

INTERNATIONAL STUDENT EDITION



Human Physiology Sixth Edition

From Cells to Systems

Lauralee Sherwood

Not for Sale in the  
United States

# Contents

Preface xxiii

## Chapter 1 Homeostasis: The Foundation of Physiology 1

### Introduction to Physiology 1

Physiology focuses on mechanisms of action. 1

Structure and function are inseparable. 2

### Levels of Organization in the Body 2

The chemical level: Various atoms and molecules make up the body. 2

The cellular level: Cells are the basic units of life. 2

The tissue level: Tissues are groups of cells of similar specialization. 4

The organ level: An organ is a unit made up of several tissue types. 5

The body system level: A body system is a collection of related organs. 5

The organism level: The body systems are packaged together into a functional whole body. 5



**Concepts, Challenges, and Controversies: Stem-Cell Science and Tissue Engineering: The Quest to Make Defective Body Parts Like New Again 6**

### Concept of Homeostasis 8

Body cells are in contact with a privately maintained internal environment. 8

Body systems maintain homeostasis, a dynamic steady state in the internal environment. 10



**A Closer Look at Cellular Physiology:  
What Is Exercise Physiology? 11**

### Homeostatic Control Systems 14

Homeostatic control systems may operate locally or bodywide. 14

Negative feedback opposes an initial change and is widely used to maintain homeostasis. 14

Positive feedback amplifies an initial change. 16

Feedforward mechanisms initiate responses in anticipation of a change. 16

Disruptions in homeostasis can lead to illness and death. 16



### Chapter in Perspective:

Focus on Homeostasis 17

Chapter Summary 17

Review Exercises 18

Points to Ponder 18

Clinical Consideration 19

PhysioEdge Resources 19

## Chapter 2 Cell Physiology 21

### Observations of Cells 21



### Concepts, Challenges, and Controversies:

**HeLa Cells: Problems in a "Growing" Industry 22**

### An Overview of Cell Structure 22

The plasma membrane bounds the cell. 23

The nucleus contains the DNA. 23

The cytoplasm consists of various organelles and the cytosol. 23

### Endoplasmic Reticulum and Segregated Synthesis 23

The rough endoplasmic reticulum synthesizes proteins for secretion and membrane construction. 24

The smooth endoplasmic reticulum packages new proteins in transport vesicles. 25

### Golgi Complex and Exocytosis 26

Transport vesicles carry their cargo to the Golgi complex for further processing. 26

The Golgi complex packages secretory vesicles for release by exocytosis. 26

### Lysosomes and Endocytosis 29

Lysosomes serve as the intracellular digestive system. 29

Extracellular material is brought into the cell by phagocytosis for attack by lysosomal enzymes. 29

Lysosomes remove useless but not useful parts of the cell. 30

### Peroxisomes and Detoxification 31

Peroxisomes house oxidative enzymes that detoxify various wastes. 31

## Mitochondria and ATP Production 31

Mitochondria, the energy organelles, are enclosed by a double membrane. 31

Mitochondria play a major role in generating ATP. 32

The cell generates more energy in aerobic than in anaerobic conditions. 37



**A Closer Look at Exercise Physiology:**

**Aerobic Exercise: What For and How Much? 38**

The energy stored within ATP is used for synthesis, transport, and mechanical work. 39

## Vaults as Cellular Trucks 39

Vaults may serve as cellular transport vehicles. 39

## Cytosol: Cell Gel 40

The cytosol is important in intermediary metabolism, ribosomal protein synthesis, and nutrient storage. 40

## Cytoskeleton: Cell “Bone and Muscle” 41

Microtubules help maintain asymmetric cell shapes and play a role in complex cell movements. 41

Microfilaments are important to cellular contractile systems and as mechanical stiffeners. 45

Intermediate filaments are important in cell regions subject to mechanical stress. 46

The cytoskeleton functions as an integrated whole and links other parts of the cell together. 47



**Chapter in Perspective:**

**Focus on Homeostasis 47**

**Chapter Summary 48**

**Review Exercises 49**

**Points to Ponder 50**

**Clinical Consideration 50**

**PhysioEdge Resources 51**

## Chapter 3

### The Plasma Membrane and Membrane Potential 53

#### Membrane Structure and Composition 53

The plasma membrane is a fluid lipid bilayer embedded with proteins. 54

The lipid bilayer forms the basic structural barrier that encloses the cell. 56

The membrane proteins perform a variety of specific membrane functions. 56



**Concepts, Challenges, and Controversies: Cystic Fibrosis: A Fatal Defect in Membrane Transport 57**

The membrane carbohydrates serve as self-identity markers. 58

#### Cell-to-Cell Adhesions 58

The extracellular matrix serves as the biological “glue.” 58

Some cells are directly linked by specialized cell junctions. 58

#### Overview of Membrane Transport 60

## Unassisted Membrane Transport 61

Particles that can permeate the membrane passively diffuse down their concentration gradient. 61

Ions that can permeate the membrane also passively move along their electrical gradient. 63

Osmosis is the net diffusion of water down its own concentration gradient. 63

## Assisted Membrane Transport 66

Carrier-mediated transport is accomplished by a membrane carrier flipping its shape. 66

Carrier-mediated transport may be passive or active. 68



**A Closer Look at Exercise Physiology:**

**Exercising Muscles Have a “Sweet Tooth” 69**

With vesicular transport, material is moved into or out of the cell wrapped in membrane. 71

## Membrane Potential 73

Membrane potential is a separation of opposite charges across the plasma membrane. 73

Membrane potential is due to differences in the concentration and permeability of key ions. 73



**Chapter in Perspective:**

**Focus on Homeostasis 80**

**Chapter Summary 80**

**Review Exercises 81**

**Points to Ponder 82**

**Clinical Consideration 83**

**PhysioEdge Resources 83**

## Chapter 4

### Principles of Neural and Hormonal Communication 85

#### Introduction to Neural Communication 85

Nerve and muscle are excitable tissues. 85

Membrane potential decreases during depolarization and increases during hyperpolarization. 86

Electrical signals are produced by changes in ion movement across the plasma membrane. 86

#### Graded Potentials 87

The stronger a triggering event is, the larger the resultant graded potential. 87

Graded potentials spread by passive current flow. 87

Graded potentials die out over short distances. 88

#### Action Potentials 89

During an action potential, the membrane potential rapidly, transiently reverses. 89

Marked changes in membrane permeability and ion movement lead to an action potential. 90

The  $\text{Na}^+ - \text{K}^+$  pump gradually restores the concentration gradients disrupted by action potentials. 92

Action potentials are propagated from the axon hillock to the axon terminals. 93

Once initiated, action potentials are conducted throughout a nerve fiber. **93**  
 The refractory period ensures one-way propagation of the action potential. **96**  
 The refractory period also limits the frequency of action potentials. **97**  
 Action potentials occur in all-or-none fashion. **98**  
 The strength of a stimulus is coded by the frequency of action potentials. **98**  
 Myelination increases the speed of conduction of action potentials. **98**



**Concepts, Challenges, and Controversies: Multiple Sclerosis: Myelin—Going, Going, Gone 100**

Fiber diameter also influences the velocity of action potential propagation. **100**

**Regeneration of Nerve Fibers 100**

Schwann cells guide the regeneration of cut peripheral axons. **101**

Oligodendrocytes inhibit regeneration of cut central axons. **101**

Researchers seek to promote regeneration of cut central axons. **101**

**Synapses and Neuronal Integration 101**

Synapses are junctions between presynaptic and postsynaptic neurons. **102**

A neurotransmitter carries the signal across a synapse. **102**

Some synapses excite whereas others inhibit the postsynaptic neuron. **103**

Each neurotransmitter–receptor combination always produces the same response. **104**

Neurotransmitters are quickly removed from the synaptic cleft. **105**

The grand postsynaptic potential depends on the sum of the activities of all presynaptic inputs. **105**

Action potentials are initiated at the axon hillock because it has the lowest threshold. **107**

Neuropeptides act primarily as neuromodulators. **107**

Presynaptic inhibition or facilitation can selectively alter the effectiveness of a presynaptic input. **108**

Drugs and diseases can modify synaptic transmission. **109**

Neurons are linked through complex converging and diverging pathways. **110**

**Intercellular Communication and Signal**

**Transduction 111**

Communication between cells is largely orchestrated by extracellular chemical messengers. **111**

Extracellular chemical messengers bring about cell responses primarily by signal transduction. **112**

Some extracellular chemical messengers open chemically gated channels. **113**

Many extracellular messengers activate second-messenger pathways. **113**

**Principles of Hormonal Communication 113**

Hormones are chemically classified as being hydrophilic or lipophilic. **114**

The mechanisms of synthesis, storage, and secretion of hormones vary according to their chemical differences. **115**  
 Hydrophilic hormones dissolve in the plasma; lipophilic hormones are transported by plasma proteins. **115**  
 Hormones generally produce their effect by altering intracellular proteins. **116**  
 Hydrophilic hormones alter pre-existing proteins via second-messenger systems. **117**



**Concepts, Challenges, and Controversies: Programmed Cell Suicide: A Surprising Example of a Signal Transduction Pathway 120**

By stimulating genes, lipophilic hormones promote synthesis of new proteins. **121**

Hormonal responses are slower and longer than neural responses. **122**

**Comparison of the Nervous and Endocrine Systems 122**

The nervous system is “wired,” and the endocrine system is “wireless.” **123**

Neural specificity is due to anatomic proximity; and endocrine specificity, to receptor specialization. **123**

The nervous and endocrine systems have their own realms of authority but interact functionally. **124**



**Chapter in Perspective: Focus on Homeostasis 124**

**Chapter Summary 125**

**Review Exercises 127**

**Points to Ponder 128**

**Clinical Consideration 128**

**PhysioEdge Resources 129**

**Chapter 5**

**The Central Nervous System 131**

**Organization of the Nervous System 132**

The nervous system is organized into the central nervous system and the peripheral nervous system. **132**

The three functional classes of neurons are afferent neurons, efferent neurons, and interneurons. **132**

**Protection and Nourishment of the Brain 133**

Glial cells support the interneurons physically, metabolically, and functionally. **133**

The delicate central nervous tissue is well protected. **136**

Three meningeal membranes wrap, protect, and nourish the central nervous system. **136**

The brain floats in its own special cerebrospinal fluid. **138**

A highly selective blood-brain barrier carefully regulates exchanges between the blood and brain. **138**



**Concepts, Challenges, and Controversies: Strokes: A Deadly Domino Effect 139**

The brain depends on constant delivery of oxygen and glucose by the blood. **139**

**Overview of the Central Nervous System 139**

**Cerebral Cortex 141**

The cerebral cortex is an outer shell of gray matter covering an inner core of white matter. **141**

The cerebral cortex is organized into layers and functional columns. **142**

The four pairs of lobes in the cerebral cortex are specialized for different activities. **142**

The parietal lobes accomplish somatosensory processing. **143**

The primary motor cortex is located in the frontal lobes. **143**

Other brain regions besides the primary motor cortex are important in motor control. **146**

Somatotopic maps vary slightly between individuals and are dynamic, not static. **147**

Because of its plasticity, the brain can be remodeled in response to varying demands. **147**

Different regions of the cortex control different aspects of language. **147**

The association areas of the cortex are involved in many higher functions. **148**

The cerebral hemispheres have some degree of specialization. **149**

An electroencephalogram is a record of postsynaptic activity in cortical neurons. **149**

Neurons in different regions of the cerebral cortex may fire in rhythmic synchrony. **150**

### **Basal Nuclei, Thalamus, and Hypothalamus 151**

The basal nuclei play an important inhibitory role in motor control. **151**

The thalamus is a sensory relay station and is important in motor control. **151**

The hypothalamus regulates many homeostatic functions. **151**

### **The Limbic System and Its Functional Relations with the Higher Cortex 153**

The limbic system plays a key role in emotion. **154**

The limbic system and higher cortex participate in controlling basic behavioral patterns. **154**

Motivated behaviors are goal directed. **154**

Norepinephrine, dopamine, and serotonin are neurotransmitters in pathways for emotions and behavior. **155**

Learning is the acquisition of knowledge as a result of experiences. **155**

Memory is laid down in stages. **155**

Memory traces are present in multiple regions of the brain. **157**

Short-term and long-term memory involve different molecular mechanisms. **157**



#### **Concepts, Challenges, and Controversies:**

#### **Alzheimer's Disease: A Tale of Beta Amyloid Plaques, Tau Tangles, and Dementia 158**

Short-term memory involves transient changes in synaptic activity. **160**

Long-term memory involves formation of new, permanent synaptic connections. **162**

### **Cerebellum 163**

The cerebellum is important in balance and in planning and executing voluntary movement. **163**

### **Brain Stem 164**

The brain stem is a vital link between the spinal cord and higher brain regions. **164**

Sleep is an active process consisting of alternating periods of slow-wave and paradoxical sleep. **164**

The sleep-wake cycle is controlled by interactions among three neural systems. **167**

The function of sleep is unclear. **167**

### **Spinal Cord 168**

The spinal cord extends through the vertebral canal and is connected to the spinal nerves. **168**

The white matter of the spinal cord is organized into tracts. **169**

Each horn of the spinal cord gray matter houses a different type of neuronal cell body. **171**

Spinal nerves carry both afferent and efferent fibers. **171**

The spinal cord is responsible for the integration of many basic reflexes. **171**



*A Closer Look at Exercise Physiology: Spin Who or Belly Flop: It's a Matter of CNS Control 174*



#### **Chapter in Perspective:**

**Focus on Homeostasis 176**

**Chapter Summary 176**

**Review Exercises 178**

**Points to Ponder 178**

**Clinical Consideration 179**

**PhysioEdge Resources 179**

## **Chapter 6**

# **The Peripheral Nervous System: Afferent Division; Special Senses 181**

### **Introduction 181**

Visceral afferents carry subconscious input whereas sensory afferents carry conscious input. **181**



*A Closer Look at Exercise Physiology:*

*Back Swings and Prejump Crouches:*

*What Do They Share in Common? 182*

Perception is the conscious awareness of surroundings derived from interpretation of sensory input. **182**

### **Receptor Physiology 183**

Receptors have differential sensitivities to various stimuli. **183**

A stimulus alters the receptor's permeability, leading to a graded receptor potential. **183**

Receptor potentials may initiate action potentials in the afferent neuron. **184**

Receptors may adapt slowly or rapidly to sustained stimulation. **184**

Each somatosensory pathway is "labeled" according to modality and location. **186**

Acuity is influenced by receptive field size and lateral inhibition. **186**

### **Pain 187**

Stimulation of nociceptors elicits the perception of pain plus motivational and emotional responses. **188**

The brain has a built-in analgesic system. **190**

### **Eye: Vision 190**

Protective mechanisms help prevent eye injuries. **190**



#### **Concepts, Challenges, and Controversies:**

##### **Acupuncture: Is It for Real? 191**

The eye is a fluid-filled sphere enclosed by three specialized tissue layers. **191**

The amount of light entering the eye is controlled by the iris. **192**

The eye refracts the entering light to focus the image on the retina. **192**

Accommodation increases the strength of the lens for near vision. **195**

Light must pass through several retinal layers before reaching the photoreceptors. **199**

Phototransduction by retinal cells converts light stimuli into neural signals. **200**

Rods provide indistinct gray vision at night, whereas cones provide sharp color vision during the day. **203**

The sensitivity of the eyes can vary markedly through dark and light adaptation. **203**

Color vision depends on the ratios of stimulation of the three cone types. **204**

Visual information is modified and separated before reaching the visual cortex. **205**

The thalamus and visual cortices elaborate the visual message. **206**

Visual input goes to other areas of the brain not involved in vision perception. **208**

Some sensory input may be detected by multiple sensory-processing areas in the brain. **208**

### **Ear: Hearing and Equilibrium 208**



#### **Concepts, Challenges, and Controversies:**

##### **"Seeing" with the Tongue 209**

Sound waves consist of alternate regions of compression and rarefaction of air molecules. **209**

The external ear plays a role in sound localization. **211**

The tympanic membrane vibrates in unison with sound waves in the external ear. **212**

The middle ear bones convert tympanic membrane vibrations into fluid movements in the inner ear. **212**

The cochlea contains the organ of Corti, the sense organ for hearing. **212**

Hair cells in the organ of Corti transduce fluid movements into neural signals. **213**

Pitch discrimination depends on the region of the basilar membrane that vibrates. **215**

Loudness discrimination depends on the amplitude of vibration. **216**

The auditory cortex is mapped according to tone. **216**

Deafness is caused by defects either in conduction or neural processing of sound waves. **217**

The vestibular apparatus is important for equilibrium by detecting position and motion of the head. **217**

### **Chemical Senses: Taste and Smell 221**

Taste receptor cells are located primarily within tongue taste buds. **222**

Taste discrimination is coded by patterns of activity in various taste bud receptors. **222**

The olfactory receptors in the nose are specialized endings of renewable afferent neurons. **224**

Various parts of an odor are detected by different olfactory receptors and sorted into "smell files." **225**

Odor discrimination is coded by patterns of activity in the olfactory bulb glomeruli. **226**

The olfactory system adapts quickly, and odorants are rapidly cleared. **226**

The vomeronasal organ detects pheromones. **227**



#### **Chapter in Perspective:**

##### **Focus on Homeostasis 227**

##### **Chapter Summary 228**

##### **Review Exercises 229**

##### **Points to Ponder 230**

##### **Clinical Consideration 231**

##### **PhysioEdge Resources 231**

## **Chapter 7**

### **The Peripheral Nervous System: Efferent Division 233**

#### **Introduction 233**

#### **Autonomic Nervous System 234**

An autonomic nerve pathway consists of a two-neuron chain. **234**

Parasympathetic postganglionic fibers release acetylcholine; sympathetic ones release norepinephrine. **235**

The sympathetic and parasympathetic nervous systems dually innervate most visceral organs. **236**

The adrenal medulla is a modified part of the sympathetic nervous system. **239**

Several different receptor types are available for each autonomic neurotransmitter. **239**

Many regions of the central nervous system are involved in the control of autonomic activities. **240**

#### **Somatic Nervous System 240**

Motor neurons supply skeletal muscle. **240**

Motor neurons are the final common pathway. **241**

#### **Neuromuscular Junction 242**

Motor neurons and skeletal muscle fibers are chemically linked at neuromuscular junctions. **242**

Acetylcholine is the neuromuscular junction neurotransmitter. **242**

Acetylcholinesterase ends acetylcholine activity at the neuromuscular junction. **244**



*In Clinical Consideration: Physiology*  
*Can the Neuromuscular Junction Be a Weak Link in a Complicated*  
*Adaptation? Study Questions 246*

The neuromuscular junction is vulnerable to several chemical agents and diseases. **247**



**Concepts, Challenges, and Controversies: Botulinum Toxin's Reputation Gets a Facelift 248**



**Chapter in Perspective:**  
**Focus on Homeostasis 248**

**Chapter Summary 249**  
**Review Exercises 249**  
**Points to Ponder 250**  
**Clinical Consideration 250**  
**PhysioEdge Resources 251**

## Chapter 8 Muscle Physiology 253

**Introduction 253**  
**Structure of Skeletal Muscle 254**

Skeletal muscle fibers are striated by a highly organized internal arrangement. **254**

Myosin forms the thick filaments. **256**

Actin is the main structural component of the thin filaments. **256**

**Molecular Basis of Skeletal Muscle Contraction 257**

During contraction, cycles of cross-bridge binding and bending pull the thin filaments inward. **258**

Calcium is the link between excitation and contraction. **259**

Contractile activity far outlasts the electrical activity that initiated it. **264**

**Skeletal Muscle Mechanics 265**

Whole muscles are groups of muscle fibers bundled together and attached to bones. **265**

Contractions of a whole muscle can be of varying strength. **265**

The number of fibers contracting within a muscle depends on the extent of motor unit recruitment. **265**

The frequency of stimulation can influence the tension developed by each muscle fiber. **266**

Twitch summation results from a sustained elevation in cytosolic calcium. **266**

There is an optimal muscle length at which maximal tension can be developed. **267**

Muscle tension is transmitted to bone as the contractile component tightens the series-elastic component. **269**

The two primary types of contraction are isotonic and isometric. **269**

The velocity of shortening is related to the load. **270**

Although muscles can accomplish work, much of the energy is converted to heat. **271**

Interactive units of skeletal muscles, bones, and joints form lever systems. **271**

## Skeletal Muscle Metabolism and Fiber Types 272

Muscle fibers have alternate pathways for forming ATP. **272**

Fatigue may be of muscle or central origin. **275**

Increased oxygen consumption is necessary to recover from exercise. **275**

There are three types of skeletal muscle fibers, based on differences in ATP hydrolysis and synthesis. **276**

Muscle fibers adapt considerably in response to the demands placed on them. **277**



*In Clinical Consideration: Physiology*  
*Are Athletes Who Use Steroids as a Performance Enhancement Truly Stronger?*  
*278*

## Control of Motor Movement 279

Multiple neural inputs influence motor unit output. **279**



**Concepts, Challenges, and Controversies: Muscular Dystrophy: When One Small Step Is a Big Deal 280**

Muscle receptors provide afferent information needed to control skeletal muscle activity. **282**

## Smooth and Cardiac Muscle 285

Smooth muscle cells are small and unstriated. **285**

Smooth muscle cells are turned on by  $Ca^{2+}$ -dependent phosphorylation of myosin. **286**

Multunit smooth muscle is neurogenic. **288**

Single-unit smooth muscle cells form functional syncytia. **289**

Single-unit smooth muscle is myogenic. **289**

Gradation of single-unit smooth muscle contraction differs from that of skeletal muscle. **290**

Smooth muscle can still develop tension yet inherently relaxes when stretched. **292**

Smooth muscle is slow and economical. **293**

Cardiac muscle blends features of both skeletal and smooth muscle. **293**



**Chapter in Perspective:**  
**Focus on Homeostasis 293**

**Chapter Summary 294**  
**Review Exercises 296**  
**Points to Ponder 297**  
**Clinical Consideration 297**  
**PhysioEdge Resources 297**

## Chapter 9 Cardiac Physiology 299

**Introduction 299**  
**Anatomy of the Heart 300**

The heart is a dual pump. **300**

Pressure-operated heart valves ensure that blood flows in the right direction through the heart. **302**

The heart walls are composed primarily of spirally arranged cardiac muscle fibers. **304**

Cardiac muscle fibers are interconnected by intercalated discs and form functional syncytia. **304**

The heart is enclosed by the pericardial sac. **305**

### **Electrical Activity of the Heart 305**

Cardiac autorhythmic cells display pacemaker activity. **305**

The sinoatrial node is the normal pacemaker of the heart. **306**

The spread of cardiac excitation is coordinated to ensure efficient pumping. **308**

The action potential of cardiac contractile cells shows a characteristic plateau. **309**

Ca<sup>2+</sup> entry from the ECF induces a much larger Ca<sup>2+</sup> release from the sarcoplasmic reticulum. **310**

A long refractory period prevents tetanus of cardiac muscle. **311**

The ECG is a record of the overall spread of electrical activity through the heart. **311**

Different parts of the ECG record can be correlated to specific cardiac events. **313**

The ECG can be used to diagnose abnormal heart rates, arrhythmias, and damage of heart muscle. **313**



*A Heart Doctor's Story: Physiology for What, Why, and When of Stress Testing* **315**

### **Mechanical Events of the Cardiac Cycle 315**

The heart alternately contracts to empty and relaxes to fill. **315**

The two heart sounds are associated with valve closures. **318**

Turbulent blood flow produces heart murmurs. **318**

### **Cardiac Output and Its Control 320**

Cardiac output depends on the heart rate and the stroke volume. **320**

Heart rate is determined primarily by autonomic influences on the SA node. **320**

Stroke volume is determined by the extent of venous return and by sympathetic activity. **322**

Increased end-diastolic volume results in increased stroke volume. **322**

Sympathetic stimulation increases the contractility of the heart. **324**

High blood pressure increases the workload of the heart. **325**

In heart failure the contractility of the heart decreases. **325**

### **Nourishing the Heart Muscle 326**

The heart receives most of its own blood supply through the coronary circulation during diastole. **327**

Atherosclerotic coronary artery disease can deprive the heart of essential oxygen. **328**



**Concepts, Challenges, and Controversies:**  
**Atherosclerosis: Cholesterol and Beyond 330**



**Chapter in Perspective:**  
**Focus on Homeostasis 332**

**Chapter Summary 332**

**Review Exercises 334**

**Points to Ponder 335**

**Clinical Consideration 335**

**PhysioEdge Resources 335**

## **Chapter 10** **The Blood Vessels and** **Blood Pressure 337**

### **Introduction 337**

To maintain homeostasis, reconditioning organs receive blood flow in excess of their own needs. **337**

Blood flow through vessels depends on the pressure gradient and vascular resistance. **338**

The vascular tree consists of arteries, arterioles, capillaries, venules, and veins. **340**



**Concepts, Challenges, and Controversies:**  
**From Humors to Harvey: Historical Highlights**  
**in Circulation 341**

### **Arteries 342**

Arteries serve as rapid-transit passageways to the organs and as a pressure reservoir. **342**

Arterial pressure fluctuates in relation to ventricular systole and diastole. **343**

Blood pressure can be measured indirectly by using a sphygmomanometer. **343**

Mean arterial pressure is the main driving force for blood flow. **345**

### **Arterioles 345**

Arterioles are the major resistance vessels. **345**

Local control of arteriolar radius is important in determining the distribution of cardiac output. **347**

Local metabolic influences on arteriolar radius help match blood flow with the organs' needs. **347**

Local histamine release pathologically dilates arterioles. **349**

Local physical influences on arteriolar radius include temperature changes, shear stress, and stretch. **350**

Extrinsic sympathetic control of arteriolar radius is important in regulating blood pressure. **351**

The medullary cardiovascular control center and several hormones regulate blood pressure. **352**

### **Capillaries 353**

Capillaries are ideally suited to serve as sites of exchange. **353**

Water-filled capillary pores permit passage of small, water-soluble substances. **356**

Many capillaries are not open under resting conditions. **357**

Interstitial fluid is a passive intermediary between blood and cells. **358**

Diffusion across the capillary walls is important in solute exchange. **358**

Bulk flow across the capillary walls is important in extracellular fluid distribution. **359**

The lymphatic system is an accessory route by which interstitial fluid can be returned to the blood. **361**

Edema occurs when too much interstitial fluid accumulates. **362**

### **Veins 363**

Venules communicate chemically with nearby arterioles. **363**

Veins serve as a blood reservoir as well as passageways back to the heart. **364**



Venous return is enhanced by a number of extrinsic factors. **364**

## **Blood Pressure 369**

Blood pressure is regulated by controlling cardiac output, total peripheral resistance, and blood volume. **369**

The baroreceptor reflex is an important short-term mechanism for regulating blood pressure. **370**

Other reflexes and responses influence blood pressure. **373**

Hypertension is a serious national public-health problem, but its causes are largely unknown. **373**

Orthostatic hypotension results from transient inadequate sympathetic activity. **375**



*A Closer Look at Exercise Physiology: The Ups and Downs of Hypertension and Exercise* **376**

Circulatory shock can become irreversible. **376**



**Chapter in Perspective:**  
**Focus on Homeostasis 379**

**Chapter Summary 379**

**Review Exercises 381**

**Points to Ponder 382**

**Clinical Consideration 382**

**PhysioEdge Resources 383**

## **Chapter 11**

### **The Blood 385**

#### **Introduction 385**

#### **Plasma 385**

Plasma water is a transport medium for many inorganic and organic substances. **385**

Many of the functions of plasma are carried out by plasma proteins. **386**

#### **Erythrocytes 387**

The structure of erythrocytes is well suited to their main function of O<sub>2</sub> transport in the blood. **387**

The bone marrow continuously replaces worn-out erythrocytes. **388**

Erythropoiesis is controlled by erythropoietin from the kidneys. **389**



*A Closer Look at Exercise Physiology: Blood Doping: Is More of a Good Thing Better?* **390**

Anemia can be caused by a variety of disorders. **390**

Polycythemia is an excess of circulating erythrocytes. **391**



**Concepts, Challenges, and Controversies: In Search of a Blood Substitute 392**

#### **Leukocytes 392**

Leukocytes primarily function as defense agents outside the blood. **393**

There are five types of leukocytes. **393**

Leukocytes are produced at varying rates depending on the changing defense needs of the body. **394**

## **Platelets and Hemostasis 396**

Platelets are cell fragments shed from megakaryocytes. **396**

Hemostasis prevents blood loss from damaged small vessels. **396**

Vascular spasm reduces blood flow through an injured vessel. **397**

Platelets aggregate to form a plug at a vessel tear or cut. **397**

Clot formation results from a triggered chain reaction involving plasma clotting factors. **397**

Fibrinolytic plasmin dissolves clots. **400**

Inappropriate clotting produces thromboembolism. **402**

Hemophilia is the primary condition that produces excessive bleeding. **402**



**Chapter in Perspective:**  
**Focus on Homeostasis 402**

**Chapter Summary 403**

**Review Exercises 404**

**Points to Ponder 405**

**Clinical Consideration 405**

**PhysioEdge Resources 405**

## **Chapter 12**

### **Body Defenses 407**

#### **Introduction 407**

Pathogenic bacteria and viruses are the major targets of the immune system. **407**

Leukocytes are the effector cells of the immune system. **408**

Immune responses may be either innate and nonspecific, or adaptive and specific. **409**

#### **Innate Immunity 410**

Inflammation is a nonspecific response to foreign invasion or tissue damage. **410**

NSAIDs and glucocorticoid drugs suppress the inflammatory response. **414**

Interferon transiently inhibits multiplication of viruses in most cells. **414**

Natural killer cells destroy virus-infected cells and cancer cells on first exposure to them. **414**

The complement system punches holes in microorganisms. **415**

#### **Adaptive Immunity: General Concepts 416**

Adaptive immune responses include antibody-mediated immunity and cell-mediated immunity. **416**

An antigen induces an immune response against itself. **417**

#### **B Lymphocytes: Antibody-Mediated Immunity 417**

Antigens stimulate B cells to convert into plasma cells that produce antibodies. **417**

Antibodies are Y shaped and classified according to properties of their tail portion. **418**

Antibodies largely amplify innate immune responses to promote antigen destruction. **419**

Clonal selection accounts for the specificity of antibody production. **419**

Selected clones differentiate into active plasma cells and dormant memory cells. **421**  
The huge repertoire of B cells is built by reshuffling a small set of gene fragments. **422**



**Concepts, Challenges, and Controversies: Vaccination: A Victory over Many Dreaded Diseases 424**

Active immunity is self-generated; passive immunity is “borrowed.” **424**

Blood types are a form of natural immunity. **424**

Lymphocytes respond only to antigens presented to them by antigen-presenting cells. **426**

**T Lymphocytes: Cell-Mediated Immunity 426**

T cells bind directly with their targets. **427**

The two main types of T cells are cytotoxic T cells and helper T cells. **429**

Cytotoxic T cells secrete chemicals that destroy target cells. **429**

Helper T cells secrete chemicals that amplify the activity of other immune cells. **431**

The immune system is normally tolerant of self-antigens. **432**

Autoimmune diseases arise from loss of tolerance to self-antigens. **433**

The major histocompatibility complex is the code for self-antigens. **434**

Immune surveillance against cancer cells involves an interplay among immune cells and interferon. **436**

A regulatory loop links the immune system with the nervous and endocrine systems. **437**



**A Closer Look at Exercise Physiology: Exercise: A Help or Hindrance to Immune Defense? 438**

**Immune Diseases 438**

Immunodeficiency diseases result from insufficient immune responses. **439**

Allergies are inappropriate immune attacks against harmless environmental substances. **439**

**External Defenses 441**

The skin consists of an outer protective epidermis and an inner, connective tissue dermis. **441**

Specialized cells in the epidermis produce keratin and melanin and participate in immune defense. **443**

Protective measures within body cavities discourage pathogen invasion into the body. **444**



**Chapter in Perspective: Focus on Homeostasis 445**

**Chapter Summary 445**

**Review Exercises 447**

**Points to Ponder 449**

**Clinical Consideration 449**

**PhysioEdge Resources 449**

## Chapter 13 The Respiratory System 451

### Introduction 451

The respiratory system does not participate in all steps in respiration. **451**

The respiratory airways conduct air between the atmosphere and alveoli. **452**

The gas-exchanging alveoli are thin-walled, inflatable air sacs encircled by pulmonary capillaries. **454**

The lungs occupy much of the thoracic cavity. **455**

A pleural sac separates each lung from the thoracic wall. **455**

### Respiratory Mechanics 455

Interrelationships among pressures inside and outside the lungs are important in ventilation. **456**

The lungs are normally stretched to fill the larger thorax. **457**

Flow of air into and out of the lungs occurs because of cyclic changes in intra-alveolar pressure. **458**

Airway resistance influences airflow rates. **463**

Airway resistance is abnormally increased with chronic obstructive pulmonary disease. **464**

Elastic behavior of the lungs is due to elastic connective tissue and alveolar surface tension. **464**

Pulmonary surfactant decreases surface tension and contributes to lung stability. **466**

The work of breathing normally requires only about 3% of total energy expenditure. **468**

The lungs normally operate at about “half full.” **469**

Alveolar ventilation is less than pulmonary ventilation because of dead space. **471**

Local controls act on the smooth muscle of the airways and arterioles to match airflow to blood flow. **473**

### Gas Exchange 475

Gases move down partial pressure gradients. **475**

Oxygen enters and CO<sub>2</sub> leaves the blood in the lungs passively down partial pressure gradients. **475**

Factors other than the partial pressure gradient influence the rate of gas transfer. **476**

Gas exchange across the systemic capillaries also occurs down partial pressure gradients. **479**

### Gas Transport 479

Most O<sub>2</sub> in the blood is transported bound to hemoglobin. **480**

The P<sub>O<sub>2</sub></sub> is the primary factor determining the percent hemoglobin saturation. **480**

Hemoglobin promotes the net transfer of O<sub>2</sub> at both the alveolar and tissue levels. **481**

Factors at the tissue level promote the unloading of O<sub>2</sub> from hemoglobin. **483**

Hemoglobin has a much higher affinity for carbon monoxide than for O<sub>2</sub>. **484**

Most CO<sub>2</sub> is transported in the blood as bicarbonate. **484**

Various respiratory states are characterized by abnormal blood-gas levels. **485**

### Control of Respiration 487

Respiratory centers in the brain stem establish a rhythmic breathing pattern. **487**



**Concepts, Challenges, and Controversies:  
Effects of Heights and Depths on the Body 488**

- The magnitude of ventilation is adjusted in response to three chemical factors:  $P_{O_2}$ ,  $P_{CO_2}$ , and  $H^+$ . **489**
- Decreased arterial  $P_{O_2}$  increases ventilation only as an emergency mechanism. **490**
- Carbon dioxide-generated  $H^+$  in the brain is normally the main regulator of ventilation. **491**
- Adjustments in ventilation in response to changes in arterial  $H^+$  are important in acid–base balance. **492**
- Exercise profoundly increases ventilation, but the mechanisms involved are unclear. **493**
- A number of factors may increase ventilation during exercise. **494**
- Ventilation can be influenced by factors unrelated to the need for gas exchange. **494**
- During apnea, a person “forgets to breathe”; during dyspnea, a person feels “short of breath.” **494**



*A Closer Look at Exercise Physiology: How to Find Out How Much Work You’re Capable of Doing* **495**



- Chapter in Perspective:  
Focus on Homeostasis 496**
- Chapter Summary 496**
- Review Exercises 498**
- Points to Ponder 499**
- Clinical Consideration 499**
- PhysioEdge Resources 499**

**Chapter 14  
The Urinary System 501**

**Introduction 501**

- The kidneys perform a variety of functions aimed at maintaining homeostasis. **501**
- The kidneys form the urine; the rest of the urinary system carries the urine to the outside. **502**
- The nephron is the functional unit of the kidney. **502**
- The three basic renal processes are glomerular filtration, tubular reabsorption, and tubular secretion. **506**

**Glomerular Filtration 507**

- The glomerular membrane is considerably more permeable than capillaries elsewhere. **507**
- Glomerular capillary blood pressure is the major force that induces glomerular filtration. **507**
- Changes in the GFR primarily result from changes in glomerular capillary blood pressure. **509**
- The GFR can be influenced by changes in the filtration coefficient. **512**
- The kidneys normally receive 20% to 25% of the cardiac output. **513**

**Tubular Reabsorption 514**

- Tubular reabsorption is tremendous, highly selective, and variable. **514**

- Tubular reabsorption involves transepithelial transport. **514**
- An active  $Na^+ - K^+$  ATPase pump in the basolateral membrane is essential for  $Na^+$  reabsorption. **515**
- Aldosterone stimulates  $Na^+$  reabsorption in the distal and collecting tubules. **516**
- Atrial natriuretic peptide inhibits  $Na^+$  reabsorption. **519**
- Glucose and amino acids are reabsorbed by  $Na^+$ -dependent secondary active transport. **519**
- In general, actively reabsorbed substances exhibit a tubular maximum. **520**
- Glucose is an example of an actively reabsorbed substance that is not regulated by the kidneys. **520**
- Phosphate is an example of an actively reabsorbed substance that is regulated by the kidneys. **521**
- Active  $Na^+$  reabsorption is responsible for the passive reabsorption of  $Cl^-$ ,  $H_2O$ , and urea. **521**
- In general, unwanted waste products are not reabsorbed. **523**

**Tubular Secretion 523**

- Hydrogen ion secretion is important in acid–base balance. **523**
- Potassium ion secretion is controlled by aldosterone. **523**
- Organic anion and cation secretion helps efficiently eliminate foreign compounds from the body. **525**

**Urine Excretion and Plasma Clearance 526**

- Plasma clearance is the volume of plasma cleared of a particular substance per minute. **526**
- If a substance is filtered but not reabsorbed or secreted, its plasma clearance rate equals the GFR. **526**
- If a substance is filtered and reabsorbed but not secreted, its plasma clearance rate is always less than the GFR. **527**
- If a substance is filtered and secreted but not reabsorbed, its plasma clearance rate is always greater than the GFR. **527**
- The kidneys can excrete urine of varying concentrations depending on the body’s state of hydration. **529**
- The medullary vertical osmotic gradient is established by countercurrent multiplication. **529**
- Vasopressin-controlled, variable  $H_2O$  reabsorption occurs in the final tubular segments. **532**
- Countercurrent exchange within the vasa recta conserves the medullary vertical osmotic gradient. **535**
- Water reabsorption is only partially linked to solute reabsorption. **535**
- Renal failure has wide-ranging consequences. **536**
- Urine is temporarily stored in the bladder, from which it is emptied by micturition. **538**



*A Closer Look at Exercise Physiology: What Problem in the Urine Does Not Pass Kidney Disease* **539**



**Concepts, Challenges, and Controversies:  
Dialysis: Cellophane Tubing or Abdominal Lining as an Artificial Kidney 540**



- Chapter in Perspective:  
Focus on Homeostasis 541**
- Chapter Summary 542**
- Review Exercises 544**
- Points to Ponder 545**

## Chapter 15 Fluid and Acid–Base Balance 547

### Balance Concept 547

The internal pool of a substance is the amount of that substance in the ECF. 547

To maintain stable balance of an ECF constituent, its input must equal its output. 548

### Fluid Balance 548

Body water is distributed between the ICF and ECF compartments. 549

The plasma and interstitial fluid are similar in composition but the ECF and ICF differ markedly. 549

Fluid balance is maintained by regulating ECF volume and osmolarity. 550

Control of ECF volume is important in the long-term regulation of blood pressure. 551

Control of salt balance is primarily important in regulating ECF volume. 551

Control of ECF osmolarity prevents changes in ICF volume. 552

During ECF hypertonicity, the cells shrink as H<sub>2</sub>O leaves them. 553



*A Closer Look at Exercise Physiology:  
A Potentially Fatal Climb: When Exercising  
Muscles and Cooling Mechanisms Compete  
for an Inadequate Plasma Volume* 554

During ECF hypotonicity, the cells swell as H<sub>2</sub>O enters them. 554

No water moves into or out of cells during an ECF isotonic fluid gain or loss. 555

Control of water balance by means of vasopressin is important in regulating ECF osmolarity. 555

Vasopressin secretion and thirst are largely triggered simultaneously. 557

### Acid–Base Balance 559

Acids liberate free hydrogen ions, whereas bases accept them. 559

The pH designation is used to express [H<sup>+</sup>]. 559

Fluctuations in [H<sup>+</sup>] alter nerve, enzyme, and K<sup>+</sup> activity. 560

Hydrogen ions are continually added to the body fluids as a result of metabolic activities. 561

Chemical buffer systems minimize changes in pH by binding with or yielding free H<sup>+</sup>. 562

The H<sub>2</sub>CO<sub>3</sub>:HCO<sub>3</sub><sup>-</sup> buffer pair is the primary ECF buffer for noncarbonic acids. 562

The protein buffer system is primarily important intracellularly. 564

The hemoglobin buffer system buffers H<sup>+</sup> generated from carbonic acid. 564

The phosphate buffer system is an important urinary buffer. 564

Chemical buffer systems act as the first line of defense against changes in [H<sup>+</sup>]. 565

The respiratory system regulates [H<sup>+</sup>] by controlling the rate of CO<sub>2</sub> removal. 565

The respiratory system serves as the second line of defense against changes in [H<sup>+</sup>]. 565

The kidneys adjust their rate of H<sup>+</sup> excretion depending on the plasma [H<sup>+</sup>] or [CO<sub>2</sub>]. 566

The kidneys conserve or excrete HCO<sub>3</sub><sup>-</sup> depending on the plasma [H<sup>+</sup>]. 567

The kidneys secrete ammonia during acidosis to buffer secreted H<sup>+</sup>. 568

The kidneys are a powerful third line of defense against changes in [H<sup>+</sup>]. 569

Acid–base imbalances can arise from either respiratory dysfunction or metabolic disturbances. 569

Respiratory acidosis arises from an increase in [CO<sub>2</sub>]. 570

Respiratory alkalosis arises from a decrease in [CO<sub>2</sub>]. 571

Metabolic acidosis is associated with a fall in [HCO<sub>3</sub><sup>-</sup>]. 572

Metabolic alkalosis is associated with an elevation in [HCO<sub>3</sub><sup>-</sup>]. 572



**Chapter in Perspective:  
Focus on Homeostasis** 573

**Chapter Summary** 574

**Review Exercises** 575

**Points to Ponder** 576

**Clinical Consideration** 576

**PhysioEdge Resources** 577

## Chapter 16 The Digestive System 579

### Introduction 579

The digestive system performs four basic digestive processes. 579

The digestive tract and accessory digestive organs make up the digestive system. 581

The digestive tract wall has four layers. 581

Regulation of digestive function is complex and synergistic. 583

Receptor activation alters digestive activity through neural reflexes and hormonal pathways. 585

### Mouth 586

The oral cavity is the entrance to the digestive tract. 586

The teeth are responsible for chewing. 586

Saliva begins carbohydrate digestion, is important in oral hygiene, and facilitates speech. 587

Salivary secretion is continuous and can be reflexly increased. 587

Digestion in the mouth is minimal; no absorption of nutrients occurs. 588

### Pharynx and Esophagus 588

Swallowing is a sequentially programmed all-or-none reflex. 588

During the oropharyngeal stage of swallowing, food is prevented from entering the wrong passageways. **588**

The pharyngoesophageal sphincter prevents air from entering the digestive tract during breathing. **589**

Peristaltic waves push food through the esophagus. **590**

The gastroesophageal sphincter prevents reflux of gastric contents. **590**

Esophageal secretion is entirely protective. **590**

## **Stomach 590**

The stomach stores food and begins protein digestion. **591**

Gastric filling involves receptive relaxation. **591**

Gastric storage takes place in the body of the stomach. **591**

Gastric mixing takes place in the antrum of the stomach. **591**

Gastric emptying is largely controlled by factors in the duodenum. **592**



### **A Closer Look at Digestive Physiology: Pregame Meal: What's In and What's Out? 594**

Emotions can influence gastric motility. **594**

The stomach does not actively participate in vomiting. **594**

Gastric digestive juice is secreted by glands located at the base of gastric pits. **595**

Hydrochloric acid activates pepsinogen. **597**

Pepsinogen, once activated, begins protein digestion. **597**

Mucus is protective. **598**

Intrinsic factor is essential for absorption of vitamin B<sub>12</sub>. **598**

Multiple regulatory pathways influence the parietal and chief cells. **598**

Control of gastric secretion involves three phases. **599**

Gastric secretion gradually decreases as food empties from the stomach into the intestine. **600**

The gastric mucosal barrier protects the stomach lining from gastric secretions. **601**

Carbohydrate digestion continues in the body of the stomach; protein digestion begins in the antrum. **601**

The stomach absorbs alcohol and aspirin but no food. **601**



### **Concepts, Challenges, and Controversies: Ulcers: When Bugs Break the Barrier 602**

## **Pancreatic and Biliary Secretions 603**

The pancreas is a mixture of exocrine and endocrine tissue. **603**

The exocrine pancreas secretes digestive enzymes and an aqueous alkaline fluid. **603**

Pancreatic exocrine secretion is regulated by secretin and CCK. **604**

The liver performs various important functions including bile production. **605**

The liver lobules are delineated by vascular and bile channels. **605**

Bile is continuously secreted by the liver and is diverted to the gallbladder between meals. **606**

Bile salts are recycled through the enterohepatic circulation. **606**

Bile salts aid fat digestion and absorption. **607**

Bilirubin is a waste product excreted in the bile. **609**

Bile salts are the most potent stimulus for increased bile secretion. **609**

The gallbladder stores and concentrates bile between meals and empties during meals. **610**

Hepatitis and cirrhosis are the most common liver disorders. **610**

## **Small Intestine 610**

Segmentation contractions mix and slowly propel the chyme. **610**

The migrating motility complex sweeps the intestine clean between meals. **611**

The ileocecal juncture prevents contamination of the small intestine by colonic bacteria. **611**

Small-intestine secretions do not contain any digestive enzymes. **612**

The small-intestine enzymes complete digestion within the brush-border membrane. **612**

The small intestine is remarkably well adapted for its primary role in absorption. **613**

The mucosal lining experiences rapid turnover. **615**

Energy-dependent Na<sup>+</sup> absorption drives passive H<sub>2</sub>O absorption. **615**

Carbohydrate and protein are both absorbed by secondary active transport and enter the blood. **616**

Digested fat is absorbed passively and enters the lymph. **616**

Vitamin absorption is largely passive. **620**

Iron and calcium absorption is regulated. **620**

Most absorbed nutrients immediately pass through the liver for processing. **621**

Extensive absorption by the small intestine keeps pace with secretion. **621**

Biochemical balance among the stomach, pancreas, and small intestine is normally maintained. **622**

Diarrhea results in loss of fluid and electrolytes. **622**

## **Large Intestine 623**

The large intestine is primarily a drying and storage organ. **623**

Haustral contractions slowly shuffle the colonic contents back and forth. **623**



### **Concepts, Challenges, and Controversies: Oral Rehydration Therapy: Sipping a Simple Solution Saves Lives 624**

Mass movements propel feces long distances. **624**

Feces are eliminated by the defecation reflex. **624**

Constipation occurs when the feces become too dry. **625**

Large-intestine secretion is entirely protective. **625**

The colon contains myriad beneficial bacteria. **625**

The large intestine absorbs salt and water, converting the luminal contents into feces. **626**

Intestinal gases are absorbed or expelled. **626**

## **Overview of the Gastrointestinal Hormones 626**



### **Chapter in Perspective:**

**Focus on Homeostasis 627**

**Chapter Summary 628**

**Review Exercises 630**

## Chapter 17

# Energy Balance and Temperature Regulation 633

### Energy Balance 633

- Most food energy is ultimately converted into heat in the body. 633
- The metabolic rate is the rate of energy use. 634
- Energy input must equal energy output to maintain a neutral energy balance. 635
- Food intake is controlled primarily by the hypothalamus. 636
- Obesity occurs when more kilocalories are consumed than are burned up. 639



*A Closer Look at Exercise Physiology:  
What the Scales Don't Tell You* 640

People suffering from anorexia nervosa have a pathologic fear of gaining weight. 641

### Temperature Regulation 641

- Internal core temperature is homeostatically maintained at 100°F (37.8°C). 641
- Heat input must balance heat output to maintain a stable core temperature. 642
- Heat exchange takes place by radiation, conduction, convection, and evaporation. 642
- The hypothalamus integrates a multitude of thermosensory inputs. 644
- Shivering is the primary involuntary means of increasing heat production. 644
- The magnitude of heat loss can be adjusted by varying the flow of blood through the skin. 645
- The hypothalamus simultaneously coordinates heat-production and heat-loss mechanisms. 645
- During a fever, the hypothalamic thermostat is “reset” at an elevated temperature. 646
- Hypothermia can occur unrelated to infection. 647



**Concepts, Challenges, and Controversies:**  
**The Extremes of Heat and Cold Can Be Fatal** 648



**Chapter in Perspective:**  
**Focus on Homeostasis** 648

**Chapter Summary** 649  
**Review Exercises** 650  
**Points to Ponder** 651  
**Clinical Consideration** 651  
**PhysioEdge Resources** 651

## Chapter 18

# Principles of Endocrinology; The Central Endocrine Glands 653

### General Principles of Endocrinology 653

- Hormones exert a variety of regulatory effects throughout the body. 654
- The effective plasma concentration of a hormone is normally regulated by changes in its rate of secretion. 655
- The effective plasma concentration of a hormone is influenced by its transport, metabolism, and excretion. 657
- Endocrine disorders result from hormone excess or deficiency or decreased target-cell responsiveness. 657
- The responsiveness of a target cell can be varied by regulating the number of hormone-specific receptors. 658

### Hypothalamus and Pituitary 662

- The pituitary gland consists of anterior and posterior lobes. 662
- The hypothalamus and posterior pituitary act as a unit to secrete vasopressin and oxytocin. 662
- Most anterior pituitary hormones are tropic. 663



*A Closer Look at Exercise Physiology:  
The Endocrine Response to the Challenge  
of Combined Heat and Starving Feet* 664

- Hypothalamic releasing and inhibiting hormones help regulate anterior pituitary hormone secretion. 664
- Target-gland hormones inhibit hypothalamic and anterior pituitary hormone secretion via negative feedback. 668

### Endocrine Control of Growth 668

- Growth depends on growth hormone but is influenced by other factors as well. 668
- Growth hormone is essential for growth, but it also exerts metabolic effects not related to growth. 669
- Bone grows in thickness and in length by different mechanisms, both stimulated by growth hormone. 670
- Growth hormone exerts some of its growth-promoting effects indirectly by stimulating somatomedins. 671
- Growth hormone secretion is regulated by two hypophysiotropic hormones. 672
- Abnormal growth hormone secretion results in aberrant growth patterns. 673



**Concepts, Challenges, and Controversies:**  
**Growth and Youth in a Bottle?** 674

- Other hormones besides growth hormone are essential for normal growth. 674
- ### Pineal Gland and Circadian Rhythms 676
- The suprachiasmatic nucleus is the master biological clock. 676
  - Melatonin helps keep the body's circadian rhythms in time with the light-dark cycle. 676



**Concepts, Challenges, and Controversies:**  
**Tinkering with Our Biological Clocks** 677



**Chapter in Perspective:**  
**Focus on Homeostasis 678**

**Chapter Summary 678**

**Review Exercises 680**

**Points to Ponder 680**

**Clinical Consideration 680**

**PhysioEdge Resources 681**

## Chapter 19

### The Peripheral Endocrine Glands 683

#### Thyroid Gland 683

The major cells that secrete thyroid hormone are organized into colloid-filled follicles. **683**

Thyroid hormone is synthesized and stored on the thyroglobulin molecule. **684**

To secrete thyroid hormone, the follicular cells phagocytize thyroglobulin-laden colloid. **684**

Most of the secreted  $T_4$  is converted into  $T_3$  outside the thyroid. **686**

Thyroid hormone is the main determinant of the basal metabolic rate and exerts other effects as well. **686**

Thyroid hormone is regulated by the hypothalamus–pituitary–thyroid axis. **686**

Abnormalities of thyroid function include both hypothyroidism and hyperthyroidism. **687**

A goiter develops when the thyroid gland is overstimulated. **689**

#### Adrenal Glands 689

Each adrenal gland consists of a steroid-secreting cortex and a catecholamine-secreting medulla. **689**

The adrenal cortex secretes mineralocorticoids, glucocorticoids, and sex hormones. **690**

Mineralocorticoids' major effects are on  $Na^+$  and  $K^+$  balance and blood pressure homeostasis. **691**

Glucocorticoids exert metabolic effects and play a key role in adaptation to stress. **691**

Cortisol secretion is regulated by the hypothalamus–pituitary–adrenal cortex axis. **692**

The adrenal cortex secretes both male and female sex hormones in both sexes. **693**

The adrenal cortex may secrete too much or too little of any of its hormones. **694**

The adrenal medulla is a modified sympathetic postganglionic neuron. **696**

Epinephrine and norepinephrine vary in their affinities for the different adrenergic receptor types. **696**

Epinephrine reinforces the sympathetic nervous system and exerts additional metabolic effects. **697**

Sympathetic stimulation of the adrenal medulla is solely responsible for epinephrine release. **698**

#### Integrated Stress Response 698

The stress response is a generalized pattern of reactions to any situation that threatens homeostasis. **698**

The multifaceted stress response is coordinated by the hypothalamus. **700**

Activation of the stress response by chronic psychosocial stressors may be harmful. **701**

#### Endocrine Control of Fuel Metabolism 701

Fuel metabolism includes anabolism, catabolism, and interconversions among energy-rich organic molecules. **701**

Because food intake is intermittent, nutrients must be stored for use between meals. **703**

The brain must be continuously supplied with glucose. **704**

Metabolic fuels are stored during the absorptive state and mobilized during the postabsorptive state. **704**

Lesser energy sources are tapped as needed. **705**

The pancreatic hormones, insulin and glucagon, are most important in regulating fuel metabolism. **705**

Insulin lowers blood glucose, fatty acid, and amino acid levels and promotes their storage. **705**

The primary stimulus for increased insulin secretion is an increase in blood glucose concentration. **707**

The symptoms of diabetes mellitus are characteristic of an exaggerated postabsorptive state. **708**



#### Concepts, Challenges, and Controversies: Diabetics and Insulin: Some Have It and Some Don't 710

Insulin excess causes brain-starving hypoglycemia. **712**

Glucagon in general opposes the actions of insulin. **713**

Glucagon secretion is increased during the postabsorptive state. **713**

Insulin and glucagon work as a team to maintain blood glucose and fatty acid levels. **713**

Glucagon excess can aggravate the hyperglycemia of diabetes mellitus. **714**

Epinephrine, cortisol, and growth hormone also exert direct metabolic effects. **714**

#### Endocrine Control of Calcium Metabolism 716

Plasma  $Ca^{2+}$  must be closely regulated to prevent changes in neuromuscular excitability. **716**

Control of  $Ca^{2+}$  metabolism includes regulation of both  $Ca^{2+}$  homeostasis and  $Ca^{2+}$  balance. **716**

Parathyroid hormone raises free plasma  $Ca^{2+}$  levels by its effects on bone, kidneys, and intestine. **717**

Bone continuously undergoes remodeling. **717**

Mechanical stress favors bone deposition. **718**

PTH raises plasma  $Ca^{2+}$  by withdrawing  $Ca^{2+}$  from the bone bank. **718**

PTH's immediate effect is to promote the transfer of  $Ca^{2+}$  from bone fluid into plasma. **719**



#### A Closer Look at Exercise Physiology: Osteoporosis: The Game of Brittle Bones 720

PTH's chronic effect is to promote localized dissolution of bone to release  $Ca^{2+}$  into plasma. **720**

PTH acts on the kidneys to conserve  $Ca^{2+}$  and eliminate  $PO_4^{3-}$ . **721**

PTH indirectly promotes absorption of  $Ca^{2+}$  and  $PO_4^{3-}$  by the intestine. **722**

The primary regulator of PTH secretion is the plasma concentration of free  $Ca^{2+}$ . **722**

Calcitonin lowers plasma  $\text{Ca}^{2+}$  concentration but is not important in the normal control of  $\text{Ca}^{2+}$  metabolism. **722**

Vitamin D is actually a hormone that increases calcium absorption in the intestine. **723**

Phosphate metabolism is controlled by the same mechanisms that regulate  $\text{Ca}^{2+}$  metabolism. **724**

Disorders in  $\text{Ca}^{2+}$  metabolism may arise from abnormal levels of PTH or vitamin D. **725**



**Chapter in Perspective:**  
**Focus on Homeostasis** **726**

**Chapter Summary** **727**

**Review Exercises** **728**

**Points to Ponder** **729**

**Clinical Consideration** **729**

**PhysioEdge Resources** **729**

## Chapter 20

# The Reproductive System **731**

### Introduction **731**

The reproductive system includes the gonads, reproductive tract, and accessory sex glands. **731**

Reproductive cells each contain a half set of chromosomes. **733**

Gametogenesis is accomplished by meiosis. **733**

The sex of an individual is determined by the combination of sex chromosomes. **735**

Sexual differentiation along male or female lines depends on the presence or absence of masculinizing determinants. **735**

### Male Reproductive Physiology **739**

The scrotal location of the testes provides a cooler environment essential for spermatogenesis. **739**

The testicular Leydig cells secrete masculinizing testosterone. **739**

Spermatogenesis yields an abundance of highly specialized, mobile sperm. **742**

Throughout their development, sperm remain intimately associated with Sertoli cells. **743**

LH and FSH from the anterior pituitary control testosterone secretion and spermatogenesis. **744**

Gonadotropin-releasing hormone activity increases at puberty. **745**

The reproductive tract stores and concentrates sperm and increases their fertility. **745**

The accessory sex glands contribute the bulk of the semen. **746**

Prostaglandins are ubiquitous, locally acting chemical messengers. **747**

### Sexual Intercourse between Males and Females **748**

The male sex act is characterized by erection and ejaculation. **748**

Erection is accomplished by penis vasocongestion. **748**

Ejaculation includes emission and expulsion. **750**



### Concepts, Challenges, and Controversies: Environmental “Estrogens”: Bad News for the Reproductive System **751**

The female sexual cycle is very similar to the male cycle. **752**

### Female Reproductive Physiology **752**

Complex cycling characterizes female reproductive physiology. **752**

The steps of gametogenesis are the same in both sexes, but the timing and outcome differ sharply. **752**

The ovarian cycle consists of alternating follicular and luteal phases. **754**

The follicular phase is characterized by the development of maturing follicles. **754**

The luteal phase is characterized by the presence of a corpus luteum. **756**

The ovarian cycle is regulated by complex hormonal interactions. **757**

Cyclic uterine changes are caused by hormonal changes during the ovarian cycle. **761**

Fluctuating estrogen and progesterone levels produce cyclical changes in cervical mucus. **762**

Pubertal changes in females are similar to those in males. **762**



### A Closer Look at Human Physiology: Menopausal Progesterone: When Cyclists and Other Female Athletes Do Not Cycle **763**

Menopause is unique to females. **763**

The oviduct is the site of fertilization. **764**

The blastocyst implants in the endometrium through the action of its trophoblastic enzymes. **766**

The placenta is the organ of exchange between maternal and fetal blood. **768**



### Concepts, Challenges, and Controversies: The Ways and Means of Contraception **770**

Hormones secreted by the placenta play a critical role maintaining pregnancy. **772**

Maternal body systems respond to the increased demands of gestation. **774**

Changes during late gestation prepare for parturition. **775**

Scientists are closing in on the factors that trigger the onset of parturition. **775**

Parturition is accomplished by a positive-feedback cycle. **777**

Lactation requires multiple hormonal inputs. **778**

Breast-feeding is advantageous to both the infant and the mother. **781**

The end is a new beginning. **781**



**Chapter in Perspective:**  
**Focus on Homeostasis** **782**

**Chapter Summary** **782**

**Review Exercises** **784**

**Points to Ponder** **785**

**Clinical Consideration** **785**

**PhysioEdge Resources** **785**



## **Appendixes**

### **Appendix A**

**The Metric System A-1**

### **Appendix B**

**A Review of Chemical Principles A-3**

### **Appendix C**

**Storage, Replication, and Expression of Genetic Information A-19**

### **Appendix D**

**Principles of Quantitative Reasoning A-31**

### **Appendix E**

**Text References to Exercise Physiology A-35**

### **Appendix F**

**Answers to End-of-Chapter Objective Questions,  
Quantitative Exercises, Points to Ponder, and Clinical  
Consideration A-37**

### **Glossary G-1**

**Credits C-1**

**Index I-1**