

## 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 to 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 hor-

mones, 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<sub>2</sub>, IP<sub>3</sub>, 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.
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.

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## SUPPLEMENTS

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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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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.

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