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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 dependence upon biochemistry, directly or indirectly, is far reaching. Medicine made important, but slow, progress before its disciples drafted the science of chemistry to its service. Within the past forty years it has advanced at a most encouraging rate, and a major part of the credit is due to the contributions of the biochemist. He has given logical chemical explanations for physiological and pathological processes. He has worked out many of the complicated secrets of nutrition and enabled physicians to use foods intelligently in preventing and combating diseases. He has provided vitamins and hormones in pure condition for use in effectively treating many diseases. He has aided in the preparation of vaccines, antitoxins, serums, etc. Last, but not least, he has provided a large number of chemical tests as aids in the recognition of disease.

We are entering the period of molecular biology and medicine in which causes and cures of disease are sought and found in intracellular structures and the chemical reactions taking place within them.

The literature of biochemistry. The subject is so vast and advances are being made so rapidly that the medical course in biochemistry cannot hope to do more than provide the student with an elementary knowledge of the facts and principles of the subject and, it is hoped, a realization of its increasing importance to medicine. The course should prepare the student with sufficient background for the successful study of his other medical courses, and it should also place him in position to read the medical literature that is becoming ever more chemical in nature.

In order that the student's training may be as broad as possible, it is desirable that he early form the habit of reading books on biochemistry other than the one adopted as a text for his class. By doing this, he will obtain knowledge of the subject from different angles. He should also become acquainted with current journals in which he may see the science in the making and learn how to weigh evidence and form his own opinions. Because the current literature of biochemistry is so vast, it is impossible to do more than read a very small fraction of the published original articles. In order that this handicap may be obviated as much as possible, review journals and books are published in which the status of important subjects at the time is summarized. These give references to the original literature for those who may wish to investigate a subject in detail. The abstract journals are among the most important publications in aiding the searcher to find any or all of the literature on a given subject, and the medical student should early become acquainted with those concerned with medicine and learn how to use them. There are various comprehensive treatises, monographs, and books dealing with the different phases of biochemistry that the student should know about and use as occasion demands. The point of the preceding admonitions is that unless the student learns how to use the literature of medicine and does so, he will regress, and the science, moving on, will leave him with an ever increasing deficiency, which after a time will become so great that he will be hopelessly out of date.