TEXTBOOK OF BIOCHEMISTRY

FOURTH EDITION

WEST / TODD / MASON / VAN BRUGGEN

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Dedicated to
Ruth West
Bertha Todd
Margaret Mason
Ruth Van Bruggen

PREFACE TO THE FOURTH EDITION

The senior authors have been particularly fortunate in having their colleagues Drs. Howard S. Mason and John T. Van Bruggen share in the revision of *Textbook of Biochemistry* and contribute their specialized knowledge to the fourth edition. This has added new viewpoints and approaches to the presentation of a subject becoming ever more intricate to the student and demanding of the teacher.

The fourth edition retains the general organization of previous editions with the same designated chapters. While several of the chapters are rather long, it is felt that coherence, integration, and clarity of presentation can be better maintained for the student than when the subjects are treated in a number of separate, small chapters.

In this revision the chief concern of the authors has been the presentation of the facts and principles of modern biochemistry, with particular attention to the experimental evidence upon which they are based, as an introduction to and foundation for molecular biology and molecular medicine.

The very rapid rate of increase in biochemical knowledge since the third edition has necessitated the deletion of much old material and the addition of new sections. This has been particularly true in the areas of metabolism, but to a considerable extent throughout the book.

As in previous editions, the physical chemistry most pertinently related to biochemistry proper has been given considerable emphasis. This has been done, as in the past, by the inclusion of several chapters on special phases of physical chemistry, and to a greater extent than formerly by the inclusion throughout the text, where indicated, of the specialized physicochemical principles and techniques that play such a major role in modern biochemical research.

While considerable effort has been directed toward the revision of each chapter as necessary to present clearly the facts and principles pertinent to the subject, major areas of revision are outlined as follows.

In the chapter on bioenergetics strong emphasis has been placed upon the experimental basis of energy concepts and their application to biology. The high-energy phosphate bond idea is carefully explained in terms of modern structural and thermodynamic concepts. Many examples of calculations of thermodynamic quantities related to biological functions are given, along with clear, thorough explanations of energy interconversions in biological systems.

The chapter on biological oxidation-reduction presents the modern theories on this subject. Mechanisms of oxidation-reduction are described from contemporary organic, inorganic, and physical points of view. The new methods for studying enzyme-substrate complexes and reaction intermediates in biological oxidation-reduction, such as electron spin resonance spectroscopy and high-speed spectroscopy of fast reactions, are described with illustrations of their applications to biochemistry. The role of conformational changes during electron transport, the biological meaning of the Franck-Condon principle, and the role of charge transfer are explained. The function of free radicals in biological oxidation-reduction is described. A comprehensive classification of the enzymes that metabolize oxygen is given, along with many details of their mechanism of action. Included also are the latest results on mitochondrial structure and function, on oxidative phosphorylation, organization of respiratory components, energy-linked reversal of electron flow in the respiratory chain, and comparative aspects of biological oxidation-reduction, with illustrations and charts.

The chapter on the chemistry of the lipids has been extensively revised. The section on the structure of fatty acids has been enlarged and includes new material on positional and geometrical isomerism. New tables of fatty acid composition determined by chromatography replace the old tables. New material on the structure of fats and phosphatides, the recent change in nomenclature of the phospholipases, and a new section on the structure of cholesterol are presented.

The chapter on proteins has been revised particularly to explain protein function in terms of modern theories of structure. The chemical and physical bases of primary, secondary, tertiary, and quaternary structure are explained, with illustrations of structure at all levels of organization. The roles of the hydrophobic bond and of van der Waals' forces in protein chemistry are pointed out. Comparative aspects of protein structure are discussed, and it is shown how the varied properties of proteins arise from modifications of a few basic principles of structural organization. The structural analysis of proteins by modern techniques is thoroughly discussed, with examples, and the most recent results of x-ray diffraction studies of proteins are illustrated with models and diagrams. Professor R. B. Corey of the California Institute of Technology kindly reviewed the discussion of the α-helix (Chapter 8), and his clarifying notes have been incorporated into the text.

The remarkable advances in the chemistry of the nucleic acids are reflected in drastic revisions. The principal lines of evidence leading to knowledge of the structures of nucleic acids, particularly recent work on the structure of soluble RNA and its relationship to gene structure, and the concept of nucleic acids as basic components of the system by which heredity is controlled and expressed are presented. DNA, messenger RNA, soluble RNA, ribosomal RNA, and virus RNA are considered separately from the point of view of their primary, secondary, and tertiary structures. The association of protein with nucleic acids, as well as the organization of nucleoproteins in chromosomes, viruses, and other particles, is explained. Particular attention is given to the physical properties of the nucleic acids that lead to an understanding of the double-stranded helix and the single-stranded, internally coiled models upon which modern concepts of nucleic acid structure and function are based.

The chapter on the metabolism of the nucleic acids and nucleoproteins has been revised to present current concepts. The origins and metabolic fates of the components of nucleic acids and nucleoproteins are described in detail, along with metabolic variations in animal species. The synthesis of nucleotides is described, and the biosynthesis of DNA and RNA is explained; many charts and illustrations are given. The mechanisms that control the rates of DNA and RNA formation are explained on the basis of the Jacob-Monod-Gros hypothesis. The overall integration of nucleic acid metabolism into the metabolic network by means of feedback mechanisms and allosteric properties of proteins is shown to produce the cellular counterpart of homeostasis.

The chapter on lipid metabolism has been essentially rewritten to replace old with new material, in keeping with the rapid advances in this area of biochemistry. The interrelations of various tissues in lipid metabolism, including the dynamic roles of the liver, adipose tissue, and muscle, are described. The mechanisms of fatty acid oxidation and the production and metabolism of the ketone bodies have been brought up to date. The biosynthesis of fatty acids in mitochondrial and extramitochondrial systems, of unsaturated fatty acids in particular, and the mechanisms for the control of fatty acid synthesis have been given in some detail. Recent findings on the relation of carnitine to fatty acid metabolism have been pointed out. The sections dealing with metabolism of the complex lipids, cholesterol biosynthesis, and cholesterol and bile acid metabolism have been revised according to current knowledge. Atherosclerosis is included in the discussion of disturbances of lipid metabolism.

Carbohydrate metabolism has been extensively revised, to present more thoroughly the modern concepts of enzymatic mechanisms and the ways in which the overall rate of carbohydrate metabolism is controlled. Particular attention has been given to the action of insulin and other hormones. A number of up-to-date tables summarizing hormonal action have been included.

The chapter on protein metabolism has undergone considerable revision. Particular attention has been given to the processes involved in, and controlling, protein biosynthesis and to the presentation of new information on the genetic code.

The chapter on composition and structure of specialized tissues has also undergone extensive revision. Current theories on the nature of muscle proteins, as well as mechanisms of muscle contraction and relaxation, are reviewed. New sections on biological membranes and adipose and epithelial tissues have been added. Sections on the structures and functions of liver and mammary glands have been enlarged.

In the chapter on hormones each section has been modified to give current theories of structure and function, including illustration of the amino acid sequences of the peptide hormones. The chapter on renal function and acid-base balance has been revised to show as clearly as possible the mechanisms of countercurrent extraction in the kidney and its fundamental role in kidney function.

The chapter on blood has been extensively revised, especially the sections dealing with the plasma proteins, blood coagulation, and the intricate structural features of hemoglobin in relation to hemoglobin function. Models of hemoglobin and myoglobin from x-ray diffraction studies are shown, and the relation of hemoglobin conformational changes to the functions of hemoglobin is discussed.

The discussion of enzyme kinetics has been expanded, and some of the significant recommendations of the Commission on Enzymes of the International Union of Biochemistry are pointed out.

New knowledge of the absorption of foods has required extensive revision; mechanisms of detoxication have been brought up to date. The chapter on vitamins has been revised primarily in relation to the function of vitamins in metabolic reactions. In the chapters on nutrition new information on the role of polyunsaturated fatty acids in human nutrition and the amino acid requirements of infants has been added, and discussion of the nutritional aspects of the inorganic elements has been updated.

Considerable new information on the mechanism of action of the antimetabolic agents has been given.

In order to limit the size of the book as much as possible, considerable material has been put in smaller print, which makes possible a more complete treatment of special subjects but which may be omitted and still leave logical discussion.

The authors feel a deep debt of gratitude to the users of the book who have taken the time and trouble to point out errors in previous editions and to make suggestions for desirable changes. It is hoped that similar constructive criticism may be accorded the fourth edition.

The authors are especially indebted to their colleagues, Drs. Clarissa Beatty, Richard Jones, Wesley Horton, John Gabourel, and Demetrios Rigas and to Mr. T. N. Morris for checking manuscripts and making valuable suggestions. Mrs. Beatrice Brunn and Miss Dianne Carlton did a superb job in typing the manuscript, and we give them our very best thanks. The authors are also deeply indebted to the many authors and publishers who kindly permitted the use of tables, charts, and figures, and to the people of The Macmillan Company, who gave aid without stint throughout the preparation of the fourth edition.

E. S. W.
W. R. T.
H. S. M.
J. T. V. B

PREFACE TO THE FIRST EDITION

Our understanding of living things is largely equivalent to what we know about the composition of protoplasm and the intricate biochemical reactions by which it is formed, broken down, and enabled to function. In particular, the recent marked advances and the future progress in the field of medicine depend upon an expanding knowledge of biochemistry. Biochemistry, which was only a fledgling twenty-five years ago, has now developed into a vastly complex science growing at an accelerated pace. This phenomenal development and its relation to the understanding of life processes is imposing ever-increasing demands upon students and the departments of biochemistry teaching them. It is also rendering increasingly difficult the writing of textbooks which encompass the current facts and theories of the general field of biochemistry.

In preparing this textbook of biochemistry the authors have attempted to outline in considerable detail the principles of physical and organic chemistry upon which biochemistry as such is based, and then to present the fundamental facts, principles, and theories which constitute biochemistry proper. Through the courtesy of The Macmillan Company large sections of West's *Physical Chemistry for Students of Biochemistry and Medicine*[1] have been incorporated in various chapters of the text to provide such background for the student when this is necessary. Special consideration has been given to explanations designed to help the student understand the subject, and these explanations contribute materially to the length of the book. Repetition of important facts and theories will be found throughout the chapters. The authors feel that such repetition is invaluable to the learning process. Also, some facts and theories have various relations necessitating their repetition in order to present well-rounded discussions of different subjects. The book will be found to contain an unusual amount of the experimental evidence, with references, upon which the principles and theories of biochemistry are based. This the authors consider desirable in order to show the student how the science develops, to increase his critical judgment, and to stimulate his interest. The amount of material contained in the book is considerably greater than usually presented in courses in biochemistry. The authors consider this to be desirable for two reasons. In the first place, different instructors emphasize different phases of the subject, and a book of broad coverage enables the student to select the sections pertinent to the course

[1] Title changed in second edition (1956) to *Textbook of Biophysical Chemistry*.

he is taking. In the second place, a rather comprehensive text provides additional material to stimulate the interest and enthusiasm of the more capable students in a class. The book is liberally provided with summaries, charts, and diagrams which enable the student to obtain information quickly when necessary.

The principles of biochemistry related to medicine have been given special attention in the chapters of the book dealing with enzymes and digestion, blood, respiration, acid-base balance, salt and water balance, hormones, metabolism, and nutrition. An understanding of the theoretical basis of nutrition is extremely important to the medical student and physician; yet the presentation of a coherent body of information relative to it is often neglected in the medical course. The authors feel that the proper place for such material is in the biochemistry course and text immediately following intermediary metabolism. This arrangement is followed in the present text and comprises chapters on the nutritional aspects of proteins, carbohydrates, fats, and minerals. Due to their importance to medicine and the mechanisms of their action, antibiotics are properly considered in a book on biochemistry. This has been done briefly in a chapter on antimetabolic agents.

The use of isotopic atoms such as deuterium, N^{15}, and C^{14} to trace the chemical pathways of substances in the body has been largely responsible for many significant recent advances in our understanding of metabolism and other biochemical phenomena. The isotopic methods utilized and the results obtained have been particularly stressed in the book. The student should early become well acquainted with the method which has done so much and promises to do so much more for the advancement of biochemistry and medicine.

The authors have approached writing this book fully cognizant of the complexity and difficulty of the task and of their limitations. Their object has been to provide a comprehensive text of biochemistry similar to those current in the field of physiology, and written from the viewpoints of both student and teacher. In such a work many errors of both omission and commission are inevitable, and the authors will appreciate having these brought to their attention.

The authors are greatly indebted to their colleague, Dr. John T. Van Bruggen, for preparation of the chapter on hormones. They also wish to express their deep appreciation to Dr. P. A. Shaffer of Washington University School of Medicine, Dr. E. A. Doisy, Saint Louis University School of Medicine, and Dr. C. G. Heller and Mr. K. B. Davison, University of Oregon Medical School, for reading portions of the manuscript and offering helpful suggestions; to Mrs. Nancy Moores, Mrs. Maxine Gross, and Mrs. Ruth West for typing the manuscript, and other aid; to Mrs. Clarice Francone and Mrs. Kay Bittick for preparation of many of the illustrations and charts; and to the many authors and publishers who have kindly granted permission to use material from books and journals. The authors are particularly indebted to The Macmillan Company for their unfailing courtesy and aid given without stint in the preparation of the book.

E. S. W.
W. R. T.

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INTRODUCTION

The scope of biochemistry. Biochemistry in its broad aspects is the most comprehensive of all the branches of chemistry. It includes inorganic, organic, and physical chemistry to the extent to which each of these is related to the chemistry of living things, both plant and animal. The chemical principles involved in the study of biochemistry are necessarily identical with those the student has learned in preliminary chemistry courses, but they are often posed in unique and intricate relationships.

The basis of all forms of life is the material called protoplasm, which in chemical composition, physical organization, and function is enormously complex; in fact, it is the most complex physicochemical system with which the chemist has to deal. The problem of biochemistry in general is to relate the properties and functions of protoplasm to its physicochemical organization. The protoplasm of each different kind of cell in each kind of animal or plant is different and characteristic, yet the chemical composition, organization, and chemical processes in these many different forms of protoplasm are in many respects strikingly similar. The study of the biochemistry of one kind of protoplasm therefore is, in effect, the study of all kinds of protoplasm. The developments in animal biochemistry have been greatly aided by investigations of the chemical processes of plants and microorganisms, and vice versa. Various chemical reactions first observed in microorganisms or plants have later been sought and found in higher animals. The reverse also is true.

A knowledge of the broad chemical principles as they apply to protoplasm in general is desirable for the biochemist whether he be concerned with pure biology or with the more specialized fields relating to agriculture, industrial processes, or medicine. The objective of the present text is to provide a broad foundation in biochemical facts and principles and, in addition, the specialized treatment of the subject desirable for students of medicine and the medical sciences.

Contents of a course in medical biochemistry. There are several particular phases of biochemistry with which the medical student is concerned. Among these may be listed the following:

The chemistry of tissues and foods. Foods are largely derived from animal or plant tissue, and the study of one is essentially identical with or closely supplementary to that of the other. Since most of the organic substances of both belong to the broad classes of carbohydrates, fatty materials, proteins, or related compounds, a rather thorough knowledge of the pure chemistry and physiological relations of these substances is of prime importance.

The chemistry of digestion and absorption. Much of our food is composed of large molecules, such as proteins and starch, which cannot be absorbed from the intestine into the blood stream and could not be utilized if they were absorbed. In fact, they might be definitely toxic, as in the case of undigested proteins. The proteins of foods contain about the same fundamental structural units (amino acids, etc.) as do the proteins of tissues, but the arrangement is different. Consequently, the various food proteins are broken into their constituent amino acids in the alimentary tract, which are then absorbed into the blood stream and distributed to the various organs; there the amino acids are recombined into proteins of structure and characteristics peculiar to the proteins of our various tissues. Similarly, much of our carbohydrate food (such as starch) is broken into simpler molecules in the digestive tract before absorption and utilization. The same applies more or less to fatty foods also. In addition to digesting the larger food molecules to smaller utilizable ones, the alimentary tract provides a method of entry for water, mineral salts, vitamins, and many other diffusible molecules of the food supply.

The chemistry of respiration. Respiration is an obligatory property of the living protoplasm of higher forms of life. In man oxygen is taken into the lungs and diffuses across the membranes into the blood, in which most of it combines loosely with the hemoglobin of the red cells; in this form it is carried to the tissues, where it is released for the oxidation of foods with the production of energy. In this process carbon dioxide is formed in volume about equal to that of the oxygen used. This carbon dioxide passes from the tissues to the blood stream and in various chemical combinations is transported to the lungs, from which it is exhaled. The gaseous exchange between air and tissues comprises many chemical and physical mechanisms.

The chemistry of tissue metabolism. Among the important problems of biochemistry is that concerned with the complicated reactions taking place within tissue cells by which protoplasm is synthesized or broken down and foods are oxidized to supply energy for the living processes. Since this problem involves a knowledge of the finer chemical composition of protoplasm as a basis for the understanding of many of the reactions, it is the most difficult phase of biochemistry and is as yet very imperfectly understood. It is commonly spoken of as intermediary metabolism and is as fundamental as life itself.

The chemistry of the glands of internal secretion. The regulation and coordination of the activity of the various organ systems of the body so that they function smoothly as an integrated whole are imperative. These are effected largely in two ways: by the hormonal control of the glands of internal secretion and by the nervous system. These systems may function either together or separately. The general process of nervous regulation of tissue functioning is well known. As an illustration of control through glands of internal secretion, consider the anatomically insignificant (in size only) pituitary gland located at the base of the brain. This gland produces a chemical substance (hormone) that regulates the activity of the thyroid gland, which in turn, among other things, controls the rate of energy production in the tissues. The pituitary gland produces hormones that regulate the development and functioning of the sex organs and is in this way vitally concerned with the process of reproduction. It secretes a hormone that determines the size to which an animal may grow, the growth hormone. Various other hormones have been attributed to the pituitary. Additional glands of internal secretion are the thyroid, pancreas, testes, ovaries, adrenals, parathyroids, and possibly thymus, each producing one or more hormones concerned in the regulation of some organ or process. The biochemistry of the glands of internal secretion is one of the most brilliant and important chapters in the records of biological achievement. This development has profoundly influenced the field of medicine both from the standpoint of understanding physiological and pathological processes and from that of furnishing effective agents of treating disease.

The chemistry of blood. The circulating blood represents the main transport system within and between the organs of the body. It carries foods to the tissues and waste products from them to the excretory organs. It transports the gases concerned in respiration. The hormones produced by the various glands of internal secretion pass into the blood and through its circulation reach the tissues for which they are specific. It serves as an efficient cooling system for the body and also distributes heat from one part of the body to another. It is actively concerned in helping maintain the proper distribution of water and salts in tissues and the acid-base balance of the body. It contains substances and cells that actively combat infection by microorganisms. The composition of blood is normally maintained relatively constant, but this constancy is a dynamic and not a static condition. For example, the quantity of glucose in the circulating blood represents a balance between that added to it from foods and body reserves and the amount removed by the tissues. In many pathological conditions the amounts of one or more constituents of the blood may become definitely increased or decreased from normal and thereby furnish valuable information for clinical diagnosis and treatment. The chemistry of blood is better understood than that of any other tissue, and a knowledge of its normal composition and pathological variations is an indispensable part of the physician's training.

The chemistry of excretion. The kidneys, lungs, intestines, and skin serve as excretory organs to remove decomposition products of tissues and foods in order that the composition of the body fluids and tissues may be kept approximately constant. Important among these decomposition products are the nitrogenous substances, urea, uric acid, and creatinine, which are formed from proteins. The metabolism of carbohydrates, fats, and proteins produces much carbon dioxide and water. The breakdown of sulfur- and phosphorus-containing proteins and other compounds leads to the formation of sulfates and phosphates. Excess salts (as $NaCl$), water, and various nonfood materials are taken with the food and absorbed into the blood and tissues. A certain range of concentration of the aforementioned substances in the body fluids and tissues is compatible with health, but much excess may lead to deranged function and illness.

The kidneys and lungs perform by far the most important roles in excretion from the body. Most of the organic waste products and excess mineral salts and water are removed from the blood by the kidneys and passed in the urine. The lungs serve especially to remove carbon dioxide and considerable water, as well as some volatile substances such as alcohol, acetone (often present in the blood and tissues of a diabetic), and gases absorbed into the blood from the intestine. Most of the excretions from the intestine (feces) represent food and bacterial residues and intestinal secretions or products derived from them. However, some materials, especially certain metals such as calcium and iron, pass from the blood into the intestine and are excreted in the feces. Normally the skin functions to only a minor extent as an excretory organ, serving to remove chiefly water, with traces of salts and organic substances. In cases of prolonged profuse perspiration, however, the loss of sodium chloride may be so great as to deplete severely the body supply and cause violent illness.

Some special phases of excretion are of particular interest to the medical student. In various diseases the excretion of certain substances may be increased or decreased, or abnormal materials may be excreted as a result of disease. In diabetes mellitus the body fails to use its sugar properly, and the blood sugar concentration rises. Consequently, the kidneys, in attempting to regulate the composition of the blood, excrete large amounts of sugar (in severe cases). In order to excrete much sugar, the kidneys must also excrete much water. As a result, the untreated severe diabetic is likely to be poorly nourished and continually hungry and thirsty. The well-trained physician quickly recognizes the significance of such facts.

A study of the chemistry of the excretions is of much importance in helping to unravel the chemical processes that take place in the body. If eating protein that contains unoxidized sulfur causes the excretion of more sulfates in the urine, it is only logical to conclude that the body can remove the sulfur from the protein and oxidize it to sulfuric acid. This is a very simple application of the knowledge of excretory products in explaining metabolic processes. In most cases the problem is much more complex.

The physical chemistry of protoplasm. The body is composed of integrated organ systems which, in turn, are aggregates of cells and specialized membranes. The cells represent masses of protoplasm, jellylike in consistency, but in reality highly organized structurally, which are enclosed in membranes. The jellylike nature of protoplasm is due to the presence of colloidal particles, composed of proteins and other cellular substances, which make up by far the greater proportion of protoplasm, aside from water, which is the major component. These colloidal particles have rather specific and unique properties as a result of their size and composition, and represent not only important structural units but also dynamic functional units of protoplasm. Some knowledge of the physicochemical principles related to the colloidal state of matter is necessary in the study of biochemistry.

Foods, hormones, and all substances necessary for the maintenance of cells, as well as the waste products formed in them, must pass through the cell membranes. These membranes are permeable to some materials and more or less impermeable to others, and different kinds of cells vary as to the substances that will diffuse through their membranes. The permeability of living membranes is often quite different from that of dead ones, so that the ordinary principles that apply to such things as collodion membranes apply only partially, for example, to the membranes of the cells of the intestinal tract. Maintenance of the normal permeability of cell membranes is necessary for normal physiological processes, and abnormal permeability is often associated with pathological conditions.

The large amount of water in protoplasm has already been stressed. A great deal of water is present in the blood and tissue fluids. Much is closely associated with protoplasmic structures, the colloidal molecules of proteins in particular holding large amounts. This protoplasmic water is an essential constituent; and when it is greatly increased or reduced, abnormal physiological functioning occurs. The proper distribution of water between the blood, lymph, and tissue cells is one of the most important processes of the body and a rather complicated one. It is related to the osmotic pressure of the various dissolved colloids and crystalloids as well as to the blood pressure and membrane permeability to the dissolved substances. The water balance of the body is closely associated with the concentrations and kinds of electrolytes present, and the proper distribution of the latter is fundamental to the composition and functioning of tissues.

Normally the reaction of the blood and lymph is very slightly alkaline, and that of the protoplasmic mass within tissue cells is more nearly neutral or faintly acid. A neutral reaction of the blood, if unrelieved, is associated with a comatose condition and death in a short time. On the other hand, a reaction slightly more alkaline than normal, if untreated, brings on a condition of hyperirritability of the tissues with tetanic contractions of the muscles and death. Such consequences of changes in reaction are not so unexpected if the relation of acidity and alkalinity (pH) to the action of enzymes, the properties of proteins, the permeability of membranes, etc., is understood. The body is equipped with various mechanisms for controlling the reaction of its tissues, and very important among these are its so-called buffer systems, which have the property of neutralizing acids and bases with only small changes in reaction. A thorough knowledge of the action of buffer systems is indispensable to an understanding of the acid-base balance of the body.

Various gases, such as oxygen, carbon dioxide, and nitrogen, are distributed throughout body fluids and tissues in physical solution and in some cases in chemical combination. A knowledge of the physical and chemical properties of these gases is essential.

Many other points of a physicochemical nature are concerned in tissue mechanisms, such as the electrical potentials across membranes, the oxidation-reduction potentials within protoplasm, and the electric charges of colloid particles. The student will realize during his studies that while the physicochemical aspects of biochemistry are rather difficult, they are at the same time exceedingly fundamental.

Importance of biochemistry to medicine. Since all protoplasm is made up of chemical substances and the normal functioning of the body ultimately involves chemical processes, the basic importance of biochemistry to other medical subjects such as physiology is obvious. In fact, physiology and biochemistry overlap and merge, so that for practical consideration they are inseparable. Pathological conditions in the body may be caused by deranged chemical composition and functioning of tissues, and many of the problems of pathology are most profitably approached from the chemical viewpoint. The bacteriologist is especially concerned with the chemical properties of bacteria and the chemical changes they produce in tissues, leading to various diseased conditions. He is also very much interested in such things as vaccines, serums, and antitoxins, which play such an important role in the treatment of disease. The pharmacologist must be acquainted with the chemical aspects of the body because the action of his drugs nearly always involves some change in the biochemical events taking place in the tissues. Since the physician utilizes all these basic sciences in the diagnosis and treatment of disease, his de-