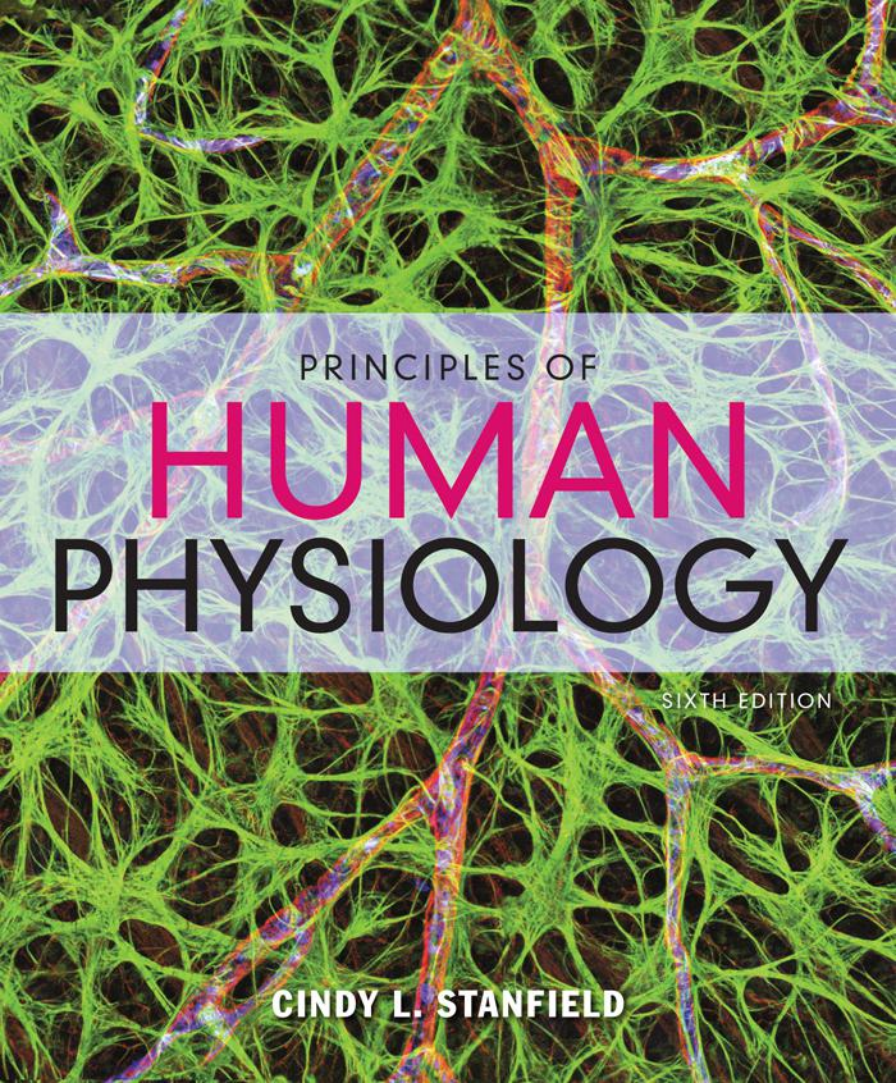

PRINCIPLES OF
HUMAN
PHYSIOLOGY
SIXTH EDITION
CINDY L. STANFIELD

Brief Contents

Solve It Tutorials

*These Solve It tutorials are not printed in the textbook, but are assignable in MasteringA&P.

Don’t just read this book…

Explore physiology with MasteringA&P®

Don’t just ask questions…

NEW! SOLVE IT tutorials engage students in a multi-step case study in which they must analyze real data. Students begin by reading a clinical scenario and answering a question in the book, with the opportunity to delve deeper in an assignable activity in MasteringA&P.

SOLVE IT!

What Happens in Your Cells During a Heart Attack?

Thirty-one-year-old Ahmed was dizzy, sweaty, having trouble catching his breath, and had chest pain radiating in his left arm and lower back. From his nursing classes, Ahmed thought these were symptoms of a heart attack; but he was so young. Since he was taught to educate patients not to ignore these symptoms, he went to the emergency department.

He was immediately taken back to a room, had blood drawn, and was connected to an electrocardiogram (ECG). When the attending physician came in, Ahmed learned that he had suffered a heart attack and would be admitted to the hospital.

The next day, a physician came in to talk to Ahmed about his results in the table to the right.

Blood Test	Normal Values	Ahmed’s Values
Total cholesterol (mg/dL)	< 200 mg/dL	350 mg/dL
Low-density lipoproteins (LDL)	< 130 mg/dL	273 mg/dL
Glucose (fasting)	70–110 mg/dL	243 mg/dL
Hemoglobin A1C	5.6% or less is normal 5.7–6.4% indicates prediabetes > 6.4% confirms diabetes	7.2%
Troponin I (TnI)	<0.034 ng/ml	0.07 ng/ml

Based on the test results, Ahmed has _____.

A. hypercholesterolemia and hyperglycemia
B. hypocholesterolemia and hypoglycemia
C. hypercholesterolemia and hypoglycemia
D. hypocholesterolemia and hyperglycemia

*Additional questions from this Solve It activity can be assigned in MasteringA&P.

Part B

Ahmed knew from his nursing classes that cardiac markers are normally found within his cardiac muscle cells, and the levels in his blood should be very
his learning, Ahmed thought about what he knew about cardiac muscle cells.

Cardiac muscle cells are excitable cells where ion diffusion across the cell membrane leads to changes in charge inside of these cells. This results in the
action potentials, which serve as the stimulus for contraction of the heart.

Using your knowledge of intracellular and extracellular ion concentrations and membrane transport, complete the statements about cardiac mu

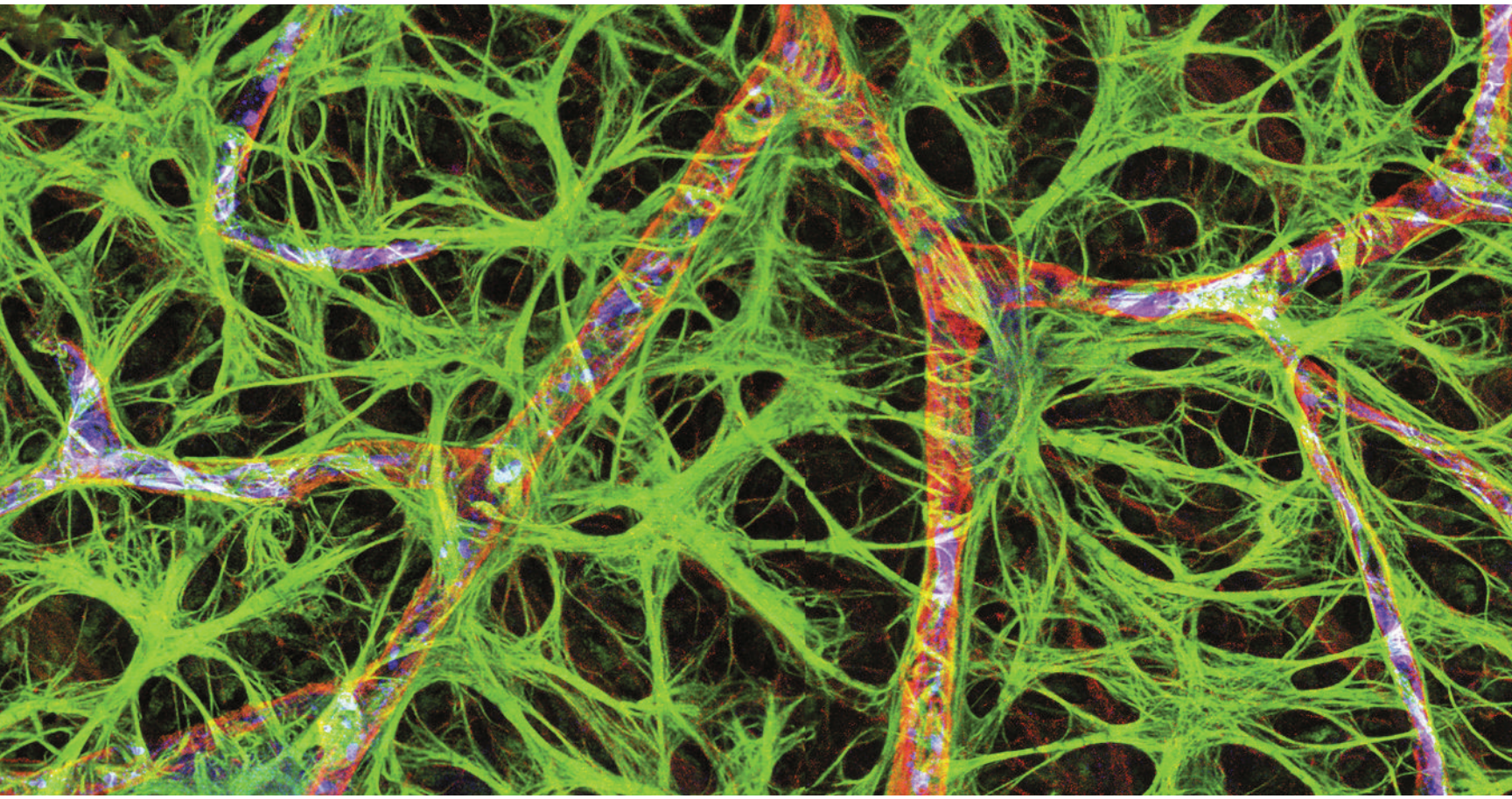
positively-charged cations
negatively-charged anions
intracellular fluid
extracellular fluid
lower
higher
into

1. Sodium, calcium, and potassium are _____.
2. Sodium and calcium ions are higher in the _____.
3. Potassium ions are higher in the _____.
4. Ions diffuse from areas of _____ concentration to areas of _____ concentration.
5. Sodium and calcium will diffuse _____ cells, and potassium will diffuse _____ cells.

PRINCIPLES OF

Human Physiology

Sixth Edition



CINDY L. STANFIELD

University of South Alabama

PEARSON

Boston Columbus Indianapolis New York San Francisco Amsterdam
Cape Town Dubai London Madrid Milan Munich Paris Montréal Toronto
Delhi Mexico City São Paulo Sydney Hong Kong Seoul Singapore Taipei Tokyo

Senior Acquisitions Editor: Kelsey Churchman
Program Manager: Chriscelle Palaganas
Project Manager: Chakira Lane
Director of Development: Barbara Yien
Editorial Assistant: Ashley Williams
Content Producer: Joe Mochnick
Text and Photo Permissions Project Manager: Tim Nicholls
Program Management Team Lead: Mike Early
Project Management Team Lead: Nancy Tabor
Project Management and Composition: Integra Software Services Pvt. Ltd.
Managing Editor: Angel Chavez
Design Manager: Marilyn Perry
Text Designer: Emily Friel
Cover Designer: Charlene Charles-Will
Marketing Manager: Allison Rona
Senior Manufacturing Buyer: Stacey Weinberger

Cover Photo Credit: Thomas Deerinck, NCMIR/Science Source

Credits and acknowledgments for materials borrowed from other sources and reproduced, with permission, in this textbook appear on the appropriate page within the text in the case of art or text material and on p. 727 in the case of photos.

Library of Congress Cataloging-in-Publication Data.
Stanfield, Cindy L.
Principles of human physiology / Cindy L. Stanfield.
pages cm
Revision of: Principles of human physiology / William J. Germann, Cindy L. Stanfield. 2002.
Includes index.
ISBN 978-0-13-416980-4 (student edition)
1. Human physiology—Textbooks. I. Title.
QP34.5.G465 2017
612—dc23

2015035509

ISBN 10: 0-134-16980-8; ISBN 13: 978-0-134-16980-4 (Student edition)
ISBN 10: 0-134-29889-6; ISBN 13: 978-0-134-29889-4; (Instructor's Review Copy)

PEARSON

www.pearsonhighered.com

1 2 3 4 5 6 7 8 9 10—V311—16 15 14 13 12

To John Thurston, the backbone of the family since losing our parents. Thanks big brother.
C.L.S.

About the Author

Cindy L. Stanfield earned a B.S. degree and a Ph.D. in physiology from the University of California at Davis. Her exposure to neurophysiology research as an undergraduate sparked her interest in pursuing a Ph.D. As a graduate student she studied the role of neuropeptides in pain modulation and taught several physiology laboratory courses, which led to her interest in teaching. She currently teaches human physiology, neuroscience, and biomedical ethics at the University of South Alabama. Cindy also serves as the director of the Health Pre-professional program.

Cindy currently serves as the national president of Alpha Epsilon Delta, the National Prehealth Honor Society. She received the College of Allied Health Professions Excellence in Served Award in 2003, and the University of South Alabama Alumni Association Excellence in Teaching Award 2004. She is an active member of several professional organizations including the American Physiology Society, the Human Anatomy and Physiology Society, and the National Association of Advisors for the Health Professions. She lives in Mobile, Alabama, with her husband Jim and their numerous cats and dogs.

Preface

The guiding philosophy for this textbook was to create a rich resource that makes it as easy as possible for students to learn the fundamentals of human physiology while also providing a solid, comprehensive, and current overview of the field. It is our belief that a physiology textbook should emphasize deeper understanding of concepts over mere memorization of facts, in concert with useful tools for students with varying levels of preparation in biology, chemistry, physics, and related sciences, to aid them in their individual studies.

In developing the sixth edition, we've made several ambitious enhancements with these goals in mind, while retaining the book's proven and trusted hallmarks: a direct and precise writing style; a clear and illuminating art program designed to maximize student learning; and pedagogical features that stimulate users' interest, help readers think about physiological processes in an integrated way, and reinforce the most important concepts.

The most wide-ranging advancement in the sixth edition is the addition of more critical thinking activities in both the text and the online tool MasteringA&P®, the most effective and widely used online tutorial, homework, and assessment platform and system for the sciences. This online tool utilizes the most current resources, including chapter quizzes, self-paced tutorials, practice tests, guided animations, interactive physiological processes, expansive laboratory simulations, and the newly added Solve It case studies and Interpreting Data.

New to the Sixth Edition

In response to the feedback we received from users, reviewers, and instructors, we have made the following key enhancements to this edition.

- **MasteringA&P®**, an integrated text and technology learning system focusing on student comprehension and instructor adaptability, with reinforced clinical content, is included in this edition. Assignable, text-specific assets include online homework, tutorial, and assessment systems; self-paced tutorials; and customizable, assignable, and automatically graded assessments. MasteringA&P® icons and references appear at appropriate places throughout each chapter to direct students to related online resources.
- SOLVE IT, clinical case studies, appear in nine chapters. These cases are presented in the text but provide the option for the instructor or the student to go to the MasteringA&P® site to further analyze the case. One case continues through four chapters to further demonstrate systems integration; the other Solve Its are independent.

INTERPRETING DATA are new exercises provided in MasteringA&P®. These exercises are found in each chapter and focus on how to read graphs and tables using related data.

Chapter 1 Introduction to Physiology

INTERPRETING DATA: Obesity and Diabetes Mellitus Type 2. Students analyze a graph showing the relationship between BMI and risk for Type II Diabetes Mellitus, and comparing men to women.

Chapter 2 The Cell: Structure and Function

INTERPRETING DATA: The Genetic Code. Students will transcribe and translate a portion of DNA.

Chapter 3 Cell Metabolism

INTERPRETING DATA: Students will analyze data on the importance of one of the enzymes of glycolysis.

Chapter 4 Cell Membrane Transport

INTERPRETING DATA: Osmolarity and Osmosis. Students will be given the concentration of solutes in water and asked to determine osmolarity and direction of water movement. There are four different scenarios, including the use of a hematocrit to determine if lysis of red blood cells has occurred.
SOLVE IT: How Can Membrane Transport Changes Lead to a Heart Attack?

Chapter 5 Chemical Messengers

INTERPRETING DATA: Receptor Antagonist Actions. Students compare graphs to determine if an antagonist had a significant effect on the actions of the messenger.

Chapter 6 The Endocrine System: Endocrine Glands and Hormone Actions

INTERPRETING DATA: Hormone Interactions. Students analyze graphs demonstrating antagonistic actions of two hormones and synergism between three hormones.

Chapter 7 Nerve Cells and Electrical Signaling

INTERPRETING DATA: Frequency of Action Potentials. Students analyze the typical trace of an action potential and refractory periods to determine the frequency of action potentials that could be generated.

Chapter 8 Synaptic Transmission and Neural Integration

INTERPRETING DATA: Quantal Release of Neurotransmitter. Students analyze data similar to that obtained by Katz to understand the concept of quantal release of neurotransmitters.

Chapter 9 The Nervous System: Central Nervous System

INTERPRETING DATA: Analyzing Magnetic Resonance Images of the Brain.

Chapter 10 The Nervous System: Sensor Systems

INTERPRETING DATA: Transduction in the Cochlea. Students analyze frequency response graphs of the basilar membrane.

Chapter 11 The Nervous System: Autonomic and Motor Systems

INTERPRETING DATA: Sympathetic and Parasympathetic Nerve Activity. Students compare graphs comparing the response of the autonomic nervous system to natural stimuli versus the effect of nerve stimulation on heart rate.
SOLVE IT: Why Does Mio Keep Falling Down? Part 4

Chapter 12 Muscle Physiology

INTERPRETING DATA: Variation in Percentage of Muscle Fiber Types. Students compare data of how different types of exercise affect the distribution of muscle fiber types.

Chapter 13 The Cardiovascular System: Cardiac Function

INTERPRETING DATA: Cardiovascular System. Students analyze how exercise and age affect cardiac efficiency.
SOLVE IT: Why Does Mio Keep Falling Down? Part 2

Chapter 14 The Cardiovascular System: Blood Vessels, Blood Flow, and Blood Pressure

INTERPRETING DATA: Blood Pressure and Velocity. Students compare graphs of blood pressure and blood velocity as blood moves through the systemic vasculature.
SOLVE IT: Why Does Mio Keep Falling Down? Part 1

Chapter 15 The Cardiovascular System: Blood

INTERPRETING DATA: Bleeding Time. Students analyze the effects of aspirin, acetaminophen, and warfarin on bleeding time compared to a placebo. Students also analyze the effects of von Willebrand's Factor on bleeding time.
SOLVE IT: Why Is Marcus Forming Blood Clots and What Problems Can They Cause?

Chapter 16 The Respiratory System: Pulmonary Ventilation

INTERPRETING DATA: Effects of Smoke on the Bronchiole Epithelium. Students analyze data from a table to determine if nicotine had any effects on the bronchiole epithelium by comparing normal epithelium properties to that of epithelium exposed to nicotine.

Chapter 17 The Respiratory System: Gas Exchange and Regulation of Breathing

INTERPRETING DATA: Hemoglobin-Oxygen Saturation Curves. Students analyze the effects of temperature and pH on the hemoglobin-oxygen saturation curve. They then analyze the differences in maternal and fetal hemoglobin.

Chapter 18 The Urinary System: Renal Function

INTERPRETING DATA: Chronic Renal Disease. Students analyze the different causes of renal failure.

Chapter 19 The Urinary System: Fluid and Electrolyte Balance

INTERPRETING DATA: Water Gain and Loss in a Kangaroo Rat and a Human. Students analyze the differences in water balance that takes place in the kangaroo rat and a human.
SOLVE IT: Why Does Mio Keep Falling Down? Part 3
SOLVE IT: What is Causing Episodes of Muscle Weakness in this Patient?*
SOLVE IT: The Car Accident: How is Breathing Related to Acid-Base Balance?*

Chapter 20 The Gastrointestinal System

INTERPRETING DATA: Hormones Regulating Long-term Metabolism. Students analyze the effects of leptin and ghrelin over 24 hours with three meals.

Chapter 21 The Endocrine System: Regulation of Energy Metabolism and Growth

INTERPRETING DATA: The Stress Response. Students will compare actions of the autonomic nervous system and hormones on the body's ability to tolerate stress.
SOLVE IT: How Are Insulin Pathways Involved in Diabetes Pathogenesis and Treatment?

Chapter 22 The Reproductive System

INTERPRETING DATA: Is it all because of hormones? Students will use a set of data comparing different aspects with a women and between men and women to determine how much the sex hormones affect appearance and behavior.
SOLVE IT: Does Sex Determination Have Only Two Possible Outcomes: Male or Female?*

Chapter 23 The Immune System

INTERPRETING DATA: AIDS-Related Deaths in the United States. Students study the pattern of AIDS-related deaths over the years.

Chapter 24 Diabetes Mellitus

INTERPRETING DATA: Ketoacidosis. Students study blood values in a chart that will help determine that a patient is suffering from ketoacidosis.
SOLVE IT: How Does Diabetes Pathogenesis Progress?

*These Solve It tutorials are not printed in the textbook, but are assignable in MasteringA&P.

Acknowledgments

As I complete the sixth edition of the textbook, my relationships with all of the supporting personnel has grown. Although the revision process is a heavy undertaking, the team at Pearson Higher Education has continued to make the experience not just manageable but actually enjoyable. Throughout the revision, I benefited from the expertise and hard work of many editors, reviewers, designers, production and marketing staff, and instructors. I extend to them my deepest and heartfelt thanks.

To begin, I want to acknowledge Frank Ruggirello, Serina Beauparlant, Barbara Yien, and Kelsey Churchman for their leadership and investment in this text. Thanks to my project and program managers, Chakira Lane and Chriscelle Palaganas, for their guidance during the work on this edition. Thanks to everyone involved in the book's production and design development, particularly Nancy Tabor (production), Marilyn Perry (design manager), Emily Friel (interior designer), and Charlene Charles-Will (cover design). Thanks also to Tim Nicholls for handling the text and art permissions and Ashley Williams for coordinating reviews and numerous other tasks. In addition, I would like to thank Joe Mochnick for his work on the Mastering and media assets, a big part of this sixth edition. Thanks also to the Pearson marketing staff Allison Rona, Christy Lesko, and Jane Campbell.

In addition, I would like to express my thanks to the numerous reviewers and contributors who provided feedback on the prior edition and suggestions for this revision. Instructor comments are valued and seriously considered during each revision cycle. Please continue to send them!

I want to give a special thanks to Heather Wilson-Ashworth of Utah Valley University and Cheryl Neudauer of Minneapolis Community and Technical College for developing the Solve It activities.

There are no words that can express the gratitude I have for the support and encouragement of my wonderful husband Jim. Without him, there would be no text. I am also grateful to my colleague Robin Mockett who also utilizes the text and provides feedback. And a special thanks goes to Theresa Allsup, who keeps my life sane by running the prehealth advising office.

Cindy L. Stanfield

Sixth Edition Reviewers

Our thanks to the following reviewers for their insightful and important contributions to the development of this edition:

Brian Antonsen
Marshall University

Ari Berkowitz
University of Oklahoma

Patrick W. Cafferty
Emory University

Geoffrey M. Goellner
Minnesota State University, Mankato

Eric Green
Salt Lake Community College

Steve Henderson
California State University, Chico

Kevin Langford
Stephen F. Austin State University

Gary Ritchison
Eastern Kentucky University

Jaya Shah
Woodland Community College

Brief Contents

Contents

List of Boxes

Chemistry Review

Toolbox

Discovery

Clinical Connections

Understanding Exercise

Focus on Diabetes

Learn how to solve problems and interpret data!

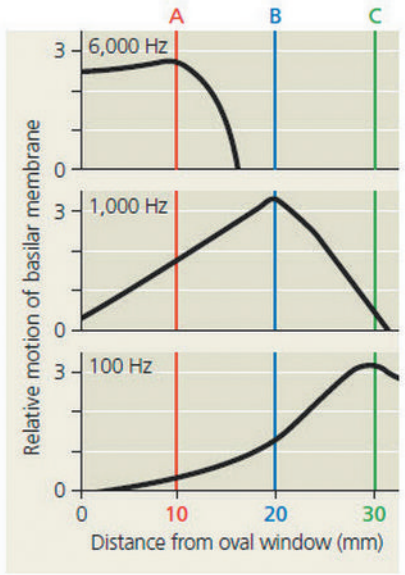
NEW! INTERPRETING DATA tutorials coach students on interpretation and analysis of graphs and charts. Ensuring that students understand and make the most of in-text graphs and figures, these tutorials are assignable in MasteringA&P

Neural Pathways for Sound

The transmitter released from hair cells binds to receptors on afferent neurons of the *cochlear nerve,* which is part of cranial nerve VIII. The hair cell transmitter depolarizes the afferent neuron: The

Part A

A musical chord consists of several notes, each formed by a sound wave of a different freque
patterns of vibration along the basilar membrane for three different frequencies, high (top), m
ation to the oval window.



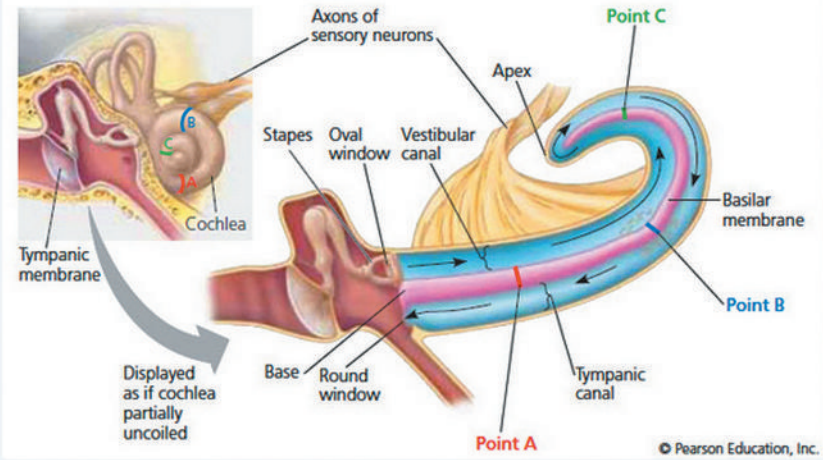
© Pearson Education, Inc.

If a chord had notes with frequencies of 100, 1,000, and 6,000 Hz, what would happen t

- It would vibrate with a peak at A only.
- It would vibrate with a peak at B only.
- It would vibrate with a peak at C only.
- It would vibrate at multiple positions, with peaks at A, B, and C.

Submit My Answers Give Up

Interpreting Data: Transduction in the Cochlea

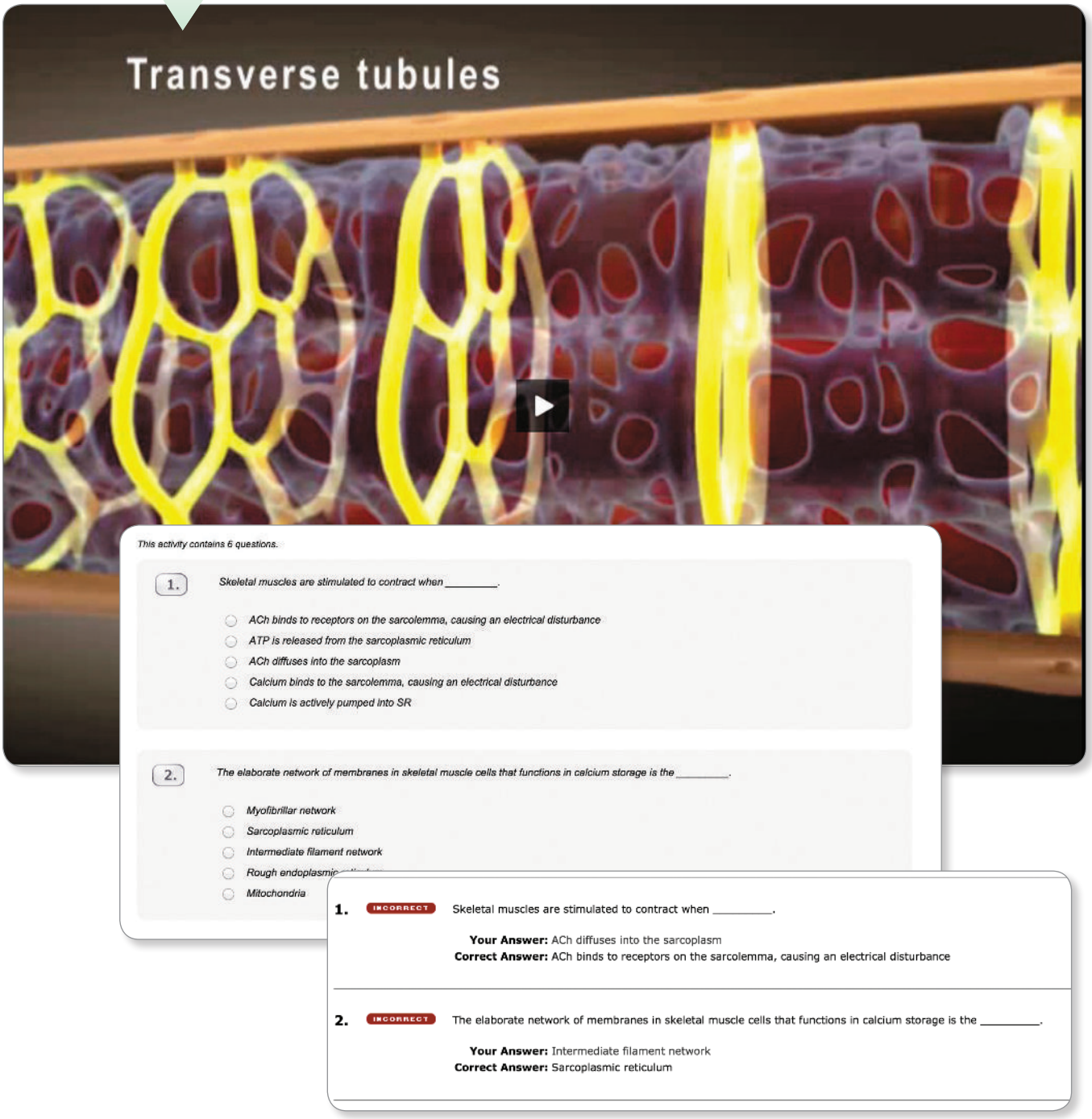


Don’t just imagine processes…

NEW! INTERACTIVE PHYSIOLOGY 1.0 AND 2.0 (IP 2.0) coaching activities help students dive deeper into complex physiological processes. Fun, interactive tutorials, games, and quizzes give students additional explanations to help them grasp complex physiological concepts and processes. Updated for today’s technology and emphasis on active-learning, IP 2.0 includes topics, such as **Cardiac Output, Resting Membrane Potential, Electrical Activity of the Heart, Factors Affecting Blood Pressure, Cardiac Cycle,** and **Generation of an Action Potential.**

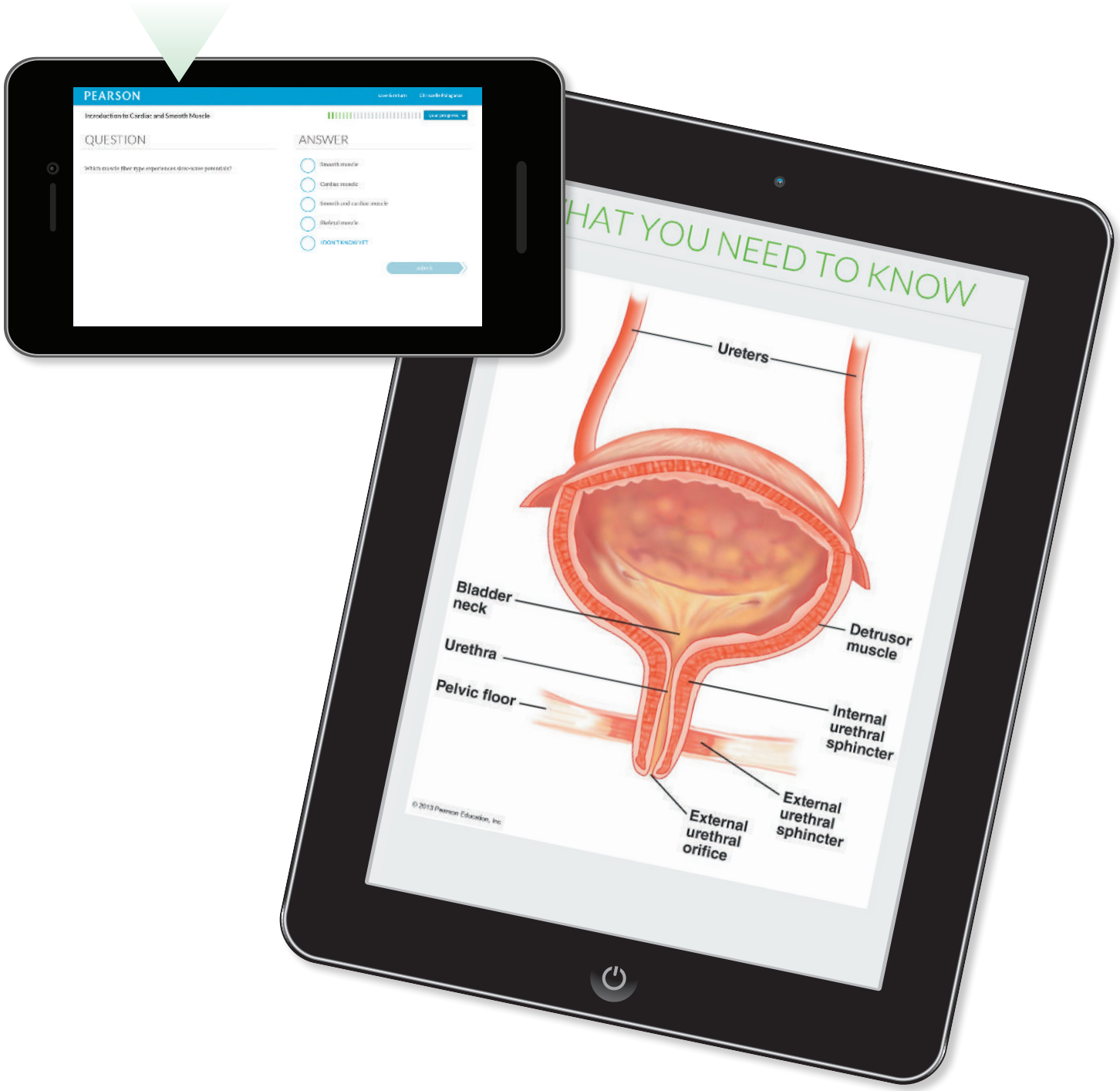
Visualize, engage, and understand!

A&PFlix™ are 3-D movie quality animations with self paced tutorials and gradable quizzes that help students master the toughest physiological topics.



Don’t just ponder…

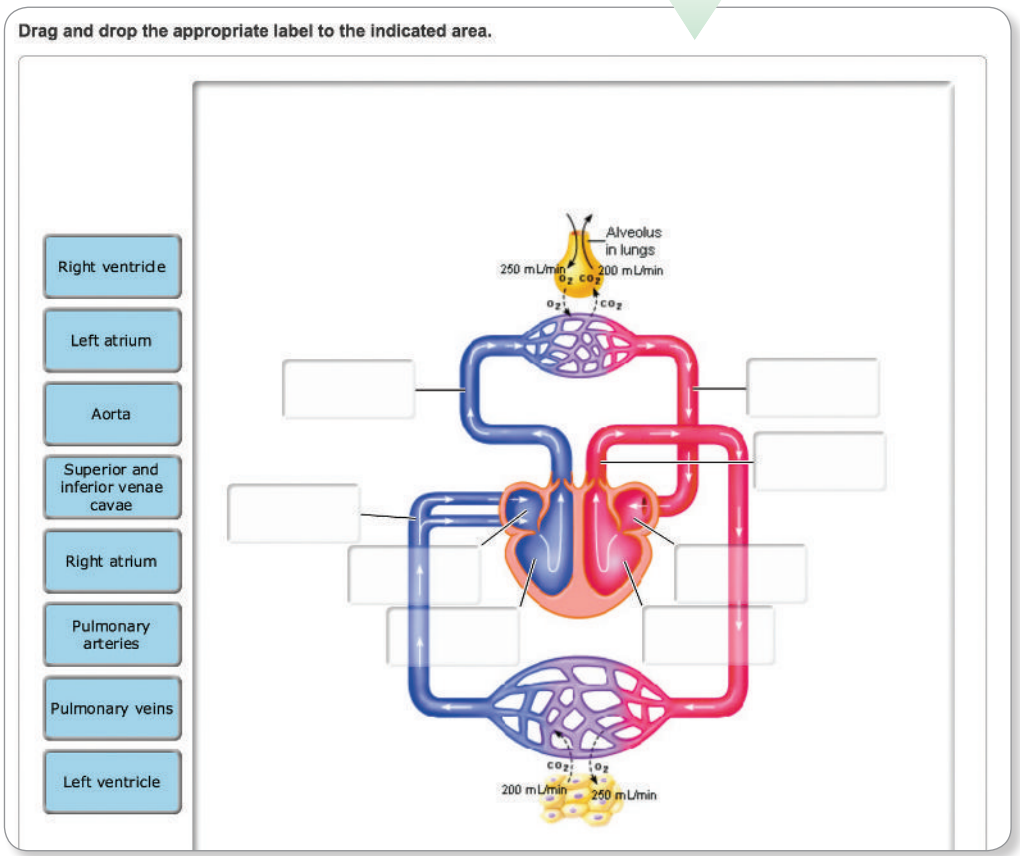
NEW! DYNAMIC STUDY MODULES offer a personalized reading experience of the chapter content. As students answer questions to master the chapter content, they receive detailed feedback with text and art from the book itself. Dynamic Study Modules help students acquire, retain, and recall information faster and more efficiently than ever before.



Practice!

NEW! learning|**catalytics**™ is a bring-your-own-device (laptop, smartphone, or tablet) student engagement, assessment, and classroom intelligent system. Instructors can assess students in real time using openended tasks to probe student understanding and facilitate peer-to-peer learning.

NEW! NURSES NEED PHYSIOLOGY coaching activities present students with a real-world scenario and guide them through problem-solving a relevant diagnosis. These case studies include worksheets that can be used as peer-to-peer learning activities in the classroom or can be assigned as homework in MasteringA&P.



Don’t just skim…

CLINICAL CONNECTIONS

From Aspirin to COX-2 Inhibitors

Aspirin is one of a number of nonsteroidal anti-inflammatory drugs (NSAIDs) that relieve pain by decreasing the production of certain prostaglandins (PG), eicosanoids that produce pain and inflammation. A critical enzyme in the synthesis of PGs is cyclooxygenase (COX). In the early 1990s, two forms of COX were identified: COX-1 and COX-2. COX-1, which is always present in the body, is generally associated with the synthesis of PGs necessary for maintaining homeostasis. In contrast, COX-2 becomes activated in the presence of chemicals released on tissue damage or infection and leads to production of PGs associated with pain and inflammation. Aspirin nonselectively inhibits the activity of both forms of COX; it is the inhibition of COX-2 that results in pain relief.

Although aspirin is used to treat pain, inflammation, and fever, its inhibition of COX-1 causes several side effects—some favorable, some not. For example, aspirin decreases the production of thromboxane A_2 a chemical involved in the formation of blood clots. However, at higher doses, aspirin also decreases the production of PGI_2 (prostacyclin), a chemical that inhibits the production of blood clots. In recognition of these effects, doctors frequently prescribe 82 mg of aspirin (“baby aspirin”) to guard against the formation of blood clots that can trigger heart attack or stroke, whereas 350 mg of aspirin is generally used to treat pain and would actually promote formation of a blood clot. In addition, aspirin inhibits production of PGE_2 in the stomach, an eicosanoid that indirectly protects the stomach lining from stomach acid. Thus major side effects of aspirin may include gastric ulcers and stomach bleeding.

In their search for safer pain relievers, pharmaceutical companies have developed drugs that selectively inhibit COX-2 to treat chronic pain and inflammatory diseases, such as arthritis. The chief advantages of COX-2 inhibitors (such as rofecoxib, also known as Vioxx, or celecoxib, also known as Celebrex) is that they do not inhibit production of PGE_2; thus they cause less harm to the stomach lining than does aspirin. Unfortunately, COX-2 inhibitors produce serious side effects of their own. For reasons that are not understood, these drugs appear to increase the risk of heart attack and stroke in individuals who are already susceptible to cardiovascular disease. Alas, the quest for a perfect “aspirin” still eludes us.

Critical Thinking Questions

1. How does inhibiting enzymes prevent the sensation of pain?
2. What negative effects do elevated doses of aspirin have on the body? How would short-term and long-term consequences compare?
3. Describe the advantages and disadvantages of using COX-2 inhibitors, rather than NSAIDs, to treat pain.

CLINICAL CONNECTIONS focus on a wide range of pertinent clinical topics designed to help students apply physiology to real-world situations and processes. Critical Thinking Questions have relatable, assignable coaching activities in MasteringA&P.

FOCUS ON DIABETES

Peripheral Neuropathy

Peripheral neuropathy, a disease of the peripheral nervous system, can affect the somatic or autonomic efferent or the afferent branch. Its symptoms vary depending on the site of disease, but the more common symptoms include numbness, tingling, or pain in the hands or feet. In autonomic neuropathy, symptoms are associated with internal organs and include dizziness, diarrhea, indigestion, and impotence. As the disease progresses, symptoms increase.

According to the Neuropathy Association, 20 million Americans suffer from neuropathy. Although many different causes are possible, 30% of neuropathies occur in conjunction with diabetes. How diabetes causes neuropathy is not known, but there are correlations between blood glucose regulation and the development of neuropathy. Thus a person with diabetes who better regulates his or her blood glucose levels is less likely to develop neuropathy. High blood glucose levels have direct effects on the ability of neurons to generate electrical signals, but can also affect blood vessels to the neurons, thereby indirectly causing nerve damage. Recent studies suggest that 30–40% of people with diabetes develop some form of neuropathy. Studies also suggest that another 30% of people with diabetes have asymptomatic neuropathy that has gone undiagnosed.

There is no cure for neuropathy, and the disease tends to progress, especially if blood glucose is not adequately regulated. Several medications can be used to treat the symptoms. Once it has set in, however, the neuropathy cannot be reversed.

FOCUS ON DIABETES boxes have been added throughout the text, making this key topic more prominent and accessible for readers. A capstone chapter on this disease reinforces the connectedness of the course material and encourages students to apply what they’ve learned to a real-world, significant problem.

Explore and apply!

DISCOVERY BOXES review current research topics in greater depth.

DISCOVERY

Circadian Rhythms and Jet Lag

The invention of air travel had an unexpected consequence: It created the phenomenon of "jet lag," or symptoms of fatigue, experienced by travelers who fly across time zones. Jet lag occurs because the body's *circadian rhythm* is disrupted. The circadian rhythm is an internal "clock" that governs many body functions. Typically, this internal clock follows a 24-hour cycle and is linked to the normal variations of light and dark that a person experiences over the course of a day (*circa* means "almost" and *dies* means "day"). When travelers fly across time zones, however, their normal exposures to light are disrupted, thereby changing their circadian rhythms. Because the circadian rhythm drives many physiological processes, alterations in the rhythm can result in symptoms—such as daytime sleepiness and loss of energy—that characterize jet lag. Jet lag can last for several days, and its duration tends to increase in proportion with the number of time zones crossed.

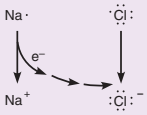
Travelers can take steps to help lessen the effects of jet lag. Because a change in the level of light exposure is what disrupts the circadian rhythm, travelers can simulate normal exposures to light with the help of a bright, artificial light while flying. Artificial light at night benefits those traveling westward, while artificial light in the morning benefits those traveling eastward. Medications may also help some travelers. The use of melatonin (a hormone of the pineal gland that is believed to be linked to circadian rhythms) to prevent jet lag has grown considerably over the last several years. However, scientific evidence of its effectiveness is not conclusive.

CHEMISTRY REVIEW

Ions and Ionic Bonds

When atoms form chemical bonds, the electrons of the atoms interact. In **Chemistry Review: Polar Molecules and Hydrogen Bonds** (p. 31), we saw how atoms could share electrons to form covalent bonds. Some atoms, however, have a tendency to gain or lose electrons completely during a chemical reaction, so that they end up with an excess or a deficit of electrons. When electrons are gained or lost from an atom or molecule, the number of negatively charged electrons no longer equals the number of positively charged protons; in such a case, a charged particle called an *ion* is formed. Atoms that gain an electron acquire a negative charge and are called *anions*, whereas atoms that lose an electron acquire a positive charge and are called *cations*.

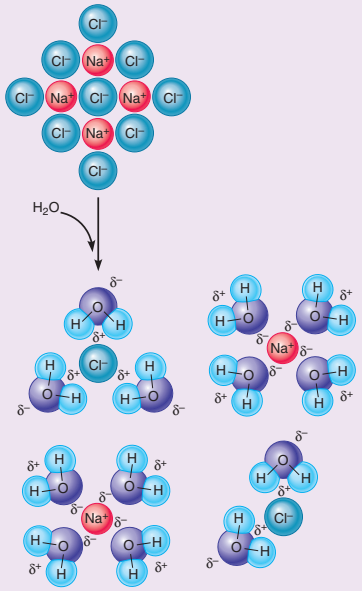
When anions and cations are present in solids, they tend to form crystals in which the cations and anions are closely associated. A familiar example is *sodium chloride (NaCl)*, also known as table salt, which contains sodium ions (Na^+) and chloride ions (Cl^-). Sodium ions form when sodium atoms lose an electron, producing an ion with 11 protons and 10 electrons. Chloride ions form when chloride atoms gain an electron, producing an ion with 17 protons and 18 electrons. This process occurs as follows:



In a crystal of NaCl, the cations (Na^+) and anions (Cl^-) are held together by electrical forces of attraction due to their opposite charges. These forces are sometimes called *ionic bonds*. When ionic solids dissolve in water, ionic bonds are disrupted by electrical attractions between the ions and polar water molecules, leaving cations and anions free to dissociate into separate particles. For sodium chloride, this process can be illustrated as shown at right.

Solutions containing dissolved ions are described as *electrolytic* because they are good conductors of electricity, and ionic substances are referred to as *electrolytes*. Body fluids are electrolytic and contain a number of small ions (known as *inorganic ions*), including sodium, potassium (K^+), calcium (Ca^{2+}), hydrogen (H^+), magnesium (Mg^{2+}), chloride, sulfate (SO_4^{2-}), and bicarbonate (HCO_3^-).

Ionized chemical groups can also be found on certain types of biomolecules. Ions and molecules containing significant numbers of ionized groups are described as *hydrophilic* because they are electrically attracted to water.



CHEMISTRY REVIEW boxes present chemistry concepts that apply to human physiology.

Don’t just lecture… Integrate powerful learning resources into your class!

INSTRUCTOR’S RESOURCE DVD features all of the art, photos, and tables from the book, in both JPEG and PowerPoint® format. Additional resources include PowerPoint lecture outlines, select figures in step-edit and label-edit format, PowerPoint art organized into chapter-specific folders, and Test Bank Microsoft Word® files. Also included are A&PFlix™ 3-D animations with quizzes (PRS-enabled, clicker questions) that focus on hard to teach concepts.

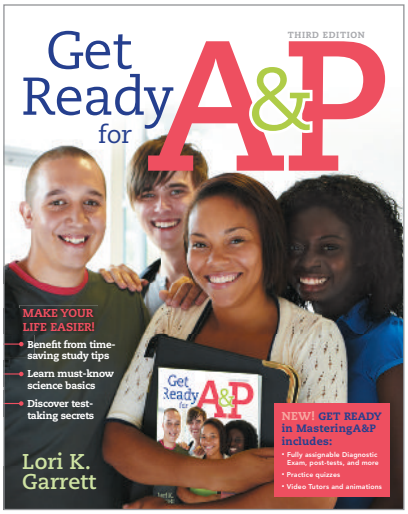
INSTRUCTOR’S GUIDE contains chapter synopses and outlines, key terms, expanded cross-references, 10 additional critical thinking questions with answers for every chapter, and suggestions for in-class activities. A detailed guide to interactive media accompanies every chapter, as well as a list of current journal articles, videos, and software, helping instructors to easily integrate outside resources into their course.

PHYSIOEX 9.1 This easy-to-use laboratory simulation software and lab manual consists of 12 exercises containing 63 physiology lab activities that can supplement or substitute for wet labs safely and cost-effectively. Now with input data variability.

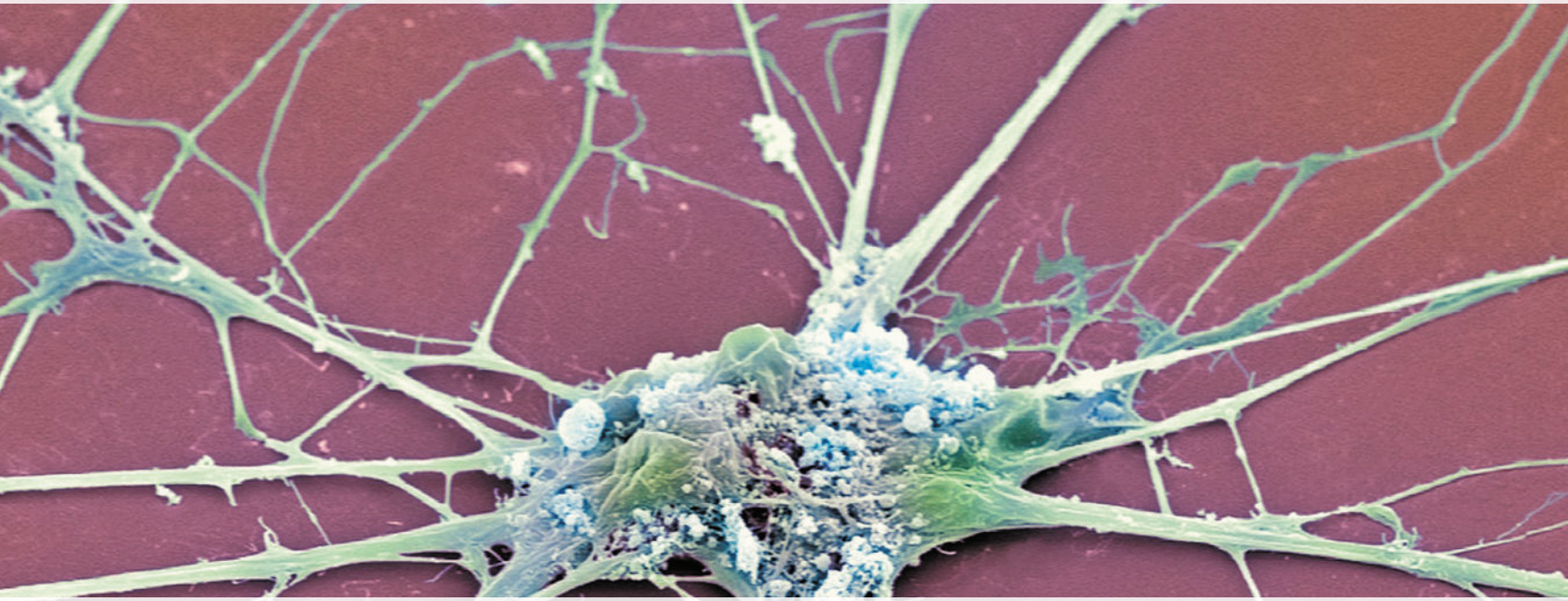
PRINTED TEST BANK contains thousands of test questions including multiple-choice, matching, true/false, short answer, and essay. Available as a print supplement and also accessible via MasteringA&P and the Instructor Resource IRDVD.

MYREADINESSTEST FOR A&P prepares students before their human physiology course even begins. It assesses students’ proficiency in the foundational concepts needed for success in human physiology and efficiently remediate gaps in targeted topics including Basic Skills, Basic Math, Biology, Chemistry, Cell, and Genetics.

GET READY FOR A&P Hands-on workbook that quickly gets students up to speed on basic study skills, math skills, anatomical terminology, basic chemistry, cell biology, and other basics of the human body. Also available in the Study Area of MasteringA&P.



1 Introduction to Physiology



Colored scanning electron micrograph (SEM) of a neuron (nerve cell).

The human body is capable of surviving in a dazzling variety of environmental conditions. It can live in jungles, mountains, crowded cities, or deserts. It can withstand the heat of a summer in India or the cold of a New England winter. With proper training, it can acclimate to altitude changes while scaling Mount Everest or survive running a 26.2-mile marathon.

How does the human body do it? As you will learn in this chapter—and throughout this textbook— our bodies have a remarkable ability to adapt to changes in the environment, thereby minimizing internal changes. For example, when a person travels from a cold environment into a warm one (which raises the body's temperature), the body quickly responds by sweating and increasing blood flow to the skin to help bring the temperature back to normal. The body's ability to maintain a normal internal environment, called **homeostasis,** is a primary theme throughout this text.

Welcome to the study of human physiology.

MasteringA&P®

Go to MasteringA&P for helpful A&P Flix 3-D animations, chapter quizzes, pre-tests, Interactive Physiology tutorials, and more!

CHAPTER OUTLINE

LEARNING OUTCOMES *After studying this chapter, you should be able to:*

- Name the four major types of cells in the human body, and describe their defining characteristics.
- Describe the distribution of water in the body, and define the different body fluid compartments.
- Define *homeostasis* and explain its significance to the function of the body.
- Describe the role of negative feedback in homeostasis.
- Explain why diabetes is considered an epidemic.

Physiology, the study of the functions of organisms, comes in many forms—plant physiology, cell physiology, microbial physiology, and animal physiology, to name a few. This book focuses on human physiology, the study of how our bodies work. We emphasize normal physiology, but occasionally describe pathophysiology—what happens when normal body function is disrupted—to better demonstrate typical body function. For example, the effects of diabetes on body function are described throughout the book to illustrate the delicacy of body function and the interdependency of organ systems.

In this book, we take the systems approach to physiology; that is, we study one organ system at a time. An **organ system** is a collection of anatomical structures that work together to carry out a specific function. For example, the cardiovascular system functions to deliver oxygen- and nutrient-rich blood to the various organs of the body. We will learn more about organ systems shortly. As we use the systems approach to studying physiology, you must remember that a single system cannot function alone. Thus a chapter on the urinary system will include some discussion of the cardiovascular system, because the two systems interact.

Because nearly everyone is curious about how the human body works, we hope that studying physiology will be one of your most satisfying academic experiences. You will also come to realize that physiology, like the other sciences, is not just a collection of well-worn facts but rather a work in progress. You will recognize that there are significant gaps in our understanding of how the body works, and you will see that much of our current understanding is subject to change as new discoveries are made.

Regardless of your background or current interests, your study of physiology will broaden your scientific outlook. You will begin to see the "big picture," understanding body function not as a collection of unrelated phenomena but rather as a connected whole. You might even discover something else—that physiology is beautiful. Most of us who have decided to make it our life's work think so.

1.1 Organization of the Body

If you have ever spent time examining a detailed anatomical chart or model of the human body, you have seen that it is an exceedingly complex and intricate structure. Despite the complexity of its structure, however, an underlying simplicity characterizes the function of the human body.

To a student, perhaps the most interesting thing about the body is that its operation can be explained in terms of a relatively small set of principles. For this reason, our approach to describing the body is to strip away all unnecessary details so that the essentials—that is, the unifying themes and principles—can be seen more clearly. To get an idea of what this means, consider **Figure 1.1**. The brain contains billions of cells that are classified into four groups according to differences in their four general shapes (morphologies). When you consider the function of these cells, however, the similarities among them outweigh the differences, allowing them to be grouped into just one category: All cells in this category are specialized to transmit information in the form of electrical signals from one body location to another. Because of this shared function, all these cells are classified as *neurons* (or *nerve cells*).

Just as the body's underlying simplicity is one of physiology's major themes, so is the degree of interaction among its various parts. Although each of the body's **cells** (cells are the smallest living units) is independently capable of carrying out its own basic life processes, the various types of cells are specialized to perform different functions important to the operation of the body as a whole. For this reason, all the cells ultimately depend on one another for their survival. Similarly, the body's organs are specialized to perform certain tasks vital to the operation of other organs. You know, for example, that your cells need oxygen to live and that oxygen is delivered to your cells by the bloodstream, but consider some of the many things that must occur to ensure that oxygen delivery is sufficient to meet the cells' needs. Oxygen is carried in the bloodstream by cells called *erythrocytes,* which are manufactured by *bone marrow,* a tissue found inside certain bones. To ensure that adequate numbers of erythrocytes are present in the blood, the synthesis of these cells is regulated by a hormone called *erythropoietin,* which is secreted by the kidneys. To ensure adequate blood flow to the body's tissues, the heart must pump a sufficient volume of blood every minute, and for this reason the rate and force of its contractions are regulated by the nervous system. To ensure that the blood carries enough oxygen, the lungs must take in sufficient quantities of air, which requires the control of breathing muscles (such as the diaphragm) by the nervous system. Finally, to provide the energy necessary to drive these and other processes, the gastrointestinal system breaks ingested food down into smaller molecules, which are absorbed into the bloodstream and distributed to cells throughout the body.

This example shows that proper body function requires not only that each part be able to carry out its own particular function, but also that the parts be able to work together in a coordinated manner. To help you better understand how the body's parts work together, the remainder of the chapter outlines broad principles pertaining to body function in general; the functions of specific organs and organ systems are the topics of later chapters.

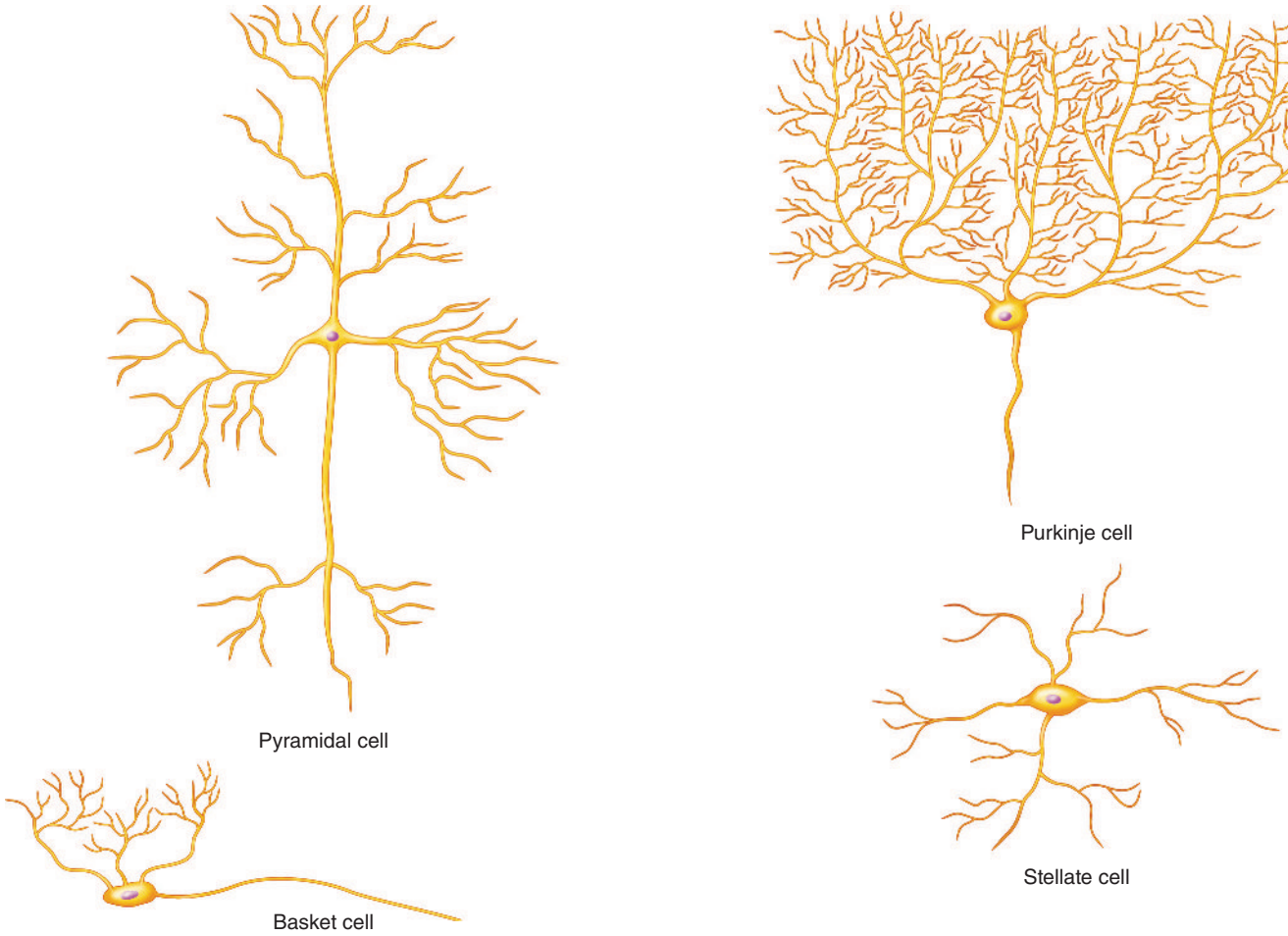


Figure 1.1 Shapes of cells found in the brain. Each of these four cells is a neuron that transmits electrical and chemical signals.

Cells, Tissues, Organs, and Organ Systems

The human body is a remarkable structure consisting of cells arranged in an orderly fashion. Cells are grouped together to form tissues, which in turn are grouped together to form organs. Organs work together as organ systems. We now describe each of these hierarchical components.

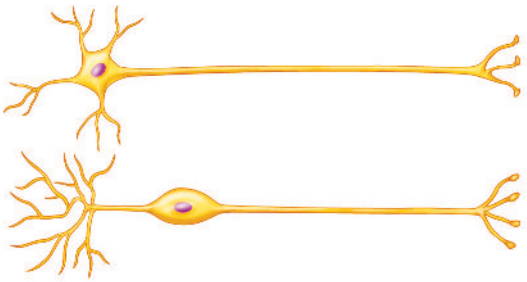
Cells and Tissues

Although more than 200 distinguishable kinds of cells are present in the body, there are only four major classes: (1) *neurons,* (2) *muscle cells,* (3) *epithelial cells,* and (4) *connective tissue cells.* Representative cells belonging to each of these cell types are shown in **Figure 1.2**. These classifications are very broad and are based primarily on functional differences. Other, more rigorous ways to classify cells have been developed based on anatomical distinctions and embryological origins.

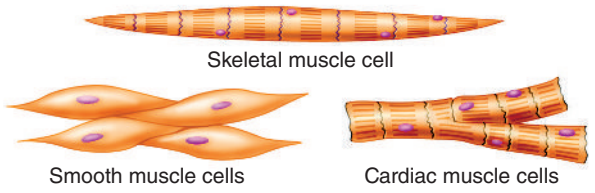
As mentioned previously, nerve cells, or **neurons** (Figure 1.2a), are specialized to transmit information in the form of electrical signals. For this purpose, neurons typically possess branches that function to receive signals from or transmit signals to other cells. Certain neurons, such as those in the eyes that respond to light or those in the skin that respond to touch, receive information from the outside environment and allow us to perceive the world through our senses. Other neurons relay signals to muscles, glands, and other organs, enabling the control of movement, hormone secretion, and other bodily functions. Still other neurons, such as those in the brain, process information, enabling us to conceptualize, remember, formulate plans of action, and experience emotion.

Muscle cells, or **muscle fibers** (Figure 1.2b), are specialized to contract, thereby generating mechanical force and movement. These cells are found in the muscles of the arms, legs, and other body parts whose movements are under voluntary control (called *skeletal muscle*), but they are also found in structures not under voluntary control, such as the heart (*cardiac muscle*) and blood vessels (*smooth muscle*). The flexing of an arm, the pumping of blood by the heart, and the mixing of food in the stomach are all examples of muscle cells in action.

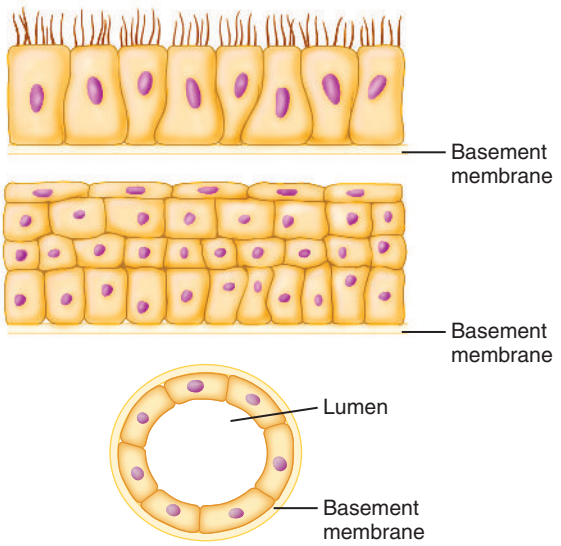
Epithelial cells are found in tissues called **epithelia** (singular: *epithelium*), which consist of a continuous, sheetlike layer of cells in combination with a thin underlying layer of noncellular material called a *basement membrane* (Figure 1.2c). Depending on the



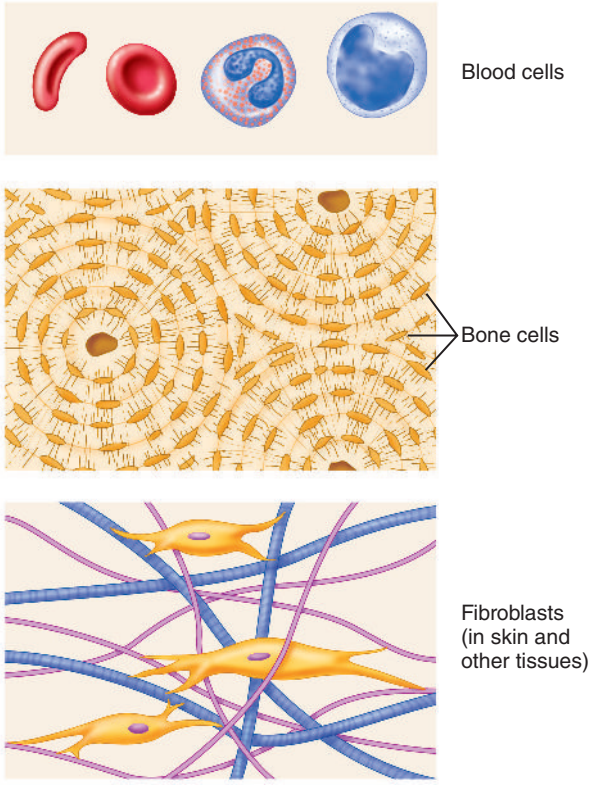
(a) Neurons



(b) Muscle cells



(c) Epithelial cells



(d) Connective tissue cells

Figure 1.2 **Major cell types in the human body.** **(a)** Neurons. **(b)** Muscle cells. **(c)** Epithelial cells. **(d)** Connective tissue cells.

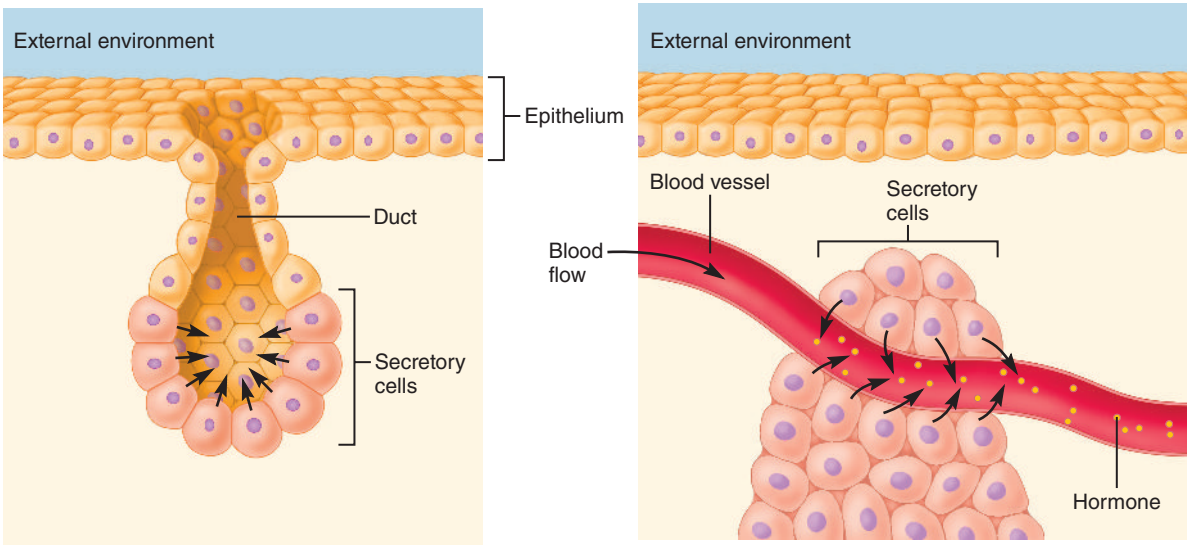
epithelium in question, the cell layer may be one cell thick (*simple*) or several cells thick (*stratified*), and the cells may vary in shape from short and flattened (*squamous*), to regular square-shaped (*cuboidal*), and in some cases to tall and oblong (*columnar*). In all cases, however, cells join closely together to form a barrier that prevents material on one side of the epithelium from mixing freely with material on the other side. Appropriately, epithelia are found wherever body fluids must be kept separate from the external environment, such as the skin surface or the lining of the lungs. Epithelia are also found in the linings of hollow organs such as the stomach, intestines, and blood vessels, where they separate fluids in the interior cavity from the surrounding body fluids. The interior cavity of a hollow organ or vessel is generally referred to as the **lumen.**

Certain epithelial cells are specialized to transport specific materials, such as inorganic ions, organic molecules, or water, from one location to another. For example, cells in the lining of the stomach transport acid (hydrogen ions) into the lumen of the stomach to aid in the digestion of food. Cells in the lining of the intestine, in comparison, transport nutrients and water from the lumen of the intestine into the bloodstream.

Some epithelial cells form **glands,** organs specialized in the synthesis and secretion of a product. Two types of glands are distinguished: exocrine and endocrine. **Exocrine glands** secrete a product into a duct leading to the external environment (**Figure 1.3**a). Examples of exocrine glands include *sweat glands* and *salivary glands.* **Endocrine glands** secrete **hormones,** chemicals that communicate a message to cells of the body, into the bloodstream (Figure 1.3b). Examples of endocrine glands include the *pituitary gland* and *adrenal gland.*

The last remaining major cell type, **connective tissue cells,** is the most diverse. This cell type includes blood cells, bone cells, fat cells, and many other kinds of cells that seem to have little in common in terms of structure or function (Figure 1.2d).

In a narrow sense, the term "connective tissue" refers to any structure whose primary function is to provide physical support for other structures, to anchor them in place, or to link them together. Familiar examples of connective tissue structures are *tendons,* which anchor muscles to bones; *ligaments,* which connect bones together; and the elastic tissue in the skin that gives it its toughness and flexibility. Another example of a connective tissue is the bones themselves, which provide direct or indirect support for all



(a) Exocrine gland **(b)** Endocrine gland

Figure 1.3 Glands. (a) Exocrine gland. The secretory cells release their product, which travels via a duct to the external environment. **(b)** Endocrine gland. The secretory cells release their product, a hormone, into the bloodstream, which transports the hormone throughout the internal environment.

of the body's structures. In most cases, connective tissue consists of widely scattered cells embedded in a mass of noncellular material called the *extracellular matrix,* which contains a dense meshwork of proteins and other large molecules. Among the most important constituents of the extracellular matrix are the long, fibrous proteins *elastin* (which gives the tissue elasticity) and *collagen* (which gives the tissue tensile strength—that is, the ability to resist stretching).

In a broader sense, the term "connective tissue" encompasses fluids such as the blood and lymph, which do not provide structural support like other connective tissue but instead serve to "connect" the various parts of the body together by providing avenues of communication. The blood, for example, delivers oxygen from the lungs to the rest of the body's tissues and carries hormones from the glands that secrete them to the tissues that respond to them. Similarly, the lymph carries water and other materials that leak out of blood vessels throughout the body and returns them to the blood.

It is a general rule that cells of a given type tend to cluster together in the body with cells of the same type. Nerve cells, for example, are always found in conjunction with other nerve cells, and epithelial cells are always joined with other epithelial cells. Any such collection of cells performing similar functions is referred to as a **tissue.** Thus tissues are also classified into four basic groups: *nervous tissue, muscle tissue, epithelial tissue,* and *connective tissue.* (The term "tissue" is also used more loosely to refer to any of the materials of which the body is composed.)

Organs and Organ Systems

Generally, when two or more tissues combine to make up structures that perform particular functions, those structures are called **organs.** The heart, for example, is an organ whose primary function is to pump blood. Although composed mostly of muscle tissue, it also contains nervous tissue (the endings of nerves that control the heartbeat), epithelial tissue (which lines the heart's chambers), and connective tissue (which makes up the heart's valves and other tissues that hold the muscle fibers together).

The various organs are organized into **organ systems,** collections of organs that work together to perform certain functions. An example is the *cardiovascular system,* whose function is to deliver blood to all the body's tissues. The cardiovascular system includes the heart, blood vessels, and the blood (which is not an organ, but rather a tissue). Another organ system is the *gastrointestinal system,* whose function is to break down food into smaller molecules and then transport these molecules into the bloodstream. This organ system includes the mouth, salivary glands, esophagus, stomach, intestines, liver, gallbladder, and pancreas. In some organ systems (for example, the cardiovascular and gastrointestinal systems), the organs are physically connected. In other cases, the organs are disconnected and more widely scattered. This is true of the *endocrine system,* which encompasses all the glands in the body that secrete hormones, and the *immune system,* which protects the body from invading microorganisms and other foreign materials. The body's organ systems and their primary functions are listed in Table 1.1.

Although the concept of an organ system is simple in principle, the distinction between one organ system and another is not always clear-cut—many organs perform functions that are integral to more than one organ system. A prime example is the pancreas, which is considered to be part of both the digestive system, because it secretes fluid and digestive enzymes into the intestines, and the endocrine system, because it secretes certain hormones.

Quick Check 1.1

1. Define *physiology*.
2. Name and describe the four basic types of cells and tissues.
3. Name the ten organ systems, and briefly state the function of each.

TABLE 1.1 Organ Systems

System	Some organs/tissues within system	Function
Endocrine	Hypothalamus, pituitary gland, adrenal gland, thyroid gland, parathyroid glands, thymus, pancreas	Provide communication between cells of the body through the release of hormones into the bloodstream
Nervous	Brain, spinal cord, peripheral nerves	Provide communication between cells of the body through electrical signals and the release of neurotransmitters into small gaps between certain cells
Musculoskeletal	Skeletal muscle, bones, tendons, ligaments	Support the body; allow voluntary movement of the body; allow facial expressions
Cardiovascular	Heart, blood vessels, blood	Transport molecules throughout the body in the bloodstream
Respiratory	Lungs, pharynx, trachea, bronchi	Bring oxygen into the body and eliminate carbon dioxide from the body
Urinary	Kidneys, ureters, bladder, urethra	Filter the blood to regulate acidity, blood volume, and ion concentrations; eliminate wastes
Gastrointestinal	Mouth, esophagus, stomach, small intestine, large intestine, liver, pancreas, gallbladder	Break down food and absorb it into the body
Reproductive	Gonads, reproductive tracts and glands	Generate offspring
Immune	White blood cells, thymus, lymph nodes, spleen, tonsils, adenoids	Defend the body against pathogens and abnormal cells
Integumentary	Skin	Protects the body from the external environment

The Overall Body Plan: A Simplified View

When physiologists attempt to understand and explain body functions, they usually try to reduce the body's complexity to its essential elements so that unifying themes and principles can be seen more easily. This tendency to simplify is nowhere more apparent than in **Figure 1.4**, which shows a physiologist's "minimalist" view of the human body. This figure does not look anything like a real body: Not only is it the wrong shape, but it is simplistic and seems to be missing some parts. The gastrointestinal system, for example, is drawn as a straight tube that extends through the body from one end to the other, and the lungs are shown as a single hollow sac. The body's intricate network of blood vessels is depicted as a simple loop, and the heart, which pumps blood around this loop, as just a box. Different cell types, such as nerve, muscle, and connective tissue cells, are drawn to look alike and are given the generic label "cells." Furthermore, the kidneys are shown simply as a single blind-ended tubule that leads to the outside.

The Body's External Environment

The most important concept highlighted by the simplistic rendering of Figure 1.4 is that a layer of epithelial tissue separates the *external environment* from the interior of the body. This epithelial barrier includes not only the skin, but also the linings of the lungs, gastrointestinal system, and kidney tubules, which are continuous with the external environment. In other words, when air enters the lungs or food enters the stomach, these materials are still actually in the external environment because they are on the external side of this epithelial barrier. Figure 1.4 also indicates that this barrier is continuous; that is, there is no real separation between the outer surface of the skin and the inside surfaces of the lungs, gastrointestinal system, and kidney tubules. They are all part of the same "fabric," if you will.

The Body's Internal Environment

To live, cells must take in oxygen and nutrients from their surroundings and release carbon dioxide and other waste products into their surroundings. The ultimate source of oxygen and nutrients, and the ultimate repository for discarded waste products (including carbon dioxide), is the external environment. As shown in Figure 1.4, however, most of the body's cells are not able to exchange materials directly with the external environment because they are not in direct contact with it. Instead, cells receive oxygen and nutrients from the bloodstream, which also carries carbon dioxide and waste products away from cells. Moreover, most cells are not in *direct* contact with the blood, but instead are surrounded by a separate fluid that exchanges materials with the blood. Because this fluid constitutes the immediate environment of most of the body's cells, it is called the **internal environment.** (The term "internal environment" also applies to the fluid in the bloodstream that surrounds blood cells.)

Figure 1.4 also shows that the blood is contained within epithelium-lined blood vessels. This epithelium differs from that of the gastrointestinal tract, airways, kidneys and skin, in that the epithelium and the blood within it have no connection with the external environment and, therefore, are part of the internal environment. Thus the epithelium that lines the blood vessels is called the endothelium (*endo* = within).

The Exchange of Materials Between the External and Internal Environments To do its job, the blood must obtain oxygen, nutrients, and other needed materials from the

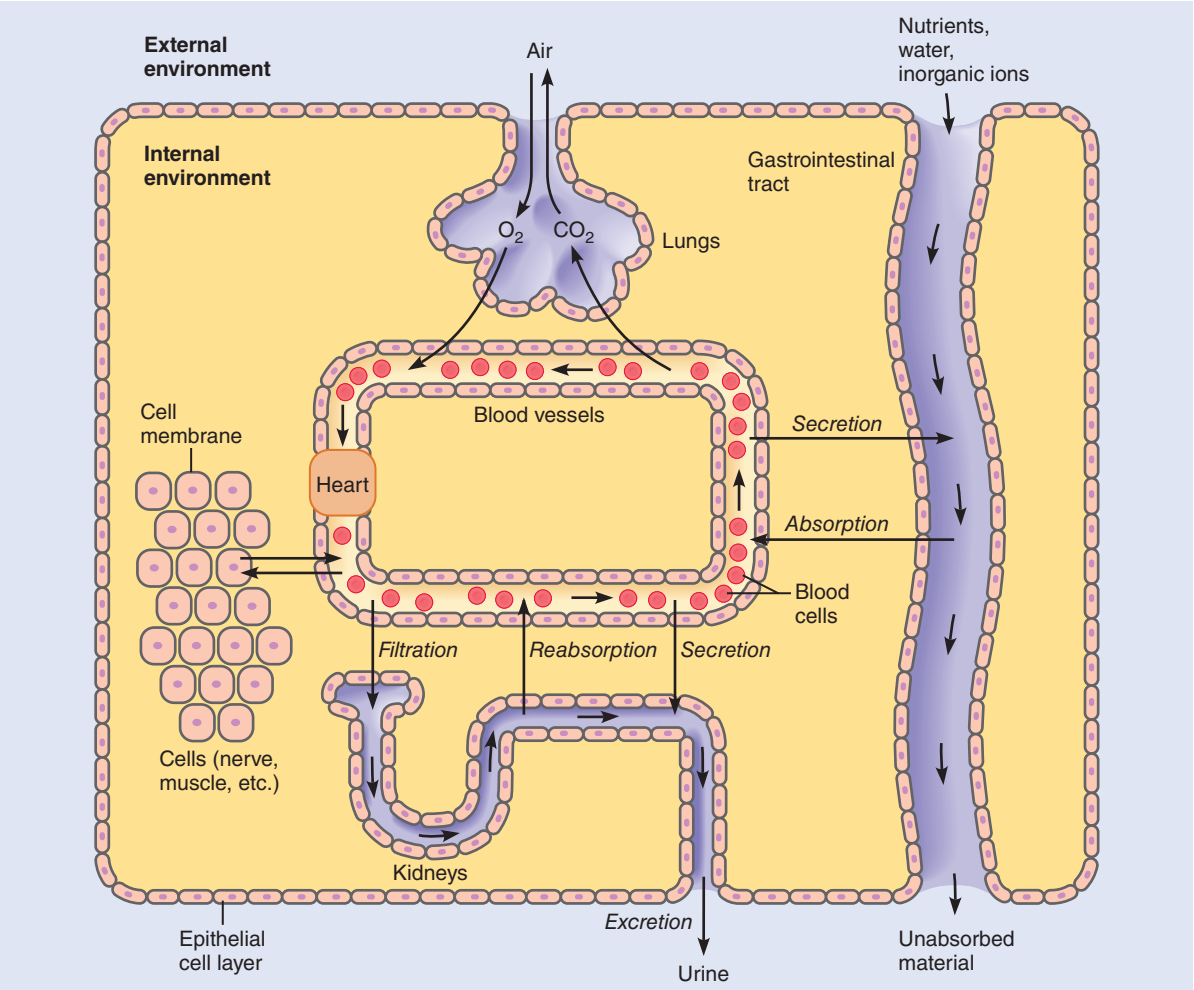


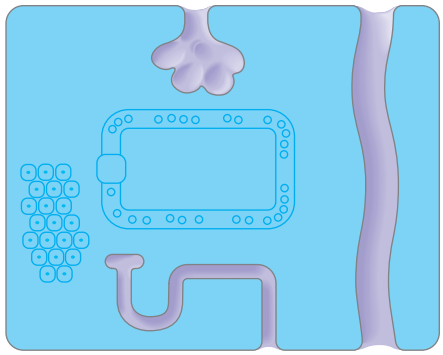
Figure 1.4 **A highly simplified view of the overall plan of the human body.** Flows of material are indicated by arrows.

external environment and must release carbon dioxide and other unneeded materials into it. As shown in Figure 1.4, material is exchanged between the blood and the external environment in a variety of places, including the lungs, the gastrointestinal tract, and the kidneys.

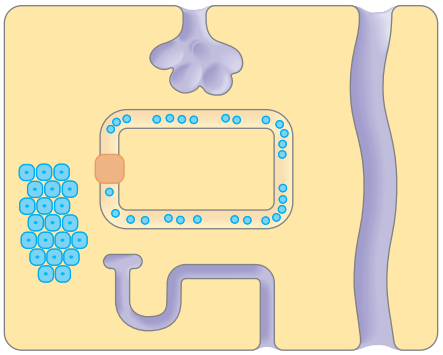
In the lungs, oxygen enters the bloodstream from the air that is breathed in during *inspiration*, whereas carbon dioxide exits the bloodstream and is expelled in the air that is breathed out during *expiration*. In the gastrointestinal tract, the water, inorganic salts, and nutrients obtained from digested food are transported from the lumen to the bloodstream, a process referred to as *absorption.* To aid in the digestion of food, the stomach uses materials from the blood to produce acids and proteins that are then transported into the lumen, a process called *secretion.* Unabsorbed materials (plus bacteria and cellular debris) remain in the gastrointestinal tract and are ultimately eliminated from the body as feces (a process called *excretion*).

In the kidneys, fluid from the bloodstream first enters tubules via a mechanism known as *filtration.* As this fluid travels along the length of the tubules, needed materials (including water, inorganic salts, and nutrients) are selectively transported back into the bloodstream, a process known as *reabsorption.* At the same time, unneeded materials are selectively transported from the bloodstream into the tubules by the secretion process. The fluid that eventually reaches the ends of the tubules constitutes the urine, which is eliminated from the body by excretion. Materials contained in the urine include cellular waste products as well as excess salts and water that are not needed by the body.

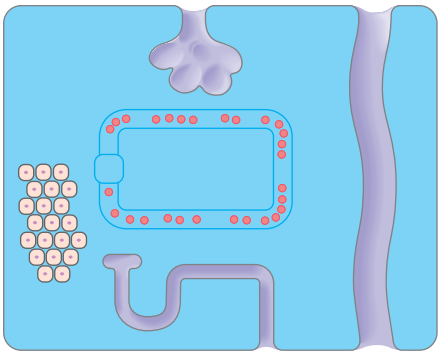
Body Fluid Compartments The most abundant substance in the body is *water,* which acts as a solvent for the great variety of solutes found in body fluids. These solutes include small molecules such as inorganic ions, sugars, and amino acids, and large molecules such as proteins. Figure 1.4 shows that the interior of the body is divided into separate compartments (which are filled with fluid) by barriers of different types, including epithelial tissues and *cell membranes,* which separate the contents of cells from their surroundings. Although these compartments are physically separated, they are still able to exchange materials with each other because the barriers that separate them are *permeable*—that is, they permit molecules to pass through them. These barriers let certain types of molecules through more easily than others, and even exclude some



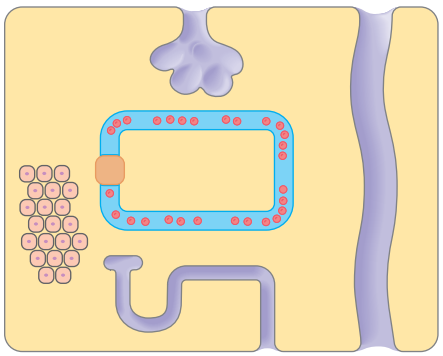
(a) Total body water (TBW)



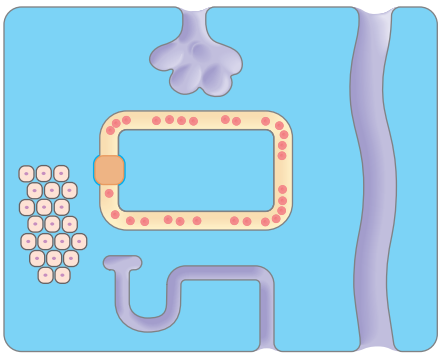
(b) Intracellular fluid (ICF)



(c) Extracellular fluid (ECF)



(d) Plasma



(e) Interstitial fluid (ISF)

Body fluid	Volume (L)
TBW	42
ICF	28
ECF	14
Plasma	3
ISF	11

(f) Distribution of TBW

Figure 1.5 Body fluid compartments. The various fluid compartments are indicated by blue in several simplified body plans similar to that shown in Figure 1.4. **(a)** Total body water. **(b)** Intracellular fluid. **(c)** Extracellular fluid. **(d)** Plasma. **(e)** Interstitial fluid. **(f)** Distribution of total body water.

Q Which of the following does not include plasma: total body water, extracellular fluid, or interstitial fluid?

molecules from entering certain compartments entirely. Thus it is more accurate to say that cell membranes and epithelial tissues are *selectively permeable* or *semipermeable.*

The volume of water contained in all the body's compartments is termed the **total body water (TBW),** meaning the total volume of fluid enclosed within the outer epithelial layer (**Figure 1.5**a). For a person weighing 70 kilograms (150 pounds), the volume of TBW is 42 liters, which accounts for approximately 60% of total body weight. Total body water includes water present in fluid located inside cells, called **intracellular fluid (ICF)** (Figure 1.5b), and fluid located outside cells, called **extracellular fluid (ECF)** (Figure 1.5c). In the body plan diagram, the volume of ECF relative to ICF is highly exaggerated; in reality, approximately two-thirds of TBW is in the ICF, and only one-third is in the ECF. (Note as well that *extracellular fluid* is synonymous with the *internal environment.*)

ICF and ECF are separated by cell membranes and differ significantly in composition. Intracellular fluid contains many proteins and is relatively rich in potassium, for example, whereas extracellular fluid contains few proteins and is relatively rich in sodium. These differences in composition support the proper functioning of cells and are made possible by the relatively low permeability of cell membranes to many solutes, such that membranes permit the selective exchange of certain solutes.

Of the total volume of extracellular fluid, approximately 20% is found in the blood, and the remainder is found outside the blood. The portion that is present in the blood (that is, the liquid, noncellular part of the blood) is **plasma** (Figure 1.5d). The portion that is present outside the blood and that bathes most of the cells in the body is called **interstitial fluid (ISF)** (Figure 1.5e). Plasma and interstitial fluid are very similar in composition; the only major difference between the two is that plasma is relatively rich in proteins, which are scarce in interstitial fluid. The similarity in composition between plasma and interstitial fluid is due to the fact that the walls of the smallest and most numerous blood vessels, called *capillaries,* are highly permeable to most solutes except proteins.

Quick Check 1.2

1. What is the difference between *absorption* and *reabsorption*?
2. Why is *extra*cellular fluid referred to as the body's *internal* environment?
3. Give the proper term for each of the following: (a) all the water that is contained in the body, (b) fluid that is contained within cells, (c) fluid that is located outside cells, (d) fluid that is located outside cells and found in the blood, and (e) fluid that is located outside cells and found outside the blood.

UNDERSTANDING EXERCISE

Challenging Homeostasis

Maintaining homeostasis can be quite challenging to the organ systems, especially when a person is faced with a stressor—that is, a stimulus that puts strain on the body. Although many stressors are deemed harmful, one stressor—exercise—is actually considered good for the body.

During exercise, the organ systems have to kick into high gear to maintain a normal internal environment. Breathing has to be deeper to bring more oxygen into the body and to eliminate carbon dioxide. The heart has to beat faster and stronger to enhance blood flow, which will rapidly transport oxygen and other nutrients to the cells and carry carbon dioxide and other waste products away from the cells. The liver releases glucose into the bloodstream and adipose tissue releases fatty acids so that exercising muscles can use these substances for energy. Increased muscle and nerve activity also causes extracellular levels of potassium to increase. Blood flow to the skin increases, and glands increase sweat production as the body releases the heat produced by the increased muscle activity.

These are just a handful of the events occurring inside the human body during exercise. With these organs working together correctly, we can lift weights, jump, and even run marathons. Although the changes described in the preceding paragraph are short-term changes that enable the body to maintain homeostasis, the benefits of exercise also persist over the long term. Our bodies adapt to repeated stressors, such as exercise. Marathon runners have slender muscles that are slow to fatigue, whereas weight trainers have large muscles that generate a lot of force but are quick to fatigue. Adaptive benefits of exercise include increased efficiency of the heart and increased metabolism. Exercise helps prevent development of diseases such as type 2 diabetes mellitus. It also burns fat. Thus, while stressors may temporarily take the body out of homeostasis, the body can learn to adapt to some stressors so that they do not seem as harsh the next time around.

1.2 Homeostasis: A Central Organizing Principle of Physiology

Our cells depend on one another for survival: If cells are removed from the body, they generally die in a short period of time. Scientists have tried to establish long-living cultures of various human cells, but with limited success (certain stem cells—undifferentiated cells—have been cultured and maintained for several years). Despite advances in technology, science still cannot duplicate the conditions of the human body necessary to sustain life.

Given our cells' sensitivity to changing conditions, how can the body tolerate the widely varying conditions it encounters in the external environment? After all, humans can live in both very hot climates, such as the tropics, and much colder climates. We can live at sea level, where oxygen is plentiful, or in the mountains, where the oxygen concentration in air is lower. We can live in the dryness of a desert or in the extreme humidity of a rain forest. How can the body adapt to such a variety of conditions?

The body has all sorts of regulatory mechanisms that work to keep conditions in its internal environment constant despite changes in the external environment. This maintenance of relatively constant conditions in the internal environment is known as **homeostasis.** As you progress through this book, you will discover that the concept of homeostasis is a central organizing principle in physiology. In fact, nine of the ten organ systems function to maintain homeostasis (the exception is the reproductive system, which functions to maintain the species, not the individual). Disruption of homeostasis can lead to disease, yet the body is also capable of adapting to mild stressors that disrupts homeostasis (see **Understanding Exercise: Challenging Homeostasis).**

To say that the internal environment is regulated to remain constant means that the *composition, temperature,* and *volume* of extracellular fluid do not change significantly under normal conditions. (Small fluctuations occur and are considered normal.) The extracellular fluid is normally kept at a temperature near 37°C or 98.6°F (normal body temperature), and concentrations of many solutes (oxygen, carbon dioxide, sodium, potassium, calcium, and glucose, for example) are kept relatively steady. The ability to maintain such constancy is important because the body continually faces potentially disruptive changes that can originate either in the external environment or within the body itself. When the environment warms up or you begin to exercise, for example, your body temperature rises. In either case, the rise in body temperature activates regulatory mechanisms that work to reduce body temperature and bring it back down toward normal. As you study physiology, you will see that the body is able to maintain relatively constant conditions in the internal environment through the efforts of different organ systems working together.

Apply Your Knowledge

Hemorrhage is the loss of whole blood, which consists of approximately 55–60% plasma. Without new fluids entering the body, how can plasma volume be elevated toward normal levels to maintain homeostasis?

Even though homeostatic regulatory mechanisms work to resist changes in the internal environment, every regulatory system has its limitations, even when it is undamaged by disease or trauma and is functioning normally. For example, body temperature can be maintained close to normal only so long as environmental temperatures are not too extreme and other stresses placed on the

CLINICAL CONNECTIONS

Heat Exhaustion and Heat Stroke

Heat exhaustion is a consequence of the body's effort to regulate its temperature—in particular, its efforts to get rid of excess heat. When the body must get rid of a large quantity of heat, it produces massive quantities of sweat, leading to a significant reduction in blood volume. In addition, blood flow to the skin increases markedly, which diverts blood from other areas of the body. Together, these changes produce a reduction in blood pressure, which reduces blood flow to the brain and precipitates symptoms such as weakness, dizziness, and even loss of consciousness.

A far more serious condition is *heat stroke,* in which the body's temperature rises out of control because of failure of the thermoregulatory system. Extreme overexertion or high environmental temperatures can overwhelm the body's capacity for getting rid of heat. When this happens, the body's temperature rises in spite of its thermoregulatory efforts. As the temperature continues to rise, the brain begins to malfunction. Delirium sets in, followed by a loss of consciousness. Eventually the brain's thermoregulatory centers begin to fail. The brain then inappropriately stops sending signals to the sweat glands that tell them to secrete fluid. As a result, sweat production comes to a halt, compromising the body's ability to get rid of heat and causing the temperature to rise even faster. If left untreated, this spiral of events leads inexorably to death.

The skin of a person experiencing heat stroke has a flushed appearance (due to increased blood flow) but will also be dry (due to the absence of sweat). These signs make it easy to distinguish heat stroke from heat exhaustion, in which sweating is profuse and the skin is flushed and wet. If someone is experiencing heat stroke or is in danger of doing so, immediate medical attention is of the utmost importance. Often, a person's life can be saved by immersing the body in ice water, which reduces the body temperature quickly to within the range at which normal thermoregulation is possible. Assuming that the elevated temperatures have not caused permanent damage to the brain's thermoregulatory centers, regulatory mechanisms can then take over.

Critical Thinking Questions

1. In what ways are the differences between heat exhaustion and heat stroke important?
2. What are the roles of blood pressure and sweat production in thermoregulation?
3. What could be alternatives to water immersion for curtailing the effects of heat stroke?

regulatory system are not too great. Intense exercise or high environmental temperatures, however, can cause body temperature to rise out of control, with potentially fatal consequences **(Clinical Connections: Heat Exhaustion and Heat Stroke)**. In fact, it is generally true that failure of any system to maintain homeostasis ultimately gives rise to signs and symptoms of disease because such failure adversely affects the function of organ systems.

Negative Feedback Control in Homeostasis

Because body temperature is not free to vary but is instead regulated to stay within relatively narrow limits, it is referred to as a **regulated variable.** Plasma concentrations of potassium, sodium, and calcium are also regulated variables because they are kept constant by homeostatic regulatory mechanisms of the organ systems. Most homeostatic regulatory mechanisms follow the same pattern: If a regulated variable increases, the system responds by making it decrease; if it decreases, the system responds by making it increase. Systems behaving in this manner are said to operate by **negative feedback.**

A familiar example of a negative feedback system is the cruise control in a car, which operates to keep the speed of the car steady at a certain desired point (**Figure 1.6**a and b). If a car running on level ground starts up a hill, the car will begin to slow down. When the control mechanism detects a difference between the actual speed of the car and the desired speed, it feeds more gasoline to the engine, and the car's speed increases. When the car's speed reaches the desired speed, the system "throttles back" to maintain that speed. As long as the car's actual speed does not differ from the desired speed, the system makes no further adjustments to the flow of gasoline.

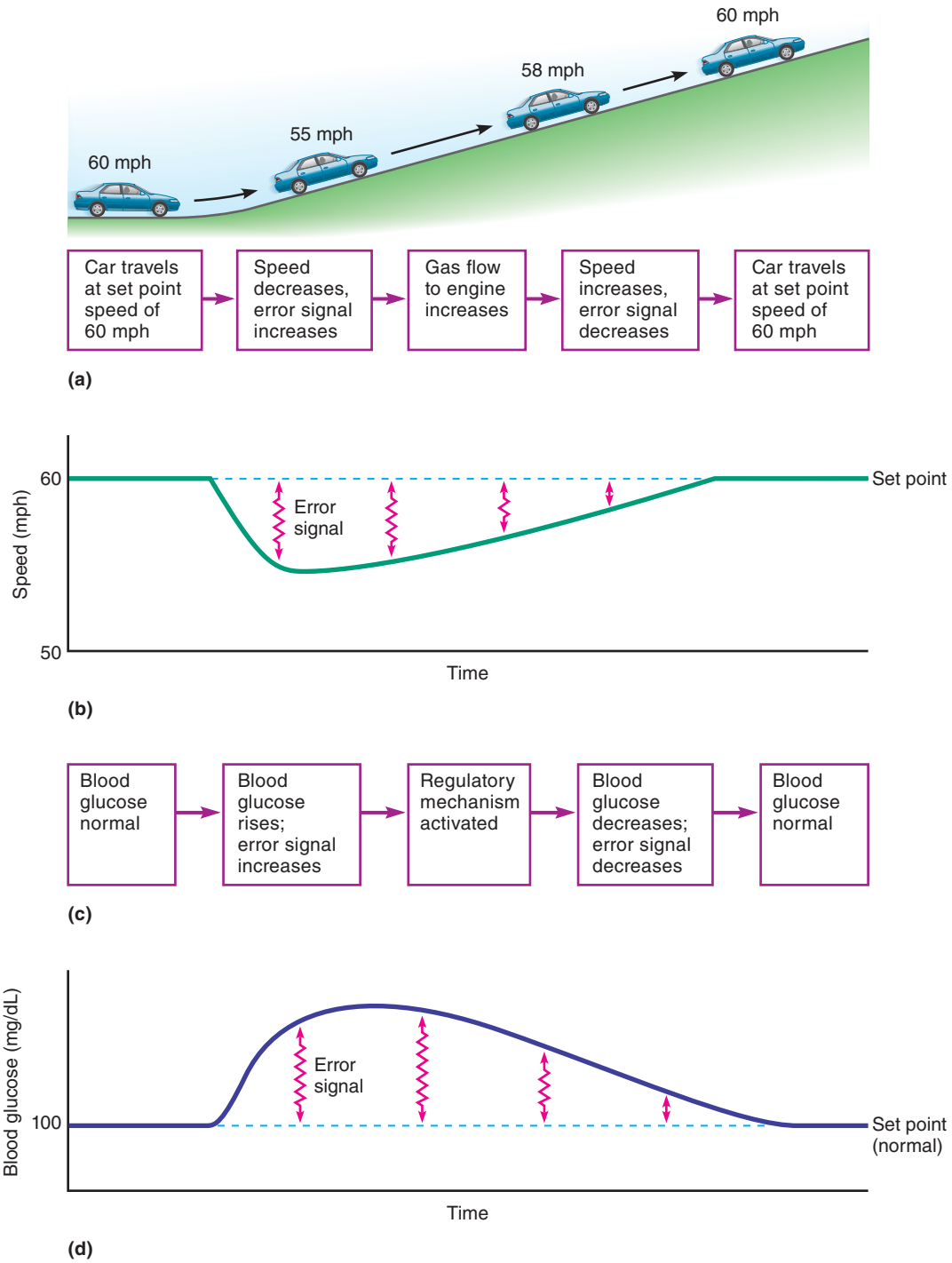


Figure 1.6 **Negative feedback control of a regulated variable.** **(a)** Events occurring as the speed of an automobile is regulated by a cruise control mechanism. **(b)** Graph showing changes in the automobile's speed as it climbs a hill. The dashed line represents the set point speed; vertical arrows indicate the error signal. **(c)** Events occurring as blood glucose is adjusted to normal following an initial rise. **(d)** Graph showing changes in blood glucose.

Like the cruise control in a car, most homeostatic regulatory mechanisms make adjustments only when they detect a difference between the actual value of the regulated variable and the normal "desired" value, called the **set point.** Any difference between the actual value and the set point constitutes an *error signal.* Because these mechanisms normally work to bring the regulated variable closer to the set point, they ultimately function to make error signals as small as possible. Note that the set point cannot be held absolutely constant, just as a car's cruise control cannot maintain a specified speed at all times. Regulated variables fluctuate

continuously, but the changes are minimized by negative feedback. For example, the normal concentration of glucose in the blood is approximately 100 mg/dL (milligrams per deciliter) of blood. After a meal, blood glucose increases, which activates regulatory mechanisms that bring the blood glucose back down to near 100 mg/dL (Figure 1.6c and d).

To operate properly, a homeostatic regulatory mechanism must have a means of detecting the regulated variable. This is accomplished through the actions of *sensors,* cells (often neurons) that are sensitive to the variable in question. For instance, certain blood vessels contain cells called *chemoreceptors* that are sensitive to concentrations of oxygen and carbon dioxide in the blood; in the brain and other parts of the body, there are neurons called *thermoreceptors* that are sensitive to temperature. Typically, such sensors relay signals (called *input*) to an **integrating center** (often a particular set of neural circuits in the brain or an endocrine gland), which then compares the regulated variable to the set point and orchestrates the appropriate response. In response to the input it receives, the integrating center relays signals (called *output*) to the cells, tissues, or organs that bring about the final response. These cells, tissues, or organs are called **effectors.**

Figure 1.7 shows an example of the homeostatic control mechanism for blood glucose. Blood glucose levels are detected by beta cells in the pancreas. When blood glucose levels increase, beta cells act as the integration center and release the hormone *insulin* into the blood. Insulin causes glucose to move from the plasma into cells throughout the body, thereby decreasing blood glucose levels. This decrease in blood glucose levels is detected by the beta cells that secreted insulin, thereby feeding back into the system's input, forming what is known as a *feedback loop*. It is called *negative* feedback because the response of the system (the fall in blood glucose) is opposite in direction to the change that set it in motion (a rise in blood glucose).

Negative feedback is important because it triggers changes in the regulated variable only when appropriate. For example, once a rise in blood glucose triggers a compensatory lowering of the blood glucose through negative feedback, the error signal decreases until blood glucose has been returned to near normal. In this way, negative feedback compensation terminates before blood glucose decreases to levels below the set point.

In addition to negative feedback systems, a few positive feedback systems are important in physiology. In **positive feedback,** the response of the system goes in the *same* direction as the change that sets it in motion. In females, for example, the pituitary gland (a small gland located at the base of the brain) secretes a hormone called *luteinizing hormone (LH)* that stimulates the ovaries to secrete hormones called *estrogens,* which regulate reproductive function. Under certain conditions, a rise in the plasma estrogen concentration can trigger an increase in the secretion of LH. This effect stimulates estrogen secretion, which enhances LH secretion even more, leading to further estrogen secretion, and so on (**Figure 1.8**). The result is a rapid rise in plasma LH, known as the *LH surge,* which triggers ovulation. Unlike negative feedback, which minimizes changes in physiological variables, positive feedback is useful in certain physiological systems because it allows a variable to change rapidly in response to a stimulus.

Even though a variable may change rapidly in positive feedback, it does not increase indefinitely or spiral out of control. Instead, some factor always acts to terminate the positive feedback loop either by removing the original stimulus or by limiting the system's ability to respond to that stimulus. During an LH surge, for example, the LH concentration rises rapidly to a peak and then begins to fall because the surge triggers ovulation, which temporarily inhibits the ovaries' ability to secrete estrogens. The resulting fall in plasma estrogen levels removes the stimulus that caused LH secretion to rise in the first place, thereby allowing LH levels to fall.

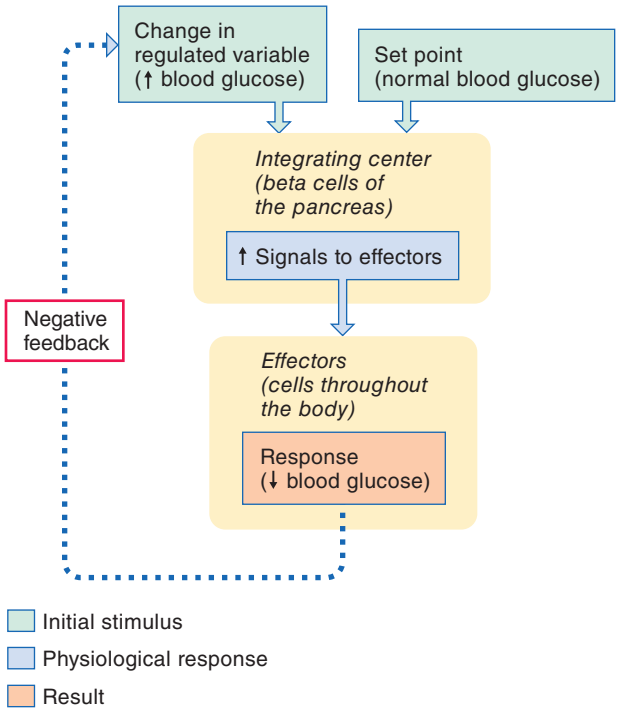


Figure 1.7 A negative feedback loop. This feedback loop operates in the control of blood glucose, as described in the text. Up and down arrows within boxes indicate increases and decreases, respectively. The dashed line indicates that the response of the system affects the input.

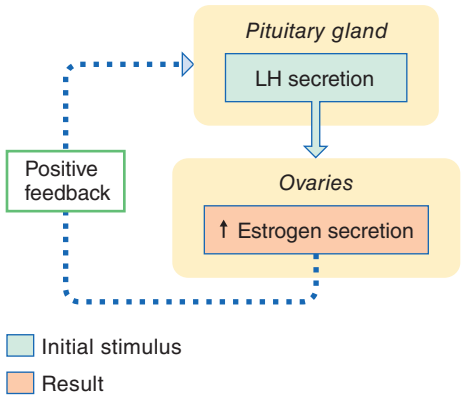


Figure 1.8 A positive feedback loop. This feedback loop operates in the control of estrogen secretion from the ovaries. LH stimulates estrogen secretion, which stimulates LH release, which stimulates more estrogen secretion, and so on.

Quick Check 1.3

1. Define *homeostasis*, and explain how it enables the body to adapt to changes in its environment.
2. Explain how negative feedback works to maintain homeostasis.
3. In certain forms of diabetes, beta cells of the pancreas fail to secrete insulin at adequate levels. Describe how a lack of insulin would affect blood glucose levels.

1.3 The Diabetes Epidemic

Diabetes mellitus is a metabolic disease that affects blood glucose levels and plasma volume and causes excessive thirst and fluid loss, among other things. In fact, diabetes affects every system in the human body. The term "diabetes" was first used in the second century a.d. by a Greek physician, Aretus the Cappadocian. *Diabetes* is a Greek word meaning "siphon" or "flow through," which describes the excessive urine flow that characterizes the disease.

Prevalence of Diabetes

Diabetes affects certain individuals more than others. **Table 1.2** shows the prevalence of diabetes among age groups in the United States. Fewer than 1% of people younger than 20 years have diabetes; however, as a person ages, he or she becomes more prone to develop diabetes. More than 20% of people older than 20 years have diabetes; among those persons older than 65 years, 26% have diabetes.

The prevalence of diabetes also varies with race or ethnicity (**Table 1.3**). Native Americans are most prone to develop diabetes, followed by African Americans and Hispanics. The prevalence of this disease in the white and Asian American populations is considerably lower.

The high prevalence of diabetes extends beyond the United States. According to the International Diabetes Federation, 387 million people (8.3% of the world population) have diabetes. Only 30 million people worldwide were diagnosed with diabetes in 1985, but by 2000 that number had increased to 150 million (**Figure 1.9**).

TABLE 1.2 Prevalence of Diabetes in the United States Based on Age and Sex Data from the American Diabetes Association

Age group	Number of people with diabetes	Percentage of people with diabetes
Younger than 20 years	200,000	0.25%
20–64 years	17.7 million	20.3%
65 years and older	11.2 million	25.9%
Women	13.4 million	11.2%
Men	15.5 million	13.6%

TABLE 1.3 Prevalence of Diabetes in the United States, 2010–2012, Age 20 and Older, Based on Race and Ethnicity

Race/ethnicity	Percentage with diabetes (%)
White, non-Hispanic	7.6
Asian American	9.0
Hispanic American	12.8
Black, non-Hispanic	13.2
Native American	15.9*

*Prevalence varies considerably among groups, with the lowest prevalence (5.5%) in Alaskan Natives and the highest prevalence (33.5%) among American Indian adults in southern Arizona.
Source: Data from the Centers for Disease Control and Prevention, *National Diabetes Fact Sheet.* 2014.

By 2035, the number of people with diagnosed diabetes is expected to reach 600 million.

The cost of treating diabetes is high, both in the United States and around the world. Direct medical costs to treat diabetes in the United States in 2012 were estimated at $176 billion. If indirect costs (including time off work, disability, and mortality) are included, this expense increases to $245 billion.

FOCUS ON DIABETES

As you make your way through this book, you will see this box in various chapters that contain information about diabetes mellitus. The prevalence of diabetes mellitus in the world population makes it a major health concern to all. According to the Centers for Disease Control and Prevention's *National Diabetes Fact Sheet, 2011,* an estimated 8.3% of the U.S. population (26 million people) have diabetes mellitus. Of these 29 million cases of diabetes mellitus, 7 million are undiagnosed. In addition, another 79 million people are prediabetic, meaning that there is a high probability that they will develop diabetes mellitus in the future.

One of the most detrimental aspects of diabetes mellitus is its pervasiveness—it affects all organ systems. As we go through the chapters of the book, we will keep coming back to diabetes as an example of what happens when homeostasis is disrupted during a disease and how the body responds in an attempt to compensate.

This feature is designed to boost your knowledge of human physiology as it pertains to the pathophysiology of diabetes and its complications—for example, how diabetes can lead to kidney disease or atherosclerosis (vessel disease). We hope you will find it informative and helpful as you advance your study of human physiology.

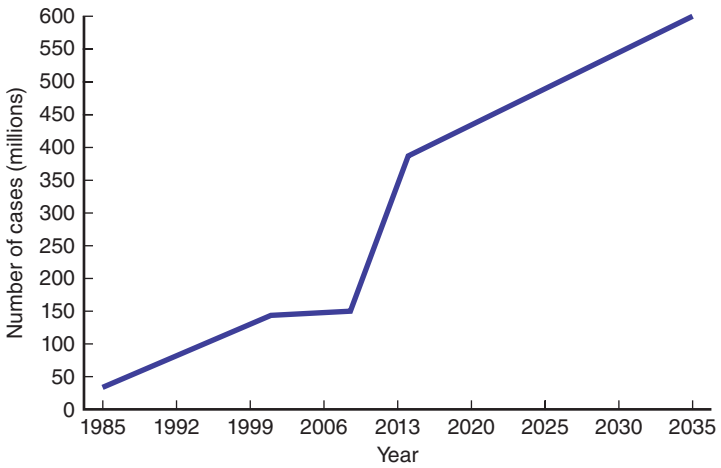


Figure 1.9 Prevalence of diabetes in the world. The 2035 data are predicted based on current trends.

Obesity and Diabetes

Why is the prevalence of diabetes increasing? One major factor is the aging of the population. People now live longer, and a large percentage of the population survives into the higher-risk ages (older than 65 years). In addition, the lifestyles of many young people may lead them to develop diabetes. Diets today incorporate more fats and carbohydrates than in years past. In addition to producing direct metabolic changes, such diets lead to obesity, the number one cause of diabetes. Many young people today also have a sedentary lifestyle, with video games replacing playground time, and physical education classes often absent from the curriculum. Such a sedentary lifestyle can lead to both metabolic changes and obesity—key factors that lead to diabetes.

The prevalence of obesity in the United States is increasing, and obesity itself is becoming an epidemic. *Obesity* is defined as having a high body fat content relative to lean body mass. It is identified using the body mass index (BMI) scale, which measures weight relative to height. The equation that measures BMI is

$$\text{BMI} = \frac{\text{Body weigth (kg)}}{\text{Height (m)}^2}$$

A BMI of 25–29 indicates a person is overweight, a BMI of 30–39 indicates obesity, and a BMI greater than 39 indicates severe obesity.

The percentage of adults who are obese has doubled over the last 30 years in the United States. According to the Centers for Disease Control and Prevention, 35% of U.S. adults are overweight and 35% are obese, up from 15% who were obese in 1980. Among children, 10% of preschoolers and 19% of children ages 6–19 years are obese. The significance of these numbers is that obesity and development of type 2 diabetes mellitus (as well as other diseases) are strongly correlated, as shown in Table 1.4.

Classification of Diabetes

When diabetes is mentioned, most people think of insulin and glucose. Insulin is a hormone released from the pancreas when blood glucose levels are elevated. It promotes glucose uptake into cells, thereby decreasing blood glucose levels—a classic negative feedback system. Once inside the cells, glucose can be used as energy or stored as glycogen or triglycerides to be used as energy at a later time. Although some diabetics must inject themselves with insulin to regulate their blood glucose levels, diabetes is actually much more complicated than that. We will focus on four types of diabetes in this text: type 1 diabetes mellitus, type 2 diabetes mellitus, gestational diabetes, and diabetes insipidus. The prevalence of diabetes described earlier refers to type 2 diabetes mellitus.

TABLE 1.4 Likelihood of Developing Type 2 Diabetes Mellitus Based on BMI

Numbers are relative to the likelihood of developing type 2 diabetes mellitus with a BMI less than 25.*

BMI	Likelihood of developing type 2 diabetes mellitus
<25	1.00*
25–29.9	2.42
30–34.9	3.35
>35	6.16

*Data are given relative to a BMI less than 25, which is assigned a value of 1.00.
Source: Based on from the American Heart Association, *A Nation at Risk: Obesity in the United States Statistical Sourcebook. 2005.*

Diabetes Mellitus

As mentioned earlier, *diabetes* is Greek for "siphon." *Mellitus* is another Greek word, which means "honey." Honey is sweet, and so is the fluid (urine) excreted by an untreated diabetic. A notable characteristic of diabetes mellitus is high blood glucose levels, such that some glucose is eliminated in the urine, giving it a sweet taste. Conversely, nondiabetics rarely excrete glucose in their urine.

Diabetes mellitus consists of two types: type 1 and type 2. Type 1 diabetes mellitus (type 1 DM) was formerly referred to as insulin-dependent diabetes mellitus or juvenile-onset diabetes mellitus: "insulin-dependent" because damage to the beta cells of the pancreas keeps them from secreting enough insulin in the blood to regulate blood glucose, and "juvenile-onset" because this form of the disease becomes apparent at an early age. Type 1 DM is the type familiar to most people, but it is by far the less common of the two types, accounting for only 5 to 10% of all diabetes mellitus cases.

Type 2 diabetes mellitus (type 2 DM) is characterized by failure to respond to insulin when its levels are normal. Type 2 DM, formerly referred to as non-insulin-dependent diabetes mellitus or adult-onset diabetes mellitus, is the disease associated with the diabetes epidemic. People with type 2 DM have normal beta cells in their pancreas that secrete insulin at appropriate levels to regulate blood glucose. Because the target cells are incapable of responding to insulin, however, they do not take up glucose from the blood. This failure has two major consequences: (1) The cells do not get the glucose they need for energy and (2) the glucose levels in the blood rise.

Gestational Diabetes

A subclass of type 2 DM is gestational diabetes, which develops in 4% of pregnant women (135,000 cases per year in the United States).

Current data suggest that hormones produced in high amounts during pregnancy induce insulin resistance. Of the women who get gestational diabetes, 5–10% develop type 2 DM after giving birth.

Prediabetes

In prediabetes, blood glucose levels are elevated, but not as much as in full diabetes. Prediabetics have fasting blood glucose levels of 100–125 mg/dL. According to the Centers for Disease Control and Prevention, 86 million Americans are considered prediabetic and many are likely to develop type 2 DM within 10 years of developing the signs of prediabetes.

Diabetes Insipidus

Diabetes insipidus differs from diabetes mellitus in that the problem lies not in regulating blood glucose levels, but rather in regulating plasma volume. The word *insipidus* is Latin for "having no flavor," thereby distinguishing the urine of people with this disease from the sweet urine of people with diabetes mellitus. Antidiuretic hormone (ADH) decreases the amount of water lost in the urine. Thus one cause of diabetes insipidus is inadequate ADH secretion. Another cause of this disease is tissue resistance to ADH, which can occur during pregnancy.

The primary symptoms shared by people with diabetes mellitus and those with diabetes insipidus include copious urination and excessive thirst. A person with diabetes insipidus may drink more than 4 gallons of water and excrete more than 3 liters of urine per day. Diagnostic procedures include measuring ADH levels in blood, magnetic resonance imaging of the brain (ADH is secreted by the pituitary gland, which is located in the brain), and a water deprivation test in which the patient is deprived of water and plasma sodium concentration is measured every hour (as plasma volume decreases due to a loss of fluid, plasma sodium concentration increases).

Diabetes insipidus is a rare disease that we will not discuss further here. We will return to diabetes insipidus later in this text (in Chapter 19), where the role of kidneys in regulating plasma volume is described.

Diagnosing Diabetes Mellitus

To test for diabetes, fasting plasma glucose levels are measured and a glucose tolerance test is performed. Random measurements of plasma glucose may give the first indication of prediabetes or diabetes; fasting plasma glucose levels and a glucose tolerance test would then confirm the diagnosis.

The fasting plasma glucose test requires that the patient not eat for 8 hours before a blood sample is taken. Normal fasting glucose levels are 60–100 mg/dL. Plasma glucose levels of 100–125 mg/dL indicate prediabetes, and levels greater than 125 mg/dL indicate diabetes.

The oral glucose tolerance test requires fasting for 8 hours, followed by consumption of a solution containing 75 grams of glucose dissolved in water. A plasma glucose measurement is taken 2 hours after the person consumes the solution. A 2-hour plasma glucose level of less than 139 mg/dL is considered normal, between 140 and 199 mg/dL is prediabetic, and greater than 200 mg/dL indicates diabetes.

Symptoms of Diabetes Mellitus

Diabetes has many symptoms, which can vary depending on the person. The symptoms most commonly identified for diagnosis purposes are elevated blood glucose and glucose in the urine. Glucose in the urine pulls water out of the body with it, resulting in loss of body fluids and dehydration.

As diabetes progresses, it affects virtually every system in the human body. Because their cells cannot utilize glucose normally, diabetics often suffer from fatigue. Fluctuations in blood glucose can lead to lethargy and, with extremely high levels, coma. The disease may affect the eyes, heart, vasculature, kidneys, stomach, and peripheral nerves. Diabetes can also cause erectile dysfunction. In addition, it promotes atherosclerosis, increasing the likelihood that the person will suffer a stroke or heart attack. All of these symptoms and more will be discussed in the context of the systems affected (see the Focus on Diabetes section earlier in this chapter) as we proceed through the text.

Treatment of Diabetes Mellitus

Current therapies used in the treatment of diabetes mellitus help control blood glucose levels. Maintaining fasting blood glucose levels between 70 and 120 mg/dL, for example, has proved effective in decreasing the incidence of eye disease, kidney disease, and nerve damage. Diabetic patients are placed on a strict diet and must test their blood glucose frequently to ensure the levels are not fluctuating too much on a daily basis. A more recently discovered test may be even better at determining blood glucose levels over a period of time—namely, measuring the amount of a certain protein, hemoglobin A_{1c}, present in the blood.

Glucose binds to hemoglobin A_{1c} inside red blood cells. Normally, glucose is transported in the plasma portion of the blood. However, when present at high levels, glucose enters the red blood cells and binds to hemoglobin A_{1c}; the higher the blood glucose levels, the more glucose bound to hemoglobin A_{1c}. Red blood cells have a short life span of 3–4 months. During this period, the cells accumulate glucose until they are removed from the blood by the spleen. Thus measurements of hemoglobin A_{1c} levels indirectly measure the average blood glucose levels for 2–3 months.

Monitoring blood glucose levels does not cure diabetes, but it provides feedback so that the patient can make lifestyle changes (for example, in diet and exercise patterns) to bring blood glucose back toward normal levels. If behavioral changes do not fix the problem, pharmaceutical interventions may be required. Individuals with type 1 DM typically have to administer insulin to control their blood glucose levels. On occasion, persons with type 2 DM may have to do the same to decrease their blood glucose levels, although other pharmaceutical options are also available. Sulfonylureas and meglitinides are drugs that stimulate beta cells to increase insulin secretion. Thiazolidinediones enhance the action of insulin on muscle and fat cells and decrease the amount of glucose produced by the liver. Biguanides decrease the amount of glucose produced by the liver. Other drugs to treat type 2 DM are also available, but their

mechanisms of action require more knowledge of physiology—we will come back to these drugs in appropriate chapters.

As diabetes progresses, treatment must also progress. As secondary problems arise from the diabetes, such as cardiovascular disease, these secondary diseases must be treated. These treatments are beyond the scope of this chapter, but will be described later in the text.

SYSTEMS INTEGRATION

In this chapter, we learned that our bodies are made up of cells of various types, and that these cells must work together in a coordinated fashion to maintain homeostasis. In future chapters, we will learn more about cells and their basic functions. We will also learn about how cells communicate with one another so that they may function as a tissue or an organ (Chapter 5). In the remainder of the book, we will discuss the organ systems—but we will always come back to the cell and its role in ensuring that the organs carry out their functions to maintain homeostasis.

CHAPTER REVIEW

SUMMARY

1.1 Organization of the Body, p. 2

- Cells—the smallest living units—are specialized to carry out different functions in the body.
- Specific types of cells are organized into tissues, which are then combined to make organs.
- Organs perform specific functions; organ systems are organs that work together to perform certain tasks.
- Four major types of cells are distinguished: neurons, muscle cells, epithelial cells, and connective tissue cells.
- The internal environment is the fluid surrounding the body's cells.
- The bloodstream delivers and removes materials to and from the internal environment and then exchanges the materials with the external environment.
- The body is divided into several fluid-filled compartments.
- Total body water (TBW) is the total volume of water in all compartments; it includes both intracellular fluid (ICF) and extracellular fluid (ECF).
- ICF is located inside cells; ECF is located outside the cells. The two types of fluids are separated by cell membranes.
- The portion of ECF in the blood is called plasma; that found outside the blood is called interstitial fluid (ISF).
- Plasma and ISF are similar in composition and are separated by the epithelial tissues that line blood vessels.

MAP iP Tissues

iP Fluid and Electrolytes, Introduction to Body Fluids

1.2 Homeostasis: A Central Organizing Principle of Physiology, p. 9

- Homeostasis is the body's ability to maintain constant conditions in the body's internal environment.
- To maintain homeostasis, regulatory mechanisms work to control regulated variables so that variations are minimized.
- Negative feedback occurs when a change in a regulated variable triggers the opposite response.
- Homeostatic regulatory mechanisms include sensors, an integrating center, and effectors.
- Positive feedback occurs in some physiological variables in which a change triggers a similar response.

1.3 The Diabetes Epidemic, p. 13

- Obesity increases the likelihood that a person will develop diabetes mellitus.
- There are two types of diabetes mellitus: type 1 DM and type 2 DM. Type 1 DM results from inadequate insulin secretion; type 2 DM results from inadequate response of tissues to insulin.
- Gestational diabetes is a subclass of type 2 DM; it develops in 4% of pregnant women.
- In prediabetes, blood glucose levels are elevated, but not as much as in full diabetes. Prediabetics are likely to develop type 2 DM in the future.
- Diabetes insipidus is associated with inadequate ADH secretion and results in copious urination.
- The major symptom of diabetes mellitus is hyperglycemia. Diagnosis of the disease depends on blood glucose levels and levels of hemoglobin A_{1c}.
- Diabetes mellitus treatment includes regulating blood glucose levels with diet, insulin injections, and/or oral medications.

EXERCISES

Multiple-Choice Questions

1. Which of the following best illustrates the concept of positive feedback?
   a) The secretion of acid by cells in the stomach lining is suppressed when the acidity of the stomach contents increases.
   b) A rise in blood pressure stimulates the elimination of water in the urine, which reduces the blood pressure.
   c) An increase in the concentration of H^+ in blood causes an increase in H^+ excretion in urine.
   d) An increase in the carbon dioxide concentration of the blood stimulates breathing, which increases the rate at which carbon dioxide is eliminated from the body.
   e) Contractions of the uterus push the fetus against the cervix, which triggers release of oxytocin into the bloodstream; oxytocin then stimulates stronger contractions of the uterus.
2. The hormone aldosterone stimulates the reabsorption of sodium ions from the lumen of a kidney tubule. Based on your knowledge of the body's cell types, you can surmise that this hormone acts on
   a) Neurons.
   b) Muscle cells.
   c) Epithelial cells.
   d) Connective tissue cells.
3. Hormones are secreted
   a) Into the blood.
   b) From exocrine glands.
   c) From endocrine glands.
   d) Both a and b are true.
   e) Both a and c are true.
4. Which cell type is specialized for contraction and generation of force?
   a) Muscle
   b) Epithelial
   c) Connective tissue
   d) Nerve
5. Normal blood glucose level is
   a) 50 mg/dL.
   b) 100 mg/dL.
   c) 50 mg/mL.
   d) 100 mg/mL.
   e) 50 mg/L.

Objective Questions

6. The body's internal environment is synonymous with (extracellular fluid/ intracellular fluid).
7. Maintenance of constant conditions in the internal environment is known as _____.
8. Plasma is extracellular fluid. (true/false)
9. In homeostasis, *all* physiological variables are regulated to stay constant. (true/false)
10. The protein elastin is found in (epithelial/ connective) tissue.
11. Plasma and interstitial fluid are identical in composition. (true/false)
12. A hormone that causes movement of glucose from plasma to cells is _____.

Essay Questions

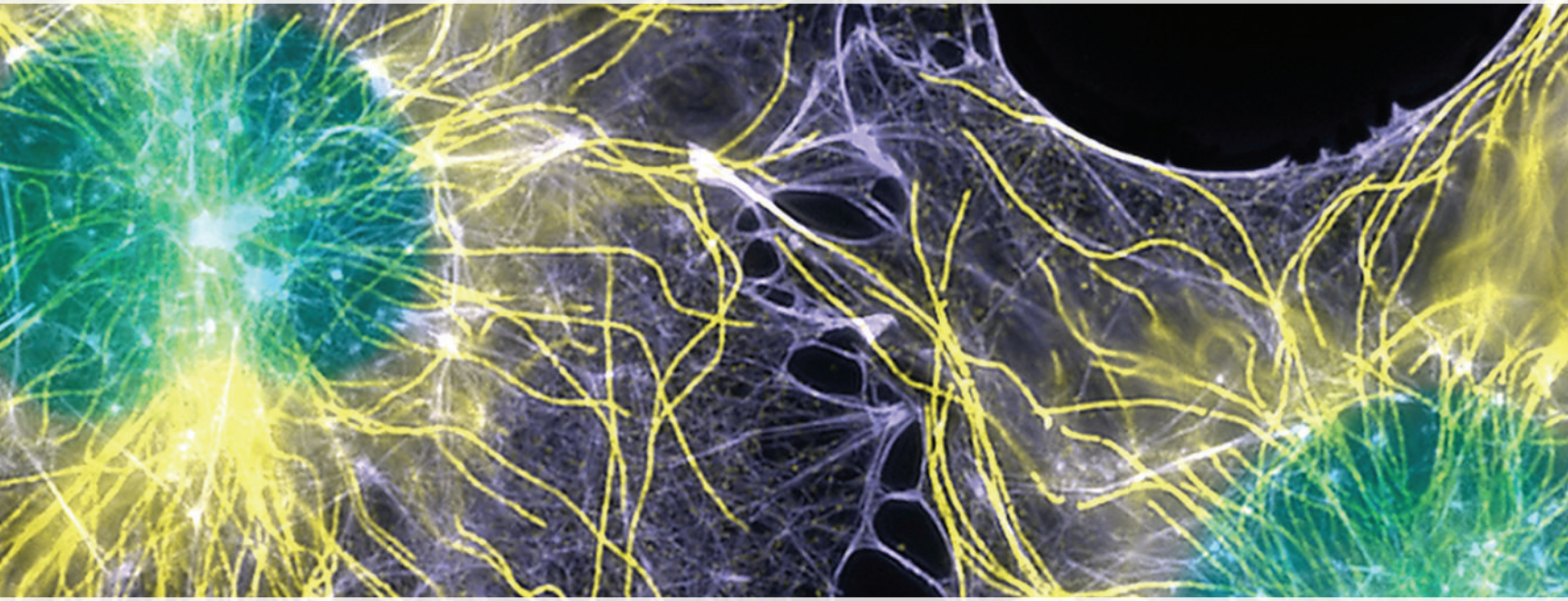
13. Draw a tree diagram illustrating the relationship between total body water, extracellular fluid, intracellular fluid, interstitial fluid, and plasma.
14. Suppose that molecules of glucose are ingested, absorbed into the bloodstream, and then converted inside muscle cells to carbon dioxide, which is eliminated through the lungs. Describe the path of these molecules as they travel through the body, being sure to mention the various barriers (epithelia or cell membranes) that must be crossed.

Critical Thinking

15. Diabetes is a growing health concern in the United States. Compare the different types of diabetes in terms of their prevalence, primary cause, and diagnostics. How might health care workers tackle the growing epidemic of diabetes?

Answers to the Figure Questions, Apply Your Knowledge, Multiple-Choice Questions, and Objective Questions are located at the back of the book.

2 The Cell
Structure and Function



Colorized electron micrograph of two nerve cells.

If you've ever taken a drop of pond water and looked at it under a microscope, then you've probably observed several single-celled organisms. These organisms take up nutrients from their environment, break them down, and convert them to usable energy or to substrates required to synthesize large molecules needed for life. They release waste products into the environment, are motile in water, and respond to various types of stimuli. Lastly, these organisms can grow and reproduce.

The cells of your body are remarkably similar to these unicellular organisms. Your cells require nutrients for energy and for synthesizing needed molecules. Your cells generate waste products that must be eliminated. Some of your cells are motile, and most of your cells can grow and reproduce. However, unlike the unicellular organisms, your cells are part of a multicellular organism—you. As such, your cells must carry out coordinated activities, with different types of cells specialized for certain functions. The ability of organ systems to carry out their functions depends on the cells that form them.

CHAPTER OUTLINE

LEARNING OUTCOMES *After studying this chapter, you should be able to:*

- Know the general characteristics of the four major classes of biomolecules (carbohydrates, proteins, lipids, and nucleic acids), and give a brief description of their functions in cells.
- Describe the structure and major functions of each of the following cellular components: plasma membrane, nucleus, ribosomes, rough endoplasmic reticulum, smooth endoplasmic reticulum, Golgi apparatus, mitochondria, lysosomes, peroxisomes, cytoskeleton.
- Define *transcription* and *translation,* and describe the role of each of the following in protein synthesis: DNA, genes, codons, genetic code, messenger RNA, transfer RNA, ribosomes, anticodons, rough endoplasmic reticulum.
- Explain how genetic information is stored in DNA, and how this information is passed on to daughter cells during mitosis.
- Briefly describe what happens to proteins following their synthesis, taking into account the different fates of membrane proteins, secreted proteins, and cytoplasmic proteins.

Before You Begin

Make sure you have mastered the following topics:

- Cell types, p. 3
- Body fluid compartments, p. 7

You've now learned about the concept of homeostasis, and you learned that physiology involves the study of how the organ systems work together to maintain homeostasis (in Chapter 1). To understand organ systems, we must understand their basic units: cells. This chapter describes the basic structures and functions of cells. To understand cells and their functions, we must also understand the molecules that form cells and that interact with cells. Most of these molecules are *biomolecules.*

2.1 Biomolecules

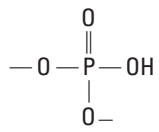
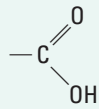
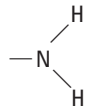
Biomolecules are molecules that are synthesized by living organisms and contain carbon atoms (**Chemistry Review: Atoms and Molecules,** p. 22). Carbon has four electrons in its outer shell and forms covalent bonds by sharing these electrons with other atoms, including other carbon atoms. Other atoms common to biomolecules include oxygen, hydrogen, and nitrogen. The ability of carbon to share four electrons and to form covalent bonds with other carbon atoms enables carbon-containing molecules to be large and complex. In biomolecules, the component carbon atoms are often arranged in chains or rings.

The four basic types of biomolecules are *carbohydrates, lipids, proteins,* and *nucleotides*. Some biomolecules are *polymers,* which consist of repeated subunits. For example, proteins are polymers of *amino acids*. The following sections discuss each class of biomolecule. Table 2.1 lists some chemical functional groups commonly found in biomolecules.

Carbohydrates

Carbohydrates are composed of carbon, hydrogen, and oxygen in a ratio of 1:2:1, with the general chemical formula $(CH_2O)_n$. The chemical formula can also be written as $C_n(H_2O)_n$, which might be interpreted as *hydrated* carbons, or carbons surrounded by water—thus the name *carbohydrates.* However, this name can be deceiving because the carbons actually bond to hydroxyl groups (—OH) and hydrogens (—H), not to water molecules. The presence of several hydroxyl groups makes carbohydrates polar molecules, so they readily dissolve in water (**Chemistry Review: Polar Molecules and Hydrogen Bonds,** p. 31).

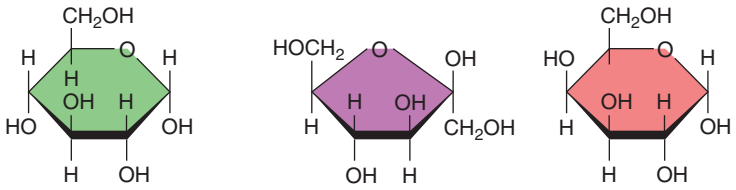
TABLE 2.1 Common Functional Groups Found in Biomolecules

Functional group	Chemical formula	Structure	Chemical property
Hydroxyl	—OH	—O—H	Polar
Sulfhydryl	—SH	—S—H	Polar
Phosphate	$-HPO_4^-$		Polar
Carboxyl	—COOH		Acid
Amino	$-NH_2$		Base

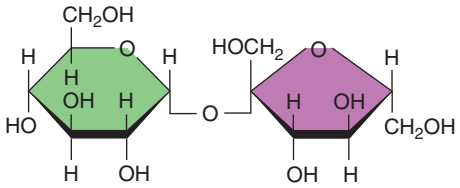
Monosaccharides, Disaccharides, and Polysaccharides

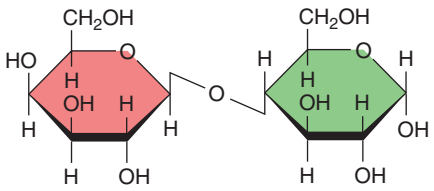
Carbohydrates can be further classified into three major groups: (1) monosaccharides, (2) disaccharides, and (3) polysaccharides. **Monosaccharides** are simple sugars, composed of a single unit (Figure 2.1a). The most common monosaccharide is **glucose,** which is an important source of energy for our cells. Glucose has the general formula $C_6H_{12}O_6$. Two other common monosaccharides, *fructose* and *galactose,* also have the general formula $C_6H_{12}O_6$ and can be converted to glucose in our cells. They are distinct molecules, however—the atoms are arranged differently in these monosaccharides, giving each its own chemical properties. *Ribose* and *deoxyribose* are two other common monosaccharides that are important components of *nucleotides,* another class of biomolecules that are described later.

Disaccharides are carbohydrates formed by the covalent bonding of two monosaccharides (Figure 2.1b). Common examples of disaccharides include *sucrose,* which is composed of a glucose

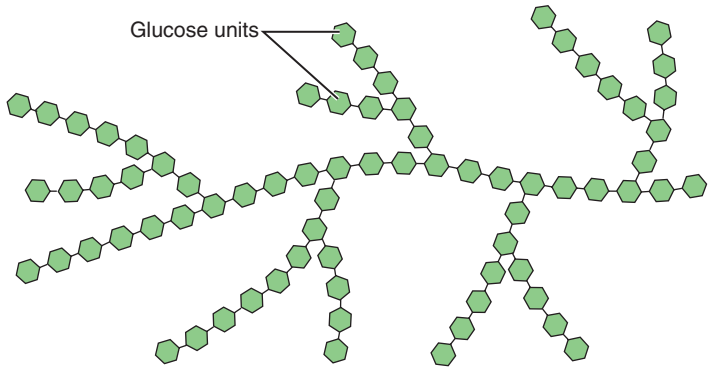


(a) Monosaccharides





(b) Disaccharides



(c) Polysaccharide

Figure 2.1 Carbohydrates. (a) Examples of three monosaccharides with the same chemical formula: $C_6H_{12}O_6$. **(b)** Examples of two disaccharides. Sucrose, or table sugar, consists of a glucose subunit and a fructose subunit. Lactose, a carbohydrate found in milk, consists of a glucose subunit and a galactose subunit. **(c)** A polysaccharide, which is a polymer of a monosaccharide. Glycogen is a glucose polymer found in animals.

Q How many hydroxyl groups are in a single glucose molecule?

subunit and a fructose subunit joined together, and *lactose,* which is composed of a glucose subunit and a galactose subunit joined together. Sucrose is also known as table sugar, whereas lactose is a carbohydrate found in milk. Notice that the names of the monosaccharides and disaccharides all end in *-ose.*

Polysaccharides are carbohydrates formed by the covalent bonding of several monosaccharides. **Glycogen** (Figure 2.1c) is a polymer of glucose subunits and is found in animal cells. Several types of cells in the body can store glucose as glycogen and later break glycogen down when they need glucose for energy. Glycogen is needed for a simple reason: If cells stored energy in the form of monosaccharides, the monosaccharides would exert an osmotic force that would draw water into the cells, making the cells swell and possibly burst. By comparison, a single large storage molecule will not draw in nearly as much water. **Starch** is a polysaccharide found in plants. Humans consume starch in various plant food products; the digestion process makes the glucose subunits of starch available as energy sources. **Cellulose,** another polysaccharide found in plants, is consumed by humans, but we are unable to digest and absorb it. Therefore, cellulose, also known as dietary fiber, passes through our gastrointestinal system. In addition to storing energy, polysaccharides are important components of cell membranes, a topic to be described later.

Synthesis and Breakdown of Saccharides

To synthesize disaccharides and polysaccharides, monosaccharides must be linked together by covalent bonds. The type of reaction that links monosaccharides together is called **condensation,** reflecting the fact that water is produced in the process. For example, when a glucose subunit and a fructose subunit react together to form sucrose, water is released. Similarly, each time a glucose subunit is added to glycogen, a molecule of water is produced.

In contrast, when disaccharides and polysaccharides must be broken down to their monosaccharide subunits, they are reacted with water. The water splits (or lyses) the larger molecule into its smaller components by a process called **hydrolysis.** During the lysis, a hydrogen atom from the water binds to one of the products, while the hydroxyl group binds to the other product of the reaction. We will see that condensation and hydrolysis are used in the synthesis and breakdown of the other biomolecules.

Lipids

Lipids are a diverse group of biomolecules that contain primarily carbon and hydrogen atoms linked together by nonpolar covalent bonds. Therefore, lipids generally are nonpolar molecules and do not dissolve in water. Most lipids also contain some oxygen, and

several contain phosphates (—HPO_4^-), which, depending on the structure, may provide areas of the molecule that are polar. A molecule that contains both polar and nonpolar regions is called **amphipathic.** The five main classes of lipids vary both structurally and functionally: (1) *triglycerides,* (2) *ketones*, (3) *phospholipids,* (4) *eicosanoids,* and (5) *steroids.*

Triglycerides

Triglycerides—what we typically call "fats"—are composed of one glycerol molecule and three fatty acid molecules. **Glycerol** is a three-carbon alcohol (**Figure 2.2a**) that functions as the "backbone" of a triglyceride; **fatty acids** are long chains of carbon atoms with a carboxyl group (!COOH) at one end (Figure 2.2b and c). **Triglycerides** are formed by linking each of three fatty acids to a different carbon in the glycerol backbone (Figure 2.2d).

Most fatty acids have an even number of carbon atoms, most commonly 16 or 18. An important feature of fatty acid chains is the number of double bonds between carbons. If there are no double bonds, then each carbon is linked to a maximum number of hydrogen atoms and, therefore, is *saturated* with hydrogen atoms. Thus *saturated fatty acids* contain carbons linked only by single bonds (Figure 2.2b). In contrast, *unsaturated fatty acids* contain one or more pairs of carbons linked by double bonds and, therefore, have fewer hydrogens per carbon (Figure 2.2c). A *monounsaturated fatty acid* contains exactly one double-bonded pair of carbons, whereas a *polyunsaturated fatty acid* contains more than

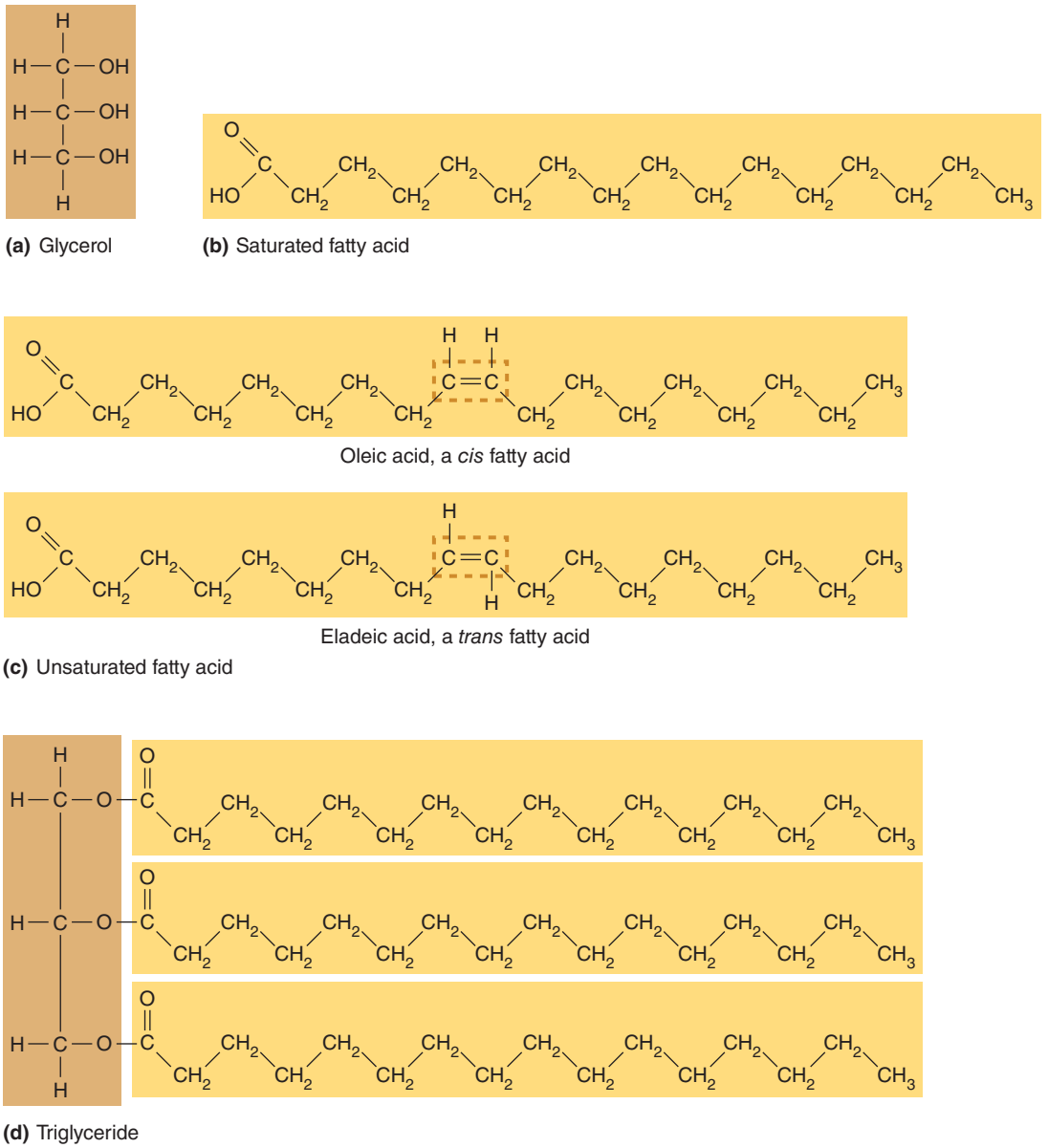


Figure 2.2 Triglycerides. (a) Glycerol, a three-carbon alcohol found in both triglycerides and phospholipids. **(b)** A fatty acid chain, which usually consists of an even number of carbon atoms with a carboxyl group (—COOH) on the end. This example is a saturated fatty acid because it has no double bonds between carbon atoms. **(c)** This fatty acid is unsaturated because of the presence of the double bond between carbons 9 and 10. Because it contains only one double bond, it is a monounsaturated fatty acid. **(d)** A triglyceride, which is composed of a glycerol backbone and three fatty acids.

Q Each of the fatty acids in Figure 2.2 (b) and (c) has 16 carbons. Which of the two fatty acids has more hydrogens?

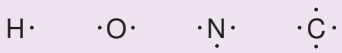
CHEMISTRY REVIEW

Atoms and Molecules

All matter is composed of fundamental units called *atoms,* which are on the order of one-billionth of a centimeter in diameter. Atoms, in turn, are made up of three types of elementary particles: (1) *protons,* which each carry one unit of positive electrical charge; (2) *electrons,* which each carry one unit of negative electrical charge; and (3) *neutrons,* which carry no charge. Normally, an atom possesses equal numbers of protons and electrons, giving it a net charge of zero. The protons and neutrons are densely concentrated at the atom's center in a core called the *nucleus,* while the electrons travel in orbits or *shells* located at various distances from the nucleus.

Atoms are distinguished from one another on the basis of their *atomic number,* which equals the number of protons (and, therefore, also the number of electrons) they possess. The atomic number also determines the chemical properties of an atom. Pure substances consisting entirely of atoms having the same atomic number are referred to as *elements.* Although more than 100 elements are known, just 4 account for more than 99% of all the atoms in the body: *hydrogen (H), carbon (C), nitrogen (N),* and *oxygen (O),* whose atomic numbers are 1, 6, 7, and 8, respectively.

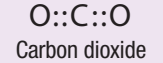
Most substances are composed of two or more atoms linked or *bonded* together to form *molecules.* Molecules of water—the most abundant substance in the body—contain two hydrogen atoms and one oxygen atom and are designated by the formula H_2O. Carbon dioxide, a waste product generated by cells, contains two oxygen atoms and one carbon atom and is designated as CO_2. Most often, a molecule's atoms are held together by *covalent bonds,* which consist of pairs of electrons shared between adjacent atoms. Because all atoms of a given type possess the same number of sharable electrons, each element has a certain capacity for forming bonds. Hydrogen atoms form only a single bond, whereas oxygen, nitrogen, or carbon can form two, three, or four bonds, respectively:



As long as each atom forms the correct number of bonds, the atoms can be combined to form a virtually unlimited variety of molecules. Molecules of water, hydrogen (H_2), and methane or *natural gas* (CH_4) can be represented as follows:

Water Hydrogen Methane

Sometimes atoms share two pairs of electrons, forming *double bonds.* This is illustrated in the following representation of a molecule of carbon dioxide:



Carbon dioxide

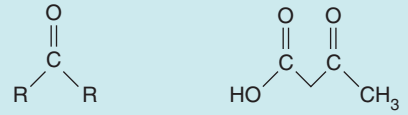
one double-bonded pair of carbons. The double bonds can also be described as *trans,* indicating that the single hydrogen and the carbon bonded with it are on opposite sides of the chain, or *cis,* indicating that the single hydrogen and the carbon bonded with it are on the same side of the chain (Figure 2.2d). The degree of saturation and the *trans* or *cis* nature of the double bonds determine important properties of a lipid, including some with significant clinical implications. *Cis* fatty acids are generally produced by natural processes, whereas *trans* fatty acids are produced artificially. For example, saturated fatty acids and *trans* fatty acids are implicated in the development of plaques that can clog arteries, which can lead to stroke or heart attack.

Triglycerides and fatty acids are nonpolar molecules because of the presence of nonpolar carbon-to-carbon and carbon-to-hydrogen bonds. They do not dissolve in water, but they readily dissolve in nonpolar solvents such as oil or benzene.

FOCUS ON DIABETES

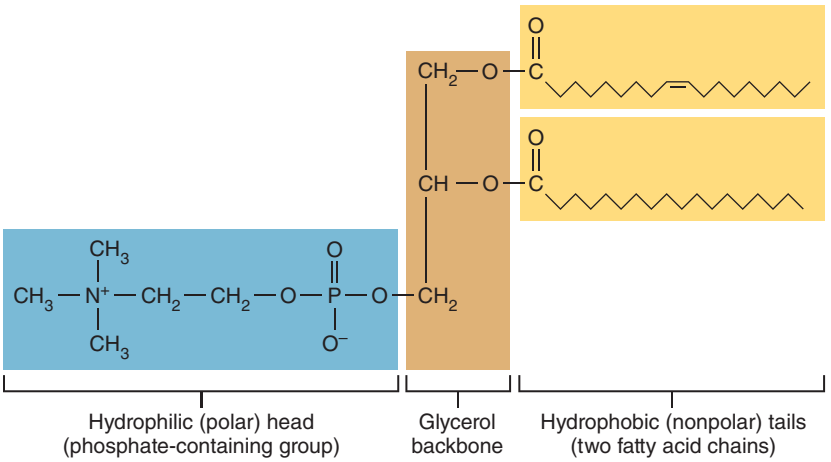
Ketone Bodies

When triglycerides are hydrolyzed in adipose tissue, free fatty acids are released into the blood as an immediate alternative source of energy (the primary energy source for cells is glucose, when it is plentiful). Some fatty acids, however, travel to the liver where they are converted to **ketone bodies** or **ketones** (see Figure 2.3). Ketone bodies include acetoacetic acid, a-hydroxybutyric acid, and acetone. When glucose levels are low, requiring the rapid breakdown of fats for energy, as occurs in low-carbohydrate diets, or in uncontrolled diabetes mellitus, where glucose cannot be used by cells for energy, then ketone bodies are rapidly produced and blood levels of these acids become elevated, producing a condition called ketosis. This buildup of acids can result in a ketoacidosis, a serious problem in diabetes mellitus. Another common, but not severe consequence of ketosis is "acetone breath."

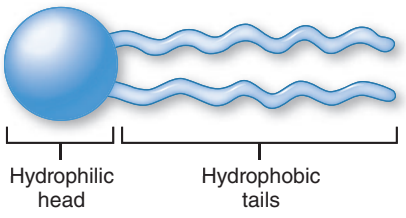


(a) Ketone structure **(b)** Acetoacetic acid

Figure 2.3 The general chemical structure of a ketone (a) and an example of a ketone, acetoacetic acid (b).



(a) Phospholipid molecule (phosphatidylcholine)



(b) Schematic representation of phospholipid molecule

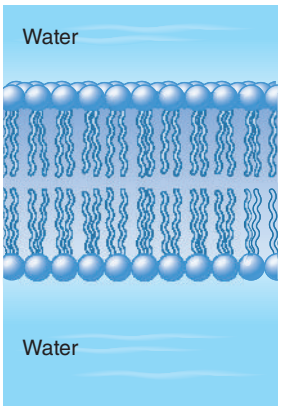
Figure 2.4 Phospholipids. (a) A phospholipid, which consists of a glycerol backbone linked to two fatty acid chains and a phosphate-containing group. The phospholipid shown here is *phosphatidylcholine*. **(b)** The standard way to schematically depict a phospholipid, emphasizing the hydrophilic head and hydrophobic tails of the molecule.

Phospholipids

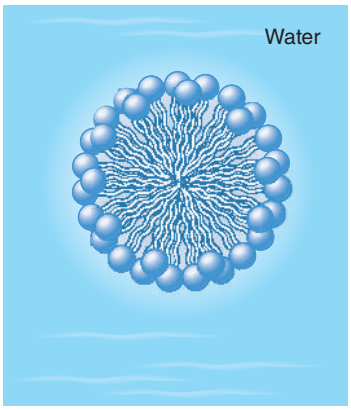
Phospholipids are lipids that contain a phosphate group. They are similar in structure to triglycerides, in that a glycerol forms the backbone. However, instead of three fatty acids, a phospholipid contains two fatty acids and has a phosphate group attached to the third carbon of glycerol (**Figure 2.4**). The two fatty acids form the *tail* region of the phospholipid, which is nonpolar because of their long chains of carbon atoms. The phosphate group is generally attached to another chemical group, and together they form the *head* region of the phospholipid, which is polar. For example, the phospholipid known as phosphatidylcholine has a choline group attached to the phosphate subunit. Because phospholipids have both a polar region and a nonpolar region, they are amphipathic molecules.

The amphipathic property of phospholipids gives them unique behaviors in an aqueous or watery environment. The polar regions can dissolve in water, but the nonpolar regions cannot. Therefore, when phospholipids are placed in an aqueous environment, the polar regions face the water, and the nonpolar regions face each other. Phospholipids form two physiologically important structures when placed in an aqueous environment: phospholipid bilayers and micelles (**Figure 2.5**). In a phospholipid bilayer (Figure 2.5a), which is the core structure of cell membranes, the phospholipids are arranged in two parallel layers: The tails of parallel phospholipids face inward toward each other, and the heads face the outside, where they come into contact with the aqueous environment. A micelle (Figure 2.5b) is a spherical structure composed of a single layer of phospholipids; it functions in the transport of nonpolar molecules in an aqueous environment. The heads of the phospholipids face outward, where they come into contact with the aqueous environment; the tails face inward, forming a hydrophobic interior.

Another benefit of the amphipathic property of phospholipids is that when applied to water, they decrease the attraction between water molecules. *Surfactants* are a type of phospholipid found in the airways of the lungs, where they decrease the attraction between water molecules lining the lung airways. The water attraction creates surface tension that tends to collapse the lungs—an effect that is prevented by surfactant. In premature babies, surfactant is not yet produced in the lung tissue; thus these babies require mechanical ventilation to keep their lungs open.



(a) Phospholipid bilayer



(b) Micelle

Figure 2.5 Structures formed by phospholipids in an aqueous environment. (a) A lipid bilayer, which consists of two sheets of phospholipids aligned such that the polar heads face the aqueous environment and the nonpolar tails face each other. **(b)** A micelle, a sphere formed by a single layer of phospholipids aligned such that the polar heads face the aqueous environment and the nonpolar tails face each other.

Apply Your Knowledge

Which types of metabolic adjustments occur when someone switches from a high-protein diet to a high-carbohydrate diet?

Eicosanoids

Eicosanoids are modified fatty acids that function in intercellular communication. An eicosanoid is derived from a 20-carbon polyunsaturated fatty acid, arachidonic acid, that is found in

phospholipid components of cell membranes (Figure 2.6). To form eicosanoids, enzymes cause the fatty acid to fold upon itself, forming a five-carbon ring in the middle with two chains of carbon atoms extending parallel to each other away from the ring. Eicosanoids are polar molecules and include *prostaglandins* and *thromboxanes.*

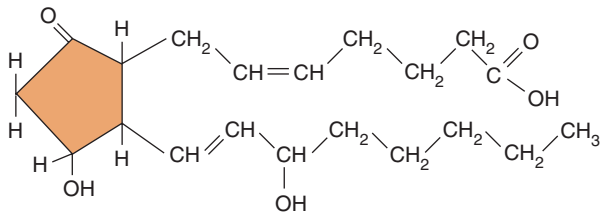
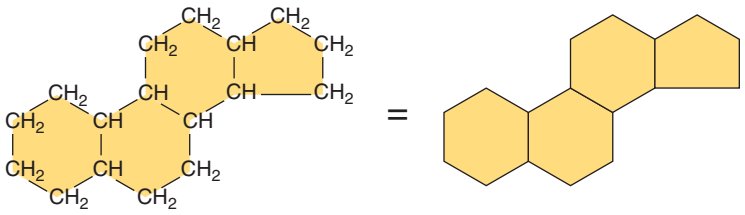


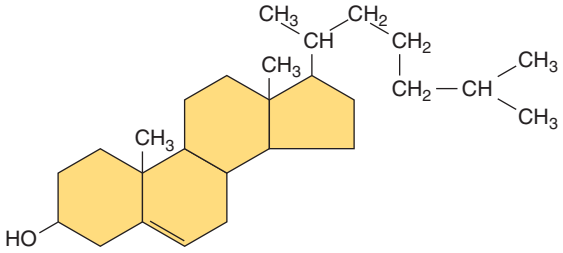
Figure 2.6 Eicosanoids. In these modified 20-carbon fatty acids, the carbons in the middle of the carbon chain form a ring that causes the molecule to fold upon itself.

Steroids

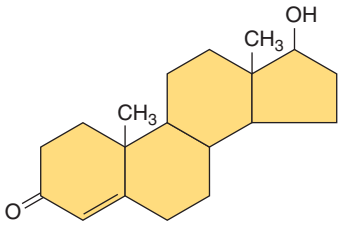
Steroids have a unique chemical structure consisting of three six-carbon rings and one five-carbon ring (Figure 2.7a). The most common steroid is cholesterol (Figure 2.7b). Because of the polar hydroxyl group on one end of the mostly nonpolar cholesterol molecule, it is a slightly amphipathic molecule. Cholesterol is an important component of the *plasma membrane,* the membrane surrounding cells. It is also the precursor molecule for the formation of *bile salts*, molecules secreted by the liver that aid in fat digestion. In addition, cholesterol is the precursor to the steroid hormones, including *testosterone* (Figure 2.7c), *estradiol, cortisol,* and *1,25-dihydroxyvitamin* D_3.



(a) Steroid ring structure



(b) Cholesterol



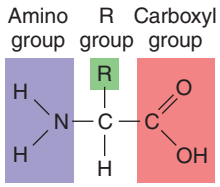
(c) Testosterone

Figure 2.7 Steroids. (a) The basic structure of all steroids, which consists of three six-carbon rings and one five-carbon ring. **(b)** Cholesterol, the most common steroid and the precursor for all other steroids in the body. **(c)** Testosterone, an example of a steroid hormone.

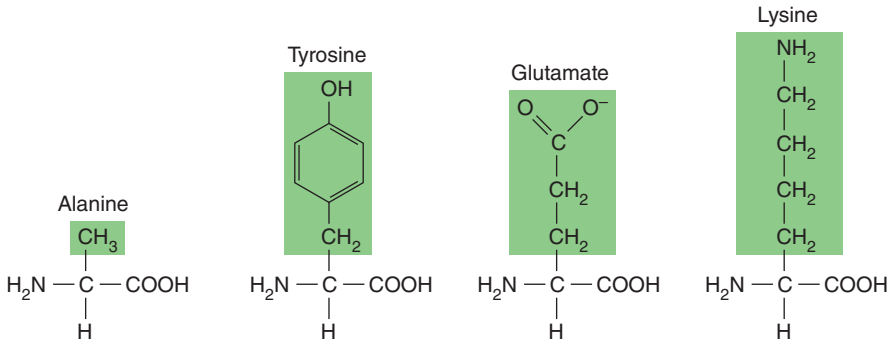
Amino Acids and Proteins

Proteins are polymers of **amino acids,** relatively small biomolecules that contain a central carbon, an amino group, a carboxyl group, a hydrogen, and a residual (R) group (Figure 2.8a). Twenty different R groups exist, so there are 20 different corresponding amino acids. The four amino acids shown in Figure 2.8b—alanine, tyrosine, glutamate, and lysine—have R groups with different chemical properties. The R group is nonpolar in alanine, a polar aromatic ring structure in tyrosine, acidic in glutamate, and basic in lysine. Although we will discuss amino acids here as components of proteins, they have other functions as well, including playing a role in intercellular communication.

Polymers of amino acids are formed by joining two amino acids together with a *peptide bond;* these polymers are, therefore, called **polypeptides.** A peptide bond forms between the amino group of one amino acid and the carboxyl group of another amino acid by a condensation reaction (Figure 2.9). Polypeptides vary in length from just two to several hundred amino acids; the name given to them differs based on their length or



(a) Amino acid



(b) Chemical structures of four amino acids

Figure 2.8 Amino acids. (a) The basic structure of an amino acid. The central carbon is bonded to an amino group, a carboxyl group, a hydrogen, and an R group. **(b)** Structures of four of the 20 amino acids. The R group is nonpolar in alanine, a polar aromatic structure in tyrosine, acidic in glutamate, and basic in lysine.

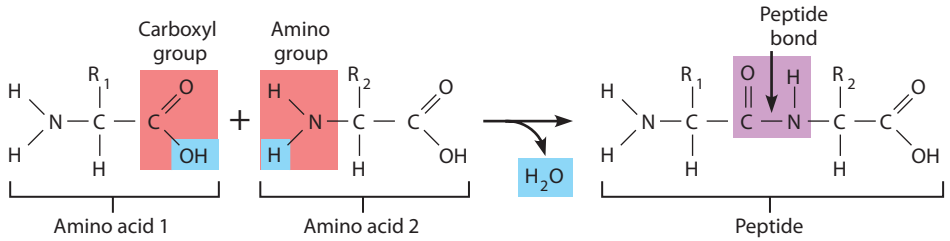
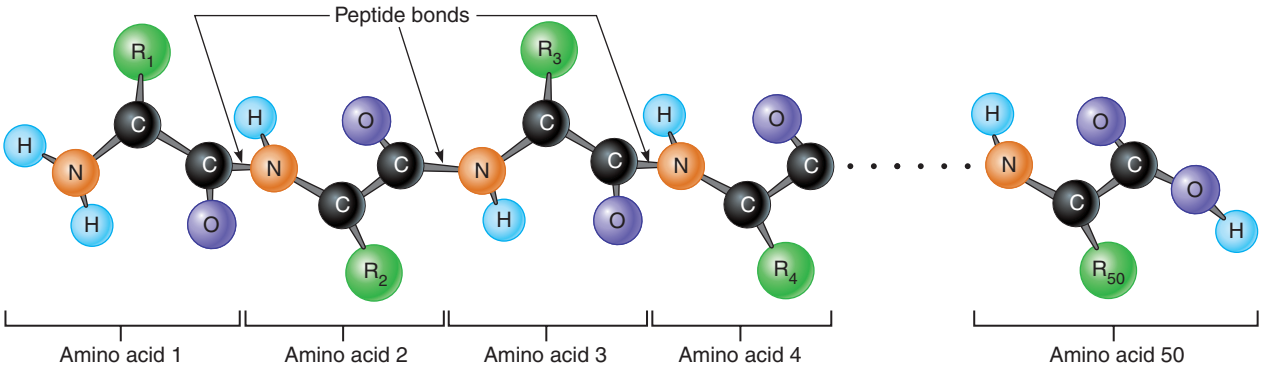
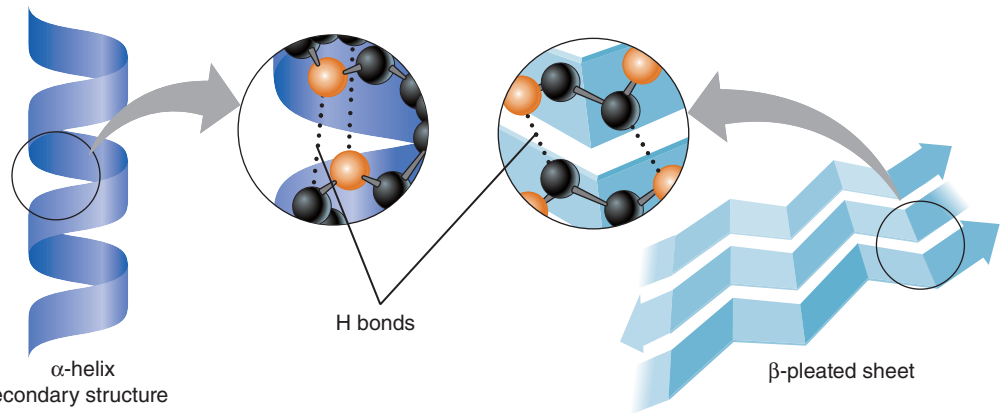


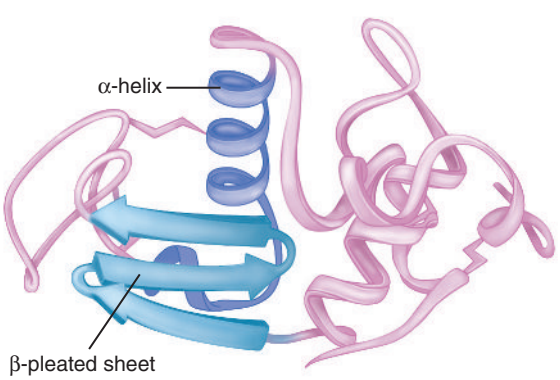
Figure 2.9 Formation of a peptide bond by a condensation reaction. The peptide bond is formed between two amino acids, and water is released.



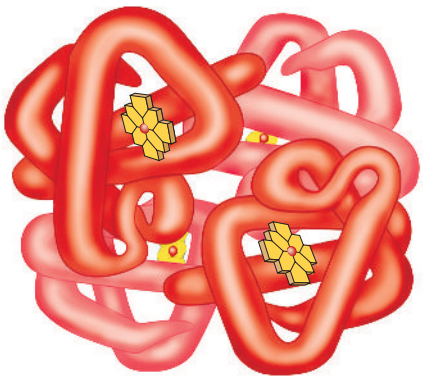
(a) Primary structure



(b) Secondary structure



(c) Tertiary structure



(d) Quaternary structure

Figure 2.10 Levels of protein structure. **(a)** Primary protein structure, which is the sequence of amino acids. **(b)** Secondary protein structure, which is caused by hydrogen bonding between the amino hydrogen of one amino acid and the carboxyl oxygen of another amino acid. Common secondary structures include a-helixes and b-pleated sheets. **(c)** Tertiary protein structure, which is the folding pattern produced by interactions between the R groups of amino acids. The protein shown here is the enzyme *lysozyme*. **(d)** Quaternary protein structure, which is the arrangement of more than one polypeptide chain in a single protein. Shown here is *hemoglobin,* which consists of four polypeptide chains.