HUMAN PHYSIOLOGY

FIFTH EDITION

HUMAN PHYSIOLOGY

THE MECHANISMS OF BODY FUNCTION

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TO OUR PARENTS
AND TO JUDY, PEGGY, AND JOE
WITHOUT WHOSE UNDERSTANDING
IT WOULD HAVE BEEN IMPOSSIBLE.

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PREFACE

To the student: You need read no further, for this preface is unashamedly aimed not at you but at your instructors.

To the instructor: Please do read further. Because a large number of competing books have appeared in the 20 years since our first edition, we feel obliged to dwell at some length upon our own goals and the profound changes made in this revision to enhance the achievement of these goals.

GOALS AND ORIENTATION

The purpose of this book remains what it was in the first four editions: to present the fundamental principles and facts of human physiology in a format that is suitable for undergraduate students, regardless of academic backgrounds or fields of study—liberal arts, biology, nursing, pharmacy, or other allied health professions. The book is also suitable for dental students, and many medical students have used previous editions to lay the foundation for the more detailed coverage they receive in their courses.

The most significant feature of this book is its clear, up-to-date, accurate explanations of mechanisms rather than the mere description of facts and events. Because there are limits to what can be covered in an introductory text, it is essential to reinforce over and over, through clear explanations, that physiology can be understood in terms of basic themes and principles. As evidenced by the very large number of flow diagrams employed, the book emphasizes understanding, based on the ability to think in clearly defined chains of causal links. Our goal is to integrate and synthesize information rather than simply t. describe, so that students will achieve a working knowledge of physiology, not just a memory bank of physiological facts.

In this regard, we must acknowledge that even an introductory course in physiology must present a rather frightening number of facts, and our book is no exception. We have made every effort, however, not to mention facts simply because they happen to be known, but rather to use facts, whenever possible, as building blocks for general principles and concepts. Since our aim has been to tell a coherent story, rather than to write an encyclopedia, we have been willing to devote considerable space to the logical development of difficult but essential concepts, such as membrane potentials.

In keeping with our goals, the book progresses from the cell to the total body, utilizing at each level of increasing complexity the information and principles developed previously. Part One presents basic cellular and molecular biology, emphasizing that all phenomena of life are ultimately describable in terms of physical and chemical laws. Part Two analyzes the concept of the internal environment, the generalized components of the homeostatic control systems that regulate this environment, and the properties and organization of the major specialized cell types that comprise these systems. Part Three then describes the coordinated body functions, emphasizing how these functions result from the precise control and integration of specialized cellular activities and serve to maintain the internal environment.

One example of this approach is as follows: The characteristics that account for protein specificity are presented in Chapter 4, and this material is then used in Chapter 5 to explain the "recognition" process exhibited by enzymes, used again in Part Two for receptors, and finally used again in Part Three for antibodies. In this manner, the student is helped to see the basic foundations upon which more complex functions are built.

Another example: Rather than presenting, in a single chapter, a gland-by-gland description of all the hormones, we give a description of the basic principles of endocrinology in Chapter 10, but then save the details of the individual hormones for later chapters. For example, insulin is described in Chapter 17, "Regulation of Organic Metabolism, Growth, and Energy Balance," and aldosterone in Chapter 15, "Regulation of the Kidneys and Inorganic Ions." This permits the student to focus on the functions of the hormones in the context of the control systems in which they participate.

A MATTER OF BALANCE

The most challenging task for those who teach physiology to the groups for which this book is intended is to strike several difficult balances: (1) that between the enormously exciting new findings in cellular and molecular biology, on the one hand, and integrated whole-person physiology, on the other; and (2) that between breadth and depth of coverage in either of these two domains. In making the infinite number of decisions that go into striking these balances, we have been led by our goal of having the student understand, at a reasonable level, the mechanisms of the events described. Thus, for example, we cover systematically the various signal-transduction mechanisms used by plasma-membrane receptors because these mechanisms are so crucial to all cellular responses to chemical and electrical signals. Moreover, in this context, the overall function of G proteins is described, as is the specific role of G_s and G_i proteins in modulating adenylate cyclase. We have chosen, however, not to go into still greater detail and describe the interaction of these proteins with GTP, since these facts are not essential to an understanding of the adenylate cyclase system.

We also frequently use the technique of presenting in depth one example of a complex phenomenon and let this example serve to flesh out the general principle. Thus, we describe the molecular mechanisms by which norepinephrine increases myocardial contractility to illustrate a full sequence of events from receptor activation to cell response.

Another difficult decision, in a book aimed at students with diverse academic backgrounds, is how to deal with the basic biology, chemistry, and physics requisite for an understanding of the physiology. We have gathered much of the chemistry into two of the chapters of Part One but have presented other basic science where relevant in the text. Students with little or no background in the sciences will find this material essential, while others, more sophisticated in those areas, should profit from this review.

ALTERNATIVE SEQUENCES

Given the inevitable restrictions of time, our organization permits a variety of sequences and approaches to be adopted when using the book. Chapter 1 should definitely be read first since it introduces the basic themes that dominate the book. Depending on the time available, the instructor's goals, and the students' backgrounds in physical science and/or cellular biology, the chapters of Part One can either be worked through systematically at the outset or be used more selectively as background reading in the contexts of Parts Two and Three. To facilitate either approach, frequent references to specific pages of Part One are made in these later chapters.

In Part Two, the absolutely essential chapters are, in order, Chapters 7, 8, 10, and 11, for they present the basic concepts and facts relevant to homeostasis, intercellular communication, signal transduction, the nervous and endocrine systems, and muscle. The material in Chapters 9 and 12 are not as critical for an understanding of later chapters.

It would be best to begin the coordinated body functions of Part Three with the circulation, Chapter 13, but otherwise the chapters of Part Three, as well as Chapters 9 and 12 of Part Two, can be rearranged and used or not used to suit individual instructors' preferences.

REVISION HIGHLIGHTS

Our three major goals for this revision were: (1) to maintain and even improve upon the clarity of our explanations; (2) to update completely all material and assure the greatest accuracy possible; and (3) to provide a comprehensive set of study aids, including a new illustration program, that would enhance learning.

The first goal was achieved by an exhaustive rewriting, based largely on the criticisms and suggestions of our editor, Irene Nunes, who served as a naïve reader. Because we continued to rewrite until the material was clear to her, we are more convinced than ever that the book can serve as a primary source of information for the student.

Helped by the input from a survey of more than 400 teachers of physiology courses, we have also made significant changes in the organization of individual chapters and in the order of the chapters.

1. Chapters 2 and 3 have been transposed so that the molecular structures of carbohydrates, fats, and pro-

teins could be used in describing cell structures. The section on membrane structure that was formerly in Chapter 6 has been moved to Chapter 3.

2. "The Sensory Systems," formerly Chapter 18, is now Chapter 9, immediately following the chapter, "Neural Control Mechanisms." This juxtaposition will help the student gain greater understanding of the sensory components of the control systems described in Chapter 8. "Control of Body Movement," formerly Chapter 19, is now Chapter 12, directly following "Muscle" so as to provide greater understanding of the neural components of muscle control. The result of these two chapter shifts is to present most of the book's neurophysiology in Part Two rather than spreading it across Parts Two and Three. We have left "Consciousness and Behavior" as the last chapter in the book, however, so we could describe in it the interactions between "mind" and the coordinated body functions described in Part Three.
3. Hemostasis has been moved from the chapter on circulation to Chapter 19, to emphasize its role as a defense mechanism and its analogies to the immune system.

Updating was, as always, a huge task. Preparation of each new edition has required us to do more reading than for the previous one, as the amount of scientific information continues to expand explosively. A great number of physiologists reviewed the manuscript (see list in the acknowledgements) to help assure not only accuracy but balance. The number of revisions are far too numerous to list, but the following are examples of topics that have been either significantly expanded because of new information or added for the first time:

Categories and characteristics of plasma-membrane channels
Molecular mechanisms of ion transport
Feedforward in control systems
Biological rhythms and their contributions to homeostasis
New signal transduction mechanisms: G proteins, cyclic GMP, phospholipase C, PIP_2, IP_3, DAG, protein kinase C, and receptors as tyrosine kinases
Synaptic effectiveness
Coding in the visual system
Synthesis of peptide hormones (preprohormones and prohormones)
Candidate hormones
New hypotheses on mechanisms of summation in muscle contraction
Lengthening contractions in muscle
Hierarchical view of motor control systems
Regulation of blood cell production (colony-stimulating factors)
Functions of endothelial cells, including endothelium-derived relaxing factors
Molecular mechanisms of catecholamine effects on the myocardium
Angiogenic factors
Blood volume and long-term regulation of arterial pressure
Atrial natriuretic factor
Insulin receptors and signal transduction
Bone growth
Growth factors and growth-inhibiting factors, including insulin-like growth factor I
Control of food intake
Acclimatization to cold
Cytokines, including interleukin 1, tumor necrosis factor, interleukin 6, and gamma interferon
Sertoli cell functions
Antigen processing and presentation, including MHC restrictions
Anticlotting factors: the fibrinolytic system, protein C, antithrombin III, heparin, tissue plasminogen activator, anticlotting roles of thrombin and endothelial cells

Coverage of still other topics was expanded in response to suggestions both from the survey of physiology teachers mentioned above and from other reviewers. Examples include:

Summary tables describing the cranial nerves
Summary of arteriolar control in specific organs and tissues
Determinants of alveolar gas pressures
Graphical presentation of pulmonary circulation pressures
Lung compliance
Bicarbonate reabsorption by the kidneys
Creatinine clearance
Summary of all major liver functions
Meiosis
Chorionic villus sampling
Contraceptive methods
EEG patterns
Exercise physiology
Pathophysiology

A separate word is needed about these last two categories. We have chosen to continue our practice of presenting exercise physiology where relevant throughout the book, rather than in a separate chapter, because we feel that the integrated tack provides an excellent way of summarizing and applying much of the material used in the individual chapters. Pathophysiology, too, is important for illustrating basic physiology and demonstrating its relevance. Examples of such topics that have been either expanded or included for the first time include: cancer and oncogenes, cataracts and presbyopia, classification of endocrine disorders (primary and secondary hyposecretion, etc.), muscle diseases, anemia, therapy of hypertension and myocardial infarctions, chronic obstructive lung disease, asthma, ventilation-perfusion inequalities, diuretics, kidney diseases, peritoneal dialysis, hypoglycemia, obesity, osteoporosis, AIDS, late-phase allergic responses, psychoneuroimmunology.

With all these additions you might assume that the total text material has increased, but such is not the case. The careful editing described earlier and a ruthless removal of material not deemed essential has permitted us to maintain the text size essentially constant. Indeed, if one excludes the end-of-chapter study aids (to be described below) added to this edition, the actual text has been decreased. For example, the text of the following chapters has been shortened by 10 to 25 percent: Chapter 4, "Molecular Control Mechanisms: DNA and Protein"; Chapter 6, "Movement of Molecules across Cell Membranes"; Chapter 8, "Neural Control Mechanisms"; Chapter 16, "The Digestion and Absorption of Food"; Chapter 20, "Consciousness and Behavior."

STUDY AIDS

A variety of pedagogical aids are used in this edition, some, as noted, for the first time:

1. **Bold face key terms** appear throughout each chapter. chapter.
2. **The illustration program** has been totally redone for this edition. The total number of figures has remained at approximately 600, but many old ones have been dropped and many new ones added. Moreover, every figure retained in this edition has been redrawn, many with extensive revisions. For the first time, full color has been employed where appropriate (approximately half the figures), a change that greatly enhances these figures' educational value. The extensive use of flow diagrams, which we introduced in 1970 (and which has been so widely imitated in other texts) has been expanded. These diagrams have been improved not only by the frequent use of full color but by the introduction of conventions that are used throughout the book and that should enhance learning. Look, for example, at Figure 19-18 on page 678. The beginning and ending boxes of the flow diagram are in light green (or in gray, in figures lacking full color), and the beginning is further clarified, when needed, by the use of a "Begin" logo. Blue three-dimensional boxes are used to denote events occurring inside organs and tissues (identified by boldface underlined labels in the upper right of the boxes), so that the reader can easily pick out the anatomic entities that participate in the sequences of events. Finally, in full-color figures, the participation of hormones in the sequences stand out by the placing of changes in their plasma concentrations in orange boxes.
3. **Summary tables.** We have doubled the number of reference and summary tables in this edition (a total of 120). Some summarize small amounts of information (for example, the summary of second messengers in Table 7-7, page 162), whereas others bring together larger amounts of information that may be scattered throughout the book (for example the summary of liver functions in Table 17-6, page 580). In several places, mini-glossaries are included as tables in the text (for example, the list of immune-system cells and chemical mediators in Table 19-13, page 684). Because the tables complement the figures, these two learning aids taken together provide a rapid means of reviewing the most important material in a chapter.
4. **End-of-chapter study aids.** These are all new for this edition:
   (*a*) Extensive **chapter summaries in outline form.**
   (*b*) Comprehensive **review questions in essay format**, including **key-word definition lists** of all boldface words in chapter. These review questions, in essence, constitute a complete list of learning objectives.
   (*c*) **Thought questions** that challenge the student to go beyond memorization of facts to solve problems, often presented as case histories or experiments. Complete **answers to thought questions** appear as Appendix A.
5. **Glossary.** For the first time, we have added **pronunciation guides** for many of the terms in this comprehensive glossary, appearing as Appendix D.
6. Other appendixes (B and C) present **English-metric interconversions** and **electrophysiology equations.**
7. **Suggested readings** are listed at the back of the book, as Appendix F.

SUPPLEMENTS

1. For this edition, a completely new **study guide** has been prepared by Dr. Sharon Russell (University of California at Berkeley). It contains a large variety of aids, including learning hints, many test questions with answers, and additional relevant contemporary material.
2. An **instructor's manual/test bank,** which contains, among other materials, a complete set of learning objectives, is available from the publisher. The test bank is also available on software for the IBM PC, Apple II, and Macintosh computers.
3. A set of 150 **overhead transparencies** representing the most important figures from the book is also available.

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First, we would like to thank the more than 400 instructors who participated in the survey that was taken prior to beginning this revision.

Secondly, we are very grateful to the many physiologists who read one or more chapters during various stages of this revision: Harold B. Falls, Southwest Missouri State University; Margaret M. Gould, Georgia State University; Bruce Grayson, University of Miami; John P. Harley, Eastern Kentucky University; Barbara J. Howell, SUNY–Buffalo; Fred J. Karsch, University of Michigan; Landis Keyes, University of Michigan; Steven Kunkel, University of Michigan; Esmail Meisami, University of Illinois, Sandy Milner-Brown, University of Colorado; Mary E. Murphy, Washington State University; Stephen R. Overmann, Southeast Missouri State University; Sharon Russell, University of California–Berkeley; Evelyn H. Schlenker, University of South Dakota, Medical School; Stanley A. Schwartz, The University of Michigan; George Simone, Eastern Michigan University; Gregory A. Stephens, University of Delaware; Jerry Stinner, University of Akron; Winton Tong, University of Pittsburgh; and George Veomett, University of Nebraska–Lincoln. Their advice was extremely useful in helping us to be accurate and balanced in our coverage. We hope they will be understanding of the few occasions when we did not heed their advice, and we are, of course, solely responsible for any errors that have crept in.

Many people participated in the development and production of this book, certainly the most gargantuan task we have all faced, not excepting preparation of the first edition. Our sponsoring editor, Denise Schanck, our production editor, Diane Renda, our editing supervisor James W. Bradley, and his assistant, Marie Gagliardi, and our designer, Jo Jones, all somehow managed to see this complex project through to completion with skill and efficiency. Deanne McKeown contributed the beautiful medical illustrations that make their appearance in this edition, and Oxford Illustrators completed the gigantic task of doing all the line art under the pressure of very tight deadlines. But one person, our basic-book editor, Irene M. Nunes, deserves the lion's share of credit for the creation of this edition. With great skill and wonderful good humor, she organized and supervised virtually every facet of the project, developed with us all the new features of this edition, and then served as a merciless reviewer of every sentence and figure in the manuscript. Irene, thank you.

Arthur J. Vander
James H. Sherman
Dorothy S. Luciano

CONTENTS

CHAPTER

1

A FRAMEWORK FOR HUMAN PHYSIOLOGY

One cannot meaningfully analyze the complex activities of the human body without a framework upon which to build, a set of viewpoints to guide one's thinking. It is the purpose of this chapter to provide such an orientation to the subject of **human physiology**—the mechanisms by which the body functions.

MECHANISM AND CAUSALITY

The **mechanist view** of life holds that all phenomena, no matter how complex, are ultimately describable in terms of physical and chemical laws and that no "vital force" distinct from matter and energy is required to explain life. The human being is a machine—an enormously complex machine, but a machine nevertheless. This view has predominated in the twentieth century because virtually all information gathered from observation and experiment has agreed with it. But **vitalism**, the view that some force beyond physics and chemistry is required by living organisms, is not completely dead, nor is it surprising that this viewpoint remains specifically in brain physiology, where scientists are almost entirely lacking in physicochemical hypotheses to explain such phenomena as thought and consciousness. Most physiologists believe that even this area will ultimately yield to physicochemical analysis, but it would be unscientific, on the basis of present knowledge, to dismiss the problem out of hand.

A common denominator of physiological processes is their contribution to survival. Unfortunately, it is easy to misunderstand the nature of this relationship. Consider, for example, the statement, "During exercise a person sweats because the body *needs* to get rid of the excess heat generated." This type of statement is an example of **teleology**, the explanation of events in terms of purpose, but it is not an explanation at all in the scientific sense of the word. It is somewhat like saying, "The furnace is on because the house needs to be heated." Clearly, the furnace is on not because it senses in some mystical manner the house's "needs" but because the temperature has fallen below the thermostat's set point and the electric current in the connecting wires has turned on the heater.

Is it not true that sweating serves a useful purpose because the excess heat, if not eliminated, might cause sickness or even death? Yes, it is, but this is totally different from stating that a need to avoid injury caused the sweating. The cause of the sweating was a sequence of events initiated by the increased heat generation: increased heat generation → increased blood temperature → increased activity of specific nerve cells in the brain → increased activity of a series of nerve cells → increased production of sweat by the sweat-gland cells. Each step occurs by means of physicochemical changes in the cells involved. In science, to explain a phenomenon is to reduce it to a causally linked sequence of physicochemical events. This is the scientific meaning of causality, of the word "because."

This is a good place to emphasize that causal chains can be not only long, as in the example just cited, but also multiple. In other words, one should not assume the simple relationship of one cause, one effect. We shall see that multiple factors often must interact to elicit a response. To take an example from medicine, cigarette smoking causes lung cancer, but the likelihood of the cancer developing in a smoker depends on a variety of other factors, including the way that person's body processes the chemicals in cigarette smoke, the rate at which damaged molecules are repaired, and so on.

That a phenomenon is beneficial to the person, while not explaining the mechanism of the phenomenon, is of obvious interest and importance. It is attributable to evolutionary processes that result in the selecting of those responses having survival value. Evolution is the key to understanding why most bodily activities do indeed appear to be purposeful. Throughout this book we emphasize how a particular process contributes to survival, but the reader must never confuse this survival value of a process with the explanation of the mechanisms by which the process occurs.

A SOCIETY OF CELLS

Cells: The Basic Units

The simplest structural units into which a complex multicellular organism can be divided and still retain the functions characteristic of life are called **cells**. One of the unifying generalizations of biology is that certain fundamental activities are common to almost all cells and represent the minimal requirements for maintaining cell integrity and life. Thus, a human liver cell and an amoeba are remarkably similar in their means of exchanging materials with their immediate environments, of obtaining energy from organic nutrients, of synthesizing complex molecules, and of duplicating themselves.

Each human organism begins as a single cell, the fertilized ovum, which divides to form two cells, each of which divides in turn, resulting in four cells, and so on. If cell multiplication were the only event occurring, the end result would be a spherical mass of identical cells. During development, however, each cell becomes specialized in the performance of a particular function, such as developing force and movement (muscle cells) or generating electric signals (nerve cells). The process of transforming an unspecialized cell into a specialized cell is known as **cell differentiation**. In addition to differentiating, cells migrate to new locations during development and form selective adhesions with other cells to form multicellular structures. In this manner, the cells of the body are arranged in various combinations to form a hierarchy of organized structures. Differentiated cells with similar properties aggregate to form **tissues** (nerve tissue, muscle tissue, and so on), which combine with other types of tissues to form **organs** (the heart, lungs, kidneys, and so on), which are linked together to form **organ systems** (Figure 1-1).

About 200 distinct kinds of cells can be identified in the body in terms of differences in structure and function. When cells are classified according to the broad types of function they perform, however, four categories emerge: (1) muscle cells, (2) nerve cells, (3) epithelial cells, and (4) connective-tissue cells. In each of these functional categories, there are several cell types that perform variations of the specialized function. For example, there are three types of muscle cells—skeletal, cardiac, and smooth-muscle cells—all of which generate forces and produce movement but differ from each other in shape, in the mechanisms controlling their contractile activity, and in their location in the various organs of the body.

Muscle cells are specialized to generate the mechanical forces that produce force and movement. They may be attached to bones and produce movements of the limbs or trunk. They may be attached to skin, as for example, the muscles producing facial expressions, or they may enclose hollow cavities so that their contraction expels the contents of the cavity, as in the case of the pumping of the heart. Muscle cells also surround many of the tubes in the body—blood vessels, for example—and their contraction changes the diameter of these tubes.

Nerve cells are specialized to initiate and conduct electric signals, often over long distances. The signal may influence the initiation of new electric signals in other nerve cells, or it may influence secretion by a gland cell or contraction of a muscle cell. Thus, nerve cells provide a major means of controlling the activities of other cells. Their activity also underlies such phenomena as consciousness, perception, and cognition.

Epithelial cells are specialized for the selective secretion and absorption of ions and organic molecules. They are located mainly at the surfaces that either cover the body or individual organs or else line the walls of various tubular and hollow structures within the body. Epithelial cells, which rest on a homogenous noncellular material called the **basement membrane**, form the boundaries between compartments and function as selective barriers regulating the exchange of molecules across them. For example, the epithelial cells at the surface of the skin form a barrier that prevents most substances in the external environment from entering the body through the skin. Epithelial cells are also found in glands that form from the invagination of the epithelial surfaces.

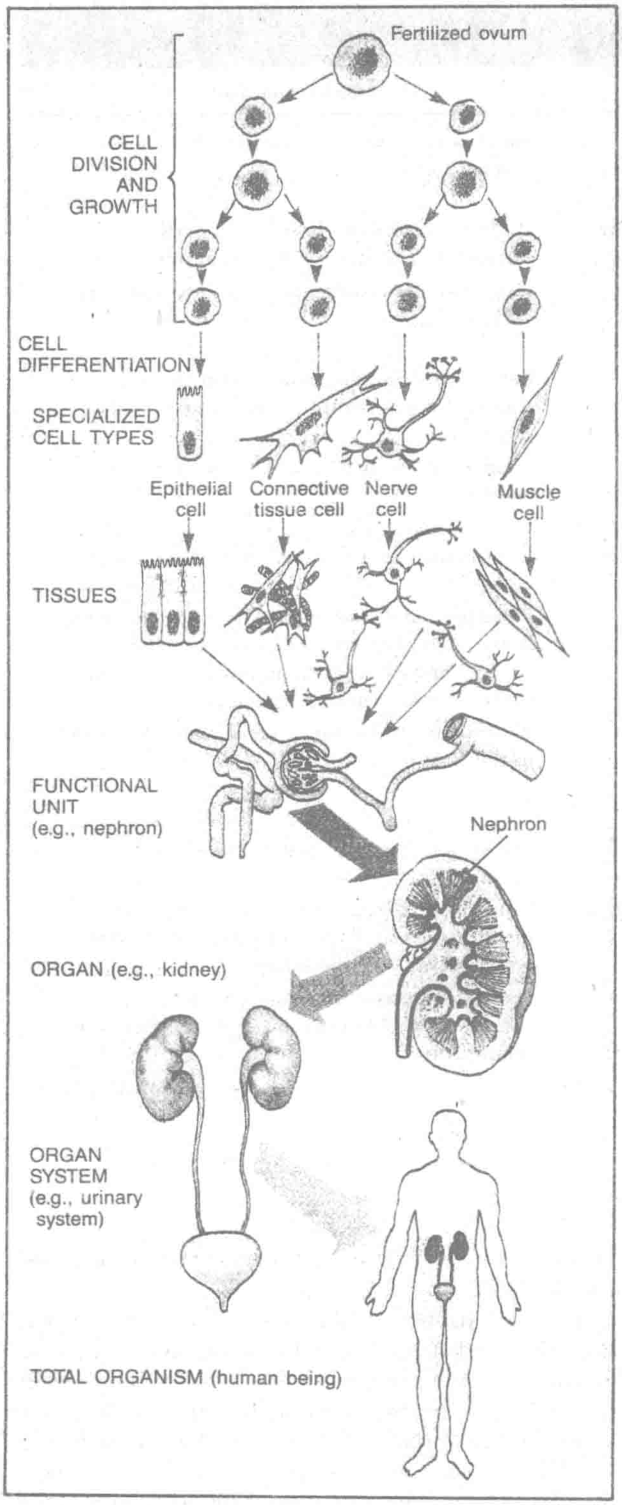

FIGURE 1-1 Levels of cellular organization.

Connective-tissue cells, as their name implies, have as their major function connecting, anchoring, and supporting the structures of the body. These cells typically have a large amount of extracellular material between them. The cells themselves include those in the loose meshwork of cells and fibers underlying most epithelial layers plus other types as diverse as fat-storing cells, bone cells, and red and white blood cells. Many connective-tissue cells secrete into the fluid surrounding them molecules that form a matrix consisting of various types of protein **fibers** embedded in a **ground substance** made of complex sugars, protein, and crystallized minerals. This matrix may vary in consistency from a semifluid gel, in loose connective tissue, to the solid crystalline structure of bone. These extracellular fibers include ropelike **collagen fibers**, which have a high tensile strength and resist stretching, rubber-band-like **elastin fibers**, and fine, highly branched **reticular fibers**.

Tissues

Most specialized cells are associated with other cells of a similar kind to form tissues. Corresponding to the four general categories of differentiated cells, there are four general classes of tissues: (1) **muscle tissue**, (2) **nerve tissue**, (3) **epithelial tissue**, and (4) **connective tissue**. It should be noted that the term "tissue" is frequently used in several ways. It is formally defined as just described, that is, an aggregate of a single type of specialized cell. However, it is also commonly used to denote the general cellular fabric of any organ or structure, for example, kidney tissue or lung tissue, each of which in fact usually contains all four classes of tissue.

Organs and Organ Systems

Organs are composed of the four kinds of tissues arranged in various proportions and patterns: sheets, tubes, layers, bundles, strips, and so on. For example, the kidneys consist largely of (1) a series of small tubes, each composed of a single layer of epithelial cells; (2) blood vessels, whose walls consist of an epithelial lining and varying quantities of smooth muscle and connective tissue; (3) nerve fibers with endings near the muscle and epithelial cells; and (4) a loose network of connective-tissue elements that are interspersed throughout the kidneys and also form enclosing capsules.

Many organs are organized into small, similar subunits often referred to as **functional units**, each performing the function of the organ. For example, the kidneys' 2 million functional units are termed nephrons, and the total production of urine by the kidneys is the sum of the amounts formed by the individual nephrons.

Finally we have the organ system, a collection of organs that together perform an overall function. For ex-

TABLE 1-1 ORGAN SYSTEMS OF THE BODY

System	Major Organs or Tissues	Primary Functions
Circulatory	Heart, blood vessels, blood (Some classifications also include lymphatic vessels and lymph in this system.)	Rapid flow of blood throughout the body's tissues
Respiratory	Nose, pharynx, larynx, trachea, bronchi, lungs	Exchange of carbon dioxide and oxygen; regulation of hydrogen-ion concentration
Digestive	Mouth, pharynx, esophagus, stomach, intestines, salivary glands, pancreas, liver, gallbladder	Digestion and absorption of organic nutrients, salts, and water
Urinary	Kidneys, ureters, bladder, urethra	Regulation of plasma composition through controlled excretion of organic wastes, salts, and water
Musculoskeletal	Cartilage, bone, ligaments, tendons, joints, skeletal muscle	Support, protection, and movement of the body
Immune	White blood cells, lymph vessels and nodes, spleen, thymus, and other lymphoid tissues	Defense against foreign invaders; return of extracellular fluid to blood; formation of white blood cells
Nervous	Brain, spinal cord, peripheral nerves and ganglia, special sense organs	Regulation and coordination of many activities in the body; detection of changes in the internal and external environments; states of consciousness; learning; cognition
Endocrine	All glands secreting hormones: Pancreas, testes, ovaries, hypothalamus, kidneys, pituitary, thyroid, parathyroid, adrenal, intestinal, thymus, and pineal	Regulation and coordination of many activities in the body
Reproductive	Male: Testes, penis, and associated ducts and glands	Production of sperm; transfer of sperm to female
	Female: Ovaries, uterine tubes, uterus, vagina, mammary glands	Production of eggs; provision of a nutritive environment for the developing embryo and fetus; nutrition of the infant
Integumentary	Skin	Protection against injury and dehydration; defense against foreign invaders; regulation of temperature

ample, the kidneys, the urinary bladder, the tubes leading from the kidneys to the bladder, and the tubes leading from the bladder to the exterior constitute the urinary system. There are ten organ systems in the human body. Their components and functions are given in Table 1-1.

To sum up, the human body can be viewed as a complex society of differentiated cells structurally and functionally combined and interrelated to carry on the functions essential to the survival of the organism. The individual cells constitute the basic units of this society, and almost all of these cells individually exhibit the fundamental activities common to all forms of life. Indeed, many of the body's cells can be removed and maintained in test tubes as free-living organisms.

There is a paradox in this analysis. If each cell performs the fundamental activities required for its own survival, what contributions do the organ systems make? How is it that the functions of the organ systems are essential to the survival of the organism when each individual cell seems capable of performing its own fundamental activities? The resolution of this paradox is found in the isolation of most of the cells of a multicellular organism from the environment surrounding the organism—the **external environment**—and the presence of an internal environment.

THE INTERNAL ENVIRONMENT

An amoeba and a human liver cell both obtain their energy by breaking down certain organic nutrients. The chemical reactions involved in this intracellular process are remarkably similar in the two types of cells and involve the utilization of oxygen and the production of carbon dioxide. The amoeba picks up oxygen directly from the fluid surrounding it (its external environment) and eliminates carbon dioxide into the same fluid. But how can the liver cell and all other internal parts of the body obtain oxygen and eliminate carbon dioxide when, unlike the amoeba, they are not in direct contact with the external environment—the air surrounding the body?

Figure 1-2 summarizes the exchanges of matter that occur in a person. Supplying oxygen is the function both of the respiratory system, comprising the lungs and the airways leading to them, which takes up oxygen from the external environment, and of the circulatory system, which distributes oxygen to all parts of the body. In addition, the circulatory system carries the carbon dioxide generated by all the cells of the body to the lungs, which eliminate it to the exterior. Similarly, the digestive and circulatory systems working together make nutrients from the external environment available to all the body's cells. Wastes other than carbon dioxide are carried by the circulatory system from the cells that produced them to the kidneys and liver, which excrete them from the body. The kidneys also regulate the concentrations of water and many essential minerals in the plasma. The nervous and hormonal systems coordinate and control the activities of all the other organ systems.

Thus the overall effect of the activities of organ systems is to create within the body an environment in which all cells can survive and function. This environment surrounding each cell is called the **internal environment**. The internal environment is not merely a theoretical physiological concept. It can be identified quite specifically in anatomical terms: The body's internal environment is the **extracellular fluid** (literally, fluid outside the cells) that bathes each cell (Figure 1-2).

In other words, the internal environment in which each cell lives is not the external environment surrounding the entire body but the local extracellular fluid surrounding that cell. It is from this fluid that the cells receive oxygen and nutrients and into which they excrete wastes. A multicellular organism can survive only as long as it is able to maintain the composition of its internal environment in a state compatible with the survival of its individual cells. In 1857, the French physiologist Claude Bernard clearly described the central importance of the extracellular fluid: "It is the fixity of the internal environment that is the condition of free and independent life. . . . All the vital mechanisms, however varied they may be, have only one object, that of preserving constant the conditions of life in the internal environment." This concept of an internal environment and the necessity of maintaining its composition relatively constant is known as **homeostasis**. It is the single most important unifying idea to be kept in mind while attempting to understand the functions of the body's organ systems and their interrelationships.

Let us illustrate homeostasis with an example. When, for any reason, the concentration of oxygen in the blood significantly decreases below normal, the nervous system detects the change and increases its output to the

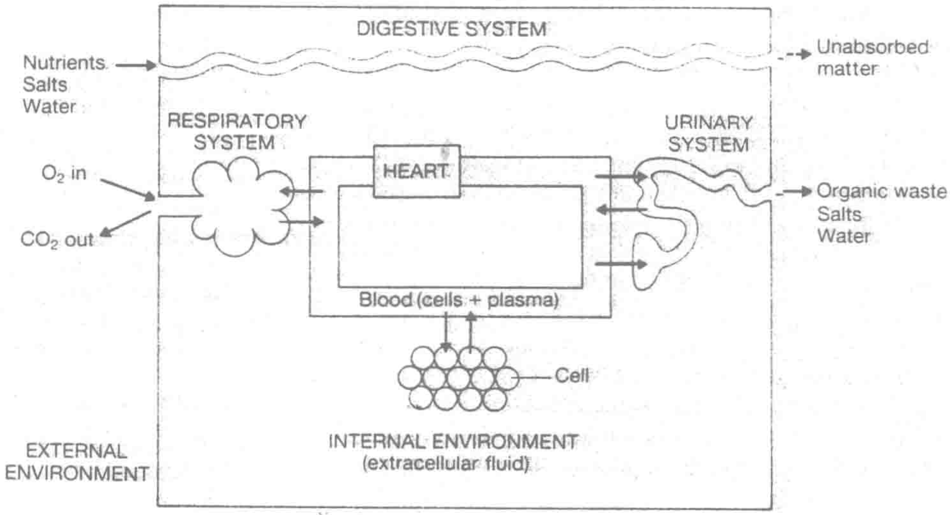

FIGURE 1-2 Exchanges of matter occur between the external environment and the circulatory system via the digestive, respiratory, and urinary systems. Extracellular fluid (plasma and interstitial fluid) is the internal environment of the body. The external environment is the air surrounding the body.

skeletal muscles responsible for breathing movements. The result is a compensatory increase in oxygen uptake by the body and a restoration of normal internal oxygen concentration.

To summarize, the total activities of every individual cell in the body fall into two categories: (1) Each cell performs for itself all those fundamental basic cellular processes—movement of materials across its membrane, extraction of energy, protein synthesis, and so on—that represent the minimal requirements for maintaining its individual integrity and life; and (2) each cell simultaneously performs one or more specialized activities that, in concert with the activities performed by the other cells of its tissue or organ system, contribute to the survival of the organism by helping maintain the stable internal environment required by all cells.

Plasma and Interstitial Fluid

Extracellular fluid exists in two locations—between cells and as the blood plasma. Approximately 80 percent of the fluid surrounds all the body's cells except the blood cells. Because it lies between cells, this 80 percent of the extracellular fluid is known as **intercellular fluid** or, more often, **interstitial fluid**. The remaining 20 percent of the extracellular fluid is the fluid portion of the blood, the **plasma**. As the blood (plasma plus suspended blood cells) is continuously circulated by the action of the heart to all parts of the body, the plasma exchanges oxygen, nutrients, wastes, and other metabolic products with the interstitial fluid surrounding the small blood vessels. Because of the exchanges between plasma and interstitial fluid, concentrations of dissolved substances are virtually identical in the two fluids, except for protein concentration.

With this major exception—higher protein concentration in plasma than in interstitial fluid—the entire extracellular fluid may be considered to have a homogeneous composition that is very different from that of the **intracellular fluid**—the fluid inside the cells.

With this introductory framework in mind, the overall organization and approach of this book should easily be understood. Because the fundamental features of cell function are shared by virtually all cells and because these features constitute the foundation upon which specialization develops, we devote the first part of the book to an analysis of basic cell physiology. Much of this cell biology is now referred to as **molecular biology** in recognition of the ultimate goal of explaining cellular processes in terms of interactions between molecules.

At the other end of the organizational spectrum, the final part of the book describes how coordinated functions (circulation, respiration, and so on) result from the precisely controlled and integrated activities of specialized cells grouped together in tissues and organs. The theme of these descriptions is that each function, with the obvious exception of reproduction, serves to keep some important aspect of the body's internal environment relatively constant.

The middle section of the book provides the principles and information required to bridge the gap between these two organizational levels, the cell and the body. Control systems are analyzed first in general terms to emphasize that the basic principles governing virtually all control systems are the same, but the bulk of Part 2 is concerned with the major components of the body's control systems (nerve cells, muscle cells, and gland cells). Once acquainted with the cast of major characters—nerve, muscle, and gland cells—and the theme—the maintenance of a stable internal environment—the reader will be free to follow the specific plot lines—circulation, respiration, and so on—of Part Three.

SUMMARY

Mechanism and Causality

I. The mechanist view of life, the view taken by physiologists, holds that all phenomena are describable in terms of physical and chemical laws.

II. Vitalism holds that some additional force is required to explain the function of living organisms.

A Society of Cells

I. Cells are the simplest structural units into which a complex multicellular organism can be divided and still retain the functions characteristic of life.

II. Cell differentiation results in the formation of four categories of specialized cells.
   - A. Muscle cells generate the mechanical activities that produce force and movement.
   - B. Nerve cells initiate and conduct electric signals.
   - C. Epithelial cells selectively secrete and absorb ions and organic molecules.
   - D. Connective-tissue cells connect, anchor, and support the structures of the body.

III. Specialized cells associate with similar cells to form tissues: muscle tissue, nerve tissue, epithelial tissue, and connective tissue.

IV. Organs are composed of the four kinds of tissues arranged in various proportions and patterns; many organs contain multiple small similar functional units.

V. An organ system is a collection of organs that together perform an overall function.

The Internal Environment

I. The extracellular fluid surrounding a cell is the cell's internal environment.

A. The function of organ systems is to maintain the internal environment relatively constant.
B. Each cell performs the basic cellular processes required to maintain its own integrity plus specialized activities that help maintain the internal environment relatively constant—homeostasis.

II. The extracellular fluid is composed of the blood plasma and the fluid between cells—the interstitial fluid.
A. Of the extracellular fluid, 80 percent is interstitial fluid and 20 percent is plasma.
B. Interstitial fluid and plasma have essentially the same composition except that plasma contains a much higher concentration of protein.
C. Extracellular fluid differs markedly in composition from the fluid inside cells—the intracellular fluid.

REVIEW QUESTIONS

1. Define:

human physiology
mechanist view
vitalism
teleology
cells
cell differentiation
tissues
organs
organ systems
muscle cells
nerve cells
epithelial cells
basement membrane
connective-tissue cells
fibers
ground substance
collagen fibers
elastin fibers
reticular fibers
muscle tissue
nerve tissue
epithelial tissue
connective tissue
functional units
external environment
internal environment
extracellular fluid
homeostasis
intercellular fluid
interstitial fluid
plasma
intracellular fluid
molecular biology

2. Describe the levels of cellular differentiation and state the four types of specialized cells and tissues.

3. List the 10 organ systems of the body and give one-sentence descriptions of their functions.

4. Contrast the two categories of functions performed by every cell.

5. What two fluids constitute the extracellular fluid, what are their relative proportions, and in what way do they differ from each other in composition?