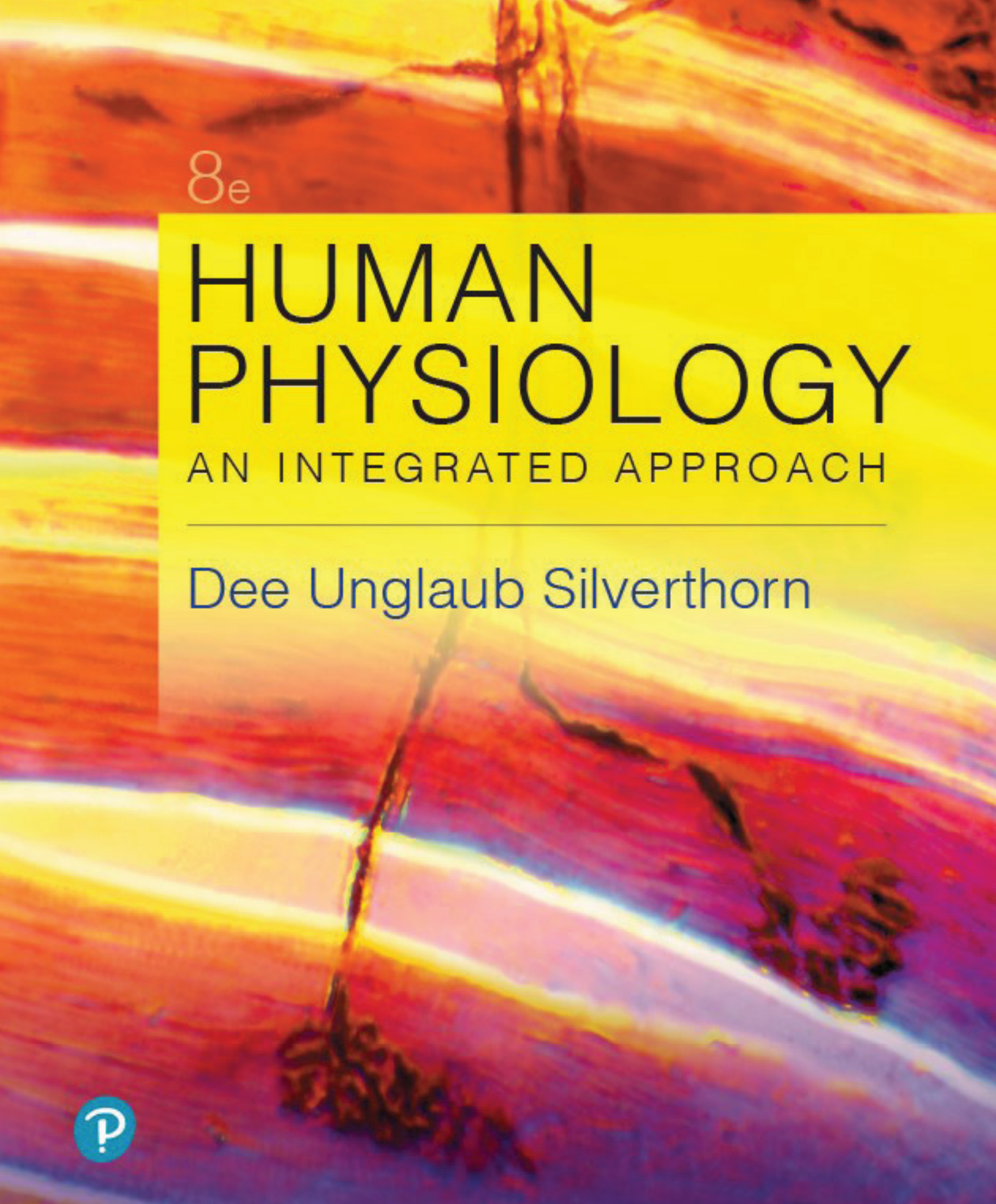

8e
HUMAN
PHYSIOLOGY
AN INTEGRATED APPROACH
Dee Unglaub Silverthorn

Contents in Brief

UNIT 1 Basic Cell Processes: Integration and Coordination

1 Introduction to Physiology 1
2 Molecular Interactions 28
3 Compartmentation: Cells and Tissues 58
4 Energy and Cellular Metabolism 92
5 Membrane Dynamics 121
6 Communication, Integration, and Homeostasis 164

UNIT 2 Homeostasis and Control

7 Introduction to the Endocrine System 194
8 Neurons: Cellular and Network Properties 223
9 The Central Nervous System 271
10 Sensory Physiology 307
11 Efferent Division: Autonomic and Somatic Motor Control 355
12 Muscles 374
13 Integrative Physiology I: Control of Body Movement 414

UNIT 3 Integration of Function

14 Cardiovascular Physiology 432
15 Blood Flow and the Control of Blood Pressure 476
16 Blood 510
17 Mechanics of Breathing 532
18 Gas Exchange and Transport 562
19 The Kidneys 587
20 Integrative Physiology II: Fluid and Electrolyte Balance 618

UNIT 4 Metabolism, Growth, and Aging

21 The Digestive System 654
22 Metabolism and Energy Balance 692
23 Endocrine Control of Growth and Metabolism 728
24 The Immune System 754
25 Integrative Physiology III: Exercise 786
26 Reproduction and Development 800

Strategies for Success

Top Ten Ways to Succeed in Classes that Use Active Learning

By Marilla Svinicki, Ph.D., former Director of the University of Texas Center for Teaching Effectiveness

1. Make the switch from an authority-based conception of learning to a self-regulated conception of learning. Recognize and accept your own responsibility for learning.
2. Be willing to take risks and go beyond what is presented in class or the text.
3. Be able to tolerate ambiguity and frustration in the interest of understanding.
4. See errors as opportunities to learn rather than failures. Be willing to make mistakes in class or in study groups so that you can learn from them.
5. Engage in active listening to what's happening in class.
6. Trust the instructor's experience in designing class activities and participate willingly if not enthusiastically.
7. Be willing to express an opinion or hazard a guess.
8. Accept feedback in the spirit of learning rather than as a reflection of you as a person.
9. Prepare for class physically, mentally, and materially (do the reading, work the problems, etc.).
10. Provide support for your classmate's attempts to learn. The best way to learn something well is to teach it to someone who doesn't understand.

Dr. Dee's Eleventh Rule:
DON'T PANIC! Pushing yourself beyond the comfort zone is scary, but you have to do it in order to improve.

Word Roots for Physiology

Simplify physiology and medicine by learning Latin and Greek word roots. The list below has some of the most common ones.

Using the list, can you figure out what *hyperkalemia* means?*

a- or **an-** without, absence
anti- against
-ase signifies an enzyme
auto self
bi- two
brady- slow
cardio- heart
cephalo- head
cerebro- brain
contra- against
-crine a secretion
crypt- hidden
cutan- skin
-cyte or **cyto-** cell
de- without, lacking
di- two
dys- difficult, faulty
-elle small
-emia in the blood
endo- inside or within
epi- over
erythro- red
exo- outside
extra- outside
gastro- stomach
-gen, -genie produce
gluco-, glyco- sugar or sweet
hemi- half
hemo- blood
hepato- liver
homo- same
hydro- water
hyper- above or excess
hypo- beneath or deficient
inter- between
intra- within
-itis inflammation of
kali- potassium
leuko- white
lipo- fat
lumen inside of a hollow tube
-lysis split apart or rupture
macro- large
micro- small
mono- one
multi- many
myo- muscle
oligo- little, few
para- near, close
patho-, -pathy related to disease
peri- around
poly- many
post- after
pre- before
pro- before
pseudo- false
re- again
retro- backward or behind
semi- half
sub- below
super- above, beyond
supra- above, on top of
tachy- rapid
trans- across, through

* Hyper = excess, kali = potassium, -emia = in the blood, or elevated blood potassium

Owner's Manual

Welcome to Human Physiology! As you begin your study of the human body, one of your main tasks will be to construct for yourself a global view of the body, its systems, and the many processes that keep the systems working. This "big picture" is what physiologists call the integration of systems, and it is a key theme in this book. To integrate information, however, you must do more than simply memorize it. You need to truly understand it and be able to use it to solve problems that you have never encountered before. If you are headed for a career in the health professions, you will do this in the clinics. If you plan a career in biology, you will solve problems in the laboratory, field, or classroom. Analyzing, synthesizing, and evaluating information are skills you need to develop while you are in school, and I hope that the features of this book will help you with this goal.

One of my aims is to provide you not only with information about how the human body functions but also with tips for studying and problem solving. Many of these study aids have been developed with the input of my students, so I think you may find them particularly helpful.

On the following pages, I have put together a brief tour of the special features of the book, especially those that you may not have encountered previously in textbooks. Please take a few minutes to read about them so that you can make optimum use of the book as you study.

Each chapter begins with a list of Learning Outcomes to guide you as you read the chapter. Within the chapters look for the **Running Problem**, **Phys in Action**, and **Try It!** activities. **Phys in Action** are online video clips that I created with the assistance of some of my students. Look for the references to Mastering A&P in the figures with associated Phys in Action clips, and watch Kevin and Michael as they demonstrate physiology in action.

Play Phys in Action
@Mastering Anatomy & Physiology

Pattern recognition is important for all healthcare professionals, so you can begin to develop this skill by learning the key concepts of physiology that repeat over and over as you study different organ systems. Chapter 1 includes two special Focus On features: one on concept mapping, a study strategy that is also used for decision-making in the clinics, and one on constructing and interpreting graphs. The Running Problem in Chapter 1 introduces you to effective ways to find information on the Internet.

Be sure to look for the Essentials and Review figures throughout the book. These figures distill the basics about a topic onto one or two pages, much as the Anatomy Summaries do. My students tell me they find them particularly useful for review when there isn't time to go back and read all the text.

We have also retained the four approaches to learning physiology that proved so popular since this book was first published in 1998.

1. Cellular and Molecular Physiology

Most physiological research today is being done at the cellular and molecular level, and there have been many exciting developments in molecular medicine and physiology in the 10 years since the first edition. For example, now scientists are paying more attention to primary cilia, the single cilium that occurs on most cells of the body. Primary cilia are thought to play a role in some kidney and other diseases. Look for similar links between molecular and cellular biology, physiology, and medicine throughout the book.

FIG. 3.5 Cilia and flagella

(a) Cilia on surface of respiratory epithelium

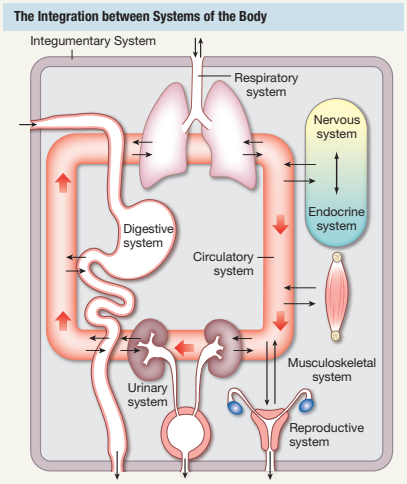
2. Physiology as a Dynamic Field

Physiology is a dynamic discipline, with numerous unanswered questions that merit further investigation and research. Many of the "facts" presented in this text are really only our current theories, so you should be prepared to change your mental models as new information emerges from scientific research.

EMERGING CONCEPTS

How to Use this Book

3. An Emphasis on Integration



The organ systems of the body do not work in isolation, although we study them one at a time. To emphasize the integrative nature of physiology, three chapters (Chapters 13, 20, and 25) focus on how the physiological processes of multiple organ systems coordinate with each other, especially when homeostasis is challenged.

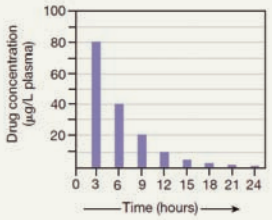
4. A Focus on Problem Solving

One of the most valuable life skills students should acquire is the ability to think critically and use information to solve problems. As you study physiology, you should be prepared to practice these skills. You will find a number of features in this book, such as the Concept Check questions and Figure and Graph Questions. These "test yourself" questions are designed to challenge your critical thinking and analysis skills. In each chapter, read the Running Problem as you work through the text and see if you can apply what you're reading to the clinical scenario described in the problem.

Also, be sure to look at the back of the text, where we have combined the index and glossary to save time when you are looking up unfamiliar words. The appendices have the answers to the Concept Check questions, Figure and Graph Questions, and end-of-chapter questions, as well as reviews of physics, logarithms, and basic genetics. The back end papers include a periodic table of the elements, diagrams of anatomical positions of the body, and tables with conversions and normal values of blood components. Take a few minutes to look at all these features so that you can make optimum use of them.

Level Four Quantitative Problems

30. The following graph represents the disappearance of a drug from the blood as the drug is metabolized and excreted. Based on the graph, what is the half-life of the drug?



It is my hope that by reading this book, you will develop an integrated view of physiology that allows you to enter your chosen profession with respect for the complexity of the human body and a clear vision of the potential of physiological and biomedical research. May you find physiology as fun and exciting I do. Good luck with your studies!

Warmest regards,
Dr. Dee (as my students call me)
silverthorn@utexas.edu

Phys in Action Video Topics:

pp. 130–131 Fig. 5.4 Osmolarity & Tonicity
pp. 154–155 Fig. 5.23 Membrane Potential
pp. 458–459 Fig.14.15 Electrocardiogram
p. 494 Fig. 15.14 Cardiovascular Control
p. 545 Fig. 17.7 The Spirometer
p. 549 Fig. 17.10 Respiratory Pressure
p. 557 Fig. 17.13 Alveolar Gases
p. 573 Fig. 18.7 Hemoglobin-Oxygen Transport
p. 610 Fig. 19.13 Renal Clearance
p. 793 Fig. 25.8 Blood Pressure & Exercise

Try It Activities:

p. 21 Graphing
p. 135 Membrane Models (Lipid bylayer)
p. 251 Action Potentials
p. 325 Salty-Sweet Taste Experiment
p. 468 Frank-Starling Law of the Heart
p. 605 Insulin
p. 682 Oral Rehydration Therapy

EIGHTH EDITION

HUMAN PHYSIOLOGY

Dee Unglaub Silverthorn, Ph.D.
UNIVERSITY OF TEXAS, AUSTIN

with contributions by

Bruce R. Johnson, Ph.D.
CORNELL UNIVERSITY

and

William C. Ober, M.D.
ILLUSTRATION COORDINATOR

Claire E. Ober, R.N.
ILLUSTRATOR

Anita Impaglizzo,
ILLUSTRATOR

Andrew C. Silverthorn, M.D.
CLINICAL CONSULTANT

Courseware Portfolio Manager: *Lauren Harp*
Content Producer: *Deepti Agarwal*
Managing Producer: *Nancy Tabor*
Courseware Director, Content Development: *Barbara Yien*
Courseware Editorial Assistant: *Dapinder Dosanjh*
Rich Media Content Producer: *Nicole Constantine*
Mastering Content Developer, Science: *Lorna Perkins*
Full-Service Vendor: *SPi Global*
Copyeditor: *Alyson Platt*

Art Project Manager: *Stephanie Marquez, Imagineering Art LLC*
Illustrators: *William C. Ober, Anita Impagliazzo, and Claire E. Ober*
Design Manager: *Maria Guglielmo Walsh*
Interior Designer: *Gary Hespenheide*
Cover Designer: *Gary Hespenheide*
Rights & Permissions Project Manager: *Katrina Mohn, Cenveo Publisher Services*
Rights & Permissions Management: *Ben Ferrini*
Manufacturing Buyer: *Stacey Weinberger, LSC Communications*
Product Marketing Manager: *Wendy Mears*

Cover Photo: *Motor Neuron in Muscle*
Credit: *Kent Wood/Science Source*

Library of Congress Cataloging-in-Publication Data
Catalogue in Publication Data is on file with the Library of Congress

ISBN 10: 0-13-460519-5; ISBN 13: 978-0-13-460519-7 (Student edition)
1 18 ISBN 10: 0-13-470434-7; ISBN 13: 978-0-13-470443-0 (Instructor's Review Copy)

www.pearson.com

ABOUT THE AUTHOR

DEE UNGLAUB SILVERTHORN studied biology as an undergraduate at Newcomb College of Tulane University, where she did research on cockroaches. For graduate school, she switched to studying crabs and received a Ph.D. in marine science from the Belle W. Baruch Institute for Marine and Coastal Sciences at the University of South Carolina. Her research interest is epithelial transport, and most recently work in her laboratory has focused on transport properties of the chick allantoic membrane. Her teaching career started in the Physiology Department at the Medical University of South Carolina but over the years she has taught a wide range of students, from medical and college students to those still preparing for higher education. At the University of Texas–Austin, she teaches physiology in both lecture and laboratory settings, and instructs graduate students on developing teaching skills in the life sciences. In 2015 she joined the faculty of the new UT-Austin Dell Medical School. She has received numerous teaching awards and honors, including a 2011 UT System Regents' Outstanding Teaching Award, the 2009 Outstanding Undergraduate Science Teacher Award from the Society for College Science Teachers, the American Physiological Society's Claude Bernard Distinguished Lecturer and Arthur C. Guyton Physiology Educator of the Year, and multiple awards from UT–Austin, including the Burnt Orange Apple Award. The first edition of her textbook won the 1998 Robert W. Hamilton Author Award for best textbook published in 1997–1998 by a University of Texas faculty member. Dee was the president of the Human Anatomy and Physiology Society in 2012–2013, has served as editor-in-chief of Advances in Physiology Education, and is currently chair of the American Physiological Society Book Committee. She works with members of the International Union of Physiological Sciences to improve physiology education in developing countries, and this book has been translated into seven languages. Her free time is spent creating multimedia fiber art and enjoying the Texas hill country with her husband, Andy, and their dogs.

Michael Chirillo, Dee Silverthorn, and Kevin Christmas

About the Illustrators

William C. Ober, M.D. (*art coordinator and illustrator*) received his undergraduate degree from Washington and Lee University and his M.D. from the University of Virginia. He also studied in the Department of Art as Applied to Medicine at Johns Hopkins University. After graduation, Dr. Ober completed a residency in Family Practice and later was on the faculty at the University of Virginia in the Department of Family Medicine and in the Department of Sports Medicine. He also served as Chief of Medicine of Martha Jefferson Hospital in Charlottesville, VA. He is currently a visiting Professor of Biology at Washington & Lee University, where he has taught several courses and led student trips to the Galapagos Islands. He was part of the Core Faculty at Shoals Marine Laboratory, where he taught Biological Illustration for 22 years. The textbooks illustrated by Medical & Scientific Illustration have won numerous design and illustration awards.

Claire E. Ober, R.N. (*illustrator*) practiced pediatric and obstetric nursing before turning to medical illustration as a full-time career. She returned to school at Mary Baldwin College where she received her degree with distinction in studio art. Following a five-year apprenticeship, she has worked as Dr. Ober's partner in Medical and Scientific Illustration since 1986. She was also on the Core Faculty at Shoals Marine Laboratory and co-taught Biological Illustration at both Shoals Marine Lab and at Washington and Lee University.

About the Clinical Consultant

Andrew C. Silverthorn, M.D. is a graduate of the United States Military Academy (West Point). He served in the infantry in Vietnam, and upon his return entered medical school at the Medical University of South Carolina in Charleston. He was chief resident in family medicine at the University of Texas Medical Branch, Galveston, and is currently a family physician in solo practice in Austin, Texas. When Andrew is not busy seeing patients, he may be found on the golf course or playing with his two rescue dogs, Molly and Callie.

About the Contributor

Bruce Johnson, Ph.D. is a Senior Research Associate in the Department of Neurobiology and Behavior at Cornell University. He earned biology degrees at Florida State University (B.A.), Florida Atlantic University (M.S.), and at the Marine Biological Laboratory in Woods Hole (Ph.D.) through the Boston University Marine Program. For three decades, he has led Cornell's highly-praised Principles of Neurophysiology course, in which students receive hands-on instruction in principles and methods in neurophysiology. He is a coauthor of *Crawdad: a CD-ROM Lab Manual for Neurophysiology* and the *Laboratory Manual for Physiology*. Bruce has directed and taught in neuroscience faculty workshops sponsored by NSF (Crawdad), ADInstruments (Crawdad and CrawFly), the Grass Foundation and the Faculty for Undergraduate Neuroscience (FUN). He has also lead workshops and neuroscience courses at the Universities of Copenhagen (Denmark), Cologne (Germany), Ibadan (Nigeria), and the Marine Biological Laboratory. Bruce has been named a Most Influential Faculty Member by the graduating senior class at Cornell and awarded the John M. and Emily B. Clark Award for Distinguished Teaching at Cornell. His other teaching awards include the FUN Educator of the Year Award, FUN Career Service Award, and co-recipient of the 2016 Award for Education in Neuroscience, sponsored by the Society for Neuroscience. He is currently the Editor-in-Chief of the *Journal of Undergraduate Neuroscience Education*. Bruce's research addresses the cellular and synaptic mechanisms of motor network plasticity.

DEDICATION

The 8th edition is dedicated to my colleagues who read every word of the first edition manuscript and provided valuable feedback that helped shape the book.

Park City, Utah, June 1995
(Standing, L to R): Judy Sullivan, Patricia Munn, Dee Silverthorn, Mary Ann Rokitka, Richard Walker, Pat Berger, Norman Scott
(Seated) Shana Ederer, Prentice Hall development editor

This page intentionally left blank

NEW TO THIS EDITION

The Eighth Edition of *Human Physiology: An Integrated Approach* builds upon the thorough coverage of integrative and molecular physiology topics that have always been the foundation of this book. The biggest change is a completely revised Chapter 24 on immunology. This field has expanded dramatically since the First Edition published in 1997, and it was time to step back and re-think the presentation of this complicated and complex subject. Neurophysiology is also changing rapidly, requiring multiple updates in Chapters 8 through 11. In nearly every chapter the latest developments in research and medicine meant changes to the presentation of information.

Continuing the revision of the art introduced in the Seventh Edition, we created additional Review and Essentials figures that students can use for quick review as well as new Anatomy Summaries and concept maps. Figures from previous editions that were significantly modified or eliminated are still available to instructors on the Instructor's DVD and in the Instructor Resources area of Mastering A&P.

In addition to the online Phys in Action videos that are referenced in related figures, we have new Try It! activities throughout the book. These activities present data, usually from classic experiments, and ask the students to interpret the results. Topics include Benjamin Franklin's little-known experiment that helped development of the phospholipid bilayer model of the membrane, and the experiments that resulted in oral rehydration therapy for treating cholera.

HIGHLIGHTS OF CONTENT UPDATES

Chapter 1 Introduction to Physiology

- New Focus on Graphing with a new Try It! activity
- Added information on the connectome and microbiome
- Updated information on literature searches and citations

Chapter 2 Molecular Interactions

- Four new element names in the periodic table, inside the back cover of the text
- Added ribbon diagram/Richardson diagram of proteins

Chapter 3 Compartmentation: Cells and Tissues

- Explanations of light and electron microscopy
- New Emerging Concepts box on induced pluripotent stem cells (iPSs)

Chapter 5 Membrane Dynamics

- New Try It! activity on lipid bilayers
- Three Phys in Action video references in Figures 5.4, 5.6, and 5.23

Chapter 6 Communication, Integration, and Homeostasis

- Juxtacrine signaling
- Updated information on NIH Common Fund's *Building Blocks, Biological Pathways, and Networks* Program
- Updated the discussion on cytokine families
- Re-classified receptor-enzymes as catalytic receptors
- GPCR for eicosanoids

Chapter 7 Introduction to the Endocrine System

- Updated information on calcitonin gene-related peptide
- Updated information on melatonin and melatonin-related drugs

Chapter 8 Neurons: Cellular and Network Properties

- Update on mechanisms of axonal transport and associated diseases: dynein, kinesin, fragile X, Alzheimer's, microcephaly
- Try It! activity on action potentials
- New link to online calculator for Nernst and GHK equations
- Added discussion of resistance of extracellular fluid to discussion of resistance to current flow
- Added space constant discussion

Chapter 9 The Central Nervous System

- Added lateral sulcus, insula, cerebral aqueduct
- Re-classification of stages of sleep
- Pericytes in blood-brain barrier formation
- Dopaminergic pathways and addiction

Chapter 10 Sensory Physiology

- New Try It! activity on sweet and salty taste
- Additional information on non-neural sensors and Merkel cells

Chapter 11 Efferent Division: Autonomic and Somatic Motor Control

- Expanded table on properties of autonomic neurotransmitter receptors
- Added N_N and N_M nicotinic subtypes
- Added discussion of sarin nerve gas
- Updated anti-nicotine vaccine
- Etiology of diabetic neuropathy

Chapter 12 Muscles

- Expanded discussion of myosin light chains in striated muscle
- New table with autonomic effects on smooth muscles

Chapter 13 Integrative Physiology I: Control of Body Movement

- Addition information on reflexes and muscle tone
- Updated Parkinson's treatments
- Expanded tetanus Running Problem

Chapter 14 Cardiovascular Physiology

- New Running problem on atypical presentation of myocardial infarction in a woman
- New section and new figure on coronary circulation
- New Try It! activity on Starling's law of the heart
- Added discussion of echocardiography
- Expanded ejection fraction discussion
- New discussion of ion channel subtypes

Chapter 15 Blood Flow and the Control of Blood Pressure

- Updated information on pericytes and their functions
- New discussion of blood-retinal barrier
- Updated discussion of angiogenesis including angiopoietin and angiopoietin/Tie signaling pathway.
- New Review quantitative question on Bernoulli's principle of fluid flow
- New sections on coronary blood flow and cerebral blood flow
- Updated statistics on CV diseases
- Added neurogenic shock

Chapter 16 Blood

- Revised art, includes Figures 16.2, 16.4, 16.6, and 16.7
- Updated information on treatment for sickle cell disease

Chapter 17 Mechanics of Breathing

- Forced vital capacity test
- FEV_1/FVC ratio
- New figure and Figure Question for forced vital capacity test
- Antenatal corticosteroids to prevent NRDS

Chapter 18 Gas Exchange and Transport

- Updated information on action of carbonic anhydrase
- Updated information on hemoglobin-based blood substitutes
- Carotid body plasticity in disease states

Chapter 19 The Kidneys

- New map for factors influencing GFR
- Updated model of organic anion transport, including OAT family transporters
- New figure and table on renal handling of some common substances
- New Try It! activity on glucosuria and the discovery of insulin
- PAH clearance and calculation of renal plasma flow discussion
- New term: renal handling
- New Figure Question
- Updated glomerular filtration barrier to include glomerular capillary glycocalyx, slit diaphragm

Chapter 20 Integrative Physiology II: Fluid and Electrolyte Balance

- New section on role of kidney in hypertension
- New Concept Check question
- Expanded discussion of K^+ handling
- Added zona gomerulosa, paraventricular and supraoptic nuclei
- New section on endocrine pathologies in fluid balance
- New Level 3 Review question on Liddle's syndrome

Chapter 21 The Digestive System

- New Try It! activity on role of the SGLT in treating diarrhea
- New information on cholera vaccine
- Updated discussion on microfold cells
- Added guanylate cyclase-C (GC-C), uroguanylin and guanylin, plecanatide

Chapter 22 Metabolism and Energy Balance

- Updated model for appetite
- Updated pharmacological trials for anorexia
- Latent autoimmune diabetes; also called type 1.5; gestational diabetes (GDM); MODY, maturity-onset diabetes of the young.
- Added mechanism of action of metformin
- Added cardiovascular risk calculator link

Chapter 23 Endocrine Control of Growth and Metabolism

- Expanded discussion of melanocortins and their receptors in the control of food intake.
- Agouti-related protein (AGRP), MC4R receptors
- Added explanation of the role of ghrelin in growth hormone release
- New figure for feedback control of growth hormone release
- Updated discussion on off-label use of growth hormone in adults
- Primary cilia in chrondrocytes and osteocytes act as mechnotransducers
- Role of calcium-sensing receptor and NALCN channel in neuronal excitability
- New figure and discussion of intestinal and renal Ca^{2+} transport
- Skeletal deformaties in ciliopathies
- New figure and discussion of bone remodeling, including RANK, RANKL, osteoprotegerin, osteoid
- New Review question on osteopetrosis

Chapter 24 The Immune System

- 6 NEW figures. Most art significantly revised.
- Added concepts include long-lived plasma cells, mucosa-associated lymphoid tissue (MALT), self-antigens, negative selection, hygiene hypothesis, Zika virus, DAMPS – danger-associated molecular patterns, B cell receptors, regulatory T cells (Tregs)
- Updated information on IgD, contact-dependent signaling

Chapter 26 Reproduction and Development

- Kisspeptin control of GNRH and role in puberty
- Origin of the acrosome
- *Flibanserin* for low libido in women

ACKNOWLEDGMENTS

Writing, editing, and publishing a textbook is a group project that requires the talent and expertise of many people. No one scientist has the detailed background needed in all areas to write a book of this scope, and I am indebted to all my colleagues who so generously share their expertise in each edition. I particularly want to acknowledge Bruce Johnson, Cornell University, Department of Neurobiology and Behavior, a superb neurobiologist and educator, who once again ensured that the chapters on neurobiology are accurate and reflect the latest developments in that rapidly changing field. I would also like to thank Michael Chirillo, a former graduate teaching assistant of mine, for his work developing the Try It! features in between interviewing for and starting a medical residency program. Peter English, a colleague and former student, has also joined the team helping with this revision.

A huge thank you goes to immunologists Natalie Steinel, from UT-Austin Dell Medical School, and Tynan A. Becker, from University of Alaska, for their assistance and critical review of the Chapter 24 revision. Brian Sumner, a 3rd year medical student at the George Washington University School of Medicine, graciously volunteered time out of his busy clinical rotations to read the revised chapter and ensure that it was student-friendly.

The art team of Bill Ober, M.D. and Claire Ober, R.N. has worked with me since the first edition, and I am always grateful for their scientifically astute suggestions and revisions. They were joined in the last edition by Anita Impagliazzo, who brought a fresh eye and new figure ideas.

Instructors and students often contact me directly about the book, and for this edition I would particularly like to thank Allison Brekke, James Mayer, and Dean A. Wiseman for comments and suggestions. Thanks also to my students who keep me informed of the typos that creep in no matter how many people look at the manuscript and pages.

Many other people devoted their time and energy to making this book a reality, and I would like to thank them all, collectively and individually. I apologize in advance to anyone whose name I have omitted.

Reviewers

I am particularly grateful to the instructors who reviewed one or more chapters of the last edition. There were many suggestions in their thoughtful reviews that I was unable to include in the text, but I appreciate the time and thought that went into their comments. The reviewers for this edition include:

Jake Brashears, San Diego City College
Trevor Cardinal, California Polytechnic State University
Michael S. Finkler, Indiana University Kokomo
Victor Fomin, University of Delaware
Jill Gifford, Youngstown State University
David Kurjiaka, Grand Valley State University
Mary Jane Niles, University of San Francisco
Rudy M. Ortiz, University of California, Merced
Jennifer Rogers, University of Iowa
Jia Sun, Imperial Valley College
Alan Sved, University of Pittsburgh

Many other instructors and students took time to write or e-mail queries or suggestions for clarification, for which I thank them. I am always delighted to have input, and I apologize that I do not have room to acknowledge them all individually.

Specialty Reviews

No one can be an expert in every area of physiology, and I am deeply thankful for my friends and colleagues who reviewed entire chapters or answered specific questions. Even with their help, there may be errors, for which I take full responsibility. The specialty reviewers for this edition were:

Natalie Steinel, UT-Austin Dell Medical School
Tynan A. Becker, University of Alaska

Photographs

I would like to thank Kristen Harris, University of Texas who generously provided micrographs from her research.

Supplements

Damian Hill once again worked with me to revise and improve the Instructor Resource Manual that accompanies the book. I believe that supplements should reflect the style and approach of the text, so I am grateful that Damian has continued to be my alter-ego for so many editions. Peter English is helping with Mastering activities this revision.

I would also like to thank my colleagues who helped with the test bank and media supplements for this edition:

Heidi Bustamante, University of Colorado, Boulder
Chad M. Wayne, University of Houston
Margaret Flemming, Austin Community College
Cheryl Neudauer, Minneapolis Community & Technical College

The Development and Production Team

Writing a manuscript is only a first step in the long and complicated process that results in a bound book with all its ancillaries. The team that works with me on book development deserves a lot of credit for the finished product. Gary Hespenheide designed a bright and cheerful cover that continues our tradition of images that show science as art. Anne A. Reid, my long-time developmental

editor, is always wonderful to work with, and provides thoughtful suggestions that improve what I wrote.

The team at Pearson Education worked tirelessly to see this edition move from manuscript to bound book. My acquisitions editor, Kelsey Volker Churchman, was joined by Lauren Harp, Senior Acquisitions Editor for the second part of this revision. Ashley Williams and Kate Abderholden, assistant editors, kept track of everyone and everything for us. Chriscelle Palaganas, Program Manager, provided excellent guidance and support throughout the whole production process.

The task of coordinating production fell to Pearson Content Producer Deepti Agarwal. Nathaniel Jones handled composition and project management, and Project Manager Stephanie Marquez at the art house, Imagineering, managed the team that prepared the art for production. Katrina Mohn was the photo researcher who found the wonderful new photos that appear in this edition. Nicole Constantine was the assistant media producer who kept my supplements authors on task and on schedule. Wendy Mears is the product marketing manager who works with the excellent sales teams at Pearson Education and Pearson International, and Derek Perrigo is the Field Marketing Manager for the anatomy and physiology list.

Special Thanks

As always, I would like to thank my students and colleagues who looked for errors and areas that needed improvement. I've learned that awarding one point of extra credit for being the first student to report a typo works really well. My graduate teaching assistants over the years have all played a huge role in my teaching, and their input has helped shape how I teach. Many of them are now faculty members themselves. They include:

Ari Berman, Ph.D.
Lawrence Brewer, Ph.D.
Kevin Christmas, Ph.D.
Michael Chirillo, M.D., Ph.D.
Lynn Cialdella Kam, M.S., M.B.A., Ph.D.
Sarah Davies Kanke, Ph.D.
Peter English, Ph.D.
Carol C. Linder, Ph.D.
Karina Loyo-Garcia, Ph.D.
Jan M. Machart, Ph.D.
Tonya Thompson, M.D.
Patti Thorn, Ph.D.
Justin Trombold, Ph.D.
Kurt Venator, Ph.D.
Kira Wenstrom, Ph.D.

Finally, special thanks to my colleagues in the American Physiological Society, the Human Anatomy & Physiology Society, and the International Union of Physiological Sciences whose experiences in the classroom have enriched my own understanding of how to teach physiology. I would also like to recognize a special group of friends for their continuing support: Penelope Hansen (Memorial University, St. John's), Mary Anne Rokitka (SUNY Buffalo), Rob Carroll (East Carolina University School of Medicine), Cindy Gill (Hampshire College), and Joel Michael (Rush Medical College), as well as Ruth Buskirk, Jeanne Lagowski, Jan M. Machart and Marilla Svinicki (University of Texas).

As always, I thank my family and friends for their patience, understanding, and support during the chaos that seems inevitable with book revisions. The biggest thank you goes to my husband Andy, whose love, support, and willingness to forgo home-cooked meals on occasion help me meet my deadlines.

A Work in Progress

One of the most rewarding aspects of writing a textbook is the opportunity it has given me to meet or communicate with other instructors and students. In the 20 years since the first edition was published, I have heard from people around the world and have had the pleasure of hearing how the book has been incorporated into their teaching and learning.

Because science textbooks are revised every 3 or 4 years, they are always works in progress. I invite you to contact me or my publisher with any suggestions, corrections, or comments about this edition. I am most reachable through e-mail at silverthorn@utexas.edu. You can reach my editor at the following address:

Applied Sciences
Pearson Education
1301 Sansome Street
San Francisco, CA 94111

Dee U. Silverthorn
silverthorn@utexas.edu
University of Texas
Austin, Texas

CONTENTS

UNIT 1 Basic Cell Processes: Integration and Coordination

CHAPTER 1
Introduction to Physiology 1

Physiology Is an Integrative Science 2
RUNNING PROBLEM **What to Believe? 2**
EMERGING CONCEPTS *The Changing World of Omics 3*
Function and Mechanism 4
Themes in Physiology 5
FOCUS ON . . . Mapping 6
Theme 1: Structure and Function Are Closely Related 8
Theme 2: Living Organisms Need Energy 8
Theme 3: Information Flow Coordinates Body Functions 9
Theme 4: Homeostasis Maintains Internal Stability 9
Homeostasis 9
What Is the Body's Internal Environment? 10
Homeostasis Depends on Mass Balance 10
Excretion Clears Substances from the Body 12
Homeostasis Does Not Mean Equilibrium 13
Control Systems and Homeostasis 13
Local Control Is Restricted to a Tissue 13
Reflex Control Uses Long-Distance Signaling 14
Response Loops Begin with a Stimulus 14
Feedback Loops Modulate the Response Loop 15
Negative Feedback Loops Are Homeostatic 15
Positive Feedback Loops Are Not Homeostatic 16
Feedforward Control Allows the Body to Anticipate Change 17
Biological Rhythms Result from Changes in a Setpoint 17
The Science of Physiology 18
Good Scientific Experiments Must Be Carefully Designed 18
FOCUS ON . . . Graphing 20
The Results of Human Experiments Can Be Difficult to Interpret 22

CHAPTER SUMMARY 25 | **REVIEW QUESTIONS** 26

CHAPTER 2
Molecular Interactions 28

RUNNING PROBLEM **Chromium Supplements 29**
Molecules and Bonds 29
Most Biomolecules Contain Carbon, Hydrogen, and Oxygen 29
Electrons Have Four Important Biological Roles 33
Covalent Bonds between Atoms Create Molecules 33
Noncovalent Bonds Facilitate Reversible Interactions 39
Noncovalent Interactions 40
Hydrophilic Interactions Create Biological Solutions 40
Molecular Shape Is Related to Molecular Function 40
Hydrogen Ions in Solution Can Alter Molecular Shape 41
Protein Interactions 46
Proteins Are Selective about the Molecules They Bind 46
Protein-Binding Reactions Are Reversible 47
Binding Reactions Obey the Law of Mass Action 47
The Dissociation Constant Indicates Affinity 48
Multiple Factors Alter Protein Binding 48
The Body Regulates the Amount of Protein in Cells 51
Reaction Rate Can Reach a Maximum 51

CHAPTER SUMMARY 55 | **REVIEW QUESTIONS** 56

CHAPTER 3
Compartmentation: Cells and Tissues 58

Functional Compartments of the Body 59
RUNNING PROBLEM **Pap Tests Save Lives 59**
The Lumens of Some Organs Are Outside the Body 59
Functionally, the Body Has Three Fluid Compartments 61
Biological Membranes 61
The Cell Membrane Separates Cell from Environment 61
Membranes Are Mostly Lipid and Protein 61
Membrane Lipids Create a Hydrophobic Barrier 62
Membrane Proteins May Be Loosely or Tightly Bound to the Membrane 62
Membrane Carbohydrates Attach to Both Lipids and Proteins 64

Intracellular Compartments 64

Cells Are Divided into Compartments 65

The Cytoplasm Includes Cytosol, Inclusions, Fibers, and Organelles 65

Inclusions Are in Direct Contact with the Cytosol 65

Cytoplasmic Protein Fibers Come in Three Sizes 68

Microtubules Form Centrioles, Cilia, and Flagella 68

EMERGING CONCEPTS *Single Cilia Are Sensors 68*

The Cytoskeleton Is a Changeable Scaffold 68

Motor Proteins Create Movement 69

Organelles Create Compartments for Specialized Functions 70

The Nucleus Is the Cell's Control Center 71

Tissues of the Body 73

Extracellular Matrix Has Many Functions 73

Cell Junctions Hold Cells Together to Form Tissues 73

Epithelia Provide Protection and Regulate Exchange 75

Connective Tissues Provide Support and Barriers 80

Muscle and Neural Tissues Are Excitable 82

Tissue Remodeling 84

Apoptosis Is a Tidy Form of Cell Death 84

Stem Cells Can Create New Specialized Cells 85

EMERGING CONCEPTS *Induced Pluripotent Stems Cells 85*

FOCUS ON . . . The Skin 86

Organs 87

CHAPTER SUMMARY 88 | **REVIEW QUESTIONS** 90

CHAPTER 4

Energy and Cellular Metabolism 92

RUNNING PROBLEM **Tay-Sachs Disease: A Deadly Inheritance 93**

Energy in Biological Systems 93

Energy Is Used to Perform Work 94

Energy Comes in Two Forms: Kinetic and Potential 94

Energy Can Be Converted from One Form to Another 95

Thermodynamics Is the Study of Energy Use 95

Chemical Reactions 96

Energy Is Transferred between Molecules during Reactions 96

Activation Energy Gets Reactions Started 96

Energy Is Trapped or Released during Reactions 96

Net Free Energy Change Determines Reaction Reversibility 98

Enzymes 98

Enzymes Are Proteins 99

Reaction Rates Are Variable 99

Enzymes May Be Activated, Inactivated, or Modulated 99

Enzymes Lower Activation Energy of Reactions 100

Enzymatic Reactions Can Be Categorized 101

Metabolism 102

Cells Regulate Their Metabolic Pathways 102

Catabolic Pathways Produce ATP 104

One Glucose Molecule Can Yield 30–32 ATP 109

Anaerobic Metabolism Makes Two ATP 109

Proteins Are the Key to Cell Function 110

DNA Guides the Synthesis of RNA 113

Alternative Splicing Creates Multiple Proteins from One DNA Sequence 114

mRNA Translation Links Amino Acids 114

EMERGING CONCEPTS *Purple Petunias and RNAi 114*

Protein Sorting Directs Proteins to Their Destination 115

Proteins Undergo Posttranslational Modification 115

CHAPTER SUMMARY 118 | **REVIEW QUESTIONS** 119

CHAPTER 5

Membrane Dynamics 121

RUNNING PROBLEM **Cystic Fibrosis 122**

Homeostasis Does Not Mean Equilibrium 122

Osmosis and Tonicity 124

The Body Is Mostly Water 124

The Body Is in Osmotic Equilibrium 124

Osmolarity Describes the Number of Particles in Solution 125

Tonicity Describes the Volume Change of a Cell 126

Transport Processes 131

Cell Membranes Are Selectively Permeable 131

Diffusion 132

Lipophilic Molecules Cross Membranes by Simple Diffusion 134

Protein-Mediated Transport 136

Membrane Proteins Have Four Major Functions 136

Channel Proteins Form Open, Water-Filled Passageways 138

Carrier Proteins Change Conformation to Move Molecules 139

Facilitated Diffusion Uses Carrier Proteins 141

Active Transport Moves Substances against Their Concentration Gradients 142

Carrier-Mediated Transport Exhibits Specificity, Competition, and Saturation 144

Vesicular Transport 146

Phagocytosis Creates Vesicles Using the Cytoskeleton 146

Endocytosis Creates Smaller Vesicles 147

CLINICAL FOCUS *LDL: The Lethal Lipoprotein 147*

Exocytosis Releases Molecules Too Large for Transport Proteins 147

Epithelial Transport 149

Epithelial Transport May Be Paracellular or Transcellular 149

Transcellular Transport of Glucose Uses Membrane Proteins 150

Transcytosis Uses Vesicles to Cross an Epithelium 151

The Resting Membrane Potential 152

Electricity Review 152

The Cell Membrane Enables Separation of Electrical Charge in the Body 152

All Living Cells Have a Membrane Potential 153

The Resting Membrane Potential Is Due Mostly to Potassium 156

Changes in Ion Permeability Change the Membrane Potential 157

Integrated Membrane Processes: Insulin Secretion 158

CHAPTER SUMMARY 160 | **REVIEW QUESTIONS** 161

CHAPTER 6

Communication, Integration, and Homeostasis 164

RUNNING PROBLEM **Diabetes Mellitus: A Growing Epidemic 165**

Cell-to-Cell Communication 165

Gap Junctions Create Cytoplasmic Bridges 165

Contact-Dependent Signals Require Cell-to-Cell Contact 165

Local Communication Uses Paracrine and Autocrine Signals 167

Long-Distance Communication May Be Electrical or Chemical 167

Cytokines May Act as Both Local and Long-Distance Signals 167

Signal Pathways 168

Receptor Proteins Are Located Inside the Cell or on the Cell Membrane 168

Membrane Proteins Facilitate Signal Transduction 170

The Most Rapid Signal Pathways Change Ion Flow through Channels 171

Most Signal Transduction Uses G Proteins 173

Many Lipophobic Hormones Use GPCR-cAMP Pathways 173

G Protein-Coupled Receptors Also Use Lipid-Derived Second Messengers 173

Catalytic Receptors Have Enzyme Activity 175

Integrin Receptors Transfer Information from the Extracellular Matrix 175

Novel Signal Molecules 175

Calcium Is an Important Intracellular Signal 176

Gases Are Ephemeral Signal Molecules 177

BIOTECHNOLOGY *Calcium Signals Glow in the Dark 177*

CLINICAL FOCUS *From Dynamite to Medicine 178*

Some Lipids Are Important Paracrine Signals 178

Modulation of Signal Pathways 179

Receptors Exhibit Saturation, Specificity, and Competition 179

One Ligand May Have Multiple Receptors 179

Up and Down-Regulation Enable Cells to Modulate Responses 180

Cells Must Be Able to Terminate Signal Pathways 181

Many Diseases and Drugs Target the Proteins of Signal Transduction 181

Homeostatic Reflex Pathways 181

Cannon's Postulates Describe Regulated Variables and Control Systems 182

Long-Distance Pathways Maintain Homeostasis 182

Control Systems Vary in Their Speed and Specificity 186

Complex Reflex Control Pathways Have Several Integrating Centers 188

CHAPTER SUMMARY 191 | **REVIEW QUESTIONS** 192

UNIT 2 Homeostasis and Control

CHAPTER 7
Introduction to the Endocrine System 194

Hormones 195

RUNNING PROBLEM **Graves' Disease 195**

Hormones Have Been Known Since Ancient Times 195

CLINICAL FOCUS *Diabetes: The Discovery of Insulin 196*

What Makes a Chemical a Hormone? 196

Hormones Act by Binding to Receptors 197

Hormone Action Must Be Terminated 197

The Classification of Hormones 199

Most Hormones Are Peptides or Proteins 199

Steroid Hormones Are Derived from Cholesterol 200

Some Hormones Are Derived from Single Amino Acids 202

Control of Hormone Release 205

The Endocrine Cell Is the Sensor in Simple Endocrine Reflexes 205

Many Endocrine Reflexes Involve the Nervous System 205

Neurohormones Are Secreted into the Blood by Neurons 205

The Pituitary Gland Is Actually Two Fused Glands 205

The Posterior Pituitary Stores and Releases Two Neurohormones 207

The Anterior Pituitary Secretes Six Hormones 207

A Portal System Connects the Hypothalamus and Anterior Pituitary 209

Anterior Pituitary Hormones Control Growth, Metabolism, and Reproduction 209

Feedback Loops Are Different in the Hypothalamic-Pituitary Pathway 211

Hormone Interactions 212

In Synergism, the Effect of Interacting Hormones Is More than Additive 213

A Permissive Hormone Allows Another Hormone to Exert Its Full Effect 213

Antagonistic Hormones Have Opposing Effects 213

Endocrine Pathologies 214

Hypersecretion Exaggerates a Hormone's Effects 214

Hyposecretion Diminishes or Eliminates a Hormone's Effects 215

Receptor or Second Messenger Problems Cause Abnormal Tissue Responsiveness 215

Diagnosis of Endocrine Pathologies Depends on the Complexity of the Reflex 215

Hormone Evolution 217

FOCUS ON . . . The Pineal Gland 218

CHAPTER SUMMARY 220 | **REVIEW QUESTIONS** 221

CHAPTER 8
Neurons: Cellular and Network Properties 223

RUNNING PROBLEM **Mysterious Paralysis 224**

Organization of the Nervous System 224

Cells of the Nervous System 226

Neurons Carry Electrical Signals 226

Establishing Synapses Depends on Chemical Signals 229

Glial Cells Provide Support for Neurons 231

Can Stem Cells Repair Damaged Neurons? 233

Electrical Signals in Neurons 234

The Nernst Equation Predicts Membrane Potential for a Single Ion 234

The GHK Equation Predicts Membrane Potential Using Multiple Ions 234

Ion Movement Creates Electrical Signals 235

Gated Channels Control the Ion Permeability of the Neuron 235

CLINICAL FOCUS *Mutant Channels 236*

Current Flow Obeys Ohm's Law 236

Graded Potentials Reflect Stimulus Strength 237

Action Potentials Travel Long Distances 239

Na^+ *and* K^+ *Move across the Membrane during Action Potentials 240*

One Action Potential Does Not Alter Ion Concentration Gradients 242

Axonal Na^+ *Channels Have Two Gates 242*

Action Potentials Will Not Fire during the Absolute Refractory Period 243

Action Potentials Are Conducted 245

Larger Neurons Conduct Action Potentials Faster 245

Conduction Is Faster in Myelinated Axons 247

Chemical Factors Alter Electrical Activity 249

BIOTECHNOLOGY *The Body's Wiring 249*

Cell-To-Cell Communication in the Nervous System 249
Neurons Communicate at Synapses 249
Neurons Secrete Chemical Signals 250
Neurotransmitters Are Highly Varied 251
CLINICAL FOCUS *Myasthenia Gravis 253*
BIOTECHNOLOGY *Of Snakes, Snails, Spiders, and Sushi 254*
Neurotransmitters Are Released from Vesicles 254
Stronger Stimuli Release More Neurotransmitter 257
Integration of Neural Information Transfer 258
Postsynaptic Responses May Be Slow or Fast 258
Pathways Integrate Information from Multiple Neurons 261
Synaptic Activity Can Be Modified 261
Long-Term Potentiation Alters Synapses 264
Disorders of Synaptic Transmission Are Responsible for Many Diseases 264

CHAPTER SUMMARY 266 | **REVIEW QUESTIONS** 268

CHAPTER 9
The Central Nervous System 271

Emergent Properties of Neural Networks 272
RUNNING PROBLEM **Infantile Spasms 272**
Evolution of Nervous Systems 272
Anatomy of the Central Nervous System 274
The CNS Develops from a Hollow Tube 274
The CNS Is Divided into Gray Matter and White Matter 274
Bone and Connective Tissue Support the CNS 277
The Brain Floats in Cerebrospinal Fluid 277
The Blood-Brain Barrier Protects the Brain 279
Neural Tissue Has Special Metabolic Requirements 280
CLINICAL FOCUS *Diabetes: Hypoglycemia and the Brain 281*
The Spinal Cord 281
The Brain 282
The Brain Stem Is the Oldest Part of the Brain 283
The Cerebellum Coordinates Movement 285
The Diencephalon Contains the Centers for Homeostasis 285
The Cerebrum Is the Site of Higher Brain Functions 287
Brain Function 288
The Cerebral Cortex Is Organized into Functional Areas 289
The Spinal Cord and Brain Integrate Sensory Information 290
Sensory Information Is Processed into Perception 291
The Motor System Governs Output from the CNS 291
The Behavioral State System Modulates Motor Output 292
Why Do We Sleep? 292
EMERGING CONCEPTS *Brain Glymphatics 294*
Physiological Functions Exhibit Circadian Rhythms 295
Emotion and Motivation Involve Complex Neural Pathways 296
Moods Are Long-Lasting Emotional States 297
Learning and Memory Change Synaptic Connections in the Brain 297
Learning Is the Acquisition of Knowledge 298
Memory Is the Ability to Retain and Recall Information 298
Language Is the Most Elaborate Cognitive Behavior 300
Personality Is a Combination of Experience and Inheritance 301

CHAPTER SUMMARY 303 | **REVIEW QUESTIONS** 305

CHAPTER 10
Sensory Physiology 307

RUNNING PROBLEM **Ménière's Disease 308**
General Properties of Sensory Systems 308
Receptors Are Sensitive to Particular Forms of Energy 309
Sensory Transduction Converts Stimuli into Graded Potentials 310
A Sensory Neuron Has a Receptive Field 310
The CNS Integrates Sensory Information 310
Coding and Processing Distinguish Stimulus Properties 312
Somatic Senses 315
Pathways for Somatic Perception Project to the Cortex and Cerebellum 315
Touch Receptors Respond to Many Different Stimuli 317
Skin Temperature Receptors Are Free Nerve Endings 318
Nociceptors Initiate Protective Responses 318
CLINICAL FOCUS *Natural Painkillers 320*
Chemoreception: Smell and Taste 322
Olfaction Is One of the Oldest Senses 322
Taste Is a Combination of Five Basic Sensations 324
Taste Transduction Uses Receptors and Channels 325
The Ear: Hearing 328
Hearing Is Our Perception of Sound 329
Sound Transduction Is a Multistep Process 329
The Cochlea Is Filled with Fluid 330
Sounds Are Processed First in the Cochlea 333
Auditory Pathways Project to the Auditory Cortex 333

Hearing Loss May Result from Mechanical or Neural Damage 334

The Ear: Equilibrium 335

The Vestibular Apparatus Provides Information about Movement and Position 335

The Semicircular Canals Sense Rotational Acceleration 335

The Otolith Organs Sense Linear Acceleration and Head Position 337

Equilibrium Pathways Project Primarily to the Cerebellum 337

The Eye and Vision 338

The Skull Protects the Eye 338

Light Enters the Eye through the Cornea 339

The Lens Focuses Light on the Retina 341

Phototransduction Occurs at the Retina 343

EMERGING CONCEPTS *Melanopsin 344*

Photoreceptors Transduce Light into Electrical Signals 344

Signal Processing Begins in the Retina 347

CHAPTER SUMMARY 352 | **REVIEW QUESTIONS** 353

CHAPTER 11

Efferent Division: Autonomic and Somatic Motor Control 355

RUNNING PROBLEM **A Powerful Addiction 356**

The Autonomic Division 356

Autonomic Reflexes Are Important for Homeostasis 357

Antagonistic Control Is a Hallmark of the Autonomic Division 358

Autonomic Pathways Have Two Efferent Neurons in Series 358

Sympathetic and Parasympathetic Branches Originate in Different Regions 359

The Autonomic Nervous System Uses a Variety of Chemical Signals 359

Autonomic Pathways Control Smooth and Cardiac Muscle and Glands 359

Autonomic Neurotransmitters Are Synthesized in the Axon 362

Autonomic Receptors Have Multiple Subtypes 363

The Adrenal Medulla Secretes Catecholamines 364

Autonomic Agonists and Antagonists Are Important Tools in Research and Medicine 364

Primary Disorders of the Autonomic Nervous System Are Relatively Uncommon 366

CLINICAL FOCUS *Diabetes: Autonomic Neuropathy 366*

Summary of Sympathetic and Parasympathetic Branches 367

The Somatic Motor Division 368

A Somatic Motor Pathway Consists of One Neuron 368

The Neuromuscular Junction Contains Nicotinic Receptors 370

CHAPTER SUMMARY 371 | **REVIEW QUESTIONS** 372

CHAPTER 12

Muscles 374

RUNNING PROBLEM **Periodic Paralysis 375**

Skeletal Muscle 376

Skeletal Muscles Are Composed of Muscle Fibers 376

Myofibrils Are Muscle Fiber Contractile Structures 377

Muscle Contraction Creates Force 380

Actin and Myosin Slide Past Each Other during Contraction 382

Myosin Crossbridges Move Actin Filaments 383

Calcium Signals Initiate Contraction 383

Myosin Heads Step along Actin Filaments 384

Acetylcholine Initiates Excitation-Contraction Coupling 385

BIOTECHNOLOGY *Watching Myosin Work 385*

Skeletal Muscle Contraction Requires a Steady Supply of ATP 388

Fatigue Has Multiple Causes 389

Skeletal Muscle Is Classified by Speed and Fatigue Resistance 390

Resting Fiber Length Affects Tension 392

Force of Contraction Increases with Summation 393

A Motor Unit Is One Motor Neuron and Its Muscle Fibers 393

Contraction Force Depends on the Types and Numbers of Motor Units 394

Mechanics Of Body Movement 395

Isotonic Contractions Move Loads; Isometric Contractions Create Force without Movement 395

Bones and Muscles around Joints Form Levers and Fulcrums 397

Muscle Disorders Have Multiple Causes 399

Smooth Muscle 400

Smooth Muscle Is More Variable Than Skeletal Muscle 401

Smooth Muscle Lacks Sarcomeres 402

Myosin Phosphorylation Controls Contraction 403

MLCP Controls Ca^{2+} Sensitivity 405

Calcium Initiates Smooth Muscle Contraction 405

Some Smooth Muscles Have Unstable Membrane Potentials 406

Chemical Signals Influence Smooth Muscle Activity 407

Cardiac Muscle 409

CHAPTER SUMMARY 410 | **REVIEW QUESTIONS** 411

CHAPTER 13

Integrative Physiology I: Control of Body Movement 414

Neural Reflexes 415

Neural Reflex Pathways Can Be Classified in Different Ways 415

RUNNING PROBLEM **Tetanus 415**

Autonomic Reflexes 417

Skeletal Muscle Reflexes 417

Golgi Tendon Organs Respond to Muscle Tension 418

Muscle Spindles Respond to Muscle Stretch 418

Stretch Reflexes and Reciprocal Inhibition Control Movement around a Joint 420

Flexion Reflexes Pull Limbs Away from Painful Stimuli 421

The Integrated Control of Body Movement 422

Movement Can Be Classified as Reflex, Voluntary, or Rhythmic 423

The CNS Integrates Movement 425

Control of Movement in Visceral Muscles 428

EMERGING CONCEPTS *Visualization Techniques in Sports 428*

CHAPTER SUMMARY 429 | **REVIEW QUESTIONS** 430

UNIT 3 Integration of Function

CHAPTER 14

Cardiovascular Physiology 432

RUNNING PROBLEM **Myocardial Infarction 433**

Overview of the Cardiovascular System 433

The Cardiovascular System Transports Materials throughout the Body 433

The Cardiovascular System Consists of the Heart, Blood Vessels, and Blood 434

Pressure, Volume, Flow, And Resistance 436

The Pressure of Fluid in Motion Decreases over Distance 436

Pressure Changes in Liquids without a Change in Volume 436

Blood Flows from Higher Pressure to Lower Pressure 438

Resistance Opposes Flow 438

Velocity Depends on the Flow Rate and the Cross-Sectional Area 439

Cardiac Muscle And The Heart 440

The Heart Has Four Chambers 440

Heart Valves Ensure One-Way Flow in the Heart 443

The Coronary Circulation Supplies Blood to the Heart 445

Cardiac Muscle Cells Contract without Innervation 446

Calcium Entry Is a Feature of Cardiac EC Coupling 447

Cardiac Muscle Contraction Can Be Graded 447

Myocardial Action Potentials Vary 448

The Heart as a Pump 452

Electrical Signals Coordinate Contraction 452

Pacemakers Set the Heart Rate 453

CLINICAL FOCUS *Fibrillation 455*

The Electrocardiogram Reflects Electrical Activity 455

The Heart Contracts and Relaxes during a Cardiac Cycle 459

CLINICAL FOCUS *Gallops, Clicks, and Murmurs 462*

Pressure-Volume Curves Represent One Cardiac Cycle 462

Stroke Volume Is the Volume of Blood Pumped per Contraction 464

Cardiac Output Is a Measure of Cardiac Performance 464

The Autonomic Division Modulates Heart Rate 464

Multiple Factors Influence Stroke Volume 466

Contractility Is Controlled by the Nervous and Endocrine Systems 467

EMERGING CONCEPTS *Stem Cells for Heart Disease 470*

EDV and Arterial Blood Pressure Determine Afterload 470

CHAPTER SUMMARY 472 | **REVIEW QUESTIONS** 474

CHAPTER 15

Blood Flow and the Control of Blood Pressure 476

RUNNING PROBLEM **Essential Hypertension 477**

The Blood Vessels 478

Blood Vessels Contain Vascular Smooth Muscle 478

Arteries and Arterioles Carry Blood Away from the Heart 478

Exchange Takes Place in the Capillaries 479

Blood Flow Converges in the Venules and Veins 480

Angiogenesis Creates New Blood Vessels 480

Blood Pressure 481

Blood Pressure Is Highest in Arteries and Lowest in Veins 481

Arterial Blood Pressure Reflects the Driving Pressure for Blood Flow 482

Blood Pressure Is Estimated by Sphygmomanometry 483

Cardiac Output and Peripheral Resistance Determine Mean Arterial Pressure 484

Changes in Blood Volume Affect Blood Pressure 484

CLINICAL FOCUS *SHOCK 485*

Resistance in the Arterioles 486

Myogenic Autoregulation Adjusts Blood Flow 486

Paracrine Signals Influence Vascular Smooth Muscle 488

The Sympathetic Branch Controls Most Vascular Smooth Muscle 489

Distribution of Blood to the Tissues 489

Cerebral Blood Flow Stays Nearly Constant 491

Coronary Blood Flow Parallels the Work of the Heart 491

Regulation of Cardiovascular Function 492

The Baroreceptor Reflex Controls Blood Pressure 492

Orthostatic Hypotension Triggers the Baroreceptor Reflex 494

Other Systems Influence Cardiovascular Function 495

Exchange at the Capillaries 495

Velocity of Blood Flow Is Lowest in the Capillaries 496

Most Capillary Exchange Takes Place by Diffusion and Transcytosis 496

Capillary Filtration and Absorption Take Place by Bulk Flow 497

The Lymphatic System 499

Edema Results from Alterations in Capillary Exchange 500

Cardiovascular Disease 501

Risk Factors for CVD Include Smoking and Obesity 501

CLINICAL FOCUS *Diabetes and Cardiovascular Disease 502*

Atherosclerosis Is an Inflammatory Process 502

Hypertension Represents a Failure of Homeostasis 502

EMERGING CONCEPTS *Inflammatory Markers for Cardiovascular Disease 504*

CHAPTER SUMMARY 505 | **REVIEW QUESTIONS** 507

CHAPTER 16

Blood 510

RUNNING PROBLEM **Blood Doping in Athletes 511**

Plasma and the Cellular Elements of Blood 511

Plasma Is Extracellular Matrix 511

Cellular Elements Include RBCs, WBCs, and Platelets 513

Blood Cell Production 513

Blood Cells Are Produced in the Bone Marrow 513

Hematopoiesis Is Controlled by Cytokines 514

Colony-Stimulating Factors Regulate Leukopoiesis 515

Thrombopoietin Regulates Platelet Production 515

Erythropoietin Regulates RBC Production 515

Red Blood Cells 517

Mature RBCs Lack a Nucleus 517

Hemoglobin Synthesis Requires Iron 517

RBCs Live about Four Months 517

FOCUS ON . . . Bone Marrow *518*

RBC Disorders Decrease Oxygen Transport 519

CLINICAL FOCUS *Diabetes: Hemoglobin and Hyperglycemia 522*

Platelets 522

Hemostasis and Coagulation 523

Hemostasis Prevents Blood Loss from Damaged Vessels 523

Platelet Activation Begins the Clotting Process 523

Coagulation Converts a Platelet Plug into a Clot 525

Anticoagulants Prevent Coagulation 527

CHAPTER SUMMARY 529 | **REVIEW QUESTIONS** 530

CHAPTER 17

Mechanics of Breathing 532

RUNNING PROBLEM **Emphysema 533**

The Respiratory System 533

Bones and Muscles of the Thorax Surround the Lungs 534

Pleural Sacs Enclose the Lungs 534

Airways Connect Lungs to the External Environment 537

The Airways Warm, Humidify, and Filter Inspired Air 538

CLINICAL FOCUS *Congestive Heart Failure 538*

Alveoli Are the Site of Gas Exchange 538

Pulmonary Circulation Is High-Flow, Low-Pressure 539

Gas Laws 540

Air Is a Mixture of Gases 540

Gases Move Down Pressure Gradients 540

Boyle's Law Describes Pressure-Volume Relationships 540

Ventilation 542

Lung Volumes Change during Ventilation 542

During Ventilation, Air Flows because of Pressure Gradients 544

Inspiration Occurs When Alveolar Pressure Decreases 544

Expiration Occurs When Alveolar Pressure Increases 546

Intrapleural Pressure Changes during Ventilation 547

Lung Compliance and Elastance May Change in Disease States 548
Surfactant Decreases the Work of Breathing 549
Airway Diameter Determines Airway Resistance 550
Rate and Depth of Breathing Determine the Efficiency of Breathing 551
Alveolar Gas Composition Varies Little during Normal Breathing 553
Ventilation and Alveolar Blood Flow Are Matched 553
Auscultation and Spirometry Assess Pulmonary Function 556

CHAPTER SUMMARY 558 | **REVIEW QUESTIONS** 559

CHAPTER 18
Gas Exchange and Transport 562

RUNNING PROBLEM **High Altitude 563**

Gas Exchange in the Lungs and Tissues 563
Lower Alveolar P_{o2} Decreases Oxygen Uptake 564
Diffusion Problems Cause Hypoxia 565
BIOTECHNOLOGY *The Pulse Oximeter 567*
Gas Solubility Affects Diffusion 567
Gas Transport In The Blood 569
Hemoglobin Binds to Oxygen 569
Oxygen Binding Obeys the Law of Mass Action 570
Hemoglobin Transports Most Oxygen to the Tissues 571
P_{O2} Determines Oxygen-Hb Binding 571
EMERGING CONCEPTS *Blood Substitutes 572*
Oxygen Binding Is Expressed as a Percentage 572
Several Factors Affect O_2-Hb Binding 573
Carbon Dioxide Is Transported in Three Ways 575

Regulation of Ventilation 578
Neurons in the Medulla Control Breathing 579
CO_2, Oxygen, and pH Influence Ventilation 580
Protective Reflexes Guard the Lungs 582
Higher Brain Centers Affect Patterns of Ventilation 582

CHAPTER SUMMARY 584 | **REVIEW QUESTIONS** 585

CHAPTER 19
The Kidneys 587

Functions of the Kidneys 588
RUNNING PROBLEM **Gout 588**

Anatomy of the Urinary System 589
The Urinary System Consists of Kidneys, Ureters, Bladder, and Urethra 589
The Nephron Is the Functional Unit of the Kidney 589

Overview of Kidney Function 592
Kidneys Filter, Reabsorb, and Secrete 592
The Nephron Modifies Fluid Volume and Osmolarity 592

Filtration 594
The Renal Corpuscle Contains Filtration Barriers 595
EMERGING CONCEPTS *Diabetes: Diabetic Nephropathy 595*
Capillary Pressure Causes Filtration 596
GFR Is Relatively Constant 598
GFR Is Subject to Autoregulation 598
Hormones and Autonomic Neurons Also Influence GFR 600

Reabsorption 600
Reabsorption May Be Active or Passive 600
Renal Transport Can Reach Saturation 602
BIOTECHNOLOGY *Artificial Kidneys 603*
Peritubular Capillary Pressures Favor Reabsorption 604

Secretion 605
Competition Decreases Penicillin Secretion 606

Excretion 607
Clearance Is a Noninvasive Way to Measure GFR 607
Clearance Helps Us Determine Renal Handling 609

Micturition 612

CHAPTER SUMMARY 614 | **REVIEW QUESTIONS** 615

CHAPTER 20
Integrative Physiology II: Fluid and Electrolyte Balance 616

Fluid and Electrolyte Homeostasis 617
ECF Osmolarity Affects Cell Volume 617
Multiple Systems Integrate Fluid and Electrolyte Balance 617
RUNNING PROBLEM **Hyponatremia 617**

Water Balance 620
Daily Water Intake and Excretion Are Balanced 620
The Kidneys Conserve Water 621
The Renal Medulla Creates Concentrated Urine 621
CLINICAL FOCUS *Diabetes: Osmotic Diuresis 623*
Vasopressin Controls Water Reabsorption 623
Blood Volume and Osmolarity Activate Osmoreceptors 625
The Loop of Henle Is a Countercurrent Multiplier 625

Sodium Balance and ECF Volume 629
Aldosterone Controls Sodium Balance 630
Low Blood Pressure Stimulates Aldosterone Secretion 630
ANG II Has Many Effects 632
Natriuretic Peptides Promote Na^+ and Water Excretion 632

Potassium Balance 635

Behavioral Mechanisms in Salt and Water Balance 636

Drinking Replaces Fluid Loss 636

Low Na^+ Stimulates Salt Appetite 636

Avoidance Behaviors Help Prevent Dehydration 636

Integrated Control of Volume, Osmolarity, and Blood Pressure 636

Osmolarity and Volume Can Change Independently 637

Dehydration Triggers Homeostatic Responses 638

Kidneys Assist in Blood Pressure Homeostasis 641

Endocrine Problems Disrupt Fluid Balance 641

Acid-Base Balance 641

pH Changes Can Denature Proteins 641

Acids and Bases in the Body Come from Many Sources 642

pH Homeostasis Depends on Buffers, Lungs, and Kidneys 642

Buffer Systems Include Proteins, Phosphate Ions, and HCO_3^- 643

Ventilation Can Compensate for pH Disturbances 644

Kidneys Use Ammonia and Phosphate Buffers 645

The Proximal Tubule Secretes H^+ and Reabsorbs HCO_3^- 645

The Distal Nephron Controls Acid Excretion 646

Acid-Base Disturbances May Be Respiratory or Metabolic 647

CHAPTER SUMMARY 651 | **REVIEW QUESTIONS** 652

UNIT 4 Metabolism, Growth, and Aging

CHAPTER 21

The Digestive System 654

RUNNING PROBLEM **Cholera in India 655**

Anatomy of the Digestive System 655

The Digestive System Is a Tube 655

The GI Tract Wall Has Four Layers 658

Digestive Function and Processes 659

We Secrete More Fluid than We Ingest 660

Digestion and Absorption Make Food Usable 661

Motility: GI Smooth Muscle Contracts Spontaneously 661

GI Smooth Muscle Exhibits Different Patterns of Contraction 663

CLINICAL FOCUS *Diabetes: Delayed Gastric Emptying 663*

Regulation of GI Function 664

The Enteric Nervous System Can Act Independently 664

GI Peptides Include Hormones, Neuropeptides, and Cytokines 665

Integrated Function: The Cephalic Phase 667

Chemical and Mechanical Digestion Begins in the Mouth 668

Saliva Is an Exocrine Secretion 668

Swallowing Moves Food from Mouth to Stomach 668

Integrated Function: The Gastric Phase 669

The Stomach Stores Food 669

Gastric Secretions Protect and Digest 670

The Stomach Balances Digestion and Defense 673

Integrated Function: The Intestinal Phase 673

Intestinal Secretions Promote Digestion 674

The Pancreas Secretes Enzymes and Bicarbonate 674

The Liver Secretes Bile 676

Most Digestion Occurs in the Small Intestine 676

FOCUS ON . . . The Liver 677

Bile Salts Facilitate Fat Digestion 678

Carbohydrates Are Absorbed as Monosaccharides 678

Proteins Are Digested into Small Peptides and Amino Acids 680

Some Larger Peptides Can Be Absorbed Intact 681

Nucleic Acids Are Digested into Bases and Monosaccharides 683

The Intestine Absorbs Vitamins and Minerals 683

The Intestine Absorbs Ions and Water 683

Regulation of the Intestinal Phase 683

The Large Intestine Concentrates Waste 684

Diarrhea Can Cause Dehydration 686

EMERGING CONCEPTS *The Human Microbiome Project 687*

Immune Functions of the GI Tract 687

M Cells Sample Gut Contents 687

Vomiting Is a Protective Reflex 687

CHAPTER SUMMARY 689 | **REVIEW QUESTIONS** 690

CHAPTER 22

Metabolism and Energy Balance 692

Appetite and Satiety 693

RUNNING PROBLEM **Eating Disorders 693**

BIOTECHNOLOGY *Discovering Peptides: Research in Reverse 694*

Energy Balance 694
Energy Input Equals Energy Output 695
Oxygen Consumption Reflects Energy Use 695
CLINICAL FOCUS *Estimating Fat–The Body Mass Index 696*
Many Factors Influence Metabolic Rate 697
Energy Is Stored in Fat and Glycogen 697
Metabolism 698
Ingested Energy May Be Used or Stored 698
Enzymes Control the Direction of Metabolism 698
Fed-State Metabolism 700
Carbohydrates Make ATP 700
Amino Acids Make Proteins 700
Fats Store Energy 700
CLINICAL FOCUS *Antioxidants Protect the Body 703*
Plasma Cholesterol Predicts Heart Disease 703
Fasted-State Metabolism 704
Glycogen Converts to Glucose 704
Proteins Can Be Used to Make ATP 705
Lipids Store More Energy than Glucose or Protein 706
Homeostatic Control of Metabolism 707
The Pancreas Secretes Insulin and Glucagon 707
The Insulin-to-Glucagon Ratio Regulates Metabolism 707
Insulin Is the Dominant Hormone of the Fed State 708
Insulin Promotes Anabolism 708
Glucagon Is Dominant in the Fasted State 711
Diabetes Mellitus Is a Family of Diseases 712
Type 1 Diabetics Are Prone to Ketoacidosis 715
Type 2 Diabetics Often Have Elevated Insulin Levels 717
Metabolic Syndrome Links Diabetes and Cardiovascular Disease 718
Multiple Hormones Influence Metabolism 719
Regulation of Body Temperature 719
Body Temperature Balances Heat Production, Gain, and Loss 719
Body Temperature Is Homeostatically Regulated 720
Movement and Metabolism Produce Heat 722
The Body's Thermostat Can Be Reset 723

CHAPTER SUMMARY 725 | **REVIEW QUESTIONS** 726

CHAPTER 23
Endocrine Control of Growth and Metabolism 728

Review Of Endocrine Principles 729
RUNNING PROBLEM **Hyperparathyroidism 729**
Adrenal Glucocorticoids 729
The Adrenal Cortex Secretes Steroid Hormones 729
Cortisol Secretion Is Controlled by ACTH 731
Cortisol Is Essential for Life 731
Cortisol Is a Useful Therapeutic Drug 733
Cortisol Pathologies Result from Too Much or Too Little Hormone 733
CRH and ACTH Have Additional Physiological Functions 734
Thyroid Hormones 734
Thyroid Hormones Contain Iodine 736
TSH Controls the Thyroid Gland 736
Thyroid Pathologies Affect Quality of Life 737
Growth Hormone 739
Growth Hormone Is Anabolic 739
Growth Hormone Is Essential for Normal Growth 741
Genetically Engineered hGH Raises Ethical Questions 741
Tissue and Bone Growth 741
Tissue Growth Requires Hormones and Paracrine Factors 741
Bone Growth Requires Adequate Dietary Calcium 742
CLINICAL FOCUS *New Growth Charts 742*
Calcium Balance 743
Plasma Calcium Is Closely Regulated 744
Three Hormones Control Calcium Balance 746
Multiple Factors Control Bone Remodeling 747
Calcium and Phosphate Homeostasis Are Linked 748
Osteoporosis Is a Disease of Bone Loss 750

CHAPTER SUMMARY 751 | **REVIEW QUESTIONS** 752

CHAPTER 24
The Immune System 754

Overview 755
RUNNING PROBLEM **HPV: To Vaccinate or Not? 755**
Anatomy of the Immune System 757
Lymphoid Tissues Are Everywhere 757
Leukocytes Are the Immune Cells 757

Development of Immune Cells 760
FOCUS ON . . . The Thymus Gland 661
Lymphocytes Mediate the Adaptive Immune Response 761
The Immune System Must Recognize "Self" 761
Early Pathogen Exposure Strengthens Immunity 762
Molecules of the Innate Immune Response 762
Many Molecules of the Innate Immune Response Are Always Present 762
Antigen Presentation and Recognition Molecules 763
Antigen-Recognition Molecules 764
B Lymphocytes Produce Antibodies 764
Pathogens of the Human Body 765
Bacteria and Viruses Require Different Defense Mechanisms 765
Viruses Can Only Replicate inside Host Cells 766
The Immune Response 766
Barriers Are the Body's First Line of Defense 766
Innate Immunity Provides Nonspecific Responses 766
Antigen-Presenting Cells Bridge Innate and Adaptive Responses 768
Adaptive Immunity Creates Antigen-Specific Responses 768
Antibody Functions 769
Integrated Immune Responses 773
Bacterial Invasion Causes Inflammation 773
Viral Infections Require Intracellular Defense 773
Specific Antigens Trigger Allergic Responses 776
MHC Proteins Allow Recognition of Foreign Tissue 777
Immune System Pathologies 778
Autoimmune Disease Results from Antibodies against Self-Antigen 779
Immune Surveillance Removes Abnormal Cells 779
Neuro-Endocrine-Immune Interactions 780
Stress Alters Immune System Function 780
Modern Medicine Includes Mind-Body Therapeutics 781

CHAPTER SUMMARY 782 | **REVIEW QUESTIONS** 784

CHAPTER 25
Integrative Physiology III: Exercise 786

RUNNING PROBLEM **Malignant Hyperthermia 787**
Metabolism and Exercise 787
Hormones Regulate Metabolism during Exercise 788
Oxygen Consumption Is Related to Exercise Intensity 789
Several Factors Limit Exercise 790
Ventilatory Responses to Exercise 790
Cardiovascular Responses to Exercise 791
Cardiac Output Increases during Exercise 791
Muscle Blood Flow Increases during Exercise 791
Blood Pressure Rises Slightly during Exercise 792
The Baroreceptor Reflex Adjusts to Exercise 792
Feedforward Responses to Exercise 793
Temperature Regulation During Exercise 794
Exercise and Health 794
Exercise Lowers the Risk of Cardiovascular Disease 795
Type 2 Diabetes Mellitus May Improve with Exercise 795
Stress and the Immune System May Be Influenced by Exercise 796

CHAPTER SUMMARY 797 | **REVIEW QUESTIONS** 798

CHAPTER 26
Reproduction and Development 800

RUNNING PROBLEM **Infertility 801**
Sex Determination 801
Sex Chromosomes Determine Genetic Sex 802
Sexual Differentiation Occurs Early in Development 802
CLINICAL FOCUS *X-Linked Inherited Disorders 805*
Basic Patterns of Reproduction 806
CLINICAL FOCUS *Determining Sex 806*
Gametogenesis Begins in Utero 806
The Brain Directs Reproduction 807
Environmental Factors Influence Reproduction 810
Male Reproduction 810
Testes Produce Sperm and Hormones 811
Spermatogenesis Requires Gonadotropins and Testosterone 814
Male Accessory Glands Contribute Secretions to Semen 815
Androgens Influence Secondary Sex Characteristics 815
Female Reproduction 815
The Ovary Produces Eggs and Hormones 818
A Menstrual Cycle Lasts about One Month 818
Hormonal Control of the Menstrual Cycle Is Complex 819
Hormones Influence Female Secondary Sex Characteristics 823
Procreation 823
The Human Sexual Response Has Four Phases 823
The Male Sex Act Includes Erection and Ejaculation 824

Sexual Dysfunction Affects Males and Females 824

Contraceptives Are Designed to Prevent Pregnancy 825

Infertility Is the Inability to Conceive 826

Pregnancy and Parturition 826

Fertilization Requires Capacitation 826

The Developing Embryo Implants in the Endometrium 827

The Placenta Secretes Hormones During Pregnancy 827

Pregnancy Ends with Labor and Delivery 830

The Mammary Glands Secrete Milk During Lactation 830

Growth and Aging 833

Puberty Marks the Beginning of the Reproductive Years 833

Menopause and Andropause Are a Consequence of Aging 833

CHAPTER SUMMARY 834 | **REVIEW QUESTIONS** 836

Appendices

Appendix A Answers A-1

Appendix B Physics and Math A-36

Appendix C Genetics A-39

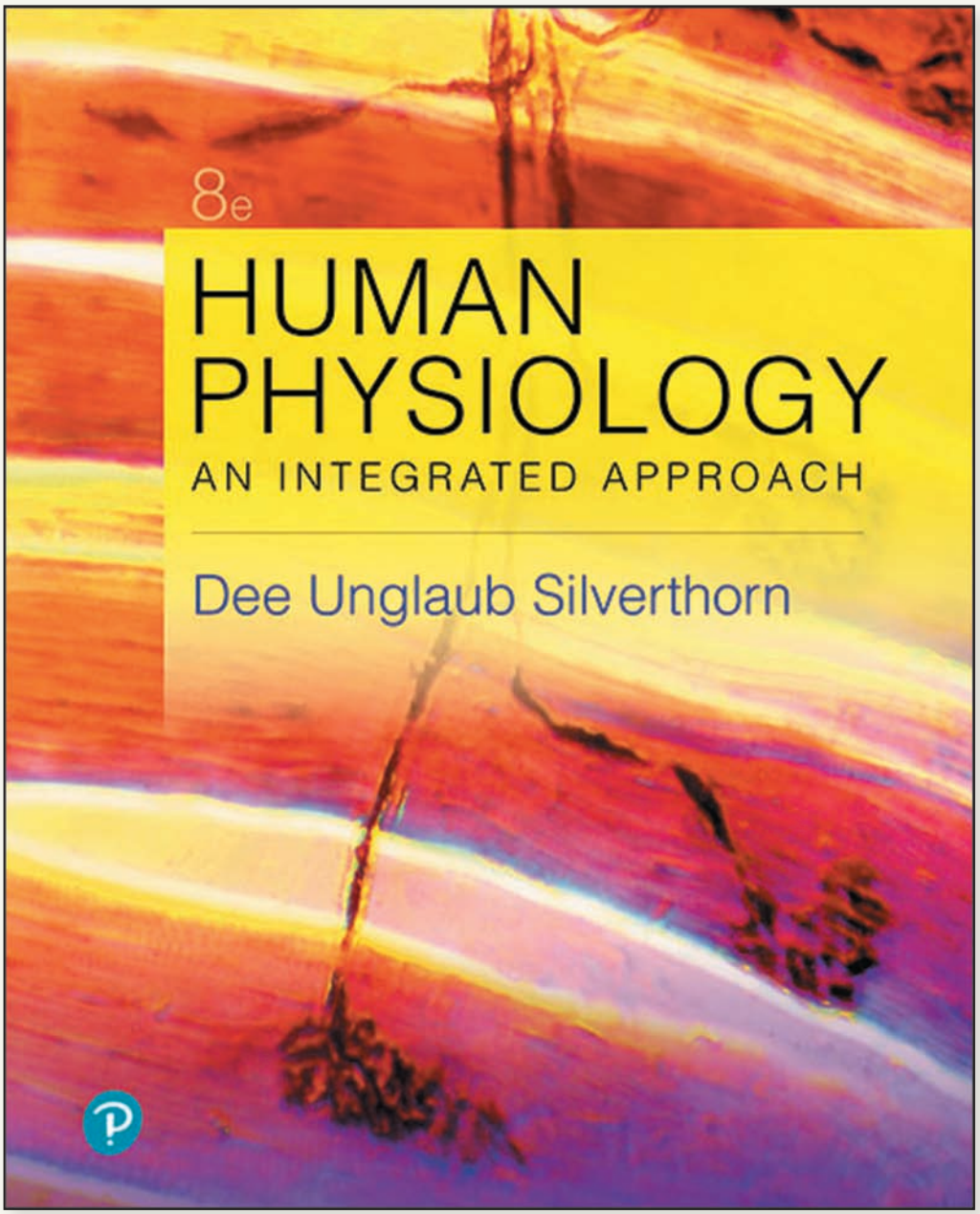
Photo Credits C-1

Glossary/Index GI-1

This page intentionally left blank

Move Beyond Memorization:
Prepare for Tomorrow's Challenges

The goals for the **Eighth Edition** of ***Human Physiology: An Integrated Approach*** are to provide an integrated and up-to-date introduction to core concepts in physiology and to equip you with skills for solving real-world problems.



Pearson

Challenge Yourself:
Apply What You Learn

Learning physiology requires that you use information rather than simply memorizing what you think will be on the test. The Eighth Edition text and Mastering™ A&P program provide multiple opportunities for you to practice answering the more challenging types of questions that you are likely to see on a test or exam.

Running Problems explore a real-world disease or disorder that unfolds in short segments throughout the chapter. You can check your understanding by comparing your answers with those in Problem Conclusion at the end of each chapter. Related Coaching Activities can be assigned in Mastering A&P.

RUNNING PROBLEM

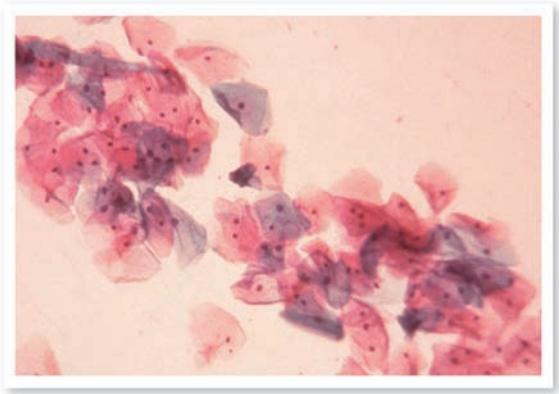
The day after Jan's visit, the computerized cytology analysis system rapidly scans the cells on the slide of Jan's cervical tissue, looking for abnormal cell size or shape. The computer is programmed to find multiple views for the cytologist to evaluate. The results of Jan's two Pap tests are shown in FIGURE 3.14.

Q6: *Has Jan's dysplasia improved or worsened? What evidence do you have to support your answer?*

Q7: *Use your answer to question 6 to predict whether Jan's HPV infection has persisted or been cleared by her immune system.*

59 61 65 79 **84** 87

see pp. 84–85



Additional Practice Questions include **Concept Check Questions,** which are placed at intervals throughout the chapter, and Review Questions, which are provided at the end of the chapter and organized into four levels of difficulty. An answer key is in Appendix A.

FIG. 7.15 Hypocortisolism

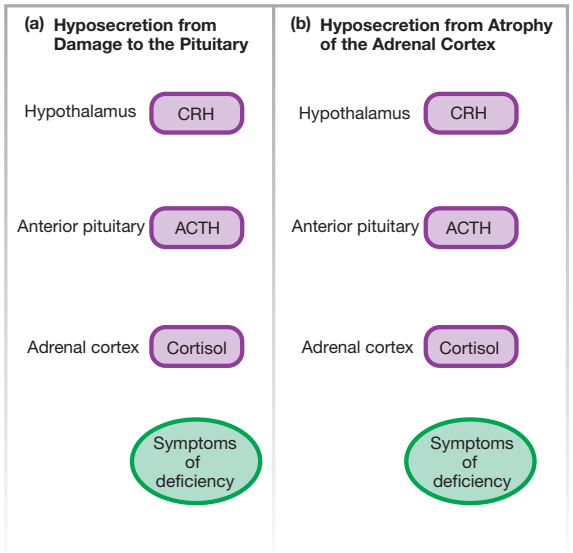


FIGURE QUESTION

For each condition, use arrows to indicate whether levels of the three hormones in the pathway will be increased, decreased, or unchanged. Draw in negative feedback loops where functional.

Figure Questions challenge you to apply visual literacy skills as you read an illustration or photo. Answers to these questions appear at the end of the text, in Appendix A.

See p. 217

Practice Solving Real-World Problems

NEW! "Try it" boxes present a real-world research problem or classic experiment and guide you through the process of analyzing the data and thinking like a scientist.

NEW! Additional questions for each "Try it" activity are available in **Mastering A&P**. Topics include Graphing (Chapter 1), Cell Membranes (Chapter 5), Action Potentials (Chapter 8), Salty-Sweet Taste Experiment (Chapter 10), Frank-Starling Law of the Heart (Chapter 14), Insulin (Chapter 19) and Oral Rehydration Therapy (Chapter 21).

Instructors: A version of this Try it! Activity can be assigned in Mastering Anatomy & Physiology

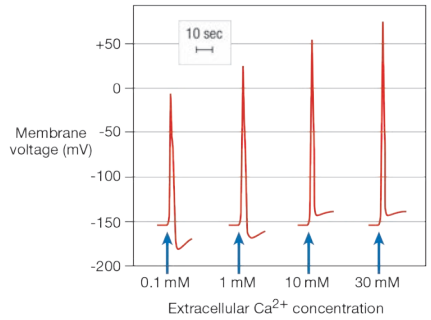
TRY IT! Action Potential

What do carnivorous plants and your neurons have in common? Most students learn that action potentials (APs) transmit information rapidly along neurons in an animal's nervous system. While this is true, APs were actually first described in algae! Another plant that uses APs is the Venus flytrap (*Dionaea muscipula*). Because these plants grow in nutrient-poor soil, they are carnivorous. The tips of their two leaves have evolved into *capture organs*, which snap shut when prey, such as a fly, moves over them. Charles Darwin himself, captivated by this phenomenon, encouraged other scientists to describe its mechanism.

In 1873, the English physiologist Sir John Scott Burdon-Sanderson was able to show that electric current flows through the Venus flytrap when a fly touches *trigger hairs* on the inner surface of the capture organs. The hairs act as mechanoreceptors that generate an action potential when bent. The AP closes the leaf tips, trapping the fly inside so the plant can digest it. In a series of experiments, researchers recorded APs in flytrap cells while varying the extracellular concentration of Ca^{2+}.

(a) The capture organ of a Venus flytrap with trigger hairs.

(b) Data from Hodick and Sievers, 1986.[1] Arrows indicate when trigger hairs were bent.



GRAPH QUESTIONS

1. Using the results shown in the graph, explain what increasing the concentration of Ca^{2+} does to the flytrap APs.
2. These results suggest that the rising phase of a flytrap AP is primarily due to which ion? Is this ion entering or leaving the cell? How does this compare to APs in your neurons?
3. What experiments could you design to determine which ion is responsible for the repolarization phase of the flytrap's AP?

[1] Hodick, D. & Sievers, A. (1986). The influence of Ca^{2+} on the action potential in mesophyll cells of *Dionaea muscipula* Ellis. *Protoplasma* 133, 83–84.

See p. 251

Graph Questions encourage you to interpret real data presented in graphs. Answers to these questions appear at the end of the text, in Appendix A.

Study More Efficiently Using the Figures

Eye-tracking research has shown that learning and comprehension levels are higher for students who study both the figures and the text together than for students who only read the text. This book offers dozens of illustrations designed to help you learn physiology more efficiently, and make the best use of your study time.

Essentials Figures distill the basics of a topic into one or two pages, helping you to see the big picture of human physiology. Instructors can assign **related Mastering A&P coaching activities** that explore these topics in greater depth.

Selected figures from the text are explored in accompanying **Phys in Action video tutors** and in **coaching activities** in **Mastering A&P**.

FIG. 5.23 ESSENTIALS Membrane Potential

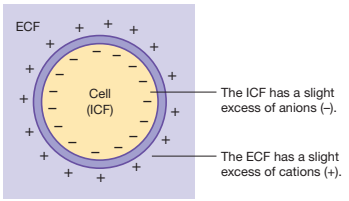
Play Phys in Action
@Mastering Anatomy & Physiology

The electrical disequilibrium that exists between the extracellular fluid (ECF) and intracellular fluid (ICF) of living cells is called the **membrane potential difference** (V_m), or membrane potential for short. The membrane potential results from the uneven distribution of electrical charge (i.e., ions) between the ECF and ICF.

What creates the membrane potential?

1. Ion concentration gradients between the ECF and ICF
2. The selectively permeable cell membrane

(a) In illustrations, this uneven distribution of charge is often shown by the charge symbols clustered on each side of the cell membrane.

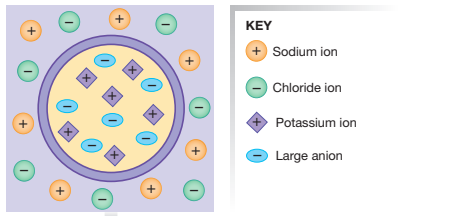


Creation of a Membrane Potential in an Artificial System

To show how a membrane potential difference can arise from ion concentration gradients and a selectively permeable membrane, we will use an artificial cell system where we can control the membrane's permeability to ions and the composition of the ECF and ICF.

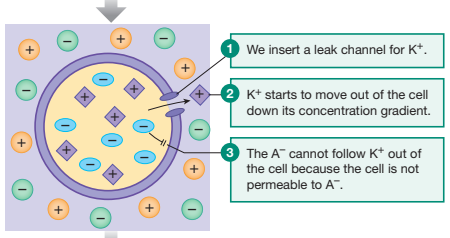
(b) When we begin, the cell has no membrane potential: The ECF (composed of Na^+ and Cl^- ions) and the ICF (K^+ and large anions, A^-) are electrically neutral.

The system is in chemical disequilibrium, with concentration gradients for all four ions. The cell membrane acts as an insulator to prevent free movement of ions between the ICF and ECF.



(c) Now we insert a leak channel for K^+ into the membrane, making the cell freely permeable to K^+.

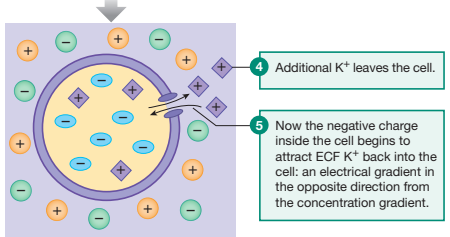
The transfer of just one K^+ from the cell to the ECF creates an electrical disequilibrium: the ECF has a net positive charge (+1) while the ICF has a net negative charge (–1). The cell now has a membrane potential difference, with the inside of the cell negative relative to the outside.



(d) As additional K^+ ions leave the cell, going down their concentration gradient, the inside of the cell becomes more negative and the outside becomes more positive.

How much K^+ will leave the cell?

If K^+ was uncharged, like glucose, it would diffuse out of the cell until the concentration outside $[K]_{out}$ equaled the concentration inside $[K]_{in}$. But K^+ is an ion, so we must consider its electrical gradient. Remember the rule for movement along electrical gradients: Opposite charges attract, like charges repel.

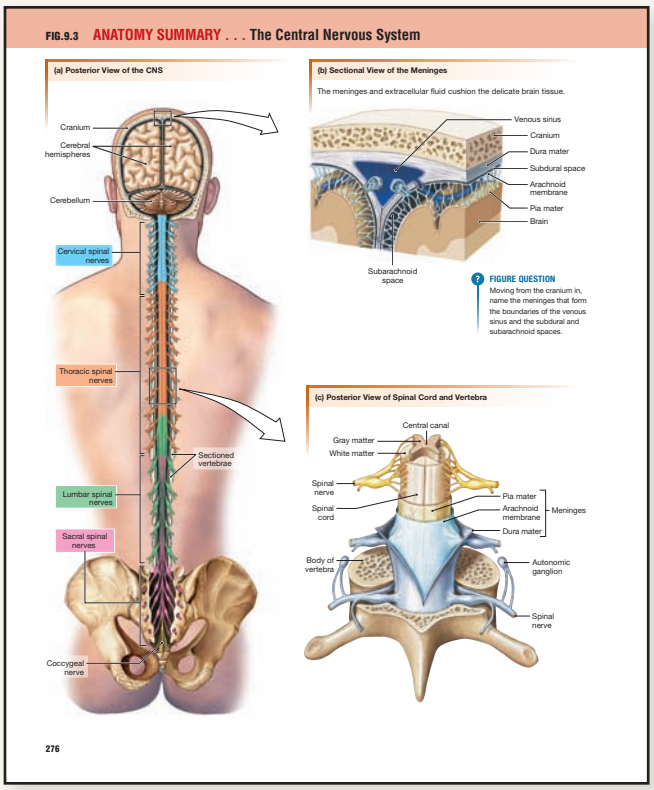


154

See p. 154

Anatomy Summary Figures provide succinct visual overviews of a physiological system from a macro to micro perspective. Whether you are learning the anatomy for the first time or refreshing your memory, these summaries show you the essential features of each system in a single figure.

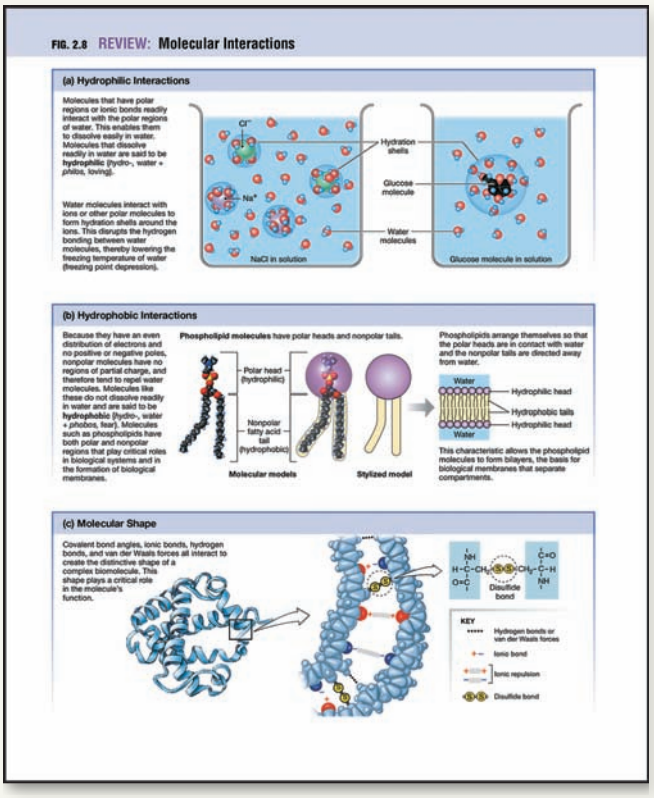
See p. 276



Review Figures visually present foundational concepts that you may already be familiar with. You may find it helpful to check out these figures before learning new physiology concepts.

Selected figures from the text can be assigned as **Art-Labeling Activities in Mastering A&P.**

See p. 44

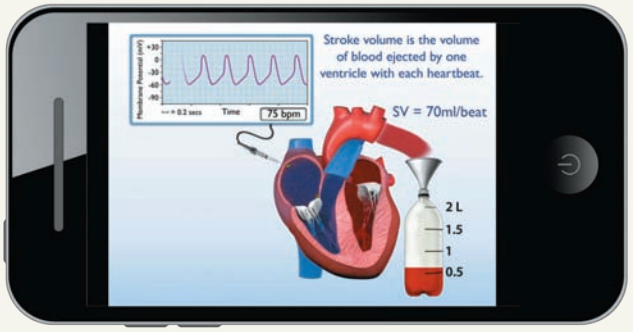


Get Online Coaching Through Mastering A&P

Mastering A&P provides tutorials and review questions that you can access before, during, and after class.

Phys in Action! Video Tutors and Coaching Activities help you visualize and master challenging physiological concepts by demonstrating laboratory procedures and real-world applications. Demonstrations include pulmonary function test, tilt table, exercise testing, and more.

EXPANDED! Interactive Physiology 2.0 Coaching Activities teach complex physiological processes using exceptionally clear animations, interactive tutorials, games, and quizzes. IP2 features new graphics, quicker navigation, and a mobile-friendly design. New topics include Generation of an Action Potential and Cardiac Cycle. IP2 and IP animations can be assigned from the Mastering A&P Item Library or accessed through the Mastering A&P Study Area.



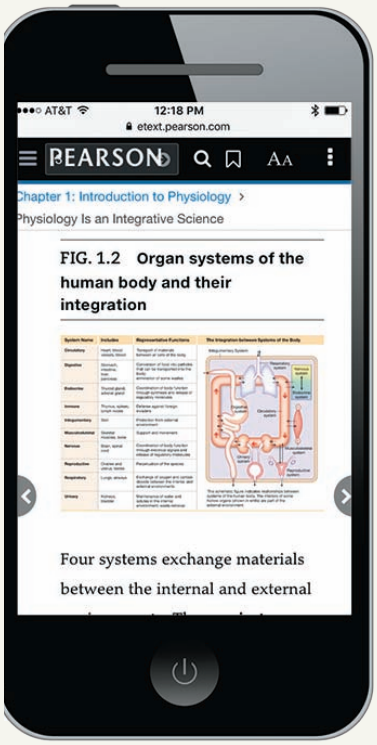
Mastering A&P offers thousands of tutorials, activities, and questions that can be used to test yourself, or assigned for homework and practice. Additional highlights include:

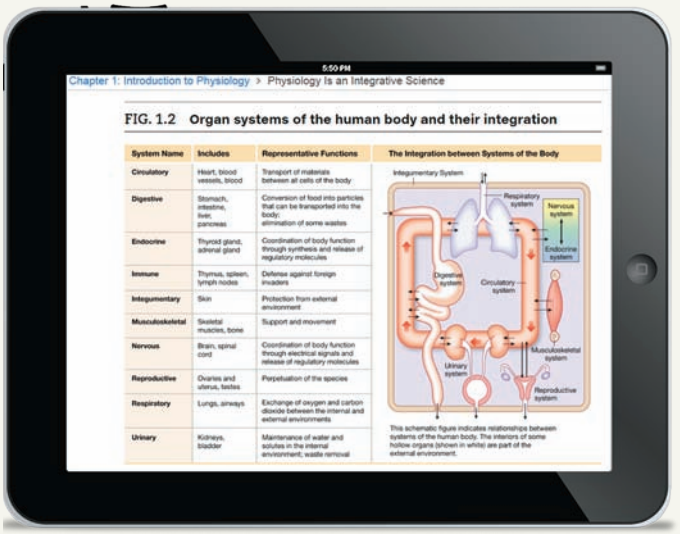
- **Nurses Need Physiology Case Studies** guide you through the steps of diagnosing and treating patients in real-world clinical scenarios.
- **A&P Flix Animations** use 3-D, movie-quality graphics to help you visualize complex physiology processes.
- **Dynamic Study Modules** are manageable, mobile-friendly sets of questions with extensive feedback for you to test, learn, and retest yourself on basic concepts.
- **PhysioEx Laboratory Simulations** offer a supplement or substitute for wet labs due to cost, time, or safety concerns.

Access the Complete Textbook Online or Offline with Pearson eText

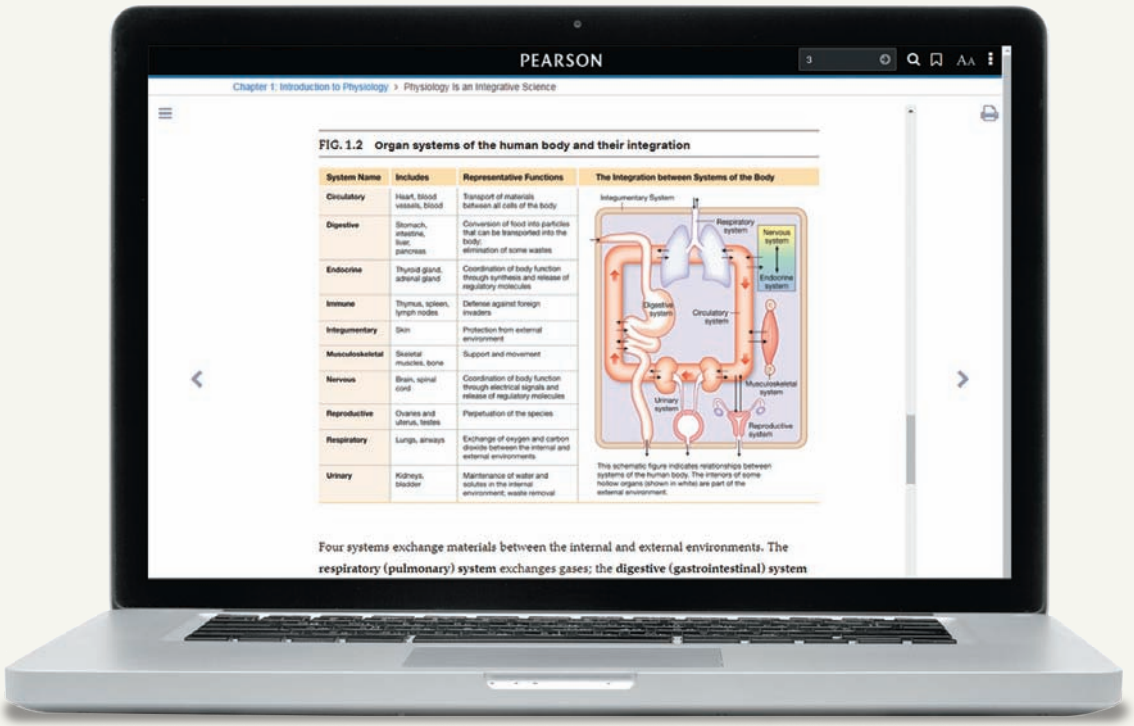
You can read your textbook without having to add weight to your bookbag.

The Pearson eText mobile app offers offline access and can be downloaded for most iOS and Android phones and tablets from the Apple App or Google Play stores.





Powerful interactive and customization functions in the eText platform include instructor and student note-taking, highlighting, bookmarking, search, and links to glossary terms.



Additional Support for Students & Instructors

NEW! Ready-to-Go Teaching Modules help instructors efficiently make use of the best teaching tools before, during, and after class. Accessed through the Instructor Resources area of Mastering A&P, and curated by author Dee Silverthorn, modules include skill development applications for Human Physiology including Concept Mapping and Graphing.

Learning Catalytics allows students to use their smartphone, tablet, or laptop to respond to questions in class. Visit learningcatalytics.com to learn more.

The Mastering A&P Instructor Resources Area includes the following downloadable tools for instructors who adopt the Eighth Edition for their classes:

- **Customizable PowerPoint® lecture outlines** include customizable images and provide a springboard for lecture prep.
- **All of the figures, photos, and tables from the text** are available in JPEG and PowerPoint® formats, in labelled and unlabelled versions, and with customizable labels and leader lines.
- **Test bank** provides thousands of customizable questions across Bloom's taxonomy levels. Each question is tagged to chapter learning outcomes that can also be tracked within Mastering Anatomy & Physiology assessments. Available in Microsoft® Word and TestGen® formats.
- **Animations and videos** bring human physiology concepts to life.
- **A comprehensive Instructor Resource Manual**, co-authored by Dee Silverthorn and Damian Hill, includes a detailed teaching outline for each chapter, along with a wealth of activities, examples, and analogies that have been thoroughly class-tested with thousands of students.
- **Customizable Study Questions**, co-authored by Dee Silverthorn and Damian Hill, help students focus their reading on the most important points in each chapters and are organized by chapter section headers for easy editing to reflect the material covered in class.

Welcome to the fascinating study of the human body! For most of recorded history, humans have been interested in how their bodies work. Early Egyptian, Indian, and Chinese writings describe attempts by physicians to treat various diseases and to restore health. Although some ancient remedies, such as camel dung and powdered sheep horn, may seem bizarre, we are still using others, such as blood-sucking leeches and chemicals derived from medicinal plants. The way we use these treatments has changed through the centuries as we have learned more about the human body.

There has never been a more exciting time in human physiology. **Physiology** is the study of the normal functioning of a living organism and its component parts, including all its chemical and physical processes. The term *physiology* literally means "knowledge of nature." Aristotle (384–322 BCE) used the word in this broad sense to describe the functioning of all living organisms, not just of the human body. However, Hippocrates (ca. 460–377 BCE), considered the father of medicine, used the word *physiology* to mean "the healing power of nature," and thereafter the field became closely associated with medicine. By the sixteenth century in Europe, physiology had been formalized as the study of the vital functions of the human body. Currently the term is again used to refer to the study of animals and plants.

Today, we benefit from centuries of work by physiologists who constructed a foundation of knowledge about how the human body functions. Since the 1970s, rapid advances in the fields of cellular and molecular biology have supplemented this work. A few decades ago, we thought that we would find the key to the secret of life by sequencing the human *genome*, which is the collective term for all the genetic information contained in the DNA of a species. However, this deconstructionist view of biology has proved to have its limitations, because living organisms are much more than the simple sum of their parts.

1.1 Physiology Is an Integrative Science

Many complex systems—including those of the human body—possess **emergent properties,** which are properties that cannot be predicted to exist based only on knowledge of the system's individual components. An emergent property is not a property of any single component of the system, and it is greater than the simple sum of the system's individual parts. Emergent properties result from complex, nonlinear interactions of the different components.

For example, suppose someone broke down a car into its nuts and bolts and pieces and laid them out on a floor. Could you predict that, properly assembled, these bits of metal and plastic would become a vehicle capable of converting the energy in gasoline into movement? Who could predict that the right combination of elements into molecules and assemblages of molecules would result in a living organism? Among the most complex emergent properties in humans are emotion, intelligence, and other aspects of brain function. None of these properties can be predicted from knowing the individual properties of nerve cells.

RUNNING PROBLEM **What to Believe?**

Jimmy had just left his first physiology class when he got the text from his mother: *Please call. Need to ask you something.* His mother seldom texted, so Jimmy figured it must be important. "Hi, Mom! What's going on?"

"Oh, Jimmy, I don't know what to do. I saw the doctor this morning and he's telling me that I need to take insulin. But I don't want to! My type of diabetes doesn't need insulin. I think he's just trying to make me see him more by putting me on insulin. Don't you think I'm right?"

Jimmy paused for a moment. "I'm not sure, Mom. He's probably just trying to do what's best for you. Didn't you talk to him about it?"

"Well, I tried but he didn't have time to talk. You're studying these things. Can't you look it up and see if I really need insulin?"

"I guess so. Let me see what I can find out." Jimmy hung up and thought. "Now what?"

2 5 9 12 16 19 24

When the Human Genome Project (*www.genome.gov*) began in 1990, scientists thought that by identifying and sequencing all the genes in human DNA, they would understand how the body worked. However, as research advanced, scientists had to revise their original idea that a given segment of DNA contained one gene that coded for one protein. It became clear that one gene may code for many proteins. The Human Genome Project ended in 2003, but before then researchers had moved beyond genomics to *proteomics*, the study of proteins in living organisms.

Now scientists have realized that knowing that a protein is made by a particular cell does not always tell us the significance of that protein to the cell, the tissue, or the functioning organism. The exciting new areas in biological research are called functional genomics, systems biology, and integrative biology, but fundamentally these are all fields of physiology. The **integration of function** across many **levels of organization** is a special focus of physiology. (To *integrate* means to bring varied elements together to create a unified whole.)

FIGURE 1.1 illustrates levels of organization ranging from the molecular level all the way up to populations of different species living together in *ecosystems* and in the *biosphere*. The levels of organization are shown along with the various subdisciplines of chemistry and biology related to the study of each organizational level. There is considerable overlap between the different fields of study, and these artificial divisions vary according to who is defining them. Notice, however, that physiology includes multiple levels, from molecular and cellular biology to the ecological physiology of populations.

At all levels, physiology is closely tied to anatomy. The structure of a cell, tissue, or organ must provide an efficient physical base for its function. For this reason, it is nearly impossible to study the physiology of the body without understanding the underlying anatomy. Because of the interrelationship of anatomy and physiology, you will find Anatomy Summaries throughout the book.

EMERGING CONCEPTS

The Changing World of Omics

If you read the scientific literature, it appears that contemporary research has exploded into an era of "omes" and "omics." What is an "ome"? The term apparently derives from the Latin word for a mass or tumor, and it is now used to refer to a collection of items that make up a whole, such as a genome. One of the earliest uses of the "ome" suffix in biology is the term *biome*, meaning all organisms living in a major ecological region, such as the marine biome or the desert biome. A genome, for example, is a collection of all the genetic material of an organism. Its physiome describes the organism's coordinated molecular, cellular, and physiological functioning.

The related adjective "omics" describes the research related to studying an "ome." Adding "omics" to a root word has become the cutting-edge way to describe a research field. For example, *pharmacogenomics* (the influence of genetics on the body's response to drugs) is now as important as *genomics*, the sequencing of DNA (the genome). There is even a journal named *OMICS!*

New "omes" emerge every year. The human connectome project (www.neuroscienceblueprint.nih.gov/connectome/) sponsored by the American National Institutes of Health is a collaborative effort by multiple institutions to map all the neural connections of the human brain. NIH also sponsors the human microbiome project (https://commonfund.nih.gov/hmp/overview), whose goal is to study the effects of microbes that normally live on or in the human body. Ignored as unimportant for many years, these microbes are now being shown to have an influence on both health and disease.

These special review features illustrate the anatomy of the physiological systems at different levels of organization.

At the most basic level of organization shown in Figure 1.1, atoms of elements link together to form molecules. Collections of molecules in living organisms form **cells,** the smallest unit of structure capable of carrying out all life processes. A lipid and protein barrier called the **cell membrane** (also called the *plasma membrane*) separates cells from their external environment. Simple organisms are composed of only one cell, but complex organisms have many cells with different structural and functional specializations.

Collections of cells that carry out related functions are called **tissues** {*texere*, to weave}. Tissues form structural and functional units known as **organs** {*organon*, tool}, and groups of organs integrate their functions to create **organ systems.** Chapter 3 reviews the anatomy of cells, tissues, and organs.

The 10 physiological organ systems in the human body are illustrated in FIGURE 1.2. Several of the systems have alternate names, given in parentheses, that are based on the organs of the system rather than the function of the system. The **integumentary system** {*integumentum*, covering}, composed of the skin, forms a protective boundary that separates the body's internal environment from the external environment (the outside world). The **musculoskeletal system** provides support and body movement.

Four systems exchange materials between the internal and external environments. The **respiratory (pulmonary) system** exchanges gases; the **digestive (gastrointestinal) system** takes up nutrients and water and eliminates wastes; the **urinary (renal) system** removes excess water and waste material; and the **reproductive system** produces eggs or sperm.

The remaining four systems extend throughout the body. The **circulatory (cardiovascular) system** distributes materials by pumping blood through vessels. The **nervous** and **endocrine systems** coordinate body functions. Note that the figure shows them as a continuum rather than as two distinct systems. Why? Because the lines between these two systems have blurred as we have learned more about the integrative nature of physiological function.

The one system not illustrated in Figure 1.2 is the diffuse **immune system,** which includes but is not limited to the anatomical structures known as the *lymphatic system*. The specialized cells of the immune system are scattered throughout the body. They protect the internal environment from foreign substances by intercepting material that enters through the intestines and lungs

FIG. 1.1 Levels of organization and the related fields of study

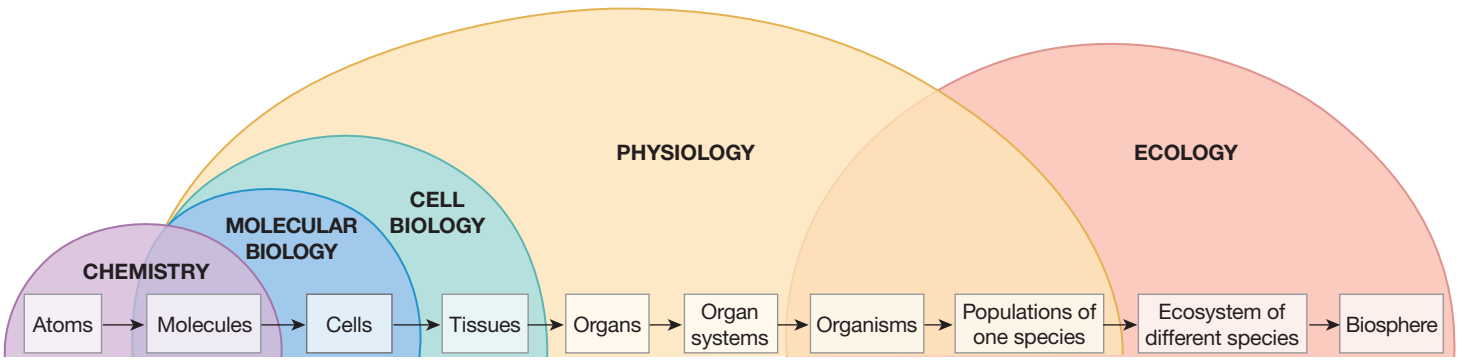
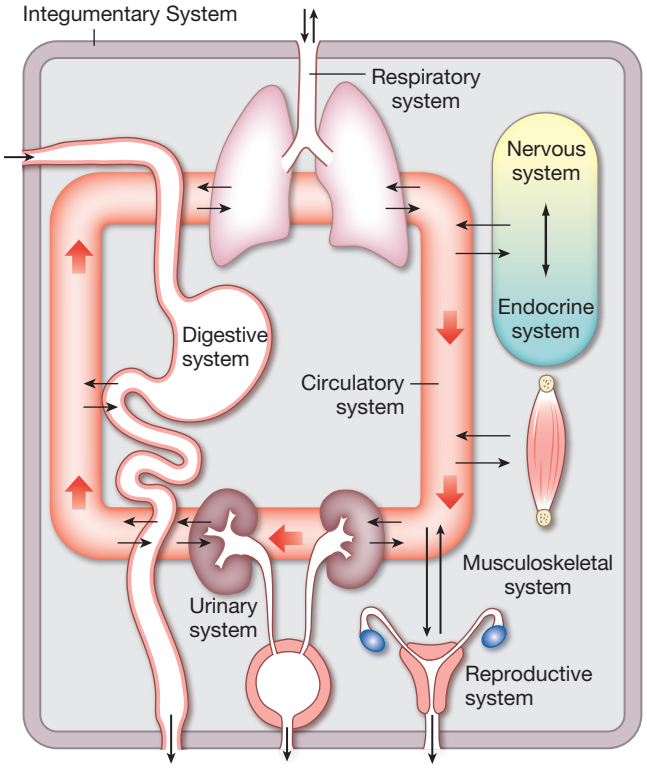


FIG. 1.2 Organ systems of the human body and their integration

FIG. 1.2 Organ Systems of the Human Body and their Integration

System Name	Includes	Representative Functions
Circulatory	Heart, blood vessels, blood	Transport of materials between all cells of the body
Digestive	Stomach, intestine, liver, pancreas	Conversion of food into particles that can be transported into the body; elimination of some wastes
Endocrine	Thyroid gland, adrenal gland	Coordination of body function through synthesis and release of regulatory molecules
Immune	Thymus, spleen, lymph nodes	Defense against foreign invaders
Integumentary	Skin	Protection from external environment
Musculoskeletal	Skeletal muscles, bone	Support and movement
Nervous	Brain, spinal cord	Coordination of body function through electrical signals and release of regulatory molecules
Reproductive	Ovaries and uterus, testes	Perpetuation of the species
Respiratory	Lungs, airways	Exchange of oxygen and carbon dioxide between the internal and external environments
Urinary	Kidneys, bladder	Maintenance of water and solutes in the internal environment; waste removal

The Integration between Systems of the Body



This schematic figure indicates relationships between systems of the human body. The interiors of some hollow organs (shown in white) are part of the external environment.

or through a break in the skin. In addition, immune tissues are closely associated with the circulatory system.

Traditionally, physiology courses and books are organized by organ system. Students study cardiovascular physiology and regulation of blood pressure in one chapter, and then study the kidneys and control of body fluid volume in a different chapter. In the functioning human, however, the cardiovascular and renal systems communicate with each other, so that a change in one is likely to cause a reaction in the other. For example, body fluid volume influences blood pressure, while changes in blood pressure alter kidney function because the kidneys regulate fluid volume. In this book, you will find several integrative physiology chapters that highlight the coordination of function across multiple organ systems.

Understanding how different organ systems work together is just as important as memorizing facts, but the complexity of interactions can be challenging. One way physiologists simplify and integrate information is by using visual representations of physiological processes called maps. The Focus on Mapping feature in this chapter will help you learn how to make maps. The first type of map, shown in **FIGURE 1.3a**, is a schematic representation of structure or function. The second type of map, shown in Figure 1.3b, diagrams a physiological process as it proceeds through time. These process maps are also called *flow charts, and they are frequently used in health care*. You will be able to practice mapping with special end-of-chapter questions throughout the book.

1.2 Function and Mechanism

We define physiology as the normal functioning of the body, but physiologists are careful to distinguish between *function* and *mechanism*. The **function** of a physiological system or event is the "why" of the system or event: Why does a certain response help an animal survive in a particular situation? In other words, what is the *adaptive significance* of this event for this animal?

For example, humans are large, mobile, terrestrial animals, and our bodies maintain relatively constant water content despite living in a dry, highly variable external environment. Dehydration is a constant threat to our well-being. What processes have evolved in our anatomy and physiology that allow us to survive in this hostile environment? One is the production of highly concentrated urine by the kidney, which allows the body to conserve water. This statement tells us *why* we produce concentrated urine but does not tell us *how* the kidney accomplishes that task.

Thinking about a physiological event in terms of its adaptive significance is the **teleological approach** to science. For example, the teleological answer to the question of why red blood cells transport oxygen is "because cells need oxygen and red blood cells bring it to them." This answer explains *why* red blood cells transport oxygen—their function—but says nothing about *how* the cells transport oxygen.

In contrast, most physiologists study physiological processes, or **mechanisms**—the "how" of a system. The **mechanistic approach** to physiology examines process. The mechanistic answer to the question "How do red blood cells transport oxygen?" is "Oxygen binds to hemoglobin molecules in the red blood cells." This very concrete answer explains exactly how oxygen transport occurs but says nothing about the significance of oxygen transport to the animal.

Students often confuse these two approaches to thinking about physiology. Studies have shown that even medical students tend to answer questions with teleological explanations when the more appropriate response would be a mechanistic explanation.[1] Often they do so because instructors ask why a physiological event occurs when they really want to know how it occurs. Staying aware of the two approaches will help prevent confusion.

Although function and mechanism seem to be two sides of the same coin, it is possible to study mechanisms, particularly at the cellular and subcellular level, without understanding their function in the life of the organism. As biological knowledge becomes more complex, scientists sometimes become so involved in studying complex processes that they fail to step back and look at the significance of those processes to cells, organ systems, or the animal. Conversely, it is possible to use teleological thinking incorrectly by saying, "Oh, in this situation the body needs to do this." *This* may be a good solution, but if a mechanism for doing *this* doesn't exist, the situation cannot be corrected.

Applying the concept of integrated functions and mechanisms is the underlying principle in **translational research,** an approach sometimes described as "bench to bedside." Translational research uses the insights and results gained from basic biomedical research on mechanisms to develop treatments and strategies for preventing human diseases. For example, researchers working on rats found that a chemical from the pancreas named *amylin* reduced the rats' food intake. These findings led directly to a translational research study in which human volunteers injected a synthetic form of amylin and recorded their subsequent food intake, but without intentionally modifying their lifestyle.[2] The drug suppressed food intake in humans, and was later approved by the Food and Drug Administration for treatment of diabetes mellitus.

[1] D. R. Richardson. A survey of students' notions of body function as teleologic or mechanistic. *Advan Physiol Educ* 258: 8–10, Jun 1990. Access free at *http://advan.physiology.org*.

[2] S. R. Smith *et al.* Pramlintide treatment reduces 24-h caloric intake and meal sizes and improves control of eating in obese subjects: a 6-wk translational research study. *Am J Physiol Endocrinol Metab* 293: E620–E627, 2007.

RUNNING PROBLEM

When Jimmy got back to his room, he sat down at his computer and went to the Internet. He typed *diabetes* in his search box—and came up with 267 million results. "That's not going to work. What about *insulin*?" Nearly 48 million results. "How in the world am I going to get any answers?" He clicked on the first sponsored ad that advertised "Information for type 2 diabetes." That might be good. His mother had type 2 diabetes. But it was for a pharmaceutical company trying to sell him a drug. "Maybe my physiology prof can help me with this search. I'll ask tomorrow."

Q1: *What search terms could Jimmy have used to get fewer results?*

2 5 9 12 16 19 24

At the systems level, we know about most of the mechanics of body function from centuries of research. The unanswered questions today mostly involve integration and control of these mechanisms, particularly at the cellular and molecular levels. Nevertheless, explaining what happens in test tubes or isolated cells can only partially answer questions about function. For this reason, animal and human trials are essential steps in the process of applying basic research to treating or curing diseases.

1.3 Themes in Physiology

"Physiology is not a science or a profession but a point of view."[3] Physiologists pride themselves on relating the mechanisms they study to the functioning of the organism as a whole. For students, being able to think about how multiple body systems integrate their function is one of the more difficult aspects of learning physiology. To develop expertise in physiology, you must do more than simply memorize facts and learn new terminology. Researchers have found that the ability to solve problems requires a conceptual framework, or "big picture," of the field.

This book will help you build a conceptual framework for physiology by explicitly emphasizing the basic biological concepts, or themes, that are common to all living organisms. These concepts form patterns that repeat over and over, and you will begin to recognize them when you encounter them in specific contexts. Pattern recognition is an important skill in healthcare professions, and it will also simplify learning physiology.

In the past few years, three different organizations issued reports to encourage the teaching of biology using these fundamental concepts. Although the descriptions vary in the three reports, five major themes emerge:

1. structure and function across all levels of organization
2. energy transfer, storage, and use
3. information flow, storage, and use within single organisms and within a species of organism

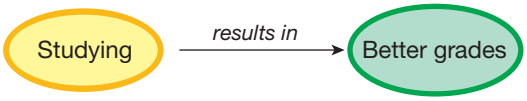
[3] R. W. Gerard. *Mirror to Physiology: A Self-Survey of Physiological Science.* Washington, DC: American Physiology Society, 1958.

FIG. 1.3 Focus on . . . Mapping

Why use maps to study physiology? The answer is simple: maps will help you organize information you are learning in a way that makes sense to you and they will make that information easier to recall on a test. Creating a map requires higher-level thinking about the relationships among items on the map.

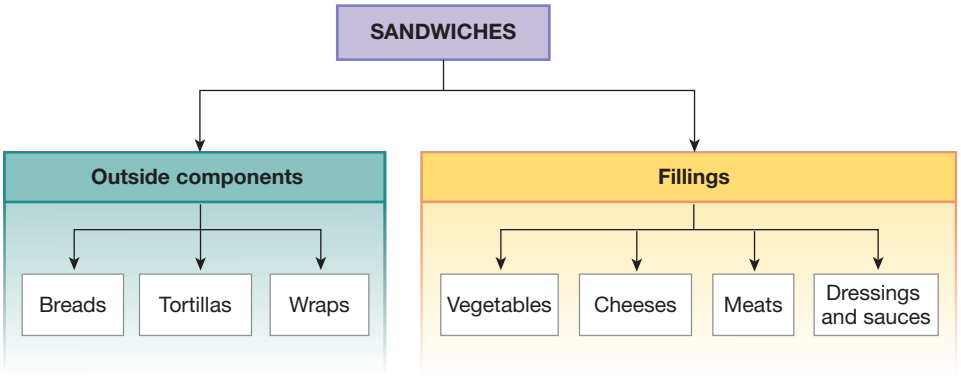
Mapping is not just a study technique. Scientists map out the steps in their experiments. Healthcare professionals create maps to guide them while diagnosing and treating patients. You can use mapping for almost every subject you study.

What is a map? Mapping is a nonlinear way of organizing material. A map can take a variety of forms but usually consists of terms (words or short phrases) linked by arrows to indicate associations. You can label the connecting arrows to describe the type of linkage between the terms (structure/function, cause/effect) or with explanatory phrases.

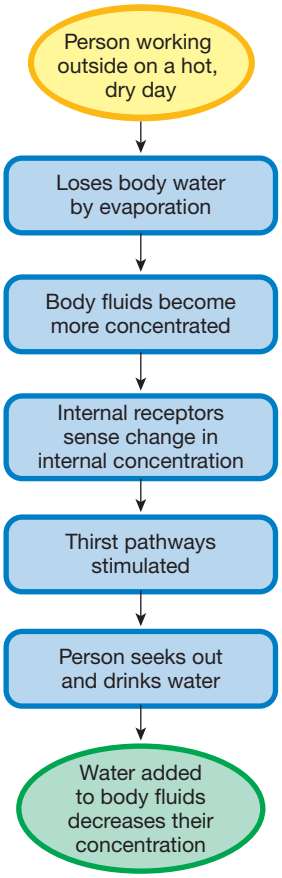


Here are two typical maps used in physiology.

Structure/function maps focus on the relationships between anatomical structures and their functions.



Process maps or **flow charts** follow normal homeostatic control pathways or the body's responses to abnormal (pathophysiological) events as they unfold over time.



Practice making maps. Many maps appear in this textbook, and they can serve as the starting point for your own maps. However, the real benefit of mapping comes from preparing maps yourself rather than memorizing someone else's maps. Your instructor can help you get started.

The next page walks you through the process of creating a structure-function map.

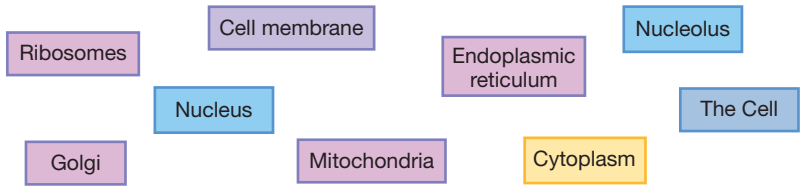
HINTS

- To help you get started, the end-of-chapter questions in this book include at least one list of terms to map for each chapter.
- Write your terms on individual slips of paper or small sticky notes so that you can rearrange the map more easily.
- Some terms may seem to belong to more than one group. Do not duplicate the item but make a note of it, as this term will probably have several arrows pointing to it or leading away from it.
- If arrows crisscross, try rearranging the terms on the map.
- Use color to indicate similar items.
- Add pictures and graphs that are associated with specific terms in your map.

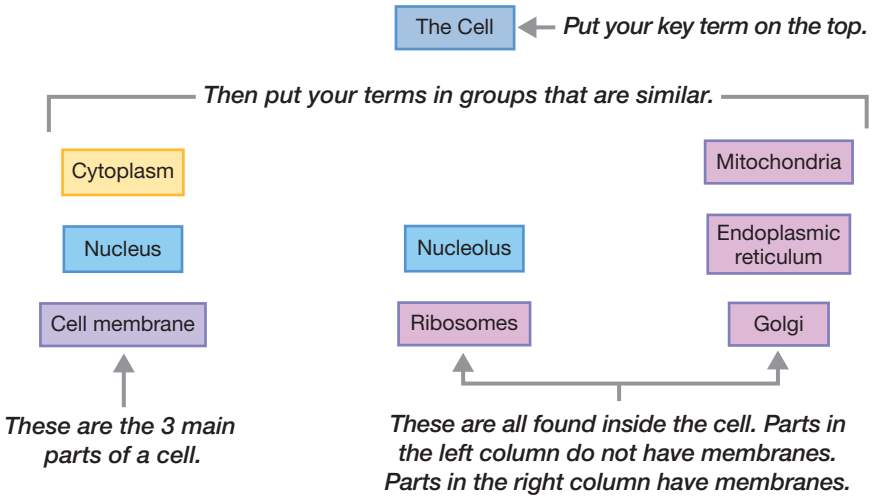
Electronic mapping. Some people do not like the messiness of hand-drawn maps. There are several electronic ways of making maps, including PowerPoint or free and commercial software programs. Free concept mapping software is available from IHMC CmapTools at http://cmap.ihmc.us. Or search for the term free concept map to find other resources on the Web. A popular commercial program for mapping is Inspiration (www.inspiration.com).

STEP 1: Write out the terms to map.

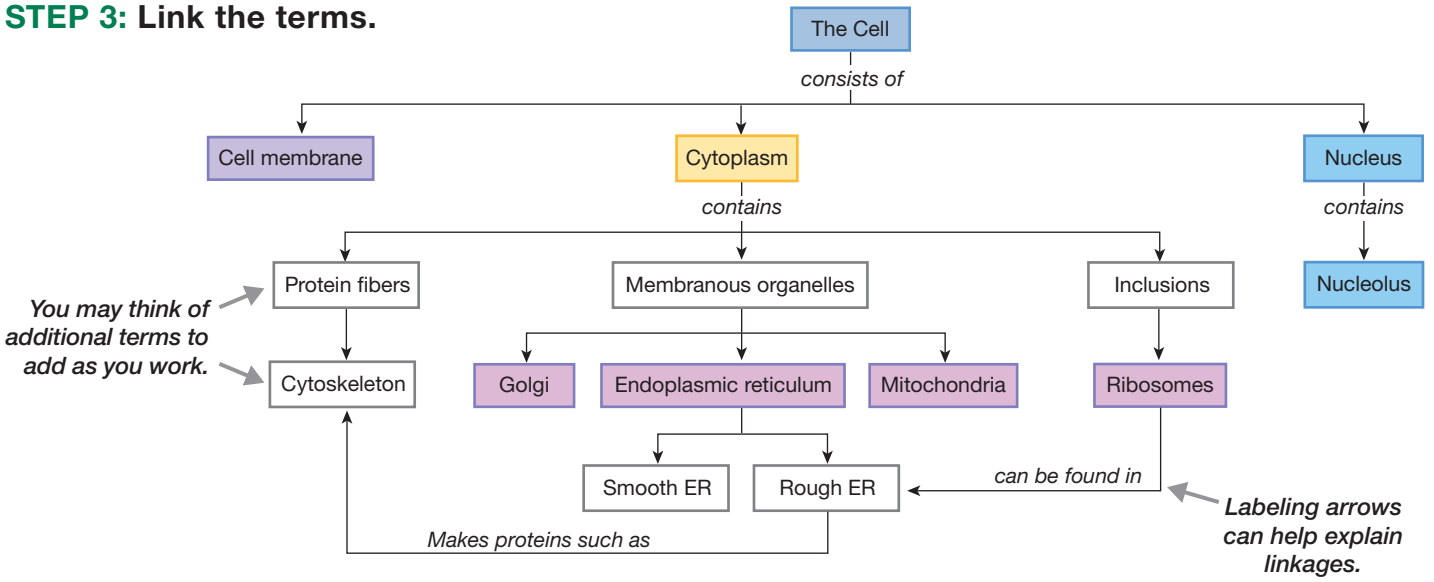
If you need help generating ideas for topics to map, the end-of-chapter mapping questions in each chapter have lists of terms to help you get started.



STEP 2: Organize the terms.



STEP 3: Link the terms.



Once you have created your map, sit back and think about it. Are all the items in the right place? You may want to move them around once you see the big picture. Add new concepts or correct wrong links. Review by recalling the main concept and then moving to the more specific details. Ask yourself questions like, What is the cause and what is the effect? What parts are involved? What are the main characteristics?

Science is a collaborative field. A useful way to study with a map is to **trade maps with a classmate** and try to understand each other's maps. Your maps will almost certainly not look the same! It's OK if they are different. Remember that your map reflects the way you think about the subject, which may be different from the way someone else thinks about it. Did one of you put in something the other forgot? Did one of you have an incorrect link between two items?

4. homeostasis and the control systems that maintain it
5. evolution

In addition, all three reports emphasize the importance of understanding how science is done and of the quantitative nature of biology. **TABLE 1.1** lists the core concepts in biology from the three reports.

In this book, we focus on the four themes most related to physiology: structure-function relationships, biological energy use, information flow within an organism, and homeostasis and the control systems that maintain it. The first six chapters introduce the fundamentals of these themes, which you may already be familiar with from earlier biology or chemistry classes. The themes and their associated concepts, with variations, then re-appear over and over in subsequent chapters of this book. Look for them in the summary material at the end of the chapters and in the end-of-chapter questions as well.

Theme 1: Structure and Function Are Closely Related

The integration of structure and function extends across all levels of organization, from the molecular level to the intact body. This theme subdivides into two major ideas: molecular interactions and compartmentation.

Molecular Interactions The ability of individual molecules to bind to or react with other molecules is essential for biological function. A molecule's function depends on its structure and shape, and even a small change to the structure or shape may have significant effects on the function. The classic example of this phenomenon is the change in one amino acid of the hemoglobin protein. (Hemoglobin is the oxygen-carrying pigment of the blood.) This one small change in the protein converts normal hemoglobin to the form associated with sickle cell disease.

Many physiologically significant molecular interactions that you will learn about in this book involve the class of biological molecules called *proteins*. Functional groups of proteins include *enzymes* that speed up chemical reactions, *signal molecules* and the *receptor proteins* that bind signal molecules, and specialized proteins that function as biological pumps, filters, motors, or transporters. Chapter 2 describes molecular interactions involving proteins in more detail.

Interactions between proteins, water, and other molecules influence cell structure and the mechanical properties of cells and tissues. Mechanical properties you will encounter in your study of physiology include *compliance* (ability to stretch), *elastance* (stiffness or the ability to return to the unstretched state), strength, flexibility, and fluidity (*viscosity*).

Compartmentation **Compartmentation** is the division of space into separate compartments. Compartments allow a cell, a tissue, or an organ to specialize and isolate functions. Each level of organization is associated with different types of compartments. At the macroscopic level, the tissues and organs of the body form discrete functional compartments, such as body cavities or the insides of hollow organs. At the microscopic level, cell membranes separate cells from the fluid surrounding them and also create tiny compartments within the cell called organelles. Compartmentation is the theme of Chapter 3.

Theme 2: Living Organisms Need Energy

Growth, reproduction, movement, homeostasis—these and all other processes that take place in an organism require the continuous input of energy. Where does this energy come from, and how is it stored? We will answer those questions and describe some of

TABLE 1.1 Biology Concepts

Scientific Foundations for Future Physicians (HHMI and AAMC)[1]	Vision and Change (NSF and AAAS)[2]	The 2010 Advanced Placement Biology Curriculum (College Board)[3]
Structure/function from molecules to organisms	Structure and function (anatomy and physiology)	Relationship of structure to function
Physical principles applied to living systems Chemical principles applied to living systems	Pathways and transformations of energy and matter	Energy transfer
Biomolecules and their functions	Information flow, exchange, and storage	Continuity and change
Organisms sense and control their internal environment and respond to external change	Systems	Regulation ("a state of dynamic balance")
Evolution as an organizing principle	Evolution	Evolution

[1] *Scientific Foundations for Future Physicians*. Howard Hughes Medical Institute (HHMI) and the Association of American Medical Colleges (AAMC), 2009. *www.aamc.org/scientificfoundations*
[2] *Vision and Change: A Call to Action*. National Science Foundation (NSF) and American Association for the Advancement of Science (AAAS). 2011. *http://visionandchange.org/finalreport*. The report mentioned the integration of science and society as well.
[3] *College Board AP Biology Course Description*, The College Board, 2010. *http://apcentral.collegeboard.com/apc/public/repository/ap-biology-course-description.pdf*. The AP report also included "Interdependence in Nature" and "Science, Technology and Society" as two of their eight themes.

the ways that energy in the body is used for building and breaking down molecules in Chapter 4. In subsequent chapters, you will learn how energy is used to transport molecules across cell membranes and to create movement.

Theme 3: Information Flow Coordinates Body Functions

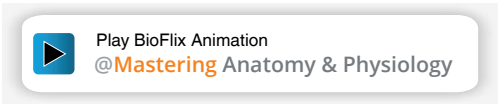
Information flow in living systems ranges from the transfer of information stored in DNA from generation to generation (genetics) to the flow of information within the body of a single organism. At the organismal level, information flow includes translation of DNA's genetic code into proteins responsible for cell structure and function.

In the human body, information flow between cells *coordinates function*. *Cell-to-cell communication* uses chemical signals, electrical signals, or a combination of both. Information may go from one cell to its neighbors (local communication) or from one part of the body to another (long-distance communication). Chapter 6 discusses chemical communication in the body.

When chemical signals reach their target cells, they must get their information into the cell. Some molecules are able to pass through the barrier of the cell membrane, but signal molecules that cannot enter the cell must pass their message across the cell membrane. How molecules cross biological membranes is the topic of Chapter 5.

Theme 4: Homeostasis Maintains Internal Stability

Organisms that survive in challenging habitats cope with external variability by keeping their internal environment relatively stable, an ability known as **homeostasis** {*homeo-*, similar + *-stasis*, condition}. Homeostasis and regulation of the internal environment are key principles of physiology and underlying themes in each chapter of this book. The next section looks in detail at the key elements of this important theme.



1.4 Homeostasis

The concept of a relatively stable internal environment is attributed to the French physician Claude Bernard in the mid-1800s. During his studies of experimental medicine, Bernard noted the stability of various physiological functions, such as body temperature, heart rate, and blood pressure. As the chair of physiology at the University of Paris, he wrote "La fixité du milieu intérieur est la condition de la vie libre, indépendante." (The constancy of the internal environment is the condition for a free and independent life.)[4] This idea was applied to many of the experimental observations of his day, and it became the subject of discussion among physiologists and physicians.

RUNNING PROBLEM

After his second physiology class, Jimmy introduced himself to his professor and explained his problem. The professor's first suggestion was simple: try to narrow the search. "One of the best ways to search is to combine terms using the connector AND. If you remember set theory from your math class, the connector AND will give you the intersection of the sets. In other words, you'll get only the results that occur in both sets."

Seemed simple enough. Jimmy went back to the Internet and tried *diabetes and insulin*. That search still had 46 million results but on the first page was a link to the American Diabetes Association, *diabetes.org*. Now he was getting somewhere.

Q2: *What kinds of websites should Jimmy be looking for in his results list, and how can he recognize them?*

2 5 9 12 16 19 24

In 1929, an American physiologist named Walter B. Cannon wrote a review for the American Physiological Society.[5] Using observations made by numerous physiologists and physicians during the nineteenth and early twentieth centuries, Cannon proposed a list of variables that are under homeostatic control. We now know that his list was both accurate and complete. Cannon divided his variables into what he described as environmental factors that affect cells (osmolarity, temperature, and pH) and "materials for cell needs" (nutrients, water, sodium, calcium, other inorganic ions, oxygen, as well as "internal secretions having general and continuous effects"). Cannon's "internal secretions" are the hormones and other chemicals that our cells use to communicate with one another.

In his essay, Cannon created the word *homeostasis* to describe the regulation of the body's internal environment. He explained that he selected the prefix *homeo-* (meaning *like* or *similar*) rather than the prefix *homo-* (meaning *same*) because the internal environment is maintained within a range of values rather than at an exact fixed value. He also pointed out that the suffix *-stasis* in this instance means a *condition*, not a state that is static and unchanging. Cannon's homeostasis, therefore, is a state of maintaining "a similar condition," similar to Claude Bernard's relatively constant internal environment.

Some physiologists contend that a literal interpretation of *stasis* {a state of standing} in the word *homeostasis* implies a static, unchanging state. They argue that we should use the word *homeodynamics* instead, to reflect the small changes constantly taking place in our internal environment {*dynamikos*, force or power}. Whether the process is called homeostasis or homeodynamics, the important concept to remember is that the body monitors its internal state and takes action to correct disruptions that threaten its normal function.

[4] C. Bernard. *Leçons sur les phénomènes de la vie communs aux animaux et aux végétaux* (Vol. 1, p. 113), Paris: J.-B. Baillière, 1885. (*http://obvil.paris-sorbonne.fr/corpus/critique/bernard_lecons-phenomenes-vie-I/body-2*)

[5] W. B. Cannon. Organization for physiological homeostasis. *Physiol Rev* 9: 399–443, 1929.