BASIC CHEMISTRY OF LIFE

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The C. V. Mosby Company

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with 155 illustrations

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Preface

The demands of society for more and better health care based on the best and latest information available continue to escalate. An important aspect in attempts to meet these demands is the ongoing effort in biochemical research. As a natural consequence of this continuous growth of knowledge, it becomes necessary, at appropriate intervals, to include the newly accepted information in a biochemistry textbook for students in the medical and allied health care professions: therefore, this edition of *Basic Chemistry of Life*.

Rapid and significant additions have been made to information about the prostaglandins and their effects on the atherosclerotic and clotting mechanisms and cellular responses to hormonal influences. These additions have been included in the chapters on the chemistry of lipids, lipid metabolism, blood, and hormones.

Because of the continuing increase in interest in nutrition, the chapter on nutrition has been expanded to emphasize the need for nutritional intervention and the formulation of intervention plans for various patients. When the close interdependency of information about nutrition and metabolic biochemistry is recognized, much of the misinformation about nutrition will hopefully be corrected.

Details about the enzymatic processes involved in the biosynthesis of fatty acids and of hemoglobin have been included in the chapters on lipid metabolism and blood. This information should provide students with a more complete knowledge base on which to build an understanding of the reasons for carrying out related procedures in the health care environment.

Scattered throughout the text are many other minor changes. As always, responsibility for the choice of what to include and what not to include is my own. Time and reasoned criticism will determine the validity of these choices.

Milton Toporek

Preface to the first edition

Progress in all phases of the life, or biomedical, sciences is being made at a relatively explosive rate. Chemistry has been, and continues to be, in the forefront of such efforts. This is so because, even though a living human being may be worth only a dollar or two as a collection of chemicals, many secrets of health are locked up in the intricate organization, functioning, and control mechanisms which nature has achieved with these chemicals.

Many of these secrets have yielded to researchers in recent years, leading to a better understanding of certain phases of the life process. At the same time many secrets remain to be solved. As a result, a continuously accelerated demand has developed for better medical and health services based on this new understanding. This in turn is leading to increased requirements for personnel properly educated in the biomedical sciences. It is difficult to see how anyone can function adequately in this field without a proper understanding of basic chemical principles. It is the purpose of this textbook to provide such a base in chemistry on which the student may build an understanding of the complex processes which go to make up the phenomenon of life as we know it, particularly in the human being. It is believed that this can be accomplished without forcing the student to become a chemist or biochemist, while exploring basic concepts to the fullest extent possible for nonspecialists in this field.

Major emphasis is placed on the dynamic nature of biochemistry and the interrelationships of the various metabolic pathways. At the same time, points along these pathways at which derangements may occur and the manner in which they occur are discussed in such a way as to stress the biochemistry involved in the underlying clinical situations. At the completion of the biochemistry chapters of this textbook, the student should see the living human being as the result of a miraculous coordination of thousands of chemical events occurring simultaneously and in sequence, with all sorts of provisions in readiness for any possible emergency which may arise to threaten the status quo. Included in this section is the almost unbelievable story of the molecule of life, DNA (deoxyribonucleic acid), and its partner, RNA (ribonucleic acid), and the roles they play in protein synthesis and reproduction.

Without energy, life as we know it could not exist. It is necessary for a proper understanding of the functioning of a living organism to learn how chemicals trap energy and how the energy, or at least a part of it, is recovered from the chemicals and converted to the forms required by the living organism. In addition, some knowledge of basic chemical reactions, structure, and physical properties of substances is also necessary. These topics are studied in the chapters on inorganic chemistry.

Many of the key compounds associated with life are from the world of organic chemistry. Some knowledge of the structure, properties, and reactions of these fascinating and extraordinary compounds also is necessary for a proper understanding of the functioning of a living organism. Care has been taken to include in the chapters on organic chemistry only as much as necessary to provide an adequate base for the subsequent discussions in the biochemistry chapters, omitting unnecessary ramblings in the realm of industrial and pharmaceutical applications, where organic chemicals undoubtedly play a very important role. Structures are used mainly to give the student some feeling for the significance of such considerations in the actions and functions of the various biochemical compounds.

Some historical material is included where appropriate to give the student an indication of the manner in which the superstructure of science is built up on the efforts of many investigators as they lay down a brick at a time on the established base. Occasionally, an entire structure goes up almost instantaneously, also on a preexisting base. Conceptually, the thread of development is more important than the specific dates, or historical detail, which are included for reference purposes.

Among the important problems encountered in courses for which this text is designed are those of disparity in scientific background of the students and wide variations in the number of hours assigned to such courses. Therefore, this text starts at a relatively elementary level in order to supply a good base for all students, and moves rapidly to a level in biochemistry which should provide a challenge to the best students. As an aid to all students, especially those in the shorter courses, an outline is provided with each chapter. This outline has been used successfully for some years by the author's students, as indicated by objective tests and unsolicited comments of the students. Their reactions have affirmed the author's opinion that such an outline would provide a more universally useful teaching tool than the conventional study questions at the end of each chapter. Such questions, therefore, have been omitted from this text.

Summary flow charts are used wherever possible to help the student appreciate the overall picture of the situation in the presence of the wealth of specific detail often required to describe a particular subject area. Although the trend in the health sciences is, hopefully, in the direction of upgrading courses in content and time, in the shorter courses these flow charts may contain the largest portion of the subject matter which can be successfully taught in the time allotted.

The list of suggested additional readings to be found in the Appendix is meant to serve merely as an introduction to the vast literature in the biomedical and related sciences for those classes or individual students with the time or inclination to track down an interesting subject. The list of references is obviously not exhaustive and is also not completely representative. However, an exploration starting with any single reference will usually illustrate the well-known cascade effect encountered in such literature, i.e., each reference has its own list of references, which in turn lead to many other lists of references.

A work of this type inevitably involves cooperation from many sources. It is a pleasure to acknowledge the help of all whose efforts and encouragement were of aid in completion of this venture. In particular, the many discussions with my colleague, Dr. Bernard Schepartz, Professor of Biochemistry at The Jefferson Medical College, have been of great value. Thanks are due to many individual scientists and commercial and nonprofit organizations for a large number of the illustrations used in the text, a practical indication of the interdependence of various research groups. An unexpected source of encouragement were my daughter and two sons, who followed the progress in writing with great interest in spite of their loss of my services for a significant period of time. The tedious task of transcribing the writing into a near-perfect manuscript was skillfully accomplished by my wife. Another important ingredient was supplied by the publisher in the form of the proper mixture of prodding, encouragement, and cooperation. To all, my sincere appreciation.

Contents

UNIT FOUR
BIOCHEMISTRY

UNIT ONE

INTRODUCTION

Overview

1

One of the most important tasks humans set for themselves was the seeking for any and all means of prolonging life and making things more comfortable during that lifetime. The search for the knowledge necessary to accomplish this task probably dates back many thousands of years to the time humans first found it possible to influence their environment. It is the purpose of this book to emphasize the central role modern biochemistry fills in this ever-expanding undertaking of determining what is life, defining the "normal" state of health, and discovering means of coping with situations of all kinds that pose a threat to this "normal" state.

BIOCHEMISTRY AND THE HEALTH SCIENCES

In recent years, the field of medicine and its allied health sciences have benefited greatly from the many advances being made as biochemists and other researchers continue attempts to explain the workings of the body on a molecular basis. These activities have led to the establishment and verification of the concept of *molecular diseases,* which, in turn, has led to more rational approaches to the investigation and treatment of such diseases.

Sickle cell anemia, a disease still very much under investigation, was the first disease proved to result from the presence of an abnormal molecule (hemoglobin S) replacing the normal type (hemoglobin A). This achievement began to unfold in 1945 when Dr. Linus Pauling, a two-time Nobel prize winner, proposed that red cells in an individual with sickle cell anemia assumed sickle shapes (from which the disease obtained its name) because a change in the hemoglobin molecule changed the physical characteristics of the cells under certain conditions so that they could not retain their normal, round shape. Within a few years, Dr. Pauling and his students showed that there was indeed a hemoglobin S that was distinctly different from hemoglobin A and that they differed from each other in only two out of a total of 574 amino acids in the hemoglobin molecule. As small as such a difference may appear to be on a quantitative basis, the consequences can be very serious or fatal. Further details about sickle cell anemia will be discussed later (p. 381).

Other important health problems related to biochemical molecules involve the production of abnormally high or low amounts of enzymes, the body's chemical catalysts. Strategic biochemical reactions may thus be forced to produce too great or too small amounts of vital substances required for the body to maintain its normal state of health. Since, as will be shown later, the information required for the synthesis of enzymes comes from genetic material, deoxyribonucleic acids (DNA) and ribonucleic acids (RNA), diseases or conditions resulting from deranged enzyme production are known as *inborn errors of metabolism.*

Another series of difficult health problems to contend with arises from derangements of a part or parts of the delicate mechanism that controls the net flow of the hundreds of biochemical reactions that are occurring in such a way as to respond properly to the ever-changing requirements of the body. As an example, changes in the acidity or alkalinity of body tissues must be controlled to a relatively small range. This involves many hormones and the processes they affect. A breakdown in any part of the control process can become a very serious threat to the health status of the individual.

It should be abundantly clear, even from this very brief listing of some of the major classes of difficulties to which the body may be subjected, that pinpointing the biochemical problem involved in a particular situation is the starting point for devising and carrying out a rational approach to correcting the problem. It therefore becomes imperative for anyone contemplating a career in the health sciences to achieve a basic understanding of the chemistry of life. For these and others, a corollary dividend would be the intellectual satisfaction of being able to better comprehend the magnitude of the miracle known as life.

THE STUDY OF CHEMISTRY

In the early history of chemistry, inorganic and organic chemistry were divided on the basis of the presence or absence of a relationship to life. It was believed that organic chemicals could be produced only by a living organism. The first indication that life was not absolutely necessary for the production of an organic chemical came in 1828 when a German chemist, Wöhler, prepared urea, a common product of animal metabolism, from two inorganic substances: ammonia and cyanic acid. Since then, many other organic chemicals have been produced in laboratories and factories until now several million such substances are known, with the element carbon as their common feature.

The ingenuity and ability of humans to produce organic compounds for specific purposes almost at will are well known and appreciated. Examples include synthetic fibers such as nylon for clothing, the wonder drugs such as the sulfonamides for curing diseases in the manner of Ehrlich's "magic bullet,"* and many items being used in space vehicles and in support of the systems that have sent these space vehicles to the moon and the planets. Yet many organic compounds found in nature have not been synthesized because of their exceedingly complex structure.

It is quite clear, then, that a mysterious "vit l force" is not required for the preparation of organic chemicals. Why, therefore, are the subjects of inorganic and organic chemistry still studied separately? The reason is mainly one of convenience. Since carbon is only one of the 105 elements now recognized, general principles involving all of the elements are studied under inorganic chemistry. These principles are then applied to the study of organic chemistry, or compounds of carbon. Also included in the study of organic chemistry are the properties peculiar to carbon that make it possible to synthesize more compounds of carbon than has been possible to produce from the other 104 elements combined.

THE STUDY OF BIOCHEMISTRY

The importance of the study of inorganic and organic chemistry to the understanding of biochemistry should be quite obvious. From the chemical viewpoint, the living organism, with particular emphasis on the human being, is simply an organized, operating collection of organic and inorganic chemicals (Fig. 1-1).

It is the ultimate purpose of biochemistry (here broadly defined to include biologic chemistry, physiologic chemistry, and molecular biology) to define the processes occurring in the living organism on the basis of the chemical principles governing the activity of the various compounds found in the organism.

Among the most important and interesting processes to be studied are those concerned with the manner in which an organism manages to reproduce itself in the image of its parents. This involves the story of DNA, deoxyribonucleic acid, or the "molecule of life" as it sometimes called. Related to this process is the one that specifies and controls the synthesis of the important class of compounds known as proteins. Among the proteins are the enzymes, the organic catalysts that allow chemical reactions to occur in the body under much milder conditions than would be possible in a test tube or a factory. The problem of the relationship between cancer and viruses, nucleic acid–containing particles, has been receiving increasing attention from researchers. Continuing intense activity in these areas has brought an understanding, in broad outline, of many of these processes and has begun to fill in the specific details of some. Enough is now known

*Paul Ehrlich, a German chemist (1854-1915), believed in the possibility of curing diseases by destroying the invading enemy, infectious bacteria, by some chemical means without affecting the normal body tissues. Hence the concept of the "magic bullet." (de Kruif, P.: Microbe hunters, New York, 1926, Harcourt Brace Jovanovich, Inc.)

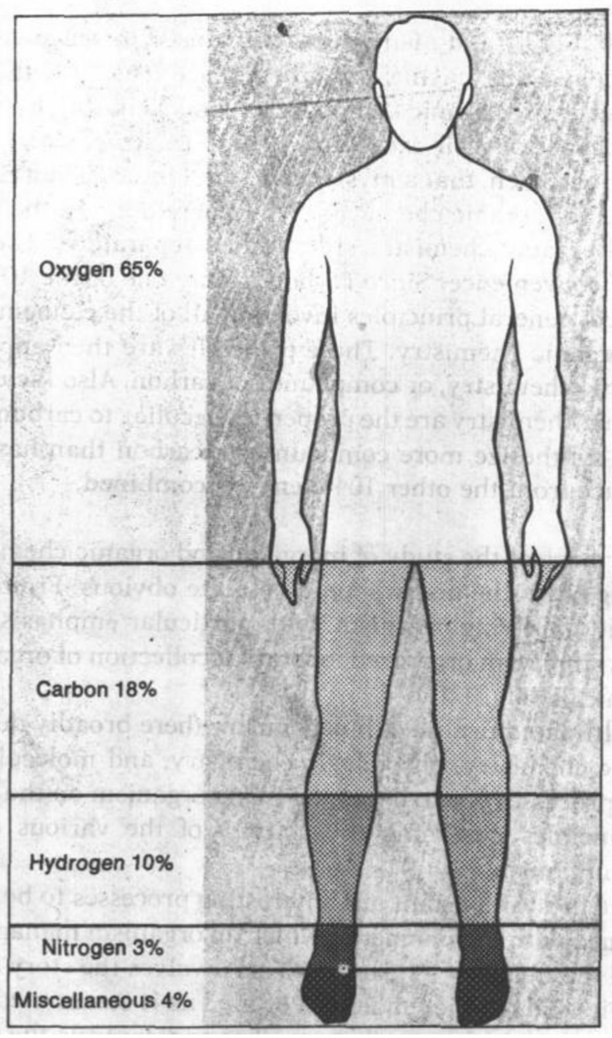

Fig. 1-1. Chemical composition of the human body.

to indicate the probability that many diseases and abnormal conditions are directly related to abnormalities found in DNA or in the processes controlled by DNA.

In fact, many studies are now under way investigating the possibilities of devising corrections for some of nature's errors and also of harnessing nature's own designs to produce large quantities of strategic substances, such as hormones, with much less effort than before or to make substances that have not yet been produced by humans. These subject areas are known popularly as genetic engineering and DNA recombinant procedures. Because of their exceedingly important social, ethical, and religious implications, the discussions of these areas of scientific innovation have been very intense among both scientists and nonscientists and will probably continue to be so in the future.

A very interesting recent example of how biochemistry progresses is found in the development of information about the prostaglandins, essential fatty acids, and aspirin. Not too many years ago it would have been very unusual to mention these substances together. Today it is known that an essential fatty acid is essential because it is used in the body to synthesize prostaglandins. One property of certain prostaglandins is that of promoting the clumping of platelets, leading to the formation of blood clots. In case of bleeding, this is a desirable property. In the case of individuals subject to heart attacks, this is a property to avoid. Recent reports have indicated that aspirin has the property of inhibiting the production of a substance, by way of prostaglandins, that causes the clumping of platelets. As a result, aspirin is now being investigated as a means of lessening the possibility of heart attacks.

An adequate background in biochemistry is required not only for an understanding of the workings of the human body, both in health and in disease states, but also for a complete realization of the potential benefits to be obtained from applications of this knowledge.

THE INFORMATION EXPLOSION

It has been estimated that the world literature in chemistry and the life sciences is doubling approximately every 8 years, and this rate has not yet leveled off. This *information explosion* can be explained on the bases that according to recent estimates, 90% of the scientists known to have lived are living now and that people are better educated in and more aware of scientific matters, generating ever-increasing pressure for more research and achievements in the life sciences.

Such a situation means that anyone contemplating a career in the life sciences must be prepared to discard old or superseded ideas and learn new ones at an alarmingly rapid rate. This is quite a challenge, but it can be a very exciting one, particularly if the base on which the student is to build is a sound one.

In addressing his medical students, Joseph Lister, an English surgeon (1827-1912) and the originator of antiseptic surgery, said:

> You must always be students, learning and unlearning till your life's end, and if, gentlemen, you are not prepared to follow your profession in this spirit, I implore you to leave its ranks and betake yourself to some third-class trade.*

With the inclusion of other areas of the life sciences and the inclusion of women also pursuing such careers, Lister's quotation is just as appropriate today as it was many years ago.

*Leeson, J. R.: Lister as I knew him, London, 1927, Baillière, Tindall, and Cassell, p. 102.

2 Energy

Energy may be defined in very simple terms as the *ability to do work.* The tremendous importance of energy considerations for living organisms cannot be overemphasized and is the reason for starting this text with a discussion of basic information about energy. Thus in the unit on inorganic chemistry, the manner in which chemicals can capture and store energy as *potential energy* will be reviewed, as will the manner by which the energy in chemicals can be extracted and utilized, or withdrawn, in the form of *kinetic energy.*

As an analogy with finances, potential energy, i.e., energy that is stored at the moment but that can be utilized as required, is like "money in the bank." Just as people must be able to keep putting money in the bank in order to pay for their needs, the supply of potential energy must be replenished in order to continue functioning properly. For the human body replenishing the supply of potential energy is accomplished by eating food. The chemical energy found in the food molecules can later be used as required for heat, motion, or metabolic reactions that require the input of energy. Thus, energy can be thought of as the "currency of life." Most of the facts about these aspects of energy will be developed in the unit on biochemistry.

The concept of constant replenishment of sources of potential energy brings up a number of questions, foremost among which is the question of the ultimate renewable source of energy that makes life possible. The answer, of course, is the sun. Green plants, through the process of photosynthesis (discussed later), capture some of the sun's energy in the form of chemical energy.

As the text develops, attention will be repeatedly focused on the energy aspects of the subject under discussion. Ultimately, although few of us would settle for the idea that we are nothing more than energy-converting machines while we live, functionally the biochemical and physiologic facts are that in many aspects this is true. In other words, the driving force behind the many reactions that make up the life process is energy.

ENERGY FORMS

Life as we know it depends on many types of energy, such as mechanical, heat, light, chemical, electrical, sound, and now, nuclear energy. One of the most important properties of these forms of energy is their interconvertibility. The different forms of energy are all easily converted to heat but some of the other interconversions still cannot be done on a practical basis.

Because the different forms of energy are all convertible to heat, all forms of energy are usually measured as heat. In these measurements, the unit of heat energy is known as the *calorie* (cal), which is defined as the heat required to raise the temperature of 1 g of water 1 Celsius (or centigrade) degree. The amount of heat energy found in foods is usually expressed in terms of the large calorie (Cal, or kilocalorie, kcal), which is equal to 1000 small calories.

PHOTOSYNTHESIS AND THE ENERGY CYCLE

For us, the sun plays a central role in providing the energy required for life. Some of the light energy reaching the earth is converted by green plants into chemical energy in the form of sugars (e.g., $C_6H_{12}O_6$), which are carbohydrates, by the combination of carbon dioxide (CO_2) and water (H_2O) in the proper proportions and in the presence of the green plant pigment, chlorophyll:

$$6CO_2 + 6H_2O + \text{light energy} \xrightarrow[\text{photosynthesis}]{\text{chlorophyll}} C_6H_{12}O_6 + 6O_2$$

This process is known as *photosynthesis* (synthesis under the influence of light) and produces oxygen at the same time that it converts light energy to chemical energy. This equation is a simple summary of the complicated events that take place. Only a very small fraction of the available light energy is converted to chemical energy by this process.

Animals cannot produce chemical energy in the form of sugars in this manner and therefore must depend on eating plants that produce sugars or eating other animals that have eaten such plants. The energy trapped in the sugars by photosynthesis can then be released by a series of chemical reactions, or *oxidations*, in the animal body and converted to the form of energy required, such as heat, mechanical, or sound energy:

$$C_6H_{12}O_6 + 6O_2 \xrightarrow[\text{by body}]{\text{oxidation}} 6CO_2 + 6H_2O + \text{energy}$$

It should be noted that this process of oxidation of the sugar by the animal body is the *reverse* of the process of photosynthesis. It requires oxygen that was produced during photosynthesis and, in turn, supplies carbon dioxide that is required for photosynthesis, completing the energy cycle diagrammed in Fig. 2-1.

The strategic position of green plants in this energy cycle should be quite clear. These plants act as the intermediary between the almost unlimited energy of the sun and the animal world, which is completely dependent on the sun as its ultimate source of energy. The appropriate management and conservation of land for planting and farming purposes are not only desirable for esthetic and economic reasons but are also necessary for survival.

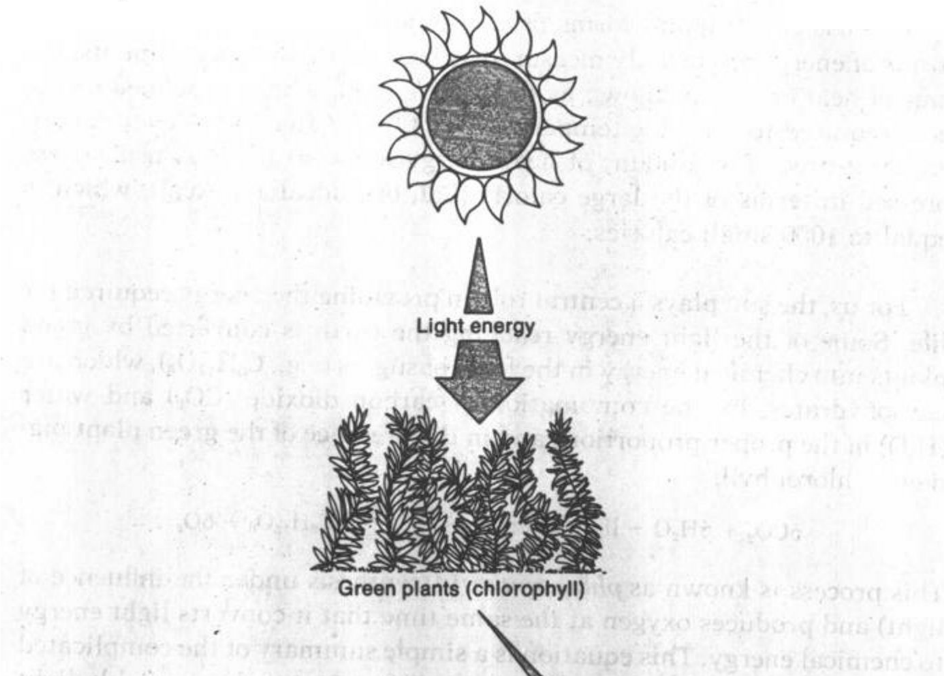

Fig. 2-1. The energy cycle that is the basis for life on earth. The sun is the ultimate source of energy input, with green plants acting as the intermediary.