

TEXTBOOK OF BIOCHEMISTRY

With Clinical Correlations

SECOND EDITION

Edited by

Thomas M. Devlin, Ph.D.

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Preface

The purposes of the second edition of the *Textbook of Biochemistry with Clinical Correlations* remain the same as the first edition: to present a clear discussion of the biochemistry of mammalian cells; to relate the biochemical events at the cellular level to the physiological processes occurring in the whole animal; and to cite examples of deviant biochemical processes in human diseases. The topics were selected to cover the essential areas of mammalian biochemistry and physiological chemistry, and they were sequenced to permit efficient development of a knowledge of biochemistry. A principal concern in the preparation of the text was to meet the needs of a course in biochemistry for medical students, but the content and depth of presentation are appropriate for a first course in biochemistry for upper-level undergraduates and graduate students.

The entire text was reviewed and edited for the second edition and significant additions of new material, clarifications, and some deletions were made in every chapter; some chapters were rewritten entirely by new contributors. The topics of protein structure, metabolic control, molecular biology, and genetic engineering, in particular, were updated because of the rapid developments in these areas. As with the previous edition, each contributor included up-to-date information that had been substantiated as being significant but avoided observations that were so new that time had not allowed adequate evaluation.

The first six chapters cover the areas of protein and enzyme chemistry, membrane structure, and bioenergetics, setting the stage for discussion of the metabolism of the principal cellular components. Presentation of metabolic interrelationships at the cellular and tissue levels is followed by chapters on the major hormones. The biochemical events in the transmittal of genetic information and the mechanism of phenotypic expression and its control, as well as recent developments in recombinant DNA research and genetic engineering, are discussed. The remaining chapters cover essential aspects of physiological chemistry, including the biochemistry of selected tissues, iron and heme metabolism, gas transport, regulation of pH, and digestion and absorption of foodstuffs. The textbook concludes with a discussion of nutrition from a biochemical perspective.

In order to emphasize the relevancy of the topics to disease problems, each chapter includes selected clinical correlations relating normal biochemical events to pathophysiological states in humans. The correlations are intended to describe the aberrant biochemistry of the disease state rather than specific case reports. In some instances the same clinical condition is presented in different chapters, each from a different perspective. Clinical correlations are presented as separate entities in order not to interrupt the flow of the biochemistry discussion. All pertinent biochemical information is presented in the main text, and an understanding of the material does not require a reading of the correlations. In some chapters clinical discussions are part of the principal text because of the close relationship of some topics to clinical conditions.

As with any textbook, selection of the material to be presented was a difficult problem. Much of our knowledge of intracellular chemical events is derived from studies of single cells such as bacteria and yeast; in fact, for some topics we have very sketchy knowledge about the events in mammalian cells. In some sections it has been necessary to discuss information derived from bacterial systems as a model for what may occur in the complex mammalian tissue.

Two new features of the second edition are the questions at the end of each chapter and an appendix containing a discussion of selected topics of organic chemistry. The questions are in multiple choice format and represent types found in national certifying examinations. Each question has an annotated answer, with references to the page in the textbook covering the content of the question. The questions cover a range of topics in each chapter. The appendix, "Review of Organic Chemistry," was designed as a reference for the nomenclature of organic groups and compounds and some chemical reactions; it is not intended as a comprehensive review. The reader might find it valuable to become familiar with the overall content and then use the appendix as a reference for specific topics when reading related sections in the main text.

The individual contributors were requested to prepare their chapters for a teaching textbook. The book is not

intended as a compendium of biochemical facts or a review of the current literature, but each chapter contains sufficient detail on the subject to make it useful as a resource. Each contributor was requested not to refer to specific researchers; our apologies to those many biochemists who rightfully should be acknowledged for their outstanding research contributions to the field of biochemistry. Each chapter contains a bibliography that can be used as an entry point to the primary research literature.

Our experience with the first edition reinforced our commitment to a multicontributor textbook as the best approach to have the most accurate and current presentation of biochemistry. Each author is involved actively in teaching biochemistry in a medical or graduate school and has an active research interest in the field in which he or she has written. Thus each has the perspective of the classroom instructor and the experience to select the topics and determine the emphasis required for students in a course of biochemistry. Every contributor, however, brings to the book an individual writing style, leading to

some differences in presentation from chapter to chapter. It was decided that this should not be an impediment to the students' ability to understand the material, as students are accustomed to learning from a variety of resources. Redundancies and inconsistencies in content have been kept to a minimum. Some repetition of topics in different chapters was retained because the topics were considered of such importance that reiteration would be helpful to the reader.

In any project, one person must accept the responsibility for the final product. The decisions concerning the selection of topics and format, reviewing the drafts, and responsibility for the final checking of the book were entirely mine. I would welcome comments, criticisms, and suggestions from the faculty and students who use this textbook. It is our hope that this work will be of value to those embarking on the exciting experience of learning biochemistry for the first time and for those who are returning to a topic in which the information is expanding so rapidly.

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The entire text was reviewed and edited for the second edition and significant additions of new material, especially in the areas of molecular biology, genetics, and biochemistry, were made. Chapters were rewritten entirely by new contributors. The topics of protein structure, metabolic control, molecular biology, and genetic engineering in particular were updated because of the rapid developments in these areas. As with the previous edition, each contributor included up-to-date information that had been substantiated as being significant but avoided observations that were so new that time had not allowed adequate evaluation.

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Acknowledgments

This project would never have been accomplished without the encouragement and participation of many people. The contributors received the support of associates and students in the preparation of their chapters, and, for fear of omitting someone, it was decided not to acknowledge individuals by name. To everyone who gave time unselfishly and shared in the objective and critical evaluation of the text, we extend our sincerest thanks. In addition, every contributor has been influenced by former teachers and colleagues, various reference resources, and, of course, the research literature of biochemistry; we are deeply indebted to these many sources of inspiration.

As editor I extend a very special thanks to all the contributors for accepting the challenge of preparing the chapters, for sharing ideas and making recommendations to improve the book, for accepting so readily suggestions to modify their contributions, and for cooperating throughout the period of preparation.

My personal and deep appreciation goes to three friends and colleagues who have been of immeasurable value to me during the preparation of the second edition. My gratitude goes to Dr. James Baggott, who patiently allowed me to use him as a sounding board for ideas and who unselfishly shared with me his suggestions and criticisms of the text, and to Dr. Carol Angstadt, who reviewed many of the chapters and who gave me valuable suggestions for improvements. A very special note of appreciation is extended to Dr. Francis Vella, who carefully read every part of the manuscript, making many excellent suggestions and corrections, and who reviewed all of the galleys. To each I extend my deepest gratitude.

I also wish to extend my deepest appreciation to the staff of John Wiley & Sons who worked with me during

the preparation of the second edition. I am indebted to Andrew Ford, Vice President, who encouraged me to undertake the project and who gave me his unqualified support. Special recognition is extended to Linda Turner, Editor, who was always available to answer my questions and who made many valuable suggestions to expedite the preparation of the book; to Beryl Matshiqi, Editorial Assistant, who handled many of the details during preparation of the manuscripts; to Bruce Williams, Editorial Supervisor, who again, as in the first edition, carefully reviewed the manuscripts; to Margery Carazzone, Production Manager, whose talents were exemplified in the transition from manuscript to book; to Denise Watov, Production Supervisor, who with unlimited patience directed the review of galleys and pages. A special thanks is due to the Illustration Department of John Wiley & Sons and the many staff members who assisted in the completion of the book.

I am deeply indebted to my own staff, including Joanne Addario, Lalise Blain, and Beth McAndrews, who faithfully and efficiently completed the multitude of little chores involved in this project. I am particularly grateful to Beverly Lyman who assisted me in the review of galleys and pages. To each I extend my heartfelt appreciation.

Finally, a very special thanks to a supportive and considerate family, particularly to my wife Marjorie, who had the foresight to encourage me to undertake this project and who created an environment in which I could devote the many hours required for the preparation of this textbook. To all my deepest and sincerest thanks.

THOMAS M. DEVLIN

CHAPTER QUESTIONS AND ANSWERS

The questions at the end of each chapter are provided to help you test your knowledge and increase your understanding of biochemistry. Since they are intended to help you learn the material, their construction does not always conform to principles for simple knowledge assessment. Specifically, you will sometimes be expected to draw on your knowledge of several areas to answer a single question, and some questions may take longer to answer than the average time allowed on certain national examinations. Occasionally, you may disagree with the answer. If

this occurs, we hope that after you read the commentary on the question, you will see the point and your insight into the biochemical problem will be increased.

The question types conform to those commonly used in objective examinations by medical school departments of biochemistry. For each question, the question type is given in parentheses after its number; for example, 5.(QT2) indicates that question 5 is of type 2. Keys for the question types are given below:

QT1: Choose the one best answer

QT2: Answer the question according to the following key:

- A. If 1, 2, and 3 are correct
- B. If 1 and 3 are correct
- C. If 2 and 4 are correct
- D. If only 4 is correct
- E. If all four are correct

QT3: Answer the question according to the following key:

- A. If A is greater than B

B. If B is greater than A

C. If A and B are equal or nearly equal

QT4: Answer the question according to the following key:

- A. If the item is associated with A only
- B. If the item is associated with B only
- C. If the item is associated with both A and B
- D. If the item is associated with neither A nor B

QT5: Match the numbered statement or phrase with one of the lettered options given above.

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1.1 CELLS AND CELLULAR COMPARTMENTS

By a process not entirely understood and in a time span that is difficult to comprehend, elements such as carbon, hydrogen, oxygen, nitrogen, and phosphorus combined, dispersed, and recombined to form a variety of molecules until a combination was achieved that was capable of replicating itself. With continued evolution and the formation of ever more com-