Fourth edition

Biochemistry

A Case-Oriented Approach

Rex Montgomery, Ph.D., D.Sc.
Robert L. Dryer, Ph.D.
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Department of Biochemistry,
The University of Iowa College of Medicine,
Iowa City, Iowa

Fourth edition with 289 illustrations

The C.V. Mosby Company

St. Louis
Toronto
London
1983

Preface

The fourth edition of this book contains significant new biochemical information while it retains material introduced in the three previous editions. New topics have also been added to the analysis of human diseases, to basic biochemical concepts, and, in the sections dealing with applications of these concepts, to analysis of health-related problems. More of the cases in this edition have been worked out for the reader. As in the other editions, many new clinical cases and discussions of the biochemical principles illustrated by them have been added. However, those clinical cases from earlier editions that served particularly well in teaching have been retained. A large number of case problems have been solved and reflect recent advances in many areas of biochemistry. More pertinent references to both solved and unsolved case problems have been included for the benefit of both student and teacher.

The fourth edition contains 13 rather than 14 chapters. On the basis of our teaching experiences we have moved cases from Chapter 14 of the third edition to appropriate parts of the other chapters, introducing the comprehensive nature of case problems earlier in the book. In the basic biochemistry sections of the text, more extensive discussion of such important topics as trace elements in nutrition, lipoproteins, glycosylated proteins, 2,6-bisphosphofructose, ion pumps, muscle contraction, inborn errors of metabolism, leukotrienes, dietary fat and atherosclerosis, hormone receptors, chromosomal structure, carcinogenesis, DNA repair mechanisms, and immunoglobulin gene rearrangements can be found. Complex figures have been broken down into more numerous, simpler ones for easier study and comprehension. Biochemical topics presented in the case problems are listed in the Table of Contents.

Aside from the case analyses, the biochemical content of the fourth edition continues to be self-standing, in contrast to the first two editions. Thus the book is appropriate for a one-semester course in human biochemistry. It is, however, organized in a manner less traditional than that of most textbooks, since significant biochemical information is incorporated into the solutions to the case problems associated with each chapter. The text thus continues to serve a dual function: first, to make students aware of biochemical principles and, second, to provide opportunities to use these principles in analyzing common diseases. We believe that the second goal is the ultimate objective of biochemical education for the health science student.

At first glance the chapter titles of this book are much like those of other biochemistry texts. The biochemical principles are needed to understand the chemical and molecular aspects of health science problems. The second part of each chapter amplifies these principles, sometimes adding others particularly relevant to the health-related problem at hand, and applies these facts and concepts to the stated solutions of health-related problems. While the purpose of the case presentations is to illustrate the *application* of biochemistry to health problems, students are often curious to know more about the physiologic or pathologic aspects of the clinical material. This curiosity can be satisfied by reading the references presented after each case. Generally, students realize that the purpose of the text is to teach biochemistry, to demonstrate *why* biochemistry is important in the health sciences, and to show *how* biochemical principles are involved in day-to-day professional practice. Experience has shown us that students grasp concepts more clearly when they see a relation between these concepts and their own professional goals. Learning seems also to be more enjoyable when the applications are made evident.

Selected clinical case descriptions and biochemical questions about them are provided with and without written analysis. Those without analysis, as well as a series of shorter additional questions at the end of each chapter, are meant to be solved by the students. Many of the questions can be answered with a knowledge of the basic biochemistry presented in the first portion of the chapter. Some cases and questions are more comprehensive. Sufficient references direct students to sources from which they can compose answers to questions that are unsolved in the main body of the text and that are identified by diamonds. Similarly, brief unsolved clinical problems are marked by diamond symbols (◆), indicating that outside reading will be required to compose a suitable solution. These questions are included because it is imperative that students become accustomed to the method and value of bibliographic research. The knowledge gained by study of the principles in the first part of the chapter can be extended by independent study of other source materials.

We have separately compiled a set of model answers for all of the case problems presented here. Interested instructors may request a copy of these answers from the authors.

The format of this book allows considerable flexibility. For some students the language statements plus the solved case problems may be sufficient. Others may wish to use the unsolved case problems or the additional study questions. As in the past editions we have selected nutrition as the topic for the first chapter in order to introduce from the beginning the case-oriented method of study. Many students have been exposed to this subject in their everyday living and in previous schooling. Knowledge of the properties of proteins follows (Chapter 2), since this material is essential for principles presented in later chapters. Chapter 3 deals with enzymes, also vital for understanding subsequent concepts. Because errors of fluid and electrolyte regulation are such frequent components of numerous diseases, principles of acid-base balance are discussed in Chapter 4. Thus early introduction to these basic topics permits selection from a wide range of case-oriented discussions. The remaining chapters may be covered in virtually any order, but we have found the sequence presented here to be satisfactory. Each chapter has been kept reasonably limited and self-contained, but we have made an effort by cross-references to guide the student toward a holistic approach.

In our one-semester course, Chapters 1 through 13 are covered in a 14-week period—for the most part, one chapter per week. Those that sometimes require a slightly longer time for completion are "Acid-base, fluid, and electrolyte control" (Chapter 4), "Carbohydrate metabolism" (Chapter 7), and "Hormonal regulation of metabolism" (Chapter 13). Weekly contact involves 5 lecture hours for the class as a whole and 2 hours of discussion and review in small groups. All 5 lecture hours are usually devoted to coverage of the basic biochemistry section of the particular chapter. In some instances, however, one of these lectures is employed to present greater amplification of some important biochemical feature taken from the clinical examples section of the text. For example, phenylketonuria in Chapter 6, diabetes mellitus in Chapter 7, and hyperlipidemia in Chapter 10 have been highlighted by special lecture time on recent developments. It is recommended that small-group discussions be devoted to the clinical examples section of each chapter. These discussions might begin with a general review of the clinical cases that have been solved in the text, in an attempt to strengthen correlation of that information with the basic biochemical principles enunciated in the earlier part of the chapter. Subsequently, students can be asked to present one or more of the cases as well as additional problems not worked out in the text, either as oral or as written presentations.

It is recommended that examinations be based entirely on the analysis of cases. We have employed questions requiring short answers, multiple choices, and brief calculations. Our examinations are largely designed to be machine graded. In all instances the questions should be based on clinical situations, real or not, designed to gauge the student's capacity to deal with applications of basic biochemistry.

The fourth edition benefits from continued refinement of this teaching program for students of medicine, a program now in its twelfth year at the University of Iowa. This

approach, which has also been used for students of dentistry, has been extended to include students in the physician assistant program. Elsewhere this book has been used in colleges of allied health sciences, medicine, nursing, osteopathic medicine, pharmacy, and veterinary medicine. In some instances it is used, as at Iowa, as the sole instructional source. In others it is used in association with a more classic text, as a source of enrichment in learning.

The third edition introduced the use of the International System of Units (SI) as an experiment, in view of the delay of its adoption by the health care institutions in the United States. We received no adverse reaction to this change. Therefore the use of SI units has been continued in the fourth edition with the exception of reintroduction of pressure units expressed in mm Hg; the SI equivalent unit in kPa is given in parentheses. Other more traditional units are also given in parentheses. It is our hope that students can learn either system but be prepared to communicate in the SI system. A more complete description of the SI system appears in Appendix E, and a table of the more common measures is contained inside the back cover of the book. We look on this editorial change as an experiment and will appreciate some expression of reader reaction to the continued use of SI units.

Past editions of this book benefited from advice and criticism of numerous friends and colleagues, whose efforts are reflected in this edition. We here express our deep appreciation to new friends, including B.J. Bergen, J.A. Buckwalter, J.F. Field, R.D. Feld, B.H. Ginsberg, M.L. Jennings, and K.L. Manchester.

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Robert L. Dryer
Thomas W. Conway
Arthur A. Spector

Contents

Chapter 1

Nutrition

Objectives

1 To analyze the biochemical role of a proper diet in maintaining homeostasis
2 To interpret the different dietary demands that result from alterations in work load, age, and normal physiologic conditions
3 To interpret the metabolic basis of some nutritional diseases

In 1980 the average resident of the United States ate 1420 lb of food. An average adult maintains a fairly constant body weight in spite of consuming six to seven times that weight of food each year. For this state of equilibrium to be maintained, energy must be supplied to satisfy the demands of the total body requirements, which include tissue maintenance. In other cases food must also provide for growth, as in children and in pregnancy. These demands vary, depending on the work load and environment. They will change with age and physiologic state. Thus the needs of a hospitalized person will likely change when he or she returns to health, and those of an athlete in training will be different. The nutritional needs of a person nearing retirement also differ from those of an adolescent.

Imposed on these variations are those of biologic individuality. The so-called average 70 kg man is not represented by any one person. Everyone is different, and nutritionally this is expressed at all biochemical and physiologic levels. For example, there are differences in the digestion and absorption of food, the supplementation of essential nutrients by the gastrointestinal flora, the transport of food to the cells, the uptake of the nutrients across the plasma membrane of the cells, and the rate of waste elimination. However, the physiologic and biochemical regulatory mechanisms, responding to all these individual factors, arrive at an equilibrium for each person that is recognized as health. In some diseases, either genetic or acquired, the resulting nutritional deficiencies of the cells cannot be overcome without external assistance.

Like all other living systems, humans survive only by means of a continual energy flux. In the broadest sense, nutrition provides the body with needed energy and essential constituents that cannot be synthesized de novo. Sound nutrition depends on a proper dietary regimen, or food intake. This must include the six major components of the diet, *carbohydrates*, *proteins*, *fats*, *vitamins*, *minerals*, and *water*. Foods often contain nonnutritive components that, together with intestinal bacteria and waste materials manufactured by our cells, comprise excreta in the form of sweat, urine, and feces.

Homeostasis

An organism as complex as the human body is an ordered aggregation of cells. Each cell obtains the nutrients essential for its well-being from the circulating extracellular interstitial fluid in which it is bathed. This same fluid also serves to remove waste products excreted from the cell. The composition of living cells is remarkably constant so long as the interstitial fluid is normal.

The interstitial fluid represents the end of a transport system through which the blood and lymph exchange materials in the external environment with those in the cells. Thus nutrients are brought to the cells from the gastrointestinal tract and oxygen is brought from the lungs while waste products are excreted in urine, feces, and expired air. Such transport in higher animals is subject to variations in load, since surges of nutrients arise from intermittent food intake. The body reacts to restore the concentration of the extracellular fluid constituents to normal and thus maintains the environment of the cells rela-