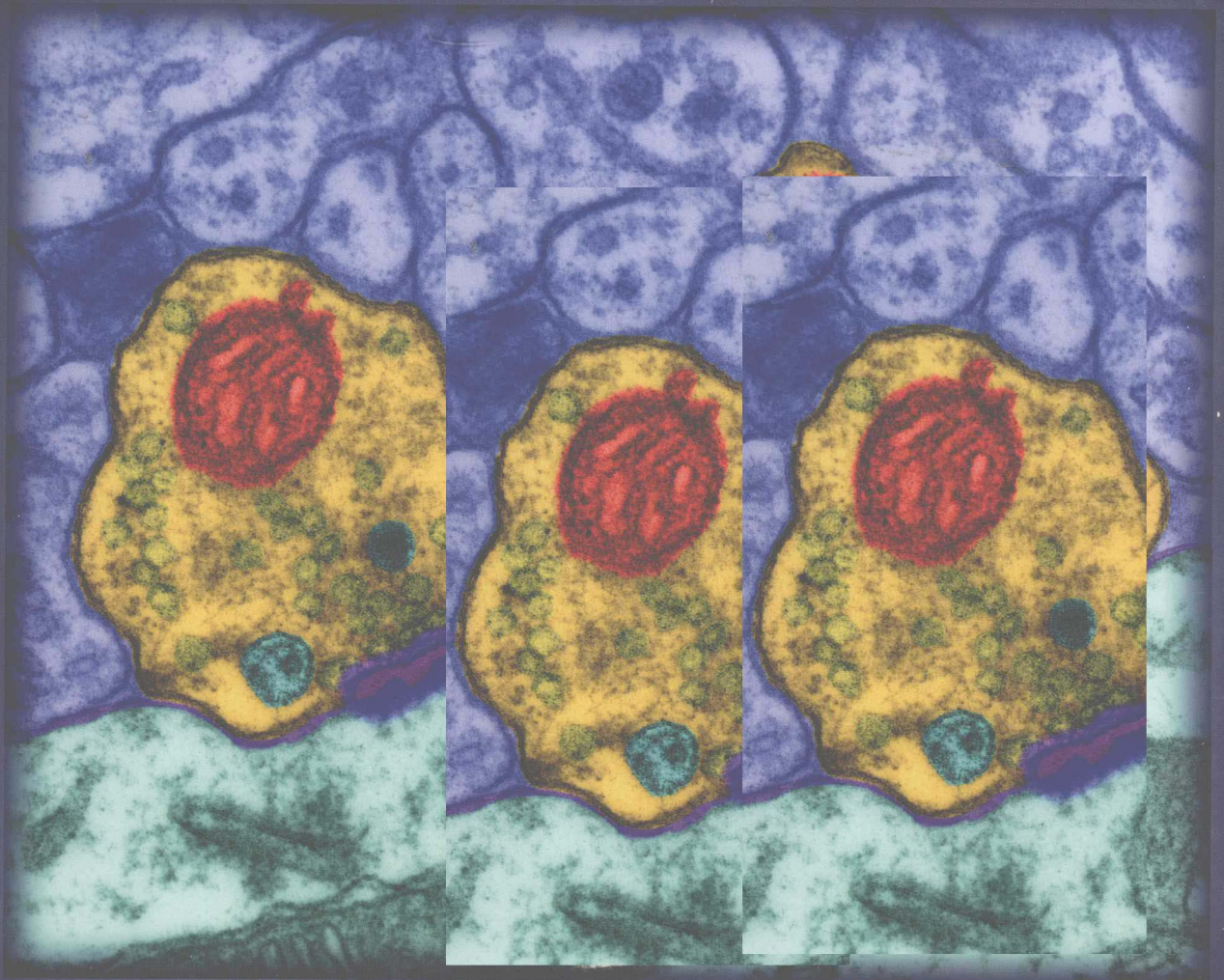


ninth edition

Vander, Sherman, & Luciano's

HUMAN PHYSIOLOGY

THE MECHANISMS OF BODY FUNCTION



Eric P. Widmaier

Hershel Raff

Kevin T. Strang

Vander, Sherman, & Luciano's

HUMAN PHYSIOLOGY

n i n t h e d i t i o n

Vander, Sherman, & Luciano's

HUMAN PHYSIOLOGY

T H E M E C H A N I S M S O F B O D Y F U N C T I O N

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I N D E D I C A T I O N

To our wives and children:

Maria, Ricky and Carrie

Judy and Jonathan

LeeAnn, Jake and Amy

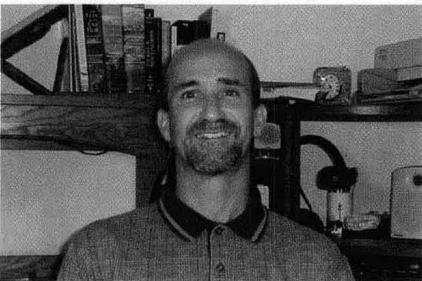
M E E T T H E N E W A U T H O R S



Eric P. Widmaier received his Ph.D. in 1984 in Endocrinology from the University of California at San Francisco. His postdoctoral training was in endocrinology and physiology at the Worcester Foundation for Experimental Biology, and The Salk Institute in La Jolla, CA. His research is focused on the control of body mass and metabolism in mammals, the mechanisms of hormone action, and the postnatal development of mature adrenal gland function. He is currently Professor of Biology at Boston University, where he has recently been recognized with the Gitner Award for Distinguished Teaching in Systems Physiology, Comparative Physiology, and General Endocrinology. He is the author of numerous scientific and lay publications, including books about physiology for the general reader. He lives outside Boston with his wife, Maria, and children, Carrie and Ricky.



Hershel Raff received his Ph.D. in Environmental Physiology from Johns Hopkins University in 1981 and did postdoctoral training in Endocrinology at the University of California at San Francisco. He is now a Professor of Medicine (Endocrine) and Physiology at the Medical College of Wisconsin and Director of the Endocrine Research Laboratory at St. Luke's Medical Center. At the Medical College of Wisconsin, he teaches systems physiology and neuroendocrinology to medical and graduate students. He was an inaugural inductee into the Society of Teaching Scholars, and he recently received the Beckman Basic Science Teaching Award from the Senior Class and the Outstanding Teacher Award from the Graduate Student Association. He also teaches at Marquette University, where he is an adjunct professor, and at the University of Wisconsin (Milwaukee) where he is a clinical professor. Dr. Raff's basic research focuses on the effects of low oxygen (hypoxia) at the organismal, cellular, and molecular levels. His clinical interest focuses on developing new methods to diagnose pituitary and adrenal diseases, with a special focus on Cushing's syndrome. His hobby is playing a variety of musical instruments including the piano, guitar, and bass. He resides outside Milwaukee with his wife, Judy, and son, Jonathan.



Kevin T. Strang received his Master's in Zoology (1988) and his Ph.D. in Physiology (1994) from the University of Wisconsin at Madison. His research area is cellular mechanisms of contractility modulation in cardiac muscle. He teaches a large undergraduate systems physiology course as well as first-year medical physiology in the UW-Madison Medical School. He was elected to UW-Madison's Teaching Academy and serves on the executive committee of the Center for Biology Education. Recent awards include the UW Medical Alumni Association's Distinguished Teaching Award for Basic Sciences, and the University of Wisconsin System's Underkoffler/Alliant Energy Excellence in Teaching Award. Interested in teaching technology, Dr. Strang has created an interactive CD-ROM tutorial called "Anatomy of a Heart Attack," and he has produced a number of animations for teaching complex physiological processes. He coaches soccer and Little League Baseball in Madison, where he lives with his wife, LeeAnn, and children, Jake and Amy.

PREFACE

Assuming the authorship of a textbook with the well-deserved reputation of Vander, Sherman, and Luciano's *Human Physiology* has been a privilege and an honor for each of the new authors. We have stayed true to the overall mission of the textbook, which is to present the topic of physiology in a sophisticated way that is suitable for any student of the science. One of the strengths of the Vander et al. text has been its thoroughness and clarity of presentation. Although the text now reflects our own writing style, we made it a priority to continue the tradition of presenting the material in each chapter in an unambiguous, straightforward way, with easy-to-follow illustrations and flow diagrams.

The eighth edition of *Human Physiology* was reviewed extensively by colleagues across the United States. Many suggestions emerged that have enabled us to improve even further the pedagogical value of the textbook. Long-time users of this textbook will notice that certain chapters have been reorganized and, in some cases, either expanded or condensed. There have also been a considerable number of new clinical applications added to most chapters, without, however, having to resort to colored "boxes" scattered throughout the text that distract the reader. Many of these new clinical features were incorporated into the body of the text, while in other cases expanded discussions were added to the end-of-chapter sections in a new feature called "Additional Clinical Examples." We feel that these additional clinical highlights will grab the interest of students interested in any area of health care, be it allied health, medicine or dentistry, biomedical engineering, or any of the other related health disciplines.

Many features of this ninth edition will be familiar to past users of the textbook. For example, key terms are featured in the text in **boldface**, while clinical terms are in **bold italics**. Key and clinical terms, with pagination, as well as succinct chapter summaries and thought questions, are still included at the end of each section and chapter. The glossary, already among the best of its kind, has been further expanded by over 400 terms. Illustrations continue to make use of clear, carefully labelled diagrams and flowcharts. However, the new edition features something new in the inclusion of photographs of individuals with clinical disorders.

The goal of this revision has been to make an excellent textbook even better by presenting the material in a sequence that is more geared to the typical sequence

of lectures offered in many human physiology courses. While we have retained the sophistication of the writing style, we have also carefully gone over each sentence to improve the flow and readability of the text for the modern student.

"... the ninth edition appears poised to carry on the excellence of its predecessors and should remain the most popular choice in the human physiology market."

John J. Lepri
University of North Carolina-Greensboro

REVISION HIGHLIGHTS FOR NINTH EDITION

Consolidation of Homeostasis

A chief feature of the new edition is the consolidation of the topic of homeostasis, which was previously split between the opening chapter and Chapter 7. The text now opens with an expanded, detailed chapter on homeostasis and feedback. This provides the student with a frame of reference, to enable him or her to appreciate the fact that homeostasis is the unifying principle of physiology. This change also reflects the fact that many teachers of physiology begin their instruction with a detailed discussion of homeostatic principles.

Streamlined Introductory Chapters

Former Chapter 2 has been retained and updated, while former Chapters 3 through 5 have been consolidated into a single chapter. The material in Chapters 2 and 3 is presented in a logical pattern, beginning with cell chemistry and cell structure, proceeding to biochemical characteristics of proteins, protein synthesis and degradation, and concluding with protein actions (including enzymes). Some of the former material on the genetics of the cell cycle and replication has been deleted, so that the focus of the introductory chapters is now directed more toward protein structure and function and its relationship to physiology. Streamlining this material has also allowed us to expand areas of particular interest in the systems physiology chapters without extending the length of the book.

"I like the idea of spending more time on organ systems. . . .consolidation of endocrine sections is a good idea."

James Porter
Brigham Young University

New Endocrinology Chapter

A third major organizational change is the consolidation of the presentations of thyroid function, endocrine control of growth, and the control of the stress response, from their previous chapters throughout the text into a single chapter on Endocrinology. The hormones involved in these processes are still referred to throughout the text in the context of different organ systems, but the major discussions of thyroid hormone, growth hormone, and cortisol are now presented as individual sections in Chapter 11. This change was made in response to numerous requests from instructors to expand the endocrine unit and make it more cohesive. We have retained the outstanding discussion of general principles of endocrinology as the first section of the revised chapter.

Improved Nervous System Coverage

The chapters on the nervous system, most notably, have been updated to include new information on neurotransmitter actions, learning and memory, and sensory transduction, to name a few examples. The discussion of electrical events in the cell has been expanded and restructured. For example, the Nernst equation and its importance in understanding membrane potential and ion flux has been moved from the appendices and incorporated directly into the body of the text.

Enhanced Clinical Coverage

Finally, dozens of new clinical features have been added to the text, in order to better help the student put this body of knowledge into a real-life context. Some of these are highlighted in the list that follows. A list of clinical terms used throughout the text has been included as a separate index in Appendix F making it easy for the reader to immediately locate where a particular disorder or disease is covered.

"To me, the clinical examples are the strongest point. . . . This makes the information more relevant, and therefore, more learnable."

James D. Herman
Texas A&M University

We believe the result of these changes is to make a great book even better and more lecture-friendly, as well as to draw the student deeper into the realm of pathophysiology in addition to normal physiological mechanisms.

CHAPTER HIGHLIGHTS

The following is a list of some of the key changes, updates, and refinements that have been made to ninth edition chapters.

Chapter 1 Homeostasis: A Framework for Human Physiology

Thorough discussion of homeostasis
Fluid composition across cell membranes
Variability and time-averaged means
Feedback at the organ and cellular levels
Quantification of physiological variables

Chapter 2 Chemical Composition of the Body

Dehydration reactions
Peptide/protein distinction
Protein structures introduced
ATP structure and importance

Chapter 3 Cell Structure and Protein Function

Condensed coverage of Chapters 3, 4, and 5 in eighth edition
Emphasis on protein biology
Logical progression from cell chemistry through protein signaling mechanisms

Chapter 4 Movement of Molecules Across Cell Membranes

Types of gated channels identified
Details on transporter mechanisms
Isotonic solutions to replace blood volume after injury

Chapter 5 Control of Cells by Chemical Messengers

Subunit structure and mechanism of G-proteins
Genomic actions of cAMP
Calcium's role in protein kinase C activation
Eicosanoid structure and function

Chapter 6 Neuronal Signaling and the Structure of the Nervous System

Revised discussion of the origin of resting and action potentials
Explanation of the Nernst equation and its importance in understanding how ions move across neuronal membranes
Updated mechanisms of neurotransmitter release and actions
Adrenergic subtypes and their actions

New Figures:

Myelin formation; Sodium and potassium channel function; Myelination and saltatory conduction; Neurotransmitter storage and release; Brain surface and midline anatomy; Cellular organization of the cortex

New Clinical Material:

Mechanism of anesthetic action; Effects of diabetes on the nervous system

Chapter 7 Sensory Physiology

Recent discoveries related to sensory receptors
Neural pathways of somatosensory system
Phototransduction

New Figures:

Pathways of pain transmission; Phototransduction in

photoreceptor; Neurotransmitter release in auditory hair cell

New Clinical Material:

Genetics of color blindness; Genetic pedigree for red-green color blindness; Loss of hearing and balance

Chapter 8 Consciousness, the Brain, and Behavior

Expansion of sleep/wake control mechanisms

New theories of memory function

Hemispheric dominance, including split-brain patients

New Figure:

Encoding and storing of memories

New Clinical Material:

Physiological changes associated with sleep; Manifestation of unilateral visual neglect; Temporal lobe dysfunction and formation of declarative memory; Amygdala lobe dysfunction and emotions; Head trauma and conscious state

Chapter 9 Muscle

Expanded description of cross-bridge cycle

Role of DHP and ryanodine receptors

Concentric versus eccentric muscle contractions

Tetanic muscle force

Oxygen debt

Latch state

New Figures:

Neuromuscular junction; Signaling at neuromuscular junction; Muscle mechanics apparatus

New Clinical Material:

Paralytic agents in surgery; Nerve gas paralysis; Botulinum toxin; Muscle cramps; Duchenne muscular dystrophy; Myasthenia gravis

Chapter 10 Control of Body Movement

Expanded discussion of proprioception

New Clinical Material:

Embryonic stem cells and Parkinson's disease; Cerebellar function and autism; Clasp-knife phenomenon; Tetanus

Chapter 11 The Endocrine System

Membrane localization of certain receptors

Acute and delayed actions of hormones

Diffusion of steroid hormones

Effect of calcium on parathyroid hormone secretion

Functions of oxytocin

Amplification of endocrine responses in three-hormone sequence

New sections on thyroid hormone, growth, and stress

New Figures:

Thyroid anatomy; Thyroid hormone synthesis; Person with goiter; Person with exophthalmia; Person with Cushing's syndrome; Person with acromegaly

New Clinical Material:

Androgen insensitivity syndrome; Autonomous hormone-secreting tumors; Hypertrophy and goiter; Effects of TH; Hyperthyroidism; Graves' disease; Exophthalmos; Hypothyroidism; Hashimoto's disease; Myxedema; Autoimmune thyroiditis; Treatment of thyroid diseases; Effects of stress-induced cortisol production on reproduction; Primary and secondary adrenal insufficiency; Cushing's syndrome; Treatment of

adrenal diseases; Laron dwarfism; Acromegaly and gigantism

Chapter 12 Cardiovascular Physiology

Updated information on pacemaker cells

L-type calcium channels

Cushing's phenomenon

Reference table for ECG leads

New Figures:

Cardiac pacemaker cell action potential; Electron micrograph of brain capillary; Person with filariasis; Dye-contrast coronary angioplasty

New Clinical Material:

Angiostatin and blood vessel growth in cancer; Causes of edema; Hypertrophic cardiomyopathy; Vasovagal syncope

"Content is appropriate level for my students, and it is rigorous enough but not too rigorous."

Charles Nicoll

University of California-Berkeley

Chapter 13 Respiratory Physiology

Law of Laplace

Steep portion of oxygen dissociation curve

New Figures:

Law of Laplace; Sleep apnea

New Clinical Material:

Nitric oxide as treatment for persistent pulmonary hypertension; Acute respiratory distress syndrome; Sleep apnea

Chapter 14 The Kidneys and Regulation of Water and Inorganic Ions

Effects of constriction and dilation of afferent and efferent arterioles; Dietary sources of vitamin D

New Figures:

Parathyroid glands; Arteriolar constriction and dilation in glomerulus; Hemodialysis

New Clinical Material:

Incontinence; Subtypes of diabetes insipidus; ACE inhibitors and angiotensin II receptor antagonists; Hyperaldosteronism; Hypercalcemia and hypocalcemia; Hyperparathyroidism; Humoral hypercalcemia of malignancy; Primary hypoparathyroidism; Pseudohypoparathyroidism

Chapter 15 The Digestion and Absorption of Food

Table on the functions of saliva

Role of CNS in GI function

Effect of pH on pepsin production

Updated average daily intakes of carbohydrate, fat, and protein

New Figure:

Endoscopy

New Clinical Material:

Inflammatory bowel disease; Malabsorption; Pernicious anemia; Sjögren's syndrome; Steatorrhea; Lithotripsy

Chapter 16 Regulation of Organic Metabolism and Energy

Balance

*Hormone-sensitive lipase**Diabetes mellitus nomenclature updated**Ketone types**Resistin and insulin resistance**Effect of temperature on rate of chemical reactions***New Clinical Material:**

Familial hypercholesterolemia; Vitamin deficiency and hyperthyroidism; Leptin resistance; Decreased leptin during starvation; Hypothalamic disease; Brown adipose tissue; Heat stroke and heat exhaustion

Chapter 17 Reproduction*Dihydrotestosterone; 5-alpha-reductase, and aromatase**New theories on initiation of parturition***New Figures:***Klinefelter's syndrome; Congenital adrenal hyperplasia***New Clinical Material:**

Male pattern baldness; Hypogonadism; Klinefelter's syndrome; Gynecomastia; Hyperprolactinemia; Toxemia; Breech presentation; Contraception methods; Amenorrhea; Cloning; Cryptorchidism; Congenital adrenal hyperplasia; Virilization; Ambiguous genitalia; Precocious puberty

Chapter 18 Defense Mechanisms of the Body*Cross-talk within immune system**Margination**Diapedesis**Types of antigens**Structure of immunoglobulins***New Clinical Material:***Kaposi's sarcoma; Systemic lupus erythematosus***John D. Buntin***University of Wisconsin***Fernando A. Carballo***St. Luke's Medical Center***John Celenza***Boston University***Allen W. Cowley***Medical College of Wisconsin***Jean-Pierre Dujardin***The Ohio State University***James Ervasti***University of Wisconsin–Madison***James W. Findling***St. Luke's Medical Center***Robert S. Fitzgerald***Johns Hopkins University***Hubert V. Forster***Medical College of Wisconsin***Kathleen French***University of California–San Diego***Norman E. Garrison***James Madison University***Thomas Gilmore***Boston University***Elizabeth Godrick***Boston University***David L. Hammerman***Long Island University***Matthew H. Hanna***St. Luke's Medical Center***Lois Jane Heller***University of Minnesota, School of Medicine–Duluth***Patrick K. Hidy***Central Texas College***Herbert W. House***Elon College***Theodore J. Hubley***St. Luke's Medical Center***Kelly Johnson***University of Kansas***Kenneth V. Kaloustian***Quinnipiac University***Harold M. Kaplan***Southern Illinois University, School of Medicine***Michael L. Kennedy***Pacific Lutheran University***Penny Knoblich***Minnesota State University, Mankato***Kiyomi Koizumi***SUNY Health Science Center at Brooklyn, College of Medicine***David Kurjiaka***Ohio University***Beth M. Lalande***St. Luke's Medical Center***John J. Lepri***University of North Carolina–Greensboro***Charles Kingsley Levy***Boston University***ACKNOWLEDGMENTS**

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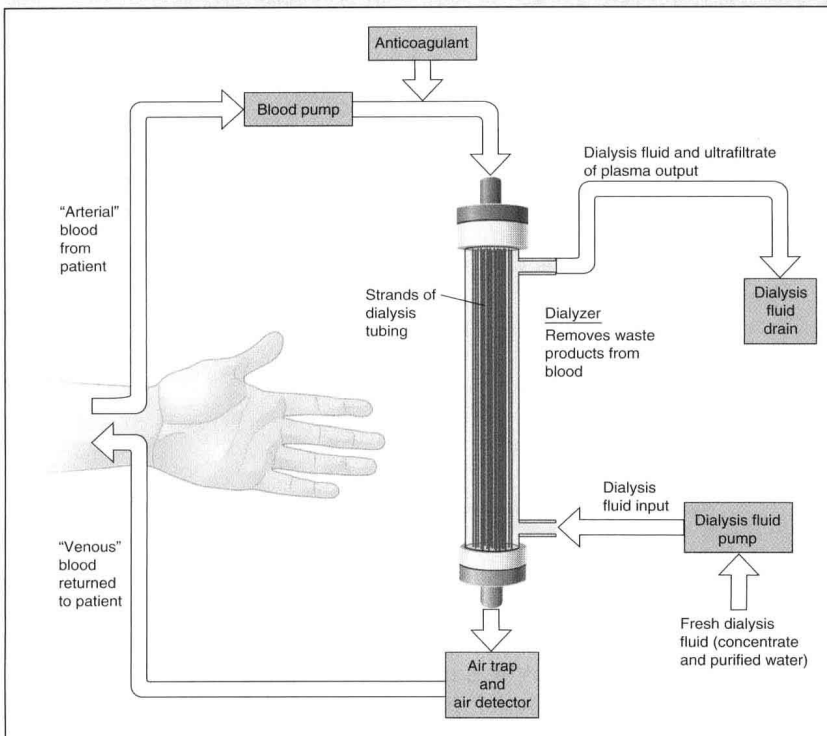
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Eric P. Widmaier
Hershel Raff
Kevin T. Strang

Textbook Tour

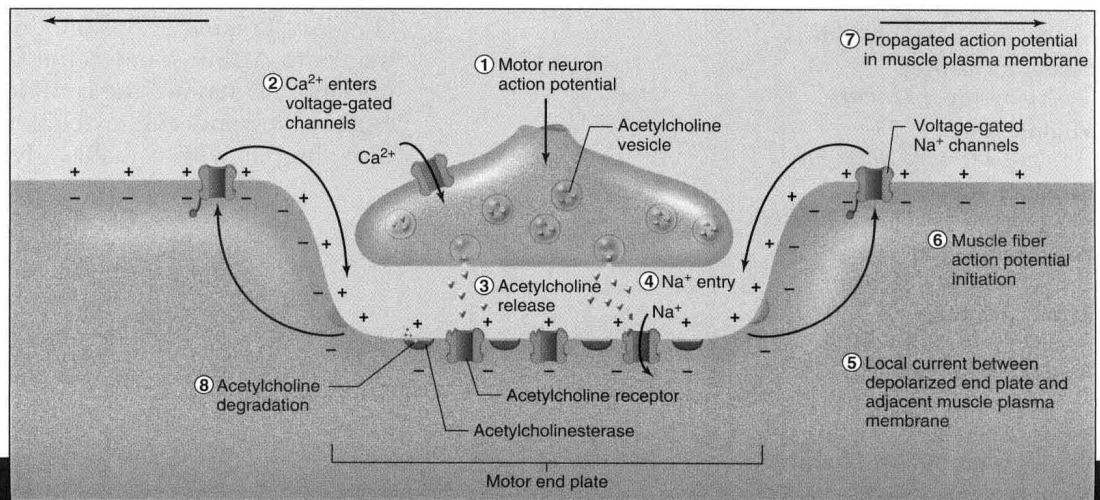


"Illustrations are one of the strong points in previous editions and this continues to be the case with the 9th edition."

Daniel Richardson
University of Kentucky

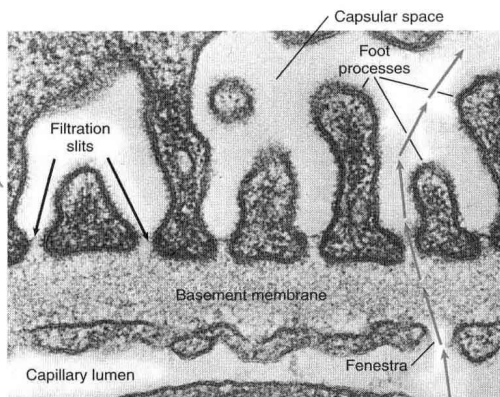
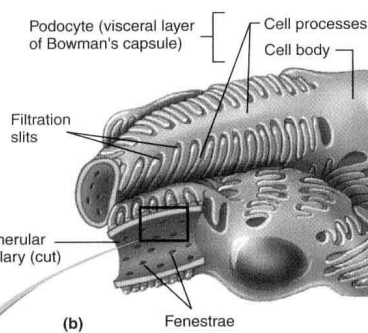
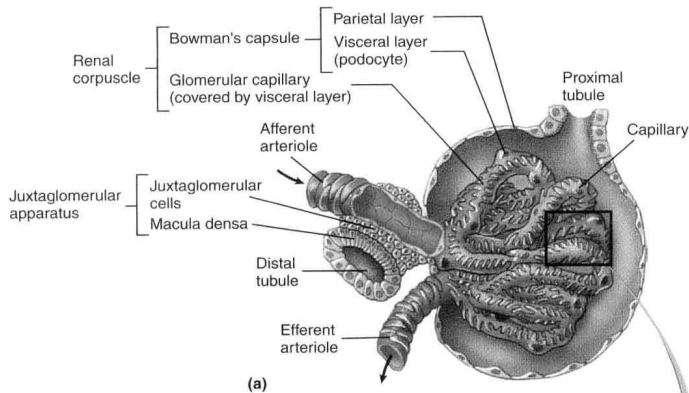
Beautifully Rendered Full-Color Art

Almost all of the figures have been redone in this edition, ranging from a complete redrawing of the figure to simple labeling changes. A realistic three-dimensional perspective has been added to many of the figures for greater clarity and understanding of the concept.



Color-Coded Illustrations

Color-coding is effectively used to promote learning. For example, there are specific colors for the extracellular fluid, the intracellular fluid, muscle, and the lumen of the renal tubules and GI tract.



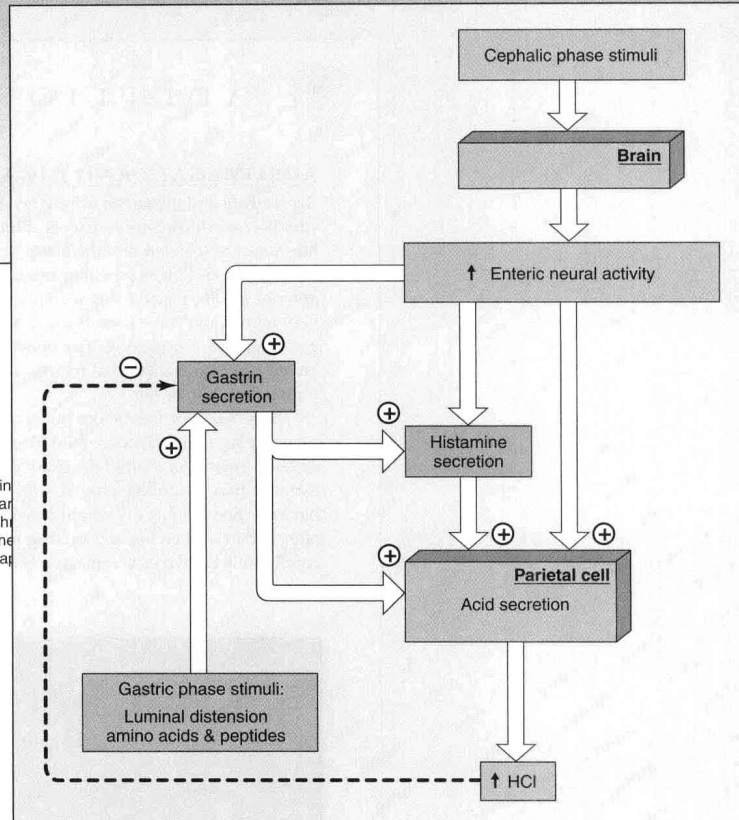
a. Blood flows in the afferent and efferent arterioles. The Bowman's capsule

b. Podocytes of Bowman's capsule surround the capillaries. Filtration slits between the podocytes allow fluid to pass into Bowman's capsule. The glomerulus is composed of capillary endothelium that is fenestrated. Surrounding the endothelial cells is a basement membrane.

c. Substances in the blood are filtered through capillary fenestrae. The filtrate then passes across the basement membrane and through slit pores between the foot processes (also called pedicels) and enters the capsular space. From here, the filtrate is transported to the lumen of the proximal convoluted tubule.

Flow Diagrams

Long a hallmark of this book, extensive use of flow diagrams has been continued in this edition. A bookmark has been included with your book to give a further explanation.



Clinical Examples

New discussions of clinical applications have been added at the ends of appropriate sections. The authors have drawn from their teaching and clinical experiences to provide students with real-life applications.



ADDITIONAL CLINICAL EXAMPLES

ACROMEGALY AND GIGANTISM

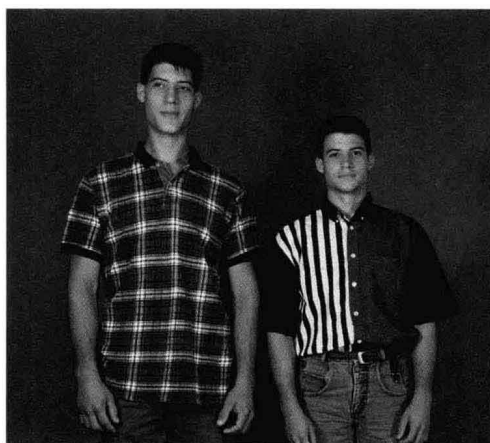
Acromegaly and *gigantism* arise when there exists a situation in which chronic, excess amounts of growth hormone are secreted into the blood. In almost all cases, acromegaly and gigantism are caused by tumors of the anterior pituitary gland that secrete growth hormone at very high rates. These tumors are typically very slow growing, and, if occurring after puberty, it may be decades before a person realizes that there is something seriously wrong with him or her.

If the tumor arises before puberty, when the epiphyseal growth plates are still open, then the individual will develop gigantism ("pituitary giant") and grow to extraordinary heights (Figure 11-28). Some pituitary giants have reached heights over eight feet! If the tumor arises after puberty, when linear growth is no longer possible, the condition is known as acromegaly. Such people will be of

normal height but will manifest many other symptoms that also occur in pituitary giants.

Even when linear growth is no longer possible (after puberty), very high plasma levels of GH result in the thickening of many bones in the body, most noticeably in the hands, feet, and head. The jaw, particularly, enlarges to give the characteristic facial appearance ("*prognathism*") associated with acromegaly. In addition, many internal organs also become enlarged, and this can interfere with their ability to function normally.

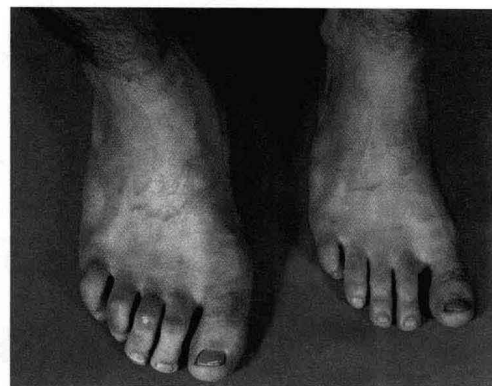
All adults continue to make and secrete GH even after growth has stopped. That is because GH has metabolic



(a)



(b)



(c)

FIGURE 11-28

Gigantism and acromegaly in one individual of a pair of identical twins. Note the increased height and facial bone thickening (a), as well as the bone thickening of hands (b) and feet (c).

"Additional clinical examples are excellent. This is definitely an improvement."

Jeffrey Walker
University of Wisconsin

TABLE 6-8 Summary of Functions of the Major Parts of the Brain

I. Forebrain

A. Cerebral hemispheres

1. Contain the cerebral cortex, which participates in perception (Chapter 7), the generation of skilled movements (Chapter 10), reasoning, learning, and memory (Chapter 8)
2. Contain subcortical nuclei, including those that participate in coordination of skeletal muscle activity (Chapter 10)
3. Contain interconnecting fiber pathways

B. Thalamus

1. Is a synaptic relay station for sensory pathways on their way to the cerebral cortex (Chapter 7)
2. Participates in control of skeletal muscle coordination (Chapter 10)
3. Plays a key role in awareness (Chapter 8)

C. Hypothalamus

1. Regulates anterior pituitary gland function (Chapter 11)
2. Regulates water balance (Chapter 14)
3. Participates in regulation of autonomic nervous system (Chapters 6 and 16)
4. Regulates eating and drinking behavior (Chapter 16)
5. Regulates reproductive system (Chapters 11 and 17)
6. Reinforces certain behaviors (Chapter 8)
7. Generates and regulates circadian rhythms (Chapters 1, 7, 11, and 16)
8. Regulates body temperature (Chapter 16)
9. Participates in generation of emotional behavior (Chapter 8)

D. Limbic system

1. Participates in generation of emotions and emotional behavior (Chapter 8)
2. Plays essential role in most kinds of learning (Chapter 8)

II. Cerebellum

- A. Coordinates movements, including those for posture and balance (Chapter 10)
- B. Participates in some forms of learning (Chapter 8)

III. Brainstem

- A. Contains all the fibers passing between the spinal cord, forebrain, and cerebellum
- B. Contains the reticular formation and its various integrating centers, including those for cardiovascular and respiratory activity (Chapters 12 and 13)
- C. Contains nuclei for cranial nerves III through XII

Summary Tables

Some summary tables summarize small or moderate amounts of information, whereas others bring together large amounts of information that may be scattered throughout the book. The tables complement the accompanying figures to provide a rapid means of reviewing the most important material in a chapter.

"... I would rank the text a 10 in valuable educational features that enhance learning."

Bruce Bennett
Community College of Rhode Island

THOUGHT QUESTIONS

(Answers are given in Appendix A.)

1. In two cases (A and B), the concentrations of solute X in two 1-L compartments separated by a membrane through which X can diffuse are

Case	CONCENTRATION OF X, mM	
	Compartment 1	Compartment 2
A	3	5
B	32	30

- a. In what direction will the net flux of X take place in case A and in case B?
- b. When diffusion equilibrium is reached, what will be the concentration of solute in each compartment in case A and in case B?
- c. Will A reach diffusion equilibrium faster, slower, or at the same rate as B?

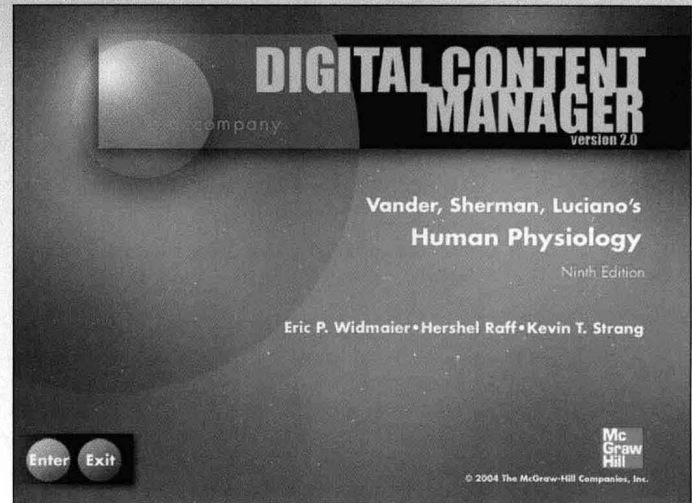
Thought Questions

At the end of each chapter are Thought Questions that challenge you to go beyond the memorization of facts to solve problems and encourage you to stop and think more deeply about the meaning or broader significance of what you have just read.

Supplements Tour

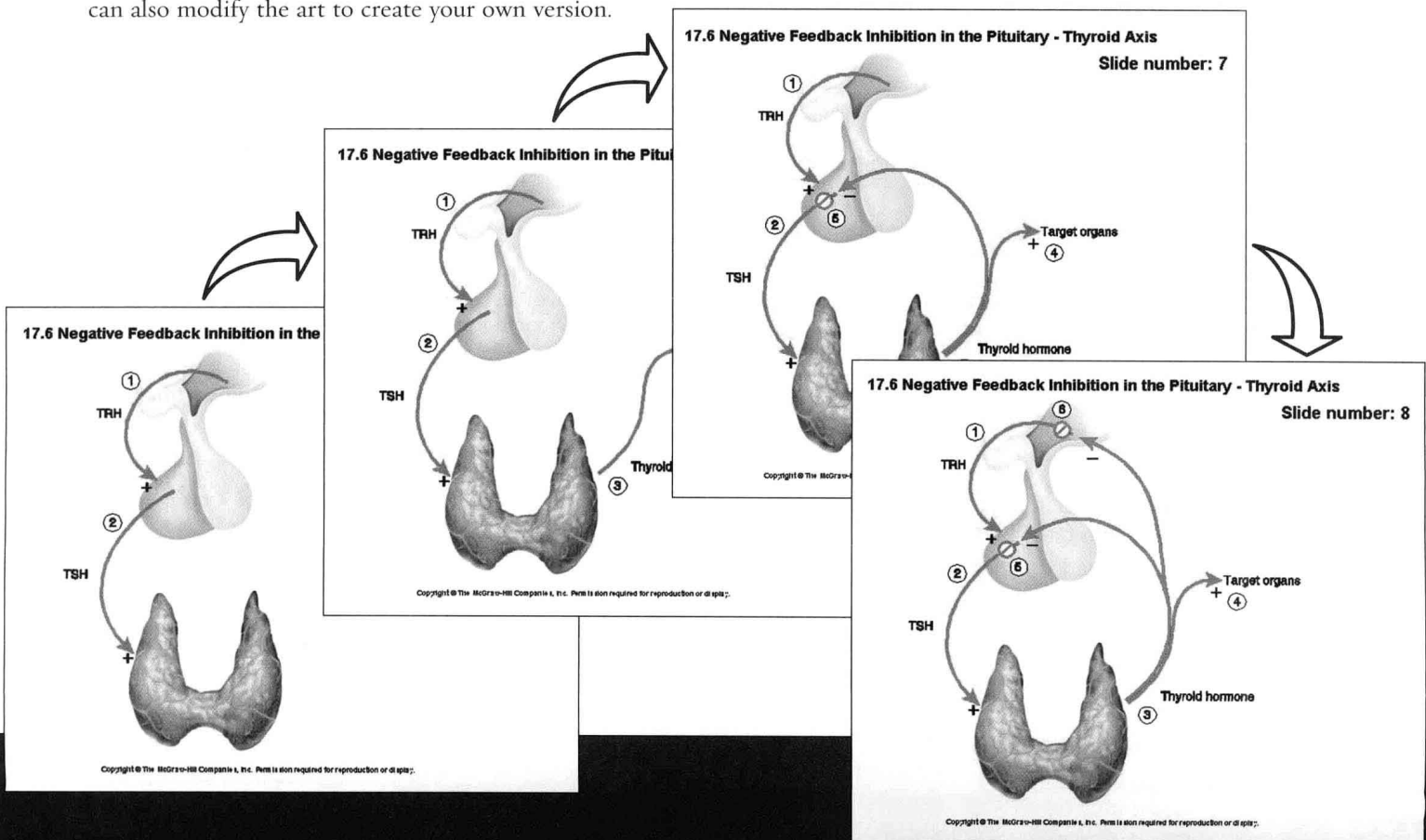
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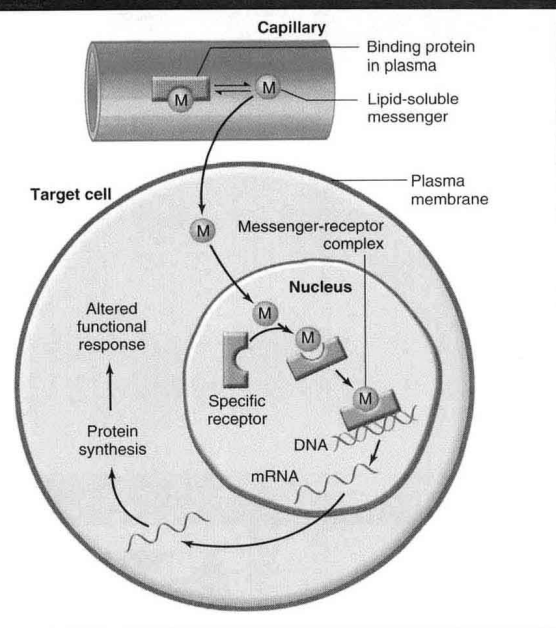
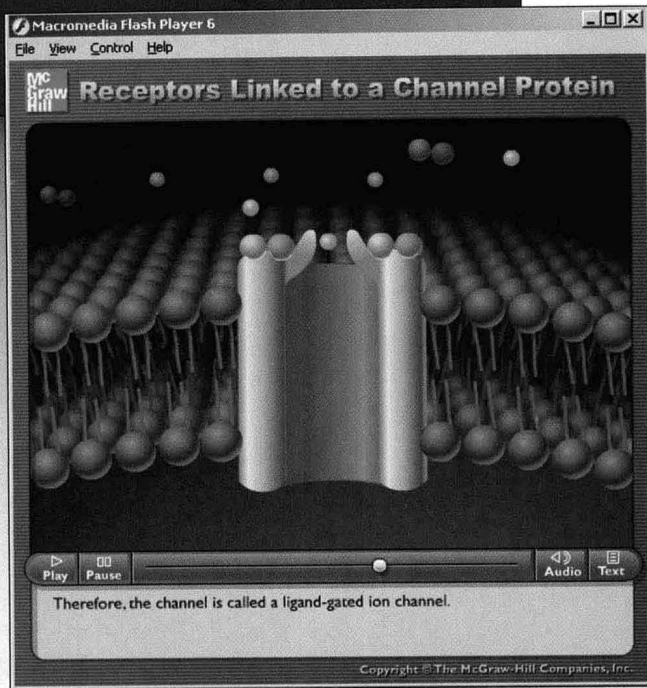
If you're looking for illustrations, photographs, tables, and animations to incorporate into your lecture presentations, handouts, or quizzes, this easy-to-use CD contains hundreds of digital assets from *Human Physiology*. Simply click on the chapter folder, select an image, and you're ready to import the image into the application of your choice. It's that easy.



Active Art

Step-by-step breakdown of key illustrations allows you to synchronize the art with your lecture presentation. You can also modify the art to create your own version.





Animations

Animations found on the Digital Content Manager allow you to harness the visual impact of processes in motion. You can import the animations into presentations or online course materials.

Illustrations, Photos, and Tables

Full-color digital files of the art and tables in *Human Physiology* can be readily incorporated into presentations, exams, or custom classroom materials.

PowerPoint Lecture Outlines

Accessible from the Digital Content Manager CD, a complete PowerPoint lecture outline with illustrations from the textbook is available for every chapter. Use the outline as is or modify it to match your specific course needs.

Leukocyte Behavior in Inflammation

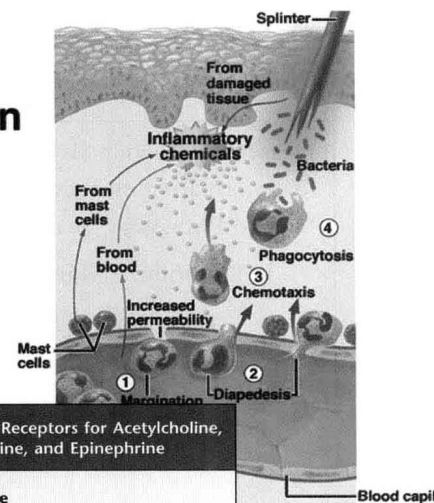


TABLE 6-12 Locations of Receptors for Acetylcholine, Norepinephrine, and Epinephrine

I. Receptors for acetylcholine

a. Nicotinic receptors

- On postganglionic neurons in the autonomic ganglia
- At neuromuscular junctions of skeletal muscle
- On some central nervous system neurons

b. Muscarinic receptors

- On smooth muscle
- On cardiac muscle
- On gland cells
- On some central nervous system neurons

Alternative functions of endocytosis:

- Transcellular transport
- 2. Endosomal processing
- 3. Recycling the membrane
- 4. Destroying engulfed materials

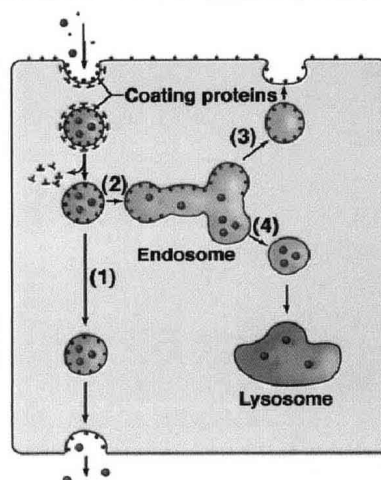


Figure 4-20