Human Biochemistry

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Preface

With the completion of the tenth edition of *Human Biochemistry,* this textbook is now approaching its fortieth anniversary, the first edition appearing in August 1945 under the authorship of the late Israel S. Kleiner. Thus it now is the senior current American textbook of biochemistry. The present edition is strikingly different from its original ancestor, both in size and in content. Many of the topics in the first edition that were incompletely understood or were vague possibilities are now well-established facts. For example, the glycolytic pathway was just being elucidated, and the citric acid cycle had been postulated only a few years earlier. DNA and RNA were scarcely mentioned, and then only casually as "nucleic acids." The entire subject of purine-pyrimidine metabolism—structures, biosynthesis, and functions—occupied only six pages! The expansion of knowledge in this as well as in the entire field indeed has been phenomenal during the past four decades—in fact, *five* decades for the senior author (JMO), this being his "golden anniversary" in biochemistry.

The continued dramatic progress in biochemistry, even since the publication of the ninth edition of this textbook, has made necessary some rather drastic changes in its organization to maintain a logical sequence of presentation. Also, the reorganization has been focused on a central theme, *the dynamic state of metabolism,* with special emphasis on application to the *human* organism. A considerable amount of older material has been deleted or condensed to make room for newer concepts and to limit the text to a practical size. References to the literature have been restricted largely to selected review-type articles, monographs, and books.

To facilitate an orderly, logical presentation, this edition has been divided into seven major sections. The first, an introductory section, deals with the nature and scope of biochemistry, the biochemical morphology of the cell, and the dynamic state of metabolism. The second section is concerned with basic principles of metabolism and its regulation, including the properties and functions of proteins, enzymes, and coenzymes, mechanisms of energy transduction, and the genetic control of metabolism. The third major section, almost completely rewritten and carefully updated, considers the metabolism of carbohydrates, lipids, amino acids, purines, and pyrimidines. This portion is followed by sections on specialized tissues and body fluids and on the chemical communication between tissues (the hormones, transport mechanisms, and metabolic interrelationships). Section six deals with some applications of human biochemistry and is composed of a reorganized and rewritten chapter on nutrition and a new chapter on molecular aspects of disease. The final section is designed for review purposes in applicable areas of organic and physical chemistry. There are three chapters devoted to the chemistry of the major cellular constituents, selected physicochemical topics, and analytical techniques frequently used in biochemistry.

Several new chapters have been added. One on coenzymes brings together coenzyme chemistry and principal functions in a way that does not detract from the flow of discussions in the chapters on metabolism and nutrition. Bioenergetics and biological oxidations also are treated in a separate chapter for the sake of emphasis and clarity. Likewise, a full chapter is devoted to transport mechanisms to discuss more advantageously recent advances in this active area and their importance in the control of metabolism. The subject of nutrition has been consolidated into a single chapter, including a concise discussion of energy metabolism as well as newer developments in this rapidly expanding area of biochemistry. The new (1980) recommended dietary allowances of the Food and Nutrition Board (N.R.C.) and the rationale for their formulation are thoroughly considered. The material on digestion and absorption has been transferred into appropriate chapters on metabolism. A new chapter on molecular aspects of disease has been added to localize and emphasize this subject of increasing medical significance.

This edition has been prepared with the needs of students in the medical and other health sciences uppermost in mind. Excessive detail, redundancy, and verbosity have been minimized as far as possible without detracting from clarity of expression and accuracy of meaning. At the same time, we have tried to avoid oversimplification and to challenge the curiosity and imagination of the more thoughtful students of biochemistry. The reorganization and revision of the text, we believe, will facilitate the study and understanding of this dynamic and challenging discipline.

In the preparation of much of the manuscript for this edition we were fortunate in having the collaboration of Dr. Francis C. Neuhaus of Northwestern University as a consultant. His critical, detailed reading and thoughtful suggestions on most of the chapters added greatly to their clarity, accuracy, and completeness. Likewise, we are indebted to Dr. Aline Underhill Orten for numerous helpful suggestions and comments, and especially for critical reviews of the chapters on nutrition and molecular aspects of disease.

We also wish to express our sincere appreciation to a number of colleagues and friends who have offered constructive comments or materials for the manuscript. Special words of gratitude are due Drs. Ray K. Brown, Samuel C. Brooks, Robert J. Peanasky, Danica Dabich, Gary D. Small, Walter H. Seegers, John A. Thomas, William W. Winder, Bennie Zak, David F. Hastings, and Paul Loach.

Finally, we thank the editors and staff of The C.V. Mosby Company for their cooperation and patience during the preparation and publication of the manuscript, and our respective departmental staffs for their generous help and encouragement over the many months required for the completion of this edition.

James M. Orten
Otto W. Neuhaus

Contents

Section One

Introduction: some perceptions of human biochemistry

Chapter 1

Nature and scope of biochemistry

Nature of biochemistry

Biochemistry, in broad terms, is the study of the chemical composition of living matter and the biochemical processes that underlie life activities during growth and maintenance. Such a general concept obviously includes plant as well as animal life. However, this book concerns primarily the biochemistry of animal life, and especially biochemistry as it applies to humans.

Early inquiries into the biochemistry of living matter by pioneering scientists such as Priestly and Laviosier in the late eighteenth century and Liebig, Berzelius, and Bernard in the nineteenth century were concerned with the whole animal and gross tissue samples. Their work was more descriptive, seeking answers to the "what" types of questions.

With the modern refinement of biochemical techniques and the development of more sophisticated and sensitive instrumentation, particularly during the last 25 years, it has become possible to delve much more deeply into these questions and to seek answers to "how" and "why" questions. For example, the development of the ultracentrifuge by Svedberg made it possible to investigate molecular problems at a cellular level and indeed even their component structural parts, i. e., the membranes, mitochondria, nuclei, endoplasmic reticulum, and other cellular parts (Chapter 2). It became possible to explore the chemical mechanisms involved in the development and differentiation of cells and what factors shape their ultimate form: how and why, for example, a primitive erythropoietic stem cell differentiates into a mature erythrocyte capable of transporting oxygen rather than into a muscle cell or a nerve cell with entirely different functions. Modern biochemistry has provided many answers to basic questions such as these.

Another exciting example is the biochemical elucidation of the structures of deoxyribonucleic acid (DNA) and ribonucleic acid (RNA). This has had far-reaching effects in biology and genetics on the understanding of the structure of genes and the transmission of genetic information and, in turn, on the development and differentiation of cells. Other examples are the chemical transformations by which glucose, amino acids, and lipids derived from foods are transformed into essential body components (anabolism) by way of so-called metabolic pathways or are used for energy (catabolism) in cells. Insight into the precise mechanisms involved in the control of these metabolic reactions in cells is another monumental accomplishment of modern biochemistry. The potential practical importance of this information is emphasized by the fact that a failure of normal metabolic control mechanisms resulting in wild growth is a unique biochemical characteristic of cancer cells. The control of the cancerous processes thus may depend on the reestablishment of normal cellular regulatory mechanisms.

Other recent accomplishments in biochemistry include the chemical isolation and determination of the molecular structures, three dimensional in many instances, of those catalysts of metabolic reactions, the various enzymes, hormones, and vitamins to be considered in later sections. In some cases even visualization of changes in molecular conformation, by x-ray diffraction techniques, in relation to the functional activity of the molecule has been achieved. Likewise of great importance has been the use of isotopic tracers in unraveling the complexities of metabolic pathways, of chromatographic procedures in isolating the minute amounts of intermediates involved in metabolic reactions, and of radioimmunoassay techniques in determining even picomolar quantities of certain vital biomolecules, such as insulin and other hormones in living tissues and body fluids. These procedures also have proven invaluable in the diagnosis of a number of human diseases. Nor should one omit mention of the current evidence linking proper nutrition with the prevention of human "killer diseases" such as ischemic heart disease, stroke, certain forms of cancer, diabetes mellitus, and possibly even hypertension. The foregoing, randomly selected examples emphasize not only the great progress made in biochemistry itself during recent years but also the tremendous impact of these advances on all other life sciences. Biochemistry has thus become the center around which studies of all life sciences must revolve.

Development of biochemistry

Biochemistry, as such, is a relatively young science; the term itself was not introduced until 1903 by the eminent German chemist Carl Neuberg. However, investigations of the chemical composition of plant and animal tissues as early as the mideighteenth century perhaps may be regarded as the beginning of biochemistry as a separate discipline. This was followed in the later eighteenth and early nineteenth centuries by chemical studies of respiration, fermentation, and the quantitative analysis of naturally occurring substances. The nature of many of these earlier discoveries and the names of the investigators involved are referred to later. From these rather fragmentary beginnings biochemistry matured into a distinct entity in the later nineteenth century, although it was then termed *physiological chemistry* or by some *pathological chemistry*. The first journal devoted exclusively to the new discipline, Hoppe-Seyler's *Zeitschrift für Physiologische Chemie,* began in 1877; its American counterpart, the *Journal of Biological Chemistry,* began publication in 1906 as the official journal of the newly formed American Society of Biological Chemists.

The period of greatest progress in biochemistry began in the 1920s with the American biochemists playing an increasingly prominent role in its development, previously accomplished primarily by German, French, English, and Swedish biochemists. This period included monumental discoveries such as the isolation, determination of the chemical structure, and synthesis of a number of the vitamins and certain hormones, the concepts of the essential amino acids and the citric acid cycle, and the beginning elucidation of metabolic pathways by means of isotopes as tracers. The post–World War II era, however, beginning in the early 1950s, was the most remarkable period of progress in biochemistry, with knowledge in the field nearly doubling every 8 years. This was due in part to the development of the new, improved research techniques and equipment and in part to the availability of more adequate funds for research, largely from federal agencies.

Biochemistry thus has developed into one of the most, if not the most, dynamic and exciting areas of human endeavor. Many of the outstanding achievements have been made by American biochemists, a number of whom have received Nobel Prizes and other prestigious awards in recognition of the quality and significance of their work.

Chemical composition of living matter

Living matter is composed of a variety of nitrogenous and nonnitrogenous organic compounds, a number of inorganic elements, and water. Water is the most abundant constituent of animal organisms, composing 75% to 85% of the weight of most tissues, with the exception, of course, of bones, teeth, and a few others.

Water

The water of the tissue and body fluids is mostly in the free state, i.e., substances may be dissolved in it and it may pass back and forth from blood to tissues, in and out of cells. A small fraction of the water is believed to be bound. In other words, some of the water in hydrophilic colloid systems is combined so that the activity of the water molecules is reduced considerably. Free water varies according to diet and physiological activity, whereas bound water is a rather constant constituent of the tissues.

Studies using deuterated water (D_2O) in dogs have shown that the average water content of the body as a whole is 61% of body weight, with a range of 55% to 67%. The water content of the human body apparently has about the same range, being less than average in fat individuals and somewhat greater in thin persons. The water content of individual tissues also varies considerably, as will be discussed later. There are several mechanisms for maintaining and controlling the water content of tissues (Chapter 15).

Water is needed for various reasons. It is a solvent, the vehicle that enables water-soluble, water-miscible, or emulsifiable substances to be transferred in the body, not only in the blood but also intercellularly and intracellularly. Ionization takes place in water, and ionization is a prerequisite to most biochemical reactions.

Organic constituents

The organic compounds found in all living matter include a wide variety of substances indispensable to life processes. Quantitatively, three major groups of organic compounds predominate: the carbohydrates, lipids, and proteins. Some of these are present partly as highly complex macromolecules, as discussed in some detail later. Various other essential biomolecules are present in smaller amounts. These include the nucleic acids (derivatives of purines and pyrimidines), many hormones, vitamins, and a number of other nitrogenous and nonnitrogenous compounds. These are discussed in subsequent chapters.

Sources

Most animal organisms, including humans, depend on plants and certain microorganisms for a preformed supply of many of the aforementioned nitrogenous and nonnitrogenous substances. Therefore they have been categorized as essential nutrients (Chapter 21). Plants and microorganisms, in turn, form them from simpler molecules, such as CO_2, N_2 or NH_3, SO_4, and H_2O, by way of photosynthesis, using energy (photons) from the sun to drive the synthetic reactions. Important constituents of animals cells such as glucose, the essential amino acids, the essential unsaturated fatty acids, and the vitamins (Chapter 21) thus are derived from food sources.

Interesting recent investigations have demonstrated that many of the previously mentioned compounds also were synthesized in prebiotic times, probably several billion years ago, from simple molecules (CO_2, CH_4, NH_3, H_2, SCN, and H_2O) using radiant energy from sources such as the sun, cosmic rays, and lightning. Indeed, a variety of organic molecules of biological importance, including glucose, a number of amino acids, adenine, ribose, malic acid, and even proteinoids, have been formed in the laboratory using these simple molecules, an electric arc for energy, and suitable temperature and pressure. Supporting evidence has come from other sources. Some 22 different amino acids have been identified in samples of pre-Cambrian sedimentary rocks that are at least 3.1 billion years old. Trace amounts of some 11 amino acids have been found in lunar rocks and other materials brought back from the surface of the moon by astronauts. Human and other contamination as a source of the amino acids apparently was ruled out. Likewise, evidence from optical spectra and radiotelescopic studies shows that porphyrin derivatives and some 31 other molecular species exist in interstellar space.

Thus the prebiotic formation of organic compounds needed for converting the sun's radiant energy into chemical energy in the form of essential substances by primordial organisms, then by photosynthetic microorganisms and plants, made possible their ultimate use as constituents of all living matter, including that of humans.

Inorganic constituents

At least 60 of the 102 or more elements known to be present in the universe occur in biological matter. Only about 22 to 26 of these are found consistently in human tissue, however, and some are present only in extremely minute amounts. About 1% of the total weight of an average soft tissue is ash, or inorganic salts, chiefly of the cations Na^+, K^+, Mg^{++}, Ca^{++}, and NH_4^+, and the anions Cl^-, $H_2PO_4^-$, $HPO_4^=$, HCO_3^-, and $SO_4^=$. Some of these may be present in organic molecules, as is also the case for the trace elements iron (Fe), iodine (I), copper (Cu), zinc (Zn), and manganese (Mn). Other trace elements consistently found in nearly all forms of living matter include boron (B), chromium (Cr), cobalt (Co), fluorine (F), molybdenum (Mo), selenium (Se), and silicon (Si). Biochemical functions of Co, F, and probably Cr, Mo, and Se, are now known, as is discussed in Chapter 21. Other elements are found in small amounts in some species, but as yet no definite function for them has been established. These include silver (Ag), aluminum (Al), arsenic (As), barium (Ba), beryllium (Be), bromine (Br), cadmium (Cd), cesium (Cs), germanium (Ge), lithium (Li), nickel (Ni), lead (Pb), rubidium (Rb), tin (Sn), strontium (Sr), titanium (Ti), and vanadium (V). A few other elements that are regarded as contaminants or accidental constituents may be found in living matter. These include argon (Ar), gold (Au), bismuth (Bi), helium (He), mercury (Hg), and thallium (Tl).

A number of elements occur in living matter as mixtures of the more common form with varying amounts of other forms of the same element. These have slightly different atomic structure and atomic weight from the more common form and are called *isotopes*. Thus ordinary chlorine, with an atomic weight of 35.457, has been found to be a mixture of two isotopes, the first and more abundant one having an atomic mass of approximately 35, and the second less abundant one an atomic mass of 37. Since isotopes in general have the same chemical and biological properties as the more abundant form, they have proved extremely valuable as tracers in biochemical research. Metabolites labeled with isotopic atoms can be followed through an organism, and metabolic pathways can thus be determined. Also, it is possible by determining the amount of an isotope, e.g., ^{14}C, in a specimen of wood or fossil to accurately estimate the age of the specimen by the isotope dating technique. The amount of the isotope present is determined by either its radioactivity, as in the case of ^{14}C or ^{3}H (tritium), or by its mass (in a mass spectrometer), as in the case of ^{13}C or ^{2}H (deuterium).

Gases

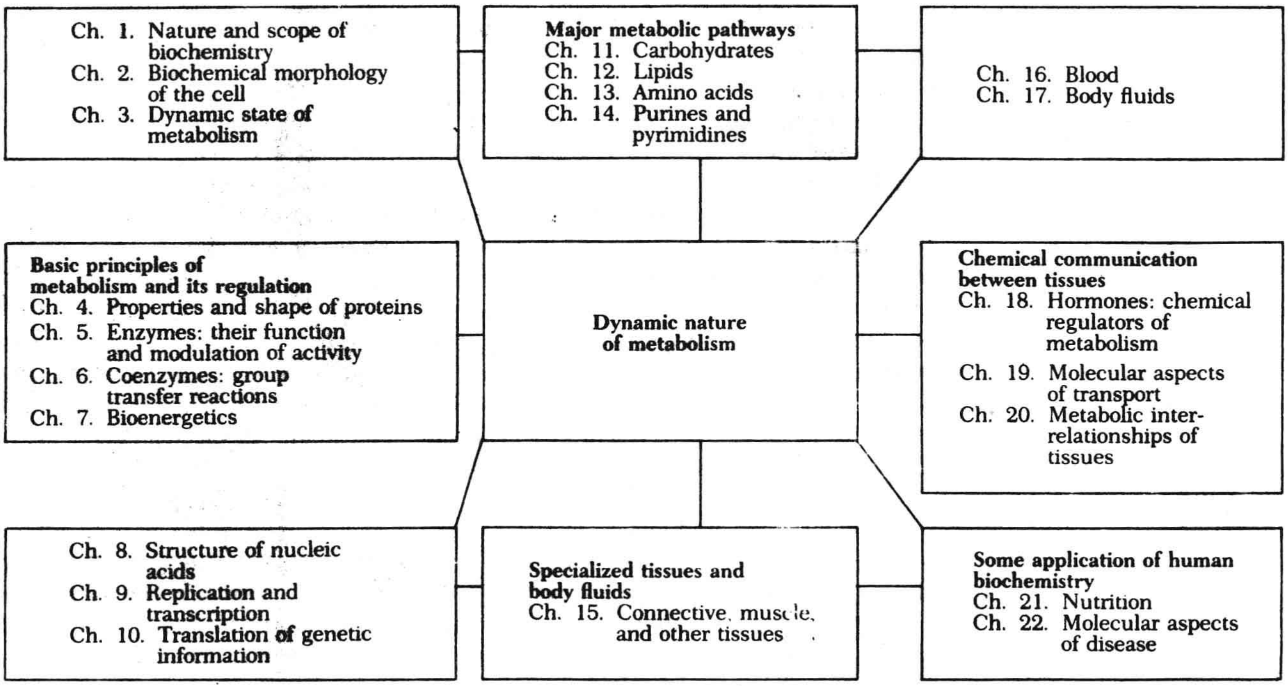
Relatively small amounts of several free gases, including oxygen, carbon dioxide, nitrogen, and traces of others, are found in animal tissues and body fluids. Oxygen and carbon dioxide have extremely important functions and are considered in Chapters 16 and 17. Larger amounts of oxygen, carbon, and nitrogen are found, of course, as constituents of a wide variety of organic and inorganic compounds.

Dynamic state of metabolism

Since biochemistry is concerned with the chemical components of and chemical reactions in living matter, it is logical at this point to inquire into the characteristics that distinguish living matter from the nonliving, inanimate molecules of which it is composed. Although knowledge of this fundamental question is far from complete, one such characteristic is the high degree of *organization* of the unit cells of which living matter is composed (Chapter 2). Each cellular subunit has specific, purposeful functions to perform in establishing and maintaining the life of the cell. Some are concerned with generating energy for use in vital cell functions such as mobility, the absorption of essential nutrients from the environment, or the replication of new molecules to replace those lost or rendered nonfunctional by the wear and tear of life processes. Also, specialization of cellular functions is common in living organisms, especially in higher forms, some functions being emphasized genetically and some being repressed (Chapter 3). Familiar examples in humans are muscle cells for locomotion, red blood cells for oxygen transport, glandular epithelial cells for special secretory products (enzymes, hormones, etc.), and nerve cells for intercellular coordination. However, all cells have in common two major general functions: energy generation and energy utilization for growth and/or maintenance. These may be termed *metabolic reactions* or more simply *metabolism*. These metabolic reactions must be maintained and regulated continuously to sustain life. Therefore they are in a *dynamic state*.

Metabolic processes in normal cells are not random but are rigidly controlled by a number of interrelated intrinsic and extrinsic checks and balances. The regulation of the dynamic state of metabolism is effected by genetic (coarse control) and fine control mechanisms (modulation of cellular enzyme activities) (Chapter 3). The dynamic state of metabolism with its highly organized regulatory mechanisms is thus a vital biochemical characteristic of "normal" living matter and is considered

Figure 1-1 The dynamic nature of metabolism with its interrelationships to the major areas of biochemistry.



to be a central theme of the present discussion of human biochemistry. The ensuing chapters of this book are in fact subtopics of this guiding theme, arranged in logical progression, as depicted schematically in Fig. 1-1.

Molecular aspects of disease

Unfortunately perhaps, animal cells, especially human, are unable to accomplish complete metabolism because of an inability to synthesize all their required components. Thus humans are dependent, nutritionally speaking, on other living organisms to supply these substances: plants for glucose as carbohydrates by photosynthesis, bacteria for nitrogen fixation, and microorganisms for the synthesis of certain amino acids and vitamins. But animal and human cellular systems themselves are not always perfect. Defective enzymes may be synthesized, or an insufficient production of an enzyme may lead to an insufficient supply of an essential intermediate or product (metabolite). A hereditary disease of metabolism thus may result from an incorrect expression of an enzyme. The molecular aspects of hereditary metabolic diseases, one of the most important and frequently occurring groups of diseases afflicting mankind, are discussed in Chapter 22.

Modern biochemistry is thus a multifaceted discipline, closely interrelated with other life sciences including the medical sciences. Consequently it encompasses a wide variety of life scientists who use chemical, biological, physical, immunological, and nutritional techniques to probe life processes—molecular events in cells, cellular organelles, tissues and body fluids, and even whole organisms. Biochemistry has become a unique blend of contributions from classical biochemists, cell biologists, physiologists, immunologists, nutritionists, medical scientists, and others. In turn, it has become a foundation for and is enriched by a wide variety of life science disciplines. Biochemistry is now a basic language for all biology and is essential to the expression and understanding of biological and medical phenomena.

Suggested readings

Anders, E., Hayatsu, R., and Studier, M.H.: Organic compounds in meteorites, Science **182**:781, 1973.

Anfinsen, C.B.: The molecular basis of evolution, New York, 1959, John Wiley & Sons, Inc.

Bronowski, J.: The ascent of man, Boston, 1974, Little, Brown & Co., Inc.

Buvet, R., and Ponnamperuma, C., editors: Chemical evolution and the origin of life, New York, 1971, American Elsevier Publishing Co., Inc.

Calvin, M.: Chemical evolution, New York, 1969, Oxford University Press, Inc.

Chittenden, R.H.: The development of physiological chemistry in the United States, American Chemical Society Monograph No. 54, New York, 1930, The Chemical Catalog Co., Inc.

FASEB Conference: Genetics and biological evolution, Fed. Proc. **35**:2077, 1976.

Florkin, M., and Stotz, E., editors: Comprehensive biochemistry, New York, 1962-1967, American Elsevier Publishing Co., Inc.

Fox, S.W., and Dose, K.: Molecular evolution and the origin of life, San Francisco, 1972, W.H. Freeman & Co., Publishers.

Johnson, F.M.: Porphyrins in space, Chem. Eng. News **49**:5, 1971.

Lewis, J.S.: The chemistry of the solar system, Sci. Am. **230**:51, 1974.

Lunar knowledge from moon samples, Chem. Eng. News **50**:35, 1973.

Nobel Foundation: Nobel lectures (1901-1962, 1963-1970): Chemistry, 4 vols.; Physiology and Medicine, 4 vols., New York, 1966 and 1972, American Elsevier Publishing Co., Inc.

Oparin, A.I.: Life: its nature, origin, and development, New York, 1962, Academic Press, Inc.

Ponnamperuma, C., et al.: Non-protein amino acids in the Murchison meteorite, Proc. Nat. Acad Sci. **69**:486, 1971.

Rohlfing, D.L., and Oparin, A.I., editors: Molecular evolution—prebiological and biological, New York, 1973, Plenum Publishing Corp.

Rose, W.C.: Recollections of personalities involved in the early history of American biochemistry, J. Chem. Educ. **46**:759, 1969.

Wilson, A.C., Carlson, S.S., and White, T.J.: Biochemical evolution, Annu. Rev. Biochem. **46**:573, 1977.

Chapter 2

Biochemical morphology of the cell

The human body is composed of a multitude of specialized tissues which in turn consist of vast clusters of cells that have differentiated into specialized chemical factories. Each human begins as a single cell, a zygote, possessing a nucleus formed by the fusion of a sperm and an egg cell. Thus all the genetic information needed to produce a person (about 10^{13} cells) is represented in the original, fertilized egg cell. With growth and development cells differentiate and become highly specialized. Even though all the cells in the body contain the same genetic information, much of it has become repressed and is silent or not expressed.

In our consideration of human biochemistry it is first appropriate to describe the nature of the unit cell and its morphological substructures. In time we must appreciate the relation of substructure to cellular function and to the function of the tissue type of the individual cell. Substructures will eventually be seen as sites where specific molecular activities occur. This view of structure related to biochemical function is *biochemical morphology*.

Concept of the cell

The cell is a living, reproducing, structural unit that contains substructures or *organelles*. Two general types of cells are recognized in nature from a biochemical-morphological point of view. These are *prokaryotes* and *eukaryotes*. As the names imply, the difference lies primarily in the presence or absence of a specific organelle, namely the nucleus.

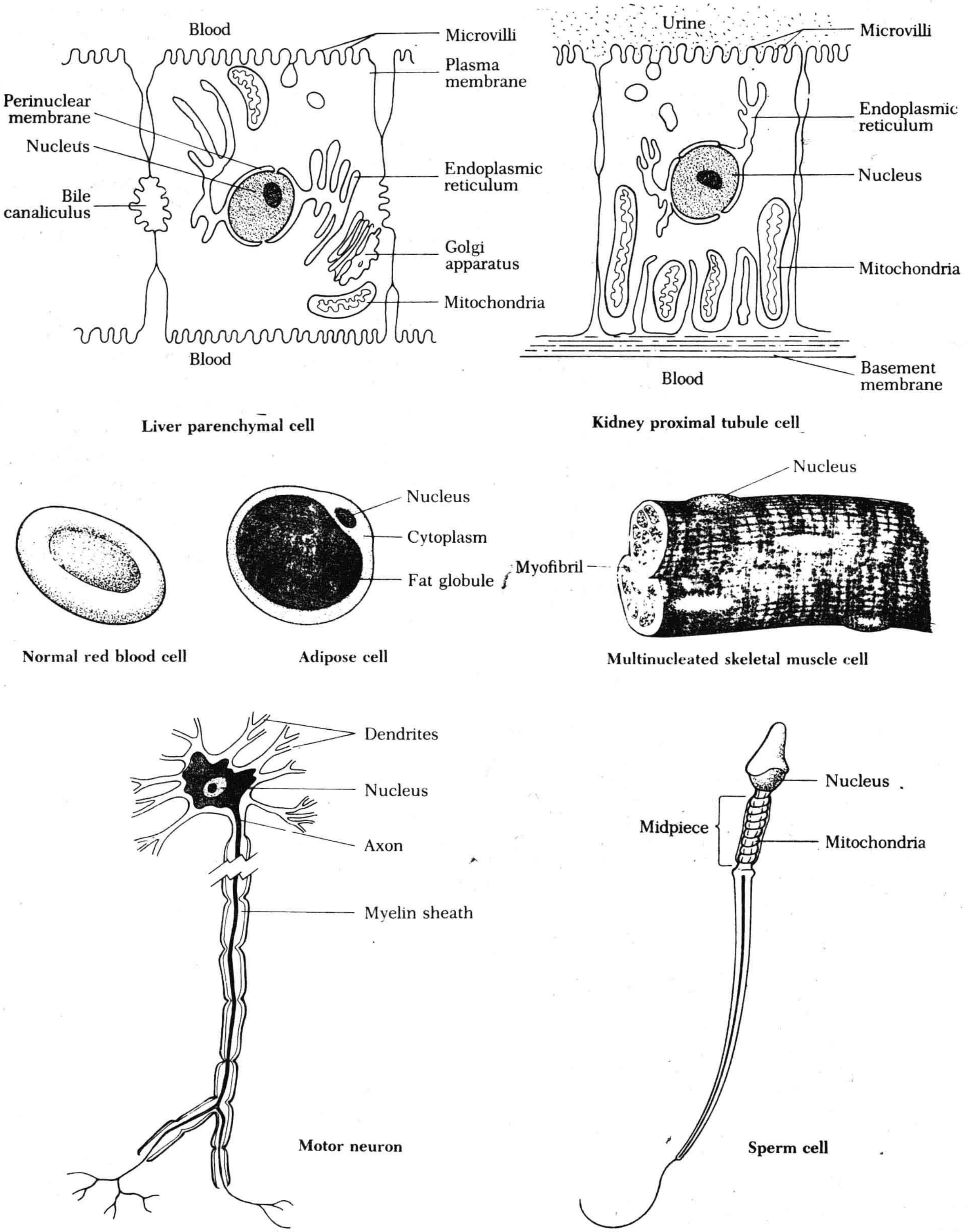
Prokaryotes are relatively simple cells representing most bacteria, as well as blue-green algae, mycoplasmas, spirochetes, and other types of microorganisms. They have no discrete nucleus and no nuclear membrane. Eukaryotic cells possess a distinct nucleus and are present in all higher organisms, both plant and animal, as well as in fungi, protozoa, and most algae.

Eukaryotic cells

In a human, eukaryotic cells exist in a variety of sizes and shapes that allow adaptation to their special functions (Fig. 2-1). Despite their diversity they have certain features in common. The nucleus is always a structure in which the DNA-containing chromosomes (Chapter 8) are separated from the rest of the cell's contents by an envelope called the perinuclear membrane. There are also other structures or subcellular organelles that involve membranes and have special functions. These are the mitochondria, the endoplasmic reticulum, the Golgi apparatus, and various kinds of vacuoles. Therefore eukaryotic cells possess a variety of internal membrane systems.

The schematic diagrams in Fig. 2-1 show that the cell units are separated from their surroundings by a *plasma membrane*. It is apparent that this membrane per-

Figure 2-1
The diversity of human cells.



forms a number of important functions: it holds the cell together; it serves as a selective barrier to the outside, permitting (and even enhancing) the entrance of essential nutrients while at the same time preventing the loss of needed substances; it secretes waste products; it keeps out toxic materials; and it binds certain regulatory substances, particularly hormones, in a locale most advantageous to the performance of their function. Obviously, a unique type of structure must be required to serve diverse functions such as mechanical support and a selective chemical barrier.

The subcellular organelles illustrated in Fig. 2-1 are also composed, in part at least, of membranes. Although internal membranes perform a diversity of functions, they all seem to share certain structural features. In other words, biological membranes are remarkably alike in structure. As a least common denominator, all membranes contain *phospholipids*.

Membrane structure

Phospholipids (Chapter 23) are distinguished by a common structure, the backbone of which is glycerol. As is evident in Fig. 2-2, two of the three hydroxyl groups of glycerol serve as points of attachment for long-chain carboxylic acids (fatty acids). To the third glycerol carbon is attached a phosphate group linking compounds such as choline, ethanolamine, inositol, and serine via a phosphodiester bond. The principal phospholipids found in cell membranes are phosphatidyl choline, phosphatidyl ethanolamine, phosphatidyl inositol, and phosphatidyl serine. In mammalian cells there are also certain neutral lipids such as cholesterol. As an example, the composition of various membranes of rat liver cells is given in Table 2-1. Since phospholipids represent many individual molecules distinguished by their constituent fatty acids (mostly 16- and 18-carbon saturated fatty acids or the

Figure 2-2
Structure of a phospholipid.