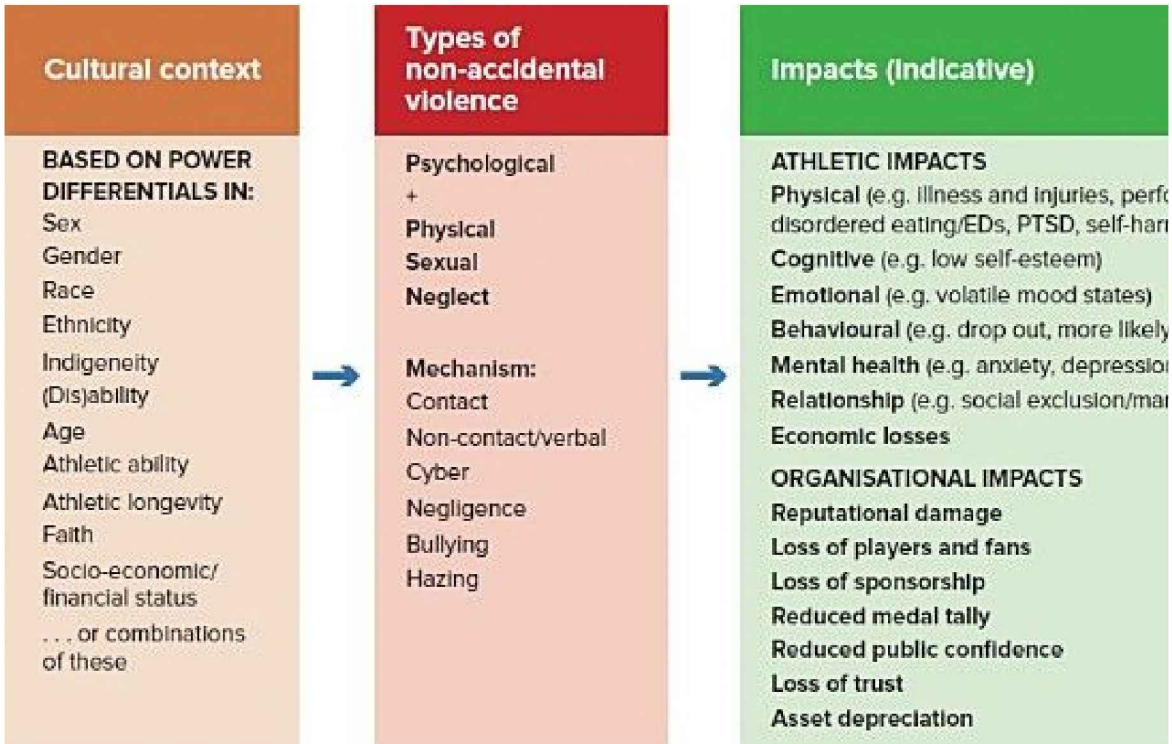


Figure 37.1 Conceptual model of harassment and abuse in sport showing cultural context, types of non-accidental violence, mechanisms and impacts

ADAPTED FROM MOUNTJOY M ET AL.[4]

ED = eating disorder; PTSD = post-traumatic stress disorder; STI = sexually transmitted infection

IOC definitions for harassment and abuse[4]

Athletes with disabilities—*Those who have long-term physical, mental, intellectual or sensory impairments that, in interaction with certain barriers, may hinder their full and effective participation in society on an equal basis with others.*

Bullying—*Bullying (or cyber-bullying if conducted online) is unwanted, repeated and intentional, aggressive behaviour usually among peers, and can involve a real or perceived power imbalance. Bullying can include actions such as making threats, spreading rumours or falsehoods, attacking someone physically or verbally and deliberately excluding someone.*

Child and adolescent—*Every human being below the age of 18 years unless, under the law applicable to the child, majority is attained earlier. Early childhood relates to those below 8 years of age. Juvenile or young person and adolescents are 10— 19 years of age.*

Hazing—*An organised, usually team-based, form of bullying in sport, involving degrading and hazardous initiation of new team members by veteran team members.*

Homophobia—*Antipathy, contempt, prejudice, aversion or hatred towards lesbian, gay or bisexual individuals.*

Neglect—*The failure of parents or caregivers to meet a child's or athlete's physical and emotional needs or failure to protect a child or athlete from exposure to danger. This definition equally applies to coaches and athlete entourages.*

Negligence—*Acts of omission regarding athlete safety. For example, depriving an athlete of food or drink; insufficient rest and recovery; failure to provide a safe physical training environment; or developmental age-inappropriate or physique-inappropriate training methods.*

Physical abuse—*Non-accidental trauma or physical injury caused by punching, beating, kicking, biting, burning or otherwise harming an athlete. This could include forced or mandated inappropriate physical activity (e.g. age-inappropriate or physique-inappropriate training loads; when injured or in pain); forced alcohol consumption; or systematic doping practices.*

Psychological abuse—*A pattern of deliberate, prolonged, repeated non-contact behaviours within a power-differentiated relationship. This form of abuse is at the core of all other forms. Some definitions refer to emotional or psychological abuse interchangeably. The term psychological abuse is used in recognition that the psyche consists of more than emotions. It also consists of cognitions, values and beliefs about oneself, and the world. The behaviours that constitute psychological abuse target a person's inner life in all its profound scope.*

Safe sport—*An athletic environment that is respectful, equitable and free from all forms of non-accidental violence to athletes.*

Sexual abuse—*Any conduct of a sexual nature, whether non-contact, contact or penetrative, where consent is coerced/manipulated or is not or cannot be given.*

Sexual harassment—*Any unwanted and unwelcome conduct of a sexual nature, whether verbal, non-verbal or physical.*

Psychological abuse and harassment

Psychological abuse is believed to be the gateway of all other forms of harassment and abuse in sport, given that all other forms of abuse and harassment are predicated on psychological underpinnings. It is recognised that psychological harassment and abuse affects the victim's emotions but may also affect the full spectrum of the different aspects of the psyche, including cognition, values and self-belief. Psychological abuse may involve one or more negative behaviours, including isolation, confinement, verbal assault, humiliation, threatening, or conversely, psychological abuse may involve passive behaviours such as ignoring or denying the athlete attention and/or support. 'Emotional abuse' is a term that has sometimes been used interchangeably with psychological abuse.[7] Normalisation of psychological abusive coaching practices prevents athlete disclosure. It has also been reported to mask sexual abuse grooming

practices.[8]

Physical abuse

Physical abuse in sport can occur on or off the field of play. Physical abusive practices in sport can be categorised as being either:

- direct-in the form of hitting, kicking, beating and forced doping practices. Extreme cases of hazing have led to severe physical consequences, including alcohol poisoning
- indirect-examples include forced over-training, age-inappropriate training loads, return to active sports participation too soon after injury, exposure to excessive heat or cold.

Reported perpetrators of physical abuse in sport include coaches, other members of the entourage, teammates, members of the public and team physicians. Team physicians have a major part to play in recognition and prevention of this type of abuse.[9]

Sexual harassment and abuse

Sexual abuse and harassment in sport were the first relational threats to children that were identified in the scientific literature.[10] Sexual harassment includes any unwelcome verbal or physical conduct that causes offence or humiliation to another person, whether through sexual jokes, gestures, threats or intimidation. It has been simply defined by Brackenridge (1997) as unwanted attention based on sex.[11] As with other forms of harassment and abuse, sexual harassment arises when there is unequal power and trust within a relationship and is manifested in conduct of a sexual nature that the victim or observers perceive as being unwanted or coerced. Sexual harassment includes homophobia (ranging from passive resentment to active victimisation of LGBT [lesbian, gay, bisexual, transgender] athletes), gender harassment (derogatory treatment of one gender or another) and hazing rituals, which often have a sexual component.[4]

Sexual abuse is an extension of sexual harassment and has been described by Brackenridge as groomed or coerced collaboration in sexual and/or genital acts where the victim has been entrapped by the perpetrator.[11] The grooming process for sexual abuse in sport is similar to the perpetrator methodology employed by perpetrators outside of sport, wherein the abuse is generally preceded by a period of grooming. During the grooming period, the perpetrator isolates the athlete, builds an emotional connection with the athlete in order to gain their trust, desensitises him or her and subsequently entraps and entices them to submit to sexual abuse or exploitation. Athletes are silenced by this grooming process and made to feel guilty and responsible.[12]

Neglect

While the definition of'neglect' outside of sport refers to the absence of protection of a child's needs by a parent or caregiver, in sport, neglect is modified to identify the victim as an athlete of any age and to identify the perpetrator as a coach or other member of the athlete's entourage. Thus, neglect in sport results from the failure of a coach, team physician or other person or sport

organisation with a duty of care to an athlete to sufficiently protect them from harm and risk. It includes the failure to ensure adequate hydration and nutrition, access to medical care and protection from exposure to excessive cold or heat. Neglect of duty of care may include sanctioning of age-inappropriate training loads and return to play too soon after injury, with insufficient time for recovery.[4] Neglect may also include the failure to provide a safe sporting environment, including both appropriate equipment and implementation of sport rules.[13] As a form of abuse, neglect can overlap with physical abuse. It is important to note that neglect of a child or adolescent athlete may have a greater impact than on an adult athlete, given the particular vulnerabilities of the youth athlete's psychological and physical development.[14] Neglect of athletes' needs can negatively affect the athlete's physical, educational, psychological or social development.[15]

A review by Mountjoy et al. (2015) presented a categorisation framework of the various forms of violence within the sporting context.[16] The framework differentiates between individual threats (often self-induced as a result of psychological trauma from abuse), relational threats (e.g. abuse between individuals; sometimes referred to as interpersonal violence) and organisational threats (caused by system failures) (Table 37.1). While that publication refers to the child athlete, this framework is relevant for all athletes and serves to ensure that all aspects of harassment and abuse are recognised. For the sport medicine clinician, all three categories are pertinent. The case of Dr Nassar presented in the introduction is an example of a relational threat, while the inaction of USA Gymnastics represents an organisational threat.

Table 37.1 Categorisation of the various forms of violence that threaten athletes

Individual	Relational	Organisational
Injury	Sexual harassment	Abuse from spectators
Depression	Sexual abuse	Discrimination
Self-harm	Physical abuse	Cultures which normalise abuse
Eating disorders	Forced physical exertion	Unhealthy training programmes
Disordered eating	Emotional abuse	Hazing
	Virtual maltreatment	Medical mismanagement
	Neglect	Systematic doping
	Bullying	Age cheating—altering documents to allow over- or underage competitors
	Doping	Inadequate provision of safe sporting environment*

DELIVERY MECHANISMS OF HARASSMENT AND ABUSE

As seen in the IOC conceptual model, there are several mechanisms through which harassment and abuse are expressed. The IOC has defined six mechanisms of expression of the forms of abuse, which, while distinct, are often utilised by perpetrators in combination. These mechanisms are:

- contact-direct physical contact between the perpetrator and victim[17]
- non-contact-indirect contact, often in the form of verbal abuse or 'trash talk'[18]

*'Inadequate provision of safe sporting environment'was not included in the original cited publication.

- *cyber mechanisms-the* use of social media for the purpose of grooming, sexting, corruption and unwanted negative content (e.g. hate messaging)[19]
- *negligence-failure* to provide a safe sporting environment[20]
- bullying-repetitive actions with the intent to taunt the victim, categorised into psychological, physical or social bullying[21]
- hazing-semi-covert initiation practices, most common in North America.[22]

Although the scientific evidence in the field of harassment and abuse in sport is not fully developed, there is much that is known. In some areas, there is little empirical data, while in other areas, comparison of research studies has proven difficult because of the widely differing means of collection and collation of data.

Harassment and abuse is known to take place at all levels within sport. Elite athletes are not exempt and are actually more vulnerable to psychological, physical and sexual abuse.[23, 24] Harassment and abuse are believed to be present in all sports and in all countries.[23, 25–28] Numerous sports have never reported incidents of harassment or abuse. Unfortunately this may be a symptom of many organisations lacking the appropriate systems to facilitate detection and/or encourage whistle-blowing.[29]

Psychological harassment and abuse

Psychological harassment and abuse is the most prevalent safeguarding concern within youth sport. Indeed, a large retrospective study of over 6000 young people in the UK and found 75% had experienced psychological abuse within organised youth sport.[30] In these instances, perpetrators were most commonly peers or teammates (around 80%). Roughly a third of young respondents also said that a coach was involved, more commonly as the athlete rose through the competitive ranks.[30]

Sexual harassment and abuse

Sexual harassment and abuse are seen in all sports, at all levels, with prevalence demonstrably greater in elite sport. Athletes with disabilities and LGBT athletes are at higher risk. Fasting et al. (2010) showed that, out of 595 women from the Czech Republic who were involved in sport at varying levels of competence, the chances of being harassed by someone in sport increased with performance levels, from 29.7% among those who participated on a recreational basis to 55.2% among the elite-level athletes.[23] Entourage members in positions of power and authority are often perpetrators of sexual harassment and abuse, although peer athletes remain the most likely offenders. Males are more often perpetrators of sexual abuse than females, although there have been reports of male victimisation that have somewhat changed this perception.[23] In a retrospective study, Vertommen et al. (2015) showed significantly higher levels of interpersonal harassment and abuse (psychological, sexual and physical) among disabled, LGBT, ethnic minority

and elite young athletes.[24] In this study, youth athletes with a disability experienced two to three times the risk of encountering psychological, physical and sexual abuse when compared with youth athletes in general.[24]

Sporting cultures at risk of sexual abuse often: lack athlete protection (e.g. a lack of safeguarding policies); have high perpertrator motivation; and have athletes considered highly vulnerable (Fig. 3 7.2).[31] High-risk locations for sexual abuse identified by athlete reports include the coach's home or car, social events (especially where alcohol is involved), the locker room, the playing field and during trips away.[32] There is no known correlation between the amount of clothing or the type of sport and the incidence of sexual harassment and abuse. Likewise, there is also no connection between the amount of physical touching in sport and sexual exploitation.[33] Sports where there is early specialisation may present greater risks of sexual exploitation, especially were intensive talent identification happens at around the age of puberty.

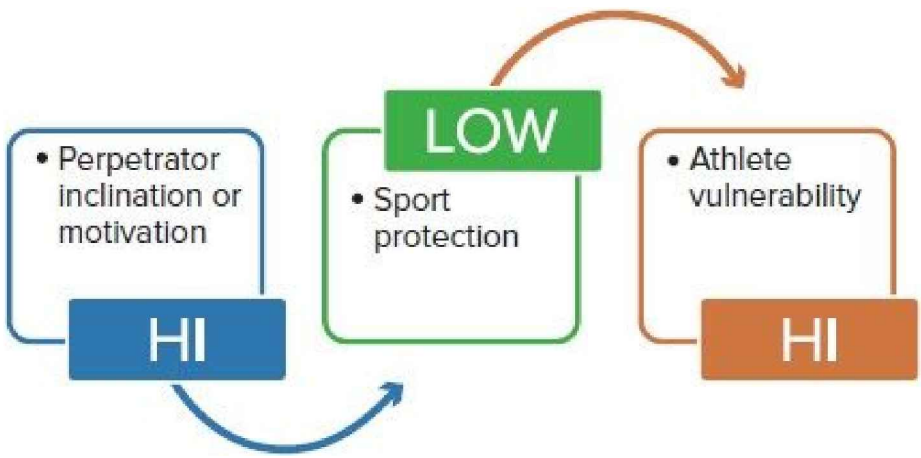


Figure 37.2 High risk sport culture for sexual harassment and abuse[31]

BRACKENRIDGE C, KIRBY S. INTERNATIONAL REVIEW FOR THE SOCIOLOGY OF SPORT (32(4)) PLAYING SAFE: ASSESSING THE RISK OF SEXUAL ABUSE TO ELITE CHILD ATHLETES PP.407-18 COPYRIGHT (C) 1997 REPRINTED BY PERMISSION OF SAGE PUBLICATIONS, INC.

Physical abuse

The physical abuse science demonstrates evidence of the infliction of physical injury through both direct physical contact or non-contact (forced physical exertion, overtraining or inappropriate training loads for age or skill level, unsafe sporting environments).[15] Coaches and members of the athlete entourage have also been reported to be perpetrators of physical abuse through erroneous weight-management practices in:

- sports with weight categories (e.g. judo, weightlifting)
- weight-dependent sports (e.g. ski jumping)

- sports requiring leanness for performance outcomes, as in judged sports (e.g. artistic swimming, gymnastics, figure skating) or timed sports (e.g. track, cross-country skiing, swimming).[34]

Physical abuse may also take place via systematic age cheating, whereby athletes are forced to compete against opponents of a falsified age, exposing athletes to a biological mismatch of skill and size, thus increasing the risk of physical injury. Age cheating has been reported in elite international level gymnastics and football.[35] Hazing practices, endorsed and practised in some sports under the guise of team building and initiation, have been reported to result in physical abuse as well as sexual abuse.[36]

Another form of physical abuse of athletes is the systematic doping of athletes with substances and methods identified on the World Anti-Doping Agency (WADA) Prohibited List.[37] The large scandals of East German doping in the 1970s, Chinese swimmers in the 1990s, and the professional cycling blood-doping schemes are well known in the public domain. More recently, the doping of Russian athletes in and around the Winter Olympic Games in Sochi, Russia, in 2014, made news headlines globally.[38] Of particular relevance is the doping of youth athletes at the elite level. For example, during the 2010 Summer Youth Olympic Games in Singapore, there were two anti-doping rule violations for diuretics used to reduce weight in order to make a weight category in wrestling. In the 2014 Summer Youth Olympic Games in Nanjing, China, one anti-doping rule violation was reported, also for a diuretic in the weight category sport of taekwondo. Finally, in the 2014 Glasgow Commonwealth Games, an anti-doping violation for diuretics was reported in a 16 year old weight lifter.[16]

The most pertinent concern for sport medicine clinicians is the physical abuse of athletes through medical mismanagement. This form of physical abuse can involve premature return to play after illness or injury, for the purposes of team selection or performance. It also includes the systemic or widespread abuse of both prescription non-prohibited medication and non-prescription nutritional supplements. For example, non-steroidal anti-inflammatory drug (NSAID) abuse has been observed in 27% of footballers at FIFA (Fédération Internationale de Football Association)-sanctioned events. While most NSAIDs were orally ingested, approximately one-third was injected intramuscularly. Analgesia was the stated rationale for use, despite NSAIDs having poor analgesic properties and significant adverse effects.[39] Abuse of non-prescription nutritional supplements among athletes is sport-culture dependent, and often mandated by a coach or members of the athlete entourage. The prevalence of nutritional substance use is reported to be as high as 85% of athletes at the IAAF (International Association of Athletics Federations) World Championships, despite the limited evidence for efficacy and high potential for both adverse effects and unintentional anti-doping rule violations.[42]

CASE STUDY

Larry Nassar—US Olympic gymnastics physician

Dr Larry Nassar was the Team USA Olympic gymnastics osteopathic physician and a sport medicine doctor. He managed gymnastics clinics at the Michigan State University, where he was a registered lecturer. In one of sport's biggest abuse scandals, he was convicted of exploiting his position of power to sexually abuse those under his care.

More than 250 women, including Team USA gymnasts, Olympic gold medal winners and girls as young as 6 years old came forward with allegations of abuse. In multiple trials Nassar was convicted of holding child pornography, and admitted abusing those under his care. The judge sentenced him to up to 175 years imprisonment. Prosecutors during the trials labelled him 'possibly the most prolific serial child sex abuser in history'.[40]

This extreme case exemplifies multiple failings within Team USA and other organisations that supported or employed Nassar. It has to be considered a large-scale failure of organisational safeguarding procedures. Accusations as long ago as 1997 were discovered, showing that Nassar evaded detection or suppressed victim reports for nearly 20 years. Rachel Denhollander, one of Nassar's principal accusers and a former gymnast, spoke about the organisational culture:

Victims were silenced, intimidated, told they were receiving medical treatment and at times sent back to be further abused. . . . this is what it looks like when institutions create a culture where a predator can behave unabated.[41]

Conclusion

A lack of safeguarding procedures led to a systemic failure to prevent further abuse. Reports of victims confiding in team members who failed to report allegations, further demonstrates the importance of a prominent, confidential and clear disclosure mechanism. It is essential to set defined codes of conduct for team members, which include procedures for the investigation of all alleged harassment abuse cases.

As a result of this case all abuse allegations in US gymnastics must now be reported to the authorities and to the US organisation SafeSport. Physicians should be aware of local organisations within their area offering similar governance procedures to encourage anyone with concerns to speak out.

Sources: references 40, 41, 60, 61, 62, 63

Neglect

Although there is little published empirical evidence on the effects of neglect in the sports context, there are many case reports of athlete illness, injury and death from the neglect of failing to ensure a safe sporting field of play, through either inadequate equipment, insufficient application of sporting rules, untrained coaching personnel or inappropriate exposure to environmental hazards such as sun, heat and cold.[43] One of the most public examples of this is the tragic death of Nodar Kumaritashvili, of Georgia, in the luge run at the Vancouver 2010 Winter Olympic Games.[44]

There is a great need for ongoing research into all aspects of harassment and abuse, with particular attention to the prevalence, incidence and efficacy of prevention interventions and knowledge translation initiatives.[4]

PRACTICE PEARL

Clinicians should develop the clinical competence to recognise the signs and symptoms of an athlete potentially suffering from harassment or abuse.[45]

CONSEQUENCES OF HARASSMENT AND ABUSE

Impacts on the athlete

Psychological abuse can impair both physical and psychological health, while having a negative effect on personal and social development. Loss of self-esteem, distorted body image, eating disorders, self-harm, suicide, somatic illness and detriment to academic performance have all been reported in the mental health literature. Ultimately, psychological abuse can lead to burnout and to premature withdrawal from sport altogether. Relative to sexual and physical abuse, childhood psychological abuse has been found to be the more powerful correlate of long-term post-traumatic and dissociative symptomatology among athletes.[46]

Physical abuse may lead to potentially devastating consequences, including developmental delays, physical injury and even death. Long-term effects on general and mental health have been reported. The consequences are generally greater in child or adolescent athletes, due to their specific growth, maturation and cognitive needs.[47]

Outside sport, childhood sexual abuse is a strong predictor of non-suicidal self-injury or self-harm. In addition, there is a risk of suicide attempts subsequent to the abuse; increasing in risk with the number of abusive episodes. Physical effects of sexual abuse include unwanted pregnancies, sexually transmitted infections and urogenital or anal trauma.[48]

Neglect can result in preventable accidents, recurrent injuries (or delay to healing), malnutrition, disordered eating, eating disorders, dehydration, the effects of exposure to adverse surrounding or atmospheric conditions (e.g. excessive cold or heat), long-term illness, self-harm behaviours, mental health problems, disability and even death.

Athletes are silenced by their abuse, compounded by the perpetrator methodology as well as by the 'bystander effect', which is defined as passive attitudes of nonintervention, denial or silence by people in positions of power. Athlete victims are then led to believe that such behaviours are socially acceptable and that there is no accountability or pathway to stop the abuse. Athletes will often hide their abuse to protect their ranking on a team, and disclosures of abuse often occur following retirement from sport. The bystander effect acts not only as a deterrent to athlete disclosure, but has also been found to compound the psychological trauma of the victim.[49]

The effects of harassment and abuse for some athletes may be very long term and devastating. Other effects of harassment and abuse in the sport context include impaired athletic performance, reduced medal opportunities and subsequent loss of sponsorship. There is a correlation between non-accidental violence and an increased willingness to dope or cheat in sport. Raakman et al. (2010) describe the phenomenon of indirect abuse that occurs when children witness the abuse of

others in sport.[50] The indirect effects of harassment and abuse on family and personal relationships within and outside sport may also be serious and may carry long-term impact. Some athlete survivors of abuse and harassment are able to recover a healthy mental state and enjoy normal lives.

Impacts on sport

If instances of harassment and abuse are discovered within a sport organisation, and in particular if they are seen to be dealt with inefficiently and non-expeditiously, the organisation itself may suffer reputational damage, loss of participation, reduced performance (including reduced medal tally), loss of trust and reduced public confidence. Another indirect impact of harassment and abuse on sport organisations is a negative economic impact through loss of sponsorship and asset depreciation.[4]

PREVENTION OF HARASSMENT AND ABUSE IN SPORT

As illustrated in Figure 37.2, harassment and abuse are most likely to occur in a sport culture where: there is a perpetrator with high inclination or motivation to harass or abuse; the sport culture has few or no athlete protection mechanisms in place; and athlete vulnerability is high. To mitigate this risk, sporting organisations have a moral, ethical and legal duty to adopt programs to protect athletes' health and wellbeing in sport. It is their responsibility to draft policies and procedures to safeguard athletes from harassment and abuse, and to take measures to eliminate any culture of secrecy. Athlete safeguarding principles are embedded in several policy documents set out by the IOC (see Table 37.2).

Table 37.2 IOC documents supporting safeguarding of athletes from harassment and abuse in sport

IOC document	Pertinent details within the doc
Olympic Charter (2015)[51]	The Olympic Charter outlines the
Olympic Agenda 2020 (2014)[52]	Recommendation 18 of the Olymp
Code of Ethics (2018)[53]	Article 1.4 of the IOC Code of Ethi
7th IOC International Athletes Forum (2015)[54]	Recommendation 2d, states the c
Olympic Movement Medical Code (2016)[55]	The Olympic Movement Medical C
IOC Consensus Statement: Harassment and Abuse in Sport (2016)[4]	According to the IOC Consensus
Safeguarding athletes from harassment and abuse in sport: IOC Toolkit for IFs and NOCs (2018)[6]	The IOC has developed a toolkit f

ROLE OF THE SPORT PHYSICIAN IN PREVENTION OF HARASSMENT AND ABUSE

Team doctors and sport physicians are in a pivotal position, given their frequent contact with athletes, to identify the potential risks and consequences of all forms of harassment and abuse. In order to work effectively as a sport physician, it is therefore essential to maintain an up-to-date knowledge and awareness of all aspects of safeguarding-the different types and manifestations of harassment and abuse, and the routes for reporting and managing allegations of harassment and abuse.[56] In addition to continuing their own personal professional education, sport medicine clinicians can play a pivotal role in the education of other stakeholders in sport, including athletes, coaches and members of the athlete entourage. Education is the cornerstone of any safe sport strategy, and prevention can be accomplished by raising awareness of harassment and abuse in sport through evidence-based education and training programs.

Page 553

Finally, clinicians should ensure that all sport organisations to which they belong have safeguarding policies and procedures, along with codes of conduct for all who have influence or contact with athletes. Codes of conduct outline standards of expected behaviours and boundaries that are explicitly defined. These codes must not only be present, but also be adhered to and enforced. Codes of conduct for team physicians and any other members of the sport medicine and sport science entourage should include clear guidelines for the clinicians' specific roles, responsibilities, relationship boundaries and appropriate professional boundaries. Sport physicians can play an active role in drafting these sport-specific guiding documents.

PRACTICE PEARL

Sport medicine clinicians and other members of the medical team should have an awareness of the safeguarding process within their organisation and how to escalate concerns.

Identification

Clinicians hold a position of trust and often, due to close contact with athletes, are in a unique position to identify signs and symptoms of harassment and abuse. The athlete may utilise the clinician as a confidant. Some of the signs and symptoms that may be observed by the clinician supporting the athlete suffering from abuse or harassment are shown in Table 37.3.

Table 37.3 Potential signs and symptoms of athlete maltreatment

- Unexplained or unwarranted injuries (e.g. bruises, sprains, fractures, overuse injuries)
- Decline in performance
- Nightmares or trouble sleeping
- Poor self-image
- Inability to trust others
- Aggressive or disruptive behaviour
- Intense anger or rage

- Acting out sexually
- Self-destructive, self-abusive or suicidal behaviour
- Appearing sad, passive, withdrawn or depressed
- Difficulty forming new relationships
- Drug or alcohol use
- Avoidance of certain places (e.g. home, training facility)
- Change in behavioural patterns
- Fear of certain adults (e.g. coaches, parents, peers)

STIRLING A, BRIDGES E, CRUZ L, ET AL. CANADIAN ACADEMY OF SPORT & EXERCISE MEDICINE POSITION STATEMENT: ABUSE, HARASSMENT, AND BULLYING IN SPORT. CLINICAL JOURNAL OF SPORT MEDICINE 201 1;21:385–391 COPYRIGHT © 2019 WOLTERS KLUWER HEALTH, INC. ALL RIGHTS RESERVED. HTTPS://JOURNALS.LWW.COM/CJSPORTSMED/FULLTEXT/2011/09000/CANADIAN_ACADEMY_OF_SPORT_AND_EXERC

Clinical management of allegations of harassment and abuse

Athletes who have been abused often feel extreme shame, guilt and fear as a result of the abusive process.[32] As discussed above, athlete victims are often silenced by their experience, resulting in a reluctance to disclose. As such, sport physicians should be vigilant, with a high index of suspicion for those athletes who clinically present with psychosomatic illnesses, injuries whose mechanisms of injury do not make sense, or injuries/illnesses that do not resolve as expected. Finally, it is important to be cognisant of athletes who portray any of the psychological or physical sequelae listed above, under 'Impacts on the athlete'.

In developing the therapeutic relationship with your athletes, emphasise safety, compassion, integrity and confidentiality at all times, to reinforce the athletes' feeling of trust. It is important to be aware that athletes have been reported to disclose harassment or abuse happening outside the sporting context to the team physician, and sport medicine clinicians should be prepared for this scenario.[58] In cases of athlete disclosure of harassment or abuse, Table 37.4 outlines the clinical guidelines and principles for the management of allegations.

Table 37.4 Clinical guidelines1 for the management of athlete disclosure of allegations of harassment or abuse

- Actively and empathetically listen to the patient/athlete
- Acknowledge his/her courage in speaking about the abuse
- Assure the athlete that this experience is not their fault
- Simultaneously encourage disclosure and yet avoid any leading questions
- Do not denigrate the perpetrator
- Keep accurate records
- Ensure the athlete's safety
- STOP the abuse: report the disclosure to the appropriate authorities, including the police and the relevant sporting organisation
- With a multi-disciplinary treatment team, investigate and manage any associated medical (physical or psychological) presentatior

- Support team mates, members of the entourage and family members
- Encourage a whistleblowing culture so that all members of the team feel comfortable speaking about possible breaches of trust

ADAPTED FROM MARKS S, MOUNTJOY M, MARCUS M. SEXUAL HARASSMENT AND ABUSE IN SPORT: THE ROLE OF THE TEAM DOCTOR. *BRJ SPORTS MED.* 2012;905-8.

Ignoring or neglecting to act on athlete disclosures of harassment or abuse through passive silence compounds the psychological harm to the athlete victim via the bystander effect, described above.[59] Doing nothing is not an option! The IOC consensus statement on harassment and abuse in sport[4] identifies the following recommendations for sport medicine and allied health professionals:

- Ensure that you are adequately trained to:
  - recognise the signs and indicators of non-accidental violence
  - effectively and appropriately respond to disclosures of non-accidental violence.
- Ensure that you have access to a multidisciplinary professional support team prior to initiating any treatment plan for athletes who are survivors of non-accidental violence.
- Know where and how to refer disclosures or suspicions.

Page 554

PRACTICE PEARL

Incidents of hazing and abuse must be reported following safeguarding guidelines.

CASE STUDY

Daniel Carcillo, ice hockey player—bullying and hazing

Some guys would get it harder than others because (they) didn't fit the mould of a typical masculine hockey player... it's amazing how you can experience a very emotional trauma and not even think about it [63]

Daniel Carcillo is a Canadian former professional ice hockey player who enjoyed a 10-year career in the NHL. Carcillo won the Stanley Cup as a member of both the 2013 and 2015 Chicago Blackhawks teams. At the end of the 2015 season, Carcillo retired from professional hockey and founded the 'Chap ter 5 Foundation', a nonprofit organisation dedicated to helping NHL players who are struggling with post-concussion syndrome and mental health problems.

In November 2018, Carcillo decided to speak out publicly about the 'toxic' culture that he and many others endured as rookies voicing his concerns on Twitter. He spoke of the widespread hockey tradition of'hazing', that he believes resulted in the acceptance of physical and emotional abuse as standard practice.

SHUTTERSTOCK/JOHN-ALEX

Carcillo provided examples of several alleged incidents involving himself and teammates. In one incident he alleges he was crowded into the washroom of a charter bus with six teammates while tobacco was spat at them through a vent. Another incident he alleges involved a teammate being tied to a table while naked and whipped with a belt. He believed that coaches and management were often aware of the events and sometimes participated. He also spoke of former teammates whom he felt had developed subsequent addiction and relationship problems due to the abuse.

Page 555

Carcillo eventually took his concerns to the league's (Ontario Hockey League) commissioner, who helped to establish procedures so that other players could raise their concerns without fear of reprisal.

Conclusion

This case study illustrates some of the forms of abuse outlined within this chapter. Separating abuse from the accepted culture of a sport or team can be difficult because coaches, management, staff and former athletes may have been exposed to abuse as rookies or juniors themselves. This risks abuse becoming a 'cultural norm' for those within the sport. Sometimes it is seen as part of 'toughening' the athlete to prepare them for the professional environment. Clinicians who observe such practices need to demonstrate strong leadership to speak up and exercise their duty of care.

Where concerns over reprisal exist, independent safeguards should be put into place to protect all parties. Without strong governance, athletes (especially rookies) may feel powerless to speak out when abuse occurs. Education about acceptable practice and reporting mechanisms are an essential part of the safeguarding process. All organisations should provide a clear path for athletes to voice their concerns in confidence.[64]

Sources: references 64, 65

SUMMARY

- As IOC Vice President Dr Ugur Erdener stated in his preamble to the IOC Toolkit for safeguarding athletes from harassment and abuse in sport: 'Sport is a microcosm of society, wider societal ills, such

as harassment and abuse, occur in sport just as they do outside of sport... Supporting athletes and safeguarding their wellbeing is very much a shared responsibility'.[6]

- Sport medicine clinicians have an important role to play in the identification, prevention and management of harassment and abuse in sport through the application of the principles outlined in this chapter.

REFERENCES

1. Raisman A. Twitter, 22 November 2017.
2. Chavez N, Levenson E. Ex-USA gymnastics doctor apologizes, pleads guilty to criminal sexual conduct. CNN, 22 November 2017. http://www.cnn.com/2017/11/22/us/us-gymnastics-doctor-plea-hearing/index.html.
3. Brackenridge C, Fasting K. Sexual harassment and abuse in sport: the research context. *J Sex Aggress* 2002; 8(2): 3–15.
4. Mountjoy M, Brackenridge C, Arrington M et al. International Olympic Committee consensus statement: harassment and abuse (non-accidental violence) in sport. *Br J Sports Med* 2016; 50(17): 1019–29.
5. Brackenridge C, Fasting K, Kirby S et al. Protecting children from violence in sport: a review with a focus on industrialized countries. Florence, Italy: UNICEF Innocenti Research Centre, 2010.
6. International Olympic Committee (IOC). Safeguarding athletes from harassment and abuse in sport: IOC Toolkit for IFs and NOCs. 1 January 2018. https://hub.olympic.org/athlete365/safeguarding/.
7. Stirling A, Kerr G. The perceived effects of the elite athletes' experiences of emotional abuse in the coach-athlete relationship. *Int J Sport Exerc Psychol* 2013; 11(1): 87–100.
8. Leahy T, Pretty G, Tenenbaum G. Perpetrator methodology as a predictor of traumatic symptomatology in adult survivors of childhood sexual abuse. *J Interpers Violence* 2004; 19(5): 521–40.
9. Marasescu M. The role of hostile and instrumental aggression in sport. *Linguistic Philosophical Investigations* 2014; 13: 170–5.
10. Brackenridge C. *Spoilsports: understanding and preventing sexual exploitation in sport*. London, UK: Routledge, 2001.
11. Brackenridge C. 'He owned me basically ...' Women's experience of sexual abuse in sport. *Int Rev Sociol Sport* 1997; 32(2): 115–30.
12. Owton H, Sparkes A. Sexual abuse and the grooming process in sport: learning from Bella's story. *Sport Educ Soc* 2017; 22(6): 732–43.

13. International Olympic Committee (IOC). Olympic Movement Medical Code: in force as from 31 March 2016. https://stillmed.olympic.org/media/Document%20Library/OlympicOrg/IOC/Who-We-Are/Commissions/Medical-and-Scientific-Commission/Olympic-Movement-Medical-Code-31-03-2016.pdf.
14. Bergeron M, Mountjoy M, Armstrong N et al. International Olympic Committee consensus statement on youth athletic development. *Br J Sports Med* 2015; 49(13): 843–51.
15. Stirling A. Definition and constituents of maltreatment in sport: establishing a conceptual framework for research practitioners. *Br J Sports Med* 2009; 43(14): 1091–9.
16. Mountjoy M, Rhind D, Tiivas A et al. Safeguarding the child athlete in sport: a review, a framework and recommendations for the IOC youth athlete development model. *Br J Sports Med* 2015; 49(13): 883–6.
17. Lang M. Adult-child touch in sport [video file]. In: Turner D. Sports Coach UK. London, UK: 2015. https://www.youtube.com/watch?v=-RzC7RCVxwE&feature=youtu.be%5d.
18. Dixon N. Trash talking, respect for opponents and good competition. *Sport Ethics Philos* 2007; 1(1): 96–106.
19. Rhind D, Brackenridge CH, Kavanagh EJ et al. '#Cyberviolence: developing a typology for understanding virtual maltreatment in sport. In: Rhind D, Brackenridge CH, eds. *Researching and enhancing athlete welfare*. London, UK: Brunel University Press, 2014: 34–43
20. Tiivas A, Billington-Wood C. *Key themes and integrity threats for elite sport*. London, UK: National Society for the Prevention of Cruelty to Children, 2015.
21. Rigby K. *New perspectives on bullying*. London, UK: Jessica Kingsley Publishers, 2002.
22. Lundy C. Hazy viewpoints: administrators' perceptions of hazing. *Int J Sport Manag Mark* 2010; 7: 119–31.
23. Fasting K, Brackenridge C, Knorre N. Performance level and sexual harassment prevalence among female athletes in the Czech Republic. *Women in Sport & Physical Activity J* 2010; 19(1): 26–32.
24. Vertommen T, Schipper-van Veldhoven N, Hartill M et al. Sexual harassment and abuse in sport: the NOC*NSF helpline. *Int Rev Sociol Sport* 2015; 50(7): 822–39.
25. Fasting K, Brackenridge C, Sundgot-Borgen J. Prevalence of sexual harassment among Norwegian female elite athletes in relation to sport type. *Int Rev Sociol Sport* 2004; 39(4): 373–86.
26. Parent S, Lavoie F, Thibodeau M et al. Sexual violence experienced in the sport context by a representative sample of Quebec adolescents. *J Interpers Violence* published online 13 April 2015; 1–21. doi: 10.1177/0886260515580366.
27. Leahy T, Pretty G, Tenenbaum G. Prevalence of sexual abuse in organized

competitive sport in Australia. *J Sex Aggress* 2004; 16–36.

28. Fasting K, Chroni S, Hervik S et al. Sexual harassment in sport toward females in three European countries. *Int Rev Sociol Sport* 2011; 46(1): 76–89.
29. Kirby S, Greaves L, Hankivisky O. *The dome of silence: Sexual harassment and abuse in sport*. Halifax, Nova Scotia: Fernwood, 2000.
30. Alexander K, Stafford A, Lewis R. *The experiences of children participating in organised sport in the UK*. London, UK: National Society for the Prevention of Cruelty to Children, 2011.
31. Brackenridge C, Kirby S. Playing safe: assessing the risk of sexual abuse to elite child athletes. *Int Rev Sociol Sport* 1997; 32(4): 407–18.
32. Cense M, Brackenridge C. Temporal and developmental risk factors for sexual harassment and abuse in sport. *Eur Phy Educ Rev* 2001; 7(1): 61–79.
33. Fletcher S. Touching practice and physical education: deconstruction of a contemporary moral panic. *Sport Educ Soc* 2013; 18(5): 694–709.
34. Sundgot-Borgen J, Fasting K, Brackenridge C et al. Sexual harassment and eating disorders in female elite athletes: a controlled study. *Scand J Med Sci Sports* 2003; 13(5): 330–5.
35. Engebretsen L, Steffen K, Bahr R et al. The IOC Consensus Statement on age determination in high-level young athletes. *Br J Sports Med* 2010; 44(7): 476–84.
36. Kowalski C, Waldron J. Looking the other way: athletes' perceptions of coaches' responses to hazing. *Int J Sports Sci Coach* 2010; 5(1): 87–100.
37. World Anti-Doping Agency (WADA). World Anti-Doping Code. International Standard. The Prohibited List, January 2018. https://www.wada-ama.org/en/resources/science-medicine/prohibited-list-documents.
38. World Anti-Doping Agency (WADA). WADA Statement regarding the IOC's decision concerning Russia. 5 December 2017. https://www.wada-ama.org/en/media/news/2017-12/wada-statement-regarding-the-iocs-decision-concerning-russia.
39. Tscholl P, Vaso M, Weber A et al. High prevalence of medication use in professional football tournaments including the World Cups between 2002 and 2014: a narrative review with a focus on NSAIDs. *Br J Sports Med* 2015; 49(9): 580–2.
40. https://www.iol.co.za/news/world/nassar-may-have-been-most-prolific-child-abuser-in-history-12921447, accessed 15 February 2019
41. https://www.bbc.com/news/world-us-canada-42812984, accessed 15 February 2019
42. Maughan R, Depiesse F, Geyer H. The use of dietary supplements by athletes. *J Sports Sci* 2007; 25 Suppl 1: S103–13.
43. Cross P, Karges J, Horkey M et al. Management of acute sports injuries and medical conditions by South Dakota high school head coaches: assessment via case scenarios. *S D Med* 2012; 65(3): 97–9, 101–5, 107.
44. Wikipedia contributors. Nodar Kumaritashvili. Wikipedia, 2010. https://en.wikipedi

a.org/wiki/Nodar_Kumaritashvili.

45. Mountjoy M. Margo Mountjoy on the Larry Nassar tragedy— never again. *BMJ Opinion*, 29 March 2018. https://blogs.bmj.com/bmj/2018/03/29/margo-mountjoy-on-the-larry-nassar-tragedy-never-again/.
46. Fasting K, Brackenridge C, Walseth K. Consequences of sexual harassment in sport for female athletes. *J Sex Aggress* 2002; 8(2): 37–48.
47. DiFliori J, Benjamin H, Brenner J et al. Overuse injuries and burnout in youth sports: a position statement from the American Medical Society for Sports Medicine. *Clin J Sport Med* 2014; 24(1): 3–20.
48. Bucchianeri M, Eisenberg M, Wall M et al. Multiple types of harassment: associations with emotional well-being and unhealthy behaviors in adolescents. *J Adolesc Health* 2014; 54(6): 724–9.
49. Fasting K, Brackenridge C, Walseth K. Women athletes' personal responses to sexual harassment in sport. *J Appl Sport Psychol* 2007; 19(4): 419–33.
50. Raakman E, Dorsch K, Rhind D. The development of a typology of abusive coaching behaviours within youth sport. *Int J Sports Sci Coach* 2010; 5(4): 503–15.
51. International Olympic Committee (IOC). Olympic Charter—in force as from 2 August 2015. https://stillmed.olympic.org/Documents/olympic_charter_en.pdf.
52. International Olympic Committee (IOC). Olympic Agenda 2020. 8 December 2014. https://stillmed.olympic.org/media/Document%20Library/OlympicOrg/Documents/Olympic-Agenda-2020/Olympic-Agenda-2020-20-20-Recommendations.pdf#_ga=2.227172442.672549019.1514930424-452720843.1503149974.
53. International Olympic Committee (IOC). Code of Ethics. 2018. https://www.olympic.org/code-of-ethics.
54. International Olympic Committee (IOC). 7th IOC International Athletes' Forum—Recommendations 8-10 October 2015, Lausanne. 8 October 2015. https://stillmed.olympic.org/Documents/IOC_Executive_Boards_and_Sessions/Executive_Board_Meetings/EB_decision-IAF_recommendations_12_2015.pdf#_ga=2.173673700.672549019.1514930424-452720843.1503149974.
55. Marks S, Mountjoy M, Marcus M. Sexual harassment and abuse in sport: the role of the team doctor. *Br J Sports Med* 2012; 46(13): 905–8.
56. Stirling A, Bridges E, Cruz L et al. Canadian Academy of Sport and Exercise Medicine Position Paper: Abuse, Harassment, and Bullying in Sport. *Clin J Sport Med* 2011; 21(5): 385–91.
57. Rhind D, McDermott J, Lambert E et al. A review of safeguarding cases in sport. *Child Abuse Review* published online 18 February 2014; 23. doi: 10.1002/car.2306.
58. Banyard V, Plante E, Moynihan M. Bystander education: bringing a broader community perspective to sexual violence prevention. *J Community Psychol* 2004; 32(1): 61–79.

59. Carcillo speaks out on alleged hazing experience in junior hockey, John Chidley-HilL, The Canadian Press, Nov. 26, 2018
60. https://www.bbc.com/news/world-us-canada-42894833
61. https://www.bbc.com/news/av/world-us-canada-42810609/larry-nassar-victim-how-much-is-a-little-girl-worth?intlink_from_url=https%3A%2F%2Fwww.bbc.com%2Fnews%2Ftopics%2Fclwx28lpp90t%2Flarry-nassar-sex-abuse-scandal&link_location=live-reporting-map
62. https://apnews.com/a8e014fb553d4b9682f32d89eaa4d71b?utm_campaign=SocialFlow&utm_source=Twitter&utm_medium=APCentralRegion
63. https://www.sbnation.com/2018/1/19/16900674/larry-nassar-abuse-timeline-usa-gymnastics-michigan-state (this has been updated since) https://www.bbc.com/news/world-us-canada-42950478?intlink_from_url=https://www.bbc.com/news/topics/clwx28lpp90t/larry-nassar-sex-abuse-scandal&link_location=live-reporting-story
64. https://en.wikipedia.org/wiki/Daniel_Carcillo
65. https://www.cbc.ca/sports/hockey/nhl/carcillo-hazing-hockey-culture-ohl-abuse-1.4922623

PART F

Practical sports medicine

Chapter 38

Emergencies

with SHANE BRUN

There's no harm in hoping for the best as long as you've prepared for the worst.
Stephen King

Highly publicised incidents of concussion, sudden cardiac death and heat-related illness have moved the topic of emergency medicine to the forefront of sports medicine discussions. Situations threatening life or limb require advanced medical knowledge, skills and appropriate equipment to ensure immediate and expert care for the best possible patient outcomes. Clinicians responsible for athlete care at any level, from grassroots to elite, should undertake a recognised and accredited medical emergency care course.

Knowledge of emergency care should not be limited to sport and exercise medicine physicians. Every potential member of the emergency care team must be well prepared for the acute management of the athlete who is injured or unexpectedly becomes ill. As athletes and accompanying clinical teams travel widely both nationally and internationally, not all athlete emergency care occurs near high-level definitive services, so all members of the emergency care team must also be prepared to deal with the unpredictable in diverse settings.

In this chapter we will discuss:

- the role of the physiotherapist in emergency care
- the sequence of events in emergency care
- the primary survey in detail
- equipment needed for emergencies
- appropriate use of analgesia in emergencies.

THE ROLE OF THE PHYSIOTHERAPIST IN EMERGENCY CARE

Although there are skills and procedures described in this chapter that are legally restricted to

physicians, this chapter is also relevant for other clinicians, such as physiotherapists. Given the countless number of people who participate in community sports, most sporting situations take place in the absence of a clinician who is trained in the management of sporting emergencies. Consequently, the responsibility of preparing for and managing an emergency may fall to other clinicians.

PRACTICE PEARL

All clinicians must be aware of the limits of their practice, as determined by their national credentialing organisation. All those responsible for sporting teams or athletes are strongly encouraged to gain further training in emergency care.

The physiotherapist has a central role in the management of sporting emergencies either as the team leader or team member. If the physiotherapist is the emergency team leader, he or she has the responsibility for preparing for and managing the emergency situation. If the physiotherapist is a member of the emergency team, they can assist the physician in preparing for an emergency situation and in the immediate management of the patient with a life- or limb-threatening condition.

THE SEQUENCE OF EVENTS IN EMERGENCY CARE

When an emergency occurs, the onus is on the most senior clinician present to assume leadership, delegate or personally perform a rapid assessment of the situation and the patient, and initiate management. Leadership and team roles must be clearly defined and outlined well in advance, and the skills related to each role should be rehearsed as a team. During training or competition, it is the medical team's responsibility to constantly monitor the athletes, so in the event of sudden injury or illness the team may prepare and rapidly respond. Observing the mechanism of an injury will provide the medical team with clues as to which injuries to expect.

Page 559

The following discusses the sequence of events for emergency care, as outlined in the box below.

Sequence of events for emergency care

1. Preparation
2. Triage
3. Primary survey
4. Resuscitate and stabilise
5. Focused history
6. Secondary survey
7. Frequent reassessment

8. Definitive care

Preparation

Preparation is divided chronologically into two components:

- pre-situation preparation
- situation preparation.

Pre-situation preparation

The clinical team must prepare and rehearse its approach to possible emergencies. A clinical team responsible for motor sports will have different emergency priorities and preparation from a team responsible for swimmers, for example. Similarly, preparation is very different for a clinical team managing athletes in a major city with ready access to pre-hospital emergency medical services (PHEMS), such as a well-developed and professionally run ambulance service, and nearby major medical facilities, compared with the clinical team taking care of athletes in a more remote location (see also Chapter 47 of *Clinical Sports Medicine Volume 1: Injuries).*

Pre-situation preparation comprises:

- emergency medical knowledge
- emergency medical skills
- emergency medical equipment/adjuncts
- clinical team rehearsal
- ensuring the clinical team, athletes and officials are aware of emergency response procedures, exit points and assembly points at the venues where they train and participate.

Mass gathering events pose their own unique challenges, with an absolute need for medical and evacuation preparedness in the event of an emergency situation.

Situation preparation

When the emergency occurs, the clinical team leader should:

- survey the scene for safety
- ensure all medical team members adopt universal precautions
- organise the clinical team.

Surveying the scene requires clinicians to ensure their own and their team's safety as an absolute priority. Establish that the environment is safe for you and the team to enter before proceeding. If the scene of the emergency is not correctly assessed prior to entering, there is the potential for harm not only to those injured but also the medical team.

Universal precautions are for the safety of the clinical team-clinical team safety must remain a priority. As an absolute minimum each team member should be issued with and wear gloves, goggles or glasses, and protective footwear. Depending on the sport and the situation, more extensive protective gear may be necessary; this must be determined in the pre-situation preparation.

Organising the clinical team requires confirming roles previously assigned, as well as which members will be responsible for which pieces of medical equipment to be brought to the scene.

Triage

Triage is the sorting of patients based on their need for treatment and the resources available. For this chapter we assume the clinical team will be confronted with either a single-casualty emergency or a multiple-casualty emergency where the number of casualties and the severity of their injuries do not overwhelm the clinical team or the resources available. Even when there are multiple casualties, the triage priorities remain: Airway, Breathing, Circulation and Disability. The topic of sporting event disaster preparedness-events with mass casualties-is beyond the scope of this book. We discuss the preparation for a sporting event in Chapter 39.

PRACTICE PEARL

At the time of triage, the clinical team leader may wish to delegate the role of notifying the pre-hospital emergency medical services (PHEMS) (also known as ambulance or emergency medical services, EMS) of the situation. It is always better to notify early rather than late.

Primary survey

The primary survey is when life-threatening conditions are identified and treated simultaneously. Although the primary survey (Fig. 38.1) is divided into system priorities for teaching purposes, in reality several life-threatening issues may be identified and treated at the same time. There are surveys after the primary survey; this chapter focuses only on the primary and secondary surveys, as these are the times to identify and treat life-threatening conditions (primary survey) and limb-threatening conditions (secondary survey).

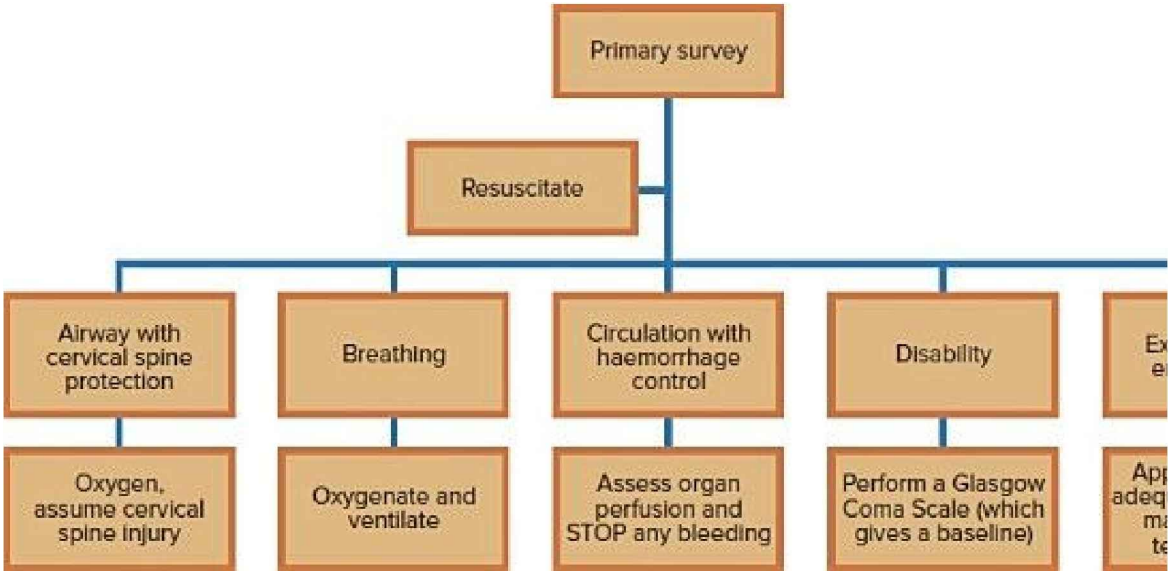


Figure 38.1 The primary survey

The primary survey is somewhat different from how a physician would usually assess and treat a patient. In the primary survey, compromise or life threat is rapidly identified and managed. Parts of the patient history are often deferred until after the primary survey is complete, and when examinations are performed they are very specific and focused. In the pre-hospital setting very few medical investigations are performed, with the exception of obtaining vital signs, blood glucose *(never forget glucose!)*, oxygen saturation and electrocardiograph (ECG).

At the time of the primary survey, the patient is positioned to facilitate assessment and treatment. In most situations, the supine position best allows the clinical team to assess, observe and treat the patient, with minimal movement and delay.

The key priorities for each system in the primary survey are as follows (these are expanded on later in this chapter):

A. Airway and cervical spine control:

1. The first priority in any emergency situation is to assess the airway and establish a patent airway, if necessary.
2. In any emergency resulting from trauma or involving an event in which the patient may have sustained a spinal injury, ensure cervical spine stabilisation at the time of establishing airway patency, using appropriate techniques and equipment.
3. At this time, high-flow oxygen may be administered to the patient. In the critically ill or injured patient, in the acute stages, assume that there is no absolute contraindication to the administration of oxygen.

B. Breathing and ventilation:

1. Airway patency does not ensure adequate ventilation.

2. Once the airway is patent and the cervical spine stabilised, assess the patient's breathing to determine whether it is adequate, or whether conditions exist that may compromise breathing.
3. The aim is that the patient will be breathing effectively alone (active ventilation). If the patient is unable to breathe, the clinical team should ventilate the patient (passive ventilation).

C. Circulation and haemorrhage control:

1. In patients who have sustained trauma and demonstrate signs and symptoms of shock, assume that the cause of shock is hypovolaemia. Bleeding is a major cause of preventable death following trauma. Thus any external bleeding must be immediately controlled by direct and firm pressure.
2. The shocked state in the patient who has not been involved in trauma is likely to be as a result of marked peripheral vasodilation, pump failure and/or inadequate heart rate.
3. In the primary survey, both traumatic shock and atraumatic shock are treated similarly.
4. Significant blood loss can occur internally especially at long bone fracture sites and internal organ rupture. Early and appropriate fracture immobilisation may be indicated during this phase of assessment.
5. Do not underestimate the importance of splinting fractures as part of haemorrhage control.

Page 561

D. Disability:

1. This refers to neurological assessment and is usually performed towards the end of the primary survey. This important assessment provides an early measure of neurological function-essential as a baseline against which to compare change as time progresses.
2. In the absence of head injury, an altered level of consciousness indicates cerebral trauma, hypoxia or hypoperfusion-this should immediately alert the clinician to reassess Airway, Breathing and Circulation.
3. Disability is best assessed using the Glasgow Coma Scale (GCS) (Table 38.2), and by assessing pupillary size and response (disability and neurological status are discussed later in this chapter).

E. Exposure/environment control:

1. One of the major pitfalls in emergency care is insufficient examination. Never assume that the injuries or compromise you initially see are all that is to be found.
2. Adequate and appropriate exposure of the patient is essential. The privacy provided on a sporting field or arena is limited. Ensure as much patient privacy and confidentiality as is possible, without compromising inspection of all body surfaces.
3. Environment control is an aspect of care that is often neglected. One must remember that a critically ill or injured patient may lose the ability to thermoregulate, thereby becoming poikilothermic, adopting the surrounding temperature. The natural inclination is to keep the patient warm, but the ideal plan is to *keep the patient normothermic.* Keep core

temperature as close to 37°C (98.6°F) as possible. Note that your own comfort level may not be accurate or appropriate as a monitor of environmental condition.

Resuscitate and stabilise

In the clinical setting, the resuscitation and stabilisation of the patient are performed at the same time during the primary survey. However, this phase is differentiated because an important aspect of emergency medical management is the use of drugs[a] and adjuncts. Adjuncts include intercostal catheters, intravenous catheters and fluids, pulse oximetry and cardiac monitoring. Because legally a physician can use emergency drugs and medical adjuncts, the physician is an important member of the clinical team in an emergency.

Focused history

The history allows the clinical team to identify injuries or potential for compromise that might otherwise be missed. Depending on the circumstances, it may be appropriate to change the sequence of events between focused history and secondary survey, thereby performing the secondary survey prior to or simultaneously with the focused history. Initially, at the time of the primary survey and resuscitation, history taking may be very basic. Apply the AMIST mnemonic:

- Age and sex of patient
- Mechanism of injury or circumstances surrounding the event
- Injuries sustained or problems identified
- Signs and Symptoms
- Treatment given so far.

This mnemonic is also useful when handing a patient over to PHEMS (ambulance, emergency care) or definitive medical care.

Once the primary survey is complete and the patient stabilised, a more focused history may be performed. Apply the AMPLE mnemonic:

- **A**llergies
- **M**edications
- **P**ast illnesses/**P**regnancy
- **L**ast oral intake (solids and liquids)
- **E**vents/**E**nvironment related to the situation.

Secondary survey

Depending on the distance from the emergency to definitive care, the severity of the condition and the response time of the PHEMS, a secondary survey may not be performed. The primary objective in emergency care is to prevent loss of life or future disability; then to identify and prevent potential compromise and limb-threatening conditions. It is only when the clinical team leader is satisfied that the patient is stable and that all aspects of the primary survey are complete and have

been addressed that attention should move to the secondary survey.

The secondary survey is a complete assessment of the patient-essentially a full systems review, with assessment of all body surfaces. A GCS assessment should also be performed, if it has not been done earlier. Also perform a log roll, with in-line spinal stabilisation, if this has not been performed already, so the back and spine may be more adequately assessed. It is during this stage that non-life-threatening conditions are identified and treated. If at any time the patient's condition changes, the priority is to recommence the primary survey and reassess Airway, Breathing, Circulation and Disability.

Page 562

Frequent reassessment

Frequent reassessment is one of the most important aspects of emergency management. You must be continuously vigilant for changes in the patient's condition and have a very low threshold for reviewing and reassessing all components of the primary survey.

PRACTICE PEARL

If at any time the patient's condition changes, you perform a significant medical intervention, the patient is moved or you are feeling overwhelmed by the situation, recommence the primary survey starting with reassessment of the airway.

It is important not to consider emergency care as a linear progression. The continuum of care should be considered as a continuous cycle of assessment and reassessment (Fig. 38.2).

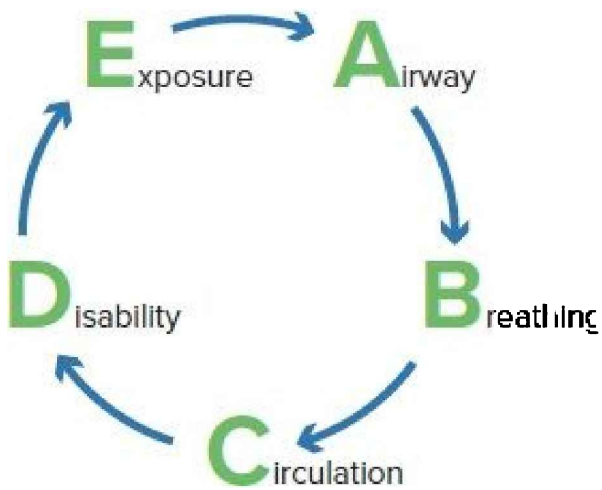


Figure 38.2 The cycle of emergency management

Definitive care

Most patients who require out-of-hospital emergency care will require transfer to definitive

medical care. In many situations this is done by a well-coordinated PHEMS. In most countries this is a highly skilled and professional paramedic ambulance service. In all situations, but particularly in rural and remote sporting locations, an important responsibility of the clinical team leader is to be familiar with the medical resources, facilities, availability and skills of the PHEMS, and the distance these are from the sporting venue and athlete accommodation. This responsibility also applies with home events.

THE PRIMARY SURVEY IN DETAIL

In this section we discuss basic life support, then each component of the primary survey. We also outline how to assess and manage each system, and we discuss the use of appropriate primary survey adjuncts. At the end of each section we discuss how to identify and manage some common clinical emergency scenarios.

Basic life support

In most countries and regions, it is a community and legal expectation that a person accepting the responsibility of clinical care for a sporting team or athletes is familiar and competent with performing basic life support. It is also an expectation that all physicians are familiar and competent with advanced life support techniques. This expectation is greater when the clinician is charged with the responsibility of care outside a hospital or clinic environment, given that the clinician is most likely to be the initial responder in an emergency situation.

Each member of the clinical team should be familiar with, skilled and practised in basic life support techniques, such as those a recognised and accredited training provider may offer. An essential component of basic life support is the immediate management of a cardiac arrest and the effective performance of cardiopulmonary resuscitation (CPR). A basic life support flowchart (DRS ABCD) is shown as Figure 38.3; the chart is available through the Australian Resuscitation Council (www.resus. org.au). Details of basic life support are beyond the scope of this chapter. Each member of the clinical team should recertify in basic life support skills annually.[1]

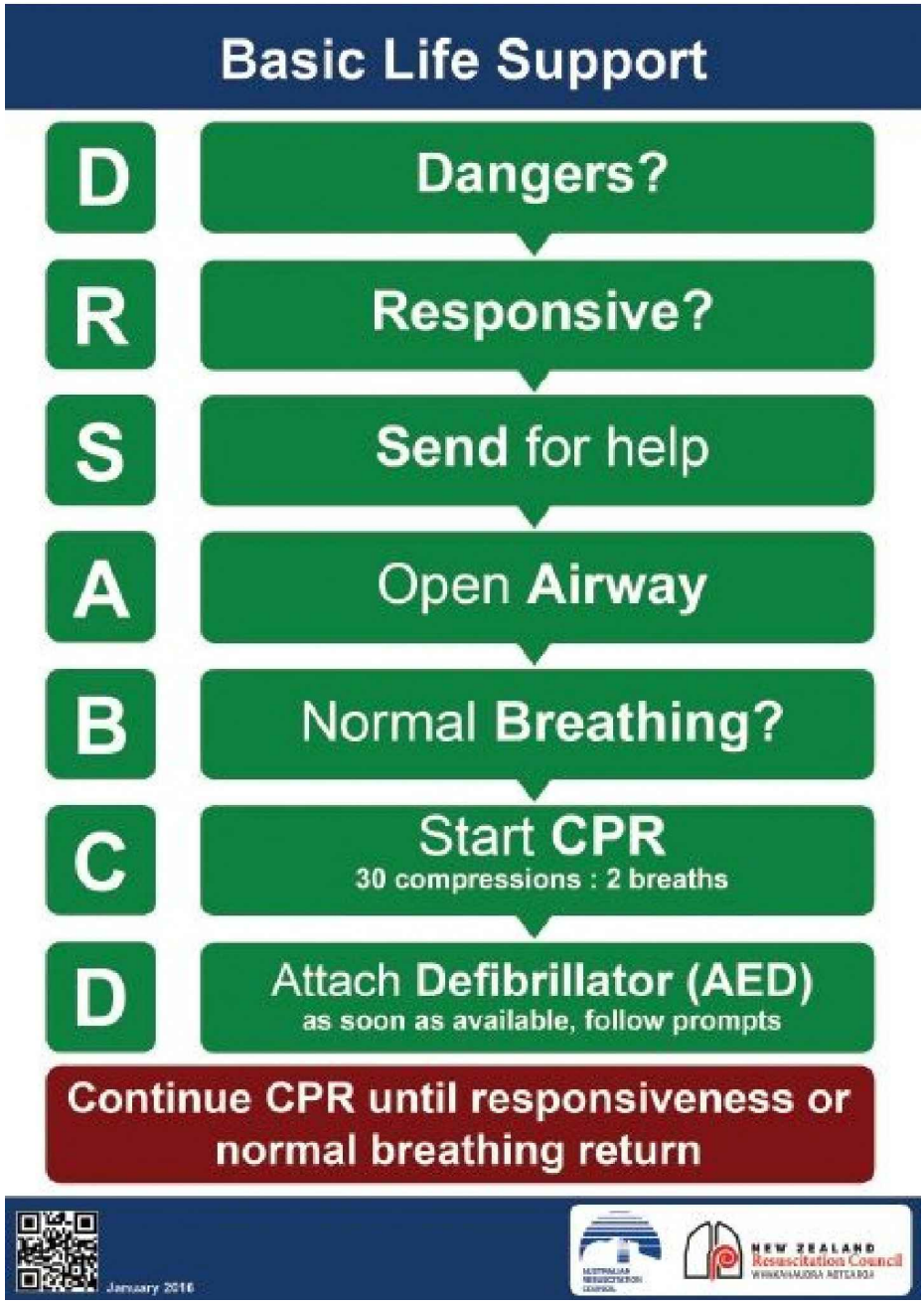


Figure 38.3 Basic life support flowchart

A very important skill for clinical team members, especially physicians, is to be confident and competent with performing bag-valve-mask (BVM) ventilation.

The mask should be held onto the face using the jaw thrust technique (Fig. 38.4). When positioning and holding the mask it is important to remember that the aim is to bring the patient's

face into the mask, rather than forcing the mask onto the patient's face. The latter causes unnecessary operator finger fatigue and has the potential of flexing the patient's head, thereby risking an occluded airway.

Figure 38.4 Applying a face mask using the jaw thrust technique. Bring the patient's face into the mask

Once the mask is positioned, the operator is able to perform either mouth-to-mask ventilation or BVM ventilation with supplemental oxygen (if available). For inexperienced operators, BVM ventilation is best performed by two operators, one securing the mask to the patient's face and the other compressing the bag firmly.

AUSTRALIAN RESUSCITATION COUNCIL, www.resus.org.au

Airway with cervical spine control

The first priority in any emergency is to establish a patent airway. The quickest way to identify the patency of the airway is to ask the patient their name and how they are. This 10-second assessment provides the clinical team with four valuable pieces of information:

- the patency of the airway
  - if the patient is unable to answer it may imply unconsciousness or an occluded airway
  - presence of stridor or noises coming from the airway suggests a degree of obstruction
- the effectiveness and ease of breathing
- the haemodynamic status of the patient, as adequate cerebral perfusion is required to respond

- the neurological status of the patient.

If the patient is maintaining his or her own airway, all that is required is constant monitoring of its patency. In many instances airway patency is relatively easy to achieve using basic airway techniques, which are discussed below.

Oxygen is one of the most valuable drugs used in the emergency situation. Along with establishing and maintaining a patent airway, the patient should have oxygen administered (if it is available). In the initial stages of all emergency situations, oxygen should be administered in high concentrations, although oxygen delivery devices providing lesser concentrations may be more appropriate to maintain optimal oxygen saturation. Excessive oxygenation can be dangerous and so administration should be managed with care. Initially, oxygen delivery is best achieved using a non-rebreather face mask, aiming for an oxygen saturation of at least 94–98% in patients without a history of lung disease.[2]

With any critically ill or injured person, it is safe to assume that there are no absolute contraindications to the administration of oxygen. Apply the mask as soon as possible and initially set the oxygen flow rate to 15 L per minute. Titrate the flow against the patient's oxygen saturation (aiming for at least 94–98%).

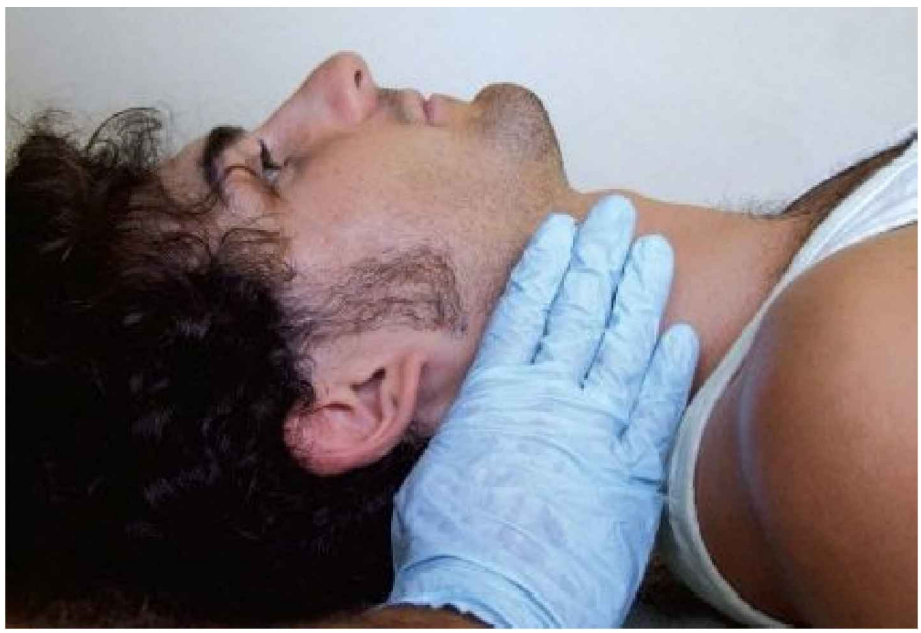
Cervical spine management

In any patient who has sustained significant trauma, an associated cervical spine injury or potential injury should be considered to be present. Thus, in-line spinal stabilisation is an essential aspect of care. Each member of the clinical team must be competent in providing and ensuring in-line stabilisation.

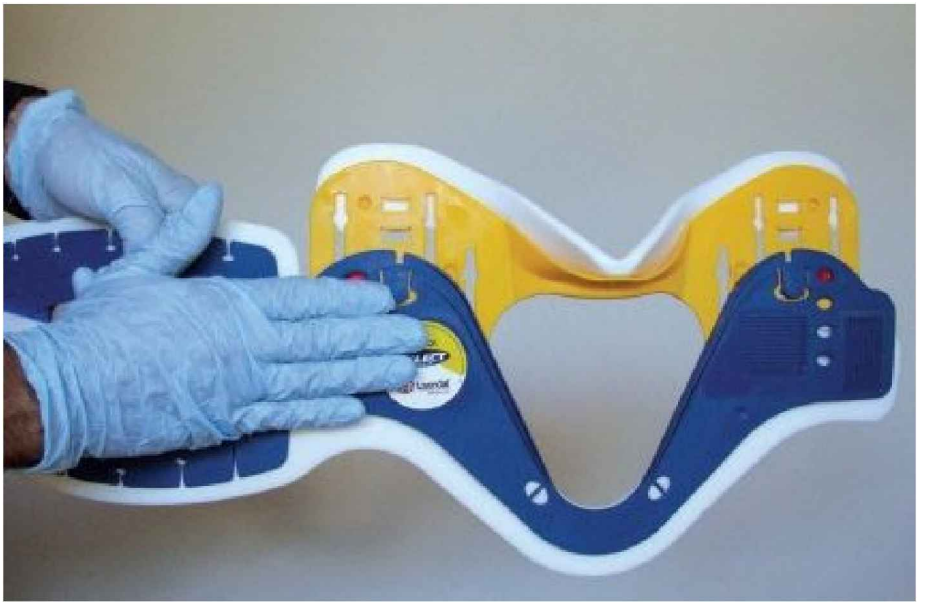
With any trauma patient, maintaining in-line spinal stabilisation is a priority. In many centres, there is a movement away from the use of semi-rigid cervical collars and transport on a spinal board. Recent evidence has demonstrated that this practice is likely to have more risks than benefits.[3–14] In patients suspected of having a spinal cord injury, ensure in-line spinal Page 564 stabilisation rather than spinal immobilisation. Placing the patient in a spine neutral position while stabilising the head and neck, with preferably a soft cervical collar and the hands of a competent and trained medical team member placed either side of the patient's head, will most likely afford the most appropriate spinal stability. A scoop stretcher, basket stretcher or vacuum mattress is the most appropriate device for moving a patient, with the standard NATO soft canvas folding stretcher to be avoided if at all possible.

Cervical collars are available in both fixed and adjustable sizes. If these devices are to be used, the adjustable semirigid collars are most appropriate in the sporting context, as they are compact and avoid the need to carry multiple collars of various sizes (Fig. 38.5a). Adjusting the collar to the correct size is essential, so as to be effective and minimise risks; this is demonstrated in Figure 38.5 b-e.

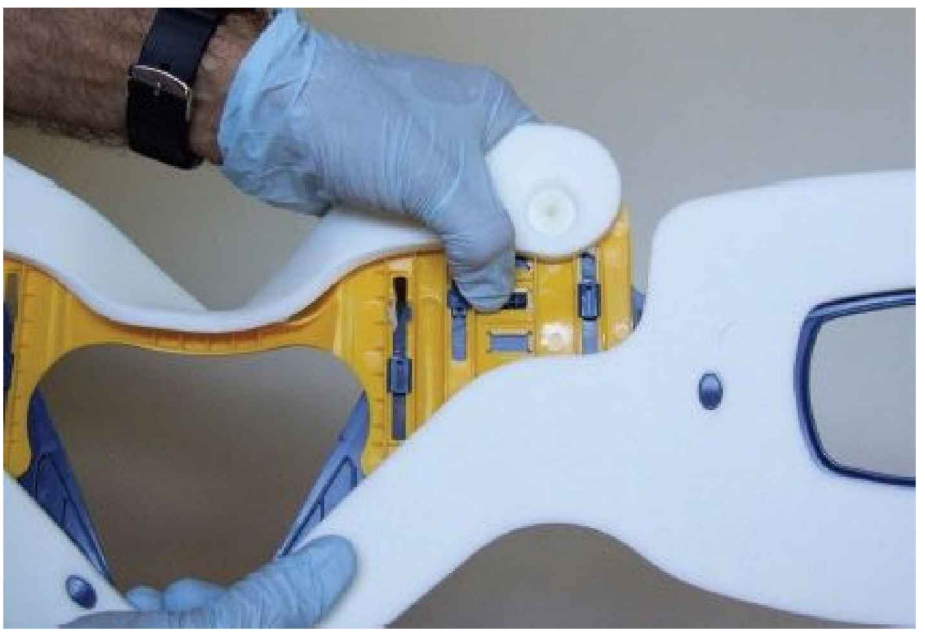
Figure 38.5 Cervical spine management (a) Laerdal®-style adjustable semi-rigid cervical collar



(b) Sizing a cervical collar using fingers as a guide



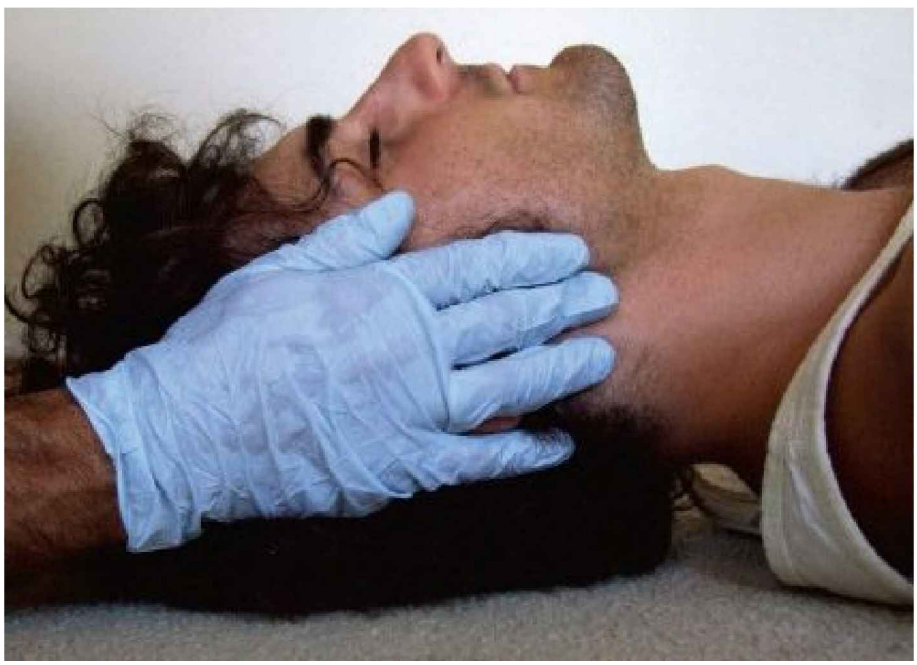
(c) Use this predetermined distance to measure from the blue plastic edge to the nearest hole



(d) Release locking lug and adjust collar so that red marker (Fig. e) aligns with the correct hole

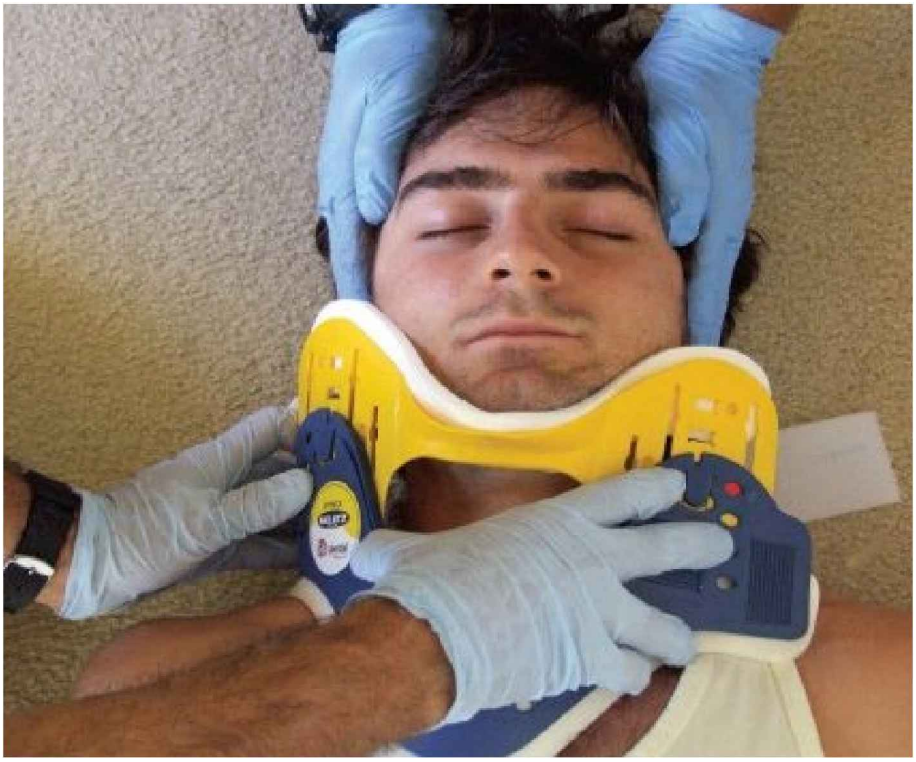
(e) Red marker positioned at the sizing hole

Initially, the cervical spine is held stable by one member of the clinical team (Fig. 38.5f), the head and spine should remain in line, with the head in the neutral position. Then slide the correctly sized collar behind the patient's neck, position it correctly and secure it quite firmly to prevent excessive movement (Fig. 38.5g-j).



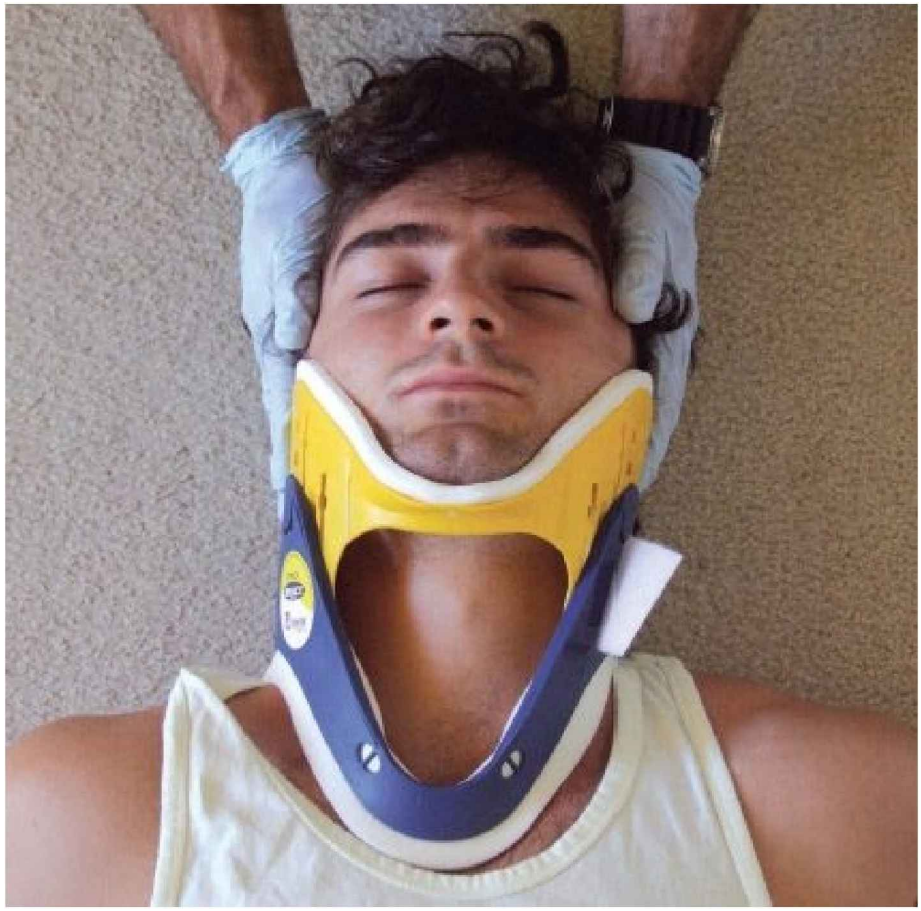
(f) In-line stabilisation of the cervical spine

(g) Positioning and securing of cervical collar—step 1



(h) Positioning and securing of cervical collar—step 2

(i) Positioning and securing of cervical collar—step 3



(j) Positioning and securing of cervical collar—step 4

PRACTICE PEARL

A cervical collar does not immobilise the cervical spine; it merely assists in stabilisation and helps remind the patient and the clinical team to assume spinal injury and manage accordingly.

Airway management technique adjuncts

Page 566

How the patient is positioned and where the clinician stands are important initial considerations. In most situations the patient is positioned supine and the clinician is either at the top or to the side of the patient's head. The priority in airway management is to maintain patency. Another priority in airway management (although less important than ensuring the patency of the airway) is protecting the airway and preventing the passage of blood or vomitus.

Maintaining a patent airway can be achieved using one or a combination of several techniques. Inspect the mouth and upper airway for obstruction (teeth, blood, vomitus, a mouth guard).

Remove any obstruction using gloved fingers, long forceps and/or suction. Once foreign matter has been removed from the airway, the next possible obstruction is the tongue and soft tissues at the back of the throat.

To facilitate airway patency, use the 'jaw lift' or 'pistol grip' (Fig. 38.6). This is achieved by grasping the lower jaw of the patient firmly and, while keeping the fingers clear of the throat, moving the jaw anteriorly so as to lift the tongue from the back of the throat. This is usually combined with head tilt, which is obtained by tilting the head, not the neck, back. Care must be taken in performing head tilt in patients with potential cervical spine injury.

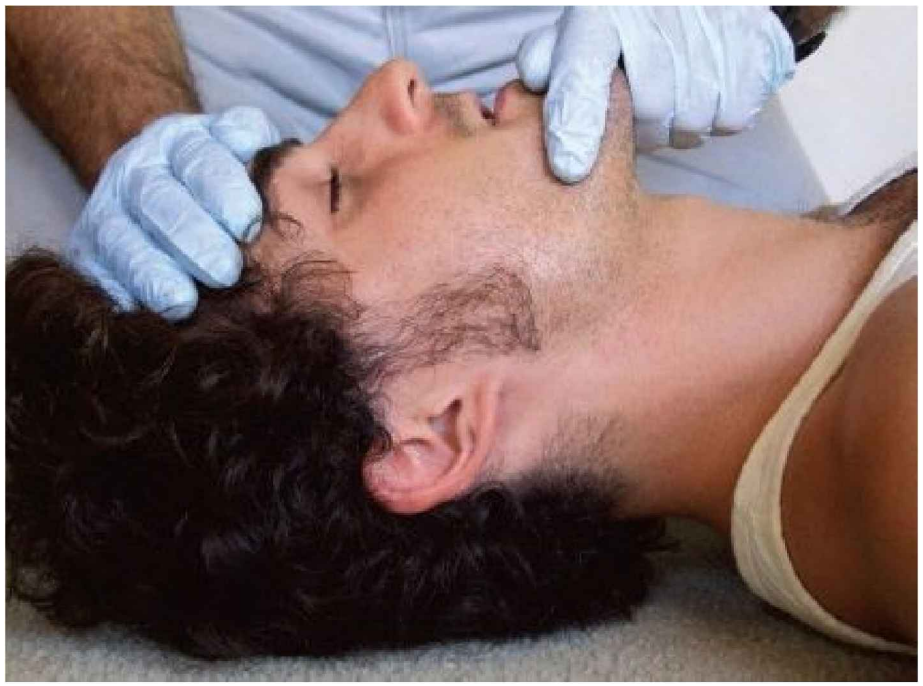


Figure 38.6 Jaw lift to clear the tongue from the back of the throat

A more effective technique is 'jaw thrust' (Fig. 38.7). This technique is performed by placing the fourth and fifth fingers behind the angles of the jaw and moving the entire mandible anteriorly. This subluxes the jaw anteriorly and moves the tongue well clear of the back of the throat.

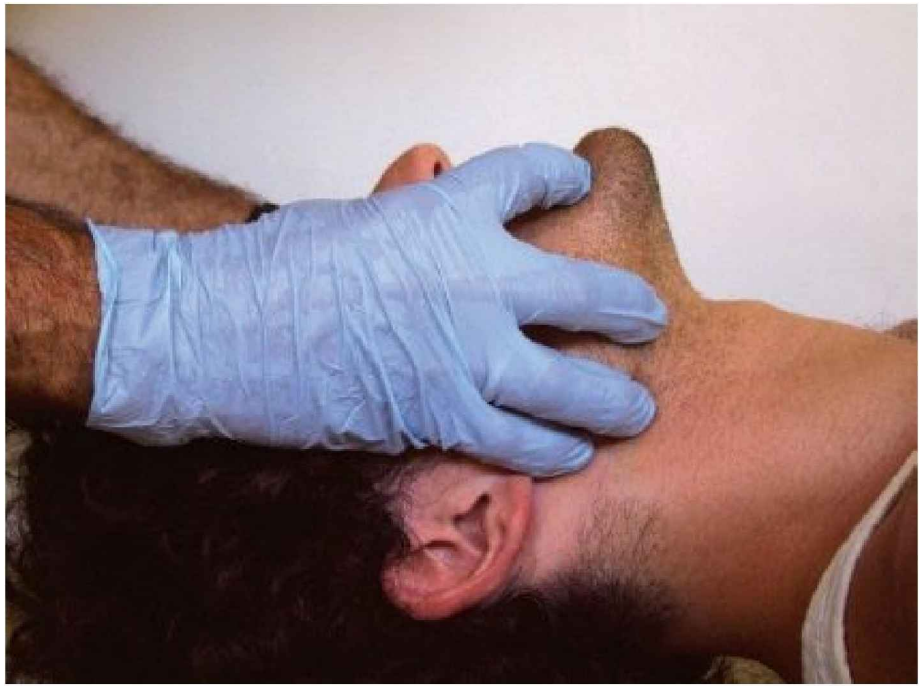
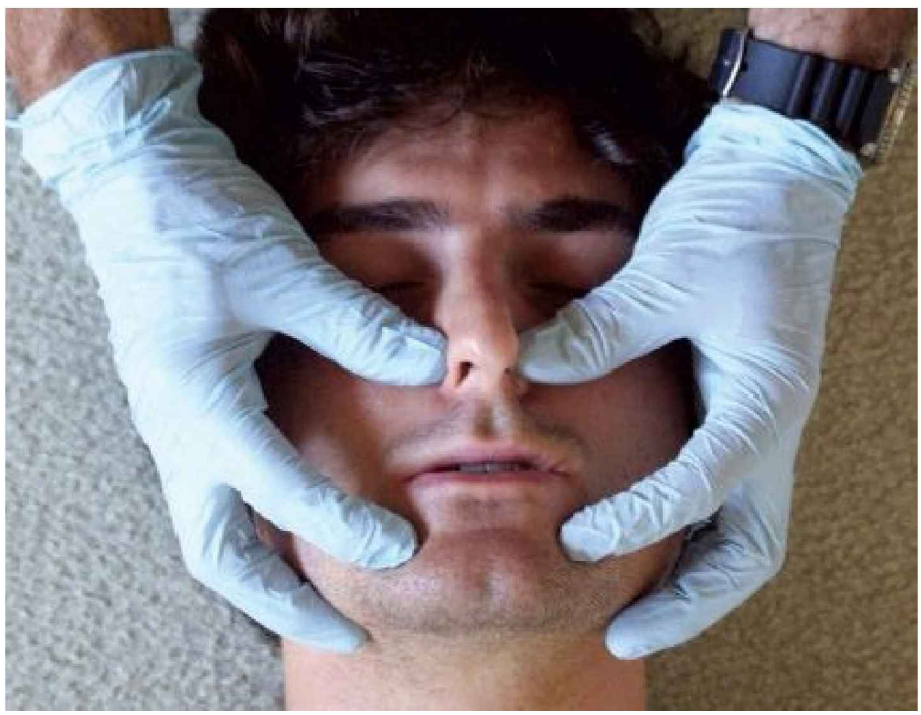


Figure 38.7 Jaw thrust—a more effective technique than the jaw lift (a) Lateral view



(b) Anterior view

Oropharyngeal airway

A useful adjunct for maintaining airway patency is the oropharyngeal airway (Fig. 38.8a). This curved piece of hollow plastic is placed into the airway and sits posterior to the tongue. It provides passage for air to flow. The lumen of an oropharyngeal airway is relatively narrow and the tube remains mobile in the airway and unsecured, so airway patency cannot be assumed. Frequent reassessment is essential.

Figure 38.8 (a) Oropharyngeal airways

Inserting the correct size of oropharyngeal airway is essential, so as not to obstruct the airway. To size an oropharyngeal airway, align the airway to the outside of the patient's mouth, so that the flange sits just anterior to the front teeth and the tail curves around the angle of the jaw (Fig. 38.8b).

(b) Sizing the oropharyngeal airway

To insert the airway, use some lubricant or water on the tube. With the patient's mouth held slightly opened, insert the tube so the distal part of the tube or its tail, is pointing towards the patient's nose (Fig. 38.9a). It is then passed over the tongue and when the tail of the tube is at the back of the patient's throat, it is rotated 180° to rest in the posterior pharynx. The flange should sit anterior to the front teeth, so that the reinforced bite area of the tube sits between the front teeth (Fig. 38.9b). Another technique for insertion, and one that should always be used for children, is to depress the tongue with a tongue depressor or wooden spatula and insert the oropharyngeal airway over the tongue with the curve of the airway following the curve of the tongue. This technique does not require the airway to be rotated 180° for its final resting position.

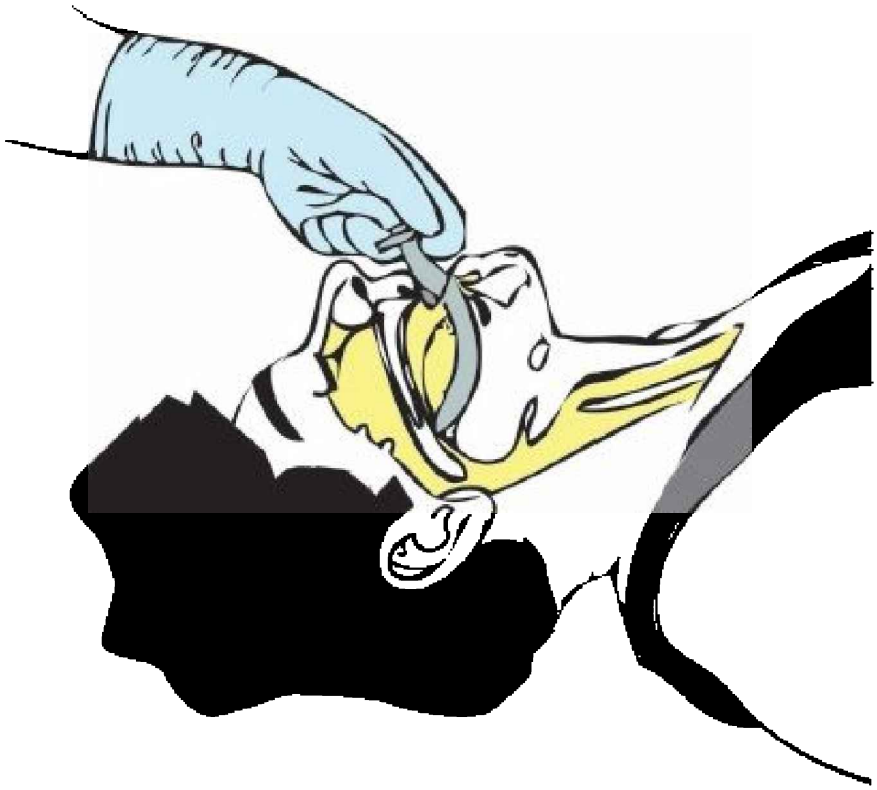
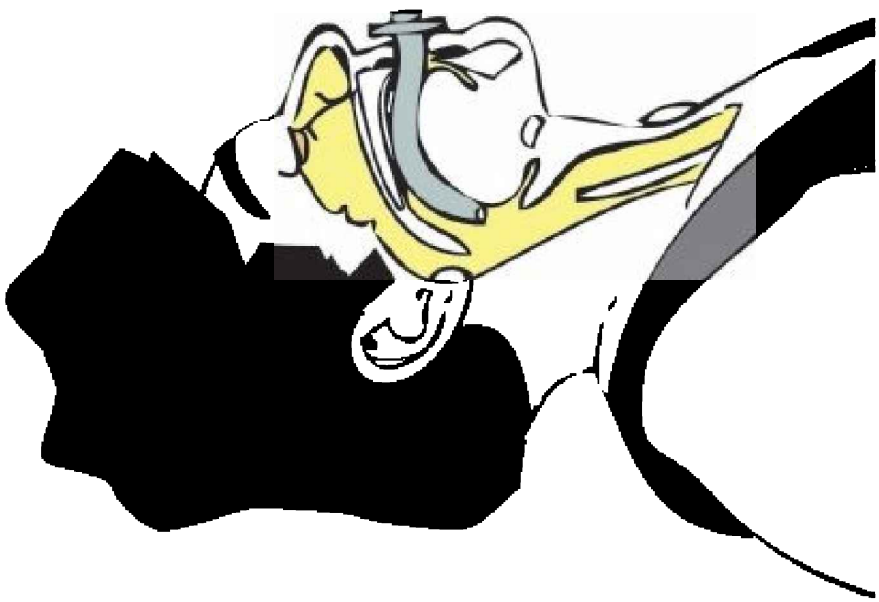


Figure 38.9 (a) Inserting the oropharyngeal airway in an adult (with the tail pointing towards the nose)
BROOKE FOWLER



(b) Final position of oropharyngeal airway (after rotating 180°) BROOKE FOWLER

Endotracheal tube

Although patency is the first priority, providing the patient with both a patent and a protected airway is ideal. This can be achieved with a cuffed tube in the trachea-an endotracheal tube (ETT). The technique requires skill and training that must be practised on a regular basis (as there is the potential for substantial risks in an inexperienced operator's hands). Inserting an ETT is made significantly more difficult when attempted in an uncontrolled environment such as in the middle of a sporting field. It also requires the use of additional instruments-such as a laryngoscope, which is costly and requires skill to use. Endotracheal intubation should only be performed by practitioners skilled and practised in the technique. The technique of ETT insertion is beyond the scope of this book.

PRACTICE PEARL

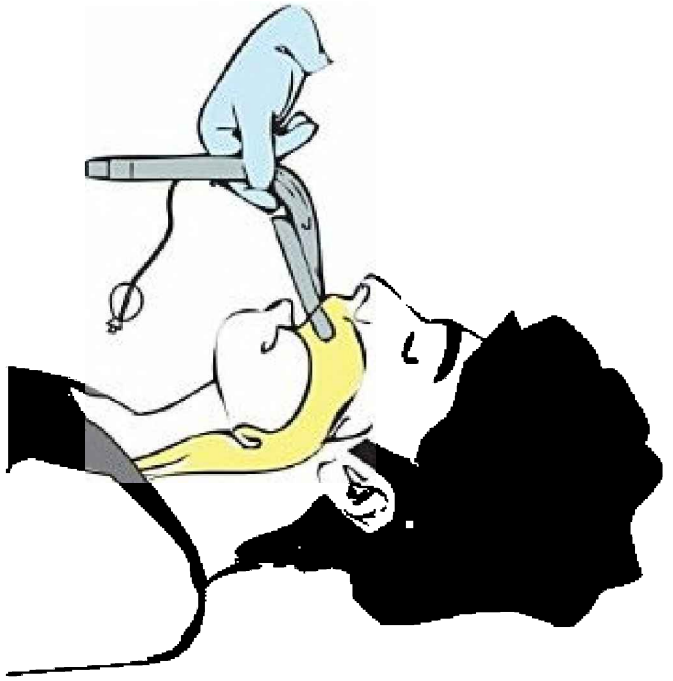
Airway patency is the priority.

Laryngeal mask airway

Page 568

A laryngeal mask airway (LMA) (Fig. 38.10) consists of an inflatable mask and a connecting tube. It is inserted into the pharynx. The use of an LMA requires skills and training that are within the expertise of many physicians. Insertion of the LMA may be simplified as a three-step process (Fi g. 38.11).

Figure 38.10 Laryngeal mask airway (LMA)



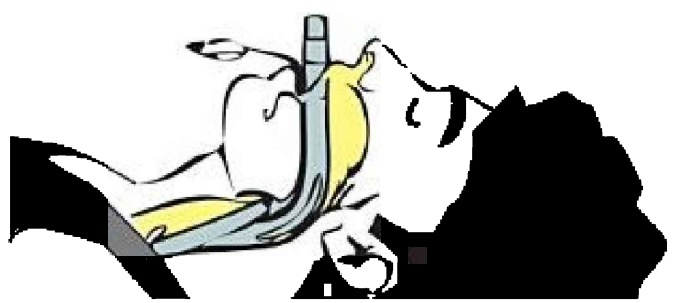


Figure 38.11 Inserting a laryngeal mask airway in three stages

BROOKE FOWLER

The LMA, once inserted and the cuff inflated, provides for a patent airway and offers partial airway protection. The patient may be ventilated through the LMA using the same technique as that used with an ETT.

Essential airway adjuncts

- Non-rebreather mask, initially connected to high-flow oxygen
- Cervical collar—sized correctly and positioned securely

Potentially life-threatening airway problems

Three potentially fatal airway problems require vigilance-choking, anaphylaxis and inability to clear the airway.

Choking—airway blockage

A common cause of partial or complete airway blockage is a foreign body. If the airway cannot be cleared by the procedures outlined above, follow the algorithm on choking as outlined by the Australian Resuscitation Council (Fig. 38.12).

AUSTRALIAN RESUSCITATION COUNCIL

NEW ZEALAND Resuscitation Council
Whakahauora, Aotearoa

MANAGEMENT OF FOREIGN BODY AIRWAY OBSTRUCTION (C

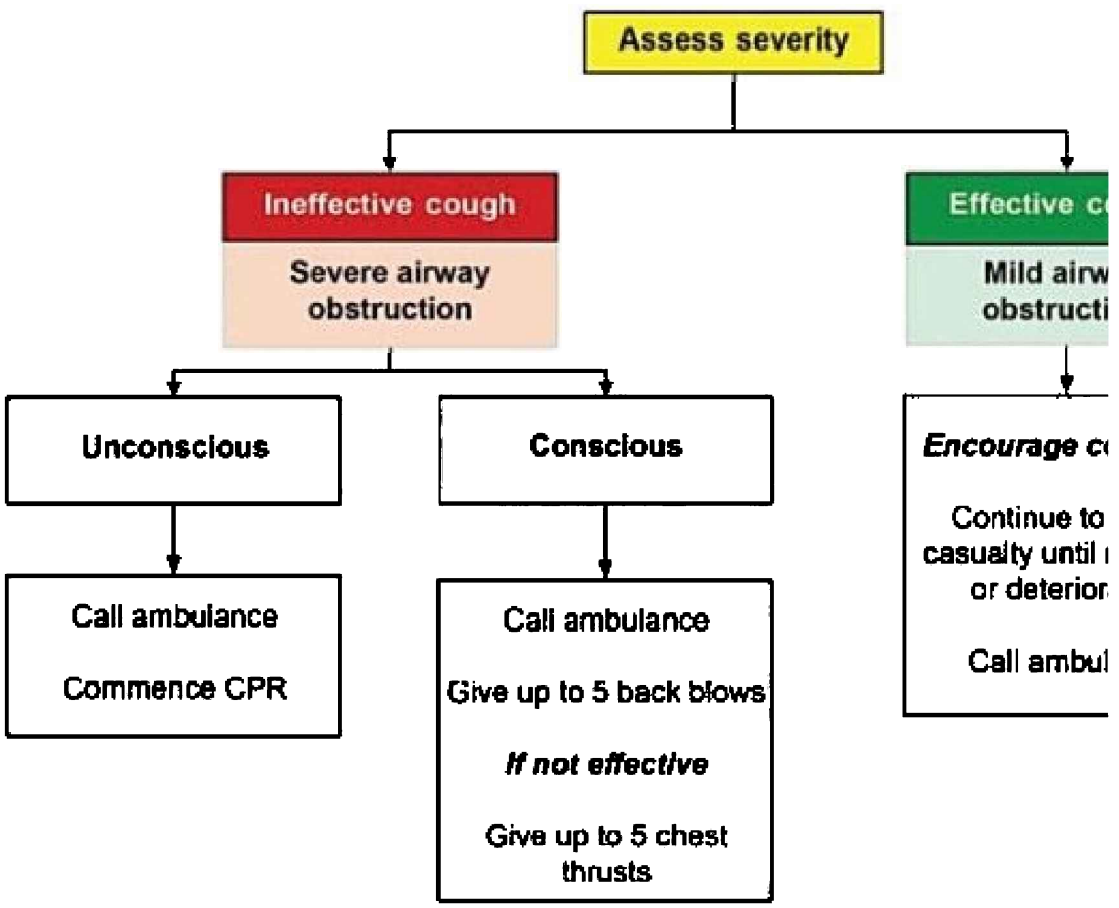


Figure 38.12 Flowchart for the management of foreign body airway obstruction

AUSTRALIAN RESUSCITATION COUNCIL, www.resus.org.au

Anaphylaxis

Anaphylaxis can occur at any time, in response to allergens to which the person has been previously sensitised (e.g. bee sting, peanuts, medications). As part of the medical screen, the clinician must be aware of any adverse, allergic or anaphylactic reactions that an athlete has previously experienced. Once identified, there must be an appropriate management plan in place to avoid exposure to the substance and to manage anaphylaxis if exposure does occur.

The recognition, and signs and symptoms of anaphylaxis are outlined in the boxes.

The immediate management of anaphylaxis is:[2]

- Follow an emergency management plan that has been previously developed for the patient.
- Remove any residual traces of the causative substance if possible (e.g. bee's sting).
- Administer oxygen, titrated to maintain saturation of at least 94%.

Recognition of anaphylaxis

- Any acute onset of hypotension or bronchospasm or upper airway obstruction where anaphylaxis is considered possible, even if typical skin features are not present, OR
- Any acute onset illness with typical skin features (urticarial rash or erythema/flushing and or angioedema), PLUS
- Involvement of respiratory and/or cardiovascular and/or persistent gastrointestinal symptoms

These features usually occur within 20 minutes of exposure, although may be delayed up to several hours.

- Give adrenaline (intramuscular):
  - 0.3-0.5 mg IM[1] injection for adult
  - 0.01 mg/kg IM injection for child.
- Repeat every 3–5 minutes if there is inadequate response.
- The patient may have their own adrenaline for self-administration, containing a predetermined dose (EpiPen®).
- Adjuncts include inhaled bronchodilators (e.g. salbutamol, ipratropium bromide) and systemic corticosteroids.
- Prolonged and biphasic reactions may occur for at least four hours after the last dose of adrenaline.
- Manage potential life-threatening symptoms as they occur.

Page 570

- Give inhaled salbutamol if there is evidence of bronchospasm (e.g. wheeze).
- Obtain intravenous access if possible.
- Commence fluid resuscitation if there is haemodynamic compromise with 20 mL/kg crystalloid solution.

Adrenaline (epinephrine) is the most important drug to be administered during anaphylaxis. Adrenaline is administered as an intramuscular (IM) injection. Intravenous access is not immediately required. The dose of adrenaline should be repeated every five minutes if there is ongoing compromise.

As anaphylaxis is a serious medical event, any patient who has experienced it must be educated appropriately, given strict instructions to always avoid the offending substance, have a well-understood and regularly reviewed management plan, carry an EpiPen® for immediate access and have close medical follow-up after the event. A delayed phase (secondary) reaction is a low frequency yet important consideration. Any patient who has experienced anaphylaxis should be assessed in a hospital emergency department after the event, even if initially managed successfully.

Significant facial swelling or trauma, or inability to clear a complete airway obstruction

Inability to clear a complete airway obstruction is a rare event, but potentially fatal. All initial interventions, as previously outlined, should be attempted first. If all attempts are unsuccessful and airway obstruction cannot be relieved, a needle cricothyroidotomy should be performed. This, although only temporising, is a life-saving procedure. It is a relatively easy technique to perform, although the physician must be rehearsed in both identifying anatomical landmarks and also the technique of needle insertion, and it should only be performed by those who are trained and legally qualified.

The purpose of this procedure is to oxygenate the patient who is attempting to breathe for him or herself on a short-term basis (usually no longer than 30–40 minutes), until a more definitive airway can be achieved. The administration of oxygen must be provided by jet insufflation as outlined below. See box for issues relating to cricothyroidotomy.

Signs and symptoms of anaphylaxis

Anaphylaxis, although also a shock state, may cause significant airway compromise. Signs and symptoms of anaphylaxis may include:

- wheezing
- stridor
- flushed, red and/or itchy skin
- hives
- swelling of the throat, tongue and/or lips
- tachycardia
- extreme anxiety

- abdominal pain or vomiting
- collapse followed by unconsciousness, if not treated immediately.

Emergency cricothyroidotomy

Equipment to prepare for needle cricothyroidotomy

- A 12G or 14G standard intravenous cannula, the lower the gauge the less airflow resistance
- A 5 mL or 10 mL syringe
- Standard oxygen therapy tubing
- A skin preparation solution or swabs
- Oxygen supply, although the delivery of expired air via the cannula may be performed if oxygen is unavailable
- A3-waytap

Anatomical landmarks and technique for performing needle cricothyroidotomy

- Assemble the cannula onto the syringe (Fig. 38.13b).
- Palpate the thyroid cartilage and thyroid notch (Adam's apple).
Page 571
- Slide your fingers inferiorly until you are in the space between the thyroid and cricoid cartilages; this is the cricothyroid membrane.
- With the region of the cricothyroid membrane identified (Fig. 38.13a), stabilise the trachea firmly with your thumb, second and third fingers.
- If time permits, clean the overlying skin.
- Insert the cannula into the centre of the cricothyroid membrane (Fig. 38.13a) and angle the cannula 45° in the caudal direction while aspirating the syringe.
- Aspiration of air identifies entry into the trachea; at this point insert the cannula several millimetres further.
- Withdraw the syringe and stylet and at the same time advance the cannula sheath into the trachea.
- Secure the cannula sheath and connect the 3-way tap with the oxygen tubing attached, ensuring all three ports of the tap are open (Fig. 38.13c).
- While holding the cannula sheath and 3-way tap securely with one hand, with the thumb of the other hand occlude the third port of the tap for 1 second to allow for oxygen flow into the trachea (Fig. 38. 13d); release your thumb for 4 seconds to allow for expiration (Fig. 38.13e).

Remember this is a temporary life-saving measure; urgent definitive medical care must be arranged.

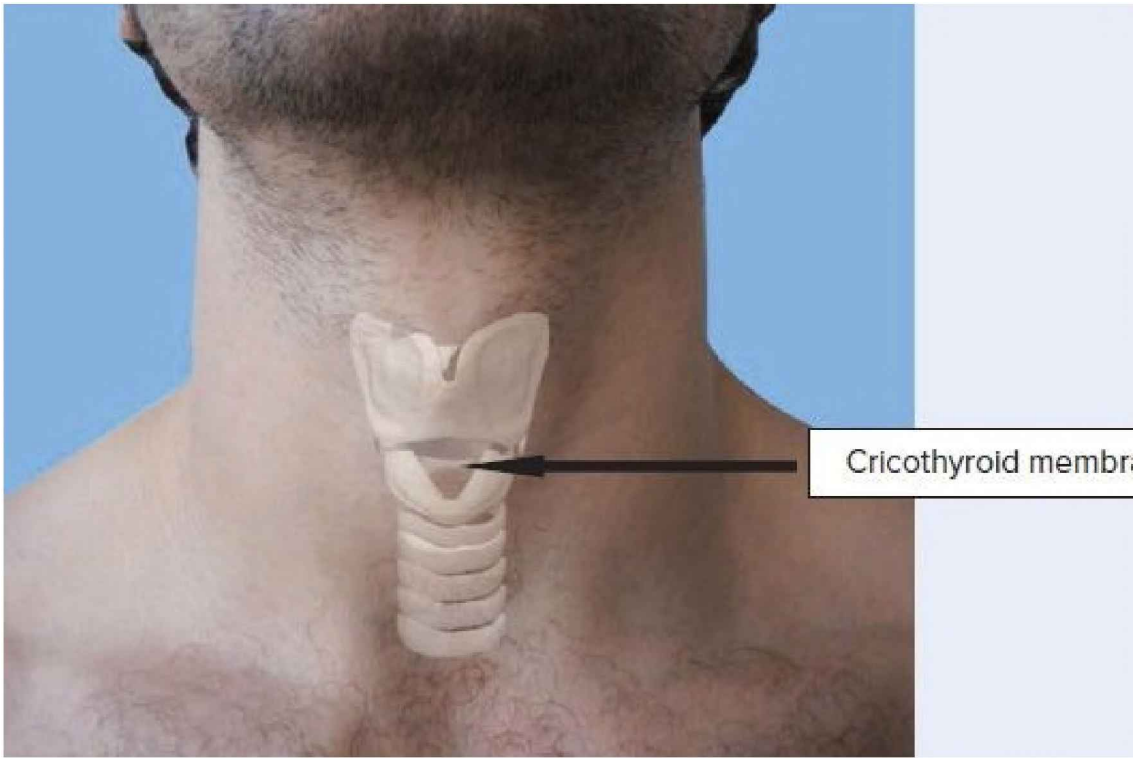
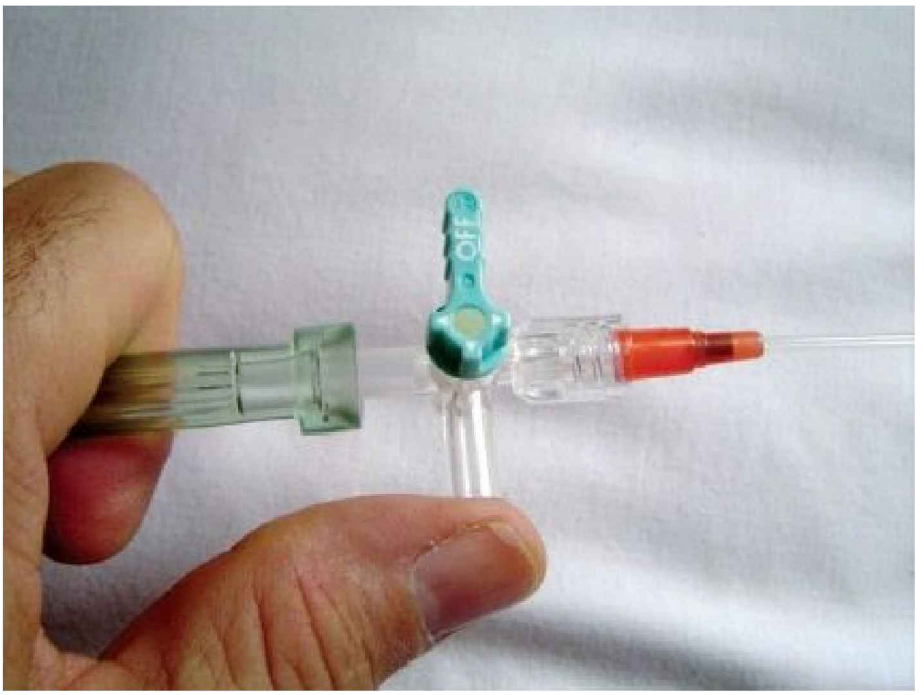


Figure 38.13 Emergency cricothyroidotomy (a) Cricothyroid membrane—position for needle cricothyroidotomy

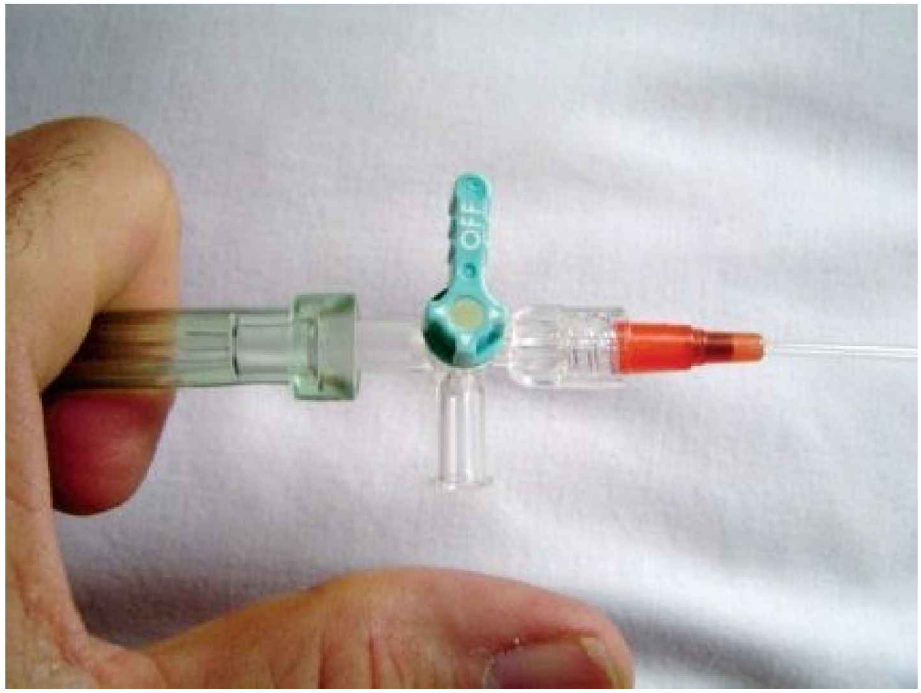
(b) Large-bore cannula attached to a syringe in preparation for a needle cricothyroidotomy

(c) Once the cannula sheath is inserted and secured in the trachea, attach the 3-way tap with oxygen

tubing



(d) Ensure all three ports are open and connected as shown and the oxygen turned on. Occlude the port open to the atmosphere with your thumb for 1 second to deliver oxygen to the patient



(e) Release the thumb over the port for 4 seconds to allow for exhalation

Breathing and ventilation

Breathing assessment and adjuncts are shown in the box. If there is no compromise to breathing or ventilation, move to the next stage of assessment, always having a low threshold for reassessment.

Breathing assessment and adjuncts

Equipment

- Stethoscope
- Pulse oximeter, if available

Once the airway is patent and secured, assess the patient's breathing and ventilation (note that performing auscultation and percussion at a noisy sporting venue can be difficult):

1. **Inspection**

   While positioned at the head of the patient with the patient's chest exposed, inspect for:

   a. accessory muscle use
   b. rate, effort and symmetry of breathing
   c. the presence of wounds or bruising to the chest or neck, which may suggest significant underlying airway or lung damage

d. evidence of distended neck veins suggesting a tension pneumothorax or cardiac tamponade.

2. **Palpation**
   a. With the patient's head in the neutral position, palpate the trachea to ensure it is midline and assess for a tracheal 'tug'. Deviation of the trachea may suggest a tension pneumothorax.
   b. Palpate the face, neck and chest for evidence of subcutaneous emphysema, suggesting a pneumothorax.
   c. Palpate the anterior chest to check for symmetry and degree of expansion.
3. **Auscultation**

   Using the stethoscope auscultate the chest at the apices, in the axillae and towards the bases, noting:
   a. equality of air entry
   b. degree of presence of breath sounds. Decreased breath sounds may suggest a pneumothorax or haemothorax, whereas completely absent breath sounds may suggest a tension pneumothorax
   c. any added sounds, such as wheezes.
4. **Percussion**
   a. Percuss all accessible regions of the chest, because as much information is gained from the feel of the percussion as from the sound.
   b. Dullness to percussion may suggest a haemothorax, especially if it is identified towards the lung bases or towards the posterior aspect in the supine patient.

Potentially life-threatening breathing and ventilation problems

Page 573

Potentially life-threatening breathing and ventilation problems include pneumothorax and acute severe asthma. Pneumothorax-the presence of air within the pleural space-can become rapidly life threatening. A pneumothorax can be closed (simple or tension) or open.

Simple pneumothorax

In most cases, a small simple pneumothorax can be managed by the administration of oxygen until definitive medical care is reached. Occasionally a spontaneous pneumothorax can become life threatening if it develops into a tension pneumothorax.

PRACTICE PEARL

Rib fractures are a common cause of pneumothorax.

Open pneumothorax

An open pneumothorax results from a penetrating chest wound where the pleural space communicates directly with the outside. This situation is best managed by applying plastic wrap over the wound and taping the wrap on three sides only, so as to produce a one-way flutter-valve effect. As the patient exhales, air from the pleural space is forced out under the wrap and when the patient inhales, the plastic wrap is sucked onto the wound, thereby preventing air entering the pleural space.

Tension pneumothorax

A tension pneumothorax is a true emergency. It may develop rapidly or gradually. If untreated, a tension pneumothorax is generally fatal. Tension pneumothoraces are made worse by active ventilation of the patient; occasionally they are the result of active ventilation. Keep this uppermost in your mind if you need to ventilate a Patient anxiety and distress patient. Signs and symptoms of a tension pneumothorax are shown in the box.

Steps for a needle thoracentesis

- Identify the appropriate anatomical landmarks (Fig. 38.14a) on the side with the suspected tension. The site where the needle should be inserted is the intersection of the fifth intercostal space and anterior to the mid axillary line on the affected side. This is best found by palpating for the angle of Louis, which is where the manubrium joins the body of the sternum. Slide your finger parallel with this joint towards the side of the suspected tension; you will meet the second rib where it articulates with the sternum—below this rib is the second intercostal space, count down to the fifth space.
- A 12G or 14G long intravenous cannula may be used and inserted its full length into the lower half of this space, so as to avoid the neurovascular bundle which runs inferior to each rib. In obese patients, a standard intravenous cannula may be too short and not enter the pleural space; subsequently a longer and more specific cannula may be required (Fig. 38.14b).
- Remove the stylet and leave the cannula sheath open to the atmosphere, sometimes aspirating the tension with a 20 or 50 mL syringe may decompress faster.

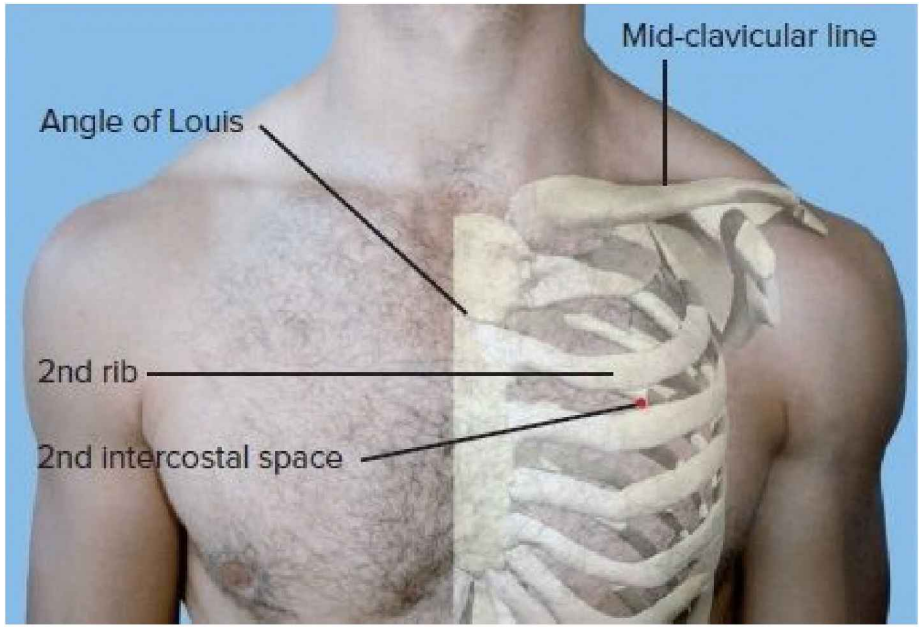
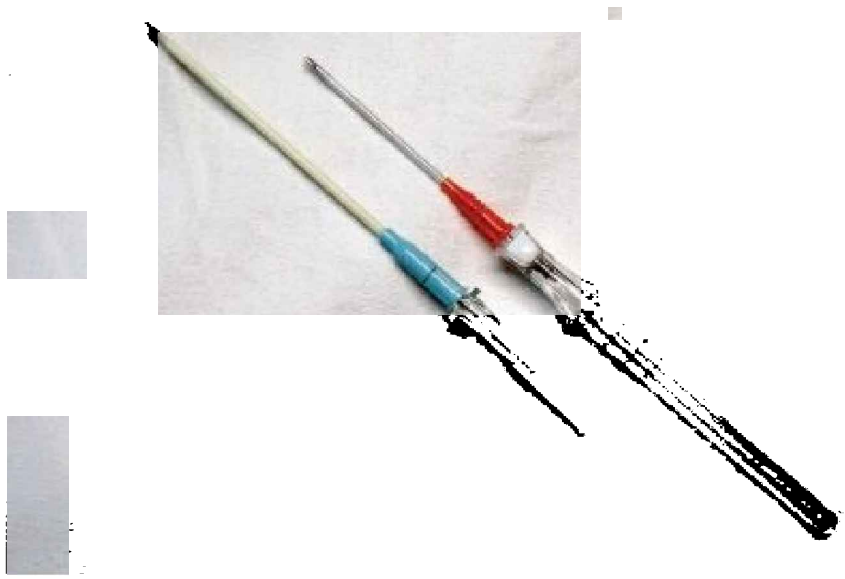


Figure 38.14 (a) Anatomical landmarks for needle thoracentesis



(b) A cannula designed for needle thoracentesis (blue) compared with a standard 14G intravenous cannula (orange)

Signs and symptoms of tension pneumothorax

- Tachypnoea
- Distended neck veins (if not hypovolaemic)
- Tachycardia
- Low oxygen saturation (although high-flow oxygen may mask this to some extent)
- Tracheal deviation to the *opposite* side of the pneumothorax, although this may be a late sign
- Absent breath sounds on the *same* side as the pneumothorax
- Hyperresonance on the *same* side as the pneumothorax
- Cyanosis may be a late sign
- If being passively ventilated, the patient may become progressively more difficult to ventilate.

Management of a tension pneumothorax requires a needle thoracentesis to relieve the tension immediately (see box). This, however, does not treat the resultant simple pneumothorax. A needle thoracentesis should only be performed by those appropriately trained and licensed.

Acute severe asthma

The clinician must be aware of all athletes under his or her care who have a diagnosis of asthma. Know the medications prescribed and the asthma action plan for the athlete. The following focuses on management of a severe asthma attack. The signs and symptoms of severe asthma are outlined in the box.

Signs and symptoms of severe asthma

- Marked dyspnoea
- Inability to speak or only speaking in single words
- Developing exhaustion
- Use of accessory muscles of respiration
- Oxygen saturation <94%
- The chest may be 'silent' to auscultation (this is an ominous sign)

Management of severe asthma

The management of severe asthma is as follows:

- Unless contraindicated, the patient should be positioned sitting up.
- Commence oxygen if the oxygen saturation is less than 95% or respiratory rate is greater than 20.
- If a nebuliser mask and oxygen supply are available, commence:
  - salbutamol 5 mg by inhalation via nebuliser, repeated every 20 minutes if indicated, or

sooner if required
  - ipratropium bromide 500 µg (adults) or 250 µg (children) 2–4 hourly.[15–17]
- If a nebuliser mask or oxygen supply is not available, use the following pressurised metered dose inhalers (pMDI) via a large volume spacer:[18, 19]
  - salbutamol 100 µg, 6–12 separate actuations by inhalation, repeated every 20 minutes if indicated, or sooner if required
  - ipratropium bromide 500 µg with a maximum of three doses in the first hour and repeat dose every 4–6 hours if required.[15–17]
- Give prednisone 50 mg orally[20] OR hydrocortisone 100 mg IV.[17]
- Start inhaled corticosteroids as soon as possible.

Circulation and haemorrhage control

If the cause of circulatory compromise or life threat is bleeding, it must be stopped. The most effective means of controlling external haemorrhage is by direct pressure to and elevation of the bleeding site.

Signs and symptoms of blood loss

Signs and symptoms of blood loss are listed in the box.

PRACTICE PEARL

Hypotension is not an early reliable sign of blood loss.

Signs and symptoms of shock due to blood loss

The most reliable early indicators of shock are:

- narrowed pulse pressure
- tachycardia (PR > 100)
- pale, cold and diaphoretic skin (i.e. peripheral shut down)
- confusion (in the absence of head injury, drugs or alcohol).

The patient usually needs to have lost up to 25% of circulating blood volume before a substantial drop in systolic blood pressure is noted. A significant systolic drop may even be less obvious in a supine patient or a very fit athlete (Fig. 38.17).

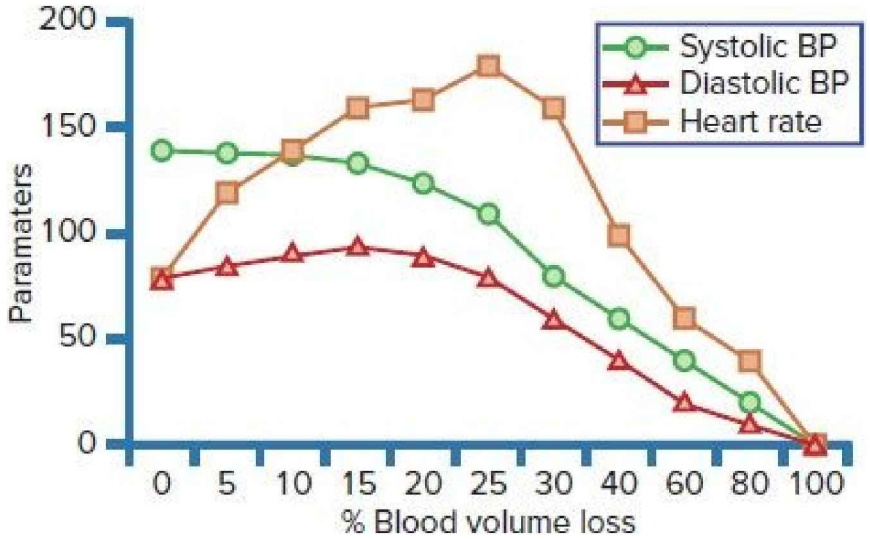


Figure 38.17 Early haemodynamic response to blood loss. Tachycardia is a much earlier sign of blood loss than hypotension

Sites of blood loss

Some sites of haemorrhage are easy to address, while others are impossible to manage outside an operating room. Possible sites of blood loss and what to do are shown in Table 38.1.

Table 38.1 Possible sites of blood loss and what to do

Site	Management
External bleeding (e.g. major lacerations)	Direct pressure and elevation of the bleeding p
	If catastrophic haemorrhage, apply a tournique
Long bones, especially the femur, which may result in 1–2 litres of internal blood loss	Immobilise and splint the fractured limb; this sig
Pelvic fractures, which have the potential for a devastating outcome	Minimise movement and handling of the pelvis
Chest, abdominal or retroperitoneal bleeds	Requires urgent transfer to a hospital for definit

Figure 38.18 Application of a pelvic binding device (a) Centre the towel or sheet over the femoral greater trochanters

(b) Pull both ends of device firmly so as to compress the pelvis circumferentially

(c) Firmly secure device with sports strapping tape or ratcheted metal clamps

(d) With the pelvic binder device firmly secured, internally rotate the legs and secure together

Circulation management principles

The priorities must always be Airway, Breathing and then Circulation. The only exception to this is life-threatening external haemorrhage likely to result in rapid exsanguination, such as from a carotid or femoral artery. In that case, initiate haemorrhage control immediately (Fig. 38.15).

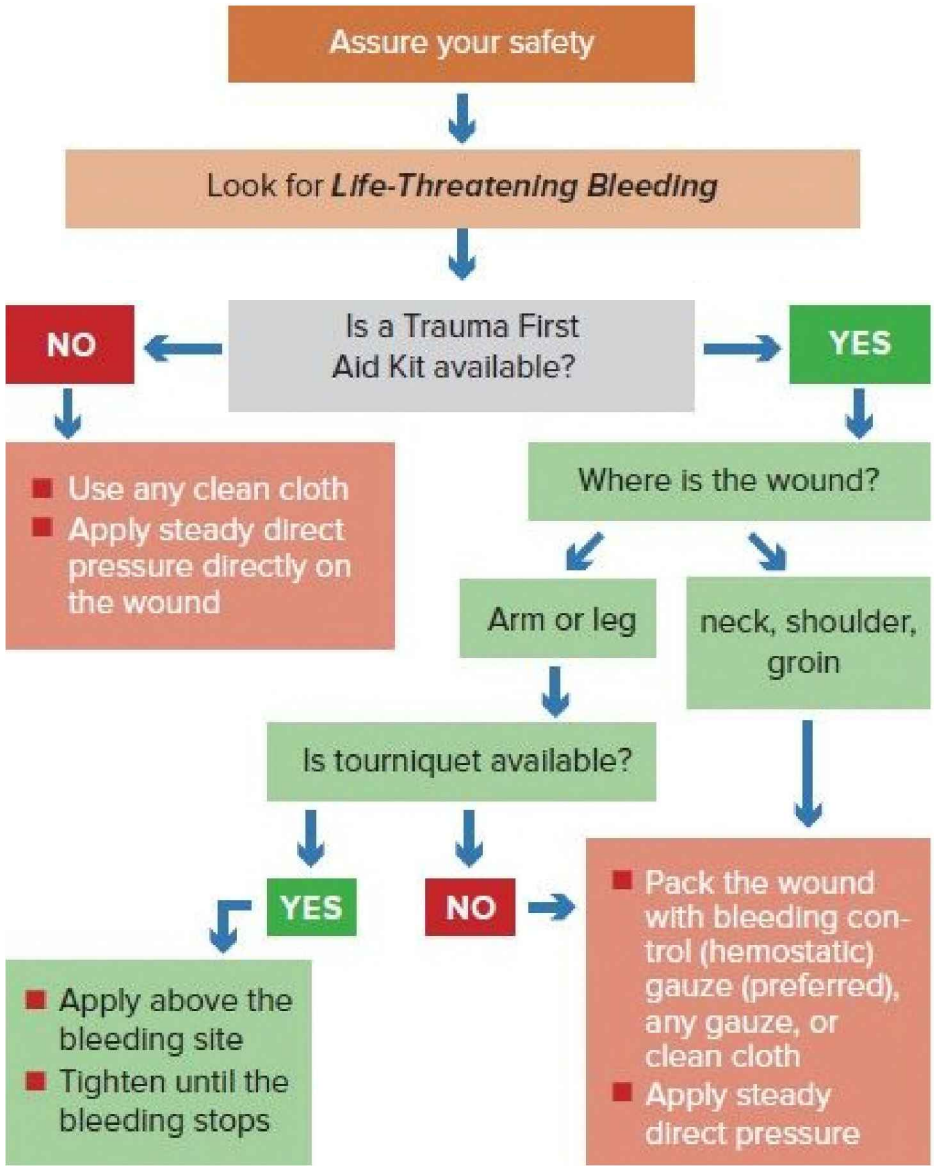


Figure 38.15 American College of Surgeons' algorithm for bleeding control

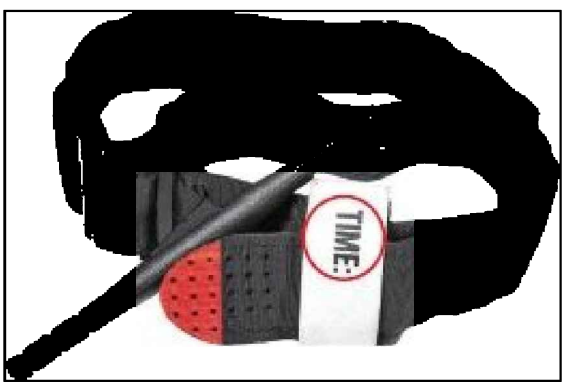
ADAPTED FROM STOPTHE BLEED.ORG

Immediate access to a tourniquet and the ability to apply it may be lifesaving. The procedure is illustrated in Figure 38.16.

1. Take the tourniquet and wrap it around the bleeding arm or leg about 2 to 3 inches above the bleeding site *(DO NOT place the tourniquet onto a joint – go above the joint if necessary)*

2. Tighten the tourniquet by pulling on the free end. Make it as tight as possible then secure it so it does not work loose

3. Twist or wind the windlass until the bleeding stops



4. Secure the windlass to ke the tourniquet tight and nc the time the tourniquet wa applied by writing it on the tourniquet

Note: Although a tourniquet will cause pain it is necessary stop life-threatening bleeding.

Figure 38.16 How to apply a tourniquet

MICHAEL PERVAK/SHUTTERSTOCK

The basic principles of haemorrhage control are outlined above. As part of the circulatory management, insert two large-bore intravenous cannulas (14G or 16G). The ideal position for these is in large veins in or around the cubital fossae, but any venous access is acceptable.

If the patient is exhibiting features of shock (see box), immediately infuse a bolus of crystalloid solution, either compound sodium lactate or sodium chloride (0.9%) (normal saline) at a dose of up to 1000 mL of 0.9% sodium chloride, or 20 mL/kg in a child. Carefully monitor the patient's response. If blood loss continues or there is inadequate or only transient response to the fluid, repeat the bolus once or twice and continue to call for urgent assistance. For patients who have ongoing and uncontrolled haemorrhage it is safer to maintain a systolic blood pressure of around 90 mmHg rather than aiming for a higher systolic pressure. A lower pressure aids in slowing the progression of coagulopathy and decreases the risk of dislodging clot formation at the bleeding site.

Ischaemic chest pain

The team clinician has medical responsibility for not only the athletes but also team coaches and officials. These persons may be at risk of ischaemic heart disease, myocardial infarction or cardiac arrest. Chest pain in any person, especially those with risks for ischaemic heart disease (IHD), should be assumed to be ischaemic heart pain until proven otherwise.

Thus, the clinical team must be competent with and well rehearsed in basic life support (see Fig. 38.3), and the physician must also be competent in advanced life support (Fig. 38.19).

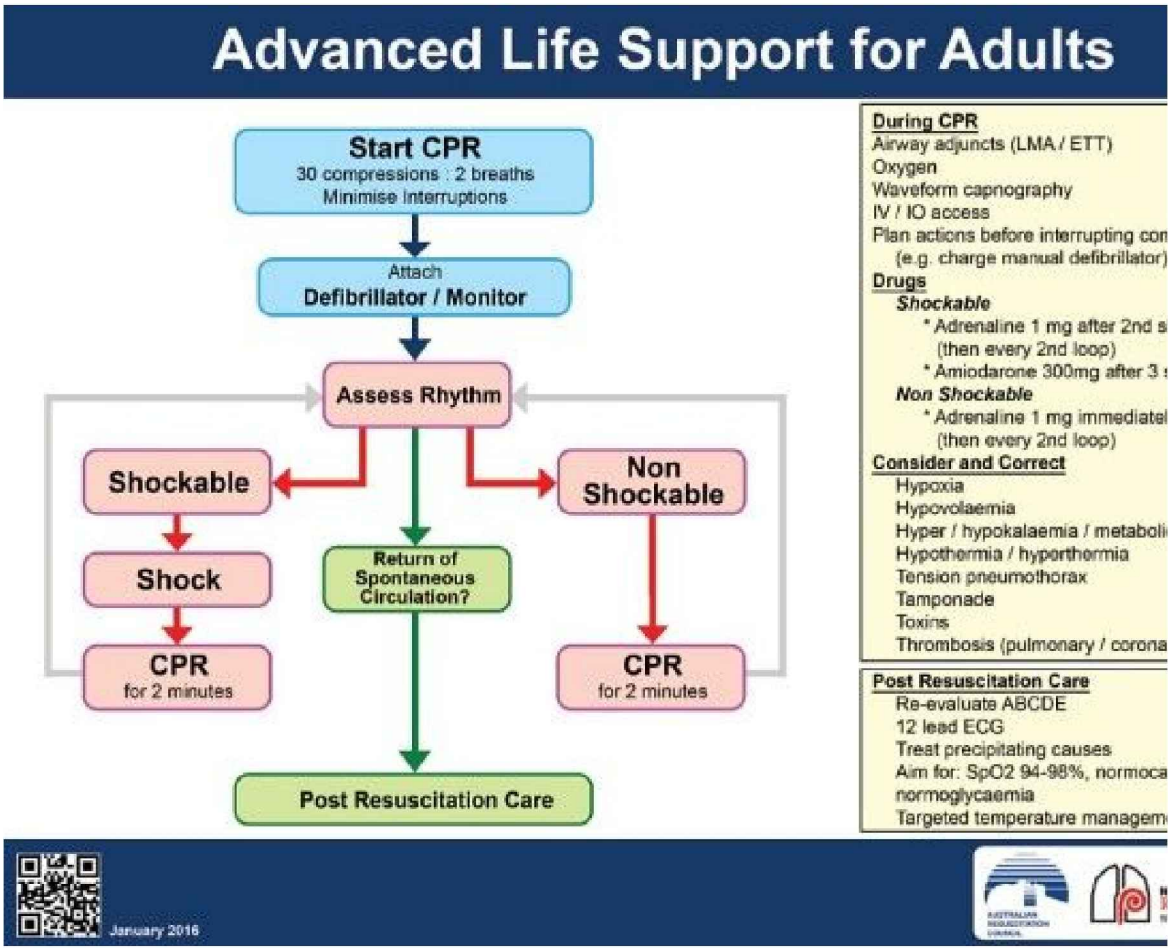


Figure 38.19 Adult advanced life support algorithm

COURTESY AUSTRALIAN RESUSCITATION COUNCIL, www.resus.org.au

In the event of a cardiac arrest, the priorities remain Airway, Breathing and Circulation. At the same time, applying the automated external defibrillator (AED) (Fig. 38.20) and following Page 577 the AED instructions are an urgent consideration and should be performed while also assessing the airway. In patients with ventricular fibrillation (VF) or pulseless ventricular tachycardia (VT), urgent defibrillation provides the patient with the best chance of survival.[21]

Circulation adjuncts

- Two large-bore cannulas
- Intravenous giving sets

- Intravenous fluids
  - compound sodium lactate (Hartmann's/Ringer's lactate)
  - normal saline (0.9% sodium chloride) Pads of automated external defibrillator (AED) Pulse oximeter
- Bandages and pads to control haemorrhage

Therefore, every physician must have rapid accessibility to an AED and accurate knowledge of the use of the device, whenever they have responsibility for the care of athletes, coaches or officials. Recognised and accredited courses in the use of AEDs for non-physicians are also available in many centres. It is essential that at least one member of the clinical team is trained and accredited to apply and use an AED in an emergency.

Management of ischaemic chest pain

The golden rule of Airway, Breathing, Circulation remains constant, and each of these are checked and established as in all other emergency care situations. In addition, the following apply:

Page 579

- Unless contraindicated, have the patient in a sitting or semi-sitting position.
- Administer oxygen if required to maintain an oxygen saturation of 94–98%.
- Attach AED pads and check monitor (Fig. 38.20).
- Obtain early intravenous access.
- Administer sublingual glyceryl trinitrate, one metered dose or one tablet. This may be repeated every 5 minutes if pain persists or to a maximum of three doses. Extreme caution should be observed if the patient has:
  - a systolic BP of < 100 mmHg or there is evidence of haemodynamic compromise
  - ingested medications such as Viagra® (sildenafil citrate) within the previous 12–24 hours.
  - For persisting pain, administer cautiously 2.5–5 mg intravenous morphine.
- Give aspirin 300 mg, either chewed and swallowed or dissolved in water and swallowed.
- Urgent transfer to more definitive medical care is essential.

Figure 38.20 Automated external defibrillator (AED). This is an essential piece of emergency medical equipment. The clinical team leader must ensure that there is ready access to an AED

Disability (and neurological status)

A brief disability assessment is included as part of the primary survey to obtain a baseline measure. Neurological status is best assessed in the emergency setting using the Glasgow Coma Scale (GCS)[22] (see Table 38.2), as well as by assessing pupillary response (size, shape and response to light). The GCS assessment should be standard practice with any head-injured athlete, no matter what the degree. A GCS score sheet should be kept in the team clinician's bag. When scoring a GCS, record the best patient response.

Table 38.2 The Glasgow Coma Scale[2]

https://www.sciencedirect.com. Due to rights and permissions restrictions, this content cannot be reproduced in a digital format. The content is available in the print edition at page 579.

REPRINTED FROM *THE LANCET*, 2(7872), TEASDALE G, JENNETT B. ASSESSMENT OF COMA AND IMPAIRED CONSCIOUSNESS. A PRACTICAL SCALE, 81–4, 1974, WITH PERMISSION FROM ELSEVIER

A normal GCS equals 15, with progressive deterioration as the score approaches a minimum of 3. A patient is usually unable to maintain or protect their airway with a GCS score of 8 or less.

Criteria for imaging the cervical spine

Page 580

Any significantly injured athlete must always be assumed to have a cervical spine injury. However, in many circumstances it may be appropriate for the clinician to assess the cervical spine and ask the following questions:

- If a collar is in position, is it safe to take the collar off?
- Should the patient undergo cervical spine imaging?
- Can the cervical spine be cleared of injury?

The National Emergency X-Radiography Utilization Study (NEXUS) cervical spine X-ray criteria[2 3–25] (see box) identify those who require further investigation of a possible cervical spine injury and those who may not. Patients who meet all five criteria have a very low probability of clinically significant injury to the cervical spine,[24] in which case they do not need radiological imaging and the cervical spine may be clinically cleared of injury.

Criteria for performing a CT scan of the brain

Where a patient has sustained multisystem or moderate or severe trauma, or where there is clinical concern, the patient must always be transferred to definitive medical care for further assessment and management.

NEXUS cervical spine X-ray criteria[23–25]

- No tenderness at posterior midline of the cervical spine
- No focal neurological deficit
- Normal level of alertness (GCS = 15)
- No evidence of intoxication
- No clinically apparent painful distracting injury (these are classified as significant injuries, especially

when involving the upper torso[3])

For those patients with an isolated head injury, where the clinician is uncertain as to the need for further investigation, the Canadian CT Head Rule[4, 26] may prove useful and should be applied to anyone who has sustained blunt trauma to the head resulting in one or more of the following:

- witnessed loss of consciousness
- definite amnesia
- witnessed disorientation (not matter how brief)
- an initial GCS <15.

This states that a patient should undergo a head CT if he or she has any one of:

- GCS < 15 at two hours after the injury
- suspected open or depressed skull fracture
- any sign of basal skull fracture
  - haemotympanum (blood in the middle ear)
  - periorbital ecchymosis ('racoon' eyes)
  - cerebrospinal fluid (CSF), otorrhea or rhinorrhea
  - bruising of the mastoid process (Battle's sign)
- two or more episodes of vomiting
- age >65 years old
- post-impact amnesia of ≥ 30 minutes
- dangerous mechanism of injury (e.g. fall > 1 m).

If the clinician is in any doubt as to the presence or absence of the above features, it is prudent to adopt a cautious approach and refer for further investigation and care.

Exposure and environment control

Although often overlooked, this part of the primary survey is as important as any other. Clinicians should adopt the mantra 'never assume'. Never assume that what you see or what the patient identifies are the only priorities needing attention. Thus, the exposure and environment control are part of the primary survey, which includes the process of a closer inspection of the patient for life-threatening problems, as well as taking action to ensure normothermia. This must be done while being mindful of ensuring patient confidentiality and privacy.

If not already performed, it is at this stage that the clinician performs a close inspection of the body parts covered by clothing and sporting gear. This also includes the back of the patient, for up until now the clinician has essentially only had vision and access to the front of the patient. It is at this time also that arrangements should be made to perform a log roll (Fig. 38.21).

Log roll

The log roll is an important skill which must be employed with any patient suspected of having a spinal injury. The technique described is also the procedure employed when moving an injured patient with the potential for spinal injury, to position a spine board or field stretcher to aid in patient transfer.

Performing the log roll for a close inspection of the patient's back or to position a spine board or field stretcher requires at least five people:

- The team leader or delegate takes control of the head and cervical spine and is responsible for coordinating the roll and ensuring neutral and in-line spinal stabilisation (Fig. 38.21a).

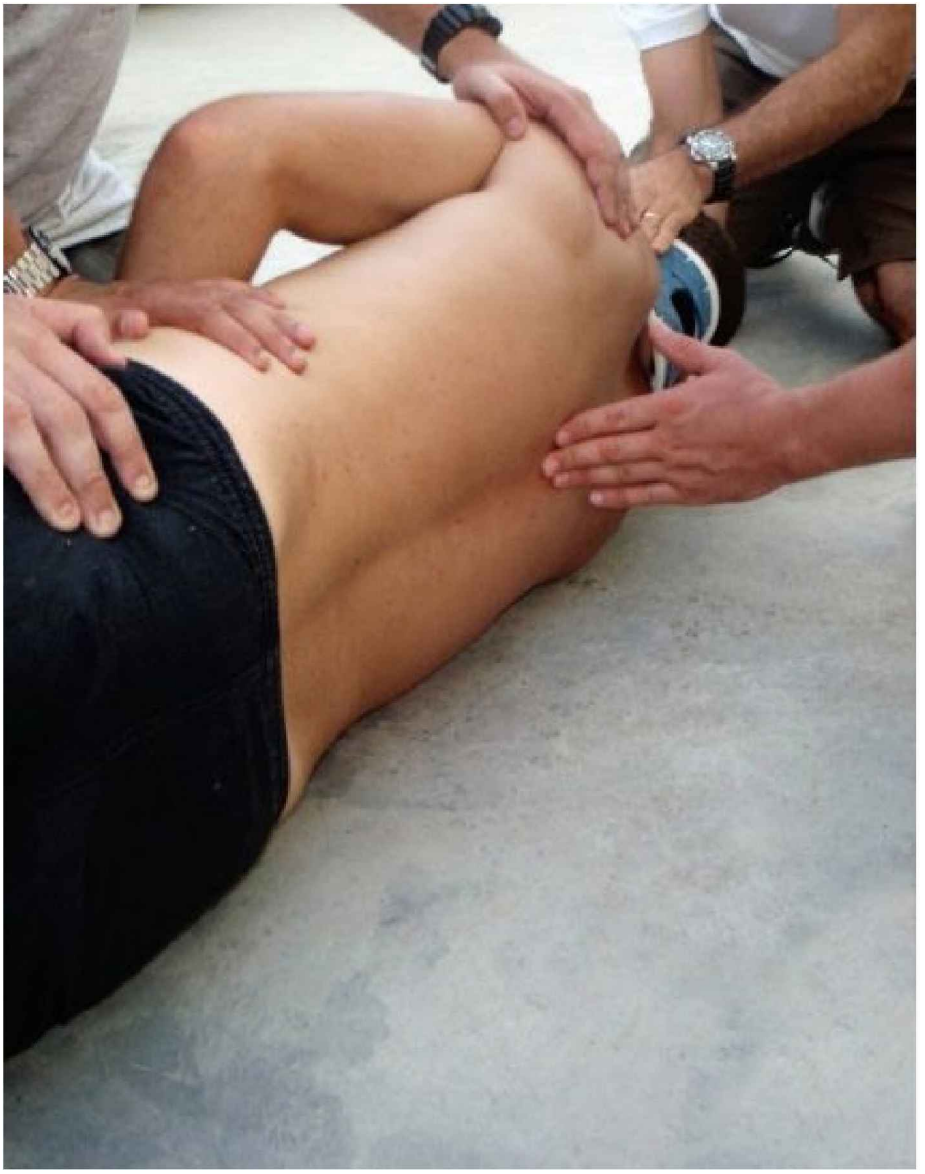
Page 581

Figure 38.21 The log roll (a) Preparing for the log roll

- Three members of the team are positioned on one side of the patient, with one being positioned alongside the patient's chest, the next alongside the patient's hips and the third alongside the region of the patient's knees.

(b) The roll is coordinated by the person controlling the cervical spine. Hand positions of the team members are demonstrated

(c) The patient is rolled in one single and smooth motion so the spine and legs remain in line



(d) Inspecting and examining the patient's back in the log roll position

- The fifth member of the team is responsible for inspecting the entire posterior aspect of the patient for injuries or objects which may result in life threat or compromise.

It is appropriate at this time to position an appropriate field stretcher so as to assist with transfer of the patient (Fig. 38.21e). The roll must be controlled and coordinated; it is strongly advised that the log roll be rehearsed by the team on a regular basis with their other clinical drills.

(e) Positioning the spine board

If used, a spine board assists with temporal spinal stabilisation to transfer the seriously injured athlete. It is not meant as a transport device and is used in most situations to move the injured athlete or the athlete suspected of spinal injury from the site where the injury occurred to an appropriate transport stretcher. Leaving a patient on a spine board for extended periods of time results in compromise to skin integrity and the potential for pressure area sores.

Ensuring normothermia

A critically ill or critically injured patient often loses his or her ability to appropriately thermoregulate. Subsequently, the patient will rapidly adopt the surrounding environmental temperature. Unless ambient temperature is 37°C (98.6°F) there is the potential for further

compromise. The aim is normothermia; therefore the clinician should aim to maintain the patient's body temperature as close to 37°C as is possible. This may mean applying blankets or warmers and sheltering the patient from the environment, or perhaps taking measures to decrease surrounding temperature so a core temperature of approximately 37°C is maintained.

APPROPRIATE USE OF ANALGESIA IN TRAUMA

The use of analgesia is important when managing emergencies, and the type of analgesia and the timing are critical. In any situation when the physician is prescribing and administering any medication, it is the absolute responsibility of the physician to understand the risks and benefits associated with administering the medication, as well as the indications, contraindications, potential adverse effects and appropriate dosages. It is also considered best practice to have appropriate medication available in the event of a subsequent allergic or anaphylactic reaction.

The physician may consider several routes of administration for analgesia in the emergency situation:

1. *Subcutaneous or intramuscular.* These routes are easy for the physician to use; however, because of variable and unpredictable absorption (especially in emergencies), these routes are usually not advised. Although these routes are not used for analgesia, adrenaline (which is used for anaphylaxis) is one of the very few drugs used via the intramuscular route in an emergency situation.
2. *Intravenous.* In most settings this is the preferred route to use for analgesia. Action of onset is rapid and doses can be titrated reasonably accurately. Obtaining intravenous access may be a challenge in certain circumstances. The use of intravenous narcotics, in some situations, may be associated with patient nausea and vomiting, in which case administering an intravenous anti-emetic prior to the narcotic may be appropriate.
3. *Regional blocks.* Using a local anaesthetic for a nerve block is a very effective form of analgesia, especially in limb and digit trauma. However, many regional blocks require the physician to have undertaken further training to be able to perform these safely and effectively. For those trained, this is an exceptionally effective modality for pain relief.
4. *Inhalational analgesia.* Most inhaled analgesics are self-administered by the patient. The onset and offset of action are quite rapid and the analgesic properties are usually predictable and reliable. These can be administered as a compressed gas in cylinders or as a solution (e.g. methoxyflurane) inserted into a dispensing device. In Australasia, the latter has become the most popular in the pre-hospital care setting and in particular as an analgesic for serious sporting injuries.

The physician should be familiar and comfortable with using at least two separate forms of analgesia. It must be recognised that different countries have different rules and regulations relating to the use and possession of certain drugs. The physician must be aware of these restrictions and ensure they are not in breach with any medications that may be in their

possession.

RECOMMENDED GENERAL AND EMERGENCY MEDICAL EQUIPMENT

The medical resources, medications and supplies required by the clinician responsible for the medical care of athletes depend at least somewhat on whether a physician is also part of the clinical team, and the sport that is being covered. However, there is basic equipment that Page 583 spans all sports and situations, and equipment that may be effectively and safely used by non-physicians. See Chapter 39 for advice on how to prepare a kit bag when working with a team and when travelling to deliver team care.

PRACTICE PEARL

It is critical for the clinical team to have ready and easy access to both an AED and an appropriate field stretcher.

REFERENCES

1. International Liaison Committee on Resuscitation. 2005 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations. Part 8: Interdisciplinary topics. *Resuscitation* 2005; 67(2–3): 305–14.
2. Brown SG. Anaphylaxis: clinical concepts and research priorities. *Emerg Med Australas* 2006; 18(2): 155–69.
3. Heffernan DS, Schermer CR, Lu SW. What defines a distracting injury in cervical spine assessment? *J Trauma* 2005; 59(6): 1396–9.
4. Stiell IG, Wells GA, Vandemheen K et al. The Canadian CT Head Rule for patients with minor head injury. *Lancet* 2001; 357(9266): P1391–6.
5. Davies G, Deakin C, Wilson A. The effect of a rigid collar on intracranial pressure. *Injury* 1996; 27(9): 647–9.
6. Brown JB, Bankey PE, Sangosanya AT et al. Prehospital spinal immobilization does not appear to be beneficial and may complicate care following gunshot injury to the torso. *J Trauma* 2009; 67(4): 774–8.
7. Barkana Y, Stein M, Scope A et al. Prehospital stabilization of the cervical spine for penetrating injuries of the neck—is it necessary? *Injury* 2000; 31(5): 305–9.
8. Kwan I, Bunn F. Effects of prehospital spinal immobilization: a systematic review of randomized trials on healthy subjects. *Prehosp Disaster Med* 2005; 20(1): 47–53.

9. Seamon MJ, Fisher CA, Gaughan J et al. Prehospital procedures before emergency department thoracotomy: 'scoop and run' saves lives. *J Trauma* 2007; 63(1): 113–20.
10. Smith JP, Bodai BI, Hill AS et al. Prehospital stabilization of critically injured patients: a failed concept. *J Trauma* 1985; 25(1): 65–70.
11. Baez AA, Schiebel N. Evidence-based emergency medicine/systematic review abstract. Is routine spinal immobilization an effective intervention for trauma patients? *Ann Emerg Med* 2006; 47(1): 110–12.
12. Hauswald M, Ong G, Tandberg D et al. Out-of-hospital spinal immobilization: its effect on neurologic injury. *Acad Emerg Med* 1998; 5(3): 214–19.
13. Hauswald M, Braude D. Spinal immobilization in trauma patients: is it really necessary? *Curr Opin Crit Care* 2002; 8(6): 566–70.
14. Hauswald M. A re-conceptualisation of acute spinal care. *Emerg Med J* 2013; 30(9): 720–3.
15. Rodrigo G, Castro-Rodriguez J. Anticholinergics in the treatment of children and adults with acute asthma: a systematic review with meta-analysis. *Thorax* 2005; 60(9): 740–6.
16. Balanag VM, Yunus F, Yang PC et al. Efficacy and safety of budesonide/formoterol compared with salbutamol in the treatment of acute asthma. *Pulm Pharmacol Ther* 2006; 19(2): 139–47.
17. Rodrigo GJ, Rodrigo C. Triple inhaled drug protocol for the treatment of acute severe asthma. *Chest* 2003; 123(6): 1908–15.
18. Dolovich MB, Ahrens RC, Hess DR et al. Device selection and outcomes of aerosol therapy: Evidence-based guidelines: American College of Chest Physicians/American College of Asthma, Allergy, and Immunology. *Chest* 2005; 127(1): 335–71.
19. Cates CJ, Welsh EJ, Rowe BH. Holding chambers (spacers) versus nebulisers for beta-agonist treatment of acute asthma. *Cochrane Database Syst Rev* 2013(9): Cd000052.
20. Fernandes RM, Oleszczuk M, Woods CR et al. The Cochrane Library and safety of systemic corticosteroids for acute respiratory conditions in children: an overview of reviews. *Evid Based Child Health* 2014; 9(3): 733–47.
21. Larsen MP, Eisenberg MS, Cummins RO et al. Predicting survival from out-of-hospital cardiac arrest: a graphic model. *Ann Emerg Med* 1993; 22(11): 1652–8.
22. Teasdale G, Jennett B. Assessment of coma and impaired consciousness: a practical scale. *Lancet* 1974; 2(7872): 81–4.
23. Hoffman JR, Schriger DL, Mower W et al. Low-risk criteria for cervical-spine radiography in blunt trauma: a prospective study. *Ann Emerg Med* 1992; 21(12): 1454–60.
24. Hoffman JR, Mower WR, Wolfson AB et al. Validity of a set of clinical criteria to rule out injury to the cervical spine in patients with blunt trauma. National Emergency

X-Radiography Utilization Study Group. *N Engl J Med* 2000; 343(2): 94–9.

25. Hoffman JR, Wolfson AB, Todd K et al. Selective cervical spine radiography in blunt trauma: methodology of the National Emergency X-Radiography Utilization Study (NEXUS). *Ann Emerg Med* 1998; 32(4): 461–9.
26. Ropper AH, Gorson KC. Clinical practice. Concussion. *N Engl J Med* 2007; 356(2): 166–72.

[a]Throughout this chapter all drug doses will assume an adult patient unless otherwise specified.

Chapter 39

Medical coverage of endurance events

with TIMOTHY NOAKES

Your body will argue that there is no justifiable reason to continue. Your only recourse is to call on your spirit, which fortunately functions independently of logic.

Professor Timothy Noakes

The organisers of endurance events are obliged to provide medical coverage, both to enable competitors to have immediate access to optimal management of medical problems and to relieve the burden on local medical services. These endurance events may include marathons, ultramarathons, triathlons and Ironman Triathlon events, as well as long-distance events such as walking, swimming, cycling and cross-country skiing. Many of these events will have large numbers of competitors with varying degrees of fitness.

Blisters, bruises, lacerations and muscle cramps are the cause of a large number of presentations to the medical tent at these events. Overuse injuries may develop or may be aggravated in athletes by competing in an endurance event, whereas traumatic injuries may occur as a result of a fall in a crowded running field or from a bike, for example. Thermal injuries (heat stroke or hypothermia) are common in endurance events (Chapters 23 and 24). As there is the possibility of cardiovascular collapse during such events, appropriate facilities must be available.

The precise details of the medical services required will depend on the particular sport, the duration and intensity of the activity and the prevailing environmental conditions. Medical teams that have worked at endurance events for years are able to predict the expected numbers of casualties. It is vital to keep medical records for all athletes treated at a particular event and to analyse these data for historical trends (Table 39.1). We will consider a marathon foot race with 1000 competitors as the basis for our recommendations. The figures should be adjusted according to the type of events and the number of competitors.

Table 39.1 Expected percentage of race starters to be admitted to central medical facility at a sporting event with 1000 competitors

Activity	Percentage of race starters
Running	
42 km	2–20
21 km	1–5
Ultratriathlon >200 km	15–30
Cycling	5
Cross-country skiing	5

HOLTZHAUSEN LM, NOAKES TD. COLLAPSED ULTRAENDURANCE ATHLETE: PROPOSED MECHANISMS AND AN APPROACH TO MANAGEMENT. CLINICAL JOURNAL OF SPORT MEDICINE 1997; 7(4): 292–301 HTTPS://EUROPEPMC.ORG/ABSTRACT/MED/93973271

RACE ORGANISATION

Specific pre-race strategies to enhance the safety of the competitors include the following.

1. Schedule the race at a time of year and day when environmental conditions will not adversely affect performance or health. The medical director of the race should have the authority to cancel the race should adverse weather conditions prevail. The American College of Sports Medicine position statement recommends that if the wet bulb globe temperature index is above 28°C (82°F), or if the ambient dry bulb temperature is below −20°C (−4°F), organisers should consider cancelling or rescheduling the event.[2]
2. Ensure adequate provision of fluids en route.

Page 586

3. Plan the race course so that the start and finish are in an area large enough to accommodate all spectators and race finishers, medical facilities and quick getaway routes for emergency vehicles. Place first-aid stations along the route at points allowing for rapid access by emergency vehicles and ideally about 3–5 km apart.
4. Set pre-participation screening and qualification standards to ensure that unfit and inexperienced athletes do not place themselves at undue medical risk during the event.
5. Provide pre-race seminars for participants presented by medical personnel, as this can reduce the number of casualties. Advice may include:
   a. correct training
   b. appropriate nutrition
   c. adequate fluids prior to and during race
   d. dangers of competing during or shortly after a febrile illness or while taking medications.
6. Ensure registration forms include questions regarding past and present medical history. This enables identification of, for example, athletes with diabetes, asthma and coronary artery disease. Such athletes could be sent specific information advising them on safety precautions, such as wearing a medical bracelet.

7. Implement an 'impaired competitor' strategy. Strategically positioned first-aid helpers should be permitted to stop athletes who appear ill and unable to finish the course. There should be vehicles to transport these competitors to the finish line.
8. Advise the local hospital emergency department of the forthcoming race and the likely number and nature of casualties.
9. Hold meetings between the various members of the medical team (see below).
10. Ensure an emergency transport service is available to bring problem cases to the central medical facility or to the nearest hospital emergency facility. Helicopter evacuation has proven invaluable for prompt treatment of athletes suffering cardiac arrest and other life-threatening conditions.

THE MEDICAL TEAM

A medical director of appropriate expertise should be appointed a number of months prior to the staging of an endurance event, to work closely with the event director. Early appointment of a medical director permits him or her to implement the pre-race strategies outlined above.

The medical director is responsible for the preparation of medical services and the supervision of the medical team on the day of the event. As endurance events are commonly held over a large area, communication between the different members of the medical team is the highest priority. The medical director should ensure adequate means of communication are available through the use of a two-way radio system or mobile phones.

The medical team should consist of appropriately trained physicians (sporting injuries and medical emergencies), physiotherapists, sports/athletic trainers, nurses, podiatrists and soft tissue therapists. For an endurance event with 1000 competitors, the medical team should number approximately 20, of which at least one-third should be physicians. Approximately 60% of the medical team should be situated in the medical areas near the finishing line, 10% of the team should be at the finish line itself, 20% should be distributed at the first-aid stations along the route and 10% should be patrolling the route in cars, ambulances or on bicycles. In shorter events, a greater proportion of the medical team should be situated near the finish line.

PRACTICE PEARL

The medical team should practise performing emergency procedures, athlete evacuation and rapid assessment of the collapsed athlete prior to the event.

At peak periods in a large race of 10 000–20 000 competitors, it is common to have four to six athletes requiring attention every minute–a much faster rate of admission than even the busiest inner-city trauma centres. Thus, the medical team must have procedures well rehearsed. This preparation period also provides the medical director the opportunity to ensure that all caregivers are using the most recent, evidence-based guidelines for the management of casualties.[3, 4] In large

events (>3000 competitors) or in adverse environmental conditions, at least one fully equipped mobile intensive care ambulance should be in attendance near the finish line. In small events, the ambulance service should be notified that the event is taking place.

FIRST-AID STATIONS

First-aid stations should be placed en route at strategic positions, providing a stretch and massage facility for cramping muscles, first aid (plasters, Band-Aids®) for chafing skin and blistered feet, and identification of the at-risk runner who is confused or delirious. These stations provide a centre from which athletes can be transported to the central medical facility or to a nearby hospital emergency department. Thus, stations should be positioned in areas that have good access to exit routes.

In running events, first-aid stations should be about 3–5 km apart. Practitioners skilled in treating common musculoskeletal problems and administering emergency first aid should staff these. A physician should staff the first-aid station and all first-aid stations should be in communication with the medical director. In larger events, a car or ambulance should patrol the course with a physician in attendance.

Drink stations are usually situated next to first-aid stations. It is important that the two be separated by at least 50 m so that the large crowds that are passing through the drink stations do not interfere with first-aid management. Additional drink stations should be situated at approximately 2–2.5 km intervals in events such as marathons.[5, 6] For events lasting less than 1 hour, water is the fluid of choice for rehydration. For longer events, a glucose-electrolyte drink is preferred by many.

MEDICAL FACILITY AT THE RACE FINISH

The layout of the central medical station will depend on the facilities available to the race organisers. Figure 39.1 shows the floor plan of the medical facility at the end of the 56 km Two Oceans ultramarathon foot race held annually in Cape Town, South Africa.[1] The green and red zones are for non-severe and severe cases, respectively. Other areas are allocated for the diagnostic laboratory, physiotherapy, medical supplies and toilets.

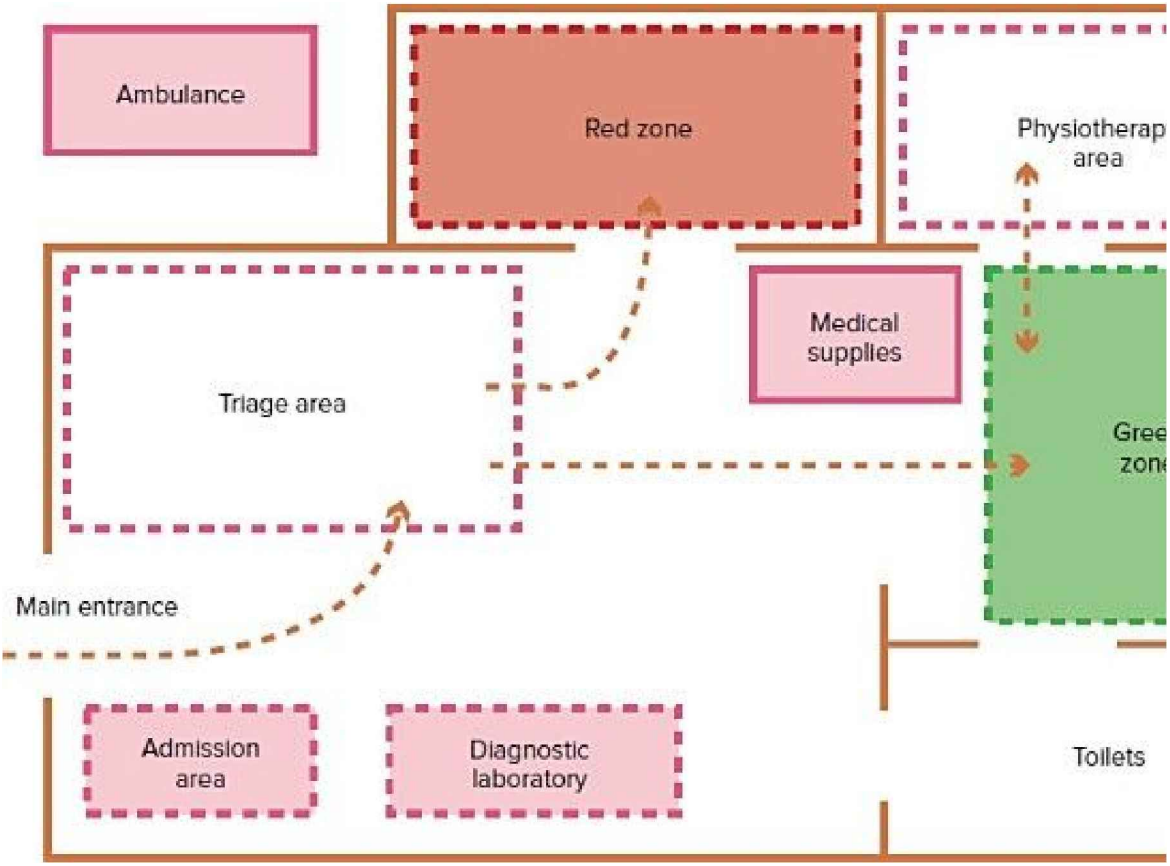


Figure 39.1 Floor plan of the medical facility at the finish line of the 56 km Two Oceans ultramarathon foot race in Cape Town, South Africa

REDRAWN WITH PERMISSION FROM HOLTZHAUSEN ET AL (1997)[1]

Note that the red zone for emergencies, such as cardiovascular collapse, hypothermia and heat stroke, is best located immediately adjacent to the triage station. The red zone can be constructed to afford a degree of privacy for distressed or seriously ill patients and permit discreet measurement of rectal temperatures. This area should be staffed by emergency-trained physicians and nurses. An ambulance should be located next to the red zone to allow rapid transport of emergency cases.

The benefit of this type of system over the undifferentiated medical tent that was prevalent in the past is that potentially lethal emergencies are much less likely to be overlooked in the general hustle and bustle of athletes with numerous important but not life-threatening musculoskeletal problems. Figure 39.2 provides guidelines for the activities that need to be completed in each of the areas.

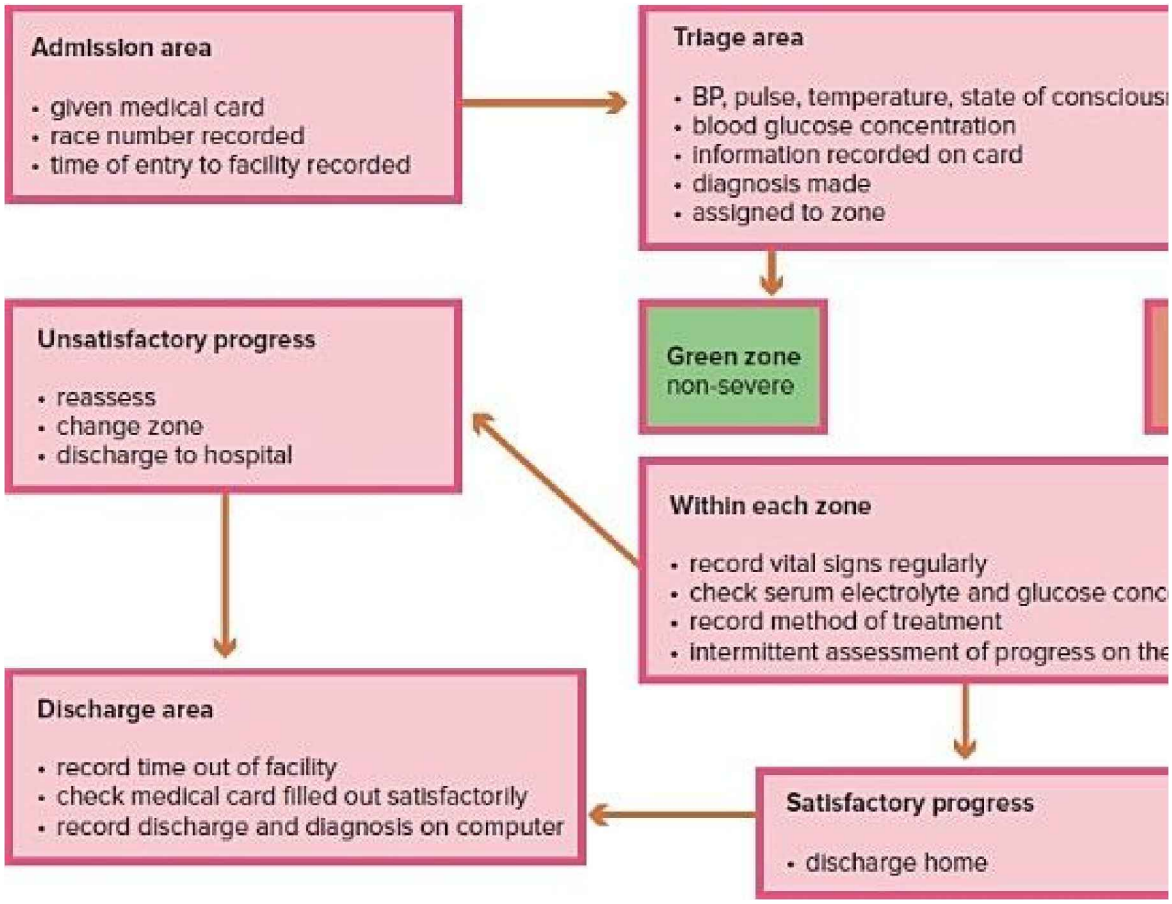


Figure 39.2 Suggested flowchart for the management of athletes once they enter the central medical facility illustrated in Figure 39.1

The equipment needs for a race medical centre include the following:

1. Chairs and tables for the computer operator at the admission area, for the laboratory technologist and the diagnostic equipment, and for the other medical equipment and drugs.
2. Stretchers for transporting collapsed athletes from the race finish to the medical facilities. These are also used for athletes to lie on in the green and red zones. Stretchers must be rigid so the foot can be elevated and collapsed athletes can be nursed, at least initially, in the head-down position. Some A-frame stands are needed to elevate the foot of the stretcher. These are removed once the athlete's cardiovascular status has normalised.
3. Blankets for each stretcher. These allow for discreet measurement of rectal temperature (Chapt er 23) and treatment of hypothermia (Chapter 24).
4. Plastic baths large enough to accommodate the torso of a 40–90 kg athlete. These are filled with

ice water and are used to treat heat stroke (Chapter 23).

5. Refrigerator facility-a mobile refrigerator truck is ideal for large races.
6. Computer terminal linked to the race finish.
7. Accurate scales should be available at race check-in and at the end of the race, and placed on a level surface. Athletes should be weighed with race-day clothing and without gear or other excess weight. Weight can be a useful tool in determining hydration status, with weight loss of >2% body weight being an indicator of dehydration, and weight gain suggestive of exercise-associated hyponatraemia (EAH).
8. Blood electrolyte and sodium analysers. Ideally, serum sodium and potassium concentrations should be measured in all patients. However, this is essential in all subjects who are diagnosed as dehydrated and in need of intravenous fluids. A serum sodium concentration below 130 mmol/L (130 mEq/L) indicates that the athlete is more likely overhydrated than underhydrated.
9. Bins for rubbish and sharps.
10. Toilet facilities.
11. Medications and equipment. Table 39.2 lists the resuscitation and medical equipment and Table 39.3 the medications required to cope with the expected emergency conditions. A pharmacist should be present to control the distribution of medications.

Table 39.2 Essential resuscitation and diagnostic tools for endurance sporting event with 1000 competitors Page 589

Resuscitation tools	Diagnostic tools
Oral airways (sizes 6–8)	Stethoscopes (5)
Resuscitation masks (disposable)	Sphygmomanometers (5)
Defibrillator	Rectal thermometers (5, with disinfectant)
Oxygen cylinder/masks (2)	Torches
	Ophthalmoscope and otoscope Glucometers for blood monitoring (2) Reflex hammer Blood electrolyte analyser Urine sticks Peak flow meter (1)

Table 39.3 Basic medications required in medical facility at endurance sporting event with 1000 competitors

Mode of administration	Medication
Injectable	Atropine (0.4 mg/mL) Dexamethasone (4 mg/mL) Morphine sulfate 15 mg/cc Dextrose 50%

	Adrenaline (epinephrine) (1:1000) (1 mg/mL) Salbutamol for nebuliser Metoclopramide Cardiac resuscitation drugs: atropine, lignocaine (lidocaine), frusemide Xylocaine (local anaesthetic) Tetanus toxoid
Inhalation	Salbutamol inhaler
Oral	Paracetamol (acetaminophen) (500 mg) Sublingual glyceryl trinitrate (nitroglycerin) (0.4 mg) Isosorbide dinitrate spray Chlorzoxazone tablets (500 mg) Loperamide capsules (2 mg)
Topical	Proparacaine (0.5%) eye anaesthetic Water-soluble lubricant Povidone iodine Tincture of benzoin

12. Given that over 60% of runners requiring attention after a marathon require physiotherapy services, it is ideal if a separate physiotherapy area can be set aside from the central medical facility. Many endurance events also provide a massage tent for athletes. As there is often a large number of minor foot injuries associated with endurance running events, the presence of a podiatrist is of great assistance also.

Additional supplies required for the medical tents and first-aid stations are shown in the boxes below.

Supplies required for medical station at finish line of a marathon with 1000 competitors

- Surgical instruments and disposables
- Scissors
- Latex gloves
- Syringes (3 mL, 5 mL, 10 mL)
- Needles (18, 21, 25 gauge)
- Steri-strips™, Band-Aids
- Skin disinfectant
- Adhesive bandages
- Gauze pads
- Suture equipment (disposable)
- Space blanket
- Fluid administration sets; cannulas, poles, giving sets (10)
- Normal saline for intravenous use (10 × 1 L)
- 3–5% saline as the IV fluid of choice for exerciseassociated hyponatraemia (10 × 1 L)
- 5% dextrose for intravenous use (2 × 1 L)

- Haemaccel for intravenous use (2 × 1 L)

Supplies required at first-aid station along course of a marathon with 1 000 competitors

- Stretchers (5)
- Blankets (5)
- 10 cm (4 inch) and 15 cm (7.5 inch) elastic bandages (6 each)
- Gauze pads
- Rigid strapping tape
- Dressing packs (5)
- Skin disinfectant
- Inflatable arm and leg splints (1 each)
- Athletic trainer's kit Petroleum jelly
- Pens and paper for record collection

Other useful equipment

- Ice and plastic bags (100 kg of ice)
- Water (500 L)
- Glucose-electrolyte drink (to make 250 L)
- Cups (2000)
- Towels
- Nebulisers (2)
- Slings (5) Eye pads
- Computer, tablet or mobile for data entry Podiatrist's kit (scalpel, sharp scissors, disinfectant, skin care pad, adhesive felt)

SUMMARY

The risks associated with endurance events can be reduced with adequate preparation, good medical coverage on the day of the event and, most importantly, education of the competitors. Educating the competitors regarding some of the pitfalls of competing in an endurance event will not only improve their performance but will also reduce the risk of any major problem developing.

Medical input into the planning of the event is essential. The risk of thermal injury is reduced if the event is held at a time that is likely to avoid extremes of heat or cold. Events held in warmer climates should be commenced early in the morning or in the evening. Adequate facilities and equipment should be provided with well-stocked, regular drink stations along the route.

The presence of experienced, trained medical and paramedical staff to deal with any emergency will dramatically reduce the risk of serious problems. A functional layout of the medical facility can permit rapid, appropriate care of all race participants.

REFERENCES

1. Holtzhausen LM, Noakes TD. Collapsed ultraendurance athlete: proposed mechanisms and an approach to management. *Clin J Sport Med* 1997; 7(4): 292–301.
2. Armstrong LE, Casa DJ, Millard-Stafford M et al. American College of Sports Medicine position stand. Exertional heat illness during training and competition. *Med Sci Sports Exerc* 2007; 39(3): 556–72.
3. Noakes TD, Sharwood K, Speedy D et al. Three independent biological mechanisms cause exercise-associated hyponatremia: evidence from 2,135 weighed competitive athletic performances. *Proc Natl Acad Sci U S A* 2005; 102(51): 18550–5.
4. Hew-Butler T, Rosner MH, Fowkes-Godek S et al. Statement of the 3rd International Exercise-Associated Hyponatremia Consensus Development Conference, Carlsbad, California, 2015. *Br J Sports Med* 2015; 49(22): 1432–46.
5. Speedy DB, Rogers IR, Noakes TD et al. Diagnosis and prevention of hyponatremia at an ultradistance triathlon. *Clin J Sport Med* 2000; 10(1): 52–8.
6. Reid SA, Speedy DB, Thompson JM et al. Study of hematological and biochemical parameters in runners completing a standard marathon. *Clin J Sport Med* 2004; 14(6): 344–53.

Chapter 40

Multisport endurance events

by ALLEN CHANG and PAUL AUERBACH

You can quit if you want and no one will care. But you will know the rest of your life.
John Collins, founder of the Ironman® World Championship triathlon, 1978

Over the past decade, the popularity of multisport endurance (MSE) athletic events has skyrocketed. As traditional distance races (marathons and 'century' cycling rides) have continued to prosper, multisport/triathlon events and obstacle course racing have shown increased participation, particularly in the young adult age group (20–39 years), and with a heavy male preponderance.[1]

Previously these were considered to be the realm of professionally sponsored outdoor athletes. Now these 'adventure races' have also become much more accessible to the general public, as the ease with which one may advance from extended obstacle course racing to self-supported MSE events is now considerably greater, both financially and logistically (Fig. 40.1).

Figure 40.1 Obstacle course racing involves various disciplines and occurs over a variety of terrain

BARRY DIOMEDE / ALAMY STOCK PHOTO

The main medical features of MSE athletic events are:

- overview of injury prevalence
- approach to physiological changes occurring in MSE athletic events
- field management of injuries
- extrication and evacuation implications.

Athletes attracted to MSE events tend to push their physiological safety envelope, both during training and on race day. Given that these events may span a variety of geographic locations, occur over multiple days and intentionally lack the number of event support services that accompany urban footraces, medical professionals should be aware of additional considerations during preparation for providing medical care at these events (Figure 40.2).

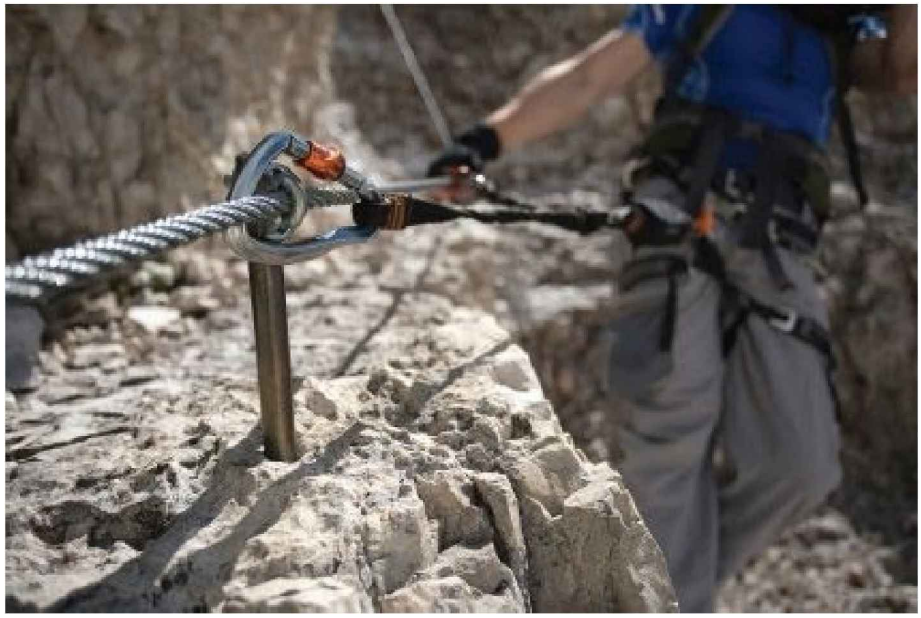


Figure 40.2 MSE events may call upon technical skills requiring additional training and equipment
DREAMPICTURES/JENSEN WALKER/BLEND IMAGES

INJURY PREVALENCE IN MULTISPORT ENDURANCE EVENTS

During previous generations of endurance racing, regimented training programs, including strict supervision and nutrition, seemed to be a factor in what may have been fewer overall and less severe injuries. The most common injuries were soft tissue injuries of the lower extremity, predominantly non-operative sprains and strains, muscle cramps and stress fractures.[2] These were followed in incidence by metabolic and environmental problems, such as dehydration, dilutional hyponatraemia, heat-related illnesses and cold-induced tissue injuries. The vast majority of these problems were treated by competitors or on-site medical staff and rarely required hospital-based intervention.[1, 3, 4]

With the evolution of MSE races to include multiday, multidiscipline events with greater (and sometimes profound) exertion over more difficult terrain and under adverse environmental conditions, the variety and severity of medical injuries became greater. In these competitions, competitors are expected to carry their own food, personal protective equipment and basic first-aid supplies. In some instances, they are provided water only at major checkpoints.

More severe lower extremity injuries include high-degree sprains (including avulsion tears), knee meniscal and ligamentous damage and fractures. Upper extremity injuries, particularly with climbing or falling onto outstretched arms, include sprains, rotator cuff tears, shoulder and elbow dislocations and fractures.[3, 4] Whether wearing or not wearing helmets, victims may suffer traumatic brain injuries. These are particularly noted in the setting of technical climbing and

traverse components among competitors who are not familiar with safe alpine ascents and self-rescue. Falls from heights and cycling accidents also contribute to head injuries.

Severe environmental and metabolic injuries include hypothermia, frostbite, heat stroke, hyponatraemia, hypoglycaemia and other electrolyte abnormalities. At their most severe, these injuries can cause irreversible damage to the brain (due to swelling or thermal injury), heart, kidneys or bowels, often due to blood shunting during prolonged endurance events that results in poor tissue perfusion and ischaemia. Poorly prepared or overly stressed participants may suffer skin blisters, subungual haematomas, sunburn, ultraviolet keratitis (snow blindness), snakebites, insect bites, jellyfish stings, spiny plant perforations, drowning and other wilderness-associated afflictions (Table 40.1).

Table 40.1 Major organ system injuries in endurance athletes

Page 592

Organ system	Major injuries
Central nervous system	Traumatic brain injury/concussion, metabolic disturbances
Cardiac	Ischaemia, heart failure
Pulmonary	Pneumonia, pneumothorax, asthma (exacerbation)
Gastrointestinal	Gastroenteritis, bowel ischaemia, ulcers
Renal	Dehydration/renal injury, metabolic disturbances, rhabdomyolysis
Musculoskeletal	Fracture, dislocation, strain, torn ligament/tendon
Skin	Laceration, abrasion, cellulitis/infection/abscess

Special consideration should be given to athletes who are exposed to extremes or large variations in altitude and/or temperature, because individuals need to undergo proper acclimatisation to achieve adequate, let alone optimal, physiological adaptation. The human body is normally capable of maintaining core temperature at 37°C (99°F), by either shivering (involuntary muscular contractions) in the cold, or by sweating and evaporative cooling in the heat. With MSE events, for many reasons, particularly exhaustion and dehydration, the body's ability to adapt to extremes of temperature is decreased, so athletes become more susceptible to heat- and cold-related injuries (Fig. 40.3, Fig. 40.4).[5, 6, 7]

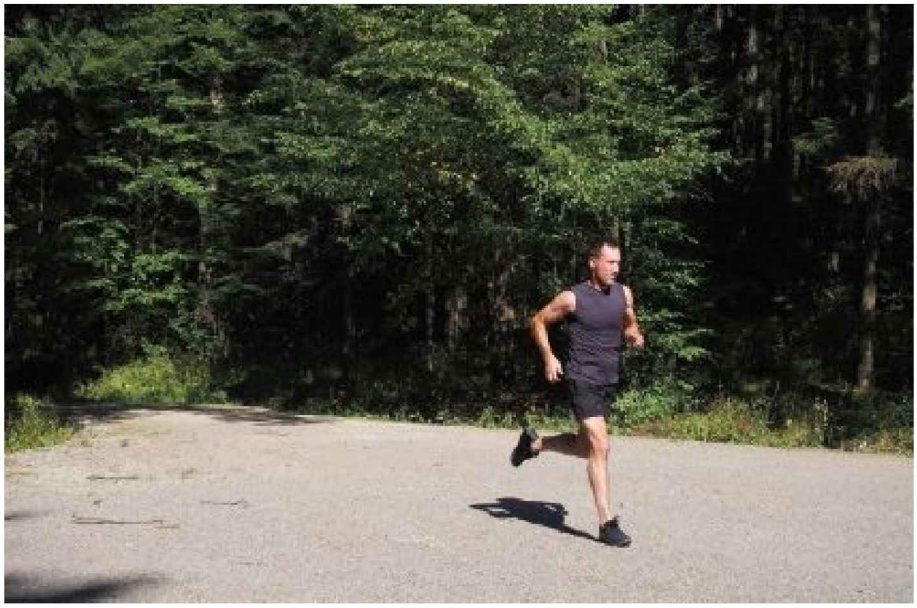


Figure 40.3 MSE events often include distance running on both developed and undeveloped courses

SHUTTERSTOCK / NINIKAS

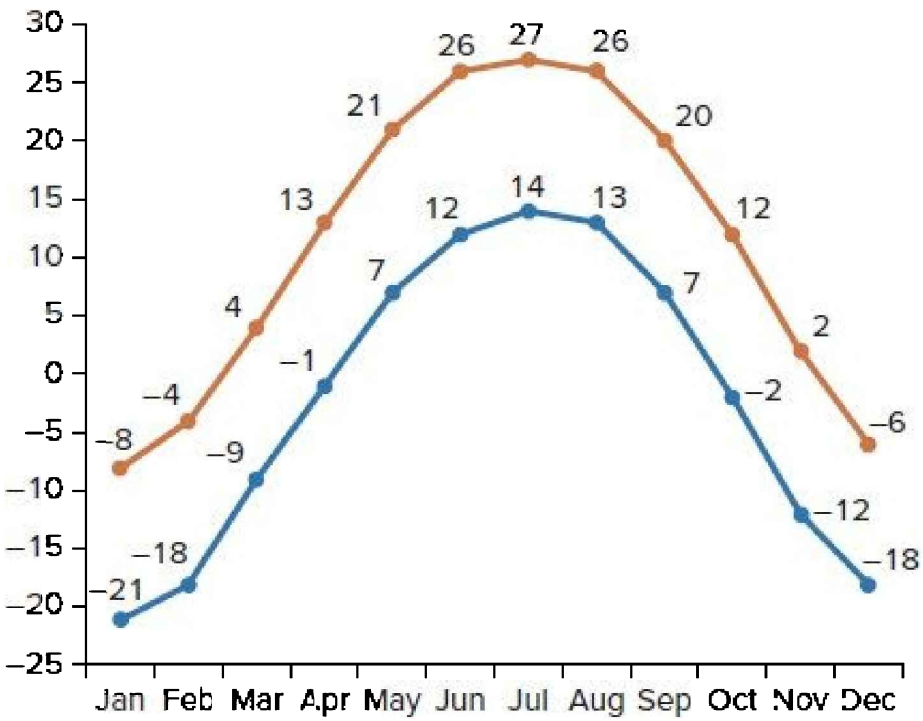


Figure 40.4 Temperatures in the Gobi Desert vary widely depending on both season and time of day

GENERAL APPROACH TO PHYSIOLOGY AS IT RELATES TO SAFETY

Proper management of fluid and electrolytes is an essential task for MSE athletes. Laboratory testing is usually unavailable, unless an athlete reports to an equipped medical tent or is pulled from a competition and taken to a testing location due to safety concerns. Thus, it is important for medical professionals to have a thorough understanding of clinical risk factors, be intuitive diagnosticians in the field and be prepared to act swiftly in the event that an athlete becomes ill in a manner consistent with a metabolic derangement. For example, a long-distance competitor who gains weight during a race and suffers from altered mental status should immediately be suspected of having ingested too much water and thereby suffering from dilutional hyponatraemia.

Page 593

Carbohydrates and sugars

In general, MSE athletes should ingest 7–12 g/kg body weight of carbohydrate each hour that they physically exert themselves after the first 60 minutes of activity. Many commercial products provide servings of simple and complex carbohydrate combinations, sugars and salts (electrolytes), to be consumed prior to each hour of strenuous activity. For a competitive edge, some products include caffeine (20–60 mg per serving), which is felt to increase short-term energy and performance.[8–11]

Whether or not there has been ingestion of performance supplements is important when evaluating MSE athletes in a medical setting. For example, excessive caffeine intake can cause tachycardia, agitation, altered mental status and/or hypertension in an otherwise healthy individual (Fig. 40.5).[12]

Figure 40.5 Supplemental nutrition may come in both pill and liquid form for ease of intake during an event

GLOW IMAGES

Glucose is the primary source of fuel for basic metabolism. The average 70 kg human requires 4 g of circulating glucose at rest and as much as 10 times that amount during strenuous athletic activity. Factoring in additional caloric needs for altitude and temperature variations (e.g. increased demand due to adaptations such as shivering or hyperventilation), MSE athletes may quickly exceed the capacity of basal glucose stores if they do not ingest supplemental nutrition.[10]

Glycogen is a storage form of glucose that exists both in muscle and the liver (approximately 100 g and 400 g, respectively, in a fasting healthy 70 kg human). During periods of alternating fasting and exertion, glycogen is released to maintain an optimal, normal serum level of glucose (3.9–6.7 mmol/L or 70–120 mg/dL).[10] Symptoms of hypoglycaemia usually do not occur in healthy individuals until serum glucose level drops to 2.8–3.3 mmol/L (50–60 mg/dL).

During short-duration races, competitors do not necessarily have to eat or refuel during the event, because the competition is often completed before glycogen stores are depleted. Self-supported MSE competitors may need to carry several kilograms of food to supply them during a multistage, multiday race. Competitors who attempt to lighten their loads by carrying less food risk hypoglycaemia, fatigue and increased injury due to episodes of weakness, fatigue and hypoglycaemia. In order to address this risk, some races require minimum-calorie packs that are checked before the event be carried.

Because the desire to carry minimal loads is always a logistics consideration, athletes may maximise calorie-dense foods, keeping in mind that, in general, fat provides 9 calories per gram while protein and carbohydrates provide 4 calories per gram (see Chapter 33). Palatability and digestibility, which are altered during exertion, must be considered. Sports nutrition is a science and often very sport-specific, which holds true for MSE athletes.[13]

Page 594

Hydration and electrolytes

While many MSE athletes are aware of basic fluid requirements and consequences of excessive water intake, some succumb to dangerous dilution of endogenous electrolytes, particularly sodium chloride. Data predict that sodium losses during extreme heat and exertion can average 4.8–6 g over an 8–12 hour event, depending on prior acclimatisation.[14] Due to variation in sweat rate between individuals, losses may be much higher and require more aggressive repletion. Proper hydration with electrolyte supplementation is absolutely essential for health, safety and optimal performance, although in extreme circumstances, it does not always fully prevent dilutional hyponatraemia (Table 40.2).[9, 15, 16]

Table 40.2 Common signs and symptoms of hyponatraemia

Signs and symptoms of hyponatraemia
• Headache

- Nausea and vomiting
- Muscle cramps
- Lethargy
- Restlessness
- Disorientation and altered mental status
- Depressed reflexes

Signs and symptoms of severe hyponatraemia

- Seizures
- Hallucinations
- Acute psychosis
- Coma

During the 2002 Boston Marathon, the incidence of dilutional hyponatraemia in runners was estimated to be approximately 13%.[17] Giving recommendations for water intake volume on an individual basis can be challenging, due to varying sweat rates, urine excretion and subjective measures of water balance. One approach suggests minimising overall body weight change during competition, although this parameter is difficult to measure and track during a race.[18] During the Ironman® World Championship, participants are weighed prior to the race. If they present to the medical tent with altered mental status without trauma, the immediate differential diagnosis includes heat stroke if they have lost or not gained weight and dilutional hyponatraemia if they have gained weight.

Athletes who completed marathons and full triathlons with slower finishing times were found to have higher prevalence of hyponatraemia, likely due to longer time on the course and more opportunities to ingest free water, compared to faster competitors.[17]

Other electrolytes, such as potassium and magnesium, are important to maintain normal physiological function. However, they may not be properly considered in nutrition planning. Male and female athletes routinely ingested inadequate amounts of daily potassium and magnesium despite an aggressive nutrition regimen.[9] This may be complicated by insensible losses during exercise. Because both potassium and magnesium are involved in energy metabolism, nerve conduction and muscle contraction, abnormalities may result in negative consequences on normal physiological function or performance. However, because intracellular concentrations of potassium and magnesium are higher than in plasma, concentration changes due to intravascular fluid shifts and dilution have less of an overall effect when compared to sodium, which is predominantly extracellular.[9]

MSE athletes who ingest non-steroidal anti-inflammatory medications before or during a race may be at higher risk for electrolyte dysregulation, because these medications can alter renal function and consequently fluid balance.[19, 20]

Treatment of MSE athletes with suspected or proven hyponatraemia includes expeditious withdrawal from the competition, fluid restriction and electrolyte supplementation, including intravenous hypertonic saline. Medical evacuation and/or escalation of care may be necessary if neurological findings (e.g. altered mental status or seizures) are present.

Rhabdomyolysis and renal injury

Rhabdomyolysis is defined as the rapid destruction and breakdown of skeletal muscle tissue resulting in release of muscle fibre protein (myoglobin) into the blood and subsequently urine.

With extended MSE races, the risk of athletes developing rhabdomyolysis increases in proportion to the event duration. Rhabdomyolysis follows breakdown of muscle tissue (release of myoglobin) from trauma, exertion, hyperthermia or prolonged immobility. Myoglobin is toxic to renal tubules.[21]

In the hospital setting, rhabdomyolysis is diagnosed clinically and with laboratory testing, usually including complete blood count, metabolic panel (potassium, sodium, chloride, glucose, creatinine, carbon dioxide, blood urea nitrogen) and specifically creatine kinase level >1000 IU/L. Urine can test positive for myoglobin without microscopic evidence of blood. Because most MSE events do not have laboratory testing support, clinical acumen is essential.

Page 595

The earliest indication of risk for rhabdomyolysis is dehydration causing decreased urine output. A healthy adult human normally produces 0.5 mL/kg/h of urine. With regular oral hydration during a race, competitors should be urinating regularly. Darker urine colour usually indicates higher concentration of excreted waste and potentially myoglobin. Persons suffering rhabdomyolysis typically have darkened ('Coca-Cola®') urine, which reflects the concentration of myoglobin. MSE athletes are advised that if their urine is not light yellow to predominantly colourless during a race, this should be a concern for hydration status and a warning of potential danger. (Fig. 40.6)

Treatment of rhabdomyolysis in the hospital usually requires aggressive intravenous hydration to protect kidney function. If suspicion is high for rhabdomyolysis, the participant should be evacuated immediately, because kidney failure may be imminent, even without obvious systemic signs and symptoms.[22]

MANAGEMENT OF INJURIES AND ADDITIONAL SAFETY CONCERNS

While prompt evacuation is sometimes an option, transport is commonly delayed, so medical providers should be prepared to treat patients in the field.

What criteria should be used to determine if a competitor can complete?

Assessment of the injured patient involves identifying severe organ dysfunction and/or failure (Ta ble 40.3).

Table 40.3 Signs and symptoms of severe organ dysfunction

Signs and symptoms of severe organ dysfunction and/or failure

Central nervous system	Altered mental status, seizure, unresponsive/coma
Cardiac	Chest pain, palpitations, irregular pulse
Pulmonary	Dyspnoea at rest, severe coughing, frothy (sometimes bloody) sputum
Gastrointestinal	Blood in stool, severe abdominal pain, intractable vomiting
Renal	Inability to urinate, blood in urine, painful urination, dark urine

Evaluation of mental status is an overarching, crucial component of medical decision making in the field. While designed for the intensive care unit and commonly used for trauma patients, the Glasgow Coma Scale (GCS) and orientation questions allow providers in various settings to quantify mental status (Table 40.4).

Table 40.4 The Glasgow Coma Scale (GCS)

Page 596

Behaviour	Response	Score
Eye opening	Spontaneous	4
	To speech	3
	To pain	2
	No response	1
Verbal response	Oriented to time, place and person	5
	Confused	4
	Inappropriate words	3
	Incomprehensible sounds	2
	No response	1
Motor response	Obeys commands	6
	Moves to localised pain	5
	Flexion withdrawal from pain	4
	Abnormal flexion (decorticate)	3
	Abnormal extension (decerebrate)	2
	No response	1
Total score:	Best response	15
	Comatose	8 or less
	Totally unresponsive	3

Causes of altered mental status (AMS) in MSE athletes include:

- temperature dysregulation
- metabolic disturbances (e.g. electrolyte imbalance, hypoglycaemia/hyperglycaemia)
- infection
- haemorrhage or anaemia
- delirium
- acute psychosis
- medication effects or adverse effects

- illicit drug use
- acute mountain sickness
- intracranial bleeding or ischaemia
- sleep deprivation.

During multiday events, athletes often minimise sleep to maintain competitiveness. This practice increases risk for delirium and elicits concern for safety. If sleep deprivation and/or extreme fatigue is present, it is very important to regularly screen individuals for AMS (Table 40.5).[23]

Table 40.5 Sample questions to evaluate levels of alertness and orientation ('A&O × 4')

1. What is your name?
2. Do you know where you are right now?
3. What is the year?
4. What are you doing or why are you here?

It is often overlooked that an athlete might be ingesting a maintenance medication(s). Any person who presents with AMS should yield a complete medical screening history with medication reconciliation. Medication effects and adverse effects, interactions and overdose each might contribute to AMS (Table 40.6).

Table 40.6 Common medications that can cause altered mental status

- Anxiolytics/benzodiazepines
- Anticonvulsants
- Narcotics
- Antihistamines (1st generation)
- Anti-emetics, including motion sickness medications
- Tricyclic antidepressants
- Lithium
- Fluoroquinolone antibiotics
- Cardiac antiarrhythmics, including beta-adrenergic blockers
- Muscle relaxants
- Corticosteroids
- Decongestants (over-the-counter)

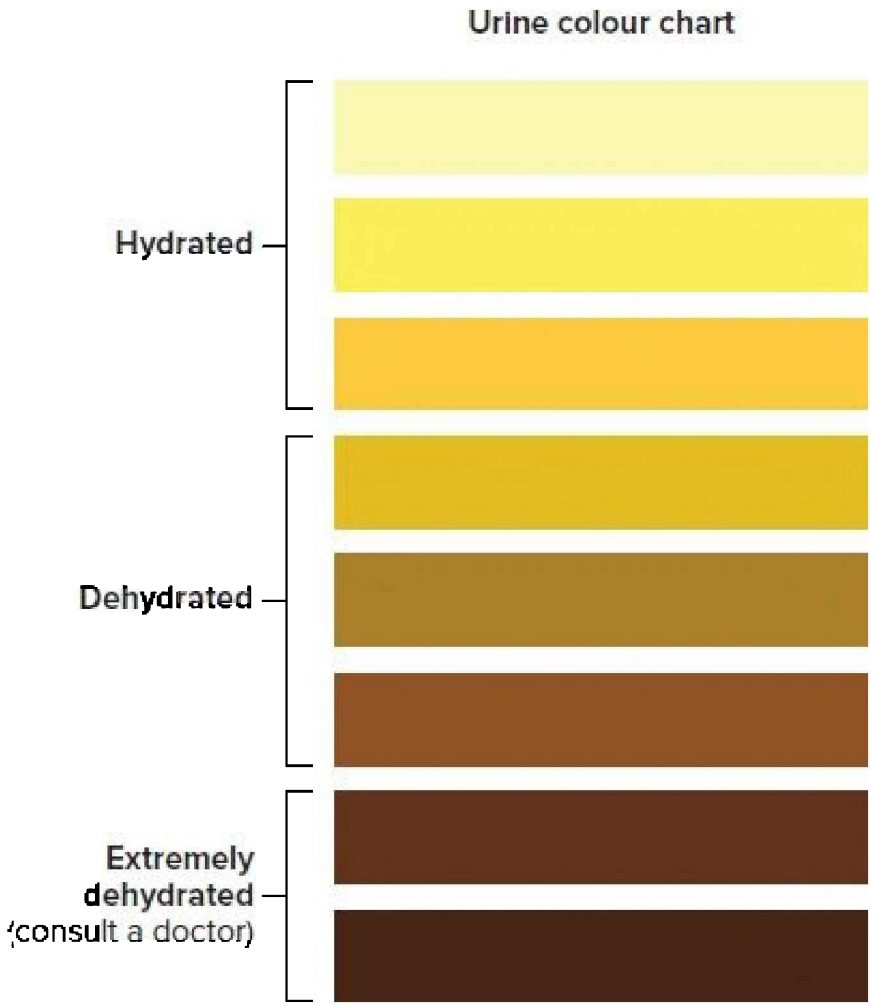


Figure 40.6 Urine colour chart depicting varying degrees of dehydration provide general guidance

Treating a metabolic or electrolyte abnormality can sometimes be accomplished at the competition site to avoid evacuation. A glucometer can identify whether a competitor is hypoglycaemic and needs to ingest or otherwise be administered glucose. Selection of administration route depends on mental status, ability to comply with treatment and available modalities (Table 40.7).[24, 25]

Table 40.7 Oral and intravenous carbohydrate/sugar concentrations

Oral carbohydrate: approximately 15 g
Glucose tabs (3–4)
Glucose gel (1 tube)
Hard candy (3–5 pieces)
Juice (120 mL)

Intravenous glucose/dextrose

D50: 50 g dextrose per 100 mL

D10: 10 g dextrose per 100 mL

Dextrose concentrations of D5 or D10 can be given via a peripheral IV; any higher concentration requires central venous access and higher level of care for close monitoring (Fig 40.7).

Figure 40.7 A glucometer requires regular calibration and compatible test strips to accurately check for serum glucose levels

Musculoskeletal injuries and improvised splints

A large proportion of race injuries involve extremities and are musculoskeletal in nature. Extremity injuries are commonly muscle spasms, sprains and fractures. Soft tissue injuries include abrasions, contusions and lacerations. Especially in MSE events, the risks to novice competitors unfamiliar with equipment or high-risk/low-occurrence activities (e.g. rappelling, rock and wall climbing, traversing swiftwater) are significant.[1, 4] Despite being very common, soft tissue and orthopaedic injuries cause only 14% and 11% of event withdrawals, respectively, compared to 25% from dehydration (Fig. 40.8, 40.9).[26]

Figure 40.8 Technical mountain rescue for injured competitors requires dedicated training for support personnel

DESIGN PICS / MICHAEL INTERISANO

Figure 40.9 Monitoring technical climbing routes for safety is paramount during an MSE event

DESIGN PICS / DAN SHERWOOD

Care providers may need to assemble commercial splints, or fashion improvised splints, depending on the injury and distance to be travelled. Common upper extremity splints include sugar tong and gutter-type, with supportive padding and wrapping.

The medical team should have access to flexible aluminium splints (e.g. SAM® splint) and elasticised or self-adherent (e.g. Coban™) bandages. The priorities are immobilisation, protection from further injury, and maintenance of circulation and sensation. With any extremity injury, it is essential to examine gross motor function, sensation and capillary refill of distal digits before and after applying a splint, in order to ensure the splint is not applied too tightly. Checking for capillary refill involves manually pressing down on a fingertip or toe until the skin blanches, releasing pressure and measuring the time until coloration returns to normal.[27] Capillary refill time should be less than 3 seconds in a healthy adult, with prolonged time indicative of impaired systemic circulation or local blood flow, which may mandate expedited transportation or evacuation (Fig. 40.10, 40.11).

Figure 40.10 Demonstration of buddy taping of injured and non-injured toes

Figure 40.11 Application of a flexible aluminium splint with elastic bandage for stabilisation

Examining the patient at regular intervals after a splint is applied is necessary to ensure that

circulation remains intact, particularly if a long transport is undertaken. Splints can be loosened or reapplied as needed.

Compartment syndrome is caused by increased pressure within one or more closed fascial compartments. This leads to insufficient blood supply to the affected tissue, predominantly muscles and nerves. Increased pressure can be due to localised swelling and oedema from extreme levels of exertion. Compartment syndrome is often a surgical emergency and may require urgent intervention within 4–6 hours to avoid irreparable damage (Table 40.8).[28]

Page 598

Table 40.8 Hallmark symptoms of compartment syndrome

The 5 Ps of compartment syndrome
1. Pain (often severe)
2. Pallor (pale skin tone)
3. Paraesthesia (numbness and tingling in the affected area)
4. Pulselessness (faint or no pulse detected on palpation)
5. Paralysis (weakness while attempting intentional movement)

If compartment syndrome is suspected, immediate evacuation is warranted. Manage pain and elevate the affected extremity at least above the level of the heart. Fasciotomy is almost always the definitive treatment, but because this is a surgical procedure, in the setting of an MSE event field management is supportive and focused on transport to definitive care (Fig. 40.12).

Figure 40.12 (a) Cross-section of fascial compartments of the lower extremity that can swell and cause tissue ischaemia if left untreated

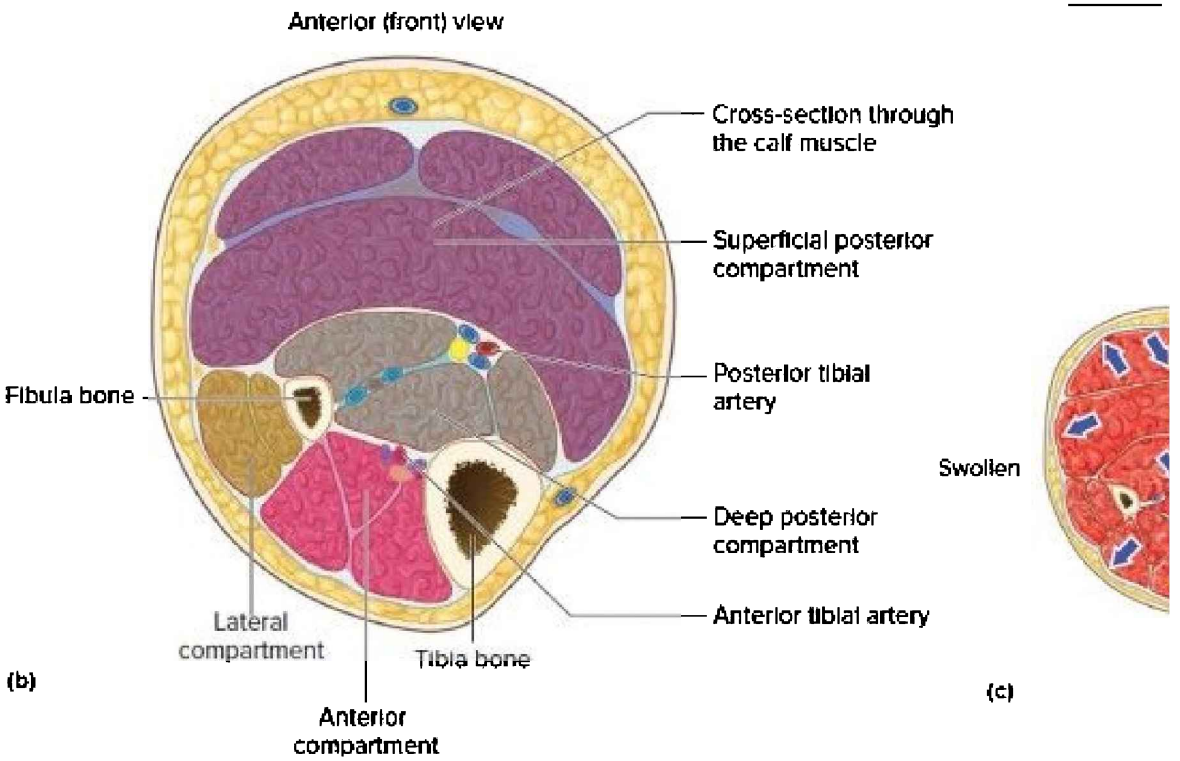


Figure 40.12 (b) cross-section through calf showing muscle compartments (c) cross-section showing swollen muscles compressing nerves and blood vessels, resulting in compartment syndrome

Soft tissue injuries and infections

Abrasions, contusions and lacerations are very common in MSE athletes, due to slips and falls on uneven and unpredictable terrain. While most superficial injuries can be self-managed with adequate cleansing, antiseptic ointment, dressings and bandages, extensive abrasions and lacerations require additional care, particularly during multiday events.

The race environment is rarely supportive of routine hygiene to counteract sweating, external dust and dirt, immersion into natural (contaminated) bodies of water and dispersal of bacteria. Surveillance of wounds for infection is paramount. A simple skin nick can develop into debilitating cellulitis or an abscess if left dirty and untreated in the wilderness environment, where immunosuppression from exhaustion and high altitude may also be factors.[29]

Evidence of worsening infection includes purulent drainage, increasing pain, swelling, and/or an expanding area of erythema around the initial injury site. Definitive treatment is centred on hygiene, meticulous wound care and, sometimes, antibiotics or drainage procedures (if purulence develops). Competitors should be encouraged to change dressings and bandages daily and perform wound care as much as is practical (Fig. 40.13).

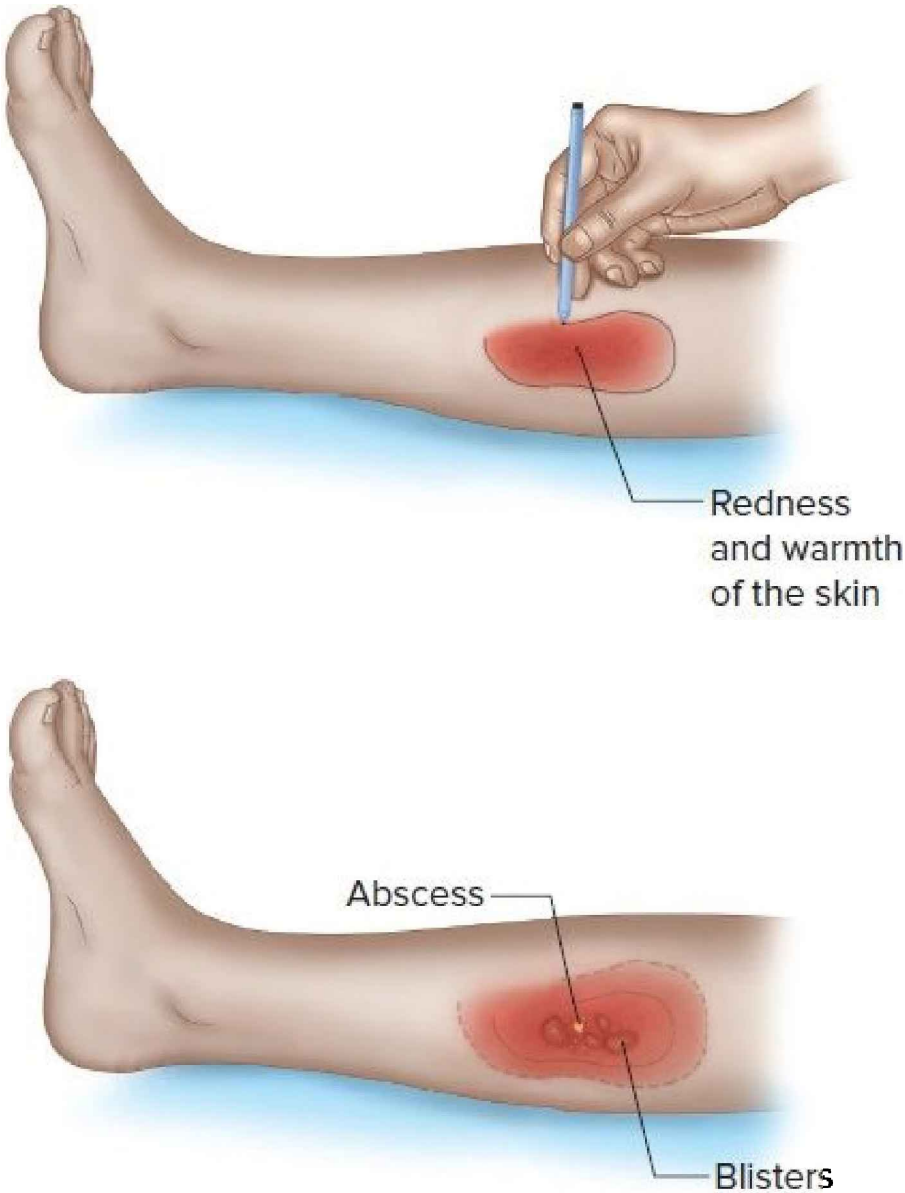


Figure 40.13 Cellulitis is a bacterial infection. It may expand and become increasingly erythematous and indurated or develop blisters if left untreated, and infection may spread to other parts of the body. Marking the borders of the red area with indelible ink (a) may aid in monitoring improvement or deterioration. Seek medical attention immediately if the area grows rapidly or develops blisters (b), or if the patient develops a fever or flu-like symptoms

Where a laceration has penetrated the epidermis and possibly the dermis, in the absence of need for a prompt deep repair (e.g. tendon, muscle, nerve or blood vessel injury), this is generally closed at the level of the top of the skin with glue, sutures, tape, staples or devices, within 6–8 hours of

injury. Due to the inherently exposed and contaminated settings of MSE events, the window to close a laceration and avoid an infection may be even shorter. In many cases, it may be more prudent to approximate the wound edges without tight closure and allow the laceration to heal by secondary intention or delayed primary closure (Fig. 40.14).[30]

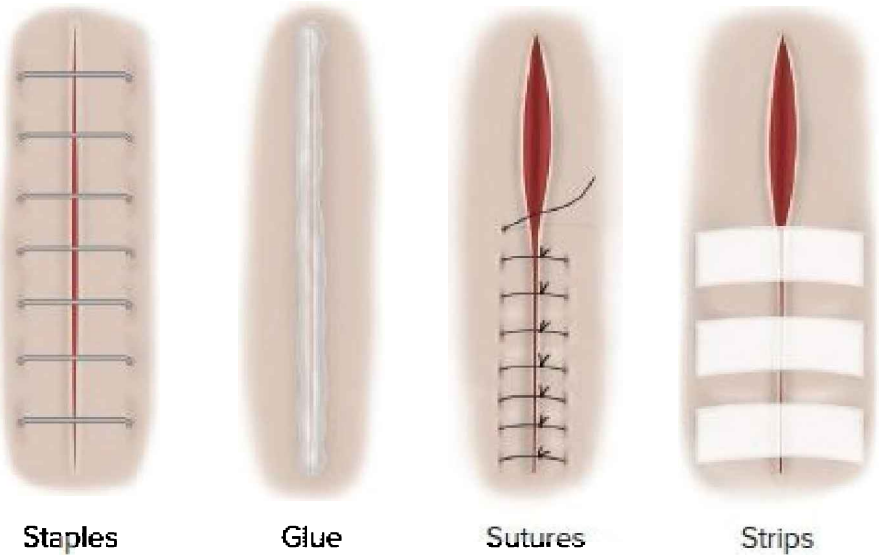


Figure 40.14 Various methods and techniques of laceration closure

Particularly with multiday events, medical practitioners should re-evaluate lacerations and other potentially infected wounds on a frequent basis. Antibiotics are considered on a case-by-case basis, depending on the nature, cause and location of the wound, presence of infection and anticipated duration and course of care throughout the race.[31] Because many antibiotics require multiple doses over days of treatment, it may not be feasible to treat a worsening or complicated infection during an MSE competition.

MEDICAL EVACUATION

The process of evacuating an athlete from the field begins well before any decision to evacuate, with early planning and asset coordination. Particularly with extended, multiday events, assets are often spread over a large geographic area, which makes their availability to multiple locations quite challenging, particularly if they are needed simultaneously for different patients.

To minimise complications with escalating medical care, medical directors and providers should be fully aware of the details of several key elements:

- host nation medical facilities and capabilities (surgical, intensive care, aviation)
- communication requirements (radio frequencies, mobile phone network availability)
- transportation requirements (ground transport vehicles and emergency road access, helicopter

availability and landing zone identification)

- plan for accessing isolated/technical areas of the course (steep trails and rock/snow/forest cover/open water/desert/high altitude [Fig. 40.15]).

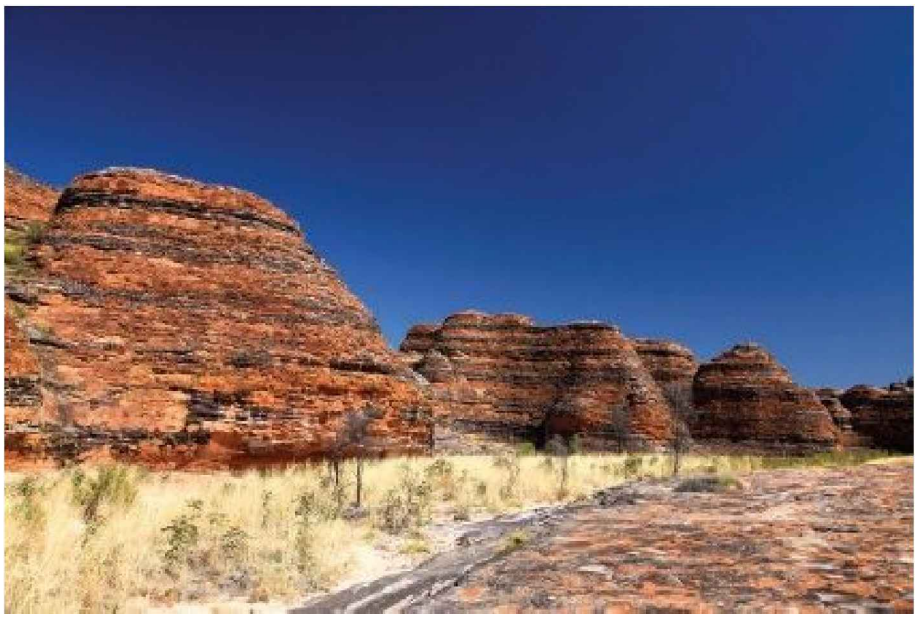


Figure 40.15 Isolated and/or technical areas of a race course may require special transportation for rescue purposes. The entire course should be surveyed comprehensively and plans for access and evacuation from every location made in advance

SHUTTERSTOCK/PIERDEST

When the decision has been made to evacuate, many specialised elements come into play. The patient must be stabilised and 'packaged' for the conveyance. He or she may clinically deteriorate en route, so additional care providers may need to accompany the patient to a higher level of care. Prolonged extrication from a remote location may require transport while the patient is immobile and exposed to the elements. Ensuring protection from both overheating and hypothermia may require special equipment and expertise. Supportive care to ensure the athlete is hydrated, fed, comfortable and with minimal pain is required.

Communication between the field medical team and race coordinators is necessary, to eliminate confusion, ensure accountability of personnel and allocate appropriate resources for transportation. A receiving medical centre with broad capabilities is generally preferred for initial in-hospital evaluation and referrals.

SUMMARY

Because MSE events have increased in popularity and are more accessible to the general public, it is very

important to be aware of medical considerations relevant to the athletes participating in these events. These considerations can range from minor medical annoyances to life-threatening situations across a large spectrum of harsh environments, with varying degrees of available medical resources.

Healthcare providers should be aware of austere environments and schooled in improvisation skills common to sport medicine and wilderness medicine. While no medical provider ever wants to withdraw a racer from competition, decisions should be made to mitigate risks and ensure the safety of all persons involved.

REFERENCES

1. Mort A, Godden D. Injuries to individuals participating in mountain and wilderness sports: a review. *Clin J Sport Med* 2011; 21(6): 530–6.
2. Andersen CA, Clarsen B, Johansen TV et al. High prevalence of overuse injury among iron-distance triathletes. *Br J Sports Med* 2013; 47(13): 857–61.
3. Fordham S, Garbutt G, Lopes P. Epidemiology of injuries in adventure racing athletes. *Br J Sports Med* 2004; 38(3): 300–3.
4. Cosca DD, Navazio F. Common problems in endurance athletes. *Am Fam Physician* 2007; 76(2): 237–44.
5. Carlsen KH. Sports in extreme conditions: the impact of exercise in cold temperatures on asthma and bronchial hyper-responsiveness in athletes. *Br J Sports Med* 2012; 46(11): 796–9.
6. Akerman AP, Tipton M, Minson CT et al. Heat stress and dehydration in adapting for performance: good, bad, both or neither? *Temperature (Austin)* 2016; 3(3): 412–36.
7. Racinais S, Cocking S, Périard JD. Sports and environmental temperature: from warming-up to heating-up. *Temperature (Austin)* 2017; 4(3): 227–57.
8. Ranchordas MK. Nutrition for adventure racing. *Sports Med* 2012; 42(11): 915–27.
9. Zalcman I, Guarita HV, Juzwiak CR et al. Nutritional status of adventure racers. *Nutrition* 2007; 23(5): 404–11.
10. Wasserman DH. Four grams of glucose. *Am J Physiol Endocrinol Metab* 2009; 296(1): E11–21.
11. Caldwell AR, Tucker MA, Butts CL et al. Effect of caffeine on perceived soreness and functionality following an endurance cycling event. *J Strength Cond Res* 2017; 31(3): 638–43.
12. Sökmen B, Armstrong LE, Kraemer WJ et al. Caffeine use in sports: considerations for the athlete. *J Strength Cond Res* 2008; 22(3): 978–86.
13. Campbell I. Macronutrients, minerals, vitamins and energy. *Anaesth Intens Care Med* 2017; 18(3): 141–6.
14. Bates GP, Miller VS. Sweat rate and sodium loss during work in the heat. *J Occup Med*

Toxicol 2008; 3:4.

15. Barrero A, Erola P, Bescós R. Energy balance of triathletes during an ultra-endurance event. *Nutrients* 2014; 7(1): 209–22.
16. Goulet ED. Dehydration and endurance performance in competitive athletes. *Nutr Rev* 2012; 70 Suppl 2: S132–6.
17. Almond CS, Shin AY, Fortescue EB et al. Hyponatremia among runners in the Boston Marathon. *N Engl J Med* 2005; 352(15): 1550–6.
18. Armstrong LE, Johnson EC, McKenzie AL et al. Ultraendurance cycling in a hot environment: thirst, fluid consumption and water balance. *J Strength Cond Res* 2015; 29(4): 869–76.
19. Wharam PC, Speedy DB, Noakes TD et al. NSAID use increases the risk of developing hyponatremia during an ironman triathlon. *Med Sci Sports Exerc* 2006; 38(4): 618–22.
20. Page AJ, Reid SA, Speedy DB. Exercise-associated hyponatremia, renal function and nonsteroidal antiinflammatory drug use in an ultraendurance mountain run. *Clin J Sport Med* 2007; 17(1): 43–8.
21. Banfi G, Colombini A, Lombardi G et al. Metabolic markers in sports medicine. *Adv Clin Chem* 2012; 56: 1–54.
22. Zimmerman JL, Shen MC. Rhabdomyolysis. *Chest* 2013; 144(3): 1058–65.
23. Martin B, Haney R. Self-selected exercise intensity is unchanged by sleep loss. *Eur J Appl Physiol Occup Physiol* 1982; 49(1): 79–86.
24. Burson R, Moran K. Hypoglycemia treatment. *Home Healthc Nurse* 2014; 32(7): 437.
25. Arnold P, Paxton RA, McNorton K et al. The effect of a hypoglycemia treatment protocol on glycemic variability in critically ill patients. *J Intensive Care Med* 2015; 30(3): 156–60.
26. Townes DA, Talbot TS, Wedmore IS et al. Event medicine: injury and illness during an expedition-length adventure race. *J Emerg Med* 2004; 27(2): 161–5.
27. Lewin J, Maconochie I. Capillary refill time in adults. *Emerg Med J* 2008; 25(6): 325–6.
28. Smith JS. Compartment syndrome. *JAAPA* 2013; 26(9): 48–9.
29. Brandenburg WE, Levandowski W, Califf T et al. Animal, microbial and fungal borne skin pathology in the mountain wilderness: a review. *Wilderness Environ Med* 2017; 28(2): 127–38.
30. Murray CK. Field wound care: prophylactic antibiotics. *Wilderness Environ Med* 2017; 28(2S): S90–102.
31. Auerbach PS. *Auerbach's Wilderness Medicine*. 7th ed. Philadelphia, PA: Elsevier, 2016.

QUOTATION SOURCES – Volume 2 - endmatter

Chapter 1

I believe that evidence supports the conclusion that physical inactivity is one of the most important public health problems of the 21st century, and may even be the most important.

Professor Steven N Blair, Arnold School of Public Health, University of South Carolina, USA
https://bjsm.bmj.com/content/43/1/1.short

Chapter 2

Eating alone will not keep a man [or woman] well; he [or she] must also take exercise.

Hippocrates (460–370 BCE)
Hippocrates: With an English Translation by W. H. S. Jones. William Heinemann, London *1953*

Chapter 3

Hippocrates said 'Walking is man's best medicine'–and this may have some personal challenges for you if you're very busy with work, or kids, or both, or you may be in pain or have other priorities . . . but my question for you is: Can you limit your sitting and sleeping to just 23 and 1/2 hours a day?

Dr Mike Evans, physician, Canada https://www.youtube.com/watch?v=aUaInS6HIGo

Chapter 4

If exercise could be packed into a pill, it would be the single most widely prescribed and beneficial medicine in the nation. Dr Robert Butler, world-renowned gerontologist, psychiatrist and author (1927–2010)
https://journals.sagepub.com/doi/pdf/10.2190/AM1W-RABB-4PJY-P1PK

Chapter 5

Obstacles don't have to stop you. If you run into a wall, don't turn around and give up. Figure out how to climb it, go through it, or work around it.

Michael Jordan
https://en.wikiquote.org/wiki/Talk:MichaelJordan

Chapter 6

Let food be thy medicine and medicine be thy food.

No confirmed source. Hippocrates (460–370 BCE)

Chapter 8

When I was first diagnosed my biggest worry was that I may not be able to play football again. Injecting myself every day was demoralising. Fortunately, I can feel the support around me–not just from my team-mates and the fans, but also the coaches, physios and nutritionists who all help me bring my A-game.

Ben Coker, English professional soccer player

https://www.telegraph.co.uk/health-fitness/body/the-athletes-who-have-triumphed-over-type-1-diabetes/

Chapter 9

Spanish footballer Nacho Barbera has died after suffering a cardiac arrest during a recent match. Barbera had been playing in the 13–14 year-old age group of Valencia-based side UD Alzira and was the captain of his team.

https://www.skysports.com/football/news/11095/11236349/spanish-teenager-nacho-barbera-dies-after-suffering-cardiac-arrest-during-match

Chapter 10

Once you're into the race, your heart isn't in rhythm, oxygen is running out and you lose power and become weaker and weaker as the race goes on. It feels like you're dragging something behind the boat.

Nathan Cohen, Olympic double sculls rowing gold medallist, London 2012

http://www.voxy.co.nz/sport/manson-replace-cohen-nz-mens-quadruple-scull/5/165635

Chapter 11

If you learn to manage your asthma and take the correct medication, there's no reason you shouldn't be the best.

Paula Radcliffe, Marathon world record holder

https://www.asthma.org.uk/advice/your-stories/paula-radcliffe-theres-no-reason-you-shouldnt-be-the-best/

Chapter 12

But there was something about me that was broken, unhealthy, unfit. Some called it allergies, some called it asthma, some just called it being out of shape. But no matter what we called it, no one knew how to fix it.

Novak Djokovic, 14-time Grand Slam winner

Novak Djokovic, *Serve to Win: The 14-Day Gluten-Free Plan for Physical and Mental Excellence,* Zinc Ink, Penguin Random House, Canada 2013

Chapter 13

The doctors told me I would never run again, [but] I'm back running. They told me I would be on dialysis for the rest of my life, but I'm not. I had a kidney transplant, it was successful and I'm back doing what I love. So, if you just stay positive and stay focused on something you really want to achieve, you will do

amazing things.

Aries Merritt, 110-metre hurdles world record holder https://www.iaaf.org/news/feature/aries-merritt-kidney-transplant-2017

Chapter 14

Even when I have an off period, I can't go too crazy because the threat of having a seizure doesn't go away. As long as you're focused and dedicated–especially in a sport–there's no reason it should dictate your life.

Dai Greene, former 400-metre hurdles world champion
https://www.mirror.co.uk/lifestyle/health/dai-greene-on-athletics-and-his-epilepsy-832938

Chapter 15

I would go to the doctor and start crying. I couldn't help it. I just want a chance to play on the same field as other people, I want to feel normal, but as frightening as the diagnosis was, it was also a relief.

Venus Williams, seven-time Grand Slam winner, on being diagnosed with Sjögren's syndrome
https://www.dailymail.co.uk/news/article-2079539/Sjogrens-Syndrome-Venus-Williams-opens-incurable-disease.html

Chapter 16

The joint lubrication was not what it was when I was competing, and I decided that not having arthritis or rheumatism for the rest of my life was a lot more important to me than returning to the track.

Edwin Moses, former world and Olympic 400-metre hurdles champion, on his decision to retire
https://www.quotetab.com/quotes/by-edwin-moses

Chapter 18

Guillermo Varela to miss German Cup final with infected tattoo and furious Frankfurt end his loan. The Manchester United loanee's infected arm artwork has spelled the premature end of his time at the Bundesliga club. Varela was instructed not to get the tattoo by Eintracht Frankfurt's club doctor ahead of the club's DFB-Pokal showdown against Borussia Dortmund on Saturday, but the 24-year-old decided to get it anyway.

www.fourfourtwo.com, 24 May 2017
https://www.fourfourtwo.com/sg/news/guillermo-varela-miss-german-cup-final-infected-tattoo-furious-frankfurt-end-his-loan

Chapter 19

Fatigue makes cowards of us all.

Vince Lombardi, NFL coach
http://connectionculture.com/post/vince-lombardis-important-lesson

Chapter 20

Even though I'm not running anymore, we still have to try to find a cure for cancer. Other people should go ahead and try to do their own thing now.

Terry Fox (1958–1981) Canadian athlete, humanitarian and cancer research activist
https://www.quotetab.com/quotes/by-terry-fox#L5Vk5TZmM4OKxPtz.97

Chapter 21

It's like a weight is pressing down on you. There are days when you just can't get out of bed. You cannot face the world. You tell yourself simple things like: 'Just get to the kitchen and get a glass of water'. But not being able to do something so basic is frightening.

Ian Thorpe, Australian swimmer and five-time Olympic gold medallist
https://www.theguardian.com/sport/2012/nov/12/ian-thorpe-swimming-depression

Chapter 22

When I let my enormous inner chimp out, I start thinking like a pessimist. I have a tremendous sense of foreboding, wondering about the what ifs, about crashes and mistakes.

Chris Hoy, six-time Olympic track cycling gold medallist, in a 2009 BBC interview
https://www.dailymail.co.uk/health/article-1100491/Like-thousands-Britons-Olympic-hero-Chris-Hoy-plagued-panic-attacks-Then-unlikely-cure-.html

Chapter 23

As far as you will be having the race in Tokyo in mid summer, none of the measures, even a pile of all measures, can ensure safety.

Professor Yokohari discussing heat stress risks facing runners at the 2020 Tokyo Olympics where temperatures could reach 39°C
https://www.theguardian.com/world/2018/jul/23/japan-heatwave-prompts-concern-over-conditions-for-2020-olympics

Chapter 24

Man in the cold is not necessarily a cold man.
David Bass, Yale University environmental physiologist, 1960
https://www.theactivetimes.com/true-or-false-facts-about-winter-running

Chapter 25

It was like I was very drunk. I couldn't walk without stumbling, and completely lost the ability to think or speak. It was a really strange feeling. I'd have some word in my mind, but I couldn't figure out how to bring it to my lips.

Dale Kruse, mountain climber, describing the effects of high-altitude cerebral oedema when climbing Mt Everest
Into Thin Air: A Personal Account of the Mt. Everest Disaster, Villard Books, New York 1997

Chapter 26

If it were bends my joints would be hurting–not the middle of my thigh, that's what all the textbooks say . . .

Textbooks aren't always right!

Richard Pyle, experienced underwater diver, after suffering decompression sickness, https://www.unix.com/war-stories/185363-confessions-mortal-diver-learning-hard-way-richard-pyle.htmll

Chapter 27

Technology, urbanization, increasingly sedentary work environments and automobile-focused community design have engineered much physical activity out of daily life.

The Toronto Charter for Physical Activity

Global Advocacy Council for Physical Activity, International Society for Physical Activity and Health. The Toronto Charter for Physical Activity: A global call for action. J *Phys Act Health* 2010 Nov; 7 (Suppl 3): S370–85.

Chapter 28

Athletes need to enjoy their training. They don't enjoy going down the track with their coach making them do repetitions until they're exhausted. From enjoyment comes the will to win.

Arthur Lydiard, New Zealand runner and legendary athletics coach, https://www.goodreads.com/quotes/210595

Chapter 29

My coach said I ran like a girl, I said if he could run a little faster he could too.

Mia Hamm, American soccer icon, Olympic gold medallist and FIFA Women's World Cup champion, https://www.goodreads.com/quotes/555037

Chapter 30

know how I look like. I know how I sound. I know how I walk. I'm just gonna be me. I do me, and you do you.

Caster Semenya

https://www.ecr.co.za/news/entertainment/caster-semenyas-wife-thought-she-was-boy/

Chapter 31

I want people to know that you can reboot your body at any age.

Dr Charles Eugster (1919–2017), British record holder in the men's 95+ category 100 m and 200 m, https://www.telegraph.co.uk/men/active/11775127/96-year-old-sets-two-new-British-sprinting-records.html

Chapter 32

When we're free to move, anything is possible.

Lauren Woolstencroft, Canadian alpine skier, eight-time Paralympic gold medallist https://www.ctvnews.ca/sports/canadian-paralympian-inspires-in-emotional-super-bowl-ad-1.3789793

Chapter 33

Nutrition is massively important if you want to train at your best.

Geraint Thomas, 2018 Tour de France Champion
https://www.cyclist.co.uk/news/1604/24-cycling-tips-from-team-gbs-olympians

Chapter 34

"One day I'm a normal person with a normal life," he said. "The next I'm standing on a street corner in Madrid with a secret phone and a hole in my arm and I'm bleeding all over, hoping I don't get arrested. It was completely crazy. But it seemed like the only way at the time."

Tyler Hamilton and Daniel Coyle, *The Secret Race: Inside the Hidden world of the Tour de France: Doping, Cover-ups, and Winning at All Costs,*
Bantam Books, Random House, New York 2012

Chapter 35

Though the ACTN3 gene does appear to influence sprinting ability, making a sports decision based on it is like deciding what a puzzle depicts when you've only seen one of the pieces. You need that piece to complete the puzzle, but you certainly can't see a meaningful picture without more pieces.

David Epstein, *The Sports Gene: Inside the Science of Extraordinary Athletic Performance,*
Penguin Random House, New York, 2013

Chapter 36

[Michael Owen, knocked unconscious in a Rugby World Cup warm-up game, pleaded not to be taken off.] Owen later admitted, "I might have told them I was OK, but I didn't feel OK." ... The last person to heed in the heat of a contest is the performer. Adrenaline overrules common sense.

Rob Hughes, Chief Sports Correspondent, *The Times,* http://www.the-times.co.uk

Chapter 37

Page 606

You used that position of trust that you had in the most vile way to abuse children. You violated the oath that you took, which is to do no harm, and you harmed them selfishly.

Judge Rosemarie Aquilinar, in the trial of Larry Nassar,
https://www.usatoday.com/story/sports/columnist/nancy-armour/2017/11/22/abuse-complaints-mount-larry-nassar-guilty-pleas-bring-some-measure-satisfaction/889869001/

Chapter 38

There's no harm in hoping for the best as long as you've prepared for the worst.

Stephen King, *Different Seasons,* The Viking Press, Penguin Random House, New York, 1982

Chapter 39

Your body will argue that there is no justifiable reason to continue. Your only recourse is to call on your spirit,

which fortunately functions independently of logic.

Professor Timothy Noakes R. Charbonneau, *Overthinking the Marathon* Y42K Publishing, 2013

Chapter 40

You can quit if you want and no one will care. But you will know the rest of your life.

John Collins, founder of the Ironman® World Championship triathlon, 1978

https://decaironman-training.com/2014/01/09/20-best-cyclingtriathlon-quotes-you-never-heard/

Index

A

AAS *see* anabolic androgenic steroid (AAS)
abrasions of the bladder wall, 189
acetaminophen (paracetamol), 242
acetazolamide, 361
acetyl coenzyme A (CoA), 59
ACSM's Guidelines for Exercise Testing and Prescription, 26
active external rewarming, 353
acute gastroenteritis, athletes, 277
acute mountain sickness, 357, 361–362
acute severe asthma, 574
adaptive protein changes, 8
adeno-associated viruses (AAVs), 505
adenoid cystic carcinoma, 310
adenosine triphosphate (ATP), 464
adenoviruses, 505
adequate intake (AI), 44
adiponectin, 302
adjunct treatment for cancer, 304–308
adrenocorticotropic hormone (ACTH), 499–500
adult onset arthritis, 211
adverse analytical findings (AAFs), 512
aerobic capacity, 389
aerobic training, 208
agoraphobia, 322
airway epithelium, 164
airway hyperreactivity (AHR), 162
airway inflammation, 162
airway patency, 560, 563, 566
Akers, Michelle, 295
alcohol, 55–56, 513
Alcott, Dylan, 449
allele, 521
α-linolenic acid (ALA), 54
altered mental status (AMS), 595–596
altitude
    chemoprophylaxis, 361–363

clinical physiology of adaptation, 363
determinants of risk, 358–360
general preventive measures, 360–361
high-altitude illness, 357–358
putting altitude training into practice, 363–366
American College of Sports Medicine (ACSM), 102, 412
American Diabetes Association (ADA), 102
American Health Care Financing Administration (1977), 76
American Heart Association, 137
American Medical Society for Sports Medicine (AMSSM), 138
amino acids, 49
amphetamines, 509
anabolic agents, 490
AAS, 493–496
ABP, 497
clenbuterol, 497
designer steroids, 497
testosterone precursors, 496–497
anabolic androgenic steroid (AAS)
adverse effects, 494–495
aggressive behaviour, 494
anabolic effect, 494
anticatabolic effect, 494
clinical uses of, 493
incidence of, 493
orally/intramuscular injection, 493
pyramid regimen, 493
toxicity
in adolescents, 496
in both sexes, 495–496
in females, 496
in males, 496
anaemia, 408–409
anaerobic capacity (power), 389
anaphylaxis, 568–570
androstenedione, 496
angioedema, 174
angiotensin-converting enzyme (ACE) inhibitors, 151, 441
angiotensin II receptor blockers, 441
ankle osteoarthritis, 235–236
ankylosing spondylitis (AS), 211, 226
anterior cruciate ligament (ACL) injuries, 234, 408
anti-cancer therapy, 304
anti-doping issues, 450–451
'anti-doping rule violations' (ADRVs), 540, 541
anti-oestrogen drugs, 502

anxiety, 9
Anxiety and Depression Association of America (ADAA), 319
anxiety disorders
    agoraphobia, 322
    athlete, 324
    clinical practice and management, 322–324
    cognitive behavioural therapy, 326
    epidemiology, 319–320
    GAD, 321
    obsessive compulsive disorder/obsessional neurosis, 321
    panic disorder/panic attack, 321
    performance anxiety, 322
    pharmacotherapy, 326–327
    physical activity, 325–326
    post-traumatic stress disorder, 321–322
    screening, 324
    signs and symptoms of, 320–321
aortic stenosis, 126
Armstrong, Kristin, 244
arrhythmogenic cardiomyopathy (AC), 119, 122–123
arterial gas embolism (AGE), 370
artificial altitude, 364
artificial oxygen carriers, 504
artificial sweeteners, 46
5 A's behavior change model
    advise, 19–20, 23
    agree, 20–21, 23
    arrange, 22, 23
    assess, 18–19, 23
    assist, 21–23
ascent rate, 359
ascorbic acid, 61
Assessment of SpondyloArthritis International Society (ASAS), 224–225
asthma, 359
    airway inflammation, 162
    bronchial hyperresponsiveness, 162
    clinical features, 161
    epidemiology, 161
    exercise-induced asthma
        aetiology, 165
        bronchial provocation challenge tests, 166–168
        clinical features, 165
        diagnosis, 165–166
        epidemiology, 163–164
        pathophysiology, 164
        treatment, 168–170

intermittent airway obstruction, 162
management, 163
risk factors
environmental exposures, 163
genetic predisposition, 162
types of, 161–162
athlete biological passport (ABP), 497
athletes
acute gastroenteritis, 277
anxiety disorders, 324
carbohydrates
feeding during exercise, 464–465
glycaemic index, 463–464
and glycaemic index, 463–464
importance of, 465
intakes, periodised approach to, 465–466
loading and muscle glycogen, 464
periodised approach, 465
post-exercise recovery period, 465
pre-exercise feeding availability, 464
super-compensation effect, 464
traditional guidelines, 465
cardiovascular symptoms *see* cardiovascular symptoms in athletes
diabetes mellitus, 293
diabetic *see* diabetic athlete
drugs *see* drugs, athlete
dyspnoea, 159, 160
dyspnoea on exertion
causes of, 391, 392
history and clinical work-up, 391
investigations, 391
VCD, 391–392
fatigue in
diabetes mellitus, 293
eating disorders, 295
hypothyroidism, 293
infectious mononucleosis (IM), 291
respiratory tract infections, 291
female *see* female athletes
HAV infection, 278
HBV infection, 278–280
HCV infection, 280
HDV infection, 280
HEV infection, 280
high-fat diets, 468
HIV infections, 280–281

infections *see specific type* infections
micronutrient requirements
calcium, 472
fat-and water-soluble vitamins, 471
iron, 472
vitamin D, 470
protein requirements, 466–467
sexually transmitted infections, 281
skin infections
bacterial, 271–273
fungal and mite skin, 273–274
viral, 270–271
tetanus, 281
tiredness, in *see* tiredness, in athletes
training during illness, 263
transgender, 430
athlete-specific performance nutrition plan
body composition analysis, 460, 462
dietary assessment methods, 458-459
dietary supplements, 473–479
energy intake assessment, 456–457, 460
energy periodisation, 484–486
macronutrient requirements, 463–470
micronutrient requirements, 470–472
nutrition periodisation, 482–484
skinfold assessment, 462
total energy expenditure, 460
athletic pseudonephritis, 189
Atkins diet, 68
atrial fibrillation, 157
attention deficit hyperactivity disorder (ADHD), 509
Australian Dietary Guidelines, 43, 45, 49
automated external defibrillators (AEDs), 117, 118, 353, 576, 579
autonomic dysreflexia, Paralympic athletes, 448

B

bacterial skin infections
carbuncle, 273
folliculitis, 272, 273
furunculosis (boil), 272–273
impetigo, 271–272
barotrauma, 368
Basal insulin, 107
bathroom scales, 75
Beck anxiety inventory (BAI), 3254
behaviour change theories, 35

benzodiazepines, 442
'Best investments for physical activity,' 6, 377, 378
beta-2 agonists, 501–502
Better Bones and Balance™, 259
bicuspid aortic valve (BAV), 126
bioelectrical impedance analysis (BIA), 74
biophysics of heat exchange, 330–331
bipolar depression, 311
blood doping, 503–504, 525
Blue Zones, 70
body fat, 74–75
Bolus insulin, 107
bone adaptation, mechanical stimuli, 245
bone health
    during adolescence and early adulthood, 248–252
    anorexia nervosa, 249
    exercise prescription, 252–260
    exercise program features, 245
    masters athletes, 260
    paralympic athletes, 448
bone morphogenetic protein (BMP), 506
Borg scale, 29
Borrelia afzelii, 219
Borrelia burgdorferi, 219
Borrelia garinii, 219
Boston Marathon (2018), 434
brain-derived neurotrophic factor (BDNF), 317
brain function and mental health
    anxiety and depression, 9
    cognitive decline, 8–9
    sleep, 9
branched amino acids (BCAAs), 467
breath-hold diving, 367
breathlessness, 159
bronchial hyperresponsiveness, 162
Brownlee, Jonathan, 334
Brugada syndrome (BrS), 120, 128–129
built environment
    clinical practice
        active travel, 384–385
        advocacy, 385
        clinical encounters, 384
        role modelling, 385
    community design
        Bogotá, Colombia, 381

complete streets, 381
connected streets, 379
cycling infrastructure, 380
footpaths, 379–380
mixed land use, 379
parks and open public spaces, 380
public transport, 380
residential density, 379
safe crossings, 380
speed limits, 380
principles of, 377
schools building design
active travel, 383
community, 384
furniture, 384
infrastructure, 383
workplace building design
active travel, 382
infrastructure, 382–383
bullous impetigo, 271
B vitamins
vitamin B_1 (thiamine), 59–60
vitamin B_9 (folate), 60
vitamin B_{12} (cobalamin), 60

C

caffeine, 56, 513
calcium pyrophosphate deposition disease (CPPD), 219–220
Canadian Society for Exercise Physiology (CSEP), 18, 19
cancer
adjunct treatment for, 304–308
biopsy techniques, 298
causes of, 297
in childhood, 394
grading, 298
hallmarks, 297–298
modifiable risk factors, 299
molecular diagnostics, 298
physical activity, 300–309
presentation, 298
prevention, 10–11
survivors
defined, 308
exercise prescription for, 309
regular physical activity, benefits of, 309

symptoms, 298
treatment, 298
candidate gene association study (CGAS), 522
cannabinoids, 510–511
carbohydrates
for athletes
feeding during exercise, 464–465
glycaemic index, 463–464
and glycaemic index, 463–464
importance of, 465
intakes, periodised approach to, 465–466
loading and muscle glycogen, 464
periodised approach, 465
post-exercise recovery period, 465
pre-exercise feeding availability, 464
super-compensation effect, 464
traditional guidelines, 465
fibre, 46–47
recommended carbohydrate intake, 45
sugar, 45–46
carbohydrates (CHO) supply, 455
carbuncle, 273
Carcillo, Daniel, 554
cardiac risks, 14
cardiometabolic health
cardiovascular disease, 11
diabetes mellitus, 11
hypertension, 12
cardiomyopathy
AC, 122–123
DCM, 124
hypertrophic, 120–122
idiopathic left ventricular hypertrophy, 122
cardiopulmonary resuscitation (CPR), 140–141
cardiorespiratory fitness (CRF), 315
cardiovascular disease (CVD), 11, 87
cardiovascular symptoms in athletes
cardiologist, 150–151
dyspnoea, 149
exertional chest pain, 148
exertional syncope, 147
fatigue, 149
heart murmur, 151
hypertension, 150–151
Marfan syndrome, 151–152
mimic syncope, 148

neurally mediated syncope (vasovagal syncope), 147
non-invasive cardiovascular testing
cardiac CT, CMR, 154
echocardiography, 154
electrocardiogram, 153–154
genetic testing, 154–155
palpitations, 148–149
post-exertional syncope, 147
potentially life/death decisions, 145
syncope/near-syncope, 146–147
temporary/permanent sports disqualification, 155–158
catecholaminergic polymorphic ventricular tachycardia (CPVT), 120, 129
catechol-O-methyltransferase (COMT) inhibitors, 200
Cavendish, Mark, 276
Centers for Medicare and Medicaid Services in the USA (2004), 76
cerebrovascular disease
considerations in prescribing physical activity for stroke patients, 197–198
effect of physical activity in the treatment of stroke, 196–197
effects of physical activity on stroke mortality, 195–196
Chand, Dutee, 427, 428
chemoprophylaxis, 361–363
childhood cancer, 394
childhood obesity, 99
Child SCAT5, 397, 398
choking-airway blockage, 568
cholesterol, 52–53
cholinergic urticaria, 174
chondrocalcinosis, 219–220
chronic fatigue syndrome (CFS), 295
chronic traumatic encephalopathy (CTE), 539
classic learning theories, 35–36
Clay, Bobby, 249
clenbuterol, 497
closed-circuit/semi-closed-circuit rebreather scuba, 367
Clostridium difficile, 47–48
Clostridium tetani, 281
CNS dysfunction, 338
cocaine, 510
coeliac disease, 180, 294–295
cognitive behavioural therapy (CBT), 12, 326
cognitive decline, 8–9
cold environment
cold air and water, 348–352
environmental and body temperature measurement, 347–348
impact of cold on performance, 348
thermoregulation, 345–347

treatment, 352–355
cold immersion, 353
cold injuries, 350, 352
combined oral contraceptive pills (COCs), 411
commotio cordis, 129, 131
compartment syndrome, 598, 599
complete androgen insensitivity syndrome (CAIS), 422–424
complex traits, 520
concussion, 397–399, 538–539
Concussion in Sport Group, 539
congenital coronary artery anomalies (CCAA), 124
consent, 530
Convention on the Elimination of All Forms of Discrimination against Women (CEDAW), 542–544
core temperature afterdrop, 353
coronary artery disease (CAD), 118–119
corticosteroids, 242
Council on Science and Public Health (CSPH), 76
Court of Arbitration for Sport (CAS), 427, 529
cow's milk, 62
Crohn's disease, 180
CrossFit®, 27
cystic fibrosis (CF), 394

D

Deaflympics, 444
decompression sickness (DCS), 371–372
deep body temperature, 345–346
defibrillation, 141–142
dehydration, 14, 336–337
dehydroepiandrosterone (DHEA), 496–497
De novo mutation, 521
depo-medroxyprogesterone (DMPA) injections, 412
depression, 9
bipolar, 311
diagnosis, 311–312
major/unipolar, 311
management, 313
pharmacological management, 318
physical activity, 313–318
psychological therapies, 318
dexamethasone, 362
diabetes
complications, 102
physical activity
aerobic activity, 105

autonomic neuropathy, 108
benefits of, 106
exercise, 106–107
high-risk sports, 108
nephropathy, 108
peripheral neuropathy, 108
program of, 109–111
retinopathy, 108
training and competition, 107
travel, 107–108
pre-participation screening, 102
treatment
dietary management, 104–105
glucose-lowering agents, 103
pharmacotherapy in, 103–104
type 1 diabetes, 101
type 2 diabetes, 101–102
diabetes mellitus, 11–12, 87, 293
diabetic athlete
diabetic ketoacidosis, 112
hypoglycaemia, 111–112
musculoskeletal manifestations
Achilles tendinopathy, 113
carpal tunnel syndrome, 113
diabetic muscle infarction, 113
DISH, 113
DRPN, 113
Dupuytren's contracture, 113
fibrosing syndromes, 112
flexor tenosynovitis, 113
gout, 112
limited joint mobility, 113
neuropathic (Charcot's) joints, 113
osteoarthritis, 112
diabetic ketoacidosis, 112
diabetic radiculoplexus neuropathy (DRPN), 113
diet, 83–84, 361
dietary approaches to stop hypertension (DASH) diet, 66–67
dietary fat types, 467–468
Dietary Guidelines (1980), 89
Dietary Guidelines for Americans, 43, 44, 49, 81–82
dietary supplements, for athlete's performance, 473–479
diffuse idiopathic skeletal hyperostosis (DISH), 113
Digestible Indispensable Amino Acid Score (DIAAS), 50
Dillema, Foekje, 425
disability-adjusted life years (DALYs), 5, 87

disease-modifying anti-rheumatic drugs (DMARDs), 220
disease-modifying osteoarthritis drugs, 242
disordered eating (DE), 412
disorders of sexual development (DSD), 424, 431, 432
diving
  case study, 374–375
  flying, 373–375
  medical certification of fitness
    coronary artery disease, 372–373
    diabetes, 373
    headaches and migraine, 373
    respiratory, 373
  methods of, 367
  pathophysiology of
    DCS, 371–372
    immersion pulmonary oedema, 372
    internal carotid artery dissection, 372
    pulmonary barotrauma, 369–370
    squeezes, 368
  physiology of, 368
Djokovic, Novak, 184–185
DNA marker, 521
DNA packaging levels, 517, 518
docosahexaenoic acid (DHA), 54, 243
dominant Mendelian traits, 519
dopamine agonists, 200
doubly labelled water (DLW), 460
drugs, athlete
  anabolic agents, 490
    AAS, 493–496
    ABP, 497
    clenbuterol, 497
    designer steroids, 497
    testosterone precursors, 496–497
  beta-2 agonists, 501–502
  beta blockers, 512
  deleted drugs, 513
  diuretics, 503
  drug testing
    athlete's responsibilities, 516
    athlete's rights, 515–516
    procedure, 514–515
    results management, 515
  hormone and metabolic modulators
    insulins, 502–503
    meldonium, 503

masking agents, 503
medico-legal issues, 539–541
non-approved substances, 490
non-intentional doping in sports, 514
peptide hormones, growth factors, related substances and mimetics
corticotrophins, 499–500
erythropoietin-stimulating agents, 497–499
hCG, 499
human growth hormone, 500–501
insulin-like growth factors, 501
permitted substances, 513
positive tests, 512
prohibited classes of, 490–492
prohibited methods
artificial oxygen carriers, 504
blood doping, 503–504
chemical and physical manipulation, 505
gene doping, 505
substances and methods prohibited in-competition
cannabinoids, 510–511
glucocorticosteroids (GCs), 511–512
narcotics, 510
stimulants, 508–510
team clinician, 516
therapeutic use, 513
WADA testing-Olympic sports, 489
dual-energy X-ray absorptiometry (DXA) scans, 74, 246–247, 460, 462
duloxetine, 241–242
dyskinesia, 201
dyspnoea on exertion, 149
symptoms, 159, 160
young athlete
causes of, 391, 392
history and clinical work-up, 391
investigations, 391
VCD, 391–392
dysthymia, 311

E

ear, nose and throat infections
infectious mononucleosis, 275–276
influenza (flu), 274–275
otitis externa, 276–277
otitis media, 277
eating disorder (ED), 295, 412
Eatwell Guide by Public Health England, 55

EIA *see* exercise-induced asthma (EIA)
eicosapentaenoic acid (EPA), 54, 243
elite sport participation risks, 319–320
emergency care
    airway with cervical spine control
        airway management technique adjuncts, 566–568
        cervical spine management, 563–565
        potentially life-threatening airway problems, 568–569
    analgesia, 582
    basic life support, 562–563
    circulation and haemorrhage control
        cervical spine, 579–580
        circulation management principles, 575–576
        CT scan, brain, 580
        disability (and neurological status), 579
        ensuring normothermia, 582
        exposure and environment control, 580
        ischaemic chest pain, 576–577
        log roll, 580–582
        signs and symptoms of blood loss, 574–576
        sites of blood loss, 575, 577
    equipment, 582
    physiotherapist role, 558
    potentially life-threatening breathing and ventilation problems
        open pneumothorax, 573
        simple pneumothorax, 573
        tension pneumothorax, 573–574
    sequence of events in
        definitive care, 562
        focused history, 561
        frequent reassessment, 562
        preparation, 559
        primary survey, 560–561
        resuscitate and stabilise, 561
        secondary survey, 561–562
        triage, 559
emergency cricothyroidotomy, 570–572
endocrine causes, of fatigue, 293
endomyocardial biopsy (EMB), 129
endorphins, 506
endothelial nitric oxide synthase, 11
endotracheal tube, 567
energy availability (EA), 412
energy imbalance, cancer development, 302
energy intake (EI), 412
energy needs, of Paralympic athletes, 448–449

energy-yielding processes, 454
ephedra, 509–510
epilepsy, 204–205
Epstein-Barr virus (EBV), 276
Erlangen Fitness Osteoporosis Prevention Study (EFOPS), 267–268
erythropoietin (EPO), 363, 497–499, 506, 524
erythropoietin receptor (EPOR) gene, 524–525
erythropoietin-stimulating agents, 497–499
essential amino acids, 466–467
estimated average requirement (EAR), 44
eumenorrhoea, 409
European Society of Cardiology (ESC), 137
excessive fatigue, 149
exercise
    and clinical infections, 262–263
    contraindications and precautions, 240–241
    hip osteoarthritis, 238–240
    and immune system, 261–262
    knee osteoarthritis, 240
    osteoarthritis, 240
    in pregnancy, 418
exercise-associated collapse (EAC), 338–339
exercise-associated hyponatraemia (EAH), 55, 339–340
exercise-associated muscle cramps, 338
exercise energy expenditure (EEE), 412
exercise-induced anaphylaxis, 173–174
exercise-induced asthma (EIA)
    aetiology, 165
    bronchial provocation challenge tests
        direct challenge tests, 166
        indirect challenge tests, 166–168
    case study, 170
    clinical features, 165
    diagnosis, 165–166
    epidemiology, 163–164
    features of, 171
    fish oil, 170
    non-pharmacological treatment
        exercise training, 168
        masks, 168
        nose breathing, 168
        refractory period, 169
        warm-up, 168
    pathophysiology, 164
    pharmacological treatment
        beta-2 agonists, 169

inhaled corticosteroids, 169
leukotriene antagonists, 169
nedocromil sodium, 169
sodium cromoglycate (cromolyn sodium), 169
theophylline, 169–170
treatment model, 170
vocal cord dysfunction (VCD)
clinical features, 171
features of, 171
investigations, 171–172
prevalence of, 170
treatment, 172
exercise-induced bronchospasm (EIB) *see* exercise-induced asthma (EIA)
exercise-induced hyperventilation, 171–173
exercise metabolism, 454–455
exercise prescription, 25
active older adult
aerobic activity, 439, 440
balance, 440
considerations for, 440
flexibility, 440
resistance, 440
bone health in middle-aged and older adults
high-risk individuals, 258
low-risk individuals, 253–255
moderate-risk individuals, 255
for cancer patients, 306
considerations, 307–308
high-intensity *vs.* low-intensity activity, 307
inactive older adult, 437–438
people with disability, 444–445
exercise-related renal impairment, 188
exertion, 360
exertional collapse, 148
exertional heat illness (EHI), 332–334
exertional heat stroke, 338–340

F

fair play, 429, 430
fat free mass (FFM), 412
fatigue, in athletes, 149
alcohol ingestion and withdrawal, 292
allergic rhinitis, 292
caffeine and medications, 292
eating disorders, 295
inadequate nutritional intake, 291–292

infectious mononucleosis, 291
iron deficiency, 292
non-infective causes, 291–292
psychological factors, 292
respiratory tract infections, 291
fats
cholesterol, 52–53
dietary fat types, 467–468
high-fat diets, athletes, 468
LCFA, 52
MCFA, 51–52
monounsaturated fatty acids, 54, 83
polyunsaturated fatty acids, 54, 83
recommended fat intake, 53
saturated, 51, 53–54
short-chain fatty acids, 51
trans fatty acids, 55
triglyceride, 50
unsaturated, 51
female athletes
ACL injuries, 408
anaemia, 408–409
breast issues, 404–405
gynaecological injuries, 405
head to toe physical differences, 403–404
hypermobility, 406–407
menstrual cycle
abnormal menstruation, 409–410
manipulation and contraception, 410–412
oestrogen and progesterone, 409, 410
patellofemoral syndrome, 407–408
pelvic floor complications, 405–406
pregnancy, 417–419
RED-S, 414–417
triad
bone health, 413–414
energy availability, 412
menstrual function, 412–413
Female Athlete Triad Coalition, 416
ferritin, 409
fibromyalgia, 226–227, 294
Fiennes, Ranulph, 351
FIMS Code of Ethics, 531, 534–536, 538, 540
FIMS Position Statement on Doping in Sport, 541
FITT principle
frequency, 31

intensity
heart rate, 29
oxygen consumption, 29–30
rating of perceived exertion (RPE), 29
progression, 32–33
time (duration), 27
total volume, 31–32
type, 26–27
flexibility training, 208–209
fluid quantity and composition, 336
fluid requirements, for athletes, 469–470
FODMAPs, 69
Fogg behaviour model, 36–37
folate/folic acid, 60
folliculitis, 272, 273
foot osteoarthritis, 236
footstrike haemolysis, 189
forced expiratory flows (FEF), 373
Fox, Terry, 300
frailty, 434
Freeman, Kris, 114
freezing of gait (FOG), 201
frostbite, 350–352
fructose, 45–46
functional ability, 433
functional hypothalamic amenorrhoea (FHA), 413
functional overreaching (FOR), 286
fungal skin infections
onychomycosis, 274
pediculosis (lice), 274
scabies, 274
tinea gladiatorum, 274
tinea pedis and cruris, 273
furunculosis (boil), 272–273

G

gallstone disease, 87
gastrointestinal and liver infections
acute gastroenteritis, 277
hepatitis, 278–280
traveller's diarrhoea, 277–278
gastrointestinal bleeding, 177–178
gastrointestinal (GI) dysfunction, 416
gastrointestinal symptoms
abdominal pain, 178
advice on, 183, 184

bleeding, 177–178
case study, 184–185
diagnostic pathway for, 182
diarrhoea, 178
with exercise, 175
exercise and gastrointestinal diseases
coeliac disease, 180
constipation, 182
Crohn's disease, 181
FODMAPs, 181
irritable bowel syndrome, 181
lactose intolerance, 179–180
small intestinal bacterial overgrowth, 181–182
Ulcerative colitis, 181
NSAIDs, 182–183
prevention of
dehydration, 183
dietary fibre intake prior to competition, 183
fat and protein intake during exercise, 183–184
ongoing symptom management, 184
pre-event meal carefully, 183
solid foods prior to the race, 183
sports psychology, 184
training, 179
treatment of, 175
upper gastrointestinal symptoms, 175–176
gene doping
animal studies, 506–507
BMP, 506
endorphins, 506
EPO, 506
gene delivery, 505–506
IGF-1, 506
myostatin, 506
PEPCK, 506
PPAR-d, 506
risks of
direct detection, 507
indirect detection, 508
in sports, 524
vascular endothelial growth factor, 506
generalised anxiety disorder (GAD), 321
generalised joint hypermobility (GJH), 397
genes, 517–518
genetic mapping, 520
genetics and sex

androgen receptors, 422–424
chromosomal variants, 422
gene variants, 422
intersex, 423
sex spectrum, 424
sex *versus* gender, 421–422
genetic testing, 523–524
genitourinary illness, in Paralympic athletes, 447–448
genome, 517, 521
genome-wide association study (GWAS), 521–523
genotype
definition, 521
vs. phenotype, 518–519
'Get Active Questionnaire,' 18
Glasgow Coma Scale (GCS), 579, 595
Global Action Plan on Physical Activity 2018–2030 (GAPPA), 6, 377
Global Burden of Disease (GBD), 85–88
Global Initiative for Asthma (GINA) guidelines3, 162
Global Physical Activity Questionnaire (GPAQ), 19
glucocorticosteroids (GCs), 511–512
glucose-lowering agents (GLAs), 103
gluten-free diet, 69
glycaemic index (GI), 44, 463–464
glycaemic load (GL), 45
goal-based motor training, 209
gold medal mutation, 524
gonadotropin releasing hormone (GnRH), 412
gonococcal arthritis, 219
gout, 219
Grant, Brian, 203
Greene, Dai, 206
Green Prescription, New Zealand, 26
Grim Reaper, 438
Grunewald, Gabriele, 310
Gryphon, Blake, 272
gut microbiota, 47–48
Guttmann, Ludwig, 443

H

haematuria
abrasions of the bladder wall, 189
athletic pseudonephritis, 189
clinical anatomy and physiology, 187–188
clinical approach, 189
exercise and the patient with renal impairment, 191–193
exercise-related renal impairment, 188

footstrike haemolysis, 189
myoglobinuria, 188–189
prevention of renal complications of exercise, 193
proteinuria, 189–191
renal trauma, 189
rhabdomyolysis, 188–189
haeme iron, 64
haemoglobin A1c (HbA1c), 12
haemoglobin oxygen carriers (HBOCs), 504
haemoglobinuria, 189
haemophilia, 394–395
Hamilton Depression Rating Scale (HAM-D), 311
hand osteoarthritis, 236–237
harassment and abuse in sport
case study, 554
consequences of, 551
delivery mechanisms of
high risk sport culture for, 549
neglect, 551
physical abuse, 549–550
psychological harassment and abuse, 549
IOC definitions for, 546–547
non-accidental violence types
homophobia, 547
neglect, 548
physical abuse, 547
psychological abuse and harassment, 547
prevention of, 552
safeguarding, 545
sport physician in prevention of, 552–554
health nutrition
dietary guidelines, 43–44
diet types
DASH, 66–67
gluten-free, 69
high fat-ketogenic, 68
high-protein, 67
intermittent fasting, 70–71
low-calorie, 65
low-carb, 67–68
low-fat, 66
low-FODMAP, 69
low-GI diet, 68
Mediterranean diet, 66
paleo, 68–69
vegetarian and vegan, 69–70

fluids, 55–56
macronutrients
carbohydrates, 44–48
fats, 50–55
protein, 49–50
micronutrients *see* micronutrients
terminology, 44
health screening, 355
healthy ageing, 433–435
healthy community design, 347
heart murmur, 151
heat acclimatisation, 335
heat illness
adaptations to chronic/repeated exposures, 333, 335
beneficial acute responses, 331
biophysics of heat exchange, 330–331
cardiovascular adaptations, 335
changes in blood volume, 335
exertional heat illness, 332–334
guidelines for medical coverage of competitive events, 337–338
guidelines for organising competitive events, 340–343
hydration, dehydration and hyponatraemia, 336–337
hyperthermia, 332–333
kinetics of acclimatisation, 336
medical management, 338–340
sweat rate, 335
heat stroke, 14
heat syncope, 338–339
hepatitis, 278–280
hepatitis A virus (HAV) infection, 278
hepatitis B virus (HBV) infection, 278–280
hepatitis C virus (HCV) infection, 280
hepatitis D virus (HDV) infection, 280
hepatitis E virus (HEV) infection, 280
hepcidin, 64
Herpes simplex virus skin infections, 270–271
high-altitude cerebral oedema (HACO), 358
high-altitude illness, 357–358
high-altitude pulmonary oedema (HAPO), 357–358, 362
high-fat diets, for athletes, 468
high-intensity interval training (HIIT), 30–31
high-intensity resistance and impact training (HiRIT), 259
high-resolution peripheral quantitative computed tomography (HR-pQCT), 248
hip osteoarthritis, 234–235
homeostasis, 7–8
homologous blood transfusions (HBT), 504

hot-tub folliculitis, 273
human chorionic gonadotrophin (hCG), 499
human growth hormone (hGH), 500–501
human immunodeficiency virus (HIV) infections, 280–281
human rights, 429–430
hyaluronic acid, 242
hydration, 336–337, 360
hydration status, practical assessment of, 469
hydroxychloroquine, 224
hyperandrogenism, 422
hypertension, 150–151
hyperthermia, 332–333
hypertrophic cardiomyopathy (HCM), 119
hypoglycaemia, 111–112
hypoinsulinaemia, 112
hyponatraemia, 336–337
hypothermia, 349–350
hypothyroidism, 293
hypoxic ventilatory response (HVR), 363

idiopathic left ventricular hypertrophy, 122
IM *see* infectious mononucleosis (IM)
immersion casualties, 353
immersion pulmonary oedema (IPO), 372
impetigo, 271–272
implantable cardioverter defibrillators (ICDs), 121, 157
industrial trans fats, 55
infections, 360–361
    in athletes *see specific type* infections
    and athletic performance, 263
    epidemiology and outbreak management, 263–269
    exercise and clinical infections, 262–263
    preventive measures, 281
infectious mononucleosis (IM)
    clinical perspective, 275
    fatigue, in athletes, 291
    investigations, 275
    splenic rupture, risk of, 275–276
    treatment, 275
infective causes, of fatigue, 291
influenza (flu), 274–275
innate immune system
    cytokines, 262
    macrophages, 262
    Natural killer cells, 261–262

neutrophils, 262
insulin-like growth factor 1 (IGF-1), 204, 301, 500, 501, 506
insulin resistance, 67, 293, 302
interleukins, 234
intermittent airway obstruction, 162
intermittent fasting, 70–71
internal carotid artery dissection, 372
International Association of Athletics Federations (IAAF), 425–428, 510
International Convention Against Doping in Sport, 529
International Federation of Sports Medicine (FIMS), 529
International Olympic Committee (IOC), 545
International Olympic Committee transgender guidelines (2015), 431
International Paralympic Committee (IPC), 443, 444
International Paralympic Games, 544
International Society for Physical Activity and Health, 6
International Society for the Advancement of Kinanthropometry (ISAK), 462, 463
International Sports Federation for Persons with Intellectual Disability, 444
intersex, 423
Intersex Society of North America, 423
intra-articular injections, 242–243
intrauterine devices (IUDs), 411
IOC Executive Board, 432
iron deficiency anaemia (IDA), 408
irritable bowel syndrome (IBS), 69, 181
ischaemic chest pain, 576–577

J

Japanese Association for the Study of Obesity (2002), 76
joint and extra-articular manifestations, 213, 216–218
joint hypermobility syndrome (JHS), 198, 397
joint injury prevention, 237
joint pain and 'pain all over,' 226–227
juvenile arthritis, 211
juvenile idiopathic arthritis (JIA), 396–397

K

ketogenic diet, 68
kinetics of acclimatisation, 336
knee osteoarthritis, 235

L

laryngeal mask airway (LMA), 568
laser-assisted in situ keratomileusis (LASIK), 360
laser photorefractive keratectomy (laser PRK), 360
late gadolinium enhancement (LGE), 129
left ventricular hypertrophy (LVH), 120, 121

Letang, Kris, 196
levonorgestrel (LNg), 411
Lifestyle integrated Functional Exercise (LiFE), 439
LIFTMOR trial, 259
locus, 521
Lomu, Jonah, 190–191
London Olympics (2012), 432
long-chain fatty acids (LCFA), 52
long QT syndromes (LQTS), 120, 126–128
low back pain and stiffness, 224–226
low-calorie diet, 65
low-calorie sweeteners (LCS), 90
low-carbohydrate diet, 67–68
low energy availability (LEA), of Para athletes, 448
low-fat diets, 66
lung spirometry, 165
lyme disease, 219

M

macronutrients
    carbohydrates
        fibre, 46–47
        recommended carbohydrate intake, 45
        sugar, 45–46
    fats
        cholesterol, 52–53
        LCFA, 52
        MCFA, 51–52
        monounsaturated fatty acids, 54
        polyunsaturated fatty acids, 54
        recommended fat intake, 53
        saturated, 51, 53–54
        short-chain fatty acids, 51
        trans fatty acids, 55
        triglyceride, 50
        unsaturated, 51
    protein, 49–50
major/unipolar depression, 311
Mäntyranta, Eero, 524
Marfan syndrome, 124–126, 149, 151–152
masters runners and cyclists, 260
McArdle disease, 396
mean corpuscular volume (MCV), 409
ME/CFS *see* myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS)
mechanotransduction, 12
medical coverage of endurance events

first-aid stations, 586–587
medical facility, race finish, 587–589
medical team, 586
race organisation, 585–586
sporting event, 585
medico-legal issues
civil law systems, 529
drugs in sport, 539–541
human rights law
disability, 544
intersex and transgender, 543
pregnancy, 543–544
single-sex sports, 542–543
international sports rules and regulations, 529
managing risky sports
head injuries, 538–539
neck injuries, 538
sports clinician/athlete relationship
consent, 530–531
creation, 529–530
local laws, 530
medical skill, 531–535
sports team clinician
managing conflict of interest, 536
medical care, 536
trust and confidence, 536–537
vicarious liability, 537
Mediterranean diet, 66
medium-chain fatty acids (MCFA), 51–52
melanoma, 305
meldonium, 503
Mendelian traits, 519–520
meniscectomies, 234
menorrhagia, 409
menstrual irregularity, 409, 410
mental illness, 87
Merritt, Aries, 193–194
mesenchymal stem cells (MSCs), 242–243
metabolic equivalents (METs), 29–31
metabolic icebox, 350
metabolic obesity, 75
methicillin-resistant *Staphylococcus aureus,* 273
micronutrients
minerals
calcium, 61–62
iodine, 63–64

iron, 64
magnesium, 62
potassium, 62–63
sodium, 63
zinc, 64–65
supplementation, 56, 57
vitamins
B vitamins, 59–60
vitamin A, 57
vitamin C, 61
vitamin D, 57–58
vitamin E, 58, 59
vitamin K, 59
mitochondrial genome (mtDNA), 521
mitochondrial myopathy (MM), 395–396, 399, 400
mitral valve prolapse (MVP), 126
modafinil, 510
moderate to vigorous physical activity (MVPA), 251, 396
molluscum contagiosum, 271
monoamine oxidase inhibitors, 316
monoamine oxidase type B inhibitors, 200
monoarthritis, 216–222
monosaccharides, 45
monounsaturated fatty acids, 54
motivational interviewing (MI)
change talk, 40
develop discrepancy, 39
example of, 41
express empathy, 38
FYSS, 38
OARS, 39–40
patient's self-efficacy, 38
roll with resistance, 39
'Moving School' initiative, 384
MSE *see* multisport endurance (MSE)
multidisciplinary cancer rehabilitation team, 309
multiple daily injections (MDI), 104
multiple sclerosis (MS), 203–204
multiple swollen joints *see* polyarthritis/polyarthralgia
multisport endurance (MSE)
injury prevalence in, 592, 593
management of injuries and safety concerns
AMS, 595–596
GCS, 595, 596
musculoskeletal injuries and improvised splints, 596–599
organ dysfunction and/or failure, 595

soft tissue injuries and infections, 598, 600
medical evacuation, 600–601
medical features of, 591
obstacle course racing, 591
physiology
carbohydrates and sugars, 593–594
hydration and electrolytes, 594
rhabdomyolysis and renal injury, 594–595
technical skills, 591
muscle glycogen and CHO loading, 464
musculoskeletal conditions, 87
musculoskeletal health, 12
musculoskeletal pain syndromes, 371
musculoskeletal risks, 13–14
myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS)
comorbidities, 294
diagnosis, 294
prevalence and aetiology, 294
symptoms, 293, 294
treatment, 294
myocarditis, 129, 130
myoglobinuria, 188–189
myostatin, 506

N

narcotics, 510
Nassar, Larry, 550
National Collegiate Athletic Association (NCAA) athletes, 117
National Emergency X-Radiography Utilization Study (NEXUS), 580
National Institute for Health and Care Excellence (NICE), 16, 17
national position statements, on infectious diseases, 281–282
neck check, 263
needle thoracentesis, 573
neighbourhood school, 384–385
Neisseria gonorrhoea, 219
neurological conditions
cerebrovascular disease, 195–198
epilepsy, 204–205
multiple sclerosis, 203–204
Parkinson's disease, 198–203
planning a physical activity program, 205–209
neuromuscular training, 209
New Zealand's Green Prescription (Green R_x), 26
NEXUS cervical spine X-ray criteria, 580
NFOR *see* non-functional overreaching (NFOR)

non-alcoholic fatty liver disease (NAFLD), 46
non-bullous impetigo, 271
non-communicable diseases (NCDs), 2, 16
non-essential amino acids, 466–467
non-freezing cold injury, 351–353
non-functional overreaching (NFOR)
    definition, 286
    diagnosis, 287–289
    prevalence, 286–287
    prevention, 289
    treatment, 290
non-haeme iron, 64
non-infective causes, of fatigue, 291–292
non-steroidal anti-inflammatory drugs (NSAIDs), 190, 241, 441
nudge, 36
number needed to treat (NNT), 15, 16
nutrient reference values (NRVs), 44
nutritional completeness, 67
nutritional ketosis, 68

O

OA *see* osteoarthritis (OA)
OARS
    affirmations, 40
    open-ended questions, 39–40
    reflections, 40
    summaries, 40
obesity
    by age, 82
    body fat, 74–75
    causes
        diet, 83–84
        energy balance, 80
        ethnicity, 79–80
        genetic factors, 76
        insulin resistance, 84
        lack of exercise, 83
        medical illnesses, 84
        medications, 84
        menopause, 84
        obesogenic environment, 84–85
        poor sleep, 84
        pregnancy, 84
        quitting smoking, 84
        sedentary lifestyle, 83
        socioeconomic disadvantage, 76, 79

stress and mental illness, 84
childhood, 99
definition, 74
disease, 76
epidemic, 92, 93
fat accumulation, 75
and illness
cancer, 87
CVD, 87
diabetes mellitus, 87
gallstone disease, 87
GBD, 85–88
mental illness, 87
musculoskeletal conditions, 87
sleep apnoea, 87
stigma, 88–89
lifestyle interventions
behavioural therapy, 90–91
lifestyle intervention programs, 91
sleep duration, 91
medical management
bariatric surgery, 91–92
medications, 91
patient management
diet, 89–90
exercise, 90
policy interventions
government action to encourage private-sector action, 98–99
policies aimed at changing the market environment, 96–98
policies supporting more-informed choice, 93–96
prevalence of, 75, 77, 78
rates of, 76, 78, 81
obesity paradox, 88
obsessional neurosis, 321
obsessive compulsive disorder (OCD), 321
oestrogen, 403
older people
definition, 433
exercise prescription in
active older adult, 439–440
inactive older adult, 437–438
healthy ageing, 433–435
medication and physical activity interact in
beta blockers, 441
cardiac drugs, 441
central nervous system, 442

diuretics, 441
insulin and oral hypoglycaemic drugs, 442
NSAIDs, 441
renin-angiotensin system, 441
physical activity in
cardiovascular system, 434–436
cognitive and psychological function, 436–437
diabetes mellitus, 436
functional independence, 436
osteoarthritis, 436
osteoporosis, 436
respiratory system, 436
risks for, 437
onychomycosis, 274
opioids, 242
oral contraceptive pills (OCPs), 360, 411
oropharyngeal airway, 566–567
osteoarthritis, 12
osteoarthritis (OA), 220–222
clinical history and diagnosis, 234–237
epidemiology, 233–234
management, 238–243
pathophysiology, 234
prevention, 237–238
Osteoarthritis Research Society International (OARSI), 233
osteogenic sarcoma, 300
osteoporosis, 12, 252
definition, 247
exercise prescription, for prevention
and management, 255
Otago Exercise Programme, 436, 437
otitis externa, 276–277
otitis media, 277
overtraining syndrome (OTS) *see also* non-functional overreaching (NFOR)
definition, 286, 287
detrimental effects, 286, 288
diagnosis, 287–289
prevalence, 286–287
prevention, 289
treatment, 290
overuse shoulder injuries, 447
overweight
by age, 81, 82
children, 90
definitions of, 74
exercise, 90

LCS, 90
obesogenic environment, 85
prevalence of, 75–77
rate of, 81

P

pain reduction, 12
palaeolithic diets, 68–69
panic disorder/panic attack, 321
papillary thyroid cancer, 310
para alpine skiing, 451
para athletes, medical issues
in summer sport, 447–449
in winter sport, 449–450
Paralympic Games
eligible impairment types, 445, 446
history, 443
Parkinson's disease (PD), 198–203
parvovirus B19, 222, 224
patellofemoral syndrome (PFS), 407–408
patent foramen ovale (PFO), 397
pathogenic mutation, 521
peak expiratory flow rate (PEFR), 163
pediculosis (lice), 274
pedometer-based walking intervention, 382
people with disability
anti-doping issues, 450–451
exercise prescription, 444–445
physical activity, 444–445
specific needs during travel, 451
sports participation, 443–444
perfluorocarbons (PFCs), 504
performance anxiety, 322
peripheral neuropathy, 102
peripheral quantitative computed tomography (pQCT), 248
peroxisome proliferator-activated receptor delta (PPAR- d), 506
pharmacotherapy
anxiety disorders, 326–327
diabetes, 103–104
phenotype
definition, 521
vs. genotype, 518–519
phenylpropanolamine, 509
phosphoenolpyruvate carboxykinase (PEPCK), 506
physical activity
and acute hepatitis infection, 280

adjunct treatment for cancer, 304–308
benefits
    brain function and mental health, 8–11
    cancer prevention, 10–11
    cardiometabolic health, 11–12
    healthy ageing, 13
    longevity, 13
    musculoskeletal health, 12
    pain reduction, 12
    social wellbeing, 13
    weight management, 12–13
best investments for, 377–378
built environment *see* built environment
and cancer risk, 300, 301
for cancer treatment
    advanced cancer patients, benefits of, 305
    anti-cancer therapy, 304
    antioxidant pathways and immunity enhancement, 302, 303
    DNA repair, epigenetic effects on, 303–304
    drug tolerance, 304
    energy imbalance and insulin resistance, 302
    gene expression, epigenetic effects on, 303–304
    insulin-like growth factor-1, 301
    overall survival, 304–305
    palliative care, 305
    patient counselling, 306–308
    survivorship, role in, 308–309
    telomere length, epigenetic effects on, 303–304
counselling
    5 A's behavior change model, 17–22
    clinical pathway for, 17
    clinicians around the world, 17, 18
    clinician's responsibility, 16
    enabling factors, 22, 24
    evidence base and guidelines, 15–16
    limited time, 22
    NICE category, 17
    primary and secondary prevention opportunity, 16
diabetes
    aerobic activity, 105
    autonomic neuropathy, 108
    benefits of, 106
    exercise, 106–107
    high-risk sports, 108
    nephropathy, 108

peripheral neuropathy, 108
program of, 109–111
retinopathy, 108
training and competition, 107
travel, 107–108
diabetic athlete
fracture reduction, 255–260
older people
cardiovascular system, 434–436
cognitive and psychological function, 436–437
diabetes mellitus, 436
functional independence, 436
osteoarthritis, 436
osteoporosis, 436
respiratory system, 436
people with disability, 444–445
physiology of, 7–8
risks
cardiac, 14
dehydration and heat stroke, 14
musculoskeletal, 13–14
respiratory, 14
and sedentary behaviour, 300, 301
Physical Activity in the Prevention and Treatment of Disease (FYSS), 26, 38, 437
physical activity on prescription (PAP), 26
Physical Activity Vital Sign Questions, 19
physical inactivity
GAPPA, 6
global burden of, 6
healthcare costs, 3–4
productivity cost, 4–5
quality of life, 5
trends, 2, 3
physiologic markers, NFOR/OTS, 287–288
plant-based diets, 70
plasmid delivery, 505
plasmid DNA (pDNA), 505
platelet-rich plasma (PRP), 242
pneumothorax, 370
policy interventions, obesity
government action to encourage private-sector action, 98–99
policies aimed at changing the market environment
fiscal measures, 96
nutrition-related standards, 98
school meals, 98
subsidies to disadvantaged consumers, 98

taxes/subsidies on foods, 96–97
workplace canteen meals, 98
policies supporting more-informed choice
advertising controls, 93–94
food labelling, 95–96
nutritional information on menus, 96
nutrition education, 94–95
social marketing, 94
polyarthritis/polyarthralgia, 222–224
polycystic ovarian syndrome (PCOS), 293
polymerase chain reaction (PCR) test, 426
polymorphism, 521
polysaccharides, 44
polyunsaturated fatty acids (PUFAs), 54
poor sleep at high altitude, 362
post-exertional syncope, 147
post-traumatic stress disorder (PTSD), 321–322
prebiotics, 48
pre-exercise medical assessments, for cancer patients, 306
pregnancy, 417–419
pregnant women at altitude, 360
prehabilitation, 237–238
premature coronary artery disease, 124, 125
pre-participation evaluation (PPE) program
diabetes, 102
SCD
cost-effectiveness and feasibility of, 138–139
incidence of, 117
in veteran athletes, 139
prescribing physical activity
behaviour change theories, 35
classic learning theories, 35–36
Fogg behaviour model, 36–37
maintenance of, 41–42
motivational interviewing (MI)
change talk, 40
develop discrepancy, 39
example of, 41
express empathy, 38
FYSS, 38
OARS, 39–40
patient's self-efficacy, 38
roll with resistance, 39
reasoned action approach, 36
social cognitive theory, 36
transtheoretical stages of change, 37

written prescription
5As component, 25
FITT principle, 26–33
sedentary behaviour, 33–34
prescription pad, 34
probiotics, 48
Profile of Mood States (POMS) questionnaire, 289
pro-inflammatory cytokines, 234
Promotion of Therapeutic Sports Activity for Children with Cancer (PASTEC), 308
prophylaxis, 277
Prospective Urban Rural Epidemiology (PURE), 45
protein degradation, 466
Protein Digestibility Corrected Amino Acids Score (PDCAAS), 50
protein requirements, for athletes, 466–467
protein synthesis, 466
proteinuria, 189–191
pseudoephedrine, 509–510
pseudogout, 219–220
Pseudomonas folliculitis, 273
psoriatic arthritis, 226
pulmonary barotrauma, 369–370
pyramid stacking, 493

R

radioallergosorbent tests (RAST), 162
randomised controlled trials (RCTs), 90
rare DNA variant, 521
rating of perceived exertion (RPE), 29
reactive arthritis, 220
rebreather diving, 367
recessive Mendelian traits, 519–520
recommended daily intake (RDI), 49
recommended dietary intake (RDI), 44
Recovery-Stress Questionnaire for Athletes (RESTQ-Sport), 289
RED-S *see* relative energy deficiency in sport (RED-S)
refractive eye surgery, 360
Reiter's syndrome, 220
relative energy deficiency in sport (RED-S)
cardiovascular, 416
definition of, 290–291
endocrine, 414
energy periodisation, 484–486
female athlete triad, 412
gastrointestinal, 416
growth and development, 416
haematological, 416

health consequences of, 414, 415
immunological, 416
metabolic, 414, 416
potential performance effects, 416
potential performance effects of, 414, 415
psychological, 416
screening and return to play, 416–417
renal impairment, exercise-related, 188
renal trauma, 189
renin-angiotensin system, 441
resistance training, 208
respiratory risks, 14
respiratory symptoms
anaphylaxis, 173–174
angioedema, 174
asthma *see* asthma
breath and wheeze shortness, 159–160
chest pain/tightness, 160–161
cholinergic urticaria, 174
cough, 160
sinus-related symptoms, 173
respiratory tract infections, 291
retirement, 325
retroviruses, 505
rewarming, 350
rhabdomyolysis, 188–189, 594–595
rheumatoid arthritis (RA), 213, 222–223
rheumatological conditions
age, 211–213
anatomical site, 213
clinical history, 213, 215
diagnosis, 227–230
joint and extra-articular manifestations, 213, 216–217
joint pain and 'pain all over,' 226–227
low back pain and stiffness, 224–226
monoarthritis, 216–222
non-pharmacological management, 230
pharmacological management, 230–231
polyarthritis/polyarthralgia, 222–224
Roughead, Jarryd, 305

S

saturated fatty acids, 51–54
sausage digits, 224–226
scabies, 274
SCD, sports *see* sudden cardiac death (SCD), sports

school-based physical activity model, 249–250
'Schools on the Move' program, 383
Scottish Physical Activity Screening Question (Scot-PASQ), 19
scuba diving, 367
seasonal affective disorder (SAD), 311
sedentary behaviour, 18
seizures, 205
selective androgen receptor modulators (SARMS), 497
selective oestrogen receptor modulators (SERMs) block, 502
selective serotonin reuptake inhibitors (SSRI), 326
self-management education, 12
Semenya, Mokgadi Caster, 427
septic arthritis, 217–219
sex spectrum, 424
sex testing in sport
    androgen receptors, 428
    chromosome testing, 426
    clinical implications of
        education, 432
        ethics of, 432
        medical issues, 431
        trust and sensitivity, 432
    DNA testing, 426
    versus doping control, 430
    future developments, 431
    on-demand multidisciplinary testing, 427
    rationale for, 429
    testosterone levels, 427–428
    visual inspection, 425–426
sexual development, 421, 422
sexually transmitted infections, athletes, 281
short-acting benzodiazepine drugs, 327
short-chain fatty acids (SCFAs), 46, 47, 51
shoulder osteoarthritis, 236
single nucleotide polymorphism (SNP), 519, 521
single swollen joint *see* monoarthritis
sinusitis, 173
sinus-related symptoms, 173
Sjögren's syndrome, 231–232
skin callipers, 75
skin infections, in athletes
    bacterial, 271–273
    fungal and mite skin, 273–274
    viral, 270–271
sleep, 9
sleep apnoea, 87

small intestinal bacterial overgrowth (SIBO), 181–182
social cognitive theory, 36
socioeconomic status (SES), 76, 79
soft drinks, 83
Soundarajan, Santhi, 426
The Special Olympics, 444
spine osteoarthritis, 236
sport nutrition, 454
sport nutritionist
    body composition analysis, 460, 462
    roles and responsibilities, 454, 455
    special considerations, 479–482
sport-related benefits, in bone mass and strength, 249
sports clinician/athlete relationship
    confidentiality and trust, 535
    consent, 530–531
    creation, 529–530
    local laws, 530
    medical skill
        difficulties, 532–533
        good Samaritans, 531
        information and advice, 534–535
        negligence, 531–532
        negligence and incident types, 533–534
        specialist sports medicine, 532
sports medicine
    medico-legal issues *see* medico-legal issues
    practice of, 528
squat jump syndrome, 188
Staphylococcus aureus, 272
state trait anxiety inventory (STAI), 324
stimulants
    amphetamines, 509
    cocaine, 510
    ephedra and pseudoephedrine, 509–510
    modafinil, 510
Stockholm consensus on sex reassignment in sports, 430
Stringer, Korey, 339
stroke *see* cerebrovascular disease
subcutaneous fat, 75
subcutaneous insulin delivery, 107
sudden arrhythmic death syndrome (SADS), 120
sudden cardiac arrest (SCA), 115, 117
sudden cardiac death (SCD), sports *see also* cardiovascular symptoms
    acquired cardiac abnormalities
        commotio cordis, 129, 131

myocarditis, 129, 130
aetiology of, 118–120
causes of, 144
common diagnostic conundrums, 133–136
conditions causing, 131–132
congenital/genetic abnormalities predisposing, primary electrical disorders
Brugada syndrome, 128–129
CPVT, 129
LQTS, 126–128
WPW, 128
congenital/genetic structural heart disease
aortic stenosis, 126
arrhythmogenic cardiomyopathy, 122–123
CCAA, 124
dilated cardiomyopathy, 124
hypertrophic cardiomyopathy, 120–122
idiopathic left ventricular hypertrophy, 122
Marfan syndrome, 124–126
MVP, 126
premature coronary artery disease, 124, 125
exercise paradox, 115
incidence of, 115–118, 143, 144
MVP, 126
primary prevention of
American Heart Association, 137
American Medical Society for Sports Medicine, 138
European Society of Cardiology, 137
PPE, 138–139
purpose of screening, 136–137
secondary prevention
cardiopulmonary resuscitation (CPR), 140–141
early defibrillation, 141–142
management of, 140
recognition of, 139–140
sugar, 83
sugar-sweetened beverages (SSBs), 83
sulphonamide, 361
Summer Olympic Games (2016), 403
summer sport illnesses, in Paralympic athletes
autonomic dysfunction, 448
bone health, 448
energy needs, 448–449
genitourinary illness, 447–448
summer sport injuries, 447
'sum of 8' skinfold (SKF) sites, 462, 463
superfood, 57

surface-supplied diving, 367
sweat rate, 335
swimmer's ear *see* otitis externa
systemic lupus erythematosus, 224

T

'talk test,' 30
tamoxifen, 502
Tasker, Bruce, 197
tension pneumothorax, 573–574
tetanus, athletes, 281
tetanus-prone injury, 281
9-tetrahydrocannabinol (THC), 511
tetrahydrogestrinone (THG), 497
therapeutic use exemption (TUE), 490, 491, 540, 541
therapeutic use exemption committee (TUEC), 513
thermoregulation in the cold, 345–347
thermoregulation, Paralympic athletes, 448
thiamine, 59–60
thiazide diuretics, 441
Thorpe, Ian, 317
thyroid hormones triiodothyronine (T3), 412
thyroid-stimulating hormone (TSH), 412
thyroxine (T4), 412
time-restricted feeding, 70–71
tinea cruris, 273
tinea gladiatorum, 274
tinea pedis, 273
tiredness, in athletes *see also* fatigue, in athletes
    assessment of, 284–285
    biopsychosocial stressors, 285
    causes, 283
    clinical investigations, 285
    coeliac disease, 294–295
    comprehensive training history, 284
    diabetes mellitus, 293
    dysfunctional sleep, 286
    eating disorders, 295
    endocrine causes, 293
    hypothyroidism, 293
    infective causes, 291
    insufficient/inadequate sleep, 286
    medical conditions, symptoms of, 284–285
    myalgic encephalomyelitis/chronic fatigue syndrome, 293–294
    non-functional overreaching, 286–290
    non-infective causes, 291–292

nutrition diary, 284
overtraining syndrome, 286–290
pathology associated with, 284
physical examination, 285
relative energy deficiency in sport, 290–291
sleep patterns, 284
T-lymphocytes, 262
topical agents, 243
total energy expenditure (TEE), 460
total iron binding capacity (TIBC), 409
trace elements, 61
traditional medical impairment types, 446, 447
Training Distress Scale (TDS), 289
trans fatty acid (TFA), 55, 98
transgender
athletes in sport, 430
definition, 424–425
transmission mode, of viral hepatitis, 279
traveller's diarrhoea
definition, 277
prophylaxis, 277
treatment, 278
Treasure, Alyx, 180
T-scores, 246, 247
type 1 diabetes, 393

U

Uhthoff's effect, 204
UK National Institute for Health and Care Excellence (NICE), 16
ultraviolet light, 361
umbilical diving, 367
Undersea and Hyperbaric Medicine Society, 375
underwater *see* diving
Union Internationale des Associations d'Alpinisme (UIAA), 360
Universal Declaration of Human Rights, 429, 529
unsaturated fatty acids, 51, 52
upper gastrointestinal symptoms, 175–176
upper limit (UL), 44
US Anti-Doping Agency (USADA), 541
uveitis, 211

V

valvular heart disease, 126
vascular endothelial growth factor, 506
vasovagal syncope, 147
VCD *see* vocal cord dysfunction (VCD)

vegetarian diets, 69–70
verrucae, 271
very-long-chain fatty acids (VLCFA), 52
very-low density lipoprotein (VLDL), 67
viral skin infections
    herpes simplex virus, 270–271
    molluscum contagiosum, 271
    warts (verrucae), 271
viral vectors, 505
visceral fat, 75
vitamin B_1 (thiamine), 59–60
vitamin B_3 (niacin), 60
vitamin B_9 (folate), 60
vitamin B_{12} (cobalamin), 60
vitamin C, 61
vocal cord dysfunction (VCD)
    case study, 172
    clinical features, 171
    features of, 171
    investigations, 171–172
    prevalence of, 170
    treatment, 172
    in young athlete, 391–392
volatile fats, 51

W

Waddell, Rob, 157
waist measurement, 75
warts (verrucae), 271
weight management in osteoarthritis, 238
Wernicke–Korsakoff syndrome, 59–60
WHO's Global Action Plan on Physical Activity (2018–2030), 6, 16, 22
Wilkinson, Jonny, 327
Williams, Ricky, 323
winter sport illness, 450
winter sport injuries, 450
Wolff-Parkinson-White syndrome (WPW), 128
Woolstencroft, Lauren, 451
World Anti-Doping Agency (WADA), 166, 489, 513, 540
World Anti-Doping Code (WADC), 489, 490, 529, 540–542
World Health Organization (WHO), 2, 15, 74, 377, 439
World Track and Field Championships (2003), 510

X

X-linked recessive Mendelian traits, 520

Y

young athletes
- aerobic capacity, 389
- anaerobic capacity (power), 389
- characteristics of, 388
- chronic childhood diseases
  - childhood cancer, 394
  - congenital coronary artery abnormalities, 397
  - cystic fibrosis (CF), 394
  - generalised joint hypermobility (GJH), 397
  - haemophilia, 394–395
  - Juvenile idiopathic arthritis, 396–397
  - McArdle disease, 396
  - mitochondrial myopathies, 395–396
  - type 1 diabetes, 393
- concussion, 397–399
- dyspnoea on exertion
  - causes of, 391, 392
  - history and clinical work-up, 391
  - investigations, 391
  - VCD, 391–392
- early specialisation, 392–391
- paediatric exercise medicine
  - dyspnoea on exertion, 391–392
  - poor exercise tolerance and fatigue, 392
- performances, 388
- strength, 389
- type 1 diabetes, 393
- VCD, 391–392
- weight-for-age competitions, 389

Z

Z-scores, 247